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Index of lectures

Paediatric Blood Management

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Through patient blood management systems, we aim to apply *evidence*-based practices to *efficiently* (in terms of both time and product use) manage *haemoglobin* concentration and *coagulation* status to minimise blood loss, morbidity and mortality. A blood management system is as a bundle that could be used to identify, risk stratify, and treat patients with critical anaemia, potential bleeding, acute and ongoing bleeding and coagulopathy.

The system should include strategies to

- identify and treat preoperative anaemia,
- strategies for blood conservation during surgery,
- guidance on the use of restrictive transfusion triggers and goal directed therapy,
- guidance in the role of point-of-care tests for coagulation management,
- and transfusion algorithms.

There is evidence that implementation of a Patient Blood Management system (PBM) decreases morbidity and mortality while decreasing cost.

RISKS OF TRANSFUSION

The complications of transfusion are well documented. Paediatric patients may be at higher risk of the non-infectious complications of transfusion. The risk of hyperkalaemia is particularly significant in children under 10 kg or less than 1 year of age. Hypocalcaemia and hypomagnesaemia (as a result of "citrate toxicity") is also more common in children. Mortality rates up to 15-30% are associated with transfusion-related acute lung injury (TRALI), transfusion-related acute circulatory overload, and haemolytic transfusion reactions. Any transfusion of red blood cells increases 30-day mortality and complication rates in children.

PREOPERATIVE OPTIMISATION

An increase (greater than three-fold) in the odds of needing a blood transfusion, whether intra- or post-operatively, can be predicted by the presence of any of 5 factors:

- Age under 1 year
- ASA class IV
- High procedure risk
- Pre-operative septic shock
- Pre-operative cardiopulmonary resuscitation

Up to 40% of children may have anaemia preoperatively, of which a great number have iron deficiency. Preoperative anaemia increases the risk of being transfused intraoperatively, which in turn increases morbidity and mortality in critically ill patients. Optimisation using iron supplementation and/or erythropoietin can be used as in adults.

Pre-operative autologous blood donation has some problems in the paediatric population. Efficacy has not been demonstrated in all results. Donation-related problems occur frequently (e.g. hypotension, problems with venous access). If autologous blood donation is considered, it should be noted that the use of erythropoietin can improve efficacy.

INTRAOPERATIVE TECHNIQUES

Basic principles must be followed: avoidance of severe haemodilution, attention to temperature control, maintenance of a normal acid-base status, and maintenance of adequate blood pressure and tissue perfusion. The EBV (estimated blood volume) should be calculated, along with an estimate of acceptable blood loss.

Tranexamic acid

There is clear evidence of benefit from tranexamic use. Types of surgery where benefit was proven in children include cranial vault remodelling, scoliosis surgery and cardiac surgery. No increased risk of thromboembolic events was demonstrated during these studies – adverse effects are rare. One concern has been a risk of seizures, but the case reports of seizures were associated with doses of 100 mg/kg and higher. If a "bolus followed by infusion" regimen is to be followed, children require a minimum 10 mg/kg bolus followed by at least 2-3 mg/kg/h infusion. Infusion rates up to 10 mg/kg/h are often used.

Cell salvage

The use of cell savers is extending to smaller children – even those younger than 6 months or less than 10 kg – as equipment and technologies improve to allow for the wash of increasingly smaller volumes of cells. Effective use has been reported for major posterior fusions of the spine and in craniosynostosis surgery.

Acute normovolaemic haemodilution

It is has not been ascertained that acute normovolaemic haemodilution is of any benefit in children. If practiced, it is imperative that hypovolaemia be avoided.

GOALS AND "TRANSFUSION TRIGGERS"

Relevant physiological differences in children include a high metabolic rate, a higher blood volume per weight in infants, different normal values for haemoglobin levels, platelets numbers and coagulation factor concentrations (especially in neonates). Neonates' platelet and fibrinogen function is also impaired compared to that of adults.

Hypovolaemic shock due to blood loss is the cause of 12% of paediatric cardiac arrests, highlighting how inadequate blood volume resuscitation can have dire consequences. The converse is true, that transfusion for reasons other than oxygen delivery failure lead to inferior outcomes. The decision when to transfuse is therefore complex and must be based on the physiological need for transfusion.

Physiological need for transfusion

Physiological need for transfusion is either due to

- Oxygen delivery failure (oxygen content and flow, globally or regionally), or
- Excessive physiological stress caused by anaemia.

Healthy adults' red blood cells deliver 2-4 times their resting oxygen requirements to tissues. While their haemoglobin (Hb) remains 8 g/dl or higher, there doesn't seem to be evidence that parameters of adequacy of oxygen delivery (lactate, MvO_2, VO_2) can be improved by transfusion. Thus, anaemia will be well tolerated by individuals with physiological reserve.

It is important to be aware of the different physiological response of paediatric patients to hypovolaemia (blood loss). Adults respond to blood loss with vasoconstriction causing a narrow pulse pressure and decreased cardiac output. The blood pressure falls, and heart rate rises concomitantly. Children will respond with a tachycardia first while maintaining their blood pressure. They are vasoconstricted and have a narrow pulse pressure and poor capillary refill. Eventually blood pressure will drop precipitously. Therefore "permissive hypotension" is a dangerous concept in children. A better approach would be "permissive tachycardia and normotension".

Transfusion triggers

A transfusion trigger, or Hb value that demands initiation of transfusion, is often sought as a simple number to use as surrogate for multiple physiological variables. However, transfusion triggers are

- Not available for many subsections of paediatric patients (if evidence base is used)
- Not indicators of minimum allowable Hb's, but rather of Hb's above one can safely NOT transfuse.

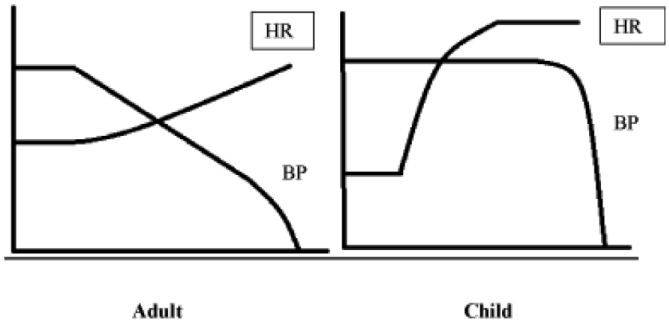

Fig. 1. Adult's versus child's physiological response to shock.*
*Adapted from The Advanced Resuscitation for Children course by the Singapore Paediatric Society

Animal studies suggest that oxygen delivery is critically impaired below an Hb of 3-4 g/dl. At an Hb of 5 g/dl healthy adults still have a normal lactate, but higher brain function may deteriorate. The same restrictive (Hb 7 g/dl) values for Hb used in adults, have been shown safe to use for infants, children, and adolescents. This holds true for children with less and more severe illness, children undergoing non-cardiac surgery, and children with acyanotic heart disease undergoing cardiac surgery.

Uncertainty exists for certain groups and situations:

- The setting of active bleeding
- Haemodynamic instability
- Acute brain injury (traumatic or stroke)
- Cyanotic heart disease
- Neonates

Evidence in the field of **neonatology** is still developing. Important aspects in the management of neonates are the concept of delayed cord clamping, and restriction of blood sampling. Term healthy neonates tolerate an Hb of 7 g/dl well. More liberal transfusion triggers are often applied to preterm neonates considering the potential risks of apnoea and impaired central nervous system development. Ideally neonates should receive leucocyte depleted, irradiated, fresh blood from a single donor.

Children with **acute brain injury** are another group needing more investigation. Consensus is that transfusion can be considered if the Hb is between 7 and 10 g/dl. The use of PbO_2 monitoring to guide transfusion decisions is not recommended.

When calculating the volume of blood to transfuse to a child it should be borne in mind that exposure to different donors (multiple units) can often be avoided or limited.

COAGULATION

Adults suffering major trauma may present with coagulopathy in about 10% of cases. This coagulopathy presents too early to be caused by fluid administration alone. Acidosis, shock and hypothermia, as well as fibrinolysis resulting in factor consumption and trauma-induced inflammation contribute to coagulopathy.

Paediatric patients display similar alterations in coagulation status, and coagulopathy in these patients is associated with mortality. Factors associated with marked elevations in coagulation studies include

- Glasgow coma scale ≤13
- Low systolic blood pressure
- Open / multiple fractures
- Major tissue wounds

Point-of-care coagulation testing

Although the use of TEG and ROTEM are often promoted, and they are expected to improve management of coagulation status, no evidence of improved morbidity or mortality in severely

bleeding patients could be demonstrated in a meta-analysis of adult data. Where invasive procedures are performed, abnormal coagulation tests were unable to predict bleeding. Paediatric data does not show any evidence for the use of TEG or ROTEM.

The use of point-of-care tests in children is hampered by the fact that “normal” test results differ for different ages.

Fresh frozen plasma (FFP)

Neonates have prolonged coagulation function tests, and often suffer coagulopathy is association with other disease processes. There is no data to show at what level of INR or PT neonates’ risk of bleeding increases. Studies of response of abnormal coagulation tests to FFP administration in neonates and infants, found minimal to no improvement in such tests. An old study showed no response of neonatal disseminated intravascular coagulation (DIC) to any treatment, including FFP.

Interestingly, a multi-institutional study found a 10-times increased rate of venous thromboembolism in neonates and children that received plasma when compared to other hospital admissions.

Cryoprecipitate

Peri-operative blood loss could be predicted by pre-operative fibrinogen levels in adolescents. The advantages of using cryoprecipitate include a lack of dilutional effect, and the fact that it can be obtained much more quickly than FFP. When used during scoliosis and craniosynostosis surgery, use of a liberal fibrinogen administration strategy significantly reduced requirements for blood products in children with craniosynostosis, but not scoliosis.

Fresh whole blood

There is no evidence of benefit to using fresh whole blood during massive transfusions, although it may decrease donor exposure. It may decrease blood loss during cardiac bypass when used to prime the cardiac bypass circuit.

Recombinant factor VII (RFVII)

Systematic reviews of RFVII use in bleeding adults (without haemophilia) could not show therapeutic advantage. Observational studies of massive transfusion protocols (MTP) could not show survival benefit either. Current paediatric data does not show benefit to RVII use for severe trauma or as part of an MTP.

MASSIVE TRANSFUSION PROTOCOLS

Massive transfusion protocols (MTP) form an integral part of a patient blood management bundle. These can be activated to streamline and protocolise management of a critical bleeding.

Massive transfusion may be defined in paediatrics as transfusion of

- >50% total blood volume (TBV) in 3 hours
- 100% TBV in 24 hours
- >10% TBV per minute
- >40 ml/kg

There is no clear inflection point, but if ≥40 ml/kg TBV is transfused (of all products) within 24 hours it indicates critical injury and carries high risk for in-hospital mortality in children. After 40-60 ml/kg total crystalloid boluses, Pediatric Advanced Life Support (PALS) recommends consideration of blood transfusion. Volume overload (over transfusion) is very common in paediatric care and should be avoided.

MTP’s often use ratios of packed red blood cells (RBC) to FFP to platelets of 1:1:1 ml. Adult data shows similar outcomes in adults if 2:1:1 is used, and paediatric data may even indicate increased mortality with higher FFP volumes. A 2:1:1 ratio therefore seems acceptable.

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Paediatric Pain Update
Analgesia for day case surgery

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With the ever-increasing number of paediatric day case surgical procedures (also commonly referred to as ambulatory surgery) being performed, it has become imperative that children's pain be effectively managed, starting in theatre and extending to the home environment. Numerous studies have demonstrated inadequate treatment of pain postoperatively with more than 30% of children noted to experience moderate to severe levels of pain for up to seven days following surgery, once they have been discharged home. Uncontrolled pain can result in significant morbidity including sleep and behavioural disturbances, poor oral intake, delayed functional recovery, re-admission to hospital and the development of chronic pain.

Multiple factors should be considered when deciding on an optimal analgesic regime, including the nature of the procedure performed, the need for an 'around the clock' versus an 'as required' dosage schedule, the patient's comorbidities and possible side effects related to the drug. Barriers to effective pain management should also be kept in mind, including child, parental, medication and system related factors. Recent recommendations by global regulatory authorities advising against the use of codeine and tramadol in children younger than 12 years, have left us with few alternative options to manage moderate to severe breakthrough pain, as there is limited data regarding the efficacy and safety of the use of alternative potent analgesics in children. This has prompted us to explore the use of new drugs (e.g. tapentadol), regional techniques and adjuvant drugs including alpha 2 agonists, ketamine, corticosteroids and gabapentin.

How effective is current pain control?

Inadequate analgesia is a common occurrence following day case surgery. Studies indicate that more than 30% of children experience moderate to severe pain.

Williams et al. conducted an observational cohort study across 8 paediatric centres in the United Kingdom to assess the prevalence and consequences of pain at home following tonsillectomy and orchidopexy day case surgery. The incidence of pain was high in the Tonsillectomy +- Adenoidectomy group (Day 2 90.1%, Day 3-7 88.1%, Day 8-14 61.8%) as well as the orchidopexy group (Day 2 70.4%, Day 3-7 34.7%, Day 8-14 17.1%). 70 % of the families reported unplanned healthcare use after they had been discharged home, with pain being the primary reason for healthcare utilisation in 79% of these cases.

How do we improve perioperative pain control?

Barriers to effective pain management

1). *Parental factors*: poor recognition and assessment of pain, misconceptions about the use and safety of analgesics.
2). *Child factors*: anxiety, refusing medication.
3). *Medication factors*: ineffective medication, inadequate formulation or dose.
4). *Hospital system factors*: lack of information, poor discharge instructions, and difficulty obtaining medication.

Assessment of Child's Pain at Home (helpful resources for parents)

Parents' Postoperative Pain Measure (PPPM)

The PPPM is a 15-item behavioural checklist that has been developed to help parents/guardians assess their child's pain at home. It has been validated for use in children aged 2-12 years of age. Scores of 6 or more out of a total of 15 signifies clinically significant pain.

Smartphone applications (Apps)
'iCanCope PostOp', 'Achy Penguin' and 'Panda' are Health Care smartphone applications currently under development. The iCanCope PostOp App is to help children and adolescents with self-management of their postoperative pain. The 'Panda' app has been designed for parents/guardians and children to use at home to help assess and manage acute postsurgical pain once discharged home. The app includes validated self-report paediatric pain scales, reminder notifications for pain assessment and the administration of analgesia. The app also includes tracking of pain scores and administered medication.

Websites
Mychildisinpain.org.uk is a website containing graphics with information and video presentations to provide information on how parents should approach pain management. It also contains information on medications to help address any concerns that parents may have.

Pharmacological interventions

Non-opioid or simple analgesics with local anaesthesia adjuncts should be used as part of a multi-modal analgesic approach to help reduce opioid exposure perioperatively. At present the evidence supports the use of the following non-opioid analgesics in the paediatric setting:

1). Paracetamol
Regardless of the route, even a single preoperative or intraoperative dose appears to be effective at reducing postoperative pain and or opioid consumption following a variety of surgical procedures, provided a therapeutic dose is used.

2). Non-steroidal anti-inflammatory drugs (NSAIDs)
Regardless of type, the perioperative use of NSAIDs decreases pain and or opioid consumption. NSAIDS have a synergistic approach when used with paracetamol. The most recent Cochrane review published in 2013, entitled 'Do non-steroidal anti-inflammatory drugs (NSAIDs) increase the risk of bleeding in children having their tonsils out?' found that there was insufficient evidence to exclude an increased risk of bleeding when NSAIDs are used for paediatric tonsillectomy. In the review, the use of NSAIDS was associated with significantly less nausea and vomiting when compared to other analgesics.

In the United Kingdom, NSAIDS such as ibuprofen and diclofenac have been licensed for use in children over the age of 3 months. In South Africa however, The Standard Treatment Guidelines and Essential Medicines List advise that NSAIDS (ibuprofen) should only be prescribed for children over the age of 12 months.

3). COX-2 selective inhibitors
COX-2 selective inhibitors are being more frequently used in paediatric practice, despite limited pharmacokinetic and pharmacodynamic data to guide their appropriate use in this population. Tan and colleagues demonstrated that Parecoxib 0.9 mg/kg in a 2 year old, 0.75 mg/kg in a 7 year old and 0.65 mg/kg in a 12 year old achieves dose equivalence of 40mg in a standard 70kg adult. There was no added analgesic benefit above dosages of 1mg/kg.

4). Dexamethasone
Meta-analyses have demonstrated that dexamethasone has a primary analgesic effect and a role in prolonging regional blockade (when used either perineurally or intravenously). It has also been shown to have an antiemetic effect. A single intraoperative dose of dexamethasone reduces pain levels in children undergoing tonsillectomy.

5). Ketamine
Intraoperative ketamine reduced early postoperative pain and or opioid consumption after a variety of minor outpatient surgeries. A single dose of Ketamine 0.25 mg/kg IV during induction decreases postop pain after adenotonsillectomy.

6). Clonidine
An oral clonidine dose of 4mcg/kg decreases postoperative pain following a variety of minor surgeries. A Cochrane systematic review conducted in 2014 evaluated how effective a preoperative dose of clonidine was for postoperative pain in children. The findings were that an oral premedication dose of 4 mcg/kg reduced the need for additional analgesia [relative risk (RR) 0.24, 95% confidence interval (CI) 0.11–0.51] with minimal side effects. It was also effective at reducing postoperative nausea and vomiting and emergence agitation. Unfortunately the overall quality of evidence was reported as low (small studies with inadequate power).

7). Dexmedetomidine
Intraoperative dexmedetomidine is 8 times more selective than clonidine for the α2 over the α1 receptors, resulting in fewer side effects. Dexmedetomidine decreases pain in a variety of day case surgeries, especially if a dose of at least 0.5 mcg/kg is given. It is especially useful as an adjunct for children known with obstructive sleep apnoea (OSA).

8). Gabapentinoids (Gabapentin and Pregabalin)
Studies conducted in adults suggest that the gabapentinoids are effective at reducing pain scores and opioid requirements in adults. These studies have prompted the American Pain Society and the American Society of Anesthesiologists to recommend the use of gabapentinoids as part of a multimodal approach to the management of postoperative pain in adults. A systematic review by Egunsola et al. evaluating the efficacy and safety of the gabapentinoids (gabapentin and pregabalin) when used as both a prophylactic measure and treatment of pain in children and adolescents reported a paucity of evidence for the analgesic effect and safety of gabapentinoids in children.

9). Other
At present there are not enough studies regarding the use of magnesium to draw conclusions regarding its analgesic effect in the paediatric population. There are no RCTs or meta-analyses assessing the efficacy of the perioperative use of IV lignocaine, amantadine, esmolol or caffeine in paediatric surgical patients.

Optimal management of breakthrough pain

In April 2017 the US Food and Drug Administration (FDA) issued a new warning that recommends **against the use of tramadol and codeine** in:

- All children under the age of 12 years.
- Adolescents (12 to 18 years) who are obese, known with obstructive sleep apnoea or have severe lung disease.
- In all children and adolescents under the age of 18 years undergoing tonsillectomy and or adenoidectomy.
- In breastfeeding mothers, due to risk of harm to their infants.

Codeine
For greater than 50 years Codeine has been the most frequently prescribed ‘weak’ opioid for the management of breakthrough pain. On 20 February 2013 the US Food and Drug Administration (FDA) added a ‘boxed warning’ to the drug label of codeine-containing preparations, advising healthcare professionals ‘to prescribe an alternative analgesic (to codeine) for postoperative pain control in children who are undergoing tonsillectomy and or adenoidectomy’. A similar warning was issued by the European Medicines Agency. The World Health Organisation (WHO) had removed codeine from its analgesic ladder in 2012.

These reviews were triggered by 2 papers that reported 3 deaths and 1 near miss in children who received normal therapeutic doses of codeine for postoperative analgesia. A review by the FDA of the Adverse Event Reporting System data from 1965 to 2015 in children who had used codeine or any codeine-containing products, revealed a total of 64 cases of severe respiratory depression and 24 codeine-related deaths, 21 of which were in children younger than 12 years of age.

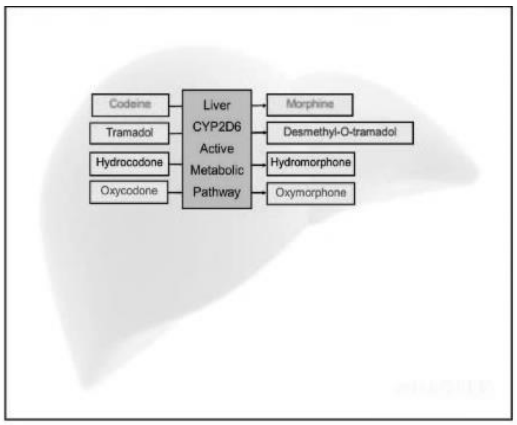
Codeine is a prodrug, requiring conversion via the cytochrome P450 2D6 enzyme to its active metabolites, namely morphine, and morphine-6-phosphate. A genetic polymorphism of the CYP2D6 enzyme results in a wide range of clinical activity.

- *'Poor metabolisers'* are unable to convert codeine to morphine, and thus codeine offers no analgesia. 5-10% of Northern European Caucasian populations are poor metabolisers.
- *'Intermediate metabolisers'* have mildly reduced activity.
- *'Extensive metabolisers'* (normal) account for 77-92% of Caucasians.
- *'Ultra-rapid metabolisers'* have more than 2 copies of the CYP2D6 gene. Phenotypically these patients have increased enzyme activity, with high concentrations of morphine produced following the administration of a normally therapeutic dose of codeine. Ultra-rapid metabolisers are prevalent in Africa (29% of Ethiopia's population are ultra-rapid metabolisers) and Saudi Arabia (21%).

What are the alternatives to codeine?

There are limited treatment options for children, particularly for neonates and young infants, with only a few analgesics specifically labelled for use in this population. Regulatory bodies are unable to recommend a specific drug to replace codeine due to a lack of comparative efficacy and safety data for the available alternatives. Therefor individuals and various institutions are devising their own policies based on current literature and experience.

A further confounding factor is that CYP2D6 is responsible for the metabolism of other drugs that have not been restricted by the FDA.



Chidambaran V. et al. Current Opinion in Anesthesiology. 2017

Tramadol

CYP2D6 is responsible for metabolism of tramadol to its active metabolite, O-desmethyltramadol. This metabolite has a mu opioid receptor affinity 200 times greater than tramadol itself. The FDA identified 9 cases of serious respiratory depression, including 3 deaths, related to tramadol in children under 18 years form January 1969 to March 2016. On 20 April 2017, the FDA announced that it was restricting the use of tramadol.

However, evidence that CYP2D6 contributes to toxicity is lacking, with the concern that these deaths were primarily related to an overdose of tramadol (the formulation was 100 mg/ml before the current concentration of 10 mg/ml) rather than a consequence of ultra-rapid metabolism.

Hydrocodone

CYP2D6 converts hydrocodone to its active metabolite, hydromorphone. Ultra-rapid metabolisers have up to an 8 times greater plasma concentration of hydromorphone, whilst poor metabolisers experience minimal analgesia. The safety and efficacy of hydrocodone have not been established in children.

Oxycodone

In the United States, many physicians have started prescribing oxycodone for analgesia. Oxycodone is twice as potent as morphine, and is an active semisynthetic opioid, not a prodrug.

A minor percentage however, does undergo metabolism by CYP2D6 to oxymorphone and noroxymorphone, which have been associated with an increased risk of opioid toxicity among ultrarapid metabolisers, and has been implicated in oxycodone related deaths in adults. At present there is insufficient data to support its use in infants and children, and one study has shown considerable variability in absorption and oral bioavailability in children.

Morphine

The advantages of oral morphine include:

- Not a prodrug, and therefor does not require any metabolism involving the CYP2D6 enzyme.
- Reasonable bioavailability.
- Can be used in children of all ages.
- Easier to titrate to effective dose (discharge doses range from 100-200 mcg/kg 4-6hrly).
- There is no indication that given equi-analgesic doses, morphine causes more side effects than other opioids.

Disadvantages include:

- Extensive experience with IV morphine, but limited clinical experience and limited comparative data in safety and efficacy in children.
- High pharmacokinetic variability, with a large inter-individual response to opioids.
- Narrow therapeutic indices of opioids.
- Controlled drug.
- Metabolites can accumulate after repeat doses.
- Associated with a high incidence of nausea (46%), vomiting and drowsiness (48%).
- Concern of opioid diversion.
- High risk of respiratory depression when used in children with OSA or respiratory disease.
- Available in a wide range of concentrations, which requires additional vigilance to avoid drug errors.

Buprenorphine

Buprenorphine is a partial mu opioid receptor agonist with a potential ceiling effect. Further PK and PD data are still needed, and it is not approved for use in children.

Tapentadol

Tapentadol is a centrally acting analgesic with a chemical structure resembling that of tramadol. It has a dual synergistic mechanism of action. It is a mu opioid receptor agonist and a noradrenaline reuptake inhibitor within the CNS. The major advantage of this drug is that it has a predictable pharmacokinetic profile, with no metabolites contributing to its analgesic effect. Only 15% of tapentadol is metabolized via CYP450, with no active metabolites.

Tapentadol provides equivalent analgesia to pure opioids, with the advantage that it has fewer opioid specific side effects due to a reduced mu-opioid receptor effect or μ-load of ≤40%. Morphine milligram equivalents to achieve equivalent analgesia are based on a conversion factor of 2.5 tapentadol: 1 morphine.

Licensed in 2011 by the FDA for use in adults, Tapentadol has recently been approved in the European Union for use in **hospitalised** children aged 2 to 18 years for treatment of moderate to severe acute pain. The labelled use is currently restricted to the hospital setting however, where there is equipment available to enable adequate respiratory monitoring and support if required. The recommended dose is 1.25 mg/kg, 4 hourly, maximum dose of 100mg per administration. At present, the duration of treatment should not exceed 3 days, as there is no data available for longer treatment periods in the paediatric population. Reported side effects include nausea, vomiting, constipation, pyrexia, somnolence, pruritus and respiratory depression.

Regional analgesia

Local anaesthetic infiltration and regional nerve blocks form an important component of multimodal analgesia. Regular analgesics should be commenced to avoid breakthrough pain when the regional block wears off. The Pediatric Regional Anesthesia Network (PRAN) and the French-Language

Society of Pediatric Anesthesiologists (ADARPEF) continue to demonstrate general overall safety with paediatric nerve blocks.

The PRAN established a database in 2007 to evaluate common practices and the risks and complications associated with regional anaesthesia performed in children. Ultrasound-guided regional anaesthesia has improved the safety profile and the efficacy of peripheral nerve blocks. In 2018 the group published its data from over 100 000 paediatric regional blocks performed. There were no permanent neurological deficits reported. The risk of severe local anaesthetic toxicity was 0.76 per 10 000, and no additional risk was associated with placing blocks under general anaesthesia.

The European Society of Regional Anaesthesia (ESRA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) formed a joint committee in 2018 to determine safe dosages of local anaesthetics in regional anaesthesia for children. They have advised a dose of 0.5-1.5 mg/kg bupivacaine or ropivacaine for ultrasound-guided upper limb peripheral nerve blocks. They also determined that dexmedetomidine is a safe adjunct to injections to prolong the nerve blocks. Useful blocks for day case procedures include upper limb blocks, penile blocks as well as:

1. *Transversus Abdominal Plane Block (TAP)*
   A TAP block is indicated for postoperative pain control for the anterior abdominal wall, particularly for laparoscopic surgeries and other abdominal incisions. Low volumes of 0.2-0.3 ml/kg of ropivacaine or bupivacaine are often used. Studies have demonstrated that TAP blocks help reduce early and late postoperative pain, as well as opioid consumption 24 hours after surgery. Complication rates range between 0.3-0.7% and include the vascular aspiration of blood and peritoneal puncture.

2. *Ilio-inguinal/ Iliohypogastric block*
   The ilioinguinal and iliohypogastric nerves supply sensation to the posterolateral gluteal region, inguinal region, and the anterior scrotum. This block is indicated for postoperative analgesia following inguinal surgery, inguinal hernia repair, orchidopexy and hydrocelectomy.

3. *Rectus sheath block*
   The rectus sheath block is for postoperative analgesia of the anterior abdominal wall. This block is particularly useful for midline abdominal incisions, umbilical hernia repair or laparoscopic procedures.

Paediatric central neuraxial techniques

Caudal

A single-shot caudal is a reliable technique for surgical procedures involving the lower abdominal and pelvic regions, as well as the lower limbs. It is preferred for children who are relatively non-ambulant. The addition of clonidine (1-2 mcg/kg) has been shown to extend the duration of regional analgesia by up to 2 to 3 times longer than administration of local anaesthetic alone, and reduces the amount of rescue analgesia required. However clonidine is often avoided as an additive in day case surgery to avoid the sedative side effects. Opioid additives should be avoided for day case surgery, due to the risk of postoperative respiratory depression.

Patients may be discharged home following a caudal, once they have passed urine. Children may be discharged home with minor residual motor and or sensory blockade provided their lower limbs are protected, their parents/guardians can understand given instructions and will be able to recognise any complications. Parents/guardians should also have access to a telephone and transport should they need to return to the hospital. Patients and their parents should be extensively counselled and be given written instructions as to the expected duration of the block, and who to contact if any complications do occur.

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Ventilation Strategies in Paediatrics

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Introduction

Paediatric ventilation is a very broad topic and would usually be covered in more than one chapter. To cover as much of the topic as possible I will focus on specific controversies and differences in the paediatric population with regards to ventilation.

Paediatric applied respiratory physiology

Infants are at risk of respiratory failure due to:

1. A decrease in respiratory reserve secondary to a smaller functional residual capacity (FRC). Their FRC is also closer to closing capacity (the lung volume at which alveoli and small airways begin to collapse)
2. The orientation of their ribs and diaphragm are more horizontal which limits the volume that can be displaced during inspiration
3. An increased oxygen consumption
4. The immature diaphragm muscle leads to quicker fatigue of inspiratory muscles
5. A decrease in airway radius causes an increase in resistance to the 4^{th} power of change in radius

The paediatric airway

1.Cuffed vs uncuffed endotracheal tubes (ETT)

Old airway beliefs:

- Funnel shaped airway
- The cricoid is the narrowest part of the airway

These old airway beliefs lead to the usage of uncuffed endotracheal tubes in children younger than 8 years; the logic being to prevent pressure necrosis caused by an inflated cuff at the level of the cricoid. This historic belief stemmed from a manuscript by Dr Eckenoff in Anesthesiology in 1951 in which he referred to work done by Bayeux. Bayeux made plaster castings of 15 paediatric cadaveric larynxes ranging in age from 4 months to 14 years. In all 15 plaster cast cadaveric larynxes the internal circumference of the cricoid ring measured narrower than other parts of the airway. The concern with this experiment is that the distending pressure of the plaster may have altered the dimensions of the distensible parts of the airway when compared to the non-distensible regions like the cricoid. More recent airway imaging using newer modalities which includes bronchoscopic examination, CT and MRI have challenged these old beliefs.

New airway beliefs:

- The airway is elliptical and not circular with a greater anterior-posterior(AP) diameter than transverse diameter
- The vocal cords and the subglottic area are the narrowest part of the airway

Implications:
From the above it becomes apparent that hearing a 'leak' with an uncuffed ETT doesn't negate the risk of pressure necrosis on the airway. There may be a leak from the AP diameter, but still significant pressure on the lateral walls of the airway with a circular ETT. The benefit of a cuffed ETT is that the

pliable cuff can seal off the airway with equal pressures at all points. To note is that although the cricoid area is not the narrowest area it may still be at risk for pressure necrosis, because it is rigid and not as displaceable as the vocal cords.

Advantages of cuffed ETT:

1. Decrease need to exchange cuffed ETT
2. Better sealing of the airway with more reliable ventilation
3. Decrease incidence of sore throat
4. Prevention of oropharyngeal contamination with inhaled anaesthetic gases and high oxygen concentrations
5. Decrease aspiration risk

The type of cuff further influences risk of aspiration. There is less risk of aspiration with the polyurethane cuff that is thinner and seals the trachea more efficiently than the polyvinylchloride cuff that may fold and thus lead to aspiration.

Disadvantages of cuffed ETT:

1. Potential of cuff herniation through the glottis when the tip of the ETT is placed in the mid-trachea. This is secondary to the position of the cuff on the shaft and the more elliptical shape of the cuff.
2. Increased risk of pressure necrosis on the transverse walls when high pressure, low volume cuffs are inflated to a pressure of 20cmH_2O, because the cuff doesn't always cover the internal trachea at this pressure and still have a leak. Higher pressures are thus needed to seal the airway with an increased risk of pressure necrosis.
3. Potential to increase work of breathing when selecting a size smaller cuffed ETT due to the bulky cuff adding to the outer diameter

The new generation cuffed ETT e.g. the Microcuff ETT:

The new generation cuffed ETT have all the advantages of the older generation cuffed ETT with the added benefit of nullifying most of the disadvantages the older generation cuffed ETT had. This is due to some new enhanced features:

- The cuff is spherical and more distal on the shaft and therefore when inflated there is less chance of cuff herniation through the glottis
- They have high volume, low pressure cuffs and therefore there is less chance for airway pressure necrosis
- They have an ultrathin cuff adding little to the outer diameter with less need to downgrade ETT sizes excessively
- The thin polyurethane cuff also seals the airway better with a resultant decreased aspiration risk

2. Oral vs nasal ETT

Oral intubations are technically easier to perform with less risk of pressure necrosis. Nasal ETTs are generally more secure with less risk of an unplanned extubation. When ventilation is anticipated post-op one should strongly consider using nasal endotracheal tubes especially in younger patients. Generally ventilated ICU patients are not deeply sedated or paralyzed and thus difficult to manage on a ventilator when they have an oral ETT in place. The disadvantages of nasal ETT are a technically more difficult intubation and the risk of pressure necrosis. It is therefore crucial that when strapping a nasal ETT in place one avoids causing any pressure on the nasal tip, nasal septum or lateral walls of the nose by strapping it in a downward fashion.

3. ETT size calculation

- Uncuffed ETT – Age/4 + 4
- Cuffed ETT – Age/4 + 3,5

4. ETT length of insertion

Formula:

- Length (cm) at lip = 12 + age/2
- Length (cm) at nose = 15 + age/2

Unfortunately these formulas don't always perform that accurately. An alternative method is to use the size of the ETT chosen as the corresponding length at which the ETT should be at the level of the vocal cords. For example if you use a size 4 ETT your ETT should be placed so that the 4cm marking on the ETT is at the level of the vocal cords. Another practical tip when placing an ETT is to make sure you confirm correct placement by auscultation in both the extended (when a roll is used under the shoulders for better airway visualization during laryngoscope) and the flexed airway position post-intubation.

Modes of ventilation

Pressure vs volume control

A pressure-controlled mode is usually preferred when there is a leak around the ETT that is commonly the case with an uncuffed ETT. In the pressure mode there is partial leak compensation, because this mode doesn't target a set tidal volume, but rather gives a set pressure for a set time. In volume-controlled mode the ventilator targets the set tidal volume that is never attained, because of the leak. The machine will automatically increase the pressure to attain the set tidal volume that could potentially lead to barotrauma in parts of the lung that is more compliant than others. Cuffed ETT's are used more commonly nowadays and therefore this is not as big a problem anymore. This led to the question being asked by many as to why pressure control is still so much preferred in paediatrics. The reason is probably because of its decelerating flow pattern. This flow pattern is more comfortable for the patient and has the potential to improve oxygenation. The improved oxygenation theory might be explained by the fact that there is minimal flow in the later part of the inspiratory phase with an inspiratory pause effectively being built into the breath that has the potential to improve V/Q matching.

The advantages and disadvantages of pressure and volume control ventilation are summarised in the table below.

Pressure control	**Volume control**
Advantages:	*Advantages:*
• Partial leak compensation	• Guaranteed minimum minute ventilation, if no leak around tube
• Decelerating flow pattern prevents air hunger and thus more comfortable	• Set tidal volume
• Avoids high inspiratory pressures	
• Potential to improve oxygenation	
Disadvantages:	*Disadvantages:*
• Change in lung compliance or resistance result in a change in tidal volume	• Fall in lung compliance will result in high alveolar pressure with risk of barotrauma
• Risk of volutrauma if an increase in lung compliance goes unnoticed	• Less suitable when uncuffed tube used
	• Constant flow pattern might result in discomfort

Ventilatory modes and their main differences

1. **Controlled mandatory ventilation**

- One of the first ventilator modes developed
- Machine can't sense patient's own effort
- Can lead to patient-ventilator asynchrony

2. Intermittent mandatory ventilation

- Set number of mandatory breaths
- Allows for spontaneous ventilation, but doesn't synchronize

3. Synchronized intermittent mandatory ventilation (SIMV)

- Set number of mandatory breaths which are synchronized with spontaneous efforts
- Patient can also take additional breaths that will be pressure supported if SIMV-PS selected

4. Assist control

- On the newer ventilators this mode is sometimes confusingly referred to as e.g. pressure control mode when in actual fact it is a pressure pre-set assist control mode
- Breaths can be initiated by patient or ventilator (in contrast to pure controlled modes where all breaths are initiated by the ventilator)
- Characteristics of each breath is the same regardless if breath is initiated by patient or ventilator (in contrast to SIMV)
- Inspiratory time is set by clinician
- Commonly used in the paediatric ICU in the form of pressure pre-set assist control mode

5. Pressure support

- Breaths initiated by patient only
- Inspiratory time controlled by patient (in contrast to assist control)
- Clinician needs to set limit when machine should cycle from on (giving the set pressure and facilitating inspiration) to off (stops delivering set pressure and allows for exhalation). Inspiratory to expiratory cycling thresholds:
    - Default approximately 30% of peak inspiratory flow (PIF)
    - In obstructive airways disease approximately 50% of PIF
    - Patients with poorly compliant lungs approximately 5% of PIF
    - In PICU mostly set to 5%, however in patients with a significant leak beware that the flow may never fall to 5% of PIF

6. Pressure regulated volume control (PRVC)

- Mode that combines features of both pressure and volume control
- Ventilator automatically adjust inspiratory pressure to achieve a set tidal volume
- Vital to set upper pressure limit appropriately to prevent excessive pressure being delivered. Ventilator monitors each breath and compare the delivered tidal volume with the set tidal volume, if delivered volume is too low it increases the inspiratory pressure on the next breath, if too high it decreases the pressure.
- Great mode for asthmatic patient where airway resistance might change quickly with treatment or neurology/ neurosurgical patients where one needs to control CO_2 tightly.

Setting the ventilator

1. **Setting tidal volume (Vt)**
    - Target Vt 5-8 ml/kg predicted body weight (PBW) in normal lungs
    - Target Vt 3-6 ml/kg PBW if poor compliance exists

There are no data to recommend optimal Vt and thus far only one observational study showed a lower mortality associated with Vt of 8 ml/kg actual body weight (ABW) compared with 10ml/kg

2. Setting the pressures

- Titrate pressure to attain above mentioned targeted tidal volumes
- Limit plateau pressure (Pplat) $\leq$ 28 cmH_2O or $\leq$ 29-32 cmH_2O if chest wall elastance is increased or $\leq$ 30 cmH_2O in obstructive airway disease
- Delta pressure $<$10 cmH_2O if no lung pathology

The delta pressure/driving pressure ($\Delta P=Vt/Crs$) that is calculated as Pplat-PEEP, best stratified the risk for mortality in adults with ARDS. They have not been able to reproduce these observations in paediatrics except for one study where there was an independent association between the airway pressure gradient (PIP – PEEP) and mortality when measured under dynamic flow conditions.

3. Setting PEEP

PEEP help to prevent alveolar collapse. In children without lung injury the suggested PEEP level is 5cmH_2O. In lung disease higher PEEP levels might be needed, but a balance needs to be found between alveolar recruitment and alveolar over-distenstion. There is no specific recommendation on how to best titrate PEEP.

The following is a list of potential parameters to utilize when titrating PEEP:

- Intrinsic PEEP measured via an expiratory hold; keep the extrinsic PEEP less than the intrinsic PEEP
- Flow-time curve; ensure the expiratory flow returns to zero when increasing PEEP
- Alveolar dead space ({$PaCO_2$-$PetCO_2$} / $PaCO_2$); take care not to increase alveolar dead space when increasing PEEP
- Oxygenation; titrate PEEP according to saturation and PaO_2
- Compliance; in pressure mode if the tidal volume starts dropping with an increase in PEEP then you are probably over-distending the lung and need to bring the PEEP level back again
- Haemodynamics; if there is a decrease in pulse pressure with an increase in PEEP then stop the upward titration

4. Setting the I:E ratio/ inspiratory time

The table below can be used as a starting point when setting inspiratory times or the respiratory rate. From this point onwards one should interrogate the flow time curve of the patient to optimize flow dynamics.

Age	Respiratory rate	Inspiratory time (sec)
Newborn	40-60 bpm	0,35-0,5
Infant (< 1year)	25-35 bpm	0,5-0,7
Child (1-5years)	20-30 bpm	0,6-0,8
Child (6-12years)	15-20 bpm	0,7-1,2
Adolescent	12-15 bpm	1,0-1,5

In figure A, inspiratory flow does not return to baseline and therefore can lead to lower tidal volumes. This can be corrected by increasing the inspiratory time or decreasing the rate.

In figure B, expiratory flow doesn't return to baseline which will lead to stacking. This can be corrected by decreasing the respiratory rate or decreasing the inspiratory time to facilitate a longer expiratory time.

□□□□□□□□□□

Figure A

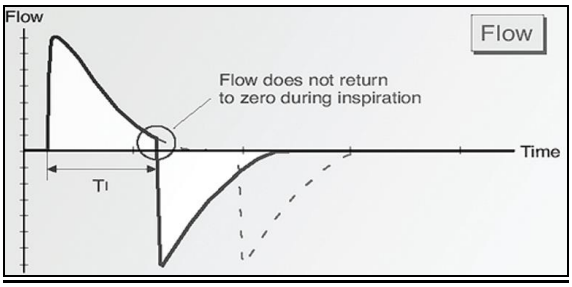
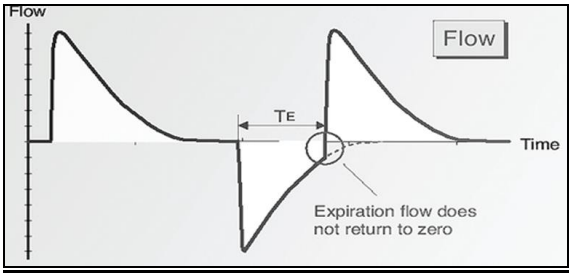


Figure B



Goals of ventilation

1. Adequate oxygenation

Strategies to improve oxygenation

Oxygenation is influenced by FiO_2 and mean airway pressure. Mean airway pressure is determined by:

- Peak inspiratory pressure
- PEEP
- Inspiratory time
- Ventilator mode

When the mean airway pressure is increased oxygenation improves via several mechanisms: the recruitment of alveoli, increasing functional residual capacity, improvement of VQ matching and decreasing intrapulmonary shunting.

Targets

- Sats > 95% in room air expected in children without lung injury or extra-pulmonary manifestations
- Permissive hypoxemia (i.e. Sats 92-97% when PEEP <10 cmH_2O and 88-92% when PEEP $\geq$10) in paediatric ARDS
- In children with congenital heart disease or chronic lung disease the clinician should be guided by trends in end organ perfusion when optimizing oxygenation. If end organ perfusion remains stable one may need to accept lower sats.
- In all situations the clinician needs to balance optimization of delivery of oxygen (DO_2) with the harmful effects of ventilation

2. Adequate ventilation

Strategies to improve ventilation

- Increase minute ventilation

This can be done by either increasing the tidal volume or the respiratory rate. However, if there is evidence of stacking, a decrease in the respiratory rate might be needed in order to increase minute ventilation

- Decrease dead space

Targets

- Normal CO_2 levels in normal lungs
- Normal pH and pCO_2 levels in traumatic brain injury and pulmonary hypertension
- Permissive hypercapnia, targeting a pH of 7,15-7,3 in moderate/ severe paediatric ARDS except in conditions where permissive hypercapnia could be harmful e.g. increased intracranial pressure, severe pulmonary hypertension, selected congenital heart disease, haemodynamic instability and in patients with significant ventricular dysfunction.
- To note is that hypocarbia is as bad as hypercarbia and should be avoided.

3. Minimise adverse effects

Respiratory complications

- Ventilator induced lung injury (VILI): barotrauma, volutrauma, atelectrauma and biotrauma
- Oxygen toxicity
- Gas trapping
- Airway trauma
- Ventilator associated pneumonia(VAP)

Cardiovascular complications

Table – The effects of positive pressure ventilation

Physiological effects	Clinical consequences
• Reduced left ventricle (LV) afterload • Reduced preload	Good for: • LV failure and pulmonary oedema • Dilated cardiomyopathy
• Increased right ventricle (RV) afterload • Reduced preload	Bad for: • Glen/ Fontan circulation • Hypovolaemia • Pericardial effusion • Pulmonary hypertension

Ventilation strategies in ARDS and Asthma

Asthma

Ventilatory goals

- Acceptable (which doesn't always equate to normal) level of oxygenation and ventilation
- Avoidance of lung hyperinflation due to incomplete exhalation

Determining an appropriate respiratory rate and exhalation time

- Interrogate the flow time curve

If expiratory flow has not returned to baseline, either decrease the respiratory rate or increase the exhalation time. However, to maintain adequate minute ventilation sufficient for CO_2 clearance, a higher tidal volume and peak inspiratory pressure might need to be tolerated. Chasing a normal CO_2 level might lead to VILI and thus permissive hypercapnia should be allowed.

The rationale for using CPAP and PEEP in asthma

CPAP in a spontaneously breathing patient with asthma:

- Decrease inspiratory work of breathing by decreasing the pressure gradient required to overcome intrinsic or auto PEEP
- Facilitates exhalation by moving the equal pressure point more proximal and towards the cartilaginous airways and thus preventing airway collapse

PEEP during positive pressure ventilation in a patient with asthma:

- By supplying extrinsic PEEP that is lower than the patient's own intrinsic PEEP, one is able to move the equal pressure point more proximal and thus prevent airway collapse, as well as maintain a pressure gradient for air to move during exhalation.

Titrate extrinsic PEEP according to

1. Intrinsic PEEP measured via an expiratory hold
2. Flow-time curve; ensure the expiratory flow returns to zero when increasing PEEP
3. Measured CO2; alveolar dead space ({PaCO2-PetCO$_2$} / PaCO$_2$) should not increase when PEEP is increased

Paediatric ARDS

Limitations in AECC and Berlin ARDS definitions when describing paediatric ARDS:

1. Focused on adult lung injury
2. The use of PaO_2 / FiO_2 (P/F) ratio

- Needs invasive measurement of PaO_2
- Ratio influenced by ventilator pressures and, in PICU, greater variability in ventilatory management than adult ICU

3. Differences in risk factors/ etiology/ pathophysiology/ outcomes not considered in AECC/Berlin definitions

Differences in Paediatric ARDS (PARDS) definition compared to Berlin definition:

1. Use of oxygenation index (OI) or oxygen saturation index (OSI) rather than P/F ratio
2. Eliminated the requirement for bilateral pulmonary infiltrates
3. Excluded patients with perinatal related lung disease
4. Included special population groups

Age	Exclude patients with peri-natal related lung disease			
Timing	Within 7 days of known clinical insult			
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload			
Chest Imaging	Chest imaging findings of new infiltrate(s) consistent with acute pulmonary parenchymal disease			
Oxygenation	**Non Invasive mechanical ventilation**	**Invasive mechanical ventilation**		
	PARDS (No severity stratification)	Mild	Moderate	Severe
	Full face-mask bi-level ventilation or CPAP ≥5 cm H_20 [2] PF ratio ≤ 300 SF ratio ≤ 264 [1]	4 ≤ OI < 8 5 ≤ OSI < 7.5[1]	8 ≤ OI < 16 7.5 ≤ OSI < 12.3[1]	OI ≥ 16 OSI ≥ 12.3[1]
Special Populations				
Cyanotic Heart Disease	Standard Criteria above for age, timing, origin of edema and chest imaging with an acute deterioration in oxygenation not explained by underlying cardiac disease. [3]			
Chronic Lung Disease	Standard Criteria above for age, timing, and origin of edema with chest imaging consistent with new infiltrate and acute deterioration in oxygenation from baseline which meet oxygenation criteria above.[3]			
Left Ventricular dysfunction	Standard Criteria for age, timing and origin of edema with chest imaging changes consistent with new infiltrate and acute deterioration in oxygenation which meet criteria above not explained by left ventricular dysfunction.			

Figure 2. Pediatric acute respiratory distress syndrome definition. OI = oxygenation index, OSI = oxygen saturation index. [a]Use Pao_2-based metric when available. If Pao_2 not available, wean Fio_2 to maintain Spo_2 ≤ 97% to calculate OSI or oxygen saturation/Fio_2 ratio. [b]For nonintubated patients treated with supplemental oxygen or nasal modes of noninvasive ventilation, see Figure 3 for at-risk criteria. [c]Acute respiratory distress syndrome severity groups stratified by OI or OSI should not be applied to children with chronic lung disease who normally receive invasive mechanical ventilation or children with cyanotic congenital heart disease. OI = (Fio_2 × mean airway pressure × 100)/Pao_2. OSI = (Fio_2 × mean airway pressure × 100)/Spo_2.

PARDS definition table taken from "PARDS: consensus recommendations from the pediatric acute lung injury consensus conference (PALICC)"

Summary of the PARDS management recommendations by the PALICC experts

For each recommendation the agreement among the experts are displayed in brackets as either weak or strong

Lung protective ventilation

1. Vt 5-8 ml/kg predicted body weight (PBW), 3-6 ml/kg PBW if poor compliance (weak)

2. Inspiratory Plat pressure <28 cmH_2O, 29-32 if decreased chest wall compliance (weak)

3. Moderate PEEP 10-15 cmH_2O titrated to oxygenation and hemodynamic response
   - PEEP >15 cmH_2O – severe PARDS, but limit Pplat (strong)
   - Monitor DO_2 (sats, PaO_2)/ respiratory compliance/ haemodynamics as you increase PEEP (strong)

4. Careful recruitment manoeuvres (weak)
   - Slow incremental and decremental PEEP steps

- Sustained inflation maneuvers cant be recommended

5. After optimizing PEEP consider lower sats levels of 88-92% in PARDS with PEEP of at least 10cmH_2O (strong)

6. When Sats <92% monitor SvO_2 and markers of oxygen delivery (strong)

7. Practice permissive hypercapnia to minimize VILI (strong)

8. Maintain pH 7,15-7,30 within lung protective guidelines (weak)
    - Exceptions – Increased intracranial pressure, severe pulmonary hypertension, selected congenital heart disease lesions, haemodynamic instability, significant ventricular dysfunction

9. Bicarbonate supplementation is not routinely recommended (strong)

Mode of ventilation

No recommendations

HFOV

- Considered in – hypoxic respiratory failure, Pplat >28 in the absence of reduced chest wall compliance (weak)

- *Paediatric evidence:*

Experience has proven its safety, but efficacy lack data.
Small RCT and observational studies show improved oxygenation, but no difference in mortality, duration of mechanical ventilation or length of stay.
PROSpect (paediatric RCT) ongoing

- *2 Adult studies:*

OSCILLATE – Use of HFOV in early mod-severe ARDS – increased mortality
OSCAR – Use of HFOV in all patients with ARDS did not decrease mortality

Cuffed ETT with conventional ventilation (strong)

Nitric oxide (strong)

- Not recommended routine
- Considered in: severe pulmonary hypertension, severe RV dysfunction, severe PARDS as rescue from or bridge to ECLS

- *Paediatric evidence:*

Studies all report improved oxygenation with no impact on mortality

Prone position (weak)

- Not recommended routine
- Considered in severe PARDS
- In paeds dramatic initial improvement in oxygenation, but survival benefit difficult to prove

- *Paediatric evidence:*

RCT supports safety, but no difference in outcomes
PROSpect ongoing

- *Adult study:*

PROSEVA – Significantly decreased mortality in prone group. Complications did not differ much between prone and supine group except increase cardiac arrest in supine group

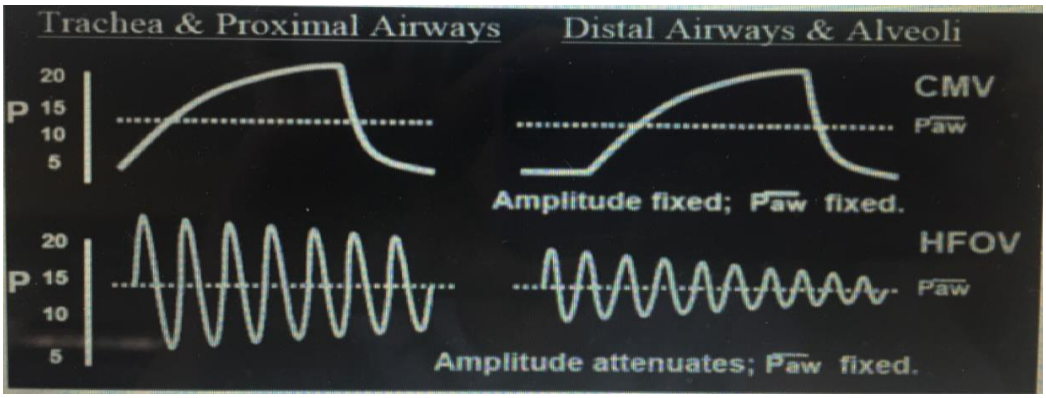
Suctioning (strong)

- Insufficient data to recommend open/close suction system
- Routine saline prior to suctioning not recommended, can use for lavage if thick secretions

High frequency oscillatory ventilation (HFOV)

The mechanism

During HFOV warmed, humidified gas (the bias flow) is oscillated via a piston pump. The piston pump causes to-and-fro displacement (amplitude) of a diaphragm at the proximal end of a rigid circuit that then produces oscillations; thus actively pumping gas into and out of the patient. This is different from conventional ventilation where only the inspiratory part is an active process. The lung is essentially being oscillated around a constant mean airway pressure at a high frequency. With conventional ventilation there is very little airway pressure dampening that occurs as air moves from the proximal airways to the distal airways. This is in contrast with HFOV where attenuation of airway pressures occurs as air moves more distally down the airway. This is demonstrated in the figure below.



The underlying principle in HFOV is to prevent VILI by utilizing very small tidal volumes (1-3 ml/kg vs the normal 5-8 ml/kg for conventional ventilation) at a very high frequency of between 4 and 12 Hz (between 240 and 720 breaths per minute). These tidal volumes are smaller than dead space and therefore would lead to hypercapnia wasn't it for the high frequency that they are being delivered with.

The features of HFOV that decreases the incidence of VILI are:

- Smaller tidal volumes which prevents alveolar over-distension and thus volutrauma
- Higher mean airway pressures (MAWP) improves alveolar recruitment and thus oxygenation
- Smaller differences between inspiratory and expiratory pressures assists with the prevention of cyclical alveolar collapse and distension and thus atelectotrauma
- Lower peak pressures help prevent barotrauma

The different theories used to explain gas exchange in HFOV are bulk convection, asymmetric velocity profiles, Taylor dispersion, turbulence, pendelluft, molecular diffusion, cardiogenic mixing and collateral ventilation.

When to consider HFOV

- Failure of conventional ventilation (unable to attain oxygenation or ventilation/ CO_2 targets despite high ventilatory settings)
- In moderate to severe PARDS patients with hypoxic respiratory failure with plateau airway pressures >28 cmH2O in the absence of clinical evidence of reduced chest wall compliance.
- Pathological air leaks e.g. broncho-pleural fistula
- Congenital diaphragmatic hernia (*To note: VICI trial showed no difference in the combined outcome of mortality or broncho-pulmonary dysplasia between the two ventilatory groups of CMV and HFOV in prenatally diagnosed CDH neonates*)

Managing a patient on HFOV

Controlling oxygenation: MAP and FiO_2

Oxygenation can be improved by adjusting your mean airway pressure (MAP) or FiO_2. FiO_2 should be adjusted according to Saturation targets set for that specific patient. A good starting point for MAP on the oscillator is 3-5 cmH2O above the MAP the patient had on conventional ventilation. After HFOV is initiated a CXR should be done to exclude under or over-distension of the lungs. The aim is to achieve lung inflation where the diaphragm lies between the 8th and 10th posterior ribs on an antero-posterior CXR.

The Royal Children's Hospital Melbourne gives the following guidelines with regards to setting MAP:

- Infant – MAP 18-25

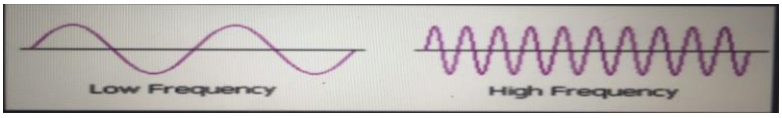
(Be cautious in preterm infants however, where MAP's as low as 8-10 could be sufficient)

- Child – MAP 20-30

Controlling ventilation: Amplitude and frequency

Adequate ventilation and thus CO_2 removal is dependant on the amplitude (delta P) of oscillations and frequency that is set. An increase in amplitude will lead to an increase in the tidal volume delivered and thus will aid in CO_2 clearance.

In conventional ventilation carefully increasing the respiratory rate, taking care not to introduce stacking, will lead to an increase in minute ventilation and thus an increase in CO_2 removal. In HFOV increasing the frequency has the opposite effect on CO_2 removal. By increasing the frequency you will decrease the area under the curve (i.e. tidal volume) and thus decrease CO_2 removal. This concept is illustrated in the figure below where the amplitude is the same in the 2 pictures, but the frequency is higher in the picture on the right leading to a decrease in area under the curve and thus smaller tidal volumes.



The guideline below is a good starting point, but thereafter amplitude should be adjusted to achieve adequate chest wall vibrations that extend down to the level of the groin, referred to as the 'chest wiggle factor'.

Royal Children's Hospital Melbourne guidelines for delta P and frequency:

- Infant - Delta P 30-40 cmH_2O, Frequency 8-12 Hz
- Child – Delta P 40-60 cmH_2O, Frequency 6-8 Hz

Another method to promote CO_2 elimination is to introduce a small cuff leak, but this might need periodic adjustment seeing that too big a leak makes it difficult to maintain a consistent MAP.

Additional settings

Bias flow

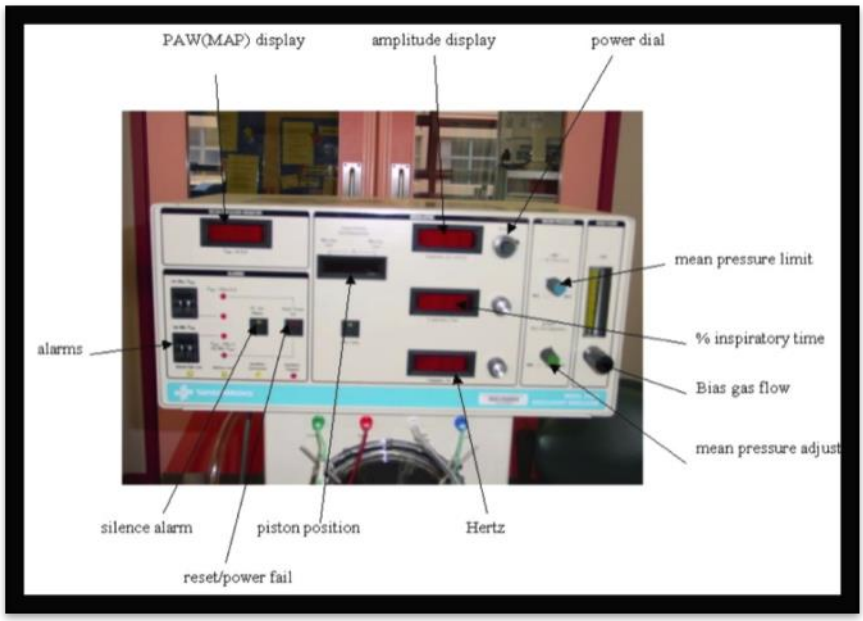
The 3100A HFOV pocket guide recommends the following flows:

- Premature baby – 10-15 litres/min
- Term baby – 10-20 litres/min
- Small child – 15-25 litres/min
- Large child – 20-30 litres/min

Inadequate bias flow will lead to an increase in dead space. Increased bias flow might be required to compensate for a leak in order to maintain the set MAP; e.g. during suctioning or in a patient with a broncho-pleural fistula.

Inspiratory time

Usually kept at 33% which translates to an I:E ratio of 1:2



Monitoring a patient on HFOV

- ***Chest wiggle factor (CWF)***

Check for symmetrical, bilateral vibration that extends from the nipple line to the groin.

A decrease in the CWF may indicate:
- Worsening compliance
- The presence of secretions
- ETT that has dislodged

Unilateral CWF may be a sign of:
- Endobronchial intubation
- A pneumothorax
- Unilateral lung collapse, consolidation or pleural effusion

The CWF may increase:
- With improvement in compliance

- ***Auscultation***

Breath sounds wont be audible, but changes in the intensity of the piston sounds might be appreciated. To hear heart or gastro-intestinal sounds the piston can be stopped temporarily; lung inflation will be maintained.

- ***Transcutaneous PCO_2 and $PaCO_2$***

End tidal CO_2 monitoring is not possible during HFOV. Transcutaneous CO_2 monitoring is used to monitor ventilation, but its drawback is its slow response time. Use regular blood gas analysis to correlate transcutaneous PCO_2 to $PaCO_2$.

A rapid rise in CO2 may be a sign of:
- Acute airway obstruction (mucous plug)
- Bronchospasm
- A pneumothorax
- Endobronchial intubation

- Extubation
- Worsening lung disease

Elevated CO2 refractory to increases in amplitude may indicate:

- A Mean airway pressure that is too low

Rule of thumb – when the set amplitude approaches three times the set MAP it usually indicates too low lung volumes resulting in poor gas exchange

- ***Oxygen saturation and transcutaneous PO_2***

To monitor oxygenation

A drop in oxygen saturation may be a sign of:

- Acute airway obstruction (mucous plug)
- Disconnection
- A pneumothorax
- Changes in mean arterial pressure
- Worsening lung disease

- ***Humidification***

Monitoring of adequate, active humidification is essential for a patient on HFOV to prevent mucous plugging and a blocked ETT.

Complications of HFOV

- Irritability necessitating increased levels of sedation/ paralysis
- Hypotension secondary to high mean airway pressures
- Pneumothorax
- ETT obstruction with secretions
- Intraventricular haemorrhages in preterm infants
- Bronchopulmonary dysplasia
- Feeding intolerance

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Approach to a Child with a Muscle Disorder

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The problem with muscle disorders in children is that they are:

- Rare
- Can react to our favourite drugs (but not always which makes us unsettled)
- There are no easy rules to fit them all
- Advanced disease has major peri-operative implications

These notes will consider:

1. What is Anaesthesia induced rhabdomyolysis (AIR) and how is it different from Malignant Hyperthermia (MH)?
2. Simple rules for known or suspected dystrophies
3. Rules for mitochondrial myopathies
4. Approach to the undiagnosed but symptomatic child
5. Anaesthetic implications of advanced disease

1. What is AIR and how is it different from MH?

AIR is associated with Duchenne's (DMD) and Becker's Muscular Dystrophy (BMD) and probably the other rarer dystrophies that all have abnormalities in the dystrophin myoglobin complex (Fig. 1). Those dystrophies are just so much more rare than DMD and BMD, and AIR is such an under-recognized event that we can't say with more certainty than this.

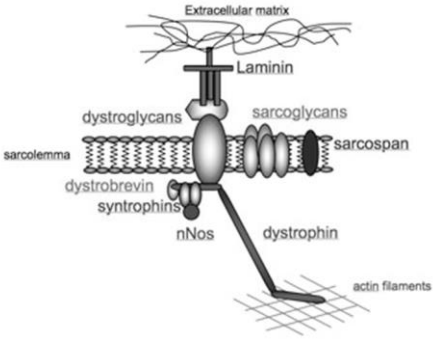

Fig 1. *Dystrophin-myoglobin complex*

Much like MH, AIR does not occur on every exposure to a triggering agent. The same child may have had several uneventful anaesthetics with triggering agents and develop AIR on subsequent exposure. As with MH, the reasons for this are uncertain.

The most catastrophic presentation of AIR is sudden cardiac arrest. This may occur in the operating room or post-operatively in the recovery room as the child is waking up and starting to move. Blood sampling will reveal a markedly elevated potassium (it is not uncommon to see this raised two or three times normal in such circumstances). AIR can also present as post-operative rhabdomyolysis (for example with the emission of cola-coloured urine) without cardiac arrest or as a gradual increase in temperature and heart rate without signs of hypermetabolism or muscle rigidity.

The rhabdomyolysis occurs as a result of exposure to suxamethonium or to the volatile anaesthetics.

Table 1 illustrates some important differences between the two crises. The key difference is that AIR's presentation is acute rhabdomyolysis and the clinical changes are as a result of the massive leak of potassium from shearing muscle membranes whereas with MH, the initial picture is one of hypermetabolism, which, if not recognized and managed early, will deteriorate to uncontrolled rhabdomyolysis.

Table 1. *The differences between Anaesthesia Induced Rhabdomyolysis and Malignant Hyperthermia*

	AIR - *rhabdomyolysis*	**MH** - *hypermetabolism*
Early signs	• Peaked T-waves → bradycardia → cardiac arrest • SaO_2 normal until arrest • Markedly ↑ K^+, myoglobin	• Muscle rigidity • Tacchycardia • ↑ CO_2 • ↑ O_2 consumption • ↓ SaO_2 • ↑ K^+
Late signs	• Acidosis • ↑ CO_2 • ±↑ Temperature	• ↑ Temperature • ↑ Myoglobin • Acidosis • Cardiac arrest

When it comes to the timing, if suxamethonium has been given to a susceptible individual one could expect a pretty rapid presentation of either emergency but with the volatiles alone the timing is variable. An unexpected cardiac arrest at the end of a case or in the recovery room should ring loud alarm bells for AIR and I would even go so far as to say that you could give a dose of calcium intravenously while you perform CPR and get a blood gas result to assess the potassium.

The major difference for treatment of these two catastrophes is the focus: with AIR you must lower the potassium to avoid heading to a cardiac arrest and protect the kidneys. With MH dantrolene will stop the process once triggers have been removed.

Treatment of AIR

1. CALL FOR HELP. Allocate specific tasks.
2. STOP trigger agents: volatiles/suxamethonium
3. HYPERVENTILATE with 100% O2 – change machine/remove vapourisers
4. If no pulse or heart rate <60, START CPR as per PEA/Asystole algorithm
5. ↑K+ most likely cause: give CALCIUM IV – see table 2 for dosing
6. TAKE BLOOD (venous or arterial blood sample):
   i) Blood gas for K+
   ii) Lab for creatine kinase (CK) and myoglobin
7. If confirmed on blood gas, TREAT HYPERKALAEMIA as per table 2.
8. Start propofol or ketamine infusion once ROSC
9. Abandon or finish surgery as soon as possible

DRUG	BOLUS DOSE	INFUSION
Calcium gluconate 10%	*0.5mL/kg IV*	*0.1 - 0.4 mL/kg/h IVI preferably via central line*
Calcium chloride 10%	*0.2ml/kg IV*	*0.04 – 0.16 ml/kg/h IVI preferably via central line*
Sodium bicarbonate 8.4%	*1-2mL/kg IV*	
Salbutamol		*5 µg/kg/min IVI for 1 hour then 1 µg/kg/min*
Insulin/50% Dextrose		*1 mL/kg/h 50% dextrose with 0.1 IU/kg/h insulin (stop if glucose < 10)*
Furosemide		*1 mg/kg IV*

Table 2. *Treatment of hyperkalaemia*

MH is definitely associated with:

- Known causative mutation of *RYR1*
- Central core disease
- Minicore, Multicore or Core rod myopathy
- Centronuclear myopathy
- King - Denborough syndrome
- Native American myopathy
- Congenital fibre type disproportion
- Periodic paralysis
- Nemaline rod myopathy
- Idiopathic hyper-CKaemia

Central core disease is one of the most common myopathies in European studies but we are fortunate to see less of it here in South Africa. We do see a fair number of children with centro-nuclear myopathy however, which does have an association with RYR1 abnormalities. Given that telling the difference between the various congenital myopathies will require a muscle biopsy, all children that have a suspected myopathy or dystrophy that present to our clinic at The Red Cross War Memorial Children's Hospital get screened for the most common abnormal RYR_1 allele before coming to theatre. However, even if they test negative for that allele we will treat them all as potentially at risk of either MH or AIR and proceed with a trigger free anaesthetic.

2. Simple rules for known or suspected dystrophies

No volatiles. Not ever, not even "just a quick whiff at induction to help get the IV up". A case report of fatal AIR in a child with DMD who was given a volatile induction has put paid to the thought that a little bit of volatile is okay.
No sux.
Machine prepared purged of all volatile agents.
Safe options: propofol, ketamine, dexmedetomidine, etomidate, NDMR as needed and regional techniques

3. Rules for mitochondrial myopathies (and a bit of background)

Mitochondrial diseases have a varied clinical presentation. There will usually be a myopathy ±encephalopathy ± intestinal disturbance ± renal abnormality ± hepatopathy etc. coupled with a metabolic disturbance (increased lactate/pyruvate/acyl carnitine). While an isolated myopathy does not rule out mitochondrial disease symptoms in other systems might be as subtle as migraines or attention deficit or as severe as intractable seizures with profound global weakness, but there will almost always be at least subtle signs of more than one system being affected.

While it's possible to diagnose some disorders on genetic analysis of blood they often require a muscle biopsy for their diagnosis. The muscle is subject to a variety of tests from histology and electron microscopy to genetics and individual enzyme analysis. This explains why some patients may come for multiple biopsies before a diagnosis is made and why it is important to have a working diagnosis to help the neurologist or paediatrician to decide which tests to send the sample for.

Aside from muscle biopsy these patients, as with the dystrophies, may come for a variety of surgeries related to their conditions such as PEG insertion, Nissen fundoplication, T's & A's for OSA or radiology scans and of course they can come for anything incidental.

Consider that mitochondria are the powerhouses of the cells, responsible for generating ATP for cellular activities. Under anaesthesia we need cells to continue with these activities as well as respond to a variety of new challenges that may arise which may increase the demand on the mitochondria. This is where the patients with mitochondrial disorders run into problems under anaesthesia and why it's essential to limit the physiological stress placed on these patients.

Patients generally do well regardless of your anaesthetic technique provided you are *well prepared, considered in your approach and vigilant*. Procedures with the potential for large fluid shifts, cardiac stress or requiring significant analgesia require the greatest attention to detail and careful intra and post-operative planning to ensure that the patient's delicate balance of metabolic and cardio-respiratory systems suffers the least disruption. Events such as prolonged hypotension and hypoxia are not good and tourniquets need very careful consideration of the pros and cons.

You should liaise closely with the physician caring for the patient to find out what energy substrate works best for these patients. They are less able to mobilise from stores and need a steady supply. Some patients require dextrose infusions, some require a ketotic diet and will need proteins in their fluids peri-operatively. Administration of the incorrect substrate is likely to result in the build-up of metabolites at whatever stage of the Krebs cycle or OxPhos pathway their defect is. You will need to be checking electrolytes regularly looking for biomarkers of decompensation for longer cases.

"Individual optimisation on a case-by-case basis is more important overall than choice of any one particular technique." (A review of anaesthetic outcomes in patients with genetically confirmed mitochondrial disorders; Eur J Pediatr (2017) 176:83–88)

While all our drugs affect mitochondrial function to some extent, in all cases it is prudent to avoid prolonged propofol infusions. In fact, many experts would avoid even short infusions opting for no more than a single dose before switching to another form of maintenance.

Patients with mitochondrial myopathies appear to be at risk of a propofol infusion syndrome (PRIS)-like clinical picture which can develop much more rapidly than the classically described syndrome, over just a few hours as opposed to several days. In fact, PRIS has been described in children after infusions as short as 3 hours. PRIS is an "all or nothing" syndrome: when it occurs it is always sudden and catastrophic and has a high mortality rate. However, cases occurring in theatre appear to have a higher survival rate (possibly because they are more intensively monitored and interventions are undertaken earlier than in ICU?). As with the dystrophies, this is an idiosyncratic reaction and incident-free propofol exposure has been shown in several case reports. By minimising metabolic stress and providing adequate fuel in the form of glucose you may avoid PRIS. Regional combined with general anaesthesia is useful in these kids. It is possible that patients without any or with only mild clinical manifestations of mitochondrial myopathy are prone to react most abnormally to propofol.

Volatile anaesthetics will not trigger a specific reaction in these patients but one should be careful of the cardiovascular effects in patients who have cardiovascular depression.

Rules with mitochondria myopathies:

1. Avoid long propofol infusions
2. Careful pre-op assessment of affected systems
3. The specific drugs or technique you use are less important than attention to detail in all aspects of the case.

4. Approach to the undiagnosed but symptomatic child

If only we could identify which patients are going to give us trouble before they come to theatre so we can tailor our anaesthetic accordingly. The trouble is that it can take a while for the disease to become clinically obvious enough for a patient to be diagnosed and they could come to theatre for any number of unrelated procedures before this and of course may need a muscle biopsy to nail their diagnosis (although thankfully genetic diagnosis is becoming increasingly possible). Picking up a potential muscle disorder requires vigilance.

The following are clues or red flags in your history and examination that a child may have an undiagnosed muscle disorder and I will ask a version of these questions in all my pre-op assessments, probing deeper if alarm bells start ringing:

Family history of a reaction to anaesthesia or of muscle disease

Developmental history, particularly motor development (see Fig 2.). Were they a "floppy infant"? Are they achieving milestones, has there been a fall off or regression? And if I get a yes to any of these I'll start asking whether they seem to tire when they play with other kids, do their parents end up carrying them around a lot? Have they ever had cola-coloured urine?

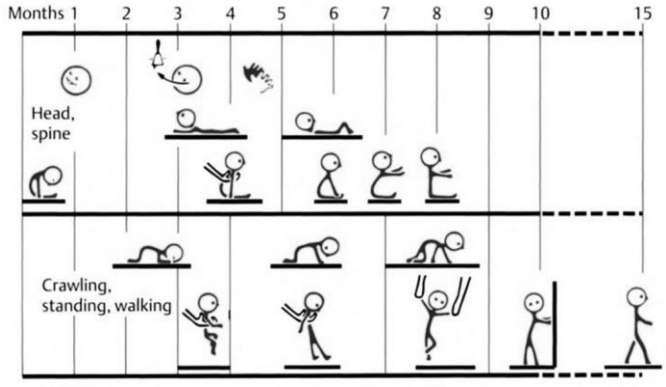

Fig 2. *Motor milestones*

Examination: resting tachycardia, enlarged calf muscles, look at their rise to standing (Gower's sign) and their gait when running (do they waddle?) (both signs of DMD), a floppy child, slips through hands

on lifting, head lag, ptosis, “carp mouth” (myopathic facies), muscle wasting are also signs of muscle disease.

To help you distinguish between possible diagnoses (particularly muscular dystrophy and mitochondrial myopathy for whom your anaesthetic may need to be different) drawing blood for creatine kinase and lactate may help. With the dystrophies, even early on, expect an elevated CK whereas the mitochondrial myopathies may have an elevated lactate, but not always. And while you’re at it check the baseline potassium level.

After you’ve made your own assessment discuss with the medical and surgical team what their hypothesis is, to help you establish the most likely diagnosis. If the child has never seen a paediatrician before and you have time to refer beforehand this may help in generating an hypothesis as to the likely diagnosis. Use all this information to help you decide on the best anaesthetic choices for your case.

If you have a patient on your list that you know or suspect to have a muscular dystrophy you should give them a TIVA. Prepare them for this pre-operatively with anxiolysis if needed and ensure that EMLA is applied at least 45 minutes before you cannulate and have a “clean” machine or an alternative oxygen source.

If you have a patient on your list with a known or suspected mitochondrial myopathy expert opinion is that you should avoid propofol and I would advocate for the use of volatile in these patients with due consideration of the cardiac function.

What if you can’t postpone for investigations? You need to work on your “best guess” hopefully after discussion with paediatricians. Avoid sux, no volatiles, favour non-propofol in cases where MM is being considered (especially if likely >2.5hrs). Be vigilant intraoperatively and in recovery: monitor appropriately and look out for potential complications (watch ECG, elecs, pH).

Send off investigations (CK, lactate) anyway and get results when they are available.

Is there an anaesthetic technique that is safe for all?

A combination of ketamine, dexmedetomidine, ±N2O and local anaesthesia, including regional techniques, are all non-triggering. Use a clean machine (take off your vapourisers, change the soda lime, get clean circuits), I get an ICU ventilator and then have a separate O2 source to which I attach a Jackson-Reece circuit (because this is the circuit I am most comfortable with). This is not my favourite anaesthetic technique but when I am in doubt, this is the one I will use.

There is absolutely no place for suxamethonium in these patients and suxamethonium should be avoided whenever a muscle disease is known or suspected. There have been case reports of the uneventful use of suggamadex in patients with muscle disorders but, as yet, there is insufficient evidence regarding its use in this heterogenous group of patients to recommend it.

5. Implications in the chronically afflicted child

The anaesthetic risks that relate to these disorders once they are advanced are varied and substantial.

The respiratory system requires careful preoperative assessment and optimisation. Kyphoscoliosis, causing restrictive lung disease, is compounded by respiratory muscle weakness that predisposes the patient to recurrent lung infections. Postoperative non-invasive ventilation may be useful, especially after major surgery such as scoliosis repair, but requires preoperative preparation of the patient. While younger children may struggle to co-operate with lung function testing this can be useful in older children and teenagers.

All patients with muscular dystrophy will develop cardiac dysfunction. The clinical manifestation of this is late because they are sedentary however the cardiac damage is happening from early on (because this is a very active muscle) but just not manifesting. Examination may reveal a resting tachycardia or other arrhythmia and ECG changes are variable and non-specific (but may be present before symptoms appear. An echocardiogram is notoriously unreliable at predicting the severity of myocardial

dysfunction, and cardiac magnetic resonance imaging or a dobutamine stress echocardiogram may be preferable as patient weakness means you can't do a traditional stress echocardiogram. If the patient with advanced disease has not been seen by a cardiologist, they should be referred pre-operatively. A course of pre-operative corticosteroids may slow down the development of cardiac dysfunction and preoperative optimisation with angiotensin converting enzyme-inhibitors may be indicated. If the heart is put under strain (e.g. hypovolaemia under anaesthesia) it may not have the capacity to respond which can lead to rapid and catastrophic decompensation under anaesthesia. Several case reports of death in such circumstances can be found.

The implication for us is that we need to be vigilant in our haemodynamic management of these patients, even when their systemic disease does not seem far advanced. Expect a slower response to your induction from low cardiac output so be patient and go slowly. Pay absolutely meticulous attention to fluid status, make sure you have adequate venous access to give rapid infusions of fluid in the face of sudden massive losses, all but the smallest of procedures should be monitored invasively, take care with myocardial depressants such as propofol and have your inotropes readily available. Transthoracic or transoesophageal echocardiography (if they can be applied intra-operatively) may be helpful in distinguishing hypovolaemia from poor function as a cause of poor output. If these patients do develop a cardiac arrest from myocardial depression and/or hypovolaemia they are notoriously difficult to resuscitate.

Patients with Duchenne muscular dystrophy are reported to have an increased bleeding risk that manifests most obviously during major surgery, such as scoliosis repair. This has been postulated to be because of impaired vascular reactivity. Adequate venous access should be secured preoperatively and blood products should be available. A cell saver is recommended. Cyclokapron infusion has been shown to reduce transfusion requirements.

A difficult airway may be anticipated because of macroglossia in Duchenne muscular dystrophy. This is from fatty infiltration of the muscle of the tongue and is found in around 20% of patients.

"Rules" (or guidance) for the child with advanced disease:

Pre-operative optimisation of cardiac and respiratory systems where possible
Go slowly and be patient with an IV induction
Meticulous fluid management and avoidance of hypovolaemia
Early inotropic support
Extubate early onto non-invasive ventilation where necessary

6. Conclusion

Children with muscle disorders require special care in assessment and management. With pre-operative vigilance appropriate plans can be put in place and with intra-operative vigilance problems can be detected and managed pre-emptively.

I am available to answer your clinical questions on the peri-operative management of these children now and after you have passed your exams. Please feel welcome to contact me on email: rebecca.gray@uct.ac.za

Recommended reading

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The Child at Risk
Mitigating against adverse outcomes in paediatric anaesthesia

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Introduction

risk /rɪsk/ *Noun* a situation involving exposure to danger

Risk stratification in adult anaesthesia, particularly cardiac and vascular anaesthesia is relatively well defined. The concept of risk in paediatric anaesthesia is evolving. Due to a growing body of robust literature, we are now able to apply evidence to our paediatric population and implement strategies that mitigate against adverse events, thereby reducing perioperative morbidity and mortality.

This paper will consider several different risks that exist in paediatric anaesthesia. Some of these are life threatening, others are threatening to quality of life. While this article is by no means comprehensive, it attempts to enable the reader to identify children at increased perioperative risk, and suggests evidence-based strategies to mitigate against this risk.

Difficult Airway Management

Difficult airway management in children is a major cause of anaesthetic-related cardiac arrest, hypoxic brain injury and death. Fortunately, a truly difficult airway (can't intubate can't ventilate) is not commonly encountered in children. Even when visualisation of the larynx and endotracheal intubation is challenging, bag mask ventilation is usually possible. Difficult airway management can often be anticipated based on pre-operative assessment, which allows for optimisation and planning. When a difficult airway is anticipated, planning must include a range of airway management strategies and should consider which personnel and what equipment should be at hand in theatre.
Challenges unique to the paediatric population:

- Comprehensive airway assessment, especially in the uncooperative/very young can be difficult. Subtle features may be missed
- Awake fibreoptic intubation is not an option
- Front of neck access is very difficult; paediatric ENT surgeons have a high failure rate
- Deterioration occurs quickly due to difficulties with pre-oxygenating, relatively high metabolic rate and low FRC, with catastrophic results

Table 1 Physical features suggestive of a difficult paediatric airway[1]

Physical feature/action	**Clinical finding predictive of difficult airway**
Upper incisor length	Longer–less available space for laryngoscope blade and endotracheal tube
Alignment of incisors	Overriding of maxillary incisors or under riding of mandibular incisors
Protrusion of mandible	Inability to protrude the mandibular incisors in front of maxillary incisors
Mouth opening	Distance between upper and lower incisors with full mouth opening: <2 fingerbreadths*. Mallampati grade 3 or 4 view
Palate	High arch or narrow
Submandibular space	Narrow, indurated, or firm
Thyromental distance	↓ to < 3 finger breadths*
Length of neck	Short
Neck size	Increased circumference
Head and neck range of motion	Limited mobility (flexion, extension, and lateral rotation)

*For evaluation in a child, use the child's own fingers.

Table 2 Syndromes in children associated with difficult airway management

Syndrome	Airway Features
Pierre Robin sequence	Micrognathia; glossoptosis (backward displacement of tongue); airway obstruction at rest; improves with age
Treacher Collins	Micrognathia; limited mouth opening; airway obstruction at rest; worsens with age (in spite having mandibular distraction)
Goldenhar	Micrognathia; hemifacial macrosomia; occipitalisation of atlas; limited mouth opening
Mucopolysaccaridoses (Hunter's and Hurler's)	Accumulation of mucopolysaccharides in various tissues, including airway; short, immobile neck; cervical instability, airway obstruction at rest; difficult mask ventilation and tracheal intubation; worsens with age
Apert	Midface hypoplasia; possible choanal stenosis; progressive calcification of cervical spine; airway obstruction
Down	Macroglossia; atlantoaxial instability; and pharyngeal hypotonia
Crouzon	Midface + maxillary hypoplasia; short neck; restricted neck movement
Pfeiffer	Midface hypoplasia and airway obstruction
Klippel-Feil	Fusion of variable number of cervical vertebrae and limited neck movement
Beckwith-Wiedemann	Macroglossia
Freeman-Sheldon	Circumoral fibrosis and microstomia

Analysis of the PEdiatric Difficult Intubation (PEDI) registry which collects data from a number of institutions in North America[2], highlighted the following risk factors and suggests these mitigation strategies:

Table 3 Risk factors for difficult airway management, increased complications and mitigation strategies

Risk factors for difficult airway	Risk factors for ↑ complications*	Mitigation strategies to ↓ complications
Age < 1 year Weight < 10kg Micrognathia Syndrome Snoring	> 2 attempts at intubation Weight < 10 kg Micrognathia > 3 attempts at direct laryngoscopy before indirect technique	Minimise attempts at direct laryngoscopy[3] Convert to indirect laryngoscopy technique early** Consider oxygenation during intubation attempts (nasal cannulae or supraglottic airway (SGA) device[3]) Experienced paediatric anaesthetist Extubate awake

*severe complications commonly include hypoxaemia and cardiac arrest
**The use of video laryngoscopy was associated with fewer attempts and higher 1st attempt success.

Emergence Delirium

The incidence of emergence delirium (ED) varies significantly, depending on the patient population studied. Although the phenomenon is self-limiting, it can be distressing for staff, as well as other patients/parents in the recovery area. There is also the possibility for injury, to both child and staff. Additionally, management of a child with ED requires intensive staffing, drawing care away from other patients. ED is not entirely benign, as maladaptive behaviours (nightmares, separation anxiety, enuresis) can persist for up to two weeks post incident.

Table 2 Risk factors and mitigation strategies for Emergence Delirium

Risk	Mitigation strategies[4, 5]
Age (3-7 years) Volatile anaesthesia ENT/ophthalmology/circumcision Patient pre-existing behaviour • Temperament • Sociability	Education and preoperative preparation Premedication*: • Ketamine • α-agonist: clonidine, dexmedetomidine • Midazolam

• Cognitive skills Parental anxiety Pain Autism Spectrum Disorder ADHD, Behavioural disorders	• Melatonin (0.2-0.4mg/kg) • Gabapentin (15mg/kg) IV induction with propofol TIVA Ensure adequate analgesia Prolong emergence • Propofol (1mg/kg at end of procedure) • Opiate • α agonist: clonidine, dexmedetomidine** Magnesium sulphate (30mg/kg IV followed by 10mg/kg/h) Acupuncture (heart 7 acupuncture site) Allow gentle awakening with minimal stimulation in a quiet recovery area

*not all of these agents are anxiolytic/sedative and do not necessarily influence mask acceptance, but given preoperatively, decreased the incidence of ED.

** Dexmedetomidine appears to be superior, regardless of timing of administration. Can be used pre/intraoperatively, or at conclusion of procedure. Doses as low as 0.15 mcg/kg IV are effective. The recent literature focuses on this newer drug, with no good studies comparing its use to a cheaper alternative – clonidine.

It is imperative that all children are assessed preoperatively for risk for ED, and that appropriate mitigation strategies are employed. Consider doing a baseline PAED[4] score at the preoperative visit. Be mindful that children with neurological, developmental or behavioural challenges may score highly and that, when stressed, children may behave in ways that are not congruent with their 'normal behaviour'. Always evaluate PAED score in relation to pain score, especially in non-verbal children. Distinguishing between pain and ED can be challenging, but patients with ED are generally unaware of their surroundings and unable to make eye contact.

Perioperative Cardiac events

Perioperative cardiac events (PCE) include arrhythmias, severe hypotension, cardiac arrest and death.

Table 3 Risk for perioperative cardiac events + suggested mitigation strategies

Risk for perioperative cardiac arrest	**Risk for death**	**Mitigation strategies**
Higher ASA PS Major/emergency surgery CHD most notably [6, 7] • Single ventricle anatomy • Unrepaired/palliated • Supra systemic PHT • LVOT obstruction • Low cardiac output PHT[8] *	Age < 1 year[9] Higher ASA PS Cardiac surgery[9] Catheterisation Lab procedure[9] CHD • Aortic stenosis • Cardiomyopathy • CCF PHT[8]	Experienced paediatric anaesthetist Anticipate, pre-empt deterioration Avoid PHT crisis, RV failure Clearly define anaesthetic goals + plan for how to achieve them iNO perioperatively and preop prostacyclin may prevent minor adverse events in PHT[8] Avoid hyperoxia + hypocapnia in neonates with PPHN[10] Appropriate postop destination**

*There are subgroups within this patient population, but beyond the scope of this article.
**patients with PHT are at higher risk for postoperative cardiac arrest and need to be monitored and cared for in an appropriate environment, regardless of surgical procedure.

CHD = congenital heart disease; ASA PS = American Society of Anaesthesiologists Physical Status; PPHN = persistent pulmonary hypertension of the newborn; PHT = pulmonary hypertension; LVOT left ventricular outflow tract; CCF = congestive cardiac failure; iNO = inhaled nitric oxide

Cardiac arrest is more likely to occur during the maintenance phase of anaesthesia than during the pre-surgical phase, and least likely during post-surgical phase[7, 11]. Patients with congenital heart disease arrested most commonly during non-cardiac surgeries, followed by cardiac surgeries and during procedures in the cardiac catheterisation lab.

My own sub-analysis of the Wits Academic Hospital Complex (WAHC) data from the SAPSOS[12] data showed that children with higher ASA PS (mean III), CHD and cancers were more likely to suffer PCE.

Perioperative Respiratory Adverse Events (PRAE)

PRAE include laryngospasm, bronchospasm, hypoxia, breath holding, airway obstruction, severe coughing and postoperative stridor. The incidence of PRAE is higher in the paediatric population. My analysis of the WAHC data from SAPSOS showed an incidence of 8.52%. Risk of developing PRAE was higher for patients with a current/recent URTI, burns, chronic lung disease, laryngeal papillomas, pulmonary tuberculosis and sickle cell disease. A number of scoring systems have been proposed to risk assess for PRAE, but have yet to be validated.

Table 4 Risk factors for PRAE and suggested mitigation strategies

↑ Risk: patient factors[11, 13, 14]	↑ Risk: surgical factors	Mitigation strategies
Age < 2 years Recent URTI (< 2 weeks) Asthma/pre-existing pulmonary condition Morbid obesity ASA >II Eczema Snoring Atopy Passive smoking Family members with asthma/ eczema	Airway surgery ENT surgery Upper abdominal surgery Cardiac surgery Eye surgery	Preoperative nebulisation with β_2 agonist for children with recent URTi[13, 15], asthmatics & bronchial hyperreactivity Experienced paediatric anaesthetist IV induction with Propofol[16] Least invasive airway instrumentation[17] (FM>LMA>ETT) Avoidance of Desflurane[13] Deep removal of SGA IV lignocaine[13]* (1-2 mg/kg) IV dexmedetomidine*

*to prevent coughing on extubation

It is important to apply the same caution and vigilance on emergence and extubation as applied during induction and intubation. Up to 1/3rd of adverse events can occur during this period[18]. Consider age, prematurity, preoperative oxygen supplementation or respiratory support, cardiac disease and ASA PS in deciding whether or not to extubate.

Table 5 Preventing PRAEs on emergence and extubation in children[19]

Factors associated with successful extubation	Number of factors present	Likelihood of successful extubation (positive predictive value) %
Tidal volume > 5ml/kg	1/5	88.4
Conjugate gaze	2/5	88.4
Facial grimace	3/5	96.3
Purposeful movement	4/5	97.4
Eye opening	5/5	100

Postoperative Vomiting (POV)

Nausea is a difficult symptom to elicit in children. Often the first sign that the child is experiencing discomfort, is vomiting. Vomiting is distressing, and can delay discharge or result in unwanted admission after day case surgery or, in extreme cases, metabolic and physiological derangement. The incidence of POV varies significantly with the patient population studied, and we (in SA) lack robust data on our patient population. A risk assessment should be conducted for every child, and a rational

approach to anti-emetic prophylaxis applied. The POVOC score has been proposed, but this scoring system is not comprehensive, and has not been validated in our patient population.

Table 6 Risk factors for POV in children[20, 21]

Patient factors*	Surgical factors	Anaesthetic factors
Age > 3 years Female (post-puberty) History of POV (or direct family history) History of motion sickness	Duration of surgery > 30 mins Strabismus surgery Adenotonsillectomy Middle ear surgery	Volatile anaesthesia Opiate use Anticholinesterase use

*There is weak evidence for patient anxiety and high BMI as risk factors. Also, weak evidence to show that passive smoking may be preventative. This risk stratification system fails to take race into account, which we appreciate anecdotally to play a role.

Table 7 A rational approach to anti-emetic prophylaxis

Number of risk factors	Recommended Intervention
2	Dexamethasone IV 0.15 mg/kg
3	Dexamethasone IV 0.15 mg/kg + Ondansetron IV 0.15 mg/kg*
>3	Dexamethasone IV 0.15 mg/kg + Ondansetron IV 0.15 mg/kg +/- Droperidol IV 25 mcg/kg Intra-operative fluid administration up to 30ml/kg

*timing of Ondansetron administration has not been found to be significant

Other strategies to decrease POV are encouraged and include avoidance of nitrous oxide, use of a multi-modal analgesic strategy to reduce opiate requirements and the consideration of a Total Intravenous Anaesthesia (TIVA) technique.

Mitigating against risk

The South African Paediatric Surgical Outcomes Study (SAPSOS) revealed an in-hospital perioperative mortality rate of 1.1% (109 per 100 000 cases)[12]. This is 10 times higher than that reported in a similar European study. Of concern, 41% of these deaths were in patients assigned an ASA status of 1 or 2. We eagerly await the further analysis of this data, which will lend some insight into the practice of anaesthesia in South Africa, and the incidence of anaesthetic complications.

Some of the above-mentioned complications are rare, but life-threatening. Others are relatively common, but cause significant distress to staff, patients and caregivers. They may delay hospital discharge, with ensuing economic implications. High risk patients should be identified preoperatively, thus allowing caregivers and clinicians to make informed decisions on patient care. Adequate counselling and consent is an ethical and legal requirement, which if carried out skilfully, improves rapport between anaesthetist and family, and de-escalates anxiety on the part of the clinician.

Guidelines and algorithms are useful cognitive aids that improve functioning and (potentially) outcomes during stressful situations. Where not universally applicable, these should be adapted for your institution or environment.

Finally, there is no substitute for experience. In the absence of governance and guidance, the profession (and society) relies on self-regulation. Identification of high risk patients is key in order to refer appropriately. Minimum caseload per year, as well as experience in the management of children with difficult airways or complex cardiac pathology are important considerations to be borne in mind.

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Nutrition In ICU
and the refeeding syndrome

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The role of nutrition in managing ICU patients

Providing adequate nutrition to the patient in the ICU is an essential part of the care but many aspects remain controversial. On the one hand the provision of nutrition is often, in practice, ignored as we struggle with the more pressing problems of oxygenation and circulation. On the other hand, dramatic claims made in the past that an excess of nutrients or that the provision of special "pharmaco-nutrients" could improve outcome have fallen away as larger trials have failed to show a special benefit.

Critically ill patients often arrive in ICU already nutritionally depleted due to pre-existing illness and then go into marked negative energy balance due to the hypermetabolic response. Observational studies have shown a survival benefit if adequate protein and energy is provided and a cluster randomised study of ICU's following a nutrition protocol as opposed to "usual care" has shown a trend towards a survival benefit.[1,2] For obvious reasons prospective randomized trials of "nutrition" vs "no nutrition" have not been done.

The most recent trend in this field is one of caution and a "less-is-more" approach particularly in the early phase of critical illness. Awareness is also growing that some ICU patients can be harmed by a covert refeeding syndrome.

The recommendations in this lecture are largely based on the 2019 guidelines of the European Society of Enteral and Parenteral nutrition.[3]

Metabolic dysfunction in critical illness

Many ICU patients are admitted following a major insult, such as sepsis, trauma or major surgery that causes a massive inflammatory response which includes profound metabolic changes. During the initial shock phase following an insult, tissue hypoxia reduces energy expenditure. This is followed by an acute phase where there is an increase in metabolic rate with an increase in energy expenditure of 25 to 50% above resting energy expenditure. Glucose is the main source of energy with some derived from fat stores. Carbohydrate stores in the body are very limited, mainly glycogen in the liver, which is rapidly depleted. At the same time relative insulin resistance develops resulting in an increased blood glucose level that may impair the immune response and particularly the function of neutrophils.

To provide this energy source there is a massive breakdown of structural protein, particularly skeletal muscle with the resulting amino-amides being converted to glucose - mainly in the liver. This can result a loss of muscle mass at a rate of 2% per day.[4] This contributes to the long-term weakness and disability commonly suffered by ICU survivors which is part of the post intensive care syndrome (PICS).

The liver also synthesizes different proteins, becoming a net albumin importer and increasing its production of acute phase proteins including clotting factors and opsonins. Albumin levels drop rapidly in acute illness and no longer reflect the nutritional status.

All these changes are governed by a network of hormones including cortisol, glucagon and catecholamines as well as the inflammatory cytokines such as TNF, IL-1 and IL-6. This metabolic response is different to the metabolic response to starvation that includes a reduction in metabolic rate, the consumption of fat stores and the conservation of protein.

During the acute phase, nutrition can only reduce, but not reverse protein catabolism until recovery begins and the patient become anabolic.

Nutritional Assessment

Ideally all ICU patients should be assessed by a dietician prior to admission. Assessment starts with a nutritional history including recent intake of micronutrients and alcohol consumption. Physical examination should particularly look for evidence of muscle wasting. Ideal body mass index (BMI) should be calculated. The **subjective global assessment** uses patient history and a specific physical examination to determine nutritional status. Actual and Height can be easily measured in the supine patient, but body mass is best obtained from a recent premorbid measurement as resuscitation fluid will increase mass. The body mass index (BMI) can be calculated:

$$BMI = Mass\ (Kg) / Height\ (meters)^{2}$$

A BMI of less than 18.5 is indicative of malnutrition and less than 17 is associated with severe malnutrition. For ICU patients the **modified NUTRIC score** gives an indication of nutritional risk and is associated with mortality.[5]

Nutritional requirements

Energy: The main focus of nutrition is to provide for the patient's energy and protein needs. This is easier said than done as energy expenditure varies between patients and from day to day. Also, providing full requirements in the early acute phase increases complications, both gastrointestinal intestinal and metabolic.

Hypocaloric feeding in the first few days of critical illness results in less hyperglycaemia and better gastrointestinal tolerance without worsening outcome and ESPEN recommends no more than 70% of requirements in the early acute phase.

A simple formula for full energy requirements is 25-30 Kcal/Kg ideal body weight that can be calculated using the height and sex of the patient. Conventionally the caloric content of enteral feeds is quoted as total calories while that of parenteral solutions is quoted as "protein free calories" – so the lower figure is advised for parenteral prescriptions. More complex formulae, such as the Harris-Benedict equation that consider age and sex, can be used to calculate resting energy expenditure to which a 25% stress factor can be added. More scientifically a metabolic monitor that uses indirect calorimetry to measure energy expenditure can be used. This is attached to the ventilator and calculates energy expenditure and respiratory quotient from the measured oxygen consumption and carbon dioxide production. Any non-nutritional energy source such as glucose and propofol infusions should be considered when calculating requirements. Obese patients require additional nutrients and the energy and protein prescription should be based on an adjusted body mass of ideal body mass plus one third of the difference between actual and ideal mass.

Carbohydrate and Fat: Both carbohydrate and fat should be used to provide non-protein energy. Glucose is the only carbohydrate used in parenteral solution while enteral feeds contain a variety of starches. Lipid should make up 30-50% of the energy supply and include a blend of medium chain triglycerides, mono- and omega-3 unsaturated lipids. While small studies on omega-3 fatty acids in ARDS and Sepsis showed promise, larger studies have been unable to show an outcome benefit. Blood glucose levels should be maintained in the 6 to 10 mmol range using an insulin infusion and/or by reducing the carbohydrate intake.

Protein requirements are thought to be higher in the critically ill and the current recommendation is 1.3 grams/Kg ideal body weight. It need not be restricted in the early acute phase. Protein intake should not be decreased in acute renal failure but should be reduced in severe hepatic failure.

Glutamine: This non-essential amino acid was thought to be beneficial in the critically ill, but a large study showed that high doses in multiple organ failure caused harm. It may be of benefit in trauma and burns patients but should not be administered to patients in hepatic or renal failure.[7]

Vitamins Patients should receive the recommended daily allowance of vitamins that are included in most enteral feeds. However, vitamins do not have magical properties in critical illness. **Vitamin C** is an anti-oxidant but a large study of antioxidants in multiple organ failure failed to show benefit.[7] There may be a benefit with modest doses but the promise of mega doses of Vitamin C and D in an observational study reducing mortality in septic shock has not been borne out in prospective

randomized trials.

Vitamin D levels should be measured and if low, a single dose of 50000 IU administered.

Thiamine should be administered to all patients with a history of heavy alcohol intake and to patients at risk of the refeeding syndrome.

Trace elements should be supplemented in patients on parenteral nutrition. Plasma zinc should be monitored in long-term ICU patients particularly if they have high gastrointestinal fluid losses and supplemented if low.

Dietary Fiber is important for proper bowel function and to slow the rate of absorption of carbohydrates. It may reduce the incidence of diarrhea and constipation. Fiber containing feeds should be introduced once bowel motility has become established.

Water and Electrolytes: Most of the daily adjustments to the nutrition prescription are related to this fluctuating requirement. Generally, ICU patients require potassium, magnesium and phosphate replacement (see section on the refeeding syndrome) and sodium and water restriction. After resuscitation, fluid restriction and diuretics may be used to improve pulmonary function hence the need for more concentrated feeding solutions. Over-restriction causes hypernatremia which may require addition water to be temporally added. Low potassium feeds are required in renal failure. In patients with high upper gastrointestinal losses sodium intake may have to be increased.

Enteral Nutrition

There is good evidence that early (24-48 hours after admission) institution of enteral feeds is beneficial with a decrease in organ failure, infections and mortality.[6] This may be due restoration of gut barrier function and gut-associated lymphoid tissue function. Low volumes of feed are as beneficial as full volume and are better tolerated.[8] Enteral feeds also reduce the risk of stress related gastrointestinal feeding. The downside of enteral feeding is that vomiting and the risk of aspiration is increased.

There is a huge variety of enteral feeds. They all come pre-packed in sterile containers usually 500ml in volume. Polymeric feeds contain whole nutrients, are cheaper and are indicated where bowel function is expected to be normal. Semi-elemental feeds mainly consist of polypeptides, small complex carbohydrates and medium chain triglyceride fats. There main indication is when bowel function is impaired and absorption compromised, particularly when the bowel may be edematous after resuscitation or due to hypoalbuminemia. Theoretically they are indicated in pancreatitis.

Naso-gastric tube feeding is the main nutritional route used in ICU and should always be tried first unless contraindicated. Contraindications are unresuscitated shock, abdominal compartment syndrome, a stapled off GIT, upper gastrointestinal fistulae and large (> 500 ml/day) nasogastric drainage. Abdominal surgery, intestinal anastomoses (except duodenal repairs) post-surgical ileus, and lack of bowel sounds are not contraindications. The location of the feeding tube should always be checked after placement on X-ray. The patient should be nursed head up at $30\text{-}40^0$ and the feed to should be started slowly, gradually increasing the feed rate every 4 hours. Critically ill patients commonly have gut dysfunction even if they have not had abdominal surgery.[9] Regular gastric aspirates to guide the rate of increase (slow down if > 250 ml) are practiced in our units but have been shown to not reduce the incidence of aspiration in medical patients. Having a feeding protocol to guide the nurses helps to ensure that the prescribed feed is all administered. If the feed is not tolerated, then metoclopramide and/or IV erythromycin should be started but not persisted with beyond 3 days.

Oral feeding should be attempted in extubated patients. Many ICU patients are anorexic, and it is difficult to achieve full nutritional requirements using this method. Supplemental sip feeds are often better tolerated than plates of unappetizing food from the kitchen.

Naso-jejunal tube feeding is an option when there is a need to bypass the stomach and duodenum as in gastric outlet obstruction and after surgery in that area. It is also useful for patients with severe pancreatitis who often have a function gastric outlet obstruction. They are difficult to insert, are easily displaced and do not reduce the risk of vomiting. Jejunostomies should not be inserted in the critically ill as they have a high complication rate.

Parenteral nutrition

Parenteral nutrition should only be used if the enteral route is not available or if enteral feeding is inadequate for more than seven days in the previously well nourished.[10] It may also be introduced earlier in malnourished patients who are not achieving full requirements via the enteral route provided the risk of refeeding syndrome is mitigated.

The intravenous nutrition solutions consist of mixtures of amino-acids, glucose and lipid and come in a variety of formulations so most patient requirements can be provided for. Most of the solutions are available with and without electrolytes. When combined the solutions are unstable and need to be refrigerated and used within a few days. There are two systems for supplying PN. Compounded bags are made to order in a central factory. Multi-chambered bags are supplied in bags with the different administration. Trace elements and vitamins also need to be supplied in IV form.
PN solutions are very hyperosmolar and the more concentrated solutions, preferred in ICU because of their lower volume, must be administered through a central venous catheter.

The main risk of parenteral nutrition is infection; either of the central venous catheter or of the bag itself as the solution is very supportive of bacterial growth. PN should be administered through a dedicated catheter or port and no additives or “piggy-back” infusions added. Each bag should not hang for more than 24 hours once spiked and the infusion set should be changed with the line using a full sterile technique. Other complications of TPN are hyperglycaemia and hyperlipidemia, hepatic dysfunction and overfeeding.

Refeeding syndrome

First described in World War II among liberated prisoners who were re-fed too rapidly, this is describes a cluster of conditions that may even be fatal. Critically ill patients are particularly at risk, perhaps because of their high metabolic rate. Risk factors are illness or stay in hospital prior to ICU admission.

During relative starvation there is a gradual decrease in the main intracellular ions: Potassium, Magnesium and Phosphate. Prior to refeeding blood levels of these electrolytes are normal, but with the reintroduction of nutrition they drop rapidly. The main culprit in refeeding syndrome is the phosphate as low levels can cause muscle weakness and affect neurological function. A decrease in blood phosphate below 0.65 mmol/l or a decrease of > 0.16 mmol/l ICU is strongly suggestive of the diagnosis.[3] In extreme cases there may be arrhythmias, seizures and coma. During refeeding basal metabolic rate increases as does blood glucose level. Phosphate becomes bound to phosphorylated carbohydrates in the liver and muscles. The increase in blood glucose increases the demand for phosphate to form ATP. There is also a decrease in red blood cell 2,3-DPG resulting in reduced oxygen delivery. Thiamine is an essential co-enzyme in the oxidative decarboxylation of pyruvate and further steps in glycolytic pathway.

All critically ill patients should have their nutrients introduced gradually and their phosphate, magnesium and potassium levels closely monitored and aggressively replaced if below normal. In patients at risk of the refeeding syndrome their initial nutrition targets should be calculated on their actual, not ideal body mass.

In conclusion providing nutrition in the ICU requires a partnership between the dietician, nurse and doctor to make a daily feeding plan and ensure it is carried out.

Recommended reading

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Anaesthesia for Lung Transplantation

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Introduction

Lung transplantation has evolved over the past four decades since the first successful transplant in the 1980's. This chapter will aim to provide a broad overview of the principals involved in the anaesthetic technique for lung transplantation and to discuss some of the controversies that still exist in this field. The number of transplants has increased every year in the United States. Both the utilization of "extended criteria" donors and ex vivo lung perfusion systems have allowed for an increase in the number of recovered donor organs. Despite transplanting more complex patients and a greater acceptance of donor organs, survival has not changed over the past 5 years (84.6% 1-year, 67.8% 3-year, and 55.5% 5-year survival). The increased number of transplants along with stable survival resulted in more lung transplant recipients being alive than ever before. Lung transplantation is a life-saving therapy for end-stage lung disease that requires perioperative physicians versatile in caring for these patients in the preoperative, intraoperative, and post-operative periods.

Indications

Lung transplantation is an established therapy for end-stage lung disease. To be considered for listing, a patient should have end-stage lung disease, a >50% mortality risk within 2 years, a >80% chance of survival for 90 days after transplantation and a >80% chance of survival for more than 5 years with preserved graft function. Lung transplantation itself poses risks for morbidity and mortality, so only those with a high risk for disease related mortality should be considered. Criteria for listing for lung transplantation according to the 2014 ISHLT update consensus document for the selection of lung transplant candidates are summarized below:

Table 1
Criteria for listing for lung transplantation for different underlying lung pathologies

Obstructive diseases	BODE index ≥7
	FEV1 <15%–20% of predicted
	Three or more severe exacerbations in the past year
	Moderate to severe pulmonary hypertension
	One severe exacerbation with acute hypercapnic respiratory failure
Suppurative diseases	Chronic respiratory failure ($Paco_2$ >50 mm Hg, Pao_2 <60 mm Hg, or a combination of the two)
	Need for noninvasive ventilation
	Pulmonary hypertension
	Frequent hospitalizations
	Rapid decline in lung function
	World Health Organization functional status IV
Interstitial diseases	≥10% decline in FVC at 6 mo of follow-up
	≥15% decline in DLCO at 6 mo of follow-up
	Desaturation <88%, 6MWD <250 m, or a >50-m decline in the 6MWD at 6-mo follow-up
	Pulmonary hypertension
	Hospitalization because of functional deterioration, pneumothorax, or acute exacerbation
Vascular diseases	NYHA class III or IV despite optimal therapy (including prostanoids)
	Cardiac index <2 L/min/m^2
	Mean right atrial pressure >15 mm Hg
	6MWD <350 m
	Hemoptysis, pericardial effusion, or signs of right heart failure

Abbreviations: 6MWD, 6-minute walking distance; BODE, body mass index, airflow obstruction, dyspnea, exercise capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NYHA, New York heart association; $PaCO_2$, partial pressure of CO_2 in arterial blood; PaO_2, partial pressure of O_2 in arterial blood. Data from Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014—an update from the pulmonary transplantation council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2015;34(1):1–15.

The lung allocation score (LAS) has changed the landscape of lung transplantation since its inception in 2005. Simply put the LAS is an algorithmic calculation of risk based on pre-transplantation waiting list urgency versus post-transplant survival. The year after the introduction of the LAS, the number of deaths on the waiting list dropped 40%, from more than 500 per year previously. Below is a table listing the definitions and formulas used in the LAS:

LAS components	Definition or formula
Waiting list urgency measure	= Expected number of days lived without a transplant during an additional year on the waiting list (area under the 1-year waiting list survival curve)
Posttransplant survival measure	= Expected number of days lived during the first year following transplantation (area under the 1-year posttransplant survival curve)
Transplant benefit	= Posttransplant survival measure − waiting list urgency measure, i.e. the number of expected additional days of life over the next year if a particular candidate received a transplant rather than remaining on the waiting list
Raw allocation score	= Transplant benefit measure − waiting list urgency measure = (posttransplant survival measure − waiting list urgency measure) − waiting list urgency measure = posttransplant survival measure − 2× (waiting list urgency measure)
Normalized lung allocation score	= 100 × (raw score + 2 × 365)/3 × 365

The possible range of values for the raw allocation score would be from +365 to −730 (the two extremes of 100% survival posttransplant but dying today without a transplant to a 100% chance of living for a year on the waiting list but a 100% probability of dying before the first day after a transplant). Because the Lung Allocation Subcommittee felt that negative allocation scores would be difficult to understand, it was decided to 'normalize' the score and produce a range from 0 to 100 according to the following formula:100 °x (raw score + 2 °x 365)/3 °x 365

Importantly, a list of absolute and relative contraindications exists to guide clinicians who not to list for transplant particularly in fledgling programs.

Box 1
Contraindications (absolute and relative) to lung transplantation

Absolute Contraindications

- Recent malignancy (5-year disease-free period for any major malignancy)
- Untreatable major organ dysfunction not paired with another transplant
- Uncorrected atherosclerotic disease with end-organ dysfunction and CAD not amenable to revascularization
- Acute medical instability (eg, sepsis, myocardial infarction, liver failure)
- Uncorrectable bleeding diathesis
- Chronic infection with highly virulent and/or resistant microbe that is poorly controlled pretransplant
- Mycobacterium tuberculosis infection
- Significant chest was deformity expected to cause severe restriction
- BMI ≥35
- Current or prolonged past medical non-adherence
- Psychiatric or psychological condition that results in an inability to cooperate with medical care
- Absence of an adequate social support system
- Severely limited functional status with poor rehab potential

Relative Contraindications

- Age >65 with low physiologic reserve and age >75 is unlikely to be successful
- BMI 30 to 35
- Progressive or severe malnutrition
- Severe, symptomatic osteoporosis
- Extensive prior chest surgery
- Mechanical ventilation or mechanical circulatory support
- Colonization or infection with highly resistant microbes
- HIV outside of experienced centers or with poorly controlled disease
- Other medical conditions that can be optimized should be before listing (eg, diabetes mellitus, epilepsy, gastroesophageal reflux)

Abbreviations: BMI, body mass index; CAD, coronary artery disease; HIV, human immunodeficiency virus.

Data from Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014—an update from the pulmonary transplantation council of the international society for heart and lung transplantation. J Heart Lung Transplant 2015;34(1):1–15.

Pre-operative considerations

Pre-operative assessment

The evaluation of a lung transplant candidate is performed by a multidisciplinary team and involves pulmonologists, thoracic surgeons, infectious disease specialists, nurses, nutritionists,

physiotherapists, psychologists, and social workers. In terms of pre-operative workup, the table below summarizes the list of investigations required.

Table 2
Standard evaluation for lung transplant candidates

Pulmonary evaluation	Pulmonary function testing Arterial blood gas on room air Chest radiography 6-min walk distance test Noncontrast computed tomography scan Quantitative ventilation and perfusion scan Fluoroscopy of the diaphragms
Cardiac evaluation	Electrocardiogram Right heart catheterization Echocardiogram with bubble study Left heart catheterization for age >40 or computed tomography coronary angiography for age >40 Cardiac MRI (for patients with lung sarcoidosis)
Gastrointestinal evaluation	Barium swallow 24-h pH probe testing Esophageal manometry Solid gastric emptying (if concern for gastroparesis) Liver ultrasound (age <55) Liver computed tomography scan (age >55)
Laboratory testing	Routine hematologic, chemistry and coagulation studies Viral serologies for the following: Cytomegalovirus Herpes simplex virus Epstein- Barr virus Varicella zoster virus Hepatitis B, C Human immunodeficiency virus Flow cytometry for HLA antibodies

Abbreviation: HLA, human leukocyte antigen.
Data from Gray AL, Mulvihill MS, Hartwig MG. Lung transplantation at Duke. J Thorac Dis 2016;8(3):E185–96.

Special considerations

Right ventricular function and the presence of pulmonary hypertension, most often pre-capillary (mean pulmonary artery pressure 25 mmHg and pulmonary artery wedge pressure 15 mmHg), warrant particular attention. Patients with idiopathic pulmonary artery hypertension, other indications for lung transplantation associated with severe pulmonary hypertension (e.g. pulmonary veno-occlusive disease, pulmonary fibrosis), or secondary pulmonary hypertension associated with right ventricular dysfunction poorly tolerate hypoxemia, hypercapnia, haemodynamic instability associated with surgical manipulation, and pulmonary artery clamping requiring proactive inotropic and vasopressor support, or elective or emergent deployment of extracorporeal mechanical circulatory support.

Patients with CF present with comorbidities specific to the underlying disease. They are more likely to have had prior thoracic procedures, such as pleurodesis for pneumothoraces, which will increase the complexity of the recipient pneumonectomy and increase the likelihood of pleural bleeding. They are also likely to be colonized with pan-resistant Pseudomonas aeruginosa, different species of Burkholderia, fungal pathogens (e.g. Aspergillus fumigatus), and nontuberculous Mycobacteria. The impact of pretransplant colonization on lung transplant outcome may result in increased peri-operative morbidity and may require more aggressive, or alternative antibiotic regimens targeted at preventing early infection. Gastrointestinal comorbidities include liver dysfunction, pancreatic exocrine insufficiency, and malnutrition. Patients with liver dysfunction limited to cholestasis are at low risk for perioperative liver decompensation; however, patients with cirrhosis may be considered unsuitable for isolated lung transplantation. The most common comorbidity associated with CF is diabetes, which occurs in 20% of adolescents and 40% to 50% of the adults.

Older patients are now being transplanted for chronic obstructive pulmonary disease (COPD), idiopathic interstitial pneumonia, and other indications, with many centres performing lung transplants on patients beyond the age of 70. Older recipients are more likely to have other comorbidities, such as coronary artery disease and osteoporosis, due to the presence of other risk factors, such as history of smoking, chronic steroid use, and vitamin D deficiency. If significant cardiac disease warrants intervention, pretransplant percutaneous coronary revascularization via stenting is preferred; however, concurrent surgical revascularization with lung transplantation can be considered for selected patients (e.g. high functional status, age <65 years).

Pre-induction

Communication with the surgical, perfusion, and nursing teams should alert them to the potential for hemodynamic instability during induction and should establish plans for deployment of cardiopulmonary bypass (CPB) or extracorporeal membrane oxygenation (ECMO) at any time during the procedure. This is extremely important, and a good cohesive team approach is fundamental to the success of any lung transplant program.

Sedation outside of the operating room, if needed, should be provided with great caution, as it may precipitate hypoxemia, hypercarbia, increase in pulmonary vascular resistance, right ventricular failure, and cardiorespiratory arrest. We establish arterial and large-bore peripheral venous access before induction with minimal or no sedation but with generous administration of local anesthetic and good counseling of the patients.

The immunosuppression and antibiotic regimen should be reviewed with the team. Standard immunosuppression regimen around the period of induction consists of the following, however, this varies from institution to institution.

1. Tacrolimus 1 mg sublingual (or 0.5 mg for patients older than 65 years) before transplantation at the time the donor lungs are deemed acceptable and the decision to proceed with transplant has been made
2. Basiliximab 20 mg administered intraoperatively
3. Mycophenolate mofetil 1000 mg administered intraoperatively
4. Solumedrol 500 mg IV on induction

At this stage, under strict sterile conditions, we will site a thoracic epidural at level T7-8 and administer a test dose of 3 mls of 2% Lignocaine. We would endeavor to use the epidural mainly for post-operative analgesia and particularly once the patient is extubated in order to facilitate early mobilization.

Standard prophylactic antibiotics will vary from patient to patient depending on the flora they are colonized with, but this would be done in close consultation with the transplant pulmonologist in charge.

Induction

Induction of anesthesia is one of the most critical periods. Most patients will have elevated pulmonary artery pressure, preexisting right ventricular dysfunction, and hypercapnia at baseline. Cardiovascular collapse on induction, especially in patients with limited cardiorespiratory reserve can result from hypoxia, hypercapnia, decreased endogenous sympathetic drive, institution of positive pressure ventilation resulting in further increase in right ventricular afterload, and hypotension due to systemic vasodilation or myocardial depression. Irrespective of the induction agents used, should be titrated judiciously.

Emphasis should be placed on a thorough airway examination and contingency plans for intubation, as these patients will not tolerate prolonged periods of apnea resulting from difficult intubation. We prefer placing a left-sided double lumen tube (DLT) for all cases, as the position of the bronchial lumen will not interfere with the surgical access to the left main stem and performing the left-sided bronchial anastomosis, irrespective of the type of the procedure performed (single or double-lung transplantation). Central line and a pulmonary artery catheter are typically placed after induction. Transoesophageal echocardiography (TOE/ TEE) probe for intraoperative TOE monitoring is performed in all cases. We would also advise a second arterial line in the left femoral artery, if possible, to ensure adequate monitoring of blood pressure especially if the patient comes off on veno-arterial ECMO.

Surgical aspects and Maintenance of Anaesthesia

During the surgical dissection, a particular challenge is the management of OLV of the diseased lungs. OLV may not only lead to hypoxia, but also to hypercapnia and acidosis with further increase in pulmonary vascular resistance and spiraling right ventricular failure and hemodynamic instability. Some of the recommendations for OLV are as follows:

1. Tidal volumes of 4-6mls/ kg of ideal body weight
2. Titrate PEEP to best compliance e.g. 3-10 cmH_2O
3. Target Plat < 30cmH_2O or driving pressure < 14 cmH_2O

Although implementing these recommendations is desirable, underlying pathology in the recipient lungs will impact OLV management. Challenges associated with each pathology and management strategies to overcome them are listed in the table below:

Table 3
Challenges and intraoperative management strategies for different underlying lung pathologies

Recipient Pathology	Intraoperative Complications	Management Strategies
Obstructive (COPD, BOS)	• Dynamic hyperinflation • Tension pneumothorax	• Use pressure control ventilation to minimize dynamic hyperinflation • Maximum exhalation time (I:E = 1:3–1:4) to minimize auto- PEEP • Check for auto-PEEP: interrupted inspiratory flow on the flow-volume curve • No or low extrinsic PEEP (3–4 cm H_2O)
Suppurative (cystic fibrosis, bronchiectasis)	• Thick, profuse secretions • Severe hypercapnia • Difficult dissection due to prior thoracic procedures	• Initial SLT intubation for BAL and suctioning • May require higher airway pressures • May require higher level of PEEP • Frequent suctioning
Restrictive (pulmonary fibrosis, hypersensitivity pneumonia)	• Severe pulmonary hypertension • May not tolerate OLV	• May need high peak inspiratory pressures (40 cm H_2O) • Maximize inspiratory time (I:E = 1:1–1:2) • Higher extrinsic PEEP (8–10 cm H_2O)
Primary pulmonary hypertension	• Severe hemodynamic instability due to right ventricular failure	• Central venous access before induction • Inotropic/vasopressor/inhaled pulmonary vasodilators on induction • Continue perioperative intravenous prostaglandins • Prepare for extracorporeal mechanical circulatory support

Maintenance of anaesthesia can be achieved with inhalational agents, propofol infusion, or both. Dose-dependent inhibition of hypoxic pulmonary vasoconstriction is well documented with older inhaled anaesthetics (e.g. halothane), but it has not been shown to occur with newer agents at less than 1 minimum alveolar concentration. A recent systematic review of randomized controlled trials of intravenous (e.g. propofol) versus inhalational (e.g. isoflurane, sevoflurane, desflurane) anaesthesia in patients undergoing OLV found that very little evidence is available to show differences in outcomes. However, end-stage lung disease and pneumonectomy of the native lungs may impact the uptake of inhaled agents, making total intravenous anesthesia more reliable. Irrespective of the anesthetic drug used, adequate depth of anesthesia should be monitored, as these patients are at increased risk of intraoperative awareness.

Although many donor and recipient characteristics determine which side is transplanted first during BOLT, generally the side that receives less perfusion is first transplanted. For the pneumonectomy of the native lung, the pulmonary vessels are divided first followed by the bronchus. The bronchial lumen of the DLT should be positioned comfortably away from the division line to avoid damage of the bronchial cuff. Clamping of right pulmonary artery of the operative lung may improve oxygenation by removing intrapulmonary shunt, but it will also divert the entire cardiac output to the contralateral lung with predictable increase of pulmonary artery pressures. This rapid increase in right ventricular afterload will be tolerated well in patients with mild pulmonary hypertension. Pre-emptive haemodynamic optimization with inotropes/vasopressors and pulmonary vasodilators before clamping of the pulmonary artery and continued efforts to reduce pulmonary vascular resistance and maintain right ventricular perfusion pressure and contractility after clamping may avoid institution of mechanical extracorporeal support. At this point continued monitoring by TOE of right ventricular function, severity of tricuspid regurgitation and pulmonary artery pressures from the PAC can provide clues into adjusting management strategies.

The implantation of the transplanted lung is conducted sequentially beginning with the most posterior structure, the bronchial anastomosis. The pulmonary artery anastomosis is fashioned next, followed by the left atrial anastomosis of the donor upper and lower pulmonary veins surrounded by a cuff of donor atrium to the recipient atrium. Surgical exposure and access to the atrium and hilum

necessitates retraction, resulting in arrhythmias and hypotension, and constant communication between the surgeon and the anesthesiologist is crucial. Before finishing the anterior aspect of the left atrial anastomosis, the left atrial clamp is removed to allow de-airing of the graft and removal of the remaining pneumoplegia. The pulmonary artery is unclamped slowly over 10 to 15 minutes, allowing controlled low-pressure perfusion of the transplanted lung. Ventilation of the transplanted lung is initiated during this time, initially by hand, with a low FiO_2 (less than 30%) and then by mechanical ventilation. A gentle Valsalva maneuver may allow for alveolar recruitment and expansion of the allograft. Severe hypotension may occur with reperfusion of the lung due to possible blood loss through leaks in the vascular anastomosis, wash-out of ischemic metabolites, and pneumoplegia from the allograft, or air entrained in the coronary arteries, most commonly the right coronary artery. Once the last anastomosis is completed, a second dose of Solumedrol 500 mg IV is given just before the clamp is released.

Ventilation strategies for the transplanted lungs

Primary graft dysfunction (PGD) after lung transplantation occurs in the early period following reperfusion of the allograft with an incidence ranging from 10-57%. The ISHLT criteria for diagnosing PGD is summarized below:

Table 4
The International Society for Heart and Lung Transplantation primary graft dysfunction definition and grading

Grade	Pao_2/Fio_2	Radiographic Infiltrates
0	>300	Absent
1	>300	Present
2	200–300	Present
3	<200	Present

Severe PGD (grade 3) is both a risk factor for early mortality following lung transplantation and for the development of bronchiolitis obliterans syndrome, one of the late complications following lung transplantation. PGD is clinically and histopathologically similar to ARDS with diffuse pulmonary infiltrates and high oxygen requirements in the first 72 hours following transplantation. Risk factors include the following:

Donor related

- Age > 45 yr or < 21 yr
- Female gender
- Smoking > 10 pack years
- Head trauma
- Prolonged mechanical ventilation

Recipient related

- Female gender
- BMI > 25
- Elevated pulmonary artery pressures at the time of induction

Operative factors

- Prolonged ischaemic time
- Use of CPB
- Use of blood products
- Single lung transplant

Management of mechanical ventilation immediately after lung transplantation is an opportunity to reduce incidence of PGD and influence short-term and long-term outcome of lung transplant recipients. Lung protective strategies with low tidal volumes (6 mL/kg ideal body weight) have been shown to benefit not only patients with ARDS but also patients at risk for ARDS surgical patients undergoing short periods of intraoperative mechanical ventilation and donor management for trans-plantation. Although not directly studied in lung transplant recipients, principles of lung protective mechanical ventilation are easily generalizable to those patients who have multiple respiratory

impairments:

1. Fresh thoracotomy wound
2. Phrenic and pleural dysfunction
3. Allograft airway mucosa and bronchial anastomosis at risk for ischemia and poor healing
4. Ischemia-reperfusion injury of the allograft

A unique aspect to lung transplantation is the situation of lungs undersized to the recipient thoracic cavity size. In this case, ventilation with tidal volumes calculated based on recipient characteristics will lead to higher tidal volumes when compared with matched or oversized allografts. There is a growing body of evidence that undersized allografts are associated with increased rates of PGD, tracheostomy, resource utilization, and risk of first-year mortality. Whether over-inflation of the undersized graft is associated with higher rates of PGD is unclear and calls more for more research in this area. In a recent international survey of practices of mechanical ventilation immediately after lung transplantation, 65% of the responders answered that they did not consider donor characteristics when setting the ventilator, and more than half (58%) answered that the team managing the ventilator did not have this information. Several studies have shown a strong association between an increased FiO_2 at reperfusion and higher incidence of PGD. The lowest FiO_2 (preferably <30%) should be used to maintain an appropriate partial pressure of oxygen in the arterial blood (70 mmHg).

Box 2
Recommendations for intraoperative mechanical ventilation of the transplanted lungs

- Tidal volume of 6 mL/kg IBW. Adjust for OLV, if needed. Consider using donor body weight if the allograft is undersized
- PEEP 6 to 8 cm H_2O
- PIP less than 30 cm H_2O
- Careful recruitment maneuvers
- Lowest Fio_2 to maintain $Pao_2 \geq 70$ mm Hg
- Normocapnia or low levels of permissive hypercapnia (if it allows for low Vt and not associated with acidosis)
- Bronchoscopic airway clearance

Abbreviations: Fio_2, fraction of inspired oxygen; IBW, ideal body weight; OLV, one-lung ventilation; Pao_2, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure; PIP, peak inspiratory airway pressure; Vt, tidal volume.
Adapted from Barnes L, Reed RM, Parekh KR, et al. Mechanical ventilation for the lung transplant recipient. Curr Pulmonol Rep 2015;4(2):92; with permission.

Controversies in the peri-operative management of lung transplantation

Inhaled pulmonary vasodilators after lung transplantation

iNO (inhaled nitric oxide) in the range of 10 to 40 ppm is a staple in the management of patients undergoing lung transplantation for providing pulmonary vasodilation selectively in the ventilated regions of the lung leading to improved ventilation-perfusion match and oxygenation. iNO may also modulate aspects of inflammation, oxidative stress, permeability, and coagulation. Beyond the haemodynamic effects, iNO may mitigate acute lung injury in the transplanted lung by decreasing the hydrostatic forces associated with reperfusion and protecting the allograft from inflammatory insults and apoptosis. Pulmonary reperfusion-ischemia injury is a complex process thought to be initiated by hypoxemia of the endothelial cells and reperfusion stress, ultimately leading to endothelial activation and dysfunction, dysregulation of pulmonary vasoreactivity, platelet aggregation, apoptosis and impaired gaseous exchange. Preclinical studies have shown that iNO may have strong effects on the pathways involved in the pathogenesis of lung ischaemia-reperfusion injury. Clinical studies, however, have shown little evidence to support this hypothesis. The inability to translate the preclinical data into the clinical setting may be due to genetic signaling related to the injury and subsequent PGD already triggered at the donor and cold ischaemia phase. However, consensus exists regarding the use of iNO for haemodynamic and oxygenation management in lung transplantation and more importantly, to avoid the need for CPB, which is a modifiable risk factor associated with the development of PGD.

Transoesophageal echocardiography in lung transplantation

Transesophageal echocardiography has become part of routine monitoring and has well-defined application during all stages of procedure (pre-transplantation, intra-transplantation, and post-transplantation), as well as in the immediate postoperative period in the intensive care unit.

Considering that lung transplantation recipients experience variable times awaiting transplantation, TOE should confirm findings of the preoperative workup regarding ventricular function and valvular lesions, especially with respect to right ventricular function and tricuspid regurgitation. TOE also should evaluate the presence of intra-cardiac shunts (e.g. patent foramen ovale, atrial septal defect) which may warrant surgical closure at the time of transplantation. At all times during lung transplantation, TOE can differentiate among different causes of haemodynamic instability, such as right ventricular failure, hypovolemia, myocardial ischemia with wall motion abnormalities, or pulmonary tamponade in cases of severe emphysema and lung hyperinflation (Fig. 1). After transplantation, TOE can assist with de-airing manoeuvres and assessment of the vascular anastomotic sites. Because intra-operatively PGD is a diagnosis of exclusion, it is important to rule out problems involving vascular anastomosis such as stenosis, torsion, or thrombosis as a cause for hypoxaemia.

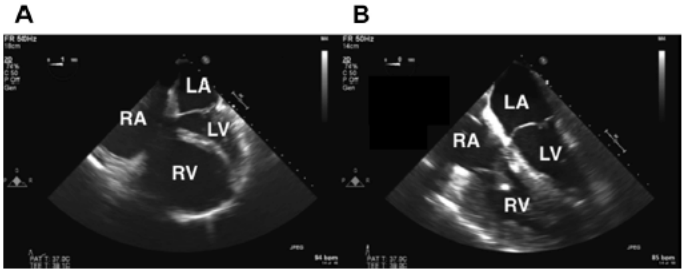

Fig. 1. Midesophageal 4-chamber view shows a severely dilated right ventricle (RV) with shift of the interventricular septum toward the left impinging on the left ventricle (LV) and likely impeding adequate filling and function (*A*) in a patient with severe pulmonary hypertension. (*B*) The same echocardiographic view after lung transplantation showing a hypertrophied, dilated RV but with a midline positioned interventricular septum. LA, left atrium; RA, right atrium.

Criteria exist to evaluate velocities through the pulmonary veins and generally, velocities of <1 m/s peak systolic flow are considered acceptable. Below are some images of the pulmonary venous structures and colour flow to illustrate flow velocities.

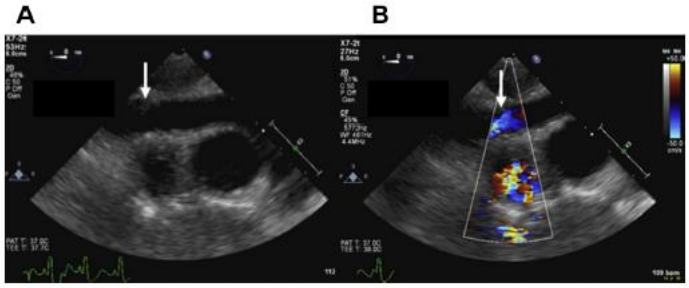

Fig. 2. Midesophageal ascending aorta short axis view with the probe turned toward the right showing (*A*) the right pulmonary artery and (*B*) with color flow Doppler. The arrow marks the most likely area of anastomosis.

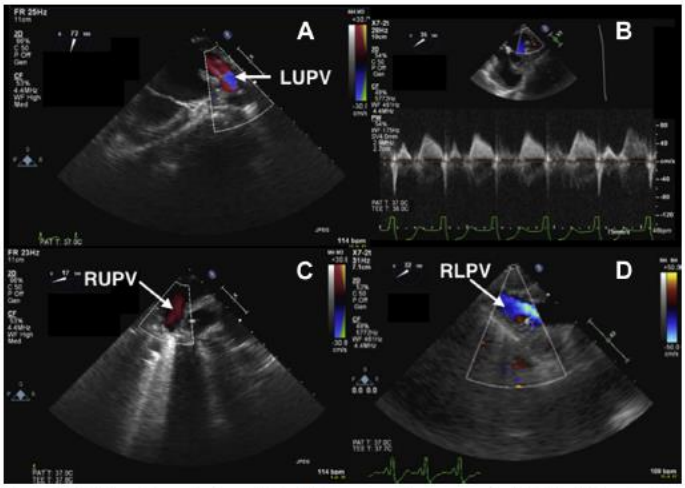

Fig. 3. (*A*) Midesophageal view of the left upper pulmonary vein (LUPV) with color flow Doppler. (*B*) Pulsed-wave Doppler of the LUPV, displaying peak velocities less than 80 cm/s. (*C*) Midesophageal view of the right upper pulmonary vein (RUPV) with color flow Doppler. (*D*) Midesophageal view of the right lower pulmonary vein (RLPV) with color flow Doppler.

Fluid management during lung transplantation

One of the pathophysiological mechanisms of PGD is alveolar decreased fluid clearance due to lymphatic drainage disruption. It is very likely, therefore, that the newly transplanted lungs are sensitive to large volume fluid administration and there is a growing body of literature that intraoperative administration of fluid is a modifiable risk factor for PGD. Geube and colleagues showed that increased intraoperative fluid volume is associated with the most severe form of PGD. In their retrospective study on a cohort of almost 500 patients, the most severe form of PGD (grade 3 PGD) occurred in 25% of patients. Each additional liter of intraoperative fluid was associated with increased odds for grade 3 PGD by approximately 22%. Patients who developed grade 3 PGD also received larger volumes of red blood cell concentrate than patients who did not develop PGD (1.1 vs 0.4, adjusted odds ratio 1.7; 95% confidence interval 1.08–2.7; P 5 .002). There was no association between non-blood components of fluid therapy (colloids and crystalloids) and grade 3 PGD. Similar findings were reported by the Lung Transplant Outcomes Group: transfusing more than 1 L of red blood cell concentrate was associated with a twofold increase in the incidence of PGD. The ISHLT cautiously recommends the correction of fluid losses while optimizing haemoglobin and coagulation status.

Other anaesthetic considerations

At the end of the procedure, the DLT must be exchanged for a single-lumen endotracheal tube and a bronchoscopy is performed to inspect the anastomoses and clear secretions. As lung transplantations tend to be lengthy procedures, the stomach should be emptied of gastric secretions with the aid of an orogastric tube before the tube exchange. The exchange should be performed under direct or video-laryngoscopic vision using a soft-tipped exchange catheter, as the airway is likely to be edematous at the end of the procedure. Inability to reintubate the patient and loss of airway may have disastrous consequences.

Role of extracorporeal mechanical support in lung transplantation

Extracorporeal mechanical circulatory support, either CPB or ECMO, is required in up to 30% to 40% of lung transplant procedures. Intraoperatively, it allows for haemodynamic stability and a larger degree of flexibility in surgical manipulation while performing the surgical anastomoses. These benefits are not without costs. In a recent prospective, multicenter cohort study by the Lung Transplant Outcomes Group, the use of CPB has been associated with a threefold increase in the incidence of PGD, although it was not possible to differentiate between planned or emergent institution of CPB for deteriorating hemodynamics and oxygenation. No randomized trials regarding the use of CPB exist, and in a recent review of the topic, including retrospective analyses and cohort studies, some studies showed significant disadvantages to the use of CPB, some showed no difference, and others showed both, depending on the postoperative outcome assessed. A growing body of evidence suggests that veno-arterial ECMO may be preferable to CPB if mechanical circulatory support is needed. Relative to CPB, ECMO is associated with fewer transfusions, fewer reoperations, less PGD, decreased rates of renal complications, shorter intensive care unit stays, and shorter hospital length of stay. Other benefits of ECMO are lower required heparin dose, less blood air interface with less inflammatory response, and the ability to convert to postoperative support.

Veno-venous ECMO (VV ECMO) can be used as a bridge to lung transplantation with comparable short-term and midterm outcomes, especially in highly experienced centers. Newer cannulation strategies with dual-lumen single cannula allow for ambulatory VV ECMO with patients being able to participate in physical therapy and rehabilitation before transplantation.

Patients with severe forms of PGD after lung transplantation and who are on maximal ventilator support (peak inspiratory pressures 30 cmH_2O, $FiO_2 > 0.6$) should be considered for VV ECMO. VV ECMO should be instituted within 24 hours of onset of severe PGD and the patients can be transitioned back to lung protective ventilator strategies and FiO_2 of 0.21.

Ex vivo lung perfusion (EVLP)

Normothermic EVLP is a technique used to preserve and treat questionable organs for transplantation. The concept of normothermic perfusion of organs for preservation, as opposed to static hypothermic flush preservation is not new, originally pioneered by Charles Lindbergh (and

others) in 1935. However, only recently has technology advanced sufficiently for the technique to become clinically useful. Several different EVLP systems are currently available, and their technical specifications and indications are beyond the scope of this chapter. Research and clinical trials are currently underway to delineate the role of EVLP in lung transplantation. Below is an example of such a system in action.

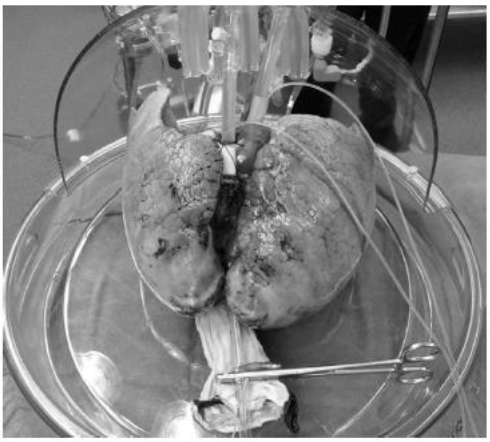

Figure 3 – *Photo depicting the early stages of ex vivo lung perfusion. After the acellular perfusate is pumped through the pulmonary artery (yellow) and out through the left atrium (green), the lungs are warmed to 32°C, the endotracheal tube is unclamped, and protective ventilation is begun. (Reprinted with permission from Perfusix USA, Inc.)*

Post-operative management

These patients are generally transferred to the ICU ventilated for +/-24hrs following the procedure. The ICU management is a continuum of the peri-operative care and is managed by the same team headed by the transplant pulmonologist. Routine ICU care including monitoring for PGD is the mainstay of care for these patients. Once the patients are eligible for extubation, the epidural is established for optimal analgesia and all systemic analgesics are discontinued. Strict infection control precautions need to be adhered to in order to ensure that these patients are not at increased risk of nosocomial infections. Immunosuppression is also escalated at this stage to ensure adequate graft protection.

Summary

Lung transplantation is a continuously evolving field with unique surgical and medical aspects. The perioperative management of the patients undergoing lung transplantation is challenging and requires constant communication among the surgical, anaesthesia, perfusion, and nursing teams. Although all aspects of the anaesthetic management are important, certain intraoperative strategies (mechanical ventilation, fluid management, extracorporeal mechanical support deployment) have tremendous impact on the subsequent evolution of the lung transplant recipient, especially with respect to allograft function and should be carefully considered.

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Pulmonary Hypertension

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Driving questions:

1. "What happens to the right ventricle when the left ventricle is broken?"
2. "What happens to the right ventricle when the lungs are broken?"
3. "How do we look after the lungs when they are broken?"
4. "How do we look after the right ventricle when it is broken?"

The right ventricle (RV) receives blood from the venae cavae and coronary circulation, and pumps it via the low-pressure pulmonary vasculature into the left ventricle (LV). Since the pulmonary vascular resistance (PVR) is a fraction of the systemic vascular resistance (SVR), the pulmonary arterial pressure (PAP) is relatively low and the wall thickness of the right ventricle (RV) is much less than that of the LV. In the patient with normal PAP, the RV thus resembles more of a passive conduit rather than a pump. Coronary perfusion to the RV occurs continuously during systole and diastole because of the low intraventricular and intramural pressures. Because of its thin myocardial wall, the RV is very compliant and can deal reasonably well with an acute increase in preload. The RV can however not cope with an acute increase in afterload, like that experienced in acute ARDS or acute Pulmonary Embolism.

The preload of the normal RV will be represented by the right atrial pressure (RAP), and therefore assessed by the central venous pressure (CVP). Normal will be anything between 4 mmHg – 12 mmHg. Of course compliance is crucial and this pressure-volume relationship is not linear in the diseased RV.

The pulmonary vascular resistance (PVR) may be calculated as an index of RV afterload, using mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure and cardiac output (CO):

$$\text{PVR} = \frac{\text{MPAP} - \text{PCWP}}{\text{CO}} \times 80 \text{ dynes.s cm}^{-5}$$

The normal PVR ranges from 90 to 150 dynes.s cm^{-5}.
CO, PAP and PCWP have to be obtained with a Pulmonary Artery Catheter (PAC) to calculate SVR and PVR.
Right ventricular stroke work index (RVSWI):

$$\text{RVSWI} = \frac{(\text{MPAP} - \text{CVP}) \times \text{SI}}{100} \times 1.36 \text{ g.m m}^{-2}$$

Normal values for RVSWI are 5–10 g.m m^{-2}.

The right ventricle plays an important role in the morbidity and mortality of patients presenting with signs and symptoms of cardiopulmonary disease. The cardiac and pulmonary systems are operating in series, but also next to each other, and pathology of the one system has a profound effect on the other. Even subtle disruption of this interventricular interaction will affect patient haemodynamics. During the perioperative period there are surgical and anaesthetic influences affecting both cardiac and pulmonary systems e.g. after lung resection there may be an acute increase in right ventricular afterload, which is not always well tolerated by this thin-walled, low-pressure chamber. This will also affect the left ventricle and compromise cardiac function, especially when the pulmonary system is mismanaged postoperatively. The principles of cardiopulmonary interaction and interventricular interdependence are crucial when dealing with the patient with Pulmonary Hypertension (PHT).

Hypoxic pulmonary vasoconstriction in the extra-alveolar pulmonary arterioles supplying the unventilated lung is an essential normal physiological response to alveolar hypoxia in poorly ventilated alveoli. This is the safety mechanism of the body to minimize shunt and hence hypoxaemia. This effect occurs when there is a reduction in alveolar partial pressure of oxygen to between 4 and 8 kPa. Poor alveolar ventilation will therefore increase the PAP and thus the afterload of the RV. Pulmonary and right ventricular haemodynamics remain unaffected by slight hypocarbia. In contrast, hypercarbia increases pulmonary vascular resistance and mean pulmonary artery pressure. This is accompanied by an increase in right ventricular end-diastolic volume, an increase in right ventricular end-systolic pressure, and a decrease in right ventricular ejection fraction. Despite an increase in right ventricular afterload, stroke volume is usually maintained because of an increase in right ventricular stroke work index due to the Starling mechanism in the healthy heart. Although patients maintain pulmonary blood flow during hypercarbia using preload augmentation, compensatory reserve might be exceeded in patients with a compromised right ventricular function.

The PAP and therefore RV afterload may also be affected by ventilator strategies in theatre and the ICU. Positive pressure ventilation with high airway pressures and high PEEP (more than 10 mmHg) will increase afterload and may compromise the delicate RV.

PHT is defined as an increase in mean pulmonary arterial pressure (mPAP) to ≥25 mmHg at rest as assessed by right heart catheterisation (Galie).

PHT severity can be quantified as:

Mild = mPAP 25-40 mmHg
Moderate = mPAP 40-55 mmHg
Severe = mPAP > 55mmHg

Untreated the morbidity and mortality of PHT is high. Therefore its accurate and prompt diagnosis is crucial (Augustine). The diagnosis of PHT requires a clinical suspicion based on symptoms, physical examination and review of a comprehensive set of investigations. Echocardiography is a key imaging modality in the assessment of patients with suspected or known PHT. PHT often complicates patient care in surgical and medical intensive care units. Severe acute pulmonary hypertension may produce right ventricular (RV) failure. PHT and RV failure may reduce left ventricular (LV) filling, decrease cardiac output, and lead to systemic hypotension and hemodynamic instability. Decreased arterial blood pressure will compromise RV coronary perfusion at a time when RV end-diastolic pressures and RV myocardial oxygen consumption are increased as a result of increased RV wall tension, thereby leading to RV ischemia. RV ischemia will exacerbate RV failure, causing a further reduction in cardiac output and blood pressure. This vicious cycle may continue unless the PAP is reduced, permitting an increased RV ejection fraction.

The classification of PHT categorizes different clinical conditions into five groups (Augustine) (Table 1).

There is an important difference between pulmonary venous PHT and pulmonary arterial PHT.

The most common form of PHT encountered in any echocardiography department will be secondary to left heart disease. Each of these groups can further be categorized as to whether there is normal pulmonary capillary wedge pressure (estimate of left atrial pressure) or elevated pulmonary capillary wedge pressure, which may be helpful in identifying the aetiology of PHT.

We must clearly distinguish between pulmonary venous PHT and pulmonary arterial PHT

WHO group	Aetiology of PHT	Mean pulmonary capillary wedge pressure	Example causes
1	Pulmonary arterial hypertension	Normal	Idiopathic, hereditary, drug or toxin induced, shunts related to congenital heart disease, connective tissue disease, portal hypertension, chronic haemolytic anaemia
2	PHT secondary to left heart disease	Increased	Valvular heart disease, systolic dysfunction, diastolic dysfunction, pericardial disease, congenital/acquired left heart inflow/outflow tract obstruction, congenital cardiomyopathies
3	PHT secondary to lung disease	Normal	Chronic obstructive pulmonary disease, severe asthma, interstitial lung disease, sleep apnoea, long term exposure to high altitude, congenital lung abnormalities
4	Chronic thromboembolic PHT (CTEPH)	Normal	Chronic pulmonary embolism
5	PHT with unclear and/ or multifactorial mechanisms	Normal or increased	Systemic diseases, sarcoidosis, vasculitis, haematological malignancies, chronic renal failure, metabolic disorders, lung tumours

Table 1: WHO Classification of PHT (Simonneau).

Hemodynamic assessment plays a crucial role when managing the critically ill and unstable patient with PHT. For the past 40 years the pulmonary artery catheter (PAC) has been the mainstay of haemodynamic monitoring in the critically ill patient, and the patient at risk of complications from haemodynamic changes. Although it was initially used to measure intracardiac pressures, the addition of cardiac output measurement by thermodilution, and the ability to measure the mixed venous blood gasses, have added value to this important monitor. The user must distinguish between indices directly measured (right atrial pressure, right ventricular pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output, etc.) and those indices derived and calculated from the measured parameters (e.g. stroke volume, stroke work index, and vascular resistances). One should never ignore the oxygen delivery parameters (mixed venous oxygen content, oxygen delivery, oxygen consumption, etc.). In response to the information obtained, the clinician may perform certain haemodynamic manipulations. Even when a PA catheter is not used, the effects of having previously learned from its use will influence a clinician's judgement in subsequent patient management. A good example of this goal-directed therapy was the guidelines described by Shoemaker in the early eighties. The problem is that the sicker the patient, often the more unreliable

the information obtained from the PA catheter. Although there was a general belief under critical care clinicians that this tool improves patient outcome, this has never been proven in a scientific way. There is a huge variability of clinician experience and PA catheter knowledge. The inappropriate placement of a PA catheter by an inexperienced clinician may cause harm, and also injudicious choice of therapy with disastrous consequences. Numerous societies and groups like the ASA Task Force (ASA Task Force), PA catheter Consensus Conference (PAC Consensus Conference), and the European Society of Intensive Care Medicine Expert Panel (Bennett), have over the years provided guidelines and qualified support to continue the use of the PA catheter in selected cases. The "UK PA Catheters in Patient Management Trial" (PAC-man) has provided interested information and lead to a decrease in the use of this tool to guide haemodynamic management. (Angus)

Intensive care units have huge variations in the use of the PA catheter (insertion rates vary from 3-76% of admissions!), according to a previous survey conducted by the Intensive Care National Audit and Research Centre (ICNARC)(Angus). There is presently no consensus on the benefits of a PA catheter in the intensive care. In the USA many PA catheters are placed every year at a high cost (Kefalides). This is not the case in many other developed countries.

The importance of data interpretation leading to alterations in patient management cannot be overemphasized (Stocking). This has been demonstrated a while ago already by some prospective randomized trials, which assessed the effects of PA catheter-directed treatment protocols, rather than just the catheter (Gattinoni, Hayes). The use of optimal goals for treatment of the critically ill patient should not be confused with the diagnostic use of the PA catheter. Selective use of the PA catheter now appears to be more appropriate than routine use.

Complementary and/or sometimes competing technologies like point-of-care (POC) transthoracic echocardiography (TTE), transoesophageal echocardiography (TOE), oesophageal Doppler ultrasound, thoracic electrical bio-impedance, pulse contour arterial measurement (PiCCO), rebreathing of end-tidal CO_2 (NICO), Lithium dilution CO (LiDCO) etc. have been developed in an attempt to find a less-invasive, safer and more reliable, cost-effective way to assess haemodynamics. However, at present the PA catheter is still a recognised monitor in the critical care physician's armamentarium.

Over the past 15 years POC echocardiography (TTE and TOE) has developed into the gold-standard perioperative haemodynamic monitor. Training in echo techniques has now been introduced into training programmes of disciplines dealing with the haemodynamically unstable patient. When assessing different cardiac pathologies, POC echocardiography is certainly adding value over and above the measurement of intracardiac pressures as measured with PAC or CVP. Where the PAC can tell the physician that something is wrong, POC echocardiography can demonstrate exactly what the mechanism of the pathology is. We can now clearly visualize the cause of cardiac pathology. This will allow more precise management of haemodynamic instability. The value of perioperative echocardiography, not only as a quantitative diagnostic tool but also as an excellent qualitative monitor, is now well established in the operating theatre and in critical care practice. (Ng) (Ng) (Lau)

The pulmonary arterial systolic pressure has been estimated with echocardiography from the peak tricuspid regurgitant velocity and adding this to an estimate of right atrial pressure/CVP, by utilizing the simplified Bernoulli equation. Studies have demonstrated a correlation between this estimate of pulmonary arterial systolic pressure and that obtained from invasive measurement with a PA catheter across a cohort of patients. For an individual patient significant overestimation or underestimation can occur. Recent guidance has suggested that echocardiographic assessment of pulmonary hypertension should be limited to determining the presence of pulmonary hypertension rather than estimating the exact pulmonary artery pressure. In those patients in whom the presence of pulmonary hypertension requires precise quantification (e.g. lung transplantation), this should be done with right heart catheterization.

There are many perioperative clinical scenarios in which information from both the pulmonary artery catheter and echocardiography are crucial and complementary. Those situations e.g. include but are not limited to:

- Lung transplantation
- Cardiac transplantation
- Ventricular Assist Device insertion

- Pulmonary endarterectomy
- Patient with severe pulmonary hypertension undergoing surgery with potential hemodynamic instability/decompensated pulmonary hypertension
- Decompensated cardiogenic shock
- Liver transplantation
- Haemodynamically unstable, critically ill patient in the Critical Care Unit

Anaesthetic and surgical goals

Achieving RV hemodynamic stability by:

- Increasing RV contractility (inotrope)
- Maintaining RV myocardial perfusion (vasoconstrictor/vasopressor)
- Decreasing RV volume load (diuretic, venous dilator, closure of intracardiac shunt, dialysis)
- Decreasing RV pressure load (oxygen, normocarbia, avoid metabolic acidosis, ventilator strategies and lung recruitment manoeuvres, normothermia, IV or inhaled pulmonary vasodilator, pharmacological and mechanical thrombolysis, embolectomy, pulmonary endarterectomy etc.)

The pharmacological perioperative treatment of pulmonary hypertension with intravenous vasodilators will worsen systemic hypotension. A number of systemic vasodilators have been evaluated for the treatment of PHT with little success. Maintaining SVR to maintain blood pressure (BP) and RV myocardial perfusion is crucial when managing the delicate RV. Therefore a calculated infusion of a vasopressor (Phenylephrine or Noradrenaline) must be considered early. On induction of anaesthesia, the consequences of administering any IV induction agent must be carefully considered. Therefore, in the presence of acute PHT, at all times preserve the BP.

Coronary Perfusion Pressure = Aortic Diastolic BP – LV end-diastolic pressure

Inhaled Nitric Oxide

The introduction of inhaled vasodilators with the ability to produce selective pulmonary vasodilation was a major advance in the treatment of PHT. Inhaled vasodilators may potentially circumvent the detrimental intravenous effects by acting predominantly in the pulmonary circulation with little or no vasodilatory effect in systemic blood vessels. A selective pulmonary vasodilator should therefore decrease PAP and PVR, without affecting systemic arterial pressure. This can potentially improve oxygenation by redistributing pulmonary blood flow to ventilated areas of lung (Lowson, Griffiths, Thunberg). In 1991, Frostell and colleagues demonstrated a therapeutic potential for inhaled NO (iNO) to act as a selective pulmonary vasodilator. iNO possesses these properties because it will preferentially increase alveolar capillary blood flow to the ventilated alveoli and therefore decrease respiratory shunt and improve arterial oxygenation. The NO molecule rapidly binds to haemoglobin (Hb) with a high affinity; therefore, the vasodilatory effect of iNO is short-lived and limited to the lung, unlike intravenous vasodilators. NO forms methaemoglobin and nitrate upon exposure to oxyhaemoglobin in the pulmonary circulation. iNO increases blood flow to well-ventilated lung areas, which may have an increased vasomotor tone. This effect of iNO is short-lived and therefore in marked contrast to the effect of intravenously administered vasodilators. IV vasodilators produce diffuse dilation to all of the pulmonary vasculature, thereby increasing blood flow to both areas of non-ventilated and ventilated lung. That will increase intrapulmonary shunt and reduce PaO_2. iNO improves perfusion of ventilated regions only, thereby reducing intrapulmonary shunting and improving arterial oxygenation. These beneficial effects of iNO have been demonstrated in some adult and paediatric patients with acute respiratory distress syndrome (ARDS). Unfortunately, this effect can be transient. The beneficial effect of iNO on outcomes in neonates and small children with respiratory distress syndrome, is well proven. Use of iNO is limited by the potential for toxicity and high cost. In humans without methaemoglobin reductase deficiency, doses <40 ppm do not cause methaemoglobinemia, and animal data suggest that long term administration at comparable doses are nontoxic. In addition to methaemoglobinemia, lung injury may occur if excessive amounts of NO are oxidized to nitrogen dioxide (NO_2), a pulmonary irritant that can cause bronchospasm and pulmonary edema. Modern iNO delivery systems include monitoring for NO and NO_2 levels. The hourly cost for use of iNO was estimated in 2012 to be around $117 in the USA. Although inhaled NO therapy results in a temporary increase in oxygenation in adult patients with ARDS, it has not been shown to improve

survival. This factor, combined with its potential toxicity, difficulties in administration and cost (major consideration), has prompted the search for alternative selective pulmonary vasodilators.

Alternatives to iNO

NO donors (inhaled sodium nitroprusside SNP, inhaled nitroglycerine NTG)

When comparing the effect of inhaled-SNP to iNO, the treatment-induced increases in PaO_2 were similar. Thus, nebulised sodium nitroprusside causes a dose-dependent increase in oxygenation in term infants with hypoxic respiratory failure, similar in magnitude to iNO. SNP administration is however limited by the potential cyanide/thiocyanate toxicity and methaemoglobinemia.

Inhaled NTG produces dose-dependent pulmonary vasodilation, which was noted to be significantly less efficacious than the other agents, including SNP. Inhaled NTG is therefore limited by its short duration of action and the need for continuous or repeated nebulisation.

Phosphodiesterase (PDE) Inhibitors (Sildenafil, Milrinone)

Nitric oxide exerts its biologic properties by increasing intracellular concentrations of cyclic guanosine monophosphate (cGMP). cGMP is rapidly metabolized by PDE, thereby terminating the effect of NO. Both cGMP and cyclic adenosine monophosphate (cAMP) are metabolized by PDE's. While cGMP is metabolized predominantly by type 5 PDEs, cAMP is metabolized mainly by type 3 PDEs. PDE-5 is expressed in relatively high amounts in the pulmonary vasculature, and animal models suggest that PDE-5 inhibitors are more effective at decreasing PA pressures than PDE-3 inhibitors.

While an intravenous infusion of the PDE-3 inhibitor milrinone reduces both pulmonary and systemic arterial blood pressure, inhalation of milrinone predominantly dilates pulmonary blood vessels, resulting in an improved pulmonary-to-systemic vascular resistance ratio (Hentschel). Repeated milrinone inhalations in 20 minute intervals causes a stable reduction of PA pressure. Inhalation of 1 mg/ml milrinone reduces PAP more effectively than the maximal intravenous dose of 1 µg/kg/min, but without exerting systemic hemodynamic effects.

Sildenafil is a selective PDE-5 inhibitor commonly used in the treatment of erectile dysfunction. Sildenafil by virtue of its action of slowing the degradation of cGMP, has been extensively used in the management of PHT in its oral and intravenous formulations. Though inhaled sildenafil is postulated to be of benefit, there are not many studies except on animal models.

Prostaglandins (Epoprostenol, Iloprost, Treprostinol, PGE1)

Inhaled Prostaglandin I2 (iPGI2-Epoprostenol) produces comparable effects to iNO in both animal and clinical ARDS studies. iPGI2 produces greater decreases in pulmonary vascular resistance while iNO produces greater improvements in oxygenation. Epoprostenol was discovered in 1976 and was the first FDA-approved therapy for the treatment of PAH as intravenous administration. It acts through cAMP whereas NO acts through cGMP. It causes vasodilation of the smaller pulmonary arteries that tightly surround the alveolar surfaces decreasing the pulmonary vasculature resistance and improving oxygenation. Inhaled Epoprostenol is associated with fewer systemic effects due to the low blood concentrations. Side effects include pulmonary oedema, headaches, jaw pain, diarrhoea, and anti-platelet effects. It has a serum half-life of 3-6 minutes and is less expensive than iNO. Epoprostenol lacks the toxic effects/metabolites of nitric oxide and therefore does not need a complicated delivery system.

Iloprost is a stable analogue of prostacyclin that can be administered by inhalation, avoiding the systemic side effects associated with intravenous administration. Administration by inhalation also causes selective vasodilation of ventilated regions of the lung, ensuring optimal gas exchange. It has a half-life of 20-30 minutes (compared with only 3 minute for PGI2). The pulmonary vasodilator effect of inhaled iloprost is approximately 20–60 min. Clinical studies have demonstrated that inhaled iloprost has comparable pulmonary haemodynamic effects to iNO and iPGI2. Inhaled iloprost showed acute effects similar to those of inhaled NO and might have a role in the short-term treatment of paediatric PHT, including in neonates. This application of inhaled Iloprost is useful especially in countries where inhaled NO may not be available.

In summary - A practical perioperative approach to manage the RV

- Optimise RV preload – avoid over-distension
- Maintain SVR, Maintain RV myocardial perfusion – Phenylephrine, Noradrenaline, IABP, RVAD
- Reduce PVR - high FiO_2, avoid hypoxia or hypercarbia, optimal ventilator strategies, inhaled NO, pulmonary dilators (PDEI-Milrinone)
- Augment RV contractility (PDEI-Milrinone)

To be discussed in the workshop session

Causes and management of acute pulmonary hypertension and acute right ventricular failure:

1. Decreased RV contractility
    - Perioperative RV injury
    - RV infarction
    - RV ischaemia e.g. intraoperative intracoronary air embolism, incomplete revascularisation, incomplete myocardial protection/ cardioplegia

2. RV pressure overload, increased afterload
    - Pulmonary embolism
    - Left sided heart dysfunction
    - Pericardial disease
    - PPV/PEEP in a patient with a delicate heart
    - Acute pulmonary HT, protamine
    - Perioperative ARDS – e.g. transfusion related

3. RV volume overload
    - Primary right heart valvular regurgitation – trauma, contusion, infective endocarditis (drug abuse), carcinioid

4. Pressure and volume overload
    - Intracardiac shunt – ASD, PFO with left to right shunt

Clinical picture and diagnosis

- Symptoms
- Clinical findings
- CXR
- ECG
- Hemodynamic alterations, CVP, PCWP, Stuart Hamilton thermodilution (influence of TR on CO reading)
- Echo imaging and use of TOE to guide intraoperative management of RV failure
- Biochemical markers
- MRI

Management

Management of RV preload

- Volume loading and offloading, intraoperative venesection from RA purse-string

Management of RV afterload - Pulmonary vascular resistance

- oxygen, morphine, frusemide, NO, PDE-3 inhibitors

Management of RV contractility

- Inotropic support, levosimendan

Management of RV perfusion

- Systemic blood pressure
- IAB counter pulsation
- right coronary artery grafting

Management of transpulmonary blood flow

- Management of LV preload
- Assist devices, ECMO

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Approach to Pre-operative Ischaemic Chest Pain
What should we do?

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Coronary artery disease in pre-operative patients

Prevalence

Coronary artery disease (CAD) is common in pre-operative patients with vascular disease. This was recognized in a study of 1000 patients with various vascular diseases (lower extremity arterial disease (LEAD), abdominal aortic aneurysms and cerebrovascular disease) published in 1984.[1] 92% had CAD, and 25% were classified as having "correctable" CAD, i.e. amenable to coronary artery bypass grafting (CABG).[1]

Patients at risk of myocardial ischaemia

Patients are at risk of myocardial ischaemia peri-operatively when they undergo: i) high-risk surgery and/or ii) are intrinsically at high risk because of their CAD. High-risk surgery includes aortic and other major vascular surgery, as CAD is a common comorbidity.[2] In addition, such surgeries are high-risk *per se* because of supply-demand mismatch, which can occur peri-operatively with haemodynamic fluctuations, e.g. as a result of aortic cross-clamping. High-risk patients have left mainstem disease, triple-vessel CAD or extensive, inducible myocardial ischaemia. Patients with high-risk CAD are prone to plaque rupture due to the peri-operative stress response, which involves cytokines, elevated levels of circulating catecholamines, coronary vasospasm, impaired fibrinolysis and platelet activation.[3] Both high-risk surgical procedures and high-risk CAD therefore predispose to peri-operative myocardial ischaemia and/or infarction.

Approaches to reduce risk

In broad terms, the risk of peri-operative myocardial ischaemia can be mitigated by: i) alleviating supply/demand mismatch, ii) bypassing areas of plaque rupture or preventing plaque rupture altogether, and iii) restoring perfusion of dysfunctional, but viable myocardial segments. Supply/demand mismatch can be corrected pharmacologically by revascularisation (including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)). Plaque rupture can be prevented with pharmacotherapeutic agents and bypassed with CABG. Dysfunctional myocardial segments, if they are viable, may have their contractile function restored with revascularisation (PCI or CABG).

Pharmacotherapy

Beta-adrenoreceptor antagonists (β-blockers) improve supply/demand mismatch by decreasing chronotropy, dromotropy, inotropy and increasing coronary vasodilation. They may also prevent ventricular tachycardia and sudden cardiac death by antagonising the cardiac sympathetic innervation. Statins prevent plaque rupture by stabilization of coronary plaque, as well as by a variety of pleiotropic effects.[4]

In a randomised study of 200 CAD (or at-risk) patients undergoing non-cardiac surgery, the pre- and postoperative administration of atenolol improved long-term survival (P=0.019) and decreased the incidence of the combined endpoint of myocardial infarction, unstable angina pectoris, heart failure hospitalisation, myocardial revascularisation and death (P=0.008), when compared to placebo.[5]

In the PeriOperative ISchemic Evaluation (POISE) trial, 8351 patients with CAD (or stroke or LEAD or heart failure hospitalisation in the past 3 years) who underwent major vascular surgery (or had any 3 of the following risk factors: intrathoracic or intraperitoneal surgery, history of heart failure, transient ischaemic attack, diabetes mellitus, serum creatinine >175 µmol/l, age >70 years or undergoing

emergent/urgent surgery), were randomly assigned to metoprolol or placebo groups.[6] The primary endpoint (a composite of cardiovascular death, non-fatal myocardial infarction and non-fatal cardiac arrest) was reduced in the group who received beta-adrenoreceptor antagonists (P=0.0399).[6] Mortality (P=0.0317) and stroke (P=0.0053), however, were more frequently observed in the metoprolol group.[6] The POISE trial was the largest randomised trial to date to evaluate the effects of beta-adrenoreceptor antagonists pre-surgery in patients with CAD, or at risk of CAD. *Post-hoc* analysis revealed that hypotension, bradycardia and stroke were the most likely mechanisms of the increased mortality risk.[6]

In a study of 100 patients undergoing vascular surgery, who were randomised to statin and placebo groups, the combined endpoint of cardiac death, non-fatal myocardial infarction, ischaemic stroke and unstable angina was reduced in the statin group after 6 months' follow-up (P=0.031).[7]

Revascularisation

Revascularisation (PCI or CABG) pre-operatively prevents supply/demand mismatch by restoring oxygen supply to the myocardium. Revascularisation can also improve contractile function in dysfunctional but viable myocardial segments that are hibernating. CABG can bypass areas of potential plaque rupture, in contrast to PCI.[8] PCI pre-operatively may actually increase risk by introducing the possibility of stent thrombosis, which carries a mortality of around 20%. Patients who discontinue dual anti-platelet therapy are at especially high risk of stent thrombosis.

The Coronary Artery Surgery Study (CASS) analysed 1834 patients with CAD and LEAD or cerebrovascular disease, from 1974 to 1979.[9] CABG was performed in 986 patients, and a decrease in the primary endpoint (death or myocardial infarction) was observed in those who underwent CABG (P<0.0001).[9] The benefit, however, was limited to recipients of CABG with triple-vessel CAD.[9] CABG in patients with triple-vessel CAD was independently associated with survival in the CASS study.[9] This registry was compiled before the modern era of optimal pharmacotherapy for CAD, i.e. statins, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) or thienopyridines.

In a carotid endarterectomy trial, 426 patients without a history of CAD were randomized to invasive coronary angiography (including PCI if appropriate) and no angiography groups.[10] The composite endpoint of post-operative myocardial ischaemic events and complications of invasive angiography was seen less frequently (P=0.01) in those undergoing revascularisation procedures (PCI or CABG).[10] During long-term follow-up, an improved survival rate was seen in patients who were revascularised.[11]

The Coronary Artery Revascularization Prophylaxis (CARP) trial enrolled 510 patients with CAD and LEAD and/or abdominal aortic aneurysms, dichotomised to revascularisation (PCI or CABG) or medical therapy.[12] No mortality benefit could be discerned in the revascularisation arm (P=0.92),[12] although limitations included the exclusion of left mainstem disease and the subjective allocation to revascularisation or medical therapy by the attending physician.

Similarly, no survival benefit (P=0.48 for the composite endpoint of all-cause mortality and non-fatal myocardial infarction) was identified in the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo (DECREASE-V) study, which enrolled 101 patients with extensive myocardial ischaemia and LEAD and/or abdominal aortic aneurysms.[13] Allocation to revascularisation (PCI/CABG) and medical groups was randomised, with all patients receiving statins, ACEIs and thienopyridines.[13] Extensive ischaemia was defined as involvement of ≥ 5 myocardial segments on dobutamine stress echocardiography or ≥ 3 segments on cardiac single-photon emission computed tomography (SPECT).[13]

The use of cardiac imaging to identify extensive myocardial ischaemia was further investigated in a study of 208 patients undergoing major vascular surgery, who were randomised to routine or selective coronary angiography (based on the presence of extensive ischaemia detected by non-invasive testing) groups.[14] More than 1 segmental defect on SPECT or ≥ 2 segments on dobutamine stress echocardiography was defined as extensive ischaemia.[14] A selective coronary angiography strategy demonstrated a long-term survival advantage (P=0.01).[14]

In a sub-analysis of the CARP trial, comprising 109 patients with evidence for inducible ischaemia on SPECT, the combined endpoint of mortality and myocardial infarction was recorded less frequently in the group who underwent imaging-guided revascularisation.[15] This benefit, however, was only seen in

the presence of anterior wall ischaemia (P=0.02), while a trend was observed for benefit in patients with medium and large ischaemic defects (P=0.09).[15] This study was limited by its retrospective nature, as well as the exclusion of left mainstem disease.

A second sub-analysis of the CARP trial revealed that patients with unprotected left mainstem CAD derived a survival benefit from pre-operative revascularisation (P<0.01), while those with triple-vessel disease did not.[16]

Risk-stratification

The limited evidence that exists for revascularisation (PCI and CABG) before high-risk surgery, suggests that the benefit is limited to certain patient subsets. In addition, PCI and CABG are not without morbidity and mortality, and the risk-benefit ratio has to be weighed up carefully.

Multimodality cardiac imaging has the potential to identify patients at highest risk, who are likely to derive most benefit from prophylactic, pre-operative revascularisation.

Cardiac imaging: approaches to risk-stratification

Inducible ischaemia can be demonstrated non-invasively with stress echocardiography, stress cardiac magnetic resonance imaging or SPECT. Stress echocardiography has the advantages of low cost, the absence of ionising radiation or potentially nephrotoxic contrast media. Suboptimal echocardiographic windows or ultrasound penetration (e.g. in obesity or chronic obstructive pulmonary disease) hamper its use, although this can be improved by employing intravenous contrast agents (see below). Stress magnetic resonance imaging is expensive and time-consuming, but not dependent on imaging windows. SPECT is less favoured in contemporary practice, because of ionising radiation, expense (although not greater than stress cardiac magnetic resonance imaging in the South African context) and the low sensitivity for detecting subendocardial ischaemia.

Stress echocardiography is performed with dobutamine (or vasodilators, e.g. adenosine, although not used in South Africa to the best of my knowledge) together or without atropine, while stress cardiac magnetic resonance imaging is performed with adenosine (or regadenoson, currently unavailable in South Africa) and intravenous, gadolinium-based contrast media.

The availability of stress echocardiography and stress cardiac magnetic resonance imaging is currently very limited in South Africa. While SPECT is fairly widespread, stress echocardiography is only available at a few governmental and private healthcare facilities. The use of stress echocardiography is currently limited to patients with good echocardiographic images due to the lack of access to intravenous echocardiographic contrast media, as well as the absence of a funding code. Stress cardiac magnetic resonance imaging is being practised only at a small number of private healthcare facilities, and, as far as I am aware, is not currently available in any governmental hospital.

Stress echocardiography, stress magnetic resonance imaging and SPECT have the added advantage of providing information on myocardial viability. Even though viability was not proven to be an independent predictor of outcome in the Surgical Treatment for Ischemic Heart Failure (STICH) trial, it may be useful in clinical decision-making.[17] The outcome of the STICH trial for viability-guided revascularisation can be attributed to methodological issues, the benefit of surgical revascularisation having been offset by the surgical risk and the fact that surgical revascularisation improves survival regardless of the presence of ischaemic tissue by bypassing diseased coronary segments where acute coronary syndromes occur (the primary mechanism of mortality in patients with chronic CAD). The role of viability assessment in ischaemic cardiomyopathy will be re-evaluated in the Study of the Efficacy and Safety of Percutaneous Coronary Intervention to Improve Survival in Heart Failure (REVIVED-BCIS2; NCT01920048).[18] Viability assessment has, to the best of my knowledge, never been evaluated in the context of a dedicated, pre-operative trial.

Emerging technologies, e.g. speckle tracking strain echocardiography and non-invasive myocardial work assessment (with speckle tracking strain echocardiography and sphygmomanometrically measured blood pressure), are promising for the non-invasive identification of CAD and appropriate pre-operative risk-stratification.[19]

I would strongly recommend liaising with a cardiologist before requesting an imaging test for inducible ischaemia or viability assessment pre-operatively.

Summary

Revascularisation (PCI or CABG) may decrease surgical risk if applied judiciously. This strategy is predicated on the following principles: i) identification of high-risk patients undergoing high-risk surgery and ii) risk-stratification by means of non-invasive cardiac imaging modalities (preferably stress echocardiography or stress magnetic resonance imaging). If extensive inducible ischaemia is demonstrated, revascularisation before surgery can be considered to reduce the peri-operative risk.

In essence, the approach to risk-stratification of patients with CAD before non-cardiac surgery is very similar to that for the risk-stratification of patients with stable CAD, although the evidence is much more limited in the pre-operative context.

The following statement from the European Society of Cardiology Guidelines on non-cardiac surgery is an accurate summary of contemporary evidence and clinical practice: “Despite the lack of extensive scientific data, myocardial revascularisation may be recommended in patients presenting with persistent signs of extensive ischaemia before elective non-cardiac surgery similar to non-surgical settings recommended by the European Society of Cardiology Guidelines.”[2]

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Day-case Surgery Made Safe

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Introduction

Day-case surgery (DCS) occurs when a patient is admitted and discharged on the same calendar day for a surgical procedure. The procedure must be planned and booked as a day case before the patient's admission. It is thus possible to develop a day-case surgery pathway from booking to discharge for these patients.

Over the past 10 years the scope and complexity of DCS has increased substantially, with a wider range of patients now suitable for day-case procedures. In South Africa, the improved patient safety and satisfaction have prompted funders (both state and private), hospitals and clinicians to increase the number of procedures performed as day cases. In 2000 the United Kingdom set a target that 75% of all elective surgery, and even some acute conditions (e.g. abscess drainage or minor trauma) requiring urgent surgical care, should be performed as day cases; stating that day-case surgery should be considered the default option for most surgical procedures.

Historically litigation related to day-case surgery has been less frequent than in inpatient-care and associated with lesser injuries and lower payouts. With the evolution of this discipline and the increase in complexity of cases and patient co-morbidities, patient consent and understanding of post-operative arrangements (and supervision) remain key in ensuring safety and limiting litigation and liability.

As day-case surgical pathways are developed, the anaesthesia care provided is a critical factor in ensuring that these patients have a low incidence of unplanned extended hospital stay, unanticipated admission or re-admissions due to complications.

Patient Selection

The selection of patients for DCS must consider local factors and surgical expertise, e.g. minor surgery for financially independent adults in a metropolitan environment is different than cancer surgery for elderly patients living in a rural setting. An important principle in facilitating DCS is that clinicians must optimize co-morbid condition at home, so that overnight pre-admission is not required.

Social factors

South Africa faces many social obstacles that many developed countries may not (geography, social inequality, burden of disease, etc.) however, with careful protocol development and pre-operative screening, DCS is an economically responsible alternative to inpatient surgery.

Patient consent and discussion of the post-operative environment (including the presence of adult supervision during the first 24 hours post-op) is an essential first step in scheduling DCS. Supervision after minor or local surgery may not be necessary and can be discussed locally. The emerging concept of a "virtual" patient and the use of telemedicine to assess post-operative patients also holds promise.

Ideally, patients having DCS should have a travelling time of less than an hour to their home.

Medical factors

A patient's functional status at the time of pre-anaesthetic assessment determines the appropriateness of DCS, and not their ASA status, age or BMI. Many chronic conditions (e.g. diabetes or epilepsy) do better with minimal disruption to daily routine. Unstable medical conditions should be assessed on an individual basis and the decision for immediate inpatient care, should be balanced by a consideration for delay of surgery, optimization and later DCS; being mindful that some surgical

indications (e.g. cancer surgery) may always necessitate inpatient care.

High BMI patients may require more in-hospital time post-operatively, but most surgical complications in these patients occur during the procedure or first stage of the recovery process, therefore they may still be considered for DCS, especially with the appropriate selection of anaesthesia technique (e.g. regional or local anaesthesia or procedural sedation). Similarly, patients with OSAS (obstructive sleep apnea syndrome) are not contra-indicated but should have a comprehensive peri-operative plan. Early mobilization is facilitated by DCS and is of benefit in both these patient populations.

The elderly and young children may also benefit from DCS, due to minimal disruption of daily life and being in familiar surroundings post-operatively.

Surgical factors

Surgical expertise and experience ensure a successful DCS program. Ideally surgeons should be senior and proficient at performing the procedure. The following surgical factors should be considered when scheduling patients for DCS:

- the incidence of significant post-operative complications that require immediate intervention (e.g. bleeding or cardio-vascular instability)
- the required period of post-operative surgical observation (e.g. resumption of bowel function)
- the post-operative pain associated with the procedure, especially if requiring multiple modalities for analgesia or intravenous analgesia
- the ability of the patient to resume normal functions rapidly, e.g. the ability to eat and drink post-operatively and mobilize independently. If mobilization is limited, DCS can still be considered with thrombo-embolic prophylaxis.

Pre-operative preparation

The three essential components of pre-operative preparation for DCS include:

1. Education of patients and their carers regarding the DCS pathway
2. Providing information regarding the procedure and the post-operative period and allowing patients to ask questions and give informed consent
3. Identifying medical risk factors and optimizing the patient's condition

Pre-operative assessment is imperative, and appropriate venues where this can occur include: the day-case surgery unit, primary care facilities, or even secure virtual/online assessments. These assessments should follow a protocol developed by the surgical, anaesthesia and nursing teams and highlight potential issues requiring management or optimization.

Ideally patients should be assessed for the DCS pathway on the same day the decision for surgery is made; this allows for early preparation for surgery and maximum time for optimization. The assessments should be made by health care practitioners experienced in DCS, and may be performed by nurses or doctors, with a low threshold for consultant review when required.

Appropriate screening and special investigations should be performed, focusing specifically on tests that will either benefit the peri-operative course or facilitate day case surgery over inpatient surgery.

Patients requiring urgent surgery for certain acute conditions can also be managed via the DCS pathway. After an initial assessment these patients may be allowed to return home and then scheduled for surgery at an appropriate time. This assessment allows for the referral of these patients from the emergency services platform to the DCS platform (which may be less congested, especially in the South African setting).

Examples of acute surgical conditions that may be successfully managed as day-case surgeries include general surgery (abscesses, cholecystitis, appendicitis), gynaecology (evacuation of retained products, stable ectopic pregnancy), trauma (MUA of fractures, tendon repairs) and maxillofacial (fractured nose or mandible).

When setting up this emergency day surgery pathway, the following should be considered:

1. *Information*: ensure the patient is adequately informed about the process
2. *Safe*: determine if the condition is safe to be left untreated for 24 hours and will be manageable at home with only oral analgesics post-operatively.
3. *Place*: identify a dedicated theatre and ensure staff are available to accommodate this surgery
4. *Case*: select procedures appropriately

Anaesthetic Management

The provision of anaesthesia for DCS should include the use of short-acting agents, local or regional anaesthesia techniques, simple oral analgesia, protocol-driven anti-emetic therapy, minimal starvation, careful use of IV fluids and early post-operative mobilization.

The anaesthesia for DCS should be provided by experienced anaesthesia providers who are comfortable working in this (sometimes remote) setting. The day-case surgery unit provides a valuable space for education and training, and medical students and junior doctors should be exposed to this setting during their pre-graduate and registrar time.

The core principles of anaesthesia in DCS are:

- rapid onset and offset of anaesthesia with clear-headed emergence
- minimal PONV (post-operative nausea and vomiting), dizziness or drowsiness
- rapid return to full cognitive function

The provision of appropriate analgesia pre-emptively, intra- and post-operatively is central to the philosophy of DCS. Analgesic regimens should ideally be multimodal and opiate sparing as far as possible, with supplementation by local or regional anaesthesia. Long-acting opiates specifically should be avoided.

The proficient use of ultrasound for the placement of local blocks and regional anaesthesia can improve the success rates of these interventions, reduced the dosage of local anaesthetic agents required, and decrease side-effects and complications. Some cases may even be performed as regional anaesthesia only procedures. The availability of a “block room” may improve efficiency and allow confirmation of adequacy of the nerve block before surgery.

Patients should be informed about the expected duration of the nerve block and may be sent home with an anaesthetized limb if it is protected and instructions are provided. Adequate analgesia must be provided for when the block wears off.

The risk for PONV should be assessed pre-operatively and prophylactic anti-emetics given, with a protocolized approach for the treatment of PONV (which includes adequate fluid administration peri-operatively)

To ensure rapid recovery the peri-operative team should aim to ensure that the patient’s body temperature is maintained with passive and active warming.

Post-operative recovery and discharge

Recovery from anaesthesia can be divided into 3 stages:

- *First stage*: period until patient is awake and protective airway reflexes have returned and pain is controlled. This stage should occur in a recovery area. Procedures performed under regional or local anaesthesia may bypass this stage. Readiness for discharge from the recovery unit may be assessed by using the Modified Aldrete Scoring System – see table below.
- *Second stage*: period commences when the patient can self-mobilize from theatre bed or trolley and lasts until discharge from hospital. This stage should occur in a ward or room adjacent to the day surgery theatre. Surveillance for post-operative problems (e.g. PONV, pain) and emergencies (e.g. haemorrhage, cardiovascular instability) should continue in this area. Readiness for hospital discharge may be facilitated by using the MPADSS (Modified Post-

Anaesthesia Discharge Scoring System) – see table below. Patients and their carers must be provided with written information upon discharge regarding potential warning signs of complications and when to contact their health care provider.

- *Late Recovery*: this period ends when the patient has made a full physiological and psychological recovery from surgery. This may take weeks to months.

Upon discharge patients should be given a copy of their discharge summary before leaving the DCS facility. This document should include information regarding the type of anaesthesia provided, the surgical procedure performed and the post-operative instructions.

All facilities providing DCS must have a post-operative pathway to enable unplanned admission or readmission should a patient require inpatient care (either into their own unit or a neighbouring hospital).

Post-operative follow-up 24-hours after discharge, either online or telephonically, is a valuable tool to ensure patient recovery and to screen for post-operative symptoms.

The modified Aldrete Scoring System		MPADSS	
Characteristic	Score	Vital Signs	Score
Level of Consciousness		BP and Pulse	
Fully awake	2	Within 20% of preoperative baseline	2
Rousable when called	1	Within 20 – 40% of preoperative baseline	1
No response	0	> 40% of the preoperative baseline	0
Oxygen saturation		Activity level	
> 90% breathing room air	2	Steady gait, no dizziness / meets pre-op level	2
Oxygen required to maintain > 90%	1	Requires assistance	1
< 90% even when breathing oxygen	0	Unable to ambulate	0
Circulation and blood pressure		Nausea and vomiting	
Sys BP within 20mmHg of pre-sedation level	2	Minimal: successfully treated with oral medication	2
Sys BP within 20 – 50mmHg of pre-sedation level	1	Moderate: successfully treated with IM medication	1
Sys BP > 50mmHg of pre-sedation level	0	Severe: continues after repeated treatment	0
Movement and activity		Pain	
Able to move all extremities on command	2	Acceptable	
Moves 2 extremities on command	1	Yes	2
Doesn't move extremities	0	No	1
Respiration		Surgical bleeding	
Able to breathe and cough freely	2	Minimal: no dressing change required	2
Dyspnea, or shallow or limited breathing	1	Moderate: up to 2 dressing changes required	1
Apnea	0	Severe: more than 3 dressing changes required	0
Require score ≥ 9 to exit the recovery room		*Score ≥ 9 indicates home readiness*	

Quality Improvement

Audit of day-case surgery units, and the procedures performed in these units, is essential in assessing, monitoring and maintaining efficiency and quality of patient care. Data should be collected at every stage of the day surgery process, from booking to post-operative patient follow-up. This data should be processed and disseminated to all role players involved in the DCS service. This allows for the improvement of services, the adaptation of protocols and the planning for and implementation of new lists.

Anaesthesia in remote day surgery units

Internationally, dedicated day-case surgery units that provide DCS autonomously from large hospitals, have been shown to provide a superior model of care and improved patient satisfaction, largely due to the avoidance of tension between inpatient and day-case lists.

In South Africa, particularly in the private sector, there are numerous day-case surgery units that function independently. Although most of these facilities are found within the large metropolitan areas, remoteness may be a potential risk to patient safety in some areas.

These facilities must have an arrangement with a larger acute hospital for unanticipated admissions / readmissions.

Key operational issues to consider when providing DCS in these facilities, include:

- Appropriate patient selection and screening.
- Ability to provide care for medical emergencies (e.g. cardiac arrest or major haemorrhage).
- Tested communications and written service level transfer agreements with the nearest acute hospital and its ICU.
- The ability to manage patients who cannot be transferred home.
- A plan for the management of post-operative complications and clear information for patients on where to go if complications occur.
- Appropriate cover until patients are discharged.
- Teaching, training, supervision and opportunities for research.

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Anaesthesia for Carotid Endarterectomy and Carotid Stenting

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INTRODUCTION

Carotid endarterectomy (CEA) or Carotid Artery Stenting (CAS) are preventative procedures undertaken to mitigate disabling or fatal stroke in patients with significant extracranial carotid stenosis.

Epidemiology[7,8,9]

In the developed world stroke is the most common cause of long term adult neurological disability. It is also attributed the third leading cause of death in the UK and US.

In South Africa a rapid epidemiological transition and longer lifespans increase the exposure to, and development of risk factors.

In 2000 stroke was the third leading cause of death following HIV/AIDS and coronary artery disease. Black women had the highest mortality rate from stroke (160 per 100 000).

The Southern African Stroke Prevention Initiative study demonstrated very high rates of stroke incidence and disability in rural SA as well.

The SA Comparative Risk Assessment Collaborating Group estimated the contribution of **8 risk factors to stroke**:

- hypertension (52%)
- tobacco use (24%)
- excess body weight (18%)
- high cholesterol (15%)
- physical inactivity (12%)
- low fruit and vegetable intake (12%)
- diabetes (8%)
- alcohol consumption (8%)

Stroke management, especially in young South Africans, is often complicated by the high prevalence of HIV/AIDS.

STROKE CLASSIFICATION AND AETIOLOGY

Globally, the proportion of strokes due to ischaemia is 68%, while haemorrhagic stroke account for 32%.

There is a higher incidence of haemorrhagic stroke in low/middle-income countries. In high income settings the proportion of all strokes due to ischaemia approaches 90%.[7]

Haemorrhagic Stroke

- Intracerebral Haemorrhage
- Subarachnoid Haemorrhage

Ischaemic Stroke

Up to 90% of ischaemic strokes occur in the carotid artery territory.

Extracranial carotid artery atherosclerosis accounts for 15-30% of all ischaemic strokes, either by causing occlusion of the artery or arterial-arterial embolization.

Cause	Example
Large-vessel disease	**atherosclerosis,** dissection, arteritis
Small-vessel disease	lipohyalinosis, fibrinoid degeneration, microatheroma
Cardioembolic disease	AF, valvular disease, chamber thrombus, MI(<1 mo), CCF(EF<30%), DCMO, endocarditis, CABG
Systemic hypoperfusion (cardiac pump failure)	cardiac arrest, arrhythmia, acute myocardial ischaemia, pulmonary embolism, pericardial effusion, hypovolaemic shock
Venous sinus thrombosis	
Blood disorders	sickle cell anaemia, polycythaemia vera, antithrombin III deficiency, antiphospholipid syndrome

Table 1. Causes of ischaemic stroke

Transient ischaemic attack (TIA)

It is a clinical definition of neurological symptoms lasting <24 hours that is caused by focal ischaemia of the brain, spinal cord or retina.

A revised definition is needed as there is frequent association with permanent brain tissue injury. The differentiation between TIA and acute ischaemic stroke is arbitrary, as the two entities share the same spectrum.

The 5 year risk of a new stroke after a TIA or stroke is 25-40%.

The risk of stroke within a week after the index TIA in a patient with high grade carotid stenosis may be as high as 20%. The highest risk is within 72hrs after the TIA.

CAROTID ATHEROSCLEROSIS

Most commonly occurs at the bifurcation of the common carotid and the proximal internal carotid arteries.

Classification of carotid artery disease:

- **Asymptomatic**
- **Symptomatic**
  - non-disabling stroke or TIA within the vascular territory of the artery (<6 months)
  - higher risk of subsequent stroke
- **Degree of stenosis**
  - Percentage of narrowest segment compared to the more distal int. carotid artery
  - Duplex ultrasound most commonly used
  - CT/MRI/ angiography in selected cases – eg delineation of difficult anatomy

The risk of stroke increases with greater degrees of narrowing, except for near occlusion, which has a lower risk. A tight stenosis can be accompanied by reduced flow and distal internal carotid artery collapse, and this might be expected pathophysiologically to confer reduced risk.

MANAGEMENT OF CAROTID ARTERY STENOSIS

Medical Therapy

Risk factor modification - stop smoking and reduce alcohol intake
Drugs – antihypertensive, diabetes treatment, statins and antiplatelet agents

Surgical – Revascularisation Interventions

The available options are **carotid endarterectomy (CEA) and carotid artery stenting (CAS).** Surgery should be performed within 2 weeks of index event. Considering the high risk of stroke after TIA, some surgeons advocate within 48 hours.

- ## Carotid Endarterectomy
  Evidence Review [4,8]: 1990's

NASCET (North American Symptomatic Carotid Endarterectomy Trial)
ESCET (European Carotid Surgery Trial)

- *Improved outcomes* demonstrated in *symptomatic patients with more than 70% stenosis*, compared with the best medical management.
- Risk reduction of stroke and death 12% (15 CEA performed to prevent 1 stroke or death).

Cochrane Group concluded that **CEA**:

- *some benefit* in patients with *50-69% symptomatic stenosis*
- *highly beneficial* for patients with *symptomatic stenosis of 70-99% without near-occlusion*.
- *marginal benefits* in patients with *near-occlusion. Benefit is most marked* in men, patients aged 75 years and above and patients randomised within 2 weeks of the last event
- *Small* magnitude of *benefit asymptomatic stenosis* (NNT is 83 to prevent one stroke in 2 years). Possibly beneficial in subgroups e.g. younger male patients with contralateral disease. It has been noted in recent literature that improvements in best medical care eg statins and newer antiplatelet agents (eg Clopidogrel) may outweigh benefits of surgery.

- ## Carotid Artery Angioplasty and Stenting

Although a less invasive option to open CEA surgery there is a higher risk of peri-operative stroke. Its use is mainly reserved for hostile neck anatomy and in patients with comorbid condition where general anaesthesia is unsuitable. Where a patient is suitable for either procedure CEA is favoured.

Improved CAS outcomes relate to greater operator experience/volumes, better patient selection and technological advancements (embolisation protection devices and newer stents).

	Favours CAS	**Favours CEA**
Periprocedural Risks		
MI	+(lower risk)	-(higher risk)
Stroke (at 30d and 4yrs)		+
Death	-	-
Age(y)		
< 70	+	
>70*		+
Local Complications		
Cranial n palsy, haematomas	+	
Tracheostomy stoma, contralateral r. laryngeal n palsy	+	
Hostile Anatomy		
Restenosis after previous CEA**	+	
Neck irradiation	+	
High/low carotid birfurcation***	+	
Tortuous vessel prox/distal to lesion		+
Significant comorbidies		
e.g.cardiopulmonary dx	+	

Table 2. Factors Affecting Surgical Approach to Carotid Artery Stenosis[9]

* > 70yo risk of stroke/death = 12% CAS cf 5.9% CEA
  Noted that stroke victims suffered more deterioration in quality of life than those who had MI
** Intimal hyperplasia has a lower peri-procedural risk than atherosclerotic plaque
***Lesions that lie high above mandible or below clavicle

ANAESTHESIA FOR CEA AND CAS

Preoperative Assessment

The history of the presenting complaint and indication for surgery must be appreciated. Understanding the symptoms and documentation of any existing neurological deficits is important, especially if the procedure is done awake since these may recur intra-operatively.

Cardiovascular co-morbidity needs to be identified and optimized (e.g.co-existing coronary artery disease). The degree of ischaemia is assessed and if the patient requires coronary angioplasty or bypass surgery, the timing thereof needs to be decided.
(see CO-EXISTING CORONARY AND CAROTID ARTERY DISEASE on p 13)

Discuss the type of anaesthesia (local/general) and what procedures and events the patient can expect in the course of the surgery. Baseline neurological testing performed (e.g. answers to personal questions) to replicate intra-operatively for awake surgery.

Medication reducing cardiovascular risk and thrombotic complications are continued:

- Statins (plaque stabilisation) and β-blocker therapy should be continued (Grade 1A evidence)
- New Statin Therapy should also be initiated in previously untreated patients (Grade 1A evidence)
- Lower dose Aspirin (if sensitive or allergic – Clopidogrel) should be continued

Caution for a sedative benzodiazepine if local/regional is being considered.

General vs Local/Regional Anaesthesia

CAS - most procedures are performed with local anaesthesia at the arterial puncture site.
CEA - patient/surgical factors or complications may favour either method.

An analysis of 26 070 cases from the NSQIP database: 85 % general anaesthesia and 15% regional[1]

Advantages	**Disadvantages**
General Anaesthesia	
Secure airway and control ventilation	Lack of direct neurological monitoring
Avoids need for urgent conversion	Intraoperative hypotension and post-operative hypertension
Ensure comfort and immobility	Increased rate of shunt use
Avoid intra-op anxiety	Delayed recovery from GA may mask post-op neurological complications
Neuro-protection with volatiles	
Regional	
Definitive real time neurological monitoring	Limited access to airway if needing to convert to GA (e.g. if seizure or cerebral ischaemia)
Coronary and cerebral autoregulation preserved	Patient may not tolerate lying flat (e.g. anxiety, claustrophobia, cough, cardiac dx-CCF)
Airway manipulation avoided	Access limited to long carotid lesions or high bifurcations
Complications of GA avoided	Patient stress/pain can cause increased risk of myocardial ischaemia
Shorter operating times and hospital LOS	Risk of excess sedation
Lower rates of death, stroke, MI	
Lower rates of wound infections, haematomas	

Table 3. *Postulated* advantages and disadvantages for GA and RA in CEA

Evidence for GA and Regional/Local

Although some data suggest that local or regional anaesthesia is beneficial, all major guidelines state no significant difference in clinical outcome when comparing GA and regional anaesthesia.

Currently, the evidence shows that the choice of anaesthetic technique should be considered individually. Morbidities, surgeon or anaesthesiologist or institutional experience should be taken into account in an attempt to optimize outcomes.

Table 4 Summary of recent literature comparing GA and RA for carotid endarterectomy [1,2]

STUDY	METHOD	RESULTS/CONCLUSIONS
Systematic Review and Meta-Analysis (2020)[2]	31 studies (n=152 376)	Differences btw RCTs and nonrandomized data (?bias) e.g. cardiac complications -significantly less frequently in LA BUT subgroup analysis of RCTs - non significant difference RCTs with small sample sizes: no significant outcome difference Nonrandomized data with larger sample sizes: small, significant differences favoured LA
Retrospective study (2019)	(n=18 945)	GA higher incidence of postoperative pneumonia and greater need for blood transfusions
Pooled Meta-analysis (2018)	21 Observational and 12 RCT (n>58 000)	LA (>14000) - lower incidences of: Stroke (odds ratio [OR] 0.66, 95% CI 0.55-0.80) TIA (OR 0.52, 95% CI 0.38-0.70) MI (OR 0.55, 95% CI0.41-0.74) Mortality (OR 0.73, 95% CI 0.56-0.94) **Subgroup analysis**: 12 RCTS (n=4453) no differences in Stroke, MI, any other outcome
Cochrane review (2008 updated 2013)	14 RCT (n=4596; 3526 fr GALA)	Incidence of stroke not significantly different (LA: 3.2%; GA: 3.5%) LA: Trend toward lower perioperative mortality (0.9 versus 1.5%, OR 0.62, 95%CI 0.63-1.07) NSQIP analysis - no significant differences for the composite outcome of perioperative stroke/myocardial infarction (MI)/death (30 day)
General Anesthesia versus Local Anesthesia (GALA) trial (2008)	largest prospective multicentre control trial (n=3526)	**Primary outcome:** composite of stroke, MI, or death 30 days after surgery – No significant difference (GA=4.8%, RA=4.5%) **Secondary outcome:** stroke, MI, death at 1 year, quality of life, and length of hospital stay (suggestion that stroke and MI at 1 year reduced in LA) **Post-hoc analysis:** LA may be more cost effective (differences in the length of intensive care unit stay and the use of consumables)

Anaesthetic Goals

Maintain airway control.

Ensure CVS stability to maintain myocardial and cerebral perfusion.

Ensure patient can comfortably lie still (if regional/sedation).

Ensure the patient is promptly lucid to be fully cooperative for neurological monitoring when done under local/regional anaesthetia. Similarly, the same end point is sought at the conclusion of a general anaesthetic.

General Anaesthetic Goals

Since the surgery is relatively short (< 90 min) appropriate medications should be used to ensure rapid emergence or prompt wake-up for a neurological examination.

Further, the choice between a ceiling concentration of volatile agent or TIVA will be made if neuro-monitoring is employed. With the aforementioned strategy, MAC between 0.5 -1 will mitigate signal suppression that would interfere with detecting brain ischaemia.

Clinical studies demonstrate equivalence of TIVA with volatile anaesthetics for maintenance of general anaesthesia, but no major advantages[1].

N_20 – may affect neuro-monitoring similarly to volatiles, additionally having a synergistic action. Nausea and vomiting possibly increases risk of postoperative neck haematoma.

Airway and ventilation management

For CEA, an endotracheal tube is preferred because of the limited access to the airway.

There are, however, deleterious effects of its use:

Intubation:

- Tracheal irritation can precipitate hypertension, tachycardia and myocardial ischaemia.

Extubation:

- Coughing and hypertension can lead to carotid haematoma if the suture line is compromised. This in turn may potentially lead to a threatened airway.
- The strategy of deep extubation could aid in avoiding haemodynamic lability.

For CAS, a supraglottic airway would address the above problems at induction and emergence.

Normocapnia is aimed for in patients undergoing CEA.

- Permissive hypercapnia, although increases cerebral blood flow during cross clamping, may contribute to a “steal” phenomenon to normally perfused brain tissue. There is also an increased risk of embolization.
- Hypocapnia is avoided as it can decrease cerebral blood flow through vasoconstriction.

Local/Regional Anaesthesia Technique

Easily titratable sedation (e.g. dexmedetomidine) is used in conjunction with a cervical plexus block. The superficial block is preferred as the deep cervical plexus block has potential serious side effects (e.g. subarachnoid injection and Horner’s syndrome). The block has good analgesic utility even if general anaesthesia is employed.

SURGICAL PROCEDURE

Patient position:

- Supine, slight head elevation and extended (bolster under shoulders) and rotated to contralateral side. Arms tucked alongside.

Incision/Dissection:

- Along anterior border of sternocleidomastoid and exposure of carotid arteries.
- Carotid arts (common, external and internal) circumferentially dissected and encircled with vascular loops.
- Heparin given before clamping of external and common carotid arts followed by clamping of internal carotid distally.
- A longitudinal arteriotomy is performed and a shunt may be inserted while excising the atheromatous plaque.
- The defect is closed by primary closure but a patch angioplasty is often performed to reduce the risk of re-stenosis. The shunt is then removed and allowing back-bleeding facilitates flushing air and debris from the artery.
- After closure of arteriotomy the clamps are removed in a specific order to preferentially allow embolization of debris to the external carotid art (first external then common and last internal carotid art).
- Doppler used to confirm flow then wound closure with possible drain insertion.
- Protamine may be used to reverse heparin.

SHUNT PLACEMENT

During carotid cross-clamping there is impoverishment of cerebral blood flow. The magnitude of which depends in the degree of collateral blood flow via the circle of Willis.

In an awake patient the decision to place a temporary artificial shunt across the operative site will be based on any evidence of cerebral ischaemia.

Under GA the placement depends on whether the surgeon uses shunts on all patients or practices selective shunting where neurological monitoring indicates poor cerebral perfusion or ischaemia.

Disadvantages:

- RCTs and retrospective studies have not demonstrated improved neurological outcome.[9]
- Potentially cause stroke by introducing air, dislodging emboli, intimal dissection, kinking or thrombosis.

NEUROLOGICAL MONITORING

The paramount goal during carotid surgery is the avoidance of cerebral ischaemia especially during the period of arterial cross-clamping.

Monitoring cerebral blood flow can aid in determining which patients may benefit from vascular shunt placement.

It should be noted that accuracy data (sensitivity and specificity) regarding neuro-monitors suffer from significant variability across sources.

Obstacles to reliable accuracy determinations:

- lack of uniform criteria for determining brain ischemia
- subjective nature of the interpretation of monitoring data
- surgical or anaesthetic intervention when a monitor suggests ischemia (e.g. shunt placement or BP elevation)
- lack of a gold standard monitor for patients under GA

Table 5 Comparison of Neurological Monitoring Strategies

	ADVANTAGES	DISADVANTAGES
AWAKE TESTING		
Gold Standard Noting answers to simple questions (baseline and repeated when carotids exposed and clamped) Motor function – handgrip strength	Direct monitor Cerebral ischaemia detected by loss of consciousness, confusion, agitation, restlessness, dysphagia or seizures	As per Table 2 Above
STUMP PRESSURE		
Pressure distal to carotid clamp reflects pressure around circle of Willis	>50mmHg High specificity (99%) for good collateral pressure	Poor sensitivity (30%) No consensus of pressure thresholds to place shunt Not continuous measurement Cannot detect emboli
TRANSCRANIAL DOPPLER (TCD)		
Measures flow in Middle Cerebral Artery (over petrous temporal bone)	Measures flow and is only monitor to detect and quantify emboli 50% reduction in flow → 100%sensitivity; 86%specificity for cerebral ischaemia	Changes in blood flow velocity may reflect arterial diameter changes rather than blood flow Acoustic window not found in 10-20% - operator dependent. Probe position may interfere with surgical site
BRAIN OXYGEN SATURATION MONITORING NEAR-INFRARED SPECTROSCOPY (NIRS)		
Produces a regional cerebral oximetry value by measuring venous and capillary oxygenation	High negative predictive value Absolute values rSO_2<50% or 15-20% decrease from baseline proposed trigger for shunt Low cost Ease of application	Poor positive predictive value Only frontal lobe sensors - small sampling window Interference from ambient light Cannot identify emboli Wide variations in baseline readings Multiple factors can cause decrease rSO_2 NOT VALIDATED
JUGULAR VENOUS BULB MONITORING ($SjVO_2$)		
Blood returning from cerebral circulation sampled at ipsilateral Internal Jugular Vein	jugular venous lactate – marker of brain ischaemia	Global not regional monitor Wide range of normal SjVO2 (55-75%) Evidence of benefit lacking

	ADVANTAGES	DISADVANTAGES
SOMATOSENSORY EVOKED POTENTIALS (SSEPs)		
EEG is recorded after stimulus representing deeper structure activity	Useful if baseline EEG abnormal Highly specific (91%)	GA can alter the signal Poorly sensitivity (58%) Cannot identify emboli Rarely used
EEG		
Waveforms obtained from scalp electrodes in multi-channel sets continuously evaluated Raw and processed data can be used	16 Lead EEG considered best available monitor WELL VALIDATED	Inability to monitor subcortical structures Difficult interpretation – need trained personnel Limited sensitivity Several functions interfere with interpretation (diathermy, BP,Tº, anaesthetic agent) Processed EEG easier to interpret but sensitivity and specificity lost

A meta-analysis of 4664 measurements from 29 studies showed the best predictor of cerebral ischemia was a combination of a low stump pressure and EEG (or TCD).[1]

CONVERSION FROM LA TO GA

The need to convert is relatively uncommon (as was appreciated in GALA trial).

Indications: Patient request, severe agitation, inadequate analgesia or seizure
Challenges: Open incision with partially covered head turned to side
Pre-oxygenation may be inadequate

Partially lifting drape, returning head to neutral position and securing airway with RSI technique to secure airway promptly would be preferable.

Conversion during CAS does not have issues of access to the airway.

HEMODYNAMIC MONITORING AND MANAGEMENT

The blood pressure and heart rate lability encountered in both CEA and CAS is attributed to:

Carotid baroreceptor dysfunction
- Altered baseline (following CVA/TIA) and intraoperative manipulation

Co-morbidity exacerbating instability:
- CVS disease, poorly controlled hypertension, autonomic dysfunction and vasoactive medication

Sequelae:
- Cerebral and Myocardial ischaemia
- Post-op hypertension – Neck haematoma, airway compromise, intracerebral haemorrhage and cerebral hyperperfusion syndrome

MONITORING	MANAGEMENT
ECG (Multiple leads) • Arrhythmias • ST-segment >1mm Depression **INVASIVE ARTERIAL MONITORING**	Anti-arrhythmic Anti-cholinergics Sympathomimetics Vasodilators Short acting β-blockers Fluids (boluses)

Periods of highest risk for CVS lability

1. INDUCTION

Anaesthetic agents → hypotension:
Removing sympathetic tone
Decreasing SVR
Direct myocardial depression
Decreased venous return
Induce bradycardia

Endotracheal intubation:
sympathetic stimulation→
tachycardia and hypertension

2. SURGICAL MANIPULATION OF THE CAROTID SINUS AND CAROTID ARTERY

CEA

Can induce either sympathetic or parasympathetic stimulation.

Carotid cross-clamping → ipsilateral cerebral ischaemia
Plaque disruption – embolization
Decreased carotid blood flow
Maintain BP 20% above baseline when clamped – optimize collateral cerebral perfusion
Modified according to neurological monitoring

Carotid unclamping and reperfusion → Hypotension

CAS

Balloon expansion → Bradycardia and Hypotension
endovascular pressure
decreased sympathetic activity
increased parasympathetic outflow

3. EMERGENCE FROM ANAESTHESIA

Extubation → hypertension
tracheal irritation, coughing

ANTICOAGULATION

A bolus of heparin is administered before carotid cross-clamping to achieve ACT 200-250s that is reversed with protamine.

It is also necessary during CAS before advancing the wires to prevent thrombosis. It is, however, unnecessary to reverse at conclusion.

Post operatively CAS patients are treated with aspirin and Clopidogrel for a minimum of 4 weeks.

POSTOPERATIVE COMPLICATIONS

1. Slow emergence from anaesthesia and stroke
Rule out residual anaesthetic effects, hypothermia or hypercarbia

If new neurological deficits consider intraoperative or postoperative stroke (24-48hrs after)

- Duplex U/S → no flow → re-explore

- CT Scan to identify intracranial haemorrhage → stop antithrombotic agents, treat supportively, neurosurgical consult
- No intracranial haemorrhage → Angiography to address emboli with lysis/extraction

2. Blood pressure control
Aim to maintain SBP 100-150mmHg

Hypertension
cerebral autoregulation disruption -> abnormally increased cerebral blood flow
disrupted baroreceptors
uncontrolled postoperative pain

Cerebral Hyperperfusion Syndrome
can occur 2-7 days post-surgery
manifests as cerebral oedema, intra-cerebral haemorrhage, unilateral headaches, seizures
TCD may be useful to monitor for increased cerebral perfusion – (increased peak MCA velocity)

Hypotension
Residual carotid hypersensitivity after plaque excision
MI
Haemorrhage

3. Neck Hematoma
Cause: Poorly controlled hypertension or on-going anticoagulation
Can threaten airway → relook surgery
Potentially difficult airway management:

- compression/ displacement of upper airway structures
- oropharyngeal/ laryngeal oedema/ bleeding
- extubate only after swelling settled

4. Pain
Opioids – may exacerbate respiratory depression if disruption of hyperventilation response to hypoxia (mediated by carotid chemoreceptors).

Paracetamol will decrease opioid requirements.

Local infiltration and cervical plexus block should provide some analgesia in the postoperative period.

5. Cranial nerve injury and Vocal cord paralysis
Caused by traction or compression
Most resolve within 6 months
Eg branches of facial n., hypoglossal, glossopharyngeal
Injury to the recurrent laryngeal nerve → ipsilateral VC paralysis→ hoarseness

6. Re-stenosis
Up to 17% at 5 years
Caused by neo-intimal hyperplasia which often spontaneously regresses
Mostly asymptomatic (CAS is the corrective procedure of choice)

CO-EXISTING CORONARY AND CAROTID ARTERY DISEASE[3]

Concomitant cerebrovascular and coronary heart disease represent a subset with advanced atherosclerosis. These patients also have a higher incidence of left main coronary disease and a reduced LVEF compared to isolated coronary heart disease.

Of consideration, is the role of combined or staged CABG, type carotid revascularization, and which strategies will result in the lowest operative morbidity and mortality.
Perioperative athero-embolism (e.g. secondary to AF, aortic atherosclerosis) and cerebral hypo-perfusion are the most common mechanisms of stroke for CABG surgery. Other causes include large and small vessel occlusive disease, perioperative MI and aortic dissection.

For long-term stroke risk reduction, all patients with significant cerebrovascular and cardiac disease, regardless of surgical intervention, warrant aggressive medical management.

Prophylactic carotid revascularization
Few RCTs addressing the effectiveness of prophylactic surgery in patients scheduled for CABG. Therefore, there is no clear consensus on the optimal strategy and we look to expert opinion.

Unilateral asymptomatic carotid stenosis of 50 to 99% is not an independent risk factor for ipsilateral ischemic stroke. These cases do not benefit from prophylactic carotid intervention.

Increased risk of stroke with CABG and would benefit from prophylactic carotid intervention:

- Symptomatic carotid stenosis of 50 to 99% in men and 70 to 99% in women
- Bilateral asymptomatic stenosis of 80 to 99%
- Unilateral asymptomatic stenosis of 70 to 99% and contralateral carotid occlusion

(Grade 2C evidence)

Carotid treatment options

Considerations for patients requiring both carotid and cardiac revascularization include the following treatment decisions:

Choice of carotid revascularization (i.e. CEA vs CAS)
Since CAS requires dual antiplatelet therapy for several weeks after procedure to prevent stent thrombosis. This precludes concomitant cardiac surgery. (Grade 1C)

Timing of revascularization (Grade 2C)

- **Staged carotid revascularization with CEA or CAS prior to CABG**

Patients with chronic stable angina in the absence of a recent myocardial infarction, severe left main coronary artery disease, or diffuse coronary heart disease without satisfactory collaterals. These patients do not need urgent coronary revascularization

- **Combined procedure of CEA plus CABG**

Severe left main coronary heart disease, diffuse coronary heart disease without satisfactory collaterals, or unstable angina. Therefore, urgent coronary intervention is required.

Retrospective data suggest that perioperative complication rates are probably similar with combined CEA and CABG compared with CEA before CABG. In addition, performing CEA during cardiopulmonary bypass does not appear to increase the incidence of bleeding or prolong hospital stay.

Timing of cardiac surgery after a stroke
Sufficient delay (at least a month unless emergent surgery)

- to allow identification of the cause of stroke
- restoration of cerebral auto-regulatory mechanism
- remodelling of the parenchymal damage to minimize the risk of haemorrhagic transformation

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Palliative Care and the Role of the Anaesthetist

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Introduction

Increased life expectancy coupled with life-prolonging treatment options through advances in medicine and technology has increased the complexity of our medical decision-making. End-of life decisions are ethically, legally and practically complex but increasingly common and therefore an important part of our practice. The mortality benefit of interventions should always be weighed against the potential for long-term suffering. We should ensure that patients die with dignity once medical therapy fails, treatment goals cannot be met and when the patient's wishes are not congruent with organ support therapies.

Anaesthetists involvement in palliative care includes palliation in critical care units, anaesthesia for the palliative care patient presenting for palliative or emergency procedures and for pain and symptom control management at the end of life. Anaesthetists should equip themselves with general palliative care principles to enable them to understand medical futility, provide appropriate patient care as well as family guidance.

'A *doctor has neither* a *duty nor* the *right* to *prescribe a lingering death' – Twycross RG*

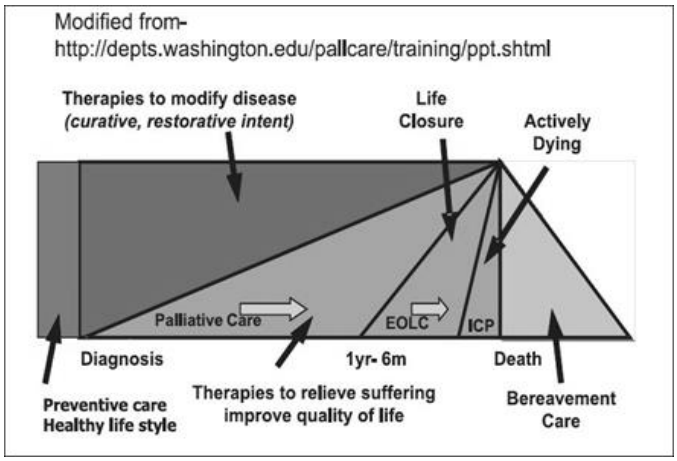
What is palliative care?

The World Health Organization defines 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."

Palliative care is a form of multidisciplinary care with the purpose of relieving suffering and improving quality of life for both patients and families affected by critical illness or injury. Palliative care addresses physical, psychosocial and spiritual aspects of a patient's care in a respectful and compassionate manner. Palliative care can be the sole treatment goal, or it can be offered in parallel with other medical treatment irrespective of prognosis. Advantages include the alleviation of physical and emotional distress, prioritizing the patient's dignity, allowing patients and their family/carers to continue living life and helping to avoid unnecessary procedures with their associated costs. This requires the skill, time and collaboration of a multidisciplinary team that includes the patient and their family in decision-making. Management decisions should be based on the patient's wishes, past and projected future quality of life, evidence based medical practice, severity and prognosis of illness, age as well as ethical reasoning. Decision-making is often complicated by differences of opinion or belief systems and causes emotional distress to all involved. Continuous reassessment of treatment goals is essential.

Common misconceptions about palliative care

- It is only for oncology patients
- It hastens death
- The administration of morphine hastens death
- Patients who stop eating die of starvation
- Palliative care can not be provided outside of a hospital
- Children should not be allowed to talk about death and dying
- Pain is a part of dying
- The use of pain medication does leads to addiction
- Palliative care implies doctors have given up hope.
- Care is withdrawn



Ethical considerations of palliative care

Clinical decision should aim to balance the four principles of Beauchamp and Childress, namely autonomy, beneficence, non-maleficence and justice.

A four quadrants approach could assist with decision-making:

- Medical indications – will the treatment have an overall benefit?
- Quality of life – how will the patient's quality of life be impacted?
- Patient preferences – does the patient want the treatment?
- Contextual features – is the treatment available? Is treatment cost justifiable?

There are several ethical considerations pertaining to palliative care that are briefly summarised in the table below.

Ethical consideration	**Example**
Autonomy and non-maleficence	Respect advanced directives Proxy informed consent Do-not-resuscitate (DNR) orders Withdrawing or withholding life-sustaining treatment
Beneficence	Achieved quality of life post treatment
Distributive justice	Equality of access to best available care
Decisional capacity and consent	Paediatric patient Intensive Care Unit (ICU) patient
Dignity	Dignified death
Honesty/truth telling	Augments patient participation in decision making
Privacy and confidentiality	Patient's wishes regarding privacy to be respected

Patients can refuse treatment but doctors are not obliged to provide life-sustaining treatment that is deemed futile or not in the best interest of the patient. These ethical considerations will be discussed further in the text below.

The need for palliative care

There is a high need for palliative care. A point prevalence survey of the need for palliative care in inpatients at 11 public sector hospital in Cape Town showed that 16,6% of all inpatients and 54,8% of medical inpatients met the criteria for palliative care.

The SPICT tool (see annexure A) can be used to identify patients with life threatening illnesses. Early identification and incorporation of palliative care principles in parallel to other clinical management is important.

The lack of palliative care results in underuse of effective therapy, overuse of aggressive therapy and misuse of several other therapies. Palliative care has been shown to improve patient and family

member symptom scores, decrease health care utilization and costs, without negatively impacting survival time. It is for these reasons that it should be an integral component of patient care.

End of life care in the Intensive Care Unit

Patient's needs in the ICU	Family's needs in the ICU
• Pain and symptom control • Human connection • Relieving the burden on family/friends • Avoidance of unwanted life support • Continuity of care • Communication • Trust in treating physician	• Honest information • Privacy • Being listened to • Respect of family member's wishes • Sensitivity to their cultural traditions • Decision making burden needs to be addressed

Comprehensive care of the critically ill should include palliative care regardless of prognosis. Palliative care helps to manage suffering and addresses the needs of patients and their families without interfering with the goals of critical care (reduce morbidity and mortality, maintain organ function and restore health). Integration of palliative care in the ICU can improve the quality of end-of-life care. It is unlikely that patients will return to their baseline life trajectory (physical and psychological) post ICU admission and palliative care helps to better prepare patients and their families for this. Pain assessment and management is the most consistent application of palliative care in the ICU whilst other aspects of palliative care are performed inconsistently and infrequently. ETHICUS 2 compares end-of-life practice between 1999-2000 vs 2015-2016 and it showed that limitations in life-prolonging therapies occurred significantly more frequently and death without limitations in life-prolonging therapies occurred significantly less frequently in 22 European ICU's.

Essential components of ICU palliative care

Multidisciplinary team palliative care assessment

A palliative care assessment should be done prior to admission to avoid invalid assumptions and recognize the dying patient. This will include:

- Pain and symptom assessment
- Cultural and spiritual assessment
- Advance care planning
    - Discussion about future care between an individual and their care providers
    - This could include: patient's concerns, wishes, important values and patient's wishes regarding interventions, organ support and resuscitation
- Advance directives
- Identify patient's mandated proxy or medical decision-maker to make decisions on the patient's behalf if the patient is no longer able to
- Prognostication- likely outcomes of ICU stay
    - It is important to discuss prognosis with patients to allow them to have realistic treatment goals, focus on important life goals and unfinished business. It is not possible to make an exact prediction and this inherent uncertainty should be communicated to patients. Do not give exact dates or numbers but rather talk about days, weeks, months or years
- Family assessment and Facilitated Values History
    - The Facilitated Values History approach helps to assist surrogate decision makers to understand incapacitated patients' values and to apply these values during decision-making

Communication – physician and critical care nurse

Communication is used as a quality of care marker in the ICU. It is highly valued by families. Compassionate truth telling is advised when having end-of-life discussions. Communication should always allow for shared decision-making. All discussions and decisions should be clearly documented. This conversation should not focus on what you cannot do but rather on what we still can do which includes symptom management, good communication and being available.

Breaking of bad news should, where possible, be done by the most senior clinician available. The clinician should be accompanied by the nurse caring for the patient. This is best approached by using the SPIKES protocol of breaking bad news.

S – Situation/Setting*: Private relative interview room*
P – Perception*: Open ended questions to try and understand what the family understand*
I – Invitation: *Obtain families invitation to give them more information*
K – Knowledge*: Honest account of history, current condition and prognosis. Discuss future care plan, DNR, autopsy or organ donation and comfort care plan options.*
E – Emotions/Empathy *– Allow for emotional responses, be empathetic*
S – Summary/Strategy *– Follow-up*

Withholding and withdrawing of organ support systems ('life support')

Consensus definitions as per the WELPICUS study:

- Withdrawing life-sustaining treatment: decision to actively stop a life-sustaining intervention presently being given
- Withholding life-sustaining treatment: decision not to start or increase a life-sustaining intervention

In clinical practice we can withhold and/or withdraw futile medical treatments when we are in the presence of death. This is different to active euthanasia and assisted suicide. Medical futility should be assessed prior to withholding and/or withdrawing treatments such as vasopressors, ventilator support, cardiopulmonary resuscitation, clinically assisted nutrition or hydration and other medical therapies. When confronted with a potentially futile situation we should ask ourselves whether quantitative, qualitative, physiological, imminent demise or overall futility applies and then direct care accordingly. The answers aren't always clear and clinicians must be comfortable dealing with uncertainties. The patient should be at the centre of all decisions and decision-making should always include the family.

The ethical equivalence of withholding and withdrawal of life sustaining treatment is debated.
The two are equivalent if a treatment is disproportionately burdensome for the patient (will not offer clinical improvement and/or may prolong suffering) because regardless of whether the treatment is stopped (withdrawal) or not started (withheld), the principle (preventing prolonged patient suffering via a non-beneficial therapy) is regarded as the same. This is supported in the guidelines of most critical care societies and medical regulatory bodies.

There are variable definitions of medical futility but essentially it is the unacceptable likelihood of achieving an effect that the patient has the capacity to appreciate as a benefit.
It has both a quantitative and qualitative component. Quantitative futility refers to the likelihood that treatment will confer patient benefit is unacceptably low and this is a medical decision. Qualitative benefit refers to the quality of the resulting patient benefit that is unacceptably low and this is a family/patient value-based decision.

Futility can also be thought of as physiological, imminent demise and clinical/overall futility.
- Physiological futility: intervention is not expected to produce its desired physiologic effect
- Imminent demise futility: medical condition is irreversible, and the patient is expected to die before discharge and not recover interactive capacity before death
- Clinical or overall futility: intervention will not restore the patient's capacity to interact with the environment and continue human development i.e. poor-quality outcome

Medical futility itself is not a widely accepted term as it implies pointlessness or uselessness. It creates the impression that nothing further can be done and although this might be true when considering cure this is not the case for overall care.

The withdrawal process requires multidisciplinary team involvement including social workers and religious/spiritual leaders. All treatments need to be critically evaluated to determine whether they are positively contributing to the care of the dying patient. All non-essential, non-beneficial procedures and medication should be continued.

Medication for pain and symptom control can be given per os, continuous subcutaneous or intravenous routes depending on the patient and clinical scenario e.g. are they able to swallow?

Examples from Providing Palliative Care in South Africa During the COVID-19 Pandemic

PALPRAC

The Association of Palliative Care Practitioners of SA
215-486 NPO
https://palprac.org/

Not anticipating rapid death after withdrawal of ventilatory support:
Approach summary:

1. Gradual scaling down of ventilatory support over 10-30 minutes to allow for the titration of medications to adequately control dyspnoea and anxiety, but not to allow for hastening or prolonging of death.
2. Once comfortable, the patient will require palliative extubation. As this is an airway procedure, this poses a significant risk to staff and the procedure needs to be performed wearing the same PPE as per the Provincial PPE Guideline section on intubation procedure.
3. Ensure neuromuscular blockade agents have worn off.
4. Turn off the multiparameter bedside monitor. Further monitoring and management will be symptom-based not based on vital sign measurement.
5. Stop inotropic infusions.
6. Administer Hyoscine Butylbromide (Buscopan) 20mg IVI or Robinul 200mcg IV.
7. Decrease Pressure Support, PEEP, F_iO_2 every 5 minutes until at 3cm H_2O & 0.21 (Room air – 21% oxygen).
8. If on an opiate infusion, continue the infusion to allow for titration – to convert later to a subcutaneous infusion.
9. Reassess symptoms every 5 minutes whilst titrating down ventilatory setting and administer additional boluses of intravenous morphine; increase the infusion rate if showing signs of breathlessness.
10. Administer bolus of available benzodiazepine if the patient develops restlessness/anxiety.
11. Use patient head coverage at the hospital (same as per intubation procedure).
12. Suction airway using in-line closed suction if available; suction mouth; extubate the patient.
13. Convert to subcutaneous medication via bolus or infusion via syringe driver. See conversion in Addendum 2.
14. Provide oxygen via nasal cannula for comfort as required - patient to wear surgical mask over nasal cannula.
15. Move to the general ward or out of ICU/High Care.
16. Continue care as per detailed End-of-Life Guideline.

Death anticipated to occur rapidly after cessation of mechanical ventilation & inotropic support:

Predictors - high PEEP & F_iO_2 or inotropic requirements or severe acidosis or obtunded.

Approach summary:

1. Gradual scaling down of ventilatory support over 10-30 minutes to allow for the titration of medications to adequately control dyspnoea and anxiety, but not to allow for hastening or prolonging of death. The patient should not be extubated for staff safety.
2. Ensure neuromuscular blockade agents have worn off.
3. Turn off the multiparameter bedside monitor. Further monitoring and management will be symptom-based and not based on vital sign measurement.
4. Stop inotropic infusions.
5. Decrease Pressure Support, PEEP, F_iO_2 every 5 minutes until at 0cmH_2O & 0.21 (Room air - 21% oxygen).
6. If on an opiate infusion, continue the infusion to allow titration.
7. Reassess symptoms every 5 minutes whilst titrating down ventilatory setting and administer additional boluses of intravenous morphine; increase the infusion rate if showing signs of breathlessness.
8. Administer bolus of available benzodiazepine if the patient develops restlessness/anxiety.
9. The patient should not be extubated until after death.

Pain and symptom control

Symptom	Management

Total pain - physical, social, emotional and spiritual pain
• Advantages
  ○ Negates unwanted systemic effects
  ○ Improves functional capacity
  ○ Manages suffering of the patient and their family
• Pain assessment with standard methods can be difficult in the dying patient
• Misconceptions
  ○ Pain management and comfort care can cause adverse haemodynamic and respiratory consequences
  ○ Aggressive pain management in the ICU can lead to opioid addiction
	• Pharmacological
	  ○ Opioids
	  ○ Paracetamol
	  ○ NSAIDs
	  ○ Ketamine
	  ○ Cannabinoids
	  ○ Neuropathic pain medication
	• Interventional
	  ○ Destructive
	  ▪ Alcohol or phenol
	  ▪ Radiofrequency
	  ▪ Surgical
	  ○ Non-destructive
	  ▪ Peripheral blocks
	  • Somatic
	  • Sympathetic

	▪ Central blocks ▪ Local anaesthetics or steroids • Non-pharmacological or complementary therapy o Social, emotional and spiritual care o Acupuncture. Massage, reflexology, aromatherapy, homeopathy etc.
Dyspnoea • Common • Opioids suppress respiratory awareness; does not hasten death	• Opioids • Benzodiazepines • Alcohol • Barbiturates • If bronchodilation required o B_2-agonists o Methylxanthines
Cough	• Opioids • Potassium iodide
Delirium • Environmental measures • Medication to reduce agitation	• Haloperidol
Secretions	• Hyoscine • Glycopyrrolate
Nausea and vomiting	• Anticholinergics - hyoscine • $5HT_3$- antagonists - ondansetron • H_1 antihistamines - promethazine • Neuroleptics - haloperidol • Prokinetics - metoclopramide • NK1- receptor antagonists – aprepitant • Adjuvants – dexamethasone, cannabinoids and benzodiazepines
Anxiety or distress	• Benzodiazepines • Propofol • Opioids
Sedation CNS stimulants	• Methylphenidate • Amphetamines • Modafinil

Other aspects of comfort care

- Assess patient and family resources and needs
- Determine preferred place of death
- Temperature control
- Wound care
- Pressure care
- Clinical assisted hydration and nutrition – provide sips of water and comfort feeding
    - Withdrawal of hydration and nutrition is emotive and debated
    - Too little or too much can be harmful. Individualise patients and take family's wishes into account
    - Mechanisms of providing hydration and nutrition can be distressing and uncomfortable e.g. nasogastric tube

Other ethical and complex issues pertaining to palliative care in the ICU

- Terminal Sedation
    - Terminal sedation aims to relieve intolerable and refractory symptoms in the terminally ill. It should not be confused with euthanasia where the goal is to hasten death. There is no evidence to support that sedation is associated with shorter survival.
- Euthanasia
    - Deliberate intervention undertaken with the intention of ending a life in order to relieve intractable suffering
        - Non- voluntary: killing of a patient who does not have capacity to request or withhold consent. This is considered murder
        - Voluntary euthanasia/assisted suicide:
            - Illegal in RSA
- Pharmacological paralysis
- Balance treating the patient with treating the family
- Presence of family members during resuscitation

Practicalities related to dying on the intensive care unit

Administration

A death certificate can be completed for a patient deemed to have died of natural causes. All unnatural deaths should get an autopsy as per the Inquest Act. If there is any doubt it should be discussed with the forensic pathologist on call.

Organ donation

Organ donation to be considered in the brain-dead patient or for donation after circulatory death if imminent cardiac arrest anticipated after withdrawal of life-sustaining treatment.

Family support and bereavement

Families should be assisted during this difficult time through relaxing unit policies to accommodate the family where possible, good communication, counselling and religious support.

It is important to establish trust prior to anticipated loss. Communication of bad news can have lasting consequences in survivors. Bereavement is determined by circumstances of loss, personality and social circumstances. Make use of available hospital services for assistance.

Kübler-Ross Grief Cycle

- *Denial*
- *Anger*
- *Depression*
- *Bargaining*
- *Acceptance*

Care team self-care

End-of-life care is associated with burnout, moral distress, cumulative grief, counter transference and compassion fatigue. Teamwork, self-care (physical, mental and social), bereavement counselling and spiritual support to care providers are essential.

Perioperative

Anaesthetists will be involved in palliative care when they are involved in critical care units, anaesthesia for palliative surgery, and for pain and symptom control management at the end of life. Palliative care is yet another example of the ever expanding role of anaesthetists as perioperative physicians.

Preoperative period

Anaesthetists are in a unique position to help with the early identification of patients in need of palliative care. Surgery should be preceded by a multidisciplinary team discussion taking into account not only the overall prognosis but also the potential and impact of postoperative complications, deterioration and long hospital stay on the patient's quality of life. Anaesthetists could provide generalist palliative care or advocate for specialist palliative care.

Advanced directives

Advanced care discussions about the patient's wishes, priorities and values should take place prior to high risk surgery. Discuss advanced directives, do not resuscitate (DNR) status and establish mandated proxy or preferred surrogate decision maker. The patient's wishes and preferences should be clearly documented. Advanced directives may change as circumstances change. In South Africa advanced directives are not legally binding but they are especially helpful and can guide decision-making if the perioperative course is complicated and the patient loses his/her capacity.

TYPES OF ADVANCE DIRECTIVES‡	
Living will	Specifies medical treatments—including cardiopulmonary resuscitation (CPR), mechanical ventilation, enteral feeding, dialysis, and antibiotics—that the patient would or would not want used to prolong their life, as well as other decisions regarding pain management or organ/tissue/body donation
Durable power of attorney	A person (with or without alternatives) named to make decisions on behalf of the patient if they are unable to do so
Do not resuscitate (DNR) order	Specific medical order instructing providers not to perform CPR if the patient's heart activity or breathing ceases
Do not intubate (DNI) order	Specific medical order instructing providers not to intubate the patient and/or place him or her on mechanical ventilation
‡**See** *www.lifecaredirectives.com*	

Perioperative Do Not Resuscitate order

Cardiopulmonary resuscitation is standard of care for cardiac arrest. It can only be withheld based on a physician's do not resuscitate (DNR) order or clear documentation of the patient's wishes.

Advanced directives and DNR orders are not routinely suspended perioperatively that presents challenges that include:

- Cardiac arrest can occur as a complication of surgery/anaesthesia as opposed to the patient's natural progression of disease
- Endotracheal intubation could be indicated for a specific surgical procedure
- Vasopressors may be indicated for brief periods to negate the effects of anaesthetic agents

It is for these reasons that conditional suspensions or waivers can be negotiated and clearly documented for the perioperative period. Negotiation outcomes can include maintaining DNR status, waiver of DNR status perioperatively, accept certain measures but refuse others or delegate to anaesthetist/surgeon to decide on appropriateness of interventions

In the scenario where full DNR status must be honoured perioperatively, the patient should be informed about the implications thereof. The physician can medically object to providing treatment deemed inconsistent with standards of care or morally object on personal grounds. If a physician

objects on moral grounds the patient's treatment must not be delayed as a consequence and an alternative willing treating team should be arranged.

Consent

Valid consent should be obtained. The patient should be aware of all risks, potential complications and medical alternatives available to them.

The consent process may be complicated in the terminally ill if they lack decisional capacity. There are variable definitions of capacity as various role players (social, political, practitioners, public health) view capacity differently based on age, individual, context and the evolution thereof.
Legal capacity consists of both age and decisional capacity. The age of full legal capacity is 18 in South Africa. It is presumed that adults have decisional capacity and that minors lack decisional capacity. A patient with decisional capacity has the ability to understand relevant information, appreciate the consequences (risks and benefits), reason and make decisions about treatment. Capacity can be decision specific and fluctuate over time.

It is difficult to assess decisional capacity. A patient's reasoning process is assessed rather than the actual choice made. The four generally accepted decision-making abilities that constitute capacity are: understanding, expressing a choice, appreciation and reasoning. There are unvalidated adult assessment tools available but there aren't agreed upon standards and criteria. Careful documentation of this process is essential.

Patients who lack decisional capacity should always remain involved in their management if possible. Honour advanced directives if appropriate to the clinical context and there is no reason to believe the patient has subsequently changed their mind. In the absence of an advanced directive or an irrelevant advanced directive a surrogate will make decisions on the patient's behalf. In order of precedence the surrogate can be a patient's mandated proxy, person authorised by law or court order, spouse or partner, parent, grandparent, adult child or a sibling. In the absence of a surrogate the healthcare professional will be expected to act on the patient's behalf adhering to the best interest principle.

Chronic medication

It would not be uncommon for these patients to be on multiple agents both for disease management as well as pain and symptom control. The impact of these drugs perioperatively should be taken into account e.g. chemotherapy, chronic opioids etc.

Intraoperative

Patients will commonly present for palliative or emergency procedures.

This particular group of patients could have increased opioids requirements and increased risk of postoperative delirium.

Postoperative

Total pain and symptom control management – see ICU

Conclusion

Palliative care should be practiced in parallel to other aspects of care. The demand for palliative care outweighs the availability of palliative care physicians and it is therefore up to us to equip ourselves with generalist palliative care skills to provide this service to our patients.

Anaesthetists as perioperative care physicians are uniquely positioned to assist with the early identification of patient's in need of palliative care, provide appropriate symptom and pain control management and to be advocates of patient's wishes perioperatively.

"You matter because you are you. You matter to the last moment of your life and we will do all we can not only to help you die peacefully but to live until you die" – Dame Cicely Saunders – founder of the first modern hospice

With special thanks to Dr Rene Krause, Dr John Turner and the Groote Schuur ICU consultant body for sharing resources and providing input during my preparation of these lecture notes.

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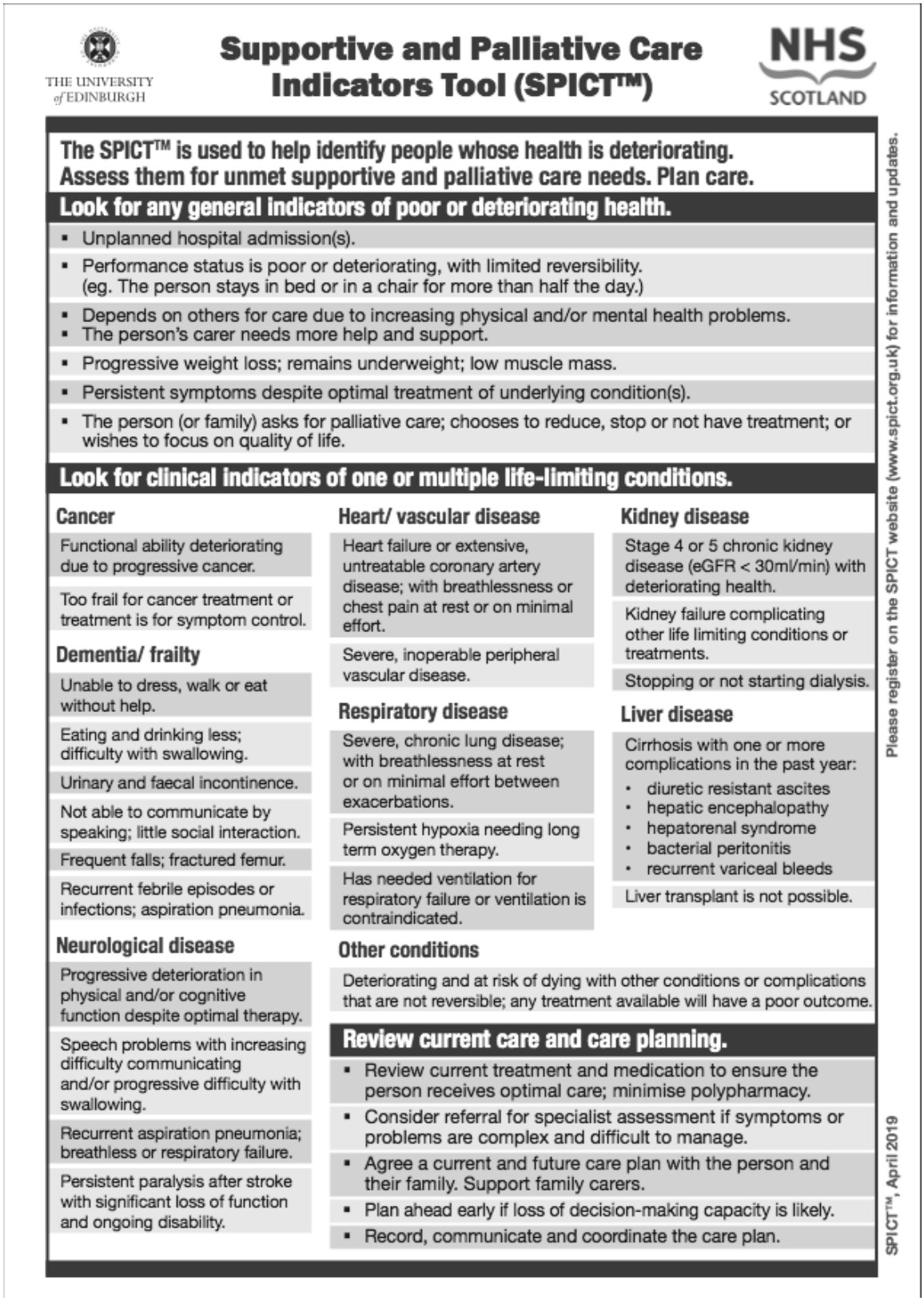
    b. Palliative care in the ICU – Dr John Turner
    c. Why Palliative Care is relevant to anaesthesiologists (and vice versa) – SASA 2016
    d. Let's talk about Death – making end of life decisions, even for the young – Dr Ivan Joubert; 2019 CCSA refresher course

Annexure A



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Supportive and Palliative Care Indicators Tool (SPICT™)

NHS SCOTLAND

The SPICT™ is used to help identify people whose health is deteriorating. Assess them for unmet supportive and palliative care needs. Plan care.

Look for any general indicators of poor or deteriorating health.

- Unplanned hospital admission(s).
- Performance status is poor or deteriorating, with limited reversibility. (eg. The person stays in bed or in a chair for more than half the day.)
- Depends on others for care due to increasing physical and/or mental health problems.
- The person's carer needs more help and support.
- Progressive weight loss; remains underweight; low muscle mass.
- Persistent symptoms despite optimal treatment of underlying condition(s).
- The person (or family) asks for palliative care; chooses to reduce, stop or not have treatment; or wishes to focus on quality of life.

Look for clinical indicators of one or multiple life-limiting conditions.

Cancer

Functional ability deteriorating due to progressive cancer.

Too frail for cancer treatment or treatment is for symptom control.

Dementia/ frailty

Unable to dress, walk or eat without help.

Eating and drinking less; difficulty with swallowing.

Urinary and faecal incontinence.

Not able to communicate by speaking; little social interaction.

Frequent falls; fractured femur.

Recurrent febrile episodes or infections; aspiration pneumonia.

Neurological disease

Progressive deterioration in physical and/or cognitive function despite optimal therapy.

Speech problems with increasing difficulty communicating and/or progressive difficulty with swallowing.

Recurrent aspiration pneumonia; breathless or respiratory failure.

Persistent paralysis after stroke with significant loss of function and ongoing disability.

Heart/ vascular disease

Heart failure or extensive, untreatable coronary artery disease; with breathlessness or chest pain at rest or on minimal effort.

Severe, inoperable peripheral vascular disease.

Respiratory disease

Severe, chronic lung disease; with breathlessness at rest or on minimal effort between exacerbations.

Persistent hypoxia needing long term oxygen therapy.

Has needed ventilation for respiratory failure or ventilation is contraindicated.

Kidney disease

Stage 4 or 5 chronic kidney disease (eGFR < 30ml/min) with deteriorating health.

Kidney failure complicating other life limiting conditions or treatments.

Stopping or not starting dialysis.

Liver disease

Cirrhosis with one or more complications in the past year:

- diuretic resistant ascites
- hepatic encephalopathy
- hepatorenal syndrome
- bacterial peritonitis
- recurrent variceal bleeds

Liver transplant is not possible.

Other conditions

Deteriorating and at risk of dying with other conditions or complications that are not reversible; any treatment available will have a poor outcome.

Review current care and care planning.

- Review current treatment and medication to ensure the person receives optimal care; minimise polypharmacy.
- Consider referral for specialist assessment if symptoms or problems are complex and difficult to manage.
- Agree a current and future care plan with the person and their family. Support family carers.
- Plan ahead early if loss of decision-making capacity is likely.
- Record, communicate and coordinate the care plan.

Please register on the SPICT website (www.spict.org.uk) for information and updates.

SPICT™, April 2019

SPICT™ THE UNIVERSITY of EDINBURGH

Why use the SPICT™?

The SPICT™ helps professionals identify people with general indicators of poor or deteriorating health and clinical signs of life-limiting conditions for assessment and care planning.

What will happen to each person and when is often uncertain. SPICT™ looks at health status not a prognostic time frame. Identifying people with deteriorating health earlier improves care.

Using SPICT™ to assess people's needs and plan care.

■ After an **unplanned hospital admission** or a **decline in health status**: review current care, treatment and medication; discuss future options; plan for managing further deterioration.

■ For people with **poorly controlled symptoms**: review and optimise treatment of underlying conditions, stop medicines not of benefit; use effective symptom control measures.

■ Identify people who are **increasingly dependent on others** due to deteriorating function, general frailty and/or mental health problems for additional care and support.

■ Identify people (and caregivers) with **complex symptoms or other needs**; consider assessment by a specialist palliative care service or another appropriate specialist or service.

■ Assess **decision-making capacity**. Record details of close family/ friends and any POA or proxy for decision-making and involve them if the person's capacity is impaired.

■ Identify people who need proactive, **coordinated care in the community** from the primary care team and/or other community staff and services.

■ Agree, record and share an **Advance/ Anticipatory Care Plan;** include plans for emergency care and treatment if the person's health (or care at home) deteriorates rapidly or unexpectedly.

Talking about future care planning

■ Ask:
- What do you know about your health problems and what might happen in the future?
- *'What matters'* to you? What are you worried about? What could help with those things?
- Who should be contacted and how urgently if your health deteriorates?

■ Talk about:
- The outcomes of hospital admission and treatments such as: IV antibiotics; surgery; interventions for stroke, vascular or cardiac disease; tube or IV feeding; ventilation.
- Treatments that will not work or have a poor outcome for this person. (eg. CPR)
- POA or proxy for decision-making in case the person loses capacity in the future.
- Help and support for family/ informal caregivers.

Tips on starting conversations about deteriorating health

- ***I wish*** *we had a treatment for…., but could we talk about what we can do if that's not possible?*
- *I am glad you feel better and* ***I hope*** *you will stay well, but* ***I am worried*** *that you could get ill again…*
- ***Can we talk*** *about how we might manage with not knowing exactly what will happen and when?*
- ***If you*** *were to get less well in the future, what would be important for us to think about?*
- ***Some people*** *want to talk about whether to go to hospital or be cared for at home….*

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Obligations of Private Practice

Dr Dirk van Zijl

Southern Anaesthetics Associates and SASA PPBU

This brief overview is partly to provide content so as to fulfil the obligations of the college syllabus as set out in domain 12 of the FCA (SA) curriculum listed on the last page of these notes.

In reality though, the majority of FCA (SA) candidates will eventually end up in some form of private practice and for this reason it is crucial that every Anaesthesiologist knows the requirements, laws and regulations needed to not only be successful, but also to make sure that they don't find themselves on the wrong side of the law, the taxman or the regulators.

South African Society of Anaesthesiologists (SASA) has for the past twelve years had a Private Practice Business Unit (PPBU) that has built up volumes of useful information regarding all the topics needed for those in private practice. Two of the most important documents are the SASA Practice Guidelines (2018 Revision) and the SASA Private Practice & Coding Guidelines (2019 Version). Both are freely available and links are provided in the references.

In addition, SASA PPBU runs regular one-day road shows around the country concentrating on practice management and presents workshops and a dedicated refresher course stream at every national SASA congress. Advanced and specialized resources are available on the member portion of the SASA website for all those who are PPBU members. The PPBU is very active in all spheres of private practice and serves member's interests, and is willing and capable of dealing with any member query. Dr Karmelle van Rensburg (a recent SASA registrar representative, and current council member and new PPBU member) has made herself personally available to anyone wanting advice on starting or joining an existing private practice. (Contact details in the acknowledgements on the last page).

Whilst you will need a trained expert when it comes to the final planning needed in the areas of accounting, taxation, income protection, staff issues and retirement planning – it is well within the capacity of each Anaesthesiologist to grasp and understand the basics. There should be no reason why anyone should be making the mistakes that many others (who did not have easy access to this information) made in the past. Everyone will have their own unique set of circumstances but for the majority these issues will be common to all.

Joining a practice or starting out on your own can be very daunting. A thorough analysis of the market in the area you want to work would be useful in establishing whether there is scope for a new practitioner. Speaking to the established practices in a particular area is a good start. In many places in South Africa (like the southern suburbs of Cape Town) the market is completely saturated with Anaesthesiologists and the prospects for new work for a new practitioner are very small, but there are other areas of South Africa where there is a dire shortage of Anaesthesiologists.

Practice structures vary greatly, and you should familiarise yourself with both the entry and the exit strategies for each unique arrangement. How does a practice resolve conflict resolution, is there a leave policy, what are the admission costs (if any), what is the probation period – these are all very important questions to ask long before you think of making a move into an established practice. SASA PPBU road shows deal with these issues on a regular basis.

Here are some general life philosophies and tips that can help you along:

You are about to start a business.
You have never received any training on how to run a business, so you need to learn and learn fast!
Your business is selling time!
Only you can do your job and you can only bill when you're working.
Arrange your life to become time efficient.
You are in-charge and completely responsible for everything.
Know and understand how every part of your practice and life works (billing, tax, retirement annuities, cash flow.) And check on it all the time.
Keep reading, learning and up to date with everything.
Use a trained expert to deal with each specialist area.
Tax advisers do tax, Insurance brokers do insurance, and anaesthetists give anaesthetics.
Watch your wallet.
You are going to need to pay for everything all the time.
Know what comes in, where it goes and why it's going there.
You will need systems for everything.
Copy other people's systems, adapt them to suit yourself and let everyone working with you know the system. SASA PPBU can give you lots of examples.
Hire slow – fire fast.
It's not worth working or persisting with staff or surgeons you don't like, can't work with or trust.
Choose your surgeons carefully - you may spend more time with them than your family.
Unlike public sector, surgeons call the shots, but it's not an adversarial relationship.
Become technologically efficient.
Don't use technology just because it's there but for what it gives you and the time it buys you.
Give yourself regular predictable time off. Plan leave, holidays and days off well ahead of time.
You can't work 24/7 365 days. Ring fence some time where you don't work each week.
Don't be afraid to say "NO", you need to look after yourself, and find "balance"
Maintain your reputation, be punctual and accommodating.
Work can dry up very quickly. You are as good as your last anaesthetic.
Find a mentor, friend, partner or confidant with whom you can discuss any aspect of your business with.
It's very lonely working for yourself and by yourself and you will have lots of questions about all sorts of aspects of your business and life.

1. The things you need to start a practice (business)

A knowledge of anaesthetics
The easiest part of your whole life and something you need no advice on: It is what you have trained for and understand. Your success depends on the 4 A's in this order:
Availability
Ability
Affability
Affordability

The Practice
Practices are run on systems. If they are not working, change them.

Paperwork
- *Patient information*: This can be given in a form of a leaflet which one emails to patients in advance or a website which one can refer their patients to. This information should contain who you are and what your responsibilities are, types of anaesthetics, risks and complications and general information related to the preparation towards one's anaesthetic.
- *Anaesthetic consent*: which relates to the procedure and complications that could possibly occur.
- *Financial consent:* Section 6 of National Health Act reads that "*every health care provider must inform a user of, inter alia, the benefits, risks, costs and consequences* of treatment options". This means that part of your consent must contain (in Rands and cents) a cost estimate on an hourly basis of what the Anaesthetic service is likely to cost.
- *POPI consent:* patients have to give you permission in terms of the storage of personal and medical information in accordance with Protection of Personal Information (POPI) Act.

- *Cost estimates:* this is very different terminology to a "quotation" which is a final amount for a service rendered. Successful practices have a system in place where cost estimates are supplied to the patients well in advance of their planned surgery, or produced at the bedside in cases of unplanned surgery.
- *Mediation:* try and get the patient to consent to mediation as the first resort of resolving a complaint.
- *SASA GREEN FORM:* this anaesthetic consent form is a free source to SASA members and offers a template for obtaining all forms of consent and includes clauses on mediation and POPI.
- *Billing:* will depend on your billing system or outsource billing company.
- *Notes:* You will need a system to take and store notes for each anaesthetic.

Staff

This depends on your personal circumstances - some doctors/anaesthesiologists do all their own admin, some outsource it all, some employ family, some do a mix of the above. Staffing can be an absolute nightmare if the wrong person is employed or disciplinary issues rear their ugly head. A thorough knowledge of the basic conditions of employment, the Labour Act, how to perform proper staff appraisals, the correct procedure to follow when it comes to disciplinary issues, dealing with unions and labour relations - these are all important issues way beyond the scope of this presentation. It is also the reason why the majority of SASA PPBU members outsource all of their accounts – so they don't have to personally deal with staff issues! It is important to remember that the staff you employ are a reflection of the service you provide, and that the HPCSA can hold YOU liable for their actions if something unethical is done.

Billing

- This can be done by yourself, a billing company, an employed staff member, family…
- There are strict rules that need to be followed as to what you can charge for and how a bill is structured. (Set out by the HPCSA). YOU MUST KNOW AND UNDERSTAND THESE.
- Read through the SASA Coding Guidelines 2019 before you even start. Basically, a bill consists of a series of codes related to a procedure, which have a number of units attached to them. Each unit gets a rand value that you must determine.
- You will bill a code for: the premed + a code for the procedure + a code for the time taken + any other modifiers that the patient may have, or you may have done. (Extremes of age, obesity, orthopaedics, CVP, blocks, ICU etc.)
- You have to determine your own billing policy and rates.
- There are no longer "medical aid rates", though medical aids all have their own unique rate.
- Get a system in place for unpaid, partly paid accounts, bad debts, etc.
- You need a system for reminders to pay, outstanding balances and refunds and to check your accounts.
- Don't expect the medical aids to be helpful, pay the bill in full or get the coding and payment correct.
- Billing needs a lot of telephone time so make sure whoever does your accounts has time available to spend hours on the phone contacting medical aids and patients.
- Sign a contract with your billing staff based either on a fixed monthly fee or a percentage of each account paid to you. Ensure your contract includes responsibilities and costs for chasing bad debt, unpaid accounts, weekly reconciliation of accounts, accounts to be written off and legal fees. Ensure your contract has a method of terminating your relationship with the billing company and the costs thereof.
- SASA PPBU has developed a very useful toolkit to evaluate a billing company.

Checks and balances on staff and billing

Have your own separate system to follow payments against what's billed and outstanding so you can see if your billing company is doing their job.

Watch out for fraud

- Get patients to only pay into your account and you send statements to your billing agency.
- Check your billing daily.
- Cash is a fraud risk.
- Wait at least a week to do refunds for any payment to avoid "reversed payment" scams.
- Fraud amongst staff working for health care providers is a lot more common than you think.

- Ideally, the person dedicated to *reconciling* the payments should be different to the person generating the account.

Bank accounts

- Use a dedicated bank account for your practice that is easily accessible for payments by patients via EFT. This means you only have practice transactions on this account, saving you time when you send your billing company statements.
- Cash and credit cards cost money to deposit so avoid them.
- Have a dedicated credit card account for your practice and use it for all your practice expenses, it gives you a record for your accountant and makes reconciliation easy.
- Have your own account into which you can pay yourself. You don't need expensive business or private banking accounts.

Data storage

Back all your practice related things up to the cloud and a portable hard-drive daily or at least weekly.

Websites

Look at other practice websites for ideas, and a place to provide information. Examples are:
http://www.southernanaesthetics.co.za/associates/associates-dvz.html
http://www.dunkeldanaestheticpractice.com/dr-ernest-welch/

Complaints

- You will get complaints! The commonest is about billing! But they could be about your anaesthetic as well.
- Develop a system to handle these that everyone in the practice is familiar with.
- Go to MPS courses on handling complaints to learn how to deal with them.
- Call someone to give you advice on how to handle specific cases.
- SASA PPBU is a very helpful resource.
- My system is: *A complaint is received either via my rooms or via my website complaint form.*
- *I handle all complaints personally. I usually phone the complainant as soon as possible and see if we can sort it out immediately. (This is usually enough to sort out the majority of complaints). If not, I suggest they escalate it to SASA to give a ruling and attempt mediation. I also then inform my insurers.*

2. Insurance

You will need insurance to cover a variety of situations that may arise during the course of your working and private life. Update and reassess it every year or when your circumstances change. Ensure they are all current and paid up at all times. Use professionals to help you here. These are some that I think are non-negotiable.

- Malpractice insurance – Don't practice without it!
- Medical aid - even as a doctor.
- Income protection – You will only earn money when you are working. Your expenses don't go away if you can't work through illness or injury. Ensure it's enough to cover at least your living and ongoing practice expenses. I suggest taking out dreaded disease and occupation specific cover as well.
- Disability insurance – you are probably more likely to be disabled and not be in a position to perform your chosen profession than dying before age 65.
- Life insurance – especially if you have dependents or a bond or debt.
- Public liability insurance – if you have a place where people may come to see you for any reason, even if it's at home.
- Cyber liability insurance – covers you if your bank accounts get hacked.
- Insuring your possessions – You need a car to get to work, make sure you have arrangements if you are suddenly without one.

3. Income Tax

South Africa has a progressive tax system where you pay more tax the more you earn.

- Up to R 700 000 income per annum you pay an average of 30% while the maximum tax rate is 45% if your income is above R 1.5 million per annum.
- Income and turnover (know the difference)
- Turnover is the total amount of money you bring in.
- It is the value of all the payments from all your accounts. It excludes your expenses and VAT, so IT IS NOT WHAT YOU EARN or have to live on.
- Income is what you have to live on and what you will pay tax on.
    - Income = Turnover - VAT - Expenses
    - What you will take home = Income – TAX
- *For example, if your turnover is R 1 000 000 for the year*
    - *Income = R1 000 000 – (R150 000 (VAT) + R500 000 Expenses) = R 350 000*
- *You will take home R350 000 – R100 000 (tax) = R 250 000 or R 20 800 per month*
- You will have to register as a provisional taxpayer as you will no longer get a salary and have someone deducting pay as you earn tax from your salary (PAYE).
- Provisional taxpayers pay tax 3 times a year, not monthly.
- You will pay 2 tax amounts. The first in August and the second in February in advance of the next tax year based on a prediction of your income for the next year and then a third (top-up) payment the following September. The tax year runs from 1 March to 28/29 February the following year and is named after the coming year. We are now in the 2021 tax year even though it's still 2020.
- As you start to earn more these amounts will rocket upwards especially once PAYE is no longer included in the predictions for your future tax payments after about 12 months in private practice. Make sure you have the money available to pay this. It may be more than R250 000 per payment.
- Tax expenses:
- You can deduct expenses that are required to run your practice from your turnover, thus decreasing your tax payment.
- Ask you accountant for a list of these (insurance, stationary, car, petrol, home office, etc.)
- You need to keep a record of all of these and the receipts.
- It is easier to do this with a dedicated practice credit card for ease of record keeping.

4. VAT

- You will have to register for VAT once your turnover reaches R1million per annum
- You will then pay 15% VAT on every rand you bill.
- This is paid every second month by the 25th of the month as a lump sum.
- Make sure you have saved 15c in every rand that you bill in an easy to access account as the penalties for late or non-payment of VAT (and tax) are severe.
- You can deduct legitimate VAT expenses from this amount so make sure you have a system of recording all your expenses and keep the receipts if you need to prove them. Unfortunately, this is always a small amount and it makes very little difference to your 15c in the rand you need to pay.

5. Managing cash flow

As you are now paying for everything you will need large sums of money available at regular intervals. Remember up to 60 cents in every Rand of turnover does not belong to you, it's the government's that you are collecting for them.

- 50% rule – You need to save 50c of every Rand you bring in just to pay tax (35% average) and VAT (15%). Once you turnover is more than 1 million rand a year this increases to 60%.
- If you have a bond, put it in there until you need it. Its easily accessible, you pay off your bond quicker and effectively make 8% interest on your tax money for each month it sits there. If you have no bond put it in a money market account that you can give short notice to when you need it.
- Monthly expenses – work out what they are and ensure you have sufficient available money to cover these.
- Paying certain things like Insurances annually can save you up to 10%.

- Pay yourself – Work out a budget what you can afford to pay yourself so that you can save to buy things you want, but don't use your tax money for this and expect to pay it back.
- Emergency fund - You need at least 3 months' expenses available at short notice to cover emergencies, which can be kept in something like a money market account.
- Don't go buying new cars or houses until you have paid 2 years' tax bills and built up an emergency fund. REMEMBER YOUR TURNOVER IS NOT WHAT YOU EARN!!!

6. Retirement / Investments

You will need to take responsibility for your retirement funding as there is no one to pay you a pension. Get a financial advisor to help here. Start saving today!

- There are many different formulas used to calculate what you need for retirement. A popular calculation is that for every R 1 million of assets you have available at retirement you will have R 3 500 a month to live on. This excludes your car and house. Work out how much you may need to cover your living expenses at today's cost of living. To get how much you need to save for retirement, double it for every 12 years you are away from retirement.
- *(E.g. If you need R 20 000 a month at present you will need to have at least R 5.75 million available to retire today. If you are 29 years old you are 36 years or 3 doubling times away from retirement. Therefore you need 5.75 x 2=11.5 x 2= 23 x 2 = R 46 million at retirement in 36 years' time)*
- Retirement annuities – Are a tax efficient mechanism to save 27% of your income up to R 350 000 a year. But look at the costs and restrictions before settling on one. Rather go for a lower monthly payment into a retirement annuity, and then "top up" twice a year depending on your income. Remember that 25% of your retirement annuity can be invested offshore.
- Tax-free savings accounts allow another R 33 000 to be saved each year free from tax – use them.
- Get a financial advisor.
- Go read Warren Ingram's books "How to become your own financial advisor" and "How to make your first million" and then keep up to date. "Rich Dad, Poor Dad" series by Robert Kiyosaki also contain solid references for basic financial planning.

7. Will and Estate planning

- Get a will drawn up preferably by a lawyer in conjunction with your financial advisor.
- Make a list of all your financial instruments and who to contact if someone else needs to do this on your behalf.
- Tell your dependents – executor where to find this information.
- Negotiate on executor fees whilst you are alive and still have the chance.

8. Steps to starting your Sole Private Practice

- Register as a Specialist Anaesthesiologist with the HPCSA. This can only be done in your last month of Registrar time (month 48) and once all requirements are completed (FCA 2 plus MMed)
- Open a Business Account
- Register with the BHF to obtain a practice number. One needs to register with your business account information and if possible, with your billing company's details if one is going to utilise them. It becomes challenging to change details later.
- Register with the various Medical Aids if you want to sign contracts for payment arrangements e.g. Discovery Classic payment arrangement, Fedhealth, etc.
- Ensure your Medical Malpractice insurance is correct for your level of turnover and active before you start your first case.
- Ensure you are registered correctly with SASA and have paid your PPBU levy.
- Prepare paperwork / stationery - draft your patient information leaflets, consent forms, anaesthetic charts and billing Sheets.
- Plan how one is going to organise your patient records according to file numbers and how one is going to digitalize the documentation, whether you are going to do paper base and scan or go paperless from the start. This is an ever-evolving system.
- Look Professional:

- Design a logo / letter head / business cards for your business. If needs be, use a graphic designer to assist.
- Create a domain email, this is not expensive (+/- R19/ month) and looks professional for patients and surgical staff.
- E.g. Patientinfo@drkvanrensburg.co.za and Theatrelists@drkvanrensburg.co.za

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Dr Ernest Welch, for the use of his 2018 Refresher Course notes. Ernest is in private practice in Johannesburg, Dunkeld Anaesthetic Practice. http://www.dunkeldanaestheticpractice.com/dr-ernest-welch/

Dr Karmelle van Rensburg, for her review and offer of personal assistance to new graduates starting out in private practice. Karmelle is in private practice in George, and a recent member of the SASA PPBU. Karmelle.vrensburg@gmail.com

Conflicts of interest

I have been in full time private practice with Southern Anaesthetics since August 2006. I was a founding member of the SASA PPBU in 2008 and have been actively involved ever since, serving twice as convenor. I have just completed seven years on SASA national council, where I served one term as SASA president. I have in the past acted as an expert witness and advisor for MPS in the defence of SASA members. I have no financial or other interests in any companies (medical, administrative, billing, etc.) other than those traded on the JSE.
http://www.southernanaesthetics.co.za/associates/associates-dvz.html

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College syllabus as set out in domain 12 of the FCA (SA) curriculum:

Organisation and Business Management of Individual Practice

The trainee will understand the organisation and management of a medical practice such as the following.

- Requirements of entering private practice
    - HPCSA rulings
    - Board of Health Care Funders
    - Council of Medical Schemes
    - National Health Act w.r.t. regulations to fee discussions
    - National Credit Act
- Principles of business management
    - Accounting
        - Budgets
        - Cash Flow
        - Balance sheet
        - Income and expenditure
        - Data collection and generation of reports
        - Prevention of fraud
        - Credit control
    - Taxation planning
        - VAT
        - Provisional tax
        - PAYE
        - Regulations re tax relief on pension contributions, travel and subsistence allowances etc.
    - Income protection insurance
    - Staff employment
        - Basic conditions of employment
        - Labour Act
        - Appraisals
        - Disciplinary issues
        - Unions and labour relations
    - Group / Associate / Sole practice
    - Computerised systems and practice management software
    - Retirement planning
- Time management strategies in determining methods of practice management
- Paid and pro bono work in the profession

The Role of Enhanced Recovery After Surgery (ERAS) in Thoracic Surgery

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Lecture outline:

1. The history of ERAS
2. The physiology of ERAS
3. The aims of ERAS (general and thoracic)
4. ERAS in South Africa

Prolonged hospital stay increases morbidity, mortality and cost. Enhanced Recovery After Surgery (ERAS) aims at enhancing recovery and shortening hospital stay after surgery. It is an evidence-based, multimodal, protocolized initiative targeting all perioperative stages.

1.The history of ERAS[1,2]

In 1994, it was found that "Fast Tracking" of cardiac surgery patients reduced intensive care stay.[3] Subsequent research showed reduced recovery times in sigmoid resection patients,[4,5] through a multimodal approach which included epidural analgesia, to improve mobility and reduce postoperative ileus. Around the same time, the benefits of metabolic support through nutrition and limitation of nil per os times became apparent.[6,7] Between 2001-2005, the ERAS® Study Group and subsequently the ERAS® Society were formed with the mission to "develop peri-operative care and to improve recovery through research, education, audit and implementation of evidence-based practice". The ERAS® Society was officially registered as a non-for-profit medical society in 2010.[2] The first ERAS® consensus protocol was published in 2005.[8] This was specific to colonic surgery. Protocols for many other types of surgery followed over the next 15 years. These include guidelines for rectal surgery[9], colonic resections[10], pancreatic resections[11], radical cystectomy[12], gastric resection[13], gynaecology,[14,15] bariatric surgery[16], liver resection[17], head-and-neck cancer surgery[18] breast reconstruction[19], thoracic surgery[20] and cardiac surgery[21].

2.The physiology of ERAS[22]

Surgical stress results in metabolic, haematological, immunological and endocrine responses. These lead to hypothalamic-pituitary-adrenal axis activation with increased cortisol, growth hormone, glucagon and catecholamine levels which increase inflammatory cytokines (Il1 and Il6) and cause insulin resistance. Reduced insulin sensitivity prolongs length of hospital stay, increases the incidence of serious postoperative complications and disturbs protein balance which results in decreased lean tissue mass with resultant decreased wound healing, immune function and muscle strength required for coughing and mobilization. Patients with altered metabolic states and reduced reserves (elderly, cancer patients, diabetics etc) often suffer severe catabolism in the perioperative state, owing to their reduced baseline reserves.

Insulin resistance is reduced through several ERAS principles. Preoperative carbohydrate loading and minimization of preoperative fasting shift cellular metabolism to an anabolic state and reduce insulin resistance. Epidural analgesia blocks pain pathways, limiting the catabolic response to tissue trauma and insulin resistance. Early feeding and perioperative glycaemic control further reduce insulin resistance.

Salt and water retention results from catabolic hormones and inflammatory mediators. Water overload impairs anastomotic integrity, causes ileus and increases prolonged hospital stay. Many perioperative factors influence water balance. These include preoperative fasting, bowel preparation, intermittent positive pressure ventilation, vasoactive drugs, regional anaesthesia, haemorrhage and sepsis. For this reason, fluid balance comprises a vital part of ERAS protocols.

Surgical stress is caused by direct tissue trauma but also by bleeding and fluid shifts, positive pressure ventilation, drugs with vasomotor effects, patient positioning, hypothermia, CO_2 pneumoperitoneum etc. Minimizing the stress response can be achieved through minimally invasive surgical techniques and close attention to optimizing these perioperative contributors to the surgical stress response.

Major surgery initiates the release of reactive oxygen species which damage lipids, proteins and DNA, resulting in cellular injury and compromised vascular permeability. Corticotropin-releasing hormone inhibits bowel function through an inflammatory response. Together with excessive fluid administration, this can result in interstitial oedema with delayed recovery of gastrointestinal function (ileus) and impaired healing of anastomoses. ERAS principles aim at reducing perioperative stress and inflammation in order to enhance gastrointestinal function and to limit ileus. Prevention of postoperative nausea and vomiting forms an important part of ERAS principles and further aims to enhance recovery of gastrointestinal function and fluid balance, ultimately enabling earlier hospital discharge.

Surgery results in the release of mediators responsible for the acute pain response. Pain results in anxiety, insomnia, disorientation, myocardial ischemia, atelectasis, pneumonia, hypoxia, paralytic ileus, decrease urinary output, thromboembolic phenomena, insulin resistance, decreased wound healing, infection, sepsis, and many other conditions which ultimately reduce mobilization and oral feeding and prevents early discharge. Multimodal analgesic strategies target the many different nociceptive sites to reduce postoperative pain, reduce surgical stress and attenuate organ dysfunction induced by uncontrolled pain, reduce opioid side effects, enable resumption of oral diet and early mobilisation to reduce length of hospital stay.

The neurohumoral surgical response results in postoperative cognitive impairment and delirium, especially in the elderly. This results in delayed discharge from hospital. ERAS principles attempt to minimise this through depth of anaesthesia monitoring, multimodal analgesia and the limited use of benzodiazepines and opioids.

Prolonged bed rest reduces cardiac function, pulmonary complications and results in muscle atrophy, loss of bone density, insulin resistance, thromboembolic phenomena, microvascular dysfunction, pressure sores and depression. ERAS encourages early mobilization through early removal of catheters and drains, adequate analgesia, prevention of nausea and vomiting, early oral intake and nutritional support, the use of short half-life drugs in the perioperative period and prescribed postoperative exercise programmes.

The ERAS principles aim at reducing the stress response of the body with the ultimate benefits of reduced length of hospital stay[23], reduction in major complications[24], reduction in onset of chemotherapy for cancer patients, cost savings[25] and reduced long-term mortality[26,27]

3.The aims of ERAS in general[1,20] and thoracic surgery[20]

As mentioned before, ERAS guidelines have been described for many different types of surgery. In 2019, the European Society of Thoracic Surgeons (ESTS) published a guideline specific to thoracic surgery.[20] The reader is encouraged to review the guideline. Many of these items correlate with general ERAS principles. They developed 45 evidence-based recommendations. Some might have an individual impact, while others have a synergistic effect when used in conjunction with other recommendations. The following provides a summary of general ERAS principles compared to the recommendations of the ERAS in Thoracic Surgery guideline.

General ERAS principles and ERAS in thoracic surgery		
Aim	**General ERAS guidelines**	**Thoracic surgery ERAS guideline**
Pre-admission phase		
Preadmission information Counselling leads to reduced fear, reduced postoperative pain and early discharge.	Dedicated preoperative counselling	Dedicated preoperative counselling
Nutrition Adequate nutrition leads to reduced insulin resistance and catabolism.	Preoperative nutritional screening and support (especially for malnourished patients)	Screening of nutritional status (Nutritional Risk Score – NRS; Malnutrition Universal Screening Tool – MUST; Subjective Global Assessment – SGA tool) and weight loss Oral supplements for malnourished patients
Smoking cessation Reduction in postoperative pulmonary complications BUT a delay in cancer surgery might result in cancer progression.	At least 4 weeks prior to surgery Intense preoperative pulmonary physiotherapy might be as effective	At least 4 weeks prior to surgery
Cessation of excessive alcohol intake Apart from chronic effects, excessive alcohol consumption impairs cardiac and immune function and blood clotting perioperatively.	Alcohol intake cessation in alcohol abusers (4 weeks prior to surgery)	Alcohol intake cessation in alcohol abusers (4 weeks prior to surgery)
Anaemia • Preoperative anaemia results in postoperative morbidity and mortality • Long-term cancer survival is reduced after blood transfusion	Correct anaemia preoperatively	Correct anaemia preoperatively Treat iron deficiency to reduce the need for erythropoiesis-stimulating agents or blood transfusion (both associated with poorer outcomes for cancer patients) There is no outcome difference between preoperative and intraoperative blood transfusion.
Pulmonary pre- and rehabilitation Pulmonary prehabilitation to	Aerobic exercise Strength training	Especially in patients with borderline lung function or exercise capacity

enhance functional capacity (as per the 6-min walk test) can reduce length of stay and postoperative complications.	Respiratory exercises	
Optimise medical conditions preoperatively Hypertension, ischaemic heart disease, hypercholesterolaemia, chronic obstructive airway disease, diabetes mellitus etc.	Reduces postoperative complications	Reduces postoperative complications
Preoperative phase		
Fasting Prolonged fasting causes fluid shifts, catabolism and insulin resistance	Follow NPO guidelines Allow fluids up to 2 hours preop	Follow NPO guidelines Allow fluids up to 2 hours preop
Carbohydrate loading Reduces postoperative insulin resistance	Carbohydrate loading recommended	Carbohydrate loading recommended
Premedication: Anxiolytics may cause postoperative cognitive impairment and delirium.	Avoid over-sedation with premedication, use short-acting anaesthetic and analgesic agents Consider relaxation techniques and music therapy for anxiolysis	Avoid routine preoperative sedatives
Intraoperative phase		
Prevention of thromboembolism	Mechanical devices (anti-embolism stockings, intermittent pneumatic compression devices, foot impulse devises) Pharmacological VTE prophylaxis	Mechanical devices Pharmacological VTE prophylaxis
Prevention of surgical site infection	Soap is as effective as chlorhexidine Limited evidence that hair removal reduces surgical site infection, but if hair is to be removed, hair clipping just before surgery is preferred.	Antibiotics: ≤ 60 minutes before skin incision Hair clipping Chlorhexidine-alcohol is preferred to povidone-iodine for skin preparation
Normothermia	Use convective active warming perioperatively Continuous temperature measurement	Use convective active warming perioperatively Continuous temperature measurement

Anaesthesia	Protective ventilation strategies Short-acting drugs Combination of regional and general anaesthesia	Lung-protective ventilation during one-lung ventilation (see below) Combination of regional and general anaesthesia (low evidence) Short-acting volatile or intravenous anaesthetics or a combination (low evidence but strongly recommended)
Fluid management • Hypovolaemia results in organ hypoperfusion • Excessive fluids cause postoperative ileus	Target euvolaemia $\leq$ 30 ml/kg net intake of intravenous fluid $\leq$ 2 kg weight gain Discontinue postoperative intravenous fluids after 24 hours Prevention of postoperative nausea and vomiting (PONV)	Pulmonary oedema after lung surgery may result from lung injury caused by pulmonary disease, chemoradiotherapy, one-lung ventilation, lung manipulation and ischaemia-reperfusion phenomena. In combination with a liberal fluid regime, acute respiratory distress syndrome, atelectasis, pneumonia, empyema and death may ensue. A target volume of 2-3 ml/kg/h should accomplish euvolaemia with a dry lung and should not result in acute kidney injury. In euvolaemic states, perfusion may be ensured by vasopressors Balanced crystalloids preferred over 0.9% NaCl Discontinue intravenous fluids and start oral fluids as soon as possible Prevent PONV
Ventilation	Lung protective ventilation strategies	Double lumen tubes (DLTs) often necessitate less repositioning than bronchial blockers (BBs) but could cause more airway injury and postoperative sore throat Fibreoptic bronchoscopy should be used to confirm placement of DLTs and BBs. Ventilating with FiO_2 = 1 just before lung collapse, results in faster non-dependent lung collapse and improved surgical access

		Lung protective ventilation strategies should be used during one-lung ventilation (Tidal volumes of 4-6 ml/kg; Positive End-expiratory pressure (PEEP) of 5-10 cmH_2O) Continuous positive airway pressure (CPAP) to the non-dependent lung reduces complete collapse with a reduction in the local inflammatory response.
Reduced surgical insult Reduces stress response, complications and pain and results in faster recovery)	Minimal invasive surgical techniques	Chest wall trauma, rib fractures and nerve and muscle damage render thoracotomy a painful procedure. Recommendations are as follows: Minimally invasive surgery (VATS, robotic surgery) where possible Anterior, muscle sparing thoracotomy approach (reduced pain but no difference in pulmonary function and complication rate) Intercostal nerve-sparing techniques (preventing crush injury of the nerve bundle by the retractor and during rib re-approximation)
Analgesia Pain results in prolonged hospital stay through: • Pulmonary complications (atelectasis/splinting/pneumonia, hypoxaemia/hypercarbia) • Increased myocardial work and ischaemia, arrhythmias • Delayed mobilization • Enhanced stress response • Ileus, postoperative nausea and vomiting, fluid imbalance • Anxiety, insomnia, delirium • Decreased urinary output • Thromboembolic phenomena • Insulin resistance, decreased wound healing, infection, sepsis	Preoperative counselling (reduces anxiety) Regional anaesthesia to reduce the endocrine stress response Postoperative multimodal analgesia should consider paracetamol, non-steroidal anti-inflammatory drugs and ketamine as opioid-sparing drugs.	Regional anaesthesia to reduce the endocrine stress response. The gold standard, thoracic epidural analgesia (TEA), may result in urinary retention, hypotension, muscular weakness and poses problems in patients on anticoagulation. Compared to TEA, paravertebral blocks may provide equivalent analgesia with better reduction in respiratory complications, PONV, pruritus, hypotension and urinary retention. Major complications, 30-day mortality and length of stay are equivalent.

		Intercostal catheters may offer equivalent analgesia compared to TEA but are more cost-effective and placement is less time consuming. Serratus anterior plane block offers good rescue analgesia. It could be considered for pleurectomy and decortication. Liposomal bupivacaine shows promise and can provide blockade at multilevel intercostal sites up to 96 hours. Cryo-analgesia could result in chronic pain and should be avoided. Postoperative multimodal analgesia should include paracetamol, non-steroidal anti-inflammatory drugs and ketamine as opioid-sparing drugs. Gabapentin may reduce acute pain in some procedures, but there is no evidence for its use in thoracic surgery and it does not reduce the ipsilateral shoulder tip pain of TEA. Glucocorticoids reduce pain and PONV, but might impair glucose homeostasis, cause gastric irritation, sodium retention and impaired wound healing. Limited evidence for pre-emptive analgesia
PONV prophylaxis	Non-pharmacological measures to decrease the baseline risk of PONV Multimodal pharmacological approach for PONV prophylaxis	Non-pharmacological measures to decrease the baseline risk of PONV Multimodal pharmacological approach for PONV prophylaxis
Prevention of postoperative atrial fibrillation	Not a concern in most other types of surgery	New onset AF is common after thoracic surgery. The risk is increased in advanced age, male sex, Caucasian race, hypertension, COPD, heart failure, valvular heart

		disease and extensive surgery. Continue beta-blockers – strong recommendation Consider diltiazem preoperatively or amiodarone postoperatively for patients at risk – weak recommendation Magnesium supplementation for magnesium depleted patients – weak recommendation. Prophylactic digoxin is ineffective and should be avoided.
Post-operative phase		
Drains (including chest drain): Drains cause pain and limit early mobilization	Avoid drains where possible Early removal of drains	Avoid routine placement Rather one than two drains (one drain is safe and effective, reduces pain scores by 40% and results in better post-removal lung function) External suction enhances air leak seal but increases chest tube drainage and reduces patient mobilization (wall suction). In the face of conflicting evidence, routine external suction is not recommended. Digital drainage systems improve decision-making (more accurate readings) and allow suction which is not connected to the wall (does not impair patient mobilization) For drain removal, accept up to 450 ml/day drainage (serous effusion)
Urinary catheter:	Avoid if possible Remove as early as possible	Routine placement of urinary catheters for urine output monitoring is not recommended. Place in patients with epidurals in situ, patients where fluid management is crucial (pneumonectomy and prolonged complicated

		surgery) and those with pre-existing renal impairment
Early mobilization: Mobilization within 24 hours as bed rest promotes physical deconditioning, reduced muscle mass, pulmonary complications and thromboembolic complications which prolong length of stay and morbidity	Avoid nasogastric tube if possible Early removal of catheters and drains Adequate analgesia Prevention of nausea and vomiting Early oral intake and nutritional support The use of short half-life drugs in the perioperative period Prescribed postoperative exercise programmes.	Early removal of urinary catheters, nasogastric tubes, drains.
Control institutional ERAS practice	Regular audit of outcomes and multidisciplinary team processes	

NSAID = Non-steroidal anti-inflammatory Drugs; PONV = postoperative nausea and vomiting; VTE = venous thromboembolism, COPD = Chronic Obstructive Pulmonary Disease, VATS = video-assisted thoracoscopic surgery, AF = atrial fibrillation, BBs = bronchial blockers, DLTs = double lumen tubes, TEA = thoracic epidural analgesia, PEEP = Positive End-expiratory Pressure, F_iO_2 = Inspiratory fraction of oxygen, NPO = Nil per Os

4. ERAS in South Africa

The South African Society of Endoscopic Surgeons (SASES) and The Association of Surgeons of South Africa (ASSSA) identified ERAS implementation as a priority in South Africa.[28] The South African Perioperative Research Group (SAPORG) listed ERAS implementation as one of its top 10 perioperative research priorities.[29] Several problems complicate the implementation of ERAS in South Africa. These include nutritional challenges, HIV and access to health care.

On the one hand, South Africa has the highest rate of obesity in Sub-Saharan Africa and on the other, 4-11% of the population is malnourished[30]. Preoperative nutritional optimization, as per ERAS protocols, will require a culture of preoperative nutritional assessment and dietitian support. This is not yet current practice in South Africa.[28] Evidence of the impact of HIV on postoperative outcomes is conflicting. As an estimated 7 million people in South Africa has HIV, ERAS guidelines might need to be revised if HIV is found to have a substantial effect on postoperative outcomes.[28]

All South Africans do not have easy access to transport and health care facilities. Delayed return to hospital when a complication arises, might result in severe morbidity or mortality. Surgeons might be hesitant to discharge patients early (as per ERAS protocols) for fear of late presentation of complications.[28]

Conclusion

As in most types of major surgery, ERAS in thoracic surgery aims to reduce hospital stay, cost, morbidity and mortality. The success of such a programme depends largely on protocol compliance. A multidisciplinary team approach and motivated patients are paramount. The benefits are however worth the effort.

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TIVA vs Volatile for Middle-ear and Sinus Surgery

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ENT surgery demands an exemplary level of cooperation between surgical and anaesthetic teams.

When analysing the potential advantages of one technique over the other, we need to consider what our specific goals for the patient and for the surgical procedure are and balance the risk and benefit of any course of action taken.

There is some specific guidance looking at the preferred technique for both middle-ear and sinus surgery procedures, with emphasis on various outcomes. It has been a topic of consideration in the literature with the aim of understanding if there is a superior modality.

These surgeries can be prolonged, with periods of minimal stimulation and a propensity toward an increased risk of PONV. Endoscopic procedures themselves require an adequate depth of anaesthesia to prevent inadvertent patient movement or responses and subsequent trauma.

Middle-ear surgery

The middle ear refers to the air-filled space between the tympanic membrane and the oval window, containing the three ossicles that transmit sound vibration to the cochlea. It is connected to the nasopharynx by the eustachian tube.

Mastoidectomy, myringoplasty or tympanoplasty and cochlear implantation are performed utilising microscopes and endoscopes. Endoscopes allow for a two-dimensional wide panoramic view of structures in small spaces, with the ability to navigate around corners. Trans-canal endoscopic ear surgery (TEES) can occasionally avoid having to create larger incisions in bones or removal of bony areas for access and surgery with a microscope.

Sinus surgery

Most procedures can be performed under local anaesthesia with sedation. The anterior ethmoidal nerve and sphenopalatine nerves innervate the nasal septum and lateral walls, and both areas can be blocked by packing the nose with local anaesthetic-soaked gauze for ten minutes. There can still be some discomfort with this technique and so general anaesthesia is favoured.

Functional endoscopic sinus surgery (FESS) is a minimally invasive technique of enlarging the nasal drainage pathway from paranasal sinuses, generally to treat chronic inflammatory and infectious sinus disease, nasal polyps, tumours and decompression of the optic nerve in Grave's ophthalmopathy. The surgery typically involves removal of the uncinate process of the ethmoid bone and opening of anterior ethmoid air cells and maxillary ostia, via an endoscope in the nasal cavity. This results in less discomfort compared with the transoral approach, which also risks damage to nerves innervating the teeth.

The "bloodless" surgical field

The aim for anaesthesia for microsurgery or endoscopic surgery in the middle-ear or sinuses is to create an environment in which bleeding is minimised and visibility for the surgeon is maximised, for speed and success. Even small amounts of blood can obscure the operating field. Capillary bleeding is the most serious problem for the surgeon in these procedures and anaesthetic goals aim to help decrease this.

Some of the literature would suggest that a 'blinded' ENT surgeon is able to discern between a TIVA and volatile-based technique and is sensitive to changes in a patient's MAP.

Other studies do not reproduce these findings, nor are able to stand up to investigator scrutiny in terms of study design and bias and are inconclusive, at best.

To achieve less intraoperative bleeding in a small space involves the manipulation of the physiological variables that would influence the rate of blood supply to, and ensure adequate venous drainage away from, the tissue being operated upon.

Surgical field bleeding is dependent upon regional flow or BP, HR, capillary perfusion and venous back-pressure.

The mainstay is a technique that induces controlled deliberate hypotension (MAP 60-70 mmHg, SBP < 100 mmHg), or typically 20% less than resting awake BP.
Patient factors may influence the safety of a chosen technique. Some patients may not tolerate deliberate hypotension with their given co-morbidities. One may even need to consider obtaining specific consent for a technique that employs an active drop in blood pressure throughout the anaesthetic.

How do we influence variables and events to minimise bleeding?
There are physical and pharmacological techniques that we can employ:

Physical techniques:

Patient positioning

Head up allows for a drop in perfusing pressure to the areas of the head and neck (every 2.5cm above the heart correlates to a drop of 2 mmHg in arterial blood supply.)

Blood pressure changes

Delivery of a smooth anaesthetic without major swings in blood pressure on induction and emergence, with avoidance of tachycardia and hypertension particularly. Ensure adequate depth of anaesthesia and avoidance of a light plane, consider the use of a NDMR agent during the procedure (if the surgeon is not concerned about facial nerve injury with surgical approach and therefore not performing nerve stimulation) and a safe deep-extubation. Intravenous lignocaine (1.5 mg/kg) may help to limit the stimuli at extubation.

Topicalise the airway to prevent coughing or bucking on the ETT – lignocaine spray to the larynx seems to reduce extubation response for up to two hours. Attempts at filling the ETT cuff with alkalinised lignocaine to facilitate this have proved effective, but with measurable systemic concentrations of drug. Consider the use of an SGA over an ETT for middle-ear procedures.

Heart rate

Aim to keep low. Less blood in per minute means less blood potentially lost per minute.

Capillary blood flow

Hydrostatic pressure within capillaries in the surgical tissues is responsible for the majority of blood loss, via oozing. Local vasoconstriction can be achieved with infiltration of an adrenaline-containing (1:50 000 - 1:200 000) local anaesthesia, wherever possible or the use of a vasoconstrictor such as phenylephrine applied topically.

Low normal CO_2 (normocarbia) is preferable here with particular avoidance of hypercarbia that would allow for increases in regional tissue perfusion and bleeding risk. IPPV will ensure the $PaCO_2$ can be manipulated carefully.

Venous pressure

To allow for improved drainage of head and neck tissues, place the patient in a slight (15 degrees) head-up position and avoid circumferential neck-ties. Limiting the amount of coughing and straining on the ETT and aim to maintain lower intrathoracic pressures. Judicious fluid management with avoidance of over-hydration.

Normal physiology

Ensure adequate haemostasis is possible by maintaining normothermia acid-base status and ionised calcium levels.

Pharmacologic techniques:

TIVA

Utilising Remifentanil seems to allow for better surgical conditions at the same blood pressure when compared to volatiles for severe sinus disease. For milder disease, there appears to be less of an appreciable difference for the surgeons.

Remifentanil allows for the added advantage of being able to rapidly titrate and drop BP, if needed, and allows for a slower HR compared to volatile anaesthesia.

TIVA provides a better recovery profile than volatile anaesthesia, particularly when it is balanced in such a way as to allow for the use of less Propofol. Most procedures with mild to moderate postoperative pain can easily be performed with a Propofol TCI targeting 3 – 3.5 mcg/mL and Remifentanil 2 – 5 ng/mL, but higher concentrations may be required.

Propofol-Remifentanil combinations have the added benefit of adequately blunting sympathetic stimulation more reliably with appropriate titration.

Ensure adequate depth of anaesthesia with processed EEG monitoring. This has an added benefit of signalling hypo-perfusion of the brain with a drop or loss in signal.

Volatiles

Volatile anaesthetics result in smooth muscle relaxation and decrease SVR. Tissue perfusion may be increased secondary to vasodilation, resulting in risk of more bleeding. Nitrous oxide should be discontinued (if utilised at all) about 15 – 30 minutes prior to graft placement during a tympanoplasty. Inhalation anaesthetics such as Isoflurane and Sevoflurane allow for blood pressure reductions to attain controlled hypotension (perhaps to a lesser degree than with TIVA). Isoflurane at moderate concentrations results in vasodilatory-induced BP drop with preservation of cerebral autoregulation, but at higher concentrations, it results in increased cerebral blood flow, increased intracranial pressure and impairment of cerebral autoregulation. Sevoflurane causes hypotension by direct vasodilatation, without changes in regional blood flow to the inner ear.

A Cochrane systematic review from 2013 did not show a demonstrably better effect in surgical field visibility (as rated by surgeons) when utilising TIVA with Propofol to create deliberate hypotension to induce less bleeding.

Other agents that may be utilised are vasodilators such as GTN or $MgSO_4$, beta-blockers such as Esmolol or Labetalol, alpha-2 adrenergic agonists such as Clonidine and Dexmedetomidine.

Prevention of post-operative nausea and vomiting is essential in this subset of patients, who are at risk for disruption of grafts or re-bleeding in the face of increasing tissue strain. TIVA reduces the incidence of PONV compared with volatile anaesthesia.

It is important to appreciate the complexity of any technique involved in inducing and maintaining general anaesthesia for these ENT surgeries. Choice may be based on patient factors or anaesthetist's skill. TIVA offers the advantage of a lower heart rate over volatile anaesthesia (without beta-blockade). Any technique, used safely, can be employed adequately for surgical needs. A good working relationship with your surgeon will facilitate discussions about the best choice for each patient. A smoother emergence can more reliably be obtained with TIVA, in experienced hands.

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Should We Be Using Perioperative Dexamethasone Routinely?

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Introduction *(Bartlett & Hartle, 2013)*

Dexamethasone is a synthetic adrenocortical steroid, used widely in numerous specialities, including anaesthesia. Dexamethasone is regarded by many anaesthetists as an ideal perioperative agent for the following reasons:

- it is usually readily available;
- it is good for the prevention of post- operative nausea and vomiting (PONV);
- it promotes appetite;
- it promotes a feeling of wellbeing;
- it is associated with earlier discharge from day surgery units; *(Coloma, Duffy, White, Kendall, & Huber, 2001) (Murphy, Szokol, & Greenberg, 2011) (Kakodkar, 2013)*
- it reduces swelling *(Fleischli & Adams, 1999)*
- it reduces post- operative pain by inhibition of the inflammatory response *(Fleischli & Adams, 1999)*

Dexamethasone is therefore used widely, and the question remains, should it be used routinely? Side-effects are generally thought of as being linked to long-term usage. What are then the problems associated with a single dose of dexamethasone at induction? Hopefully the reader of this set of notes will be equipped to contribute constructively to this debate.

Pharmacology dexamethasone and pathophysiology *(Britain, 2013)*
(Robinson, Harrison-Hansley, & Spencer, 2000) (Bartlett & Hartle, 2013)

Dexamethasone has very high glucocorticoid activity, 6–7 times greater than that of prednisolone. Peak serum levels occur 2–12 hours after injection, and the drug is completely cleared within 3–5 days. However, cortisol levels are suppressed by 64–81% at 24 hours after injection, with most patients' values returning to normal by one week. Dexamethasone clearance is inversely related to age.

Benefits of a single dose of dexamethasone:

1. Postoperative nausea and vomiting (PONV)

Dexamethasone has been used as an antiemetic in patients receiving chemotherapy for more than three decades and was first studied in surgical patients in the early nineties. The precise mechanism of action is not known, but it has been suggested that the anti-emetic effect could be due to inhibition of prostaglandins, prevention of serotonin release in the gut, reduction in neural 5-hydroxytrytophan levels or a reduction in the release of endorphins. *(Kakodkar, 2013)*

Work done by multiple researchers have illustrated that dexamethasone is an effective perioperative antiemetic:

1. Carlisle and Stevenson calculated in their Cochrane Review, a risk ratio for dexamethasone of 0.48 (95% CI 0.43–0.54) for the prevention of postoperative nausea and vomiting. This was similar to ondansetron (RR 0.56 (95% CI 0.50–0.62)) and marginally better than Cyclizine (0.67(0.56–0.79)) and droperidol (0.62 (0.58–0.67)). They also confirmed the findings of the IMPACT Group *(Carlisle & Stevenson, 2006)*

2. The IMPACT Group showed that when combined with other antiemetics, dexamethasone had an additive effect and the magnitude of the effect of combined antiemetic agents was equal to the product of the risk ratio for each agent. *(Apfel, Korttila, & Abdalla, 2004)*
3. Work done by Henzi et al showed in a meta-analysis (17 trials, 1946 patients) that dexamethasone had a more pronounced effect on late emesis (6–24 h). The findings were similar to that of the IMPACT Group. *(Henzi, Walder, & Tramer, 2000)*

2. Analgesia *(Kakodkar, 2013)*

Dexamethasone has shown to have analgesic effects:

De Oliveira et al. analysed 24 randomised controlled trials (n = 2751) published between 1997 and 2010 and concluded that an intermediate dose (0.11–0.2 $mg.kg^{-1}$) of dexamethasone conferred significant benefits in early as well as late pain. It was also shown to have a significant morphine-sparing effect. However, the differences in pain scores and morphine consumption between patients receiving dexamethasone and controls were small. The authors argued that an antiemetic with analgesic properties able to provide lower pain scores at lower doses of analgesics should be an obvious first choice in surgical patients. *(De Oliveira, Almeida, Benzon, & McCarthy, 2011)*

3. Reduction of the incidence of sore throat (*Kakodkar, 2013*)

Thomas and Beevi showed that dexamethasone reduced both the incidence and the severity of a sore throat in patients undergoing tracheal intubation *(Thomas & Beevi, 2007)*. These findings were confirmed in a randomised controlled trial by Bagchi and colleagues (*Bagchi, et al., 2012)*

4. Earlier discharge *(Kakodkar, 2013)*

It has also been shown that the use of dexamethasone results in a quicker attainment of discharge criteria, a shorter hospital stay, and a better quality of recovery (*Murphy, Szokol, & Greenberg, 2011)*

5. Earlier oral intake after tonsillectomy *(Kakodkar, 2013)*

A single dose of dexamethasone resulted in earlier oral intake after tonsillectomy *(Steward, Grisel, & Meinzen-Derr, 2011)*

6. Reduced swelling after dental extractions *(Baxendale, Vater, & Lavery, 1993)*

Potential for harm in the surgical population *(Kakodkar, 2013)*

On the basis of dexamethasone's known benefits in surgical patients, it would be logical to suggest that it should be routinely used as a perioperative antiemetic. The caveat, however, is that the harm caused by dexamethasone should not outweigh the benefits, and its safety profile must be comparable with alternative anti-emetics.

The following concerns are associated with the usage of intraoperative dexamethasone:

1. **Risk of bleeding** (especially with tonsillectomies)

- In a well-conducted meta-analysis, the incidence of bleeding episodes and hospital admission for bleeding was found to be similar in patients who had received dexamethasone compared with those who did not receive the drug. However, operative re- intervention for bleeding was higher in the dexamethasone group. In a subgroup analysis, this effect was confined to children and those who had concurrent administration of non-steroidal anti-inflammatory drugs (NSAIDs). Furthermore, when studies with high risk of bias were excluded, there was no clear association between steroid use and the incidence of operative re-intervention. *(Plante, Turgeon, & Zarychanski, 2012)*
- A randomised controlled trial conducted by Gallagher et al showed no increased risk of bleeding with dexamethasone *(Gallagher, Hill, & Ojha, 2012)*

- A meta-analysis conducted by Shargorodsky et al did not show any increased risk of bleeding with dexamethasone. *(Shargorodsky, Hartnick, & Lee, 2012)*

There is currently no clear evidence that a single dose of dexamethasone leads to an increased bleeding risk but caution should be exercised when combining dexamethasone with NSAIDs in surgical procedures where postoperative bleeding is an issue. *(Kakodkar, 2013)*

2. Risk of infection

What do we know?

- Large doses of glucocorticoids influence innate and acquired immunity which predisposes a patient to infection *(Fauci, Dale, & Balow, 1976)*
- Opportunistic or atypical organisms occur over 40 times more often in patients receiving glucocorticoids *(Saag, Koehnke, & Caldwell, 1994)*
- Dexamethasone is contraindicated in systemic fungal infections and it is also contraindicated before the administration of live or attenuated vaccines because of the unpredictable response to the vaccines. *(Bartlett & Hartle, 2013)*

However, from my reading and research, the risk of infection following a single dose of dexamethasone appears to be negligible:

- De Oliviera et al. (mentioned earlier) also looked at the incidence of wound infection in their meta-analysis and found no difference in patients receiving dexamethasone compared with placebo. As a worst-case scenario, they estimated the possibility of increased incidence of infection to be 1.2% in patients receiving intermediate (0.11–0.2 $mg.kg^{-1}$) doses of dexamethasone. *(De Oliveira, Almeida, Benzon, & McCarthy, 2011)*
- In a post hoc analysis of the ENIGMA-II trial, the authors concluded that intraoperative dexamethasone was not associated with postoperative wound infection. *(Corcoran, et al., 2017)*

I am hoping that the PADDI Trial (**P**erioperative **AD**ministration of **D**examethasone and **I**nfection Trial) will be giving us a clear answer soon on this front. *(Sidhu, n.d.) (Corcoran, et al., 2019)*

The PADDI trial is a pragmatic, multicenter, randomised, controlled, non-inferiority trial. A total of 8880 patients who underwent major elective surgery have been enrolled from March 2016 until middle 2019. Participants are followed-up for six months post procedure and the publication of the results is anticipated to occur in 2020.

Study population characteristics:

- adult patients
- ASA physical status 1-4
- elective or expedited (non-cardiac) surgery of at least two hours duration
- general anaesthesia with or without regional block,
- single (or multiple) surgical skin incision(s) of >5 cm in length,
- a minimum anticipated hospital stay of at least one night.

Participants have been randomly allocated to receive dexamethasone 8 mg or placebo intravenously following the induction of anaesthesia in a 1:1 ratio, stratified by centre and diabetes status.

Primary outcome:
Surgical site infection at 30 days following surgery, defined according to the Centre for Disease Control criteria.

Let's watch this space for the results!

3. Perioperative hyperglycaemia

Current knowledge:

- A single dose of dexamethasone induces whole body insulin resistance and it alters cardiac glucose metabolism. *(Qi, Pulinilkunnil, & Ding, 2004)* This may result in hyperglycaemia in patients both with and without diabetes mellitus, which is associated with poor outcomes, particularly for cardiac surgery and subarachnoid haemorrhage. *(De Oliveira G. , Almeida,*

Benzon, & McCarthy, 2011).

- Dexamethasone is also known to cause hyperglycaemia in major neurosurgical procedures. *(Lukins & Manninen, 2005)*
- Waldron et al found in a meta-analysis that blood glucose is higher for 24 hours after administration of dexamethasone but markedly higher in those with obesity and poor glycaemic control. *(Waldron, Jones, Gan, Allen, & Habib, 2013)*

With the above in mind, randomised studies examining changes in blood glucose after a single dose of dexamethasone have failed to demonstrate a significant impairment of blood glucose homeostasis in both non-diabetic and diabetic patients. Although there was a statistically significant rise in blood glucose levels in non-diabetic patients, the peak levels reached (8 ± 1 $mmol.l^{-1}$) were within the recommended perioperative glycaemic range. *(Nazar, Flores, Lacassie, & Munoz, 2009)*

Data, however, suggest that obese patients with impaired glucose tolerance may be at particular risk. *(Hans, Vanthuyne, Dewandre, Brichant, & Bonhomme, 2006)*

It is recommended to monitor capillary blood glucose hourly in diabetic patients for at least 4 hours after the administration of dexamethasone. *(Barker, et al., 2015)*

4. Psychiatric disturbances

Steroid therapy is known to cause a range of psychiatric disturbances including labile mood, hallucinations, sleep disturbances, suicidal thoughts and aggravation of schizophrenia. These manifestations are usually seen with higher doses and prolonged therapy. There are no reliable data on psychiatric manifestations following a single dose of dexamethasone and as such it is difficult to comment on the harm that might result from a single perioperative dose. *(Kakodkar, 2013)*

5. Hypothalamic pituitary axis *(Bartlett & Hartle, 2013)*

Even a single dose of 8 mg dexamethasone partially suppresses the hypothalamic pituitary axis for up to a week. *(Williamson, Lorson, & Osbon, 1980)* The degree of suppression is greatest and most prolonged when given at night. 1 mg taken orally at night inhibits corticotrophin secretion for 24 hours *(Britain, 2013).* This suppression has minor effects and is of unknown clinical significance. *(Bartlett & Hartle, 2013)*

6. Wound healing *(Bartlett & Hartle, 2013)*

The effect of a single dose of dexamethasone on wound healing remains a controversial topic. It was illustrated in an animal study that a single dose of dexamethasone significantly reduced collagenisation, epithelisation and fibroblast content. *(Durmus, Karaaslan, & Ozturk, 2003)*
It was also demonstrated that dexamethasone increases the risk of post-dural puncture headache after spinal anaesthesia for caesarean section when compared with placebo. *(Basurto, Uriona, & Martinez, 2013)*

One of the secondary outcomes of the PADDI trial will be looking at the incidence of wound dehiscence and hopefully we will have a more definitive answer soon.

7. Gastric ulceration *(Bartlett & Hartle, 2013)*

Use of steroids may increase the risk of perforation in patients with peptic ulcers, diverticulitis, new anastomoses and non-specific ulcerative colitis. There are no data on the risk of gastric ulceration after a single dose of dexamethasone, however, a study in rats demonstrated a 30% ulcer rate, 24 hours after a 1 $mg.kg^{-1}$ intramuscular dose of dexamethasone. It was associated with an 83-87% reduction in prostaglandin action via inhibition of prostaglandin synthase and peroxidise, and a doubling in gastric acid secretion. *(Bandyopadhyay, Biswas, Ganguly, & Banerjee, 1999)*

8. Musculoskeletal problems (*Bartlett & Hartle, 2013)*

It is a well-known fact that long-term glucocorticoids cause musculoskeletal problems. Patients taking long-term dexamethasone have a 4% risk of avascular necrosis *(eHealthMe, n.d.)* The risk is

multifactorial but it is higher with older age, a low albumin, high lipid levels and the amount of dexamethasone exposure *(Kawedial, 2011)*. The shortest use of dexamethasone associated with avascular necrosis in case reports is one week, but the onset of symptoms is usually only after six months to three years of exposure. (*van Schaardenburg, van den Brink, & Wieringa, 2001)*. The significance of one perioperative dose is unknown.

9. **Tumour lysis syndrome** (*Bartlett & Hartle, 2013)*

This syndrome is an oncological emergency and it can be fatal. It occurs in haematological tumours that grow at a fast rate or in tumours with a large bulk. It is characterised by rapid onset of hyperkalaemia, hyperphosphataemia, lactic acidosis, hyperuricaemia and acute renal failure. It usually occurs after cytotoxic chemotherapy and the administration of dexamethasone. *(Chanimov, Koren-Michowitz, Cohen, Pilipodi, & Bahar, 2006*). Dexamethasone has a known lympholytic effect by arresting growth and inducing apoptosis in lymphocytes. There are case reports of tumour lysis syndrome following treatment with dexamethasone alone. *(Lerza, Botta, & Barsotti, 2002)*. Peri-operative death has also followed a single dose of dexamethasone causing tumour lysis syndrome in a 3-year old undergoing adenotonsillectomy. (*McDonnell, Barlow, Campisi, Grant, & Malkin, 2008)*. It is therefore suggested that dexamethasone (and other corticosteroids) should be avoided in patients with a haematological tumour and clinicians should maintain a high index of suspicion if such a diagnosis is not confirmed yet.

10. **Dexamethasone-induced perineal irritation** *(Bartlett & Hartle, 2013)*

This phenomenon is not fully understood, but intravenous administration of dexamethasone to awake patients can lead to acute, short- lived (3–45 seconds) perineal pain, irritation, burning or tingling. It is postulated that the phosphate ester in dexamethasone sodium phosphate plays a significant role. Females seem to be affected more than males *(Perron, Dolbec, Germain, & Bechard, 2003)*. There are several case reports of patients who, after receiving dexamethasone 8 mg before induction, experience distressing effects, leading to the suggestion that it should only be given after induction of anaesthesia *[37 (Crandell, 2004)]*.

Conclusion *(Kakodkar, 2013)*

There are ample data on the benefits of dexamethasone in dental, ENT, laparoscopic and day case surgery procedures. In addition, it has a long duration of action with consequent effectiveness in late emesis.

Reliable data is currently not available to estimate the number of patients who might be harmed from using a single perioperative dose of dexamethasone. As a worst-case scenario based on the data from two meta-analyses, it is possible that 1–3 patients in every hundred might be coming to harm from bleeding or postoperative infection. *(De Oliveira G. , Almeida, Benzon, & McCarthy, 2011) (Plante, Turgeon, & Zarychanski, 2012)*

Whether more patients come to harm from complications of diabetes, psychiatric disturbances, exacerbation of peptic ulcer disease and immunosuppression from a single dose of dexamethasone is unknown. It is also worth noting that other alternative agents in use for the prevention of PONV have an excellent safety profile, and that severe adverse effects such as prolongation of QT intervals and extrapyramidal manifestations are rare.

I agree with the opinion of Kakodkar on the safety and efficacy of a single perioperative dose of dexamethasone. Some clinicians may argue against the routine usage of perioperative dexamethasone based on the theoretical potential for harm and the known harmful effects caused by high dose and prolonged steroid therapy *(Bartlett & Hartle, 2013)* This outlook may deprive low risk surgical patients from the benefits of a single dose perioperative dexamethasone. Kakodkar recommends that extra caution should be exercised when using dexamethasone in combination with NSAIDs in surgical procedures where postoperative bleeding is an issue, in patients with diabetes (particularly those with a high BMI), patients with peptic ulcer disease, patients with a psychiatric history, and oncology patients where tumour lysis syndrome is likely to develop.

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Phaeochromocytoma

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A phaeochromocytoma is a neoplasm of chromaffin tissue that synthesises catecholamines. Paraganglionomas are neuroendocrine tumours that arise from the extra-adrenal autonomic ganglia and are indistinguishable from phaeochromocytomas at a cellular level. They can secrete catecholamines and present clinically identically to phaeos, so the anaesthetic concerns for these patients are the same.

Biochemical tests

Traditionally, plasma and urinary catecholamine levels have been used to diagnose phaeochromocytoma definitively. However, due to the relatively low specificity and sensitivity of these tests, the modern technique measures plasma or urinary levels of the catecholamine metabolites: normetadrenaline and metadrenaline. Plasma metabolite levels are easier to collect and are more sensitive; urine tests are more specific.

Imaging

After positive biochemical tests, tumour localisation is achieved by either CT or MRI scanning. Their sensitivities are comparable but MRI has better specificity in localising paraganglionomas. MIBG-123 (meta-iodobenzylguanidine) scintigraphy is a form of functional imaging essential for all patients with paraganglionomas and those with a high likelihood of metastatic or multi-focal disease.

Since treatment of these tumours almost always includes surgical resection, most phaeo patients will require anaesthesia. Because of the rarity of the condition, most data on mortality and perioperative outcomes have been reported in multiple small case series: mortality and morbidity (particularly myocardial infarction and stroke) are uniformly low but most patients do exhibit labile blood pressure, arrhythmias and tachycardia perioperatively. Significant risk factors for adverse events include large tumour size, increased levels of preoperative catecholamines and longer duration of surgery (perhaps related to tumour size).

Risks are much higher for patients undergoing unrelated surgery with undiagnosed phaeochromocytoma. In these cases, patients may suffer any of the complications mentioned above with cardiovascular collapse after induction of anaesthesia or, indeed, at any time during surgery. Mortality in these cases may exceed 80%.

Pre-operative evaluation

The ‘catchwords’ for the perioperative management of a patient with phaeochromocytoma are: *multidisciplinary* and *individualised.* The multidisciplinary should include the surgeon, anaesthetist and endocrinologist.

The endocrinologist should institute medical therapy to limit the physiological impact of the paroxysmal catecholamine release. This should be done over about one to two weeks to allow for the medication to be titrated to effect. The anaesthetist should also be involved at this early stage, if enough lead time can be given by the surgical team. This may be challenging in a resource-poor environment where it may not be feasible for patients to travel backwards and forwards to consult specialists, nor may it be possible for them to spend weeks in hospital receiving oral medication. Compromises may need to be made and the treatment regimen and monitoring for effect will have to be individualised for each patient.

There are, however, some steps not to be skipped or modified at this stage:

- **Clinical assessment**: the classic phaeochromocytoma triad of headache, sweating and palpitations. Ninety percent of patients will be hypertensive but it will be paroxysmal in about half of these. Patients may also describe a sense of impending doom during these periods. Other symptoms include blurry vision, weight loss, polyuria and polydipsia. Papilloedema may be present on fundoscopy. About one third of patients may have associated conditions: MEN 2A and 2B, Von Hippel-Lindau disease and neurofibromatosis.

- **Evaluation of target-organ damage**: catecholamine excess can result in volume depletion, postural hypotension, ischaemia, angina and myocardial infarction, aortic dissection, cardiomyopathy, cardiac failure and arrhythmias. An ECG would screen for ischaemic changes and arrhythmias; and may be used as a tool to evaluate the effectiveness of therapy as ST and T wave changes should resolve with medical intervention. An echocardiogram will assess cardiac function, more particularly: systolic and diastolic dysfunction, chamber size and wall motion. It will also rule out a primary cardiac paraganglionoma which is fortunately vanishingly rare.

Goals of therapy

- **Blood pressure control**
  There is no universally effective regimen. Options include alpha-adrenergic blockade with or without beta-adrenergic blockade, calcium channel blockers and metyrosine. ACE-inhibitors are not recommended.

  Alpha-adrenergic blockade is initiated first and as vasodilation unmasks the intravascular depletion, the patient is likely to develop, or worsen a pre-existing tachycardia. Intravascular volume must be replaced, and it is hoped that the heart rate will fall. If the patient is adequately alpha-blocked and volume-replete but remains tachycardic, a low dose **beta-adrenergic blocker** can be added cautiously. This is usually required in cases where the tumour secretes large amounts of adrenaline that causes tachycardia and arrhythmias.

  > The beta-adrenergic blocker should ***never*** be started before the alpha-adrenergic blocker because the blockade of the peripheral vasodilatory beta-adrenergic receptors with unopposed 'phaeo' alpha-adrenergic stimulation can lead to a hypertensive crisis.

  c
  Calcium channel blockers inhibit noradrenaline-induced calcium influx in vascular smooth muscle and can be added to supplement the regimen if the hypertension is refractory.

  Metyrosine is a competitive inhibitor of tyrosine hydroxylase, an enzyme involved in the production of catecholamines. It is mainly restricted to use in conjunction with alpha-adrenergic blockade in the management of unresectable, malignant tumours as its side-effects of hypersomnolence, depression, negative inotropy, and the potentiation of the extra-pyramidal side-effects of haloperidol make it undesirable.

- **Intravascular volume expansion**
  There are some options here that can be used in isolation or in combination, as the situation requires. The patient can be encouraged to take free water orally and can be placed on a high sodium diet. If necessary, volume expansion can be achieved by intravenous clear fluid administration and can be titrated using serial haematocrits.

Therapy is instituted to prevent or reduce pre- and intra-operative hypertensive episodes, to allow intravascular volume expansion and to improve cardiac function in those patients with catecholamine-induced cardiomyopathy.

Effectiveness of the medical preparation is assessed by twice-daily haemodynamic monitoring in the standing and seated/lying positions. There is no consensus on haemodynamic targets and the old Roizen criteria are no longer cited. It is suggested that recumbent BP should be < 130/80 mmHg and HR 60-70 bpm, standing BP should show relative orthostatic hypotension with systolic values of >90 mmHg and HR 70-80 bpm. Some centres feel orthostatic hypotension is not a necessity.

Alpha-adrenergic blockade

Despite some recent work questioning the need for preoperative alpha-adrenergic blockade, these drugs remain the cornerstone of preoperative preparation of phaeochromocytoma patients. They work to reduce hypertension during surgery prior to the clamping and control of the effluent venous drainage of the tumour, but after that may cause hypotension when the catecholamine secretion drops sharply. No one alpha blocker is superior to another.

- **Phenoxybenzamine (not available in SA)** is an irreversible, non-selective, non-competitively bound alpha blocker. It has a long duration of action and so works well for peri-operative blood pressure control but may result in prolonged post-resection hypotension. It should be stopped 24 to 48 hours before surgery. As it is non-selective, the central $alpha_2$-blockade results in somnolence, headache and nasal congestion.

- **Doxazosin/ Prazosin/ Terazosin/ Urapidil** are reversible, selective, competitively bound $alpha_1$-blockers. They are comparable to phenoxybenzamine in terms of preoperative blood pressure control, and the recovery to normal blood pressure post-resection may be quicker. Prazosin and Terazosin have significantly shorter half-lives than Doxazosin and so need frequent dosing. A missed dose may result in inadequate blockade for the time of surgery.

Surgical approach

Adrenalectomy for phaeochromocytoma resection can be performed via laparotomy or laparoscopy; and will depend on the size of the tumour and its relationship to surrounding structures (usually vascular). Laparoscopic procedures can be converted to open at any stage; and open procedures are performed via midline or subcostal incisions, or via the retroperitoneal (‘kidney position’) flank approach. The laparoscopic approach favours the lateral ‘kidney position’ which requires a significant table break to improve access.

Intra-operatively, the entire procedure can be divided into two stages: the first includes dissection of the tumour from the surrounding tissues and the isolation of its blood supply. The second involves the subsequent clamping of the effluent venous drainage which may not be entirely straightforward as these tumours tend to be vascular, blood loss may be brisk and there may be multiple collaterals that make definitive clamping of the effluent vessels (and therefore the catecholamines they contain) difficult.

The first stage is characterised by surges of severe hypertension and periods of arrhythmias as the surgeon needs to manipulate the tumour and the surrounding tissue resulting in catecholamine release. The second stage is marked by a precipitous drop in endogenous catecholamines and hypotension. This is aggravated by the presence of the alpha-adrenergic blockade, down-regulation of the alpha-adrenergic receptors and volume depletion. Inotropic support may be required.

It behoves one to continue to communicate with the surgeon, particularly during these periods so that major blood pressure issues may be anticipated, and management becomes pro-active rather than reactive.

Anaesthetic management

Phaeochromocytoma resection is performed under general anaesthesia. If the case is open or likely to convert to open, an epidural may be used for analgesia. It is suggested that the epidural itself not be activated during the procedure as the resulting sympathectomy and hypotension, whilst potentially favourable in the management of intra-operative hypertension, will aggravate any post-resection or hypovolaemic hypotension.

Some argue that the pre-operative placement of the epidural can precipitate hypertensive episodes due to the positioning required and the anxiety it may induce. With this complication in mind, coupled

with the fact that the epidural is not usually activated until the post-operative period, the placement of an epidural (even for known open cases) is not a prerequisite – there are many other options available for multimodal analgesia, including wound infusion catheters.

Standard ASA monitors must be applied. Large bore peripheral intravenous access is required and a crossmatch should be sent to blood bank. Invasive arterial monitoring must be established pre-induction, or as soon after induction as possible in paediatric patients i.e. before intubation. A central venous catheter should be inserted after induction and intubation for the infusion of vasoactive drugs. Despite the lack of evidence to support the routine use of cardiac output monitoring, it should probably be used as the assessment of circulatory volume can be challenging in the context of cardiomyopathy and ischaemia. This is provided the anaesthetist is aware of the potential shortfalls and is able to use whichever method is the most familiar to them: trans-oesophageal echocardiography, LidCo/ Rapid™, Vigileo™, EV1000™, pulmonary artery catheter.

Aim for a smooth induction with adequate depth of anaesthesia to prevent a hypertensive response to intubation. Occasionally, a seemingly unprovoked hypertensive surge can occur post-induction but pre-intubation. Be prepared for this potential event. Other stimulating periods, besides actual manipulation of the tumour, are the initiation of the pneumoperitoneum in laparoscopic procedures, continuously high insufflation pressures and the ensuing hypercarbia.

Virtually any drugs and combination of drugs can be used in the induction and maintenance of anaesthesia in these cases and it may be simpler to be aware of those that should be avoided:

- Ketamine – sympathomimetic
- Ephedrine – indirect acting alpha- and beta- agonist. Should be avoided until the tumour is resected; and even then should be used with care as possible unknown metastases or remaining tumour tissue may be stimulated to release catecholamines.
- Halothane - arrhythmogenic
- Desflurane – may cause tachycardia and hypertension in high doses
- Metoclopramide – inhibits dopaminergic suppression of noradrenaline release
- Morphine – histamine release in large doses but can be used safely if given slowly and in incremental doses. Other agents associated with histamine release are: Pethidine, Atracurium and Pancuronium.

Intra-operative haemodynamic management

Despite careful preparation and optimisation and regardless of pre-operative catecholamine levels, it is common for patients to experience hypertensive surges during the first stage of the procedure and subsequent hypotension post-resection.

Vasopressors, vasodilators and anti-arrhythmic agents should be prepared in advance and be ready for immediate administration. These drugs should preferably have rapid on- and offset to respond quickly to the changing haemodynamics. Some of the options are mentioned below:

- **Sodium nitroprusside (not available in SA)** is a nitric oxide donor. It is an ultra-short acting vasodilator (arteriole dilator) administered as an infusion of 0.5-5 mcg/kg/min but should not exceed 3 mcg/kg/min for any length of time to prevent thiocyanate toxicity. Reflex tachycardia may need to be treated with a short-acting beta-blocker.

- **Glyceryl trinitrate** is a nitric oxide donor. It is principally an ultrashort-acting venodilator which may play a greater role in patients with ischaemic heart disease as it increases coronary blood flow and suppresses coronary vasospasm. It is administered as an intravenous infusion at 0.5-1.5 mcg/kg/min.

- **Phentolamine (not available in SA)** is a non-selective alpha-blocker, usually administered as 0.5-1 mg/minute intravenously. Like SNP, it is causes vasodilation and reflex tachycardia.

- **Nicardipine (unsure of SA availability)** is a calcium channel blocker similar to Nifedipine (Adalat®). It is administered at 3-5 mg/hour and increased by 0.5-1 mg/hour every 15 minutes,

not exceeding 15 mg/hour. It has a strong arterial vasodilatory effext and relatively long half-life.

- **Labetalol** is an intravenous combined alpha- and beta-blocker.

- **Esmolol** is an intravenous ultrashort-acting selective $beta_1$-adrenergic blocker and can be administered as either bolus (10-50 mg) or infusion (25-250 mcg/kg/min).

- **Remifentanil** is an intravenous ultrashort-acting opiate which facilitates rapid titration to effect. It is very effective in blunting responses to pain or intubation but is inadequate to prevent the hypertensive surges associated with tumour manipulation if used as a single agent.

- **Dexmedetomidine** is a centrally acting, selective $alpha_2$-agonist with sedative and analgesic properties. Its central sympatholytic effect results in a reduction in plasma noradrenaline levels but much like Remifentanil, it is not suitable as a single agent to manage hypertension during tumour handling.

Magnesium sulphate

Magnesium is mainly an arteriole dilator, thereby reducing afterload whilst maintaining preload, that inhibits catecholamine release from the adrenal medulla. It antagonises alpha-adrenergic receptors, is a calcium antagonist, is anti-arrhythmic and has membrane-stabilising effects. It is widely available, inexpensive and has a high therapeutic index.

In our practice, we use magnesium as the primary intra-operative agent to treat hypertension. It is administered as both intravenous boluses (0.5-1 g) and run as a background infusion of 2 g per estimated hour of surgery per 200ml normal saline, titrated to haemodynamic effect.

At high doses it potentiates the effect of the non-depolarising muscle relaxants – a peripheral nerve stimulator should be used to guide the reversal of these agents before extubation. At very high doses (serum Mg > 5 mmol/litre), it interferes with coagulation and may result in a hypocoaguable state.

Hypotension

Post-resection hypotension must be aggressively treated with volume replacement (with balanced-salt crystalloids or colloids, or blood products). Vasodilator infusions must be stopped and vasopressors administered. The initial pressor of choice is Phenylephrine: it is a pure alpha agonist with a short half life that can be given as boluses or an infusion, titrated to effect.

Please see the note above regarding Ephedrine.

Severe and refractory hypotension can be treated with noradrenaline which is a combined alpha and beta agonist administered via intravenous infusion at 2-20 mcg/minute, titrated to effect.

Vasopressin is another option, if available, and usually used in conjunction with other pressors. It acts via V1 and V2 receptors to increase the amount of free water resorbed back into the circulation from the renal tubule filtrate and it constricts arterioles to increase peripheral vascular resistance. It is administered via intravenous infusion at 0.03-0.04 units/minute.

Before instituting any of these measures it is vital to exclude blood loss and hypovolaemia as a cause of the refractory hypotension. These can be very vascular tumours with many collaterals and may lie adjacent to large intra-abdominal vascular structures. The blood loss, if any, is usually evident but may not always be easy to assess in the retroperitoneal space, particularly in laparoscopic surgery. Surgical bleeding must be treated appropriately with fluids, blood products or redo surgery.

Post-operative management

It is our practice to refer all post-operative phaeochromocytoma resection patients, regardless of whether they are extubated or not, or whether they require blood pressure support or not, to the intensive care unit.

Having said that, if the case has proceeded smoothly and there has been no significant blood loss, and if the patient does not require vasopressor infusions, the arterial blood gas is close to normal and the effect of the magnesium dose on the neuromuscular blockade is assessed to be minimal, then the patient can be reversed, extubated and referred to a post-surgical high care unit, depending on the competency of the unit.

If there is an epidural *in situ*, it can be activated for post-operative analgesia provided that the patient is haemodynamically stable.

Hypertension may be the result of pain post-operatively but may also be due to co-existing essential hypertension, urinary retention or fluid overload. Delayed hypertension may be due to accidental ligation of the renal artery and hyper-reninism. Persistent hypertension may indicate something more sinister such as incomplete tumour resection or metastatic disease. Even discounting disease recurrence, hypertension is present in approximately one quarter of all patients at five years, and approximately one half of all patients at ten years. All patients should have biochemical and clinical reviews at six weeks and six months post-operatively, followed by annual follow-up for ten years.

Diabetes occurs in over 30% of phaeochromocytoma patients due to catecholamine-induced insulin resistance and/ or suppression, increased glycogenolysis, lipolysis and increased glucagon release. Hypoglycaemia can occur post-operatively because of a rebound increase in insulin secretion as the catecholamine inhibition is removed when the tumour is resected. Blood glucose must be assiduously monitored intra- and post-operatively, and it is prudent to stop any insulin infusions as the patient may easily be rendered dangerously hypoglycaemic.

Patients who undergo adrenalectomy are at risk for post-operative acute adrenal insufficiency and need steroid (glucocorticoid) supplementation peri-operatively. If they have had bilateral adrenalectomy, lifelong steroid replacement therapy (gluco- and mineralocorticoid) is required.

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Sedation for GIT Endoscopy

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Providing sedation to patients undergoing GIT endoscopy forms a significant component of anaesthetic practice. The majority of procedures are diagnostic gastroscopies and colonoscopies or ERCP's, but longer and more complex procedures are being performed endoscopically by gastroenterologists and surgeons. GIT endoscopies are often performed in older, sicker patients and may be elective or emergency procedures. GIT procedures entail more risk than other procedures done under sedation, resulting in more than half of all sedation related complications, usually related to over-sedation and/or inadequate monitoring.

Preparation

These procedures may be done in doctors' rooms, endoscopy suites, radiology suites or the operating theatre. It is important to familiarise yourself with the environment before the procedure. The SASA sedation guidelines have a comprehensive list of drugs and equipment required for the area in which sedation is to be performed. Ensure that everything is in place before the day of the procedure, ideally. Ensure that you know how to obtain any drugs and equipment that may be elsewhere in the hospital (pharmacy or theatre) if necessary. Confirm that you have a trained assistant.

You also need to make sure that the space is optimised for efficiency. You need an area in which to see the patient beforehand as well as an appropriately equipped and staffed recovery area. The procedure room must also have enough space and lighting to work and make notes.

Patients will be nil per os for 6-8 hours pre-op. They can take their routine medications with a sip of water. Anticoagulant medications can be continued unless there is a high risk of bleeding during the procedure.

Informed consent is mandatory. Patients should be told that they may be aware of events and have some recall of the procedure, but will be comfortable. Some patients may choose to have sedation-free endoscopy, but most request some form of sedation. It may be helpful to have information leaflets that the proceduralist gives to the patient at the time of booking. The patient must have an assistant to transport them home as they will not be able to drive, operate dangerous machinery or sign legal documents for 12 hours after the procedure.

Protective equipment will be necessary if radiation is involved (e.g. ERCP). Endoscopy is considered an aerosol generating procedure in patients with COVID-19.

Patient assessment

There are 2 goals of the preprocedural assessment. The medical assessment is the same as the assessment before general anaesthesia, with particular attention to the airway, cardiorespiratory status and risk factors for complications e.g. obstructive sleep apnoea. Routine pre-procedure testing is not usually indicated.

The appropriateness of the setting is also important to assess. Patients who have an ASA status of 3 or greater should be done in theatre, as well as patients undergoing more complicated procedures e.g. ERCP's, endoscopic ultrasound and oesophageal dilatation.

Patients who are not suitable for sedation include those at high risk for aspiration e.g. upper GIT haemorrhage, achalasia, oesophageal strictures and gastric outlet obstruction. They should undergo general anaesthesia, rapid sequence induction and endotracheal intubation. Patients undergoing ERCP who may be better suited for general anaesthesia with endotracheal intubation include those with ascites, obstructive sleep apnoea, BMI >35, COPD, ASA ≥3, anticipated airway difficulty or moderate to heavy alcohol use. General anaesthesia for all patients having ERCP's is also acceptable, especially for anaesthetists less comfortable with sedation. Longer, more complex

procedures are often better managed with GA than sedation.

Performance of sedation

Many procedures are performed in positions other than supine. Discuss the required position with the operator. Gastroscopies and colonoscopies are often performed with the patient in the lateral position, while patients are often semi-prone for ERCP's.

Monitoring includes NIBP and pulse oximetry for ASA 1 and 2 patients, with ECG monitoring for patients ASA 3 or greater and longer, more complex procedures. Intravenous access is necessary. Apply nasal prongs to the patient and ensure that local anaesthesia is applied to the oropharynx, the bite block is in situ and the patient is comfortable in the optimal position before starting the sedation. Oxygen may be started immediately (e.g. in ERCP and patients with ischaemic heart disease or respiratory disease) or when the peripheral oxygen saturation decreases. Capnography may be used for deeper sedation for complex procedures e.g. ERCP, endoscopic ultrasound. Nasal oxygen cannulae with integrated capnography tubing are useful for this purpose. Continuous observation of the patient to assess chest movement and signs of airway obstruction is particularly important. Local anaesthesia is commonly used to facilitate passage of the endoscope into the upper oesophagus. It probably is unnecessary if deep sedation is used. Lignocaine spray is commonly used and the patient is asked to gargle before swallowing.

The most stimulating part of the procedure is endoscope insertion for gastroscopy. For colonoscopy, the most stimulating manoeuvres are gas insufflation and manipulation of the colonoscope around corners. Deeper levels of sedation or added analgesia may be required at these times.

There are many pharmacological options for sedation. Caution and patience are important principles to use in sedation practice. Titration of drugs to effect will help avoid both unwanted depth of sedation and cardiorespiratory adverse effects. Ensure the dose of any drug has had time to reach full effect before giving another dose.

Midazolam and fentanyl in combination are commonly used by non-anaesthetists. Benzodiazepine use increases the risk of respiratory depression from opioids. The opioid is usually given first and bolus doses of fentanyl should be limited to 50 µg or less. The initial dose of midazolam is 0,25-2mg given after the opioid has reached peak effect. Repeat doses of the medications should not be administered at the same time.

Propofol infusions are commonly used by anaesthetists. Initial bolus dose is usually less than 0,5 mg/kg, with infusion rates in the order of 1-4 mg/kg/hr. TCI is a useful technique. Schnider or Marsh models may both be used successfully. The effect site target is around 1-2 µg/ml, with targets as low as 0,6 µg/ml in the elderly. Propofol has the advantages of rapid titratability, quick recovery and prevention of nausea and vomiting. Pre-treatment with intravenous lidocaine is useful to prevent burning on injection.

A bolus dose of midazolam may be given before propofol to provide amnesia and decrease the propofol requirements. Opioids may also be used, most commonly fentanyl, alfentanil or remifentanil. Ketamine may be useful to decrease the dose of propofol and subsequent respiratory depression and hypotension. Ketamine may be administered as repeat boluses, infusion or mixed with propofol. Ketamine mixed with propofol has been called ketofol and appears to be stable and safe. The recommended ratio is 10:1 (propofol : ketamine) e.g. 20mg of ketamine in 200mg of propofol.
My practice is generally to use only propofol by TCI using the Marsh model to target a plasma concentration, but many options are available. I increase my target incrementally until the desired level of sedation is achieved.

Other drugs may be used at the request of the proceduralist e.g. glucagon or hyoscine to manage GIT motility. Prophylactic antibiotics are seldom necessary, but may be used in patients with an obstructed biliary system for ERCP, recent vascular grafts or for percutaneous gastrostomy placement.

Complications

Complications may be related to the sedation or the procedure. The most common sedation related complications are cardiorespiratory, including laryngospasm, hypoventilation with hypoxia and

hypercarbia, airway obstruction, aspiration, hypotension, vasovagal episodes and arrhythmias. Significant complications are uncommon, occurring in less than 1% of procedures. More complications occur outside operating theatres and inadequate monitoring is a common contributing factor. The rate of cardiorespiratory complications is 2-5,4 per thousand cases and mortality is 0,3-0,6 per thousand cases.

Procedure related complications can be severe. Venous gas embolism is most common with ERCP, but has been described during other upper or lower GIT endoscopy. Risk factors for gas embolism during ERCP are previous biliary tract intervention, TIPS, liver trauma, sphincterotomy, metallic stent placement and hepatic abscess or tumour. Gas embolism should be considered in the event of unexplained cardiovascular collapse.

Perforation of the GI tract can lead to pneumomediastinum, pneumothorax, pneumoperitoneum and subsequent sepsis.

Bleeding and infection related to the procedure are uncommon. Pancreatitis may occur after ERCP.

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Preoperative Screening
Who, When and How?

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INTRODUCTION

With more than 300 million operations performed annually world-wide, 30-day postoperative mortality is the third most common cause of death; higher than deaths from TB, malaria and HIV combined! Appropriate, evidence-based preoperative screening and interventions may play a role in reducing postoperative morbidity and mortality.

Screening

For screening to be effective it must identify a disease or relevant psychosocial entity which could result in appropriate planning; be amenable to intervention/s and subsequently lead to an improvement in health and/or economic outcome.

The purpose of preoperative screening:

1. Is there likely to be a **benefit** to the patient?
2. **Avoid cancellation** of surgery once deemed important to proceed
3. Improvement of **long-term outcomes**
4. Identify suitability for **day case surgery**
5. Formulate an appropriate **perioperative plan**

1. Benefit
It is important to realise that all surgery carries at least some risk to patients. The risk is not evenly distributed and predominantly depends on the underlying patient's health status as well as the invasiveness of the surgical procedure. Risk stratification models (general such as NSQIP, POSSUM, RCRI, ASOS surgical risk calculator; and specific ones to the type of surgery: Euroscore II for cardiac surgery, aneurysm scores for vascular surgery (DAS, GAS, VSS) and there are others) play an important role not so much in giving a predicted risk/value of complications or mortality to an individual patient but rather as a tool to begin a facilitated shared-decision process.

The discussion process should incorporate:

Implication of:
- Disease progression without surgical intervention
  - Prognosis
  - Impact (pain, mobility, complications, on family and carers)
- Surgery
  - Realistic expectation (best case vs worst case scenarios)
  - Recovery period
  - Complications
  - QOL after surgery
- Alternative treatments
  - this may include less aggressive (palliative) surgery or less invasive modalities e.g. radio-, chemo-, hormone therapy

Avoid *unnecessary surgery*
- Surgery that is either not needed, not indicated, or not in the patient's best interest when considered against other available options which include conservative measures. Ideally surgery that has a long-term benefit for the patient and society should be performed. It is thus important to stay up to date with credible evidence.

2. Avoiding cancellation
Surgery is a scare and expensive resource. Once a decision to operate is made, cancelling the procedure particularly on the day of scheduled surgery, has far reaching consequences for the patient, healthcare system and society.

3. Long-term outcome
Screening may identify conditions which have been missed or inadequately managed in the primary health care setting and lead to the initiation of appropriate strategies or optimising chronic treatment. These include but are not limited to:

a. Anaemia
b. Hypertension
c. Diabetes
d. Prehabilitation

4. Day case surgery
Health expenditure on surgery is massive and finding appropriate ways of limiting this mushrooming cost has led to a large proportion of cases being performed as day cases. Day case surgery limits the cost of an overnight admission (beds, nursing staff, linen, food). Medically appropriate patients, with appropriate social support and ability to contact and return to hospital; and those scheduled for appropriate surgery should be identified during the screening process. Additional benefits include favourable patient satisfaction scores, no increased risk of complications and fewer hospital acquired infections.

5. Perioperative plan
Preoperative assessment allows for planning. Does the patient require any specific modification to the routine plan e.g. type of anaesthetic (sedation only, GA, regional, neuraxial, trigger free (MH or myopathy); additional monitoring (a-line, central line, EEG/EMG, TOE, NIRS); specialised airway technique (inhalation induction, awake fibre optic, VL); appropriate postoperative care (high care, ICU)?

Screening process

Who?

All patients for elective surgery should undergo some form of preoperative evaluation. Who performs the evaluation and how this is done has to be contextualised within local resource availability. Preoperative assessment clinics have become commonplace in Europe and US and are predominantly nurse-led with support from Anaesthesia for evaluation of higher risk patients.

Because cardiovascular pathology is the leading cause of postoperative morbidity, a significant proportion of the consultation focuses on identifying and managing CV risk.

a) Ischaemic heart disease (IHD)
- (1) High risk - avoid elective surgery in patients with:
  - (i) unstable angina
  - (ii) within 6 weeks of MI*, balloon angiography, bare metal stent insertion, CABG
    * risk of MACE in patients undergoing surgery following an MI
    < 1 month: +/- 30%
    1-2 months: +/- 20%
    > 3 months < 10%
  - (iii) within 6 months of insertion of drug eluting stent (DES)
  - (iv) poor exercise tolerance following myocardial infarction (MI)
- (2) Lower risk
  - (i) > 3 months since MI and good exercise tolerance
  - (ii) stable angina

b) *Heart failure (HF)*
- (1) High risk
  - (i) Avoid elective surgery in patients with decompensated HF
- (2) Moderate risk
  - (i) Compensated HF

c) Valvular heart disease (VHD)
- (1) High Risk
  - (i) Severe aortic stenosis
    1. Mean pressure gradient > 40mmHg
    2. Aortic valve area < $1cm^2$
    3. Symptomatic patients
  - (ii) Symptomatic mitral stenosis
    1. Progressive dyspnoea on exertion
    2. Exertional syncope
    3. HF

d) Arrythmias
- (1) Avoid elective surgery (and refer to cardiologist) in patients with symptomatic arrythmias
- (2) High risk arrhythmias include:
  - (i) Mobitz II AV block
  - (ii) Third-degree AV block
  - (iii) Symptomatic ventricular arrhythmias
  - (iv) SVT (including AF) with HR >100 bpm
  - (v) Symptomatic bradycardia
  - (vi) Newly recognized ventricular tachycardia

e) Hypertension
- (1) Does not increase perioperative risk
- (2) However, if not treated, is associated with an increased morbidity and mortality due to IHD, stroke, chronic kidney disease (CKD)
- (3) A significant number of patients with hypertension have poor blood pressure control
- (4) Undiagnosed hypertension in patients presenting for surgery should be identified

f) Diabetes Mellitus
- (1) Poorly controlled plasma glucose increases septic complications
- (2) Patients suffering from diabetes undergoing elective surgery should have an HbA_1c measured within the last 3 months
- (3) Aim for an HbA_1c < 8.5mmol/L; but <10mmol/L may unfortunately be more realistic

g) Obesity
- (1) Pathological changes occur in almost all vital organs if BMI > 30
- (2) BMI > 40 increases operative risk
  - (i) Not suitable for day case surgery
  - (ii) Exclude OSA

h) Stroke
- (1) Delay elective surgery by 3 months since last CVA/TIA

It is important to realise that other organ systems also contribute significantly to postoperative morbidity and mortality and thus need to be addressed. The list below includes conditions that should be considered/managed, but clearly this is not an exhaustive list. An appropriate screening history should be undertaken (often best protocolised to avoid missing out on crucial information) exploring all organ systems. This can be conducted either as a Self-administered Patient Questionnaire or performed by a healthcare worker (nurse or physician).

1) Respiratory
   - i) Asthma/COPD
     - (1) Identify and manage reversibility
     - (2) Management of intercurrent infections
2) Endocrine
   - i) Appropriate treatment of Hypo/hyperthyroidism
     - (1) Clinical and biochemical assessment
3) Renal
   - i) Obtain an impression of the baseline renal function

   ii) Ideally undergo surgery when renal function is “back to baseline” and avoid ‘multiple hits’ which increase the risk of AKI
4) CNS
   i) Frailty
   ii) Dementia
   iii) Depression/anxiety
   iv) Chronic pain
5) Previous Surgery and Anaesthesia and related complications

How?

Special investigations
Most preoperative investigations are aimed at
1) Minimising the postponement of surgery
2) Shortening the preoperative inpatient days

Absence of preoperative testing does not appear to be associated with increased morbidity and mortality in surgical patients undergoing general anaesthesia. Tests should be *selective* and *NOT routine,* directed by history and examination. Patient characteristics have a greater role than type of surgery in deciding which preoperative investigations should be requested. Tests ordered should affect change in practice or assist in decision making.

1) Chest x-rays
a) Abnormal in 2.5 – 37% and result in a management change in 0-2.1% of cases.
b) Should NOT be used routinely for predicting the risk of postoperative pulmonary complications (POPC)
c) Indication:
   i) Patients with new or unstable cardiopulmonary signs or symptoms (*weak recommendation)*
   ii) Patients at increased risk of POPC but only if results will alter perioperative management e.g. inform decisions or postpone surgery (*weak recommendation)*

2) ECG
a) Abnormal in 4.6-31.7% and management changes in 0-2.2% of cases.
b) NOT INDICATED
   i) If no clinical risk factors (*strong recommendation)*
   ii) Asymptomatic going for low risk surgery *(strong recommendation)*
c) INDICATED
   (1) Ischaemic or structural cardiovascular disease for intermediate/high-risk surgery (*weak recommendation)*

3) Lung Function Test
a) Patient related:
   (1) INDICATED
      (a) Active wheezing
      (b) Impaired lung exercise tolerance unexplained by history and examination
   (2) REASONABLE in the following if there has been an interval from the last evaluation (generally 12 months)
      (a) Asthmatic
      (b) Symptomatic COPD
      (c) Patients with scoliosis with restrictive function
   (3) COULD CONSIDER for ASA 3/4 with respiratory disease going for intermediate/high risk surgery (particularly open upper abdominal surgery).
b) Surgery related: lung resection

4) Trans-thoracic echo (TTE)
a) NOT INDICATED in asymptomatic patients for low or intermediate risk surgery (*strong recommendation)*
b) INDICATED
   i) in clinically suspected moderate or severe valvular stenosis or regurgitation if a TTE has

not been performed in the last 12 months (*strong recommendation)*

ii) in patients with a significant change in clinical status since the last TTE (*strong recommendation)*

5) *Haemoglobin*

a) Literature suggests that Hb of less than 10g/dL occurs in less than 5% of patients however this does not reflect low- and middle-income countries where at least a third of patients have anaemia and probably at least half of those have moderate or severe disease.

b) Screening and developing strategies to manage anaemia is taking centre stage in both high- and low-income countries

6) Other common investigations and their recommendations

Patient	Type of surgery	Test	Recommendation
ASA 1	Minor or intermediate	nil	strong
	Major	FBC	strong
		U&E	weak
ASA 1 and > 65y	Major	ECG (if not done in last 12 months)	weak
ASA 2	Minor	nil	strong
	Intermediate	U&E	weak
ASA 2 and Cardiovascular or renal disease or DM	Intermediate	ECG	strong
	Major	FBC, U&E, ECG	strong
ASA 3/4	Any surgery	U&E	weak

When?

Timing of when to screen is contentious and lacks robust evidence.

High disease severity – majority of specialists would advocate to see the patient before the day of surgery (even for low risk surgery).

Low disease severity – majority of specialists would advocate that only high surgical invasiveness would warrant a before the day of surgery review. Medium and low risk procedures could be seen on or before the day of surgery.

In summary, the more invasive the procedure and the greater the severity of disease, the more appropriate it is to see the patient before the day of surgery. In deciding how long before surgery depends on a number of factors. Importantly the disease process and how much time is needed to correct it has to be considered:
e.g.

1. Anaemia – meaningful interventions will probably require 3-4 weeks
2. Hypertension – probably 2-3 weeks
3. Reactive airway/ reversibility – probably 2-3 weeks
4. Decompensated Heart failure – Depends on aetiology (probably at least 2 weeks but may well be longer)
    a. Non-compliance
    b. Infective,
    c. Arrythmias
    d. Hypertension
    e. Ischaemic
    f. PE
    g. Endocrine

5. Thyroid disease
    a. Hypothyroidism: treatment initiation depends on patient co-morbidities (go slow in the elderly). Thyroid function should be reviewed and adjusted after 4-6 weeks. Thus, purely elective surgery may well need to be postponed by 2 to 3 months.
    b. Hyperthyroidism: probably 3-8 weeks

Seeing the patient in excess of 1 month may lead to significant changes in the patient's condition such as development of new chest infections and decompensation of heart failure which may lead to cancellation of elective surgery.

Summary

Preoperative screening should be a structured evidence-based process that incorporates locally available resources to identify and manage modifiable contributors of adverse outcomes in both the individual and society.

Useful References

1. Preoperative Testing for Noncardiac Surgery - www.dynamed.com
2. Preoperative assessment. M. Bachmann et al EBM Guidelines 2018. www.bestpractice.bmj.com
3. Duceppe et al Can J Cariology 2017; 33(1):17-32
4. S. Cohn. Preoperative evaluation for non-cardiac surgery. Ann Intern Med 2016

Approach to ECG Analysis and Interpretation

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We have prepared short notes on ECG analysis and interpretation for the Anaesthesia Refresher Course. The text and images herein are predominantly from our ECG reference app, ***ECG APPtitude****. The material is the intellectual property of the University of Cape Town and should not be used or shared in any other way than the purposes of this refresher course, without prior permission of the authors.* ***ECG APPtitude*** *is available for download from the App Store and Google Play.*

Always be systematic with ECG analysis and interpretation. Start with the **basic observations**, progress to working out the **mechanism** of the rhythm. **Diagnosis** comes last. Beware snap ("blink") diagnoses and hasty conclusions.

Step 1: Rhythm analysis

The first step in analysing the 12-lead ECG is to do a rhythm analysis.

The rhythm is described by analysing:

- The **regularity** of the rhythm
  - Regular
  - Irregular (no pattern, group beating, pauses, premature beats, respiratory variation)

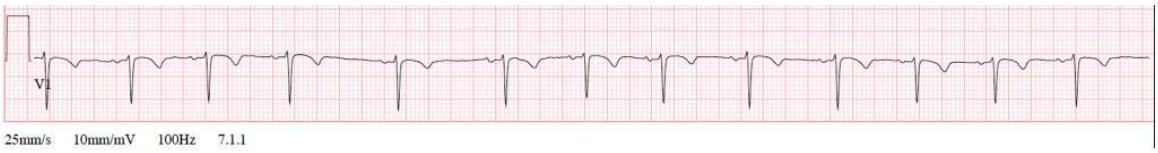
- The **rate**
  - Normal: 50-100 /min. While 50-60 is 'bradycardia', not usually pathological.
  - Slow (bradycardia): ≤50 /min.
  - Fast (tachycardia): >100 /min. Important tachycardias are usually >120 /min.

The simplest way of determining the ventricular rate is by looking at the full-length rhythm strip of the 12-lead ECG:

Number of QRS complexes X 6 = rate per minute

NB: to apply this calculation, the ***paper speed*** *must be set at* ***25 mm/s***

At a paper speed of 25mm/s, the 12 lead ECG accounts for 10 seconds. Therefore, to calculate the rate over 60 seconds (1 minute), you need to multiply the 10 second rhythm strip by 6.



In the above rhythm strip, there are 13 QRS complexes, which multiplied by 6, tells you that the rate is 78. This method allows for the calculation of the ventricular rate despite irregularity, as shown in the rhythm strip above.

Normal rate

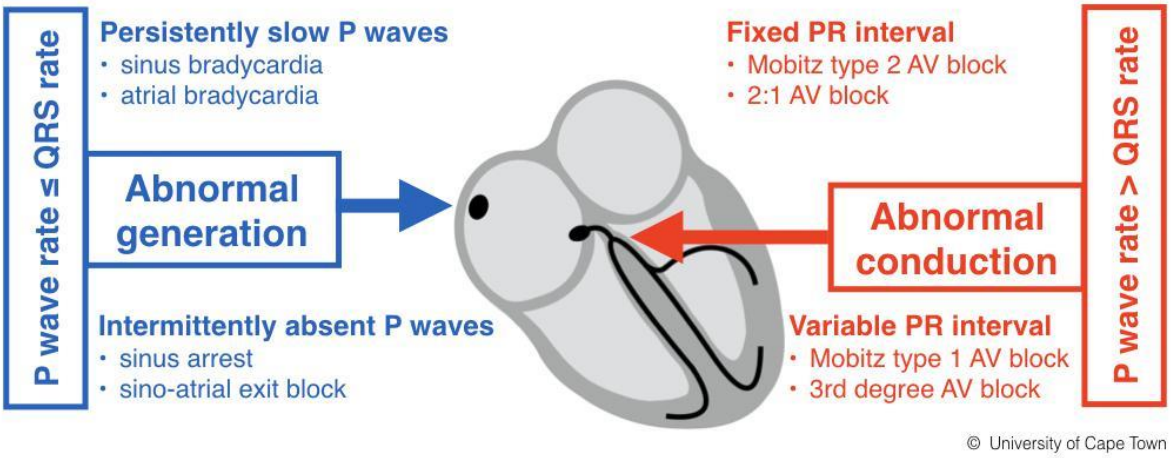
Usually sinus, but may be other atrial rhythms, accelerated junctional and ventricular rhythms or paced rhythms. If the QRS is wide, first decide on the mechanism of the wide QRS (see 'Wide QRS Rhythms, below). Pay particular attention to P wave axis and morphology and relationship to QRS. A

randomly irregular rhythm at a normal rate may be atrial fibrillation (AF) or atrial flutter with variable AV block.

Bradycardia

2 main mechanisms:

- Abnormal impulse generation – sinus node dysfunction
- Abnormal conduction – 2nd & 3rd degree AV block



Bradycardia due to a **generation abnormality** refers to **slowed or absent atrial activity**.

Sinus dysfunction

- Intrinsic (sinus node dysfunction, i.e. SA arrest or SA block)
- Extrinsic ("sick bradycardia")

  - Hyperkalaemia
  - Hypothermia
  - Hypothyroidism
  - Hypoxia
  - Hypercarbia
  - Head injury
  - Hyperautonomia ("vasovagal")
  - Myocardial infarct
  - Drugs (e.g. calcium channel blocker + beta blocker)

Bradycardia due to conduction abnormality refers to **defective atrioventricular (AV) conduction**, in which atrial depolarisations do not conduct to the ventricles, as it would in normal physiology.

Differential diagnoses for bradycardia due to conduction abnormality include

- 2nd degree AV block
  - Mobitz type 1 / Wenckebach
  - Mobitz type 2
  - 2:1 AV block

- High grade AV block
  - 3:1 or higher conduction ratios
  - Predominantly 3rd degree AV block with occasional conduction

- 3rd degree AV block / complete heart block

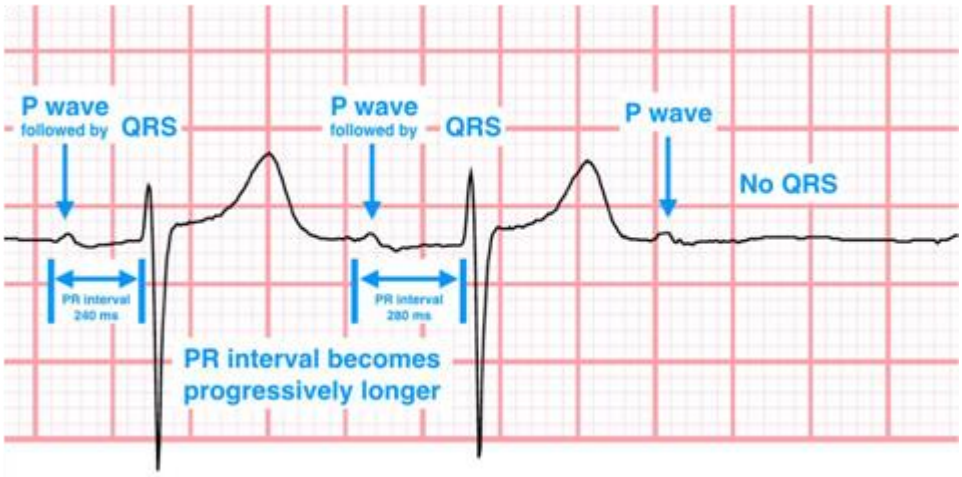
Bradycardia due to a conduction abnormality is recognised on the ECG by **more P waves than QRS complexes** ("Missing QRS complexes").

- In 2nd degree AV block, **not all P waves are followed by QRS complexes** (some conduct, some don't).
- In high grade AV block, most P waves are not followed by QRSs, but occasional Ps conduct.
- In 3rd degree AV block, there is **AV dissociation** (no relationship between P waves and QRS complexes). In atrial fibrillation with complete heart block, the ventricular response becomes regular, with either a narrow (junctional) or wide (ventricular) escape.

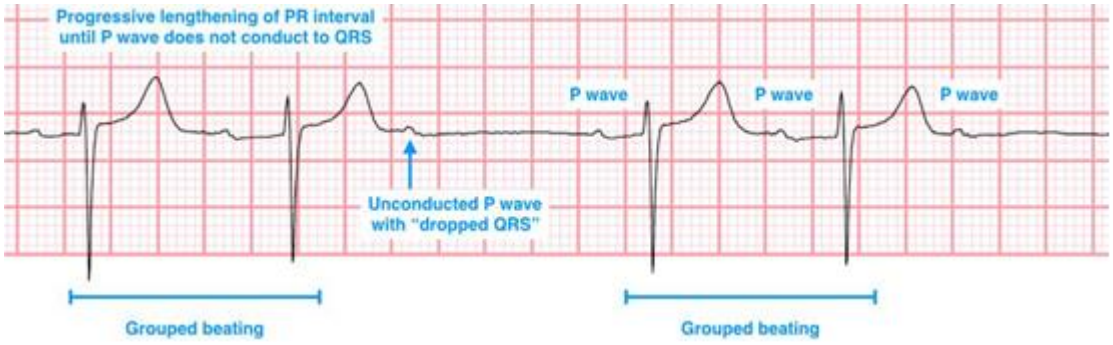
Mobitz type I second degree AV block (Wenckebach)

ECG features of Mobitz type I (Wenckebach type) second degree AV block:

- Irregular rhythm (grouped beating)
- Uniform P wave morphology
- **PR interval becomes progressively longer until the P wave is not followed by a QRS** ("dropped beat"). The cycle then repeats.
  - The PR interval is longest before the dropped QRS
  - The PR interval is shortest after the dropped QRS



The cycle then repeats:



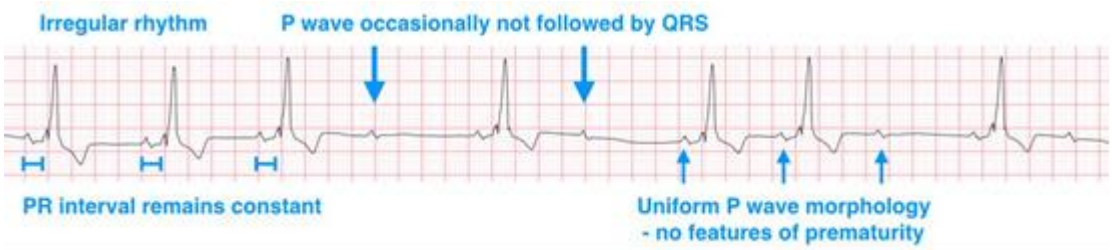
Occasionally, Wenckebach AV block occurs intermittently, without a pattern of grouped beating.

Mobitz type II second degree AV block

ECG features of Mobitz type II second degree AV block:

- Irregular rhythm (regular, with intermittent pauses)
- Uniform P wave morphology (with no features of prematurity)

- **PR interval remains fixed / constant** (no variation in PR interval length). The PR following the pause is equal to the one preceding the dropped QRS.
- **Occasionally the P wave is not followed by a QRS complex**, i.e. intermittently (and unpredictably), the P wave does not conduct to the QRS.

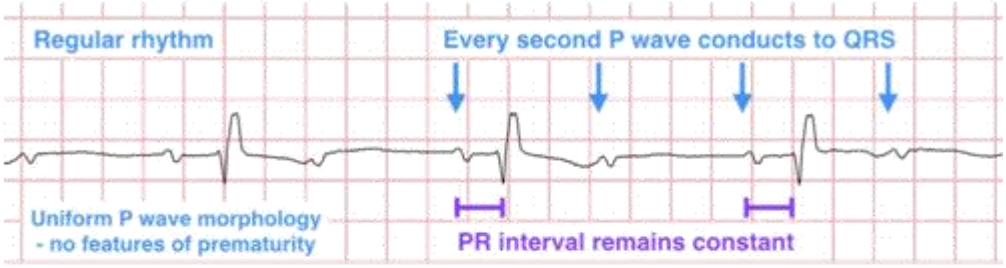


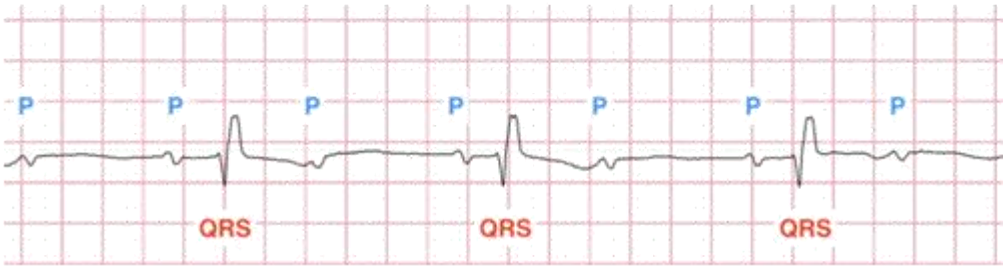
Second degree AV block, with 2:1 conduction

ECG features of 2:1 AV block:

- Regular rhythm
- Uniform P wave morphology (with no features of prematurity)
- **PR interval remains fixed / constant** (no variation in PR interval length)
- **Every second P wave is not followed by a QRS complex**.

2:1 AV block is often mistakenly called Mobitz II, but 2:1 AV block cannot be classified as Mobitz I or Mobitz II, as at least 2 consecutively conducted Ps are necessary to differentiate Mobitz I and II





Third degree AV block (complete heart block)

In third degree AV block there is no conduction from the atria to the ventricles.

ECG features of third degree AV block:

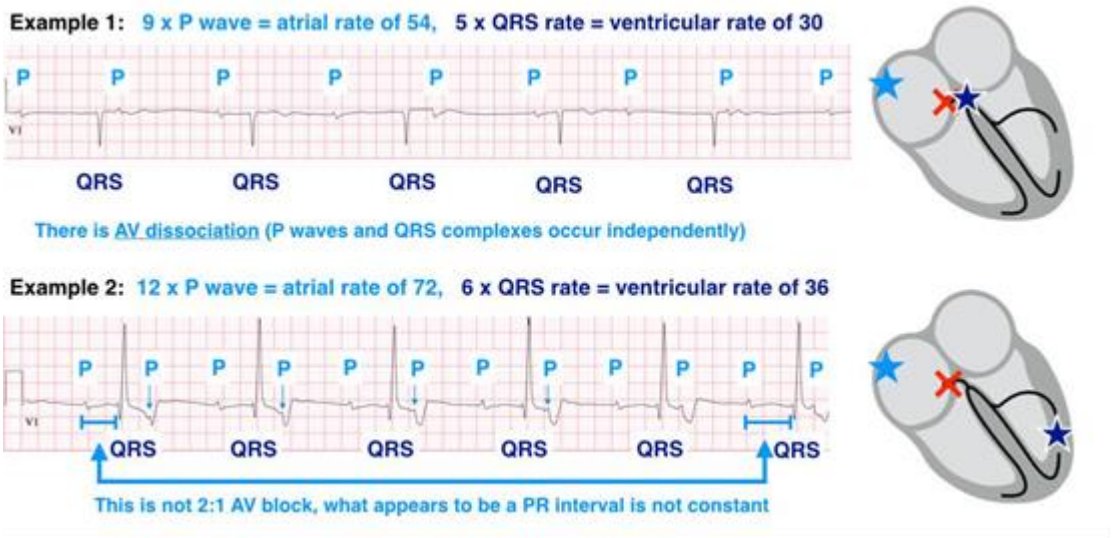
- Regular bradycardia

There are more P waves than QRS complexes (the atrial rate is faster than the ventricular rate)
The atrial rate can be regular or irregular (including atrial fibrillation or flutter), but the ventricular rate is regular

- There is **AV dissociation**

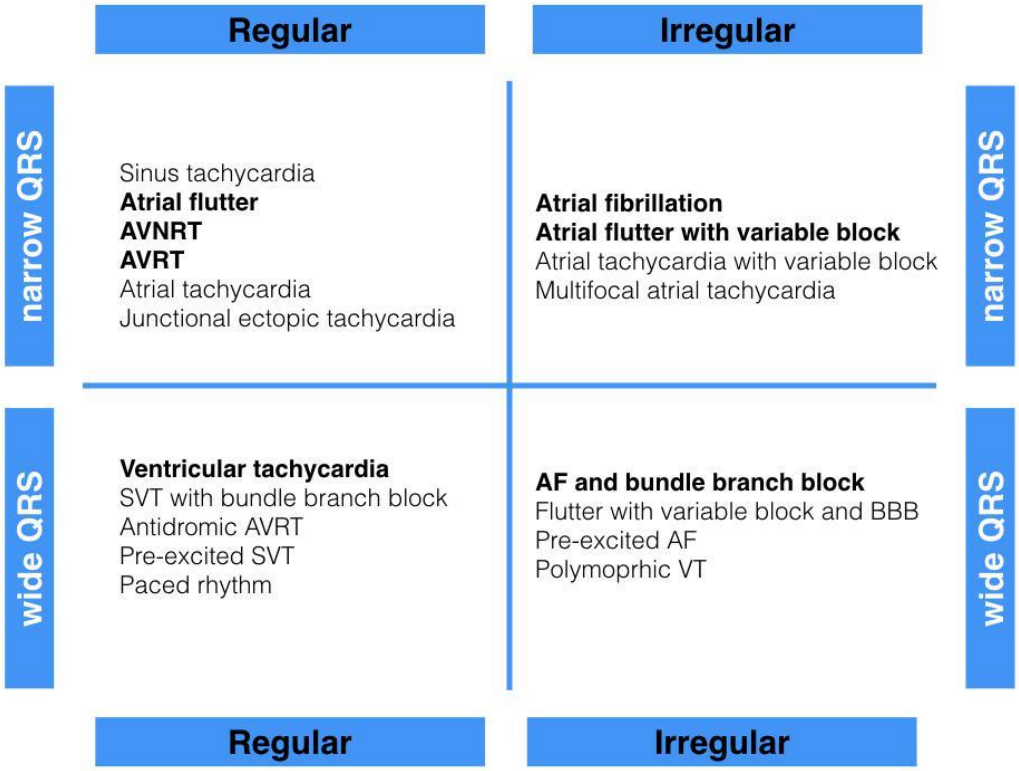
No atrial impulses are conducted to the ventricles (there is no AV conduction)
The atrial and ventricular activation are independent

- What appears to be a PR interval with varying lengths, cannot be called a PR interval, because of the AV dissociation



Tachycardia

Rather than trying to decide a priori the nature of a tachycardia, start by placing it in one of 4 groups, based on objective measurements: regular or irregular, narrow or wide QRS. Each category has a limited number of possible mechanisms.



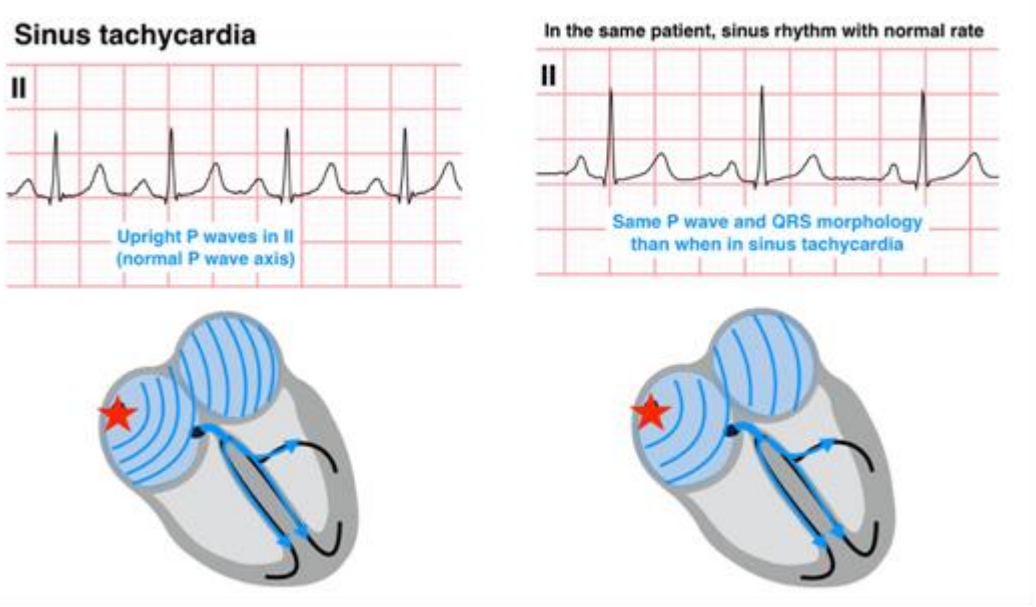
Importantly, when one analyses the wide QRS tachycardias, start by looking at the QRS morphology first, before looking for P waves.

Sinus tachycardia

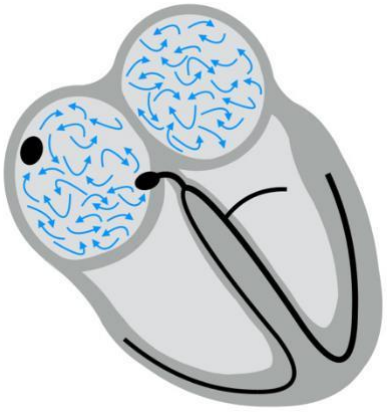
Sinus tachycardia is not purely an ECG diagnosis. There must be a clinical reason (e.g. fever, thyrotoxicosis etc) to explain the tachycardia.

ECG features of sinus tachycardia:

- Sinus rhythm, but rate > 100 per minute
  - Rate usually less than *130 bpm at rest* in adults
  - Maximum rate allowed: 220 minus the patient's age (in years) at peak exercise
- P wave axis normal (0 to +70º)
- The PR interval is usually less than 200ms, because of catecholamine effects on the AV node. If it is 200ms or longer, suspect atrial tachycardia, even if the P wave axis is normal.
- QRS morphology in sinus tachycardia should be the same as the QRS morphology when in sinus rhythm with normal rate



Atrial fibrillation



As opposed to the uniform and concentric spread of the electric impulse in normal atrial depolarisation, **there is chaotic, asynchronous atrial impulse propagation in atrial fibrillation**. The numerous wavelets course irregularly through the atria, reaching the AV node at irregular intervals and causing irregular AV node conduction. Some wavelets reach the AV node when it is not yet repolarized, and thus not all fibrillatory waves are conducted to the ventricles, which is fortunate, otherwise ventricular fibrillation would result.

ECG features of **atrial fibrillation** are:

- **Irregularly irregular rhythm**

There is no pattern to the irregularity, the ventricular beats occur at an unpredictable time and give rise to random RR intervals

- **The rate can vary**

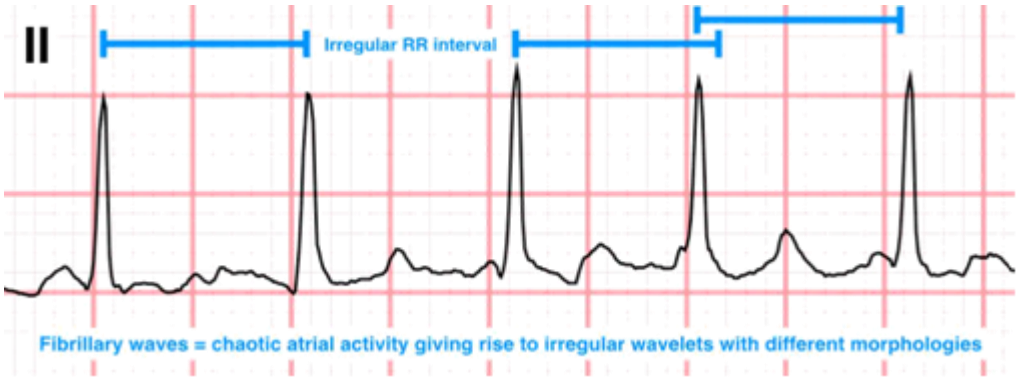
  - Uncontrolled rate > 100
  - Controlled rate < 100
  - Bradycardia < 60

- No P waves

  - there are **fibrillatory waves** (irregular undulations of the baseline),
  - which can be coarse or fine, *best seen in lead V1*
  - atrial activity is very rapid (400-700/minute)

- QRS complexes

  - **Usually narrow QRS complexes**
  - (unless there is a coincidental bundle branch block)
  - Often vary in amplitude



Atrial flutter

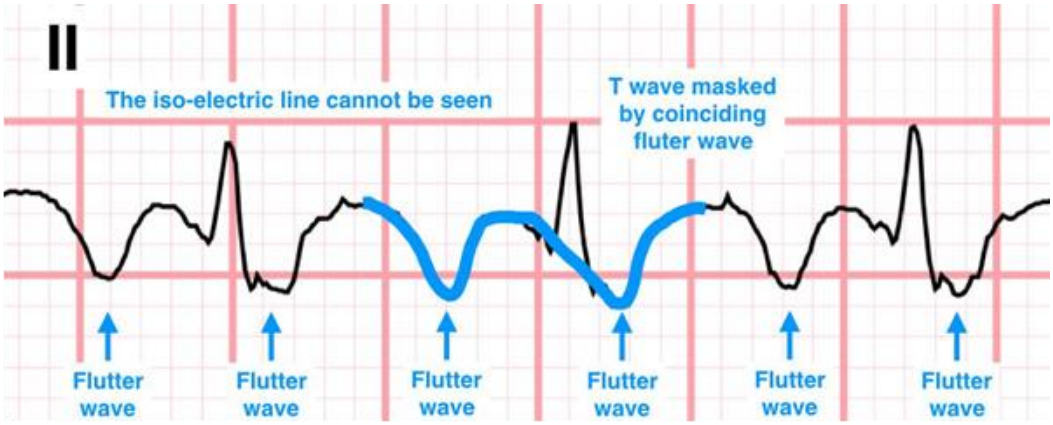
The mechanism of **atrial flutter** is a large re-entry circuit, usually in the right atrium.

ECG features of atrial flutter:

- **Regular** atrial rate can be from 240 to 360 (average 300) with uniform pattern

  - Look for **flutter waves** – usually negative in lead II, positive in V1
  - Look for blocked flutter wave at the end of the QRS / beginning of the ST segment

The ventricular rate in atrial flutter depends on the degree of AV block (e.g. QRS rate of approximately 150 in 2:1 block, QRS rate of approximately 100 in 3:1 block, approximately 75 in 4:1 block etc.)

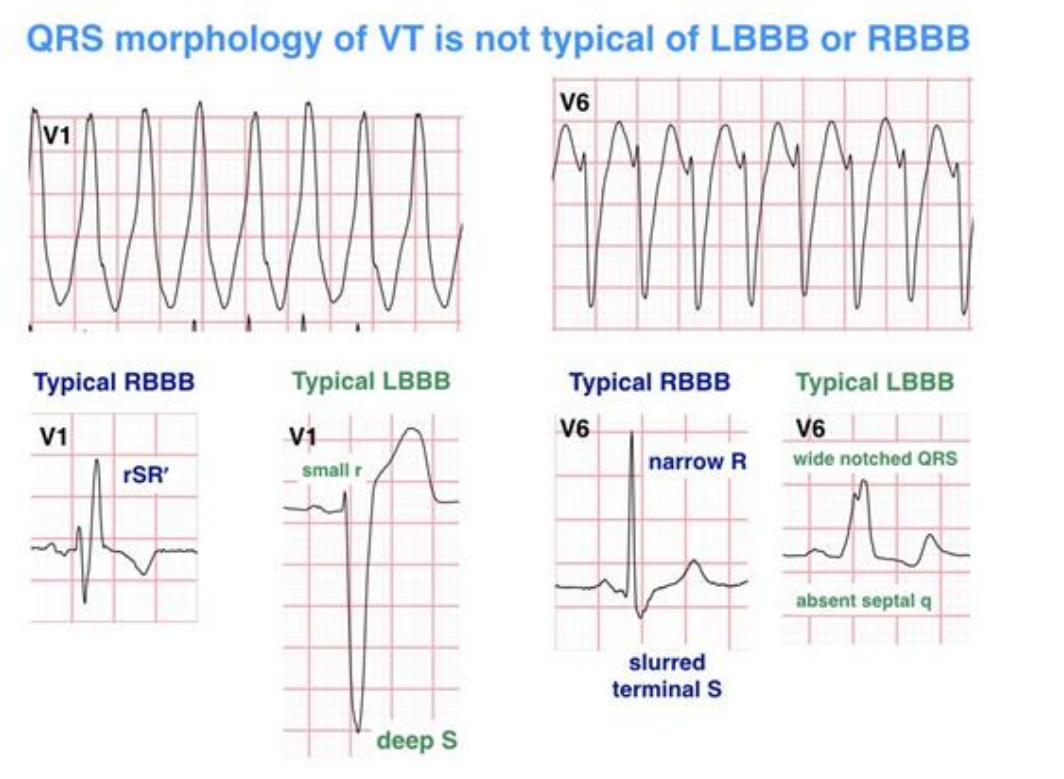


Ventricular tachycardia

For the reasons of safety and probability, **VT** is the default diagnosis in the setting of **regular broad complex tachycardia** (VT is by far (>80%) the most common diagnosis).

ECG features to look out for:

- **Primary analysis: analyse the QRS morphology** (look especially in V1 and V6)
  - the QRS does not have a typical right or left bundle branch morphology
  - slow initial and terminal depolarisation
  - QS waves in V5 and V6 are pathognomonic of VT



- **Secondary analysis: look for P waves** (only once your analysis of QRS is done)
  - P waves can be masked by the QRS complexes and not seen at all
  - P waves occur after the QRS complex with abnormal P wave axis (this is not diagnostic of VT though)
  - AV dissociation is diagnostic of VT (no relationship between P waves and QRS complexes, P waves seen intermittently)

Step 2: Waveform analysis

The P wave

When analysing the P wave, one should look at:

1. the location of the P wave, i.e. its relation to the QRS complex
2. the P wave deflection, i.e. the P wave axis
3. the P wave morphology, including its amplitude (height) and duration (width)

Characteristics of a normal P wave:

1. Location / relation to QRS

- The P wave should proceed the QRS complex
- There should be one P wave for every QRS complex

2. Deflection / P wave axis

- Upright in standard lead I, II, aVF, V2 – V6
- Inverted in aVR
- Commonly biphasic in V1

3.1. Morphology

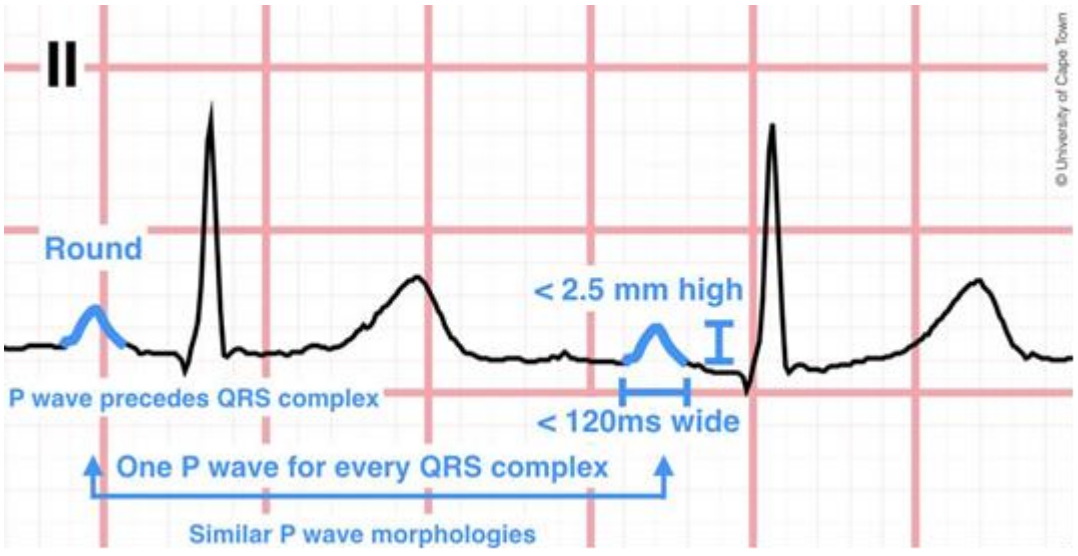
- Consecutive P waves should have a uniform morphology
- Usually round in I, II, aVF, V2 – V6
- Can be biphasic in V1 (starts with upright deflection and ends with downwards deflection)

3.2. Amplitude

- ≤ 2.5 mm high in standard lead II (two and a half small blocks)

3.3. Duration

- < 120 ms wide in standard lead II (three small blocks)



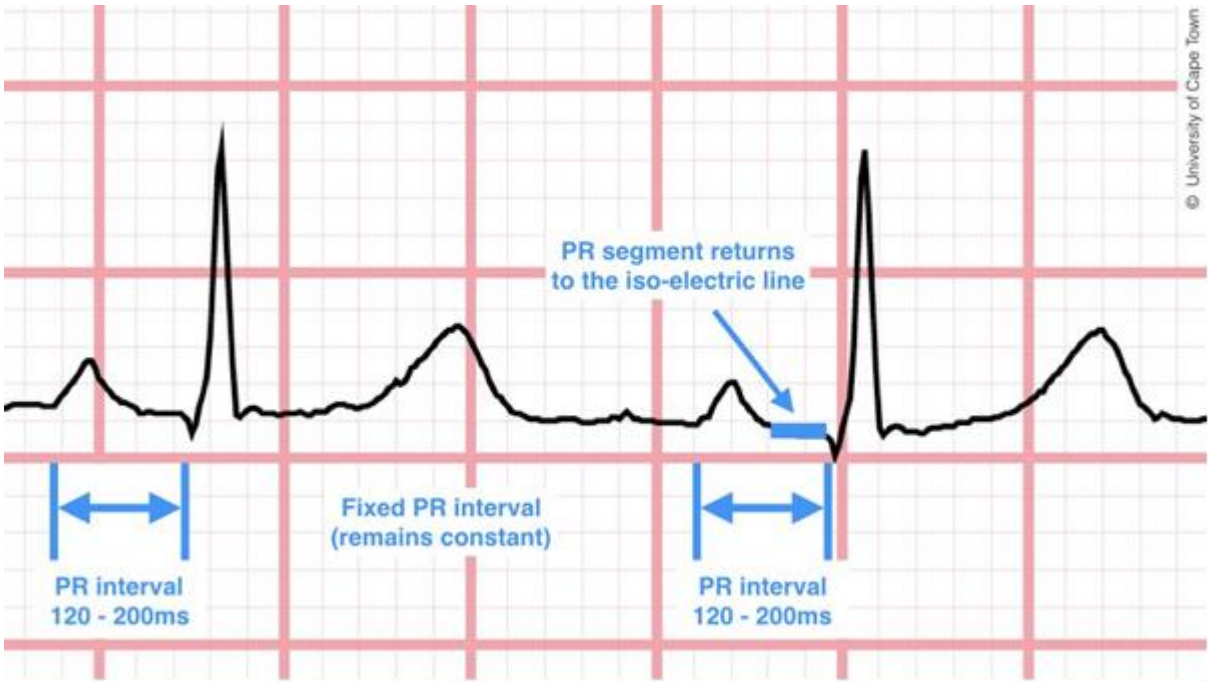
PR interval

When analysing the PR interval, one should:

1. Measure the PR interval - from the onset of the P to the beginning of the QRS complex
2. Determine whether the PR interval remains fixed / constant throughout the rhythm strip
3. Determine whether the PR segment is on the iso-electric line

Characteristics of a normal PR interval:

- **Is between 120ms and 200ms long**
  (between 3 small blocks and 5 small blocks or 1 big block; each small block is 40ms long)
- **Has a fixed / constant length**
  (remains consistent in length throughout the rhythm strip)
- The **PR segment** should be **on the iso-electric line**
  (segment after the P wave and before the first deflection of the QRS)

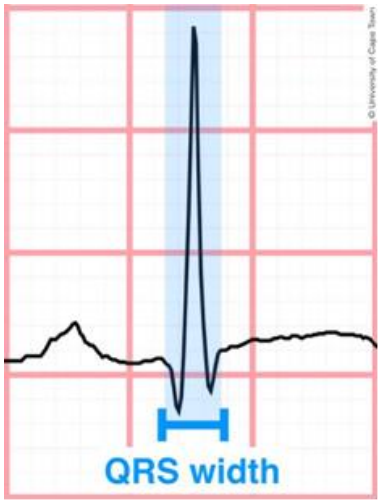


QRS complex

When analysing the QRS complex, there are 4 aspects to consider:

1. QRS width
2. QRS axis
3. QRS voltage / size
4. Q waves

1. QRS width



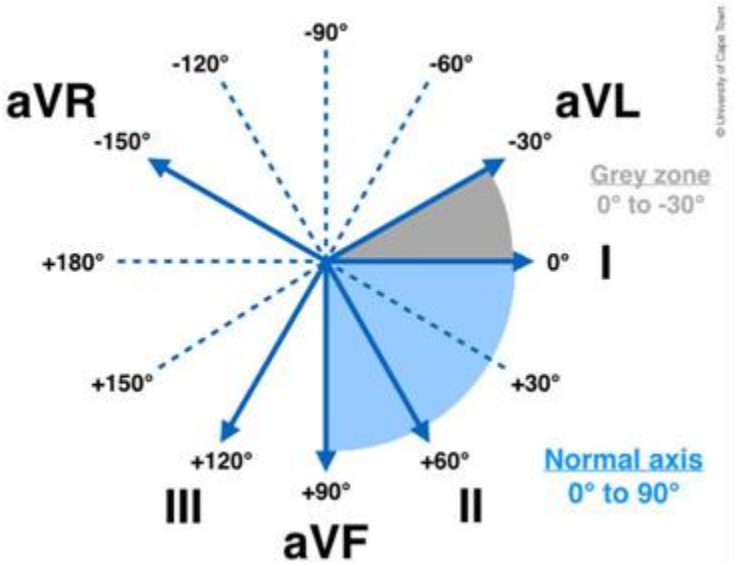
The QRS width (total QRS duration) represents the **time that it takes for ventricular depolarisation to occur**. A narrow QRS complex indicates normal, rapid distribution of the depolarisation wave via the His-Purkinje system to the ventricular myocardium.

In order to measure the QRS width, the widest QRS complex in the 12 lead ECG should be used. Measure from the beginning to the end of the complex. The **normal QRS width is between 60ms and 100ms** (1.5 and 2.5 small blocks). A QRS width of 120ms and above is broad or wide and is considered abnormal. In the setting of a wide QRS complex, the morphology of the QRS should be carefully examined for bundle branch blocks, in particular. *Refer to the approach to the wide QRS complex for more detail.*

2. QRS axis

The QRS axis represents the mean vector of ventricular depolarisation (a sum of the different electrical forces during ventricular activation), as measured in the limb leads. The direction of this vector depends on the sequence of depolarisation through the His-Purkinje system in the left ventricle mainly. The right ventricle has only a small contribution to this vector in normal hearts.

The normal QRS axis in adults is between 0° and +90°, with 0° to -30° being a grey zone.



To measure the QRS axis, look at the limb leads (I, II, III, aVR, aVL and aVF):

1. Establish the lead with the most equiphasic QRS complex, i.e. the lead where the R and S waves are the most similar in size. This lead is perpendicular to the axis.

2. Look at the lead perpendicular to the lead with the most equiphasic QRS complex:

a. If the QRS complex in this lead is predominantly positive (i.e. the R is taller than the S wave), this means that the axis is moving towards this lead
b. If the QRS complex in this lead is predominantly negative (i.e. the R is smaller than the S wave), this means that the axis is moving away from this lead

3. QRS voltage / size

In the normal heart:

V1 and V2

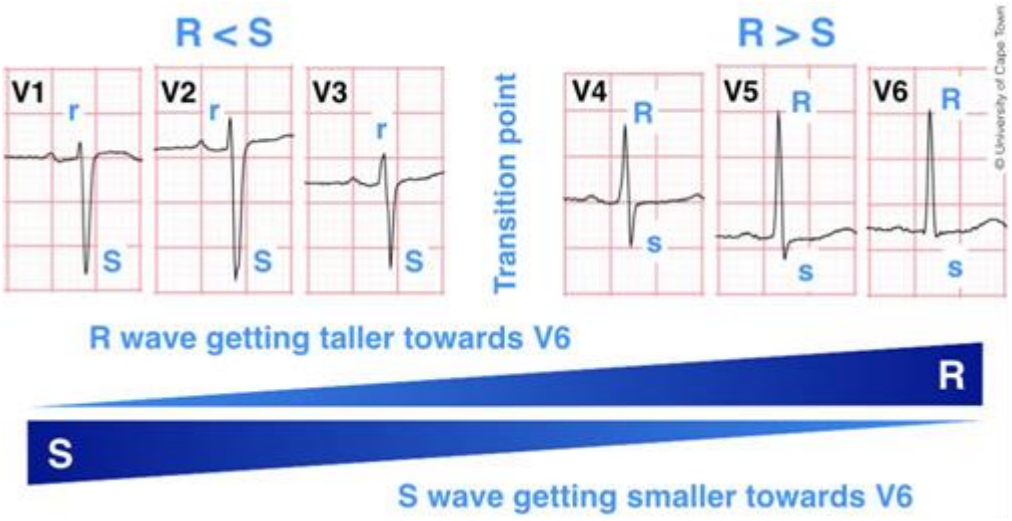
- rS complex, i.e. small R wave with deep S wave
- Any Q wave (no matter how small) is abnormal in V1, V2, V3. However, a Q in V1 can be due to incorrect lead placement, above the 4th interspace.

V2 and V3

- Transition point, i.e. the R becomes taller than the S wave.
- There is good R wave progression if the R wave is taller than the S wave in lead V4.

V5 and V6

- qRs complex, i.e. the R wave size > S wave size. The R in V5 is usually taller than in V6.
- Normal to have a small Q wave (septal depolarisation)



The QRS complexes should be

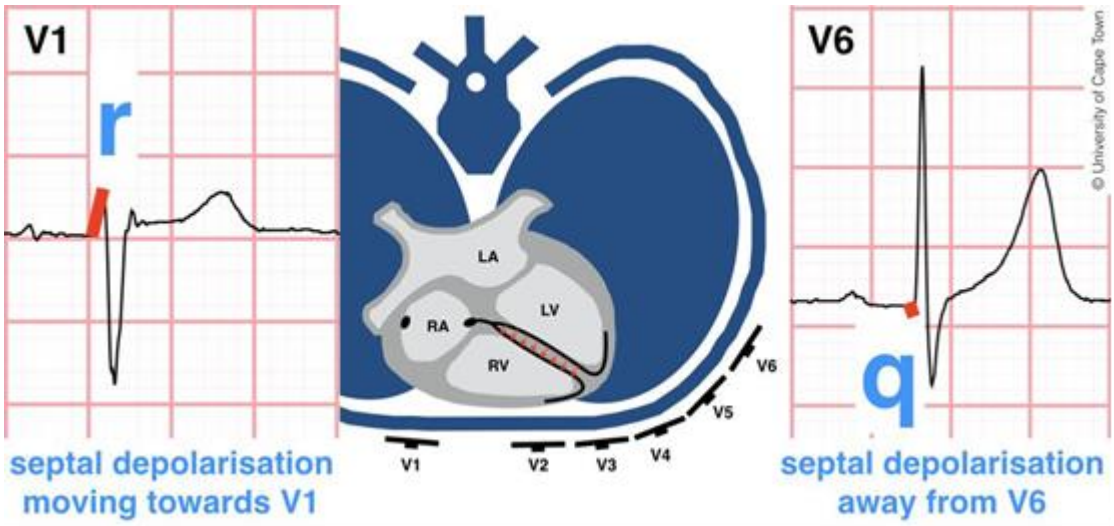
- at least 10mm in the chest leads (V1 – V6)
- at least 5mm in the limb leads (I, II, III, aVR, aVL and aVF)

But, in adults

- no R wave should be taller than 25mm
- no S wave should be deeper than 25 mm

4. Q waves

In normal physiology, the septum depolarises from left to right.

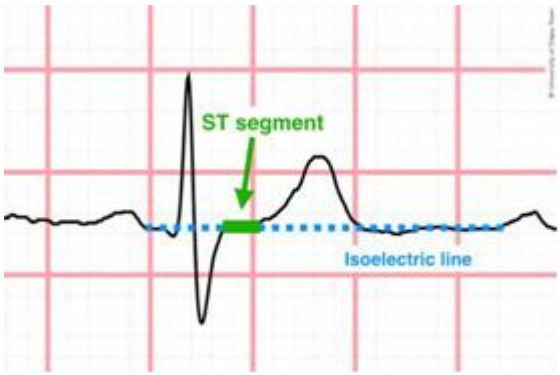


On the ECG, this causes small Q waves (i.e. **less than 1 small block wide** and **less than 2 small blocks deep**) in the left sided leads (i.e. **I, II, aVL, V5 and V6**).

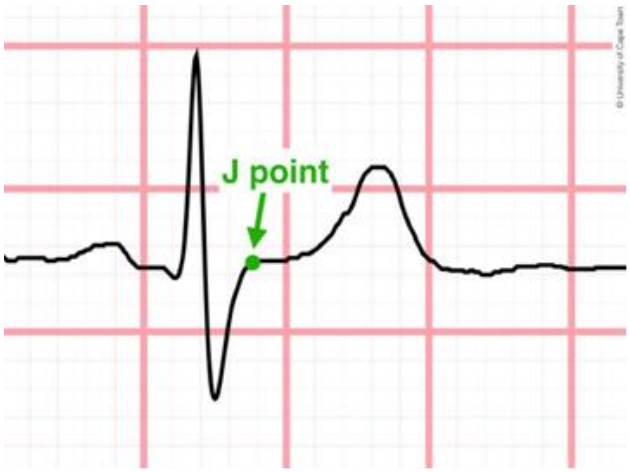
A small Q wave in standard lead III is also considered a normal variant.

The ST segment

In normal physiology, the vectors of the end of depolarisation and the vectors of the beginning of repolarisation neutralize each other, causing the ST segment to be on the isoelectric line.



The ST segment should be assessed for elevation or depression at the J point.



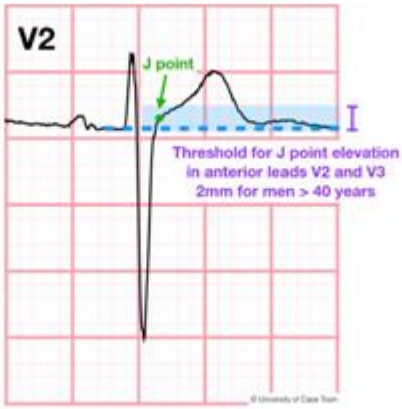
The thresholds for ST elevation depend on gender and age:

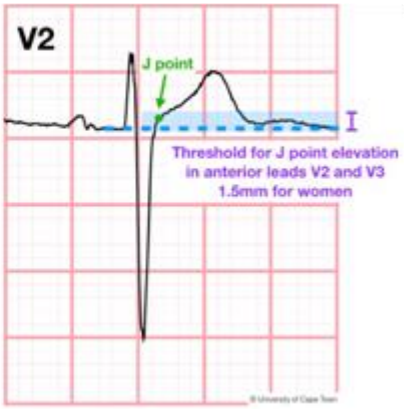
- Anterior leads: **V2** and **V3**
  - 2.5mm for men younger than 40 years
  - 2mm for men older than 40 years
  - 1.5mm for women

- Leads: **V1, V4 – V6, I, II, III, aVL, aVF** and **aVR**
  - 1mm for all ages, both genders

- Right sided leads: **V3R** and **V4R**
  - 0.5mm for all ages, both genders

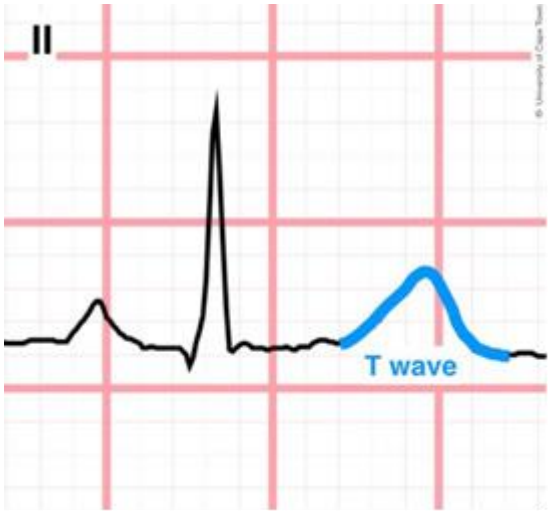
- Posterior leads: **V7, V8, V9**
  - 0.5mm for all ages, both genders





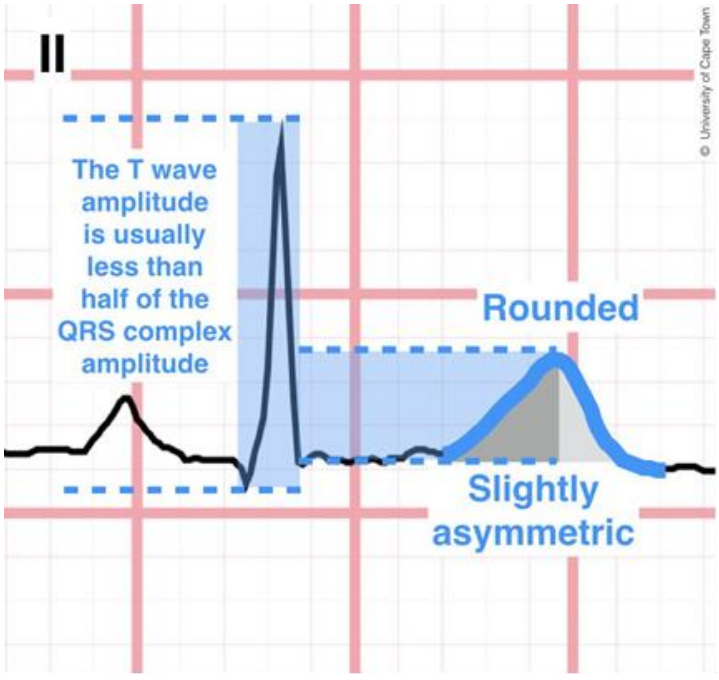
The T wave

The T wave is the rounded deflection that follows the QRS complex and is due to ventricular repolarisation.



When analysing the T wave, one should pay attention to:

1. The polarity of the T wave
2. The size of the T wave
3. The shape / morphology of the T wave

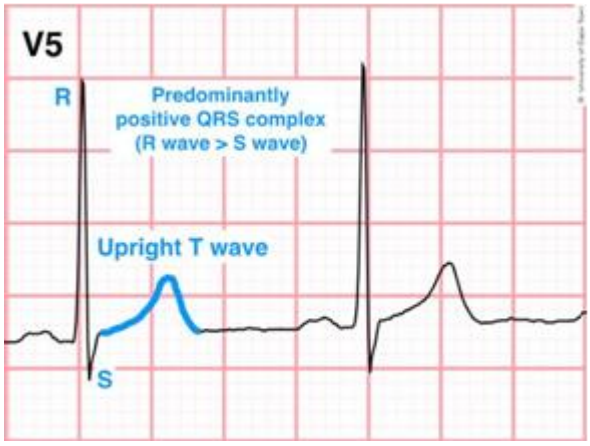


Characteristics of the normal T wave

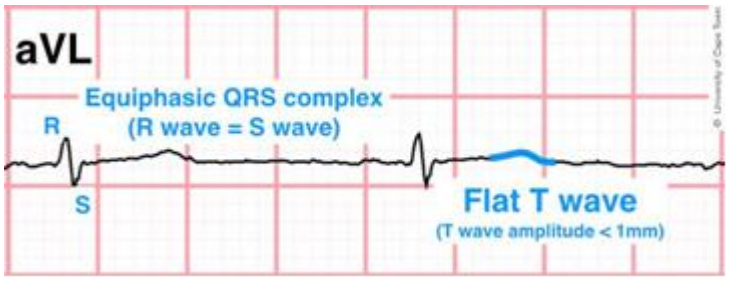
1. **T wave polarity**

The T wave is usually concordant to the QRS complex in the same lead (i.e. the T wave usually has the same polarity as the QRS complex):

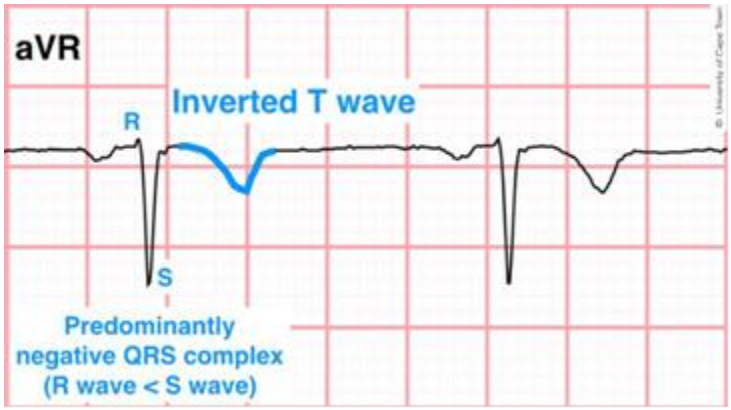
- If the QRS complex is predominantly upright (i.e. R wave amplitude > S wave amplitude), the T wave is usually upright



- If the QRS complex is equiphasic (i.e. R wave amplitude = S wave amplitude), the T wave could be upright or flat (iso-electric)

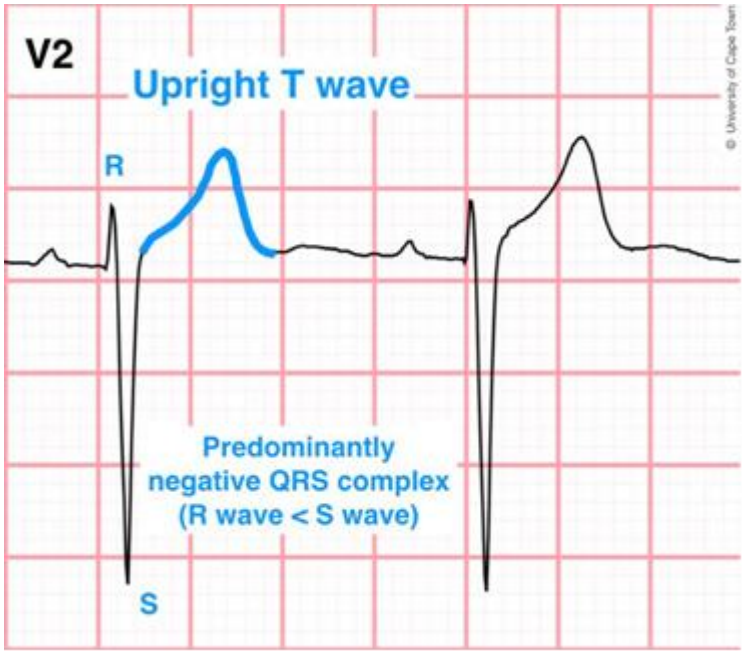


- If the QRS complex is predominantly negative (i.e. R wave amplitude < S wave amplitude), the T wave is usually inverted

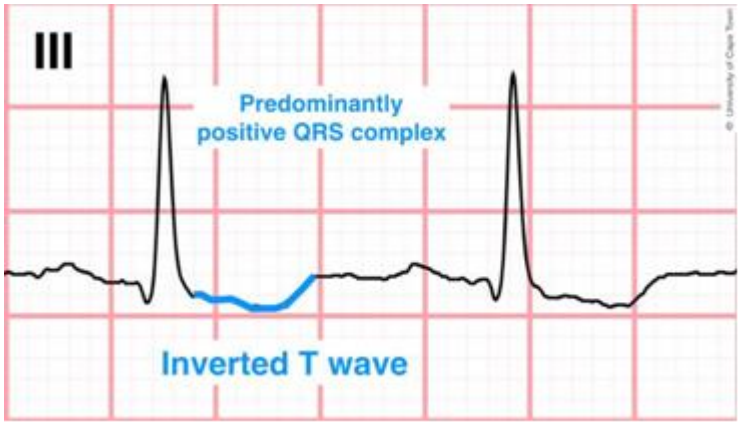


The exceptions to this rule are:

- In leads V1 and V2, the T wave is usually upright, despite the predominantly negative QRS (R < S)



- In standard lead III, the T wave can be inverted despite the predominantly upright QRS (R > S), in normal individuals

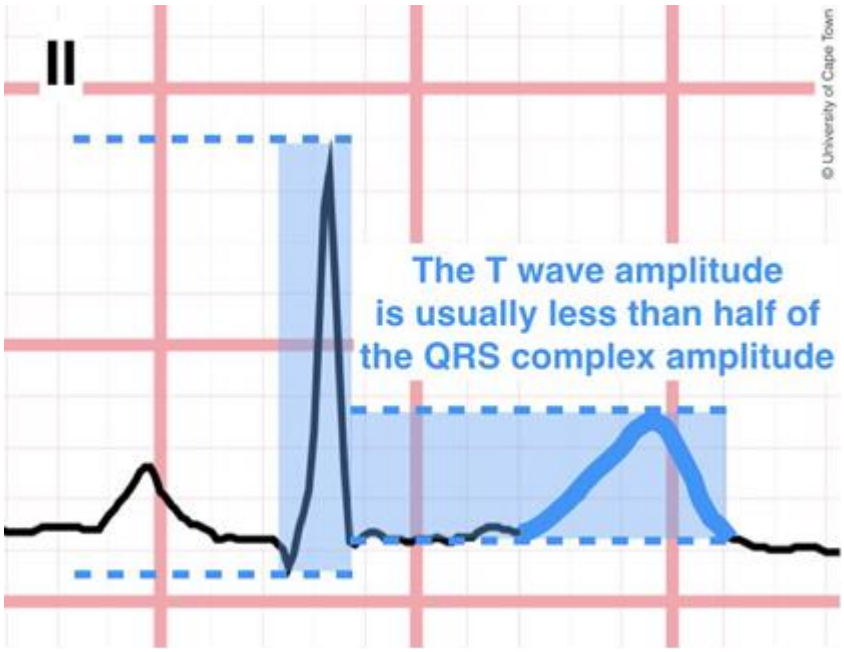


To definitively determine whether T wave inversion in the limb leads is abnormal, the angle between the QRS axis and T wave axis should be calculated. The T wave axis is calculated in the same way as the QRS complex (i.e. determine the lead with most equiphasic T wave, then look at the T wave polarity in the perpendicular lead). If the angle between the QRS complex and T wave axes are more than 60°, the T wave axis is abnormal.

2. T wave size

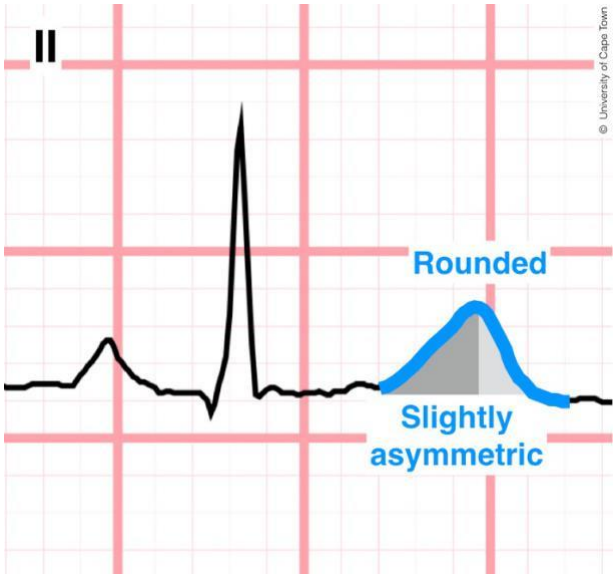
Though there is no uniform definition of normal T wave size, the T wave amplitude is usually less than half of the preceding QRS complex's amplitude. For simplicity, one could summarise normal T wave size as:

- T wave amplitude in the limb leads is usually < 5mm
- T wave amplitude in the chest leads is usually < 10mm



3. T wave shape / morphology

The normal T wave is slightly asymmetric and has a rounded peak.



The QT interval

Normal values are

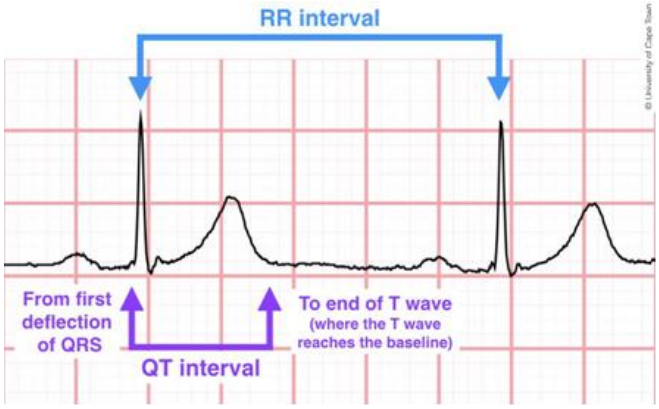
- ≤ 440ms in men
- ≤ 460ms in women

How to calculate the corrected QT (QTc) interval:

For heart rates between 60 and 100, use the **Bazett's formula**:

$$QTc = \frac{\textbf{QT interval} \text{ (calculated in seconds, not milliseconds)}}{\sqrt{\textbf{RR interval}} \text{ (calculated in seconds, not milliseconds)}}$$

The QT interval is measured taking the first deflection of the QRS up until where the T wave reaches the iso-electric line.



Bazett's formula tends to overcorrect at rapid heart rates and under-correct at slow heart rates. Thus, for bradycardia (heart rate < 60 bpm) or tachycardia (heart rate > 100 bpm) rather use:

- **Fridericia's formula**: $QTc = QT / RR^{1/3}$
- **Framingham formula**: $QTc = QT + 0.154(1 – RR)$

These formulae are impractical for routine use, but important for research use, e.g. assessment of drug effects on the QT.

The "eyeball test" is the QT interval should be less than half of the preceding RR interval

Common waveform abnormalities

Left bundle branch block

The ECG features of **complete LBBB** include:

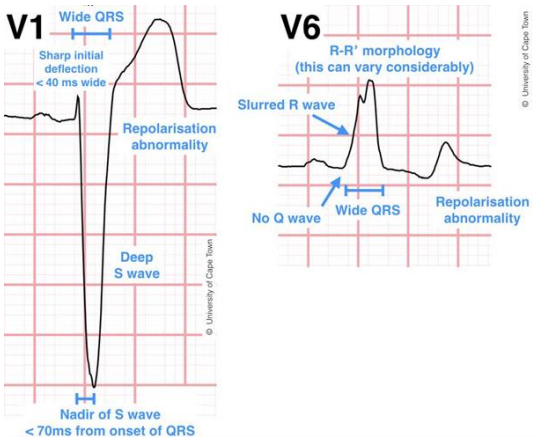
- A **QRS width** of ≥ 120ms with complete LBBB
- The **QRS axis** can be normal, left or right.
- The **QRS morphology** has a typical appearance:

  - In V1 or V2 there is an **rS pattern**

Sharp initial deflection (r wave), with small r wave that is narrow (< 40ms)
Deep S wave, with onset of QRS complex to nadir of S wave <70ms

  - In V5 or V6

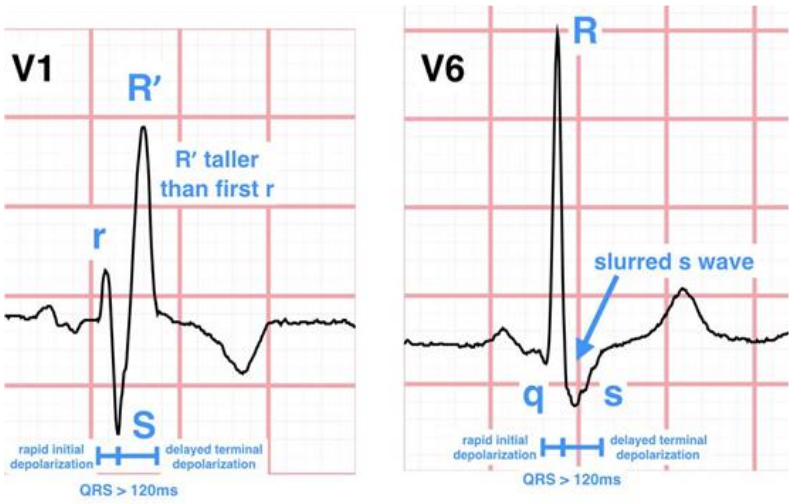
Absent septal Q wave
The R wave is broad / slurred and can be monophasic (R) or notched (R-R') – the morphology can be variable.



Right bundle branch block

The ECG features of **complete RBBB** include:

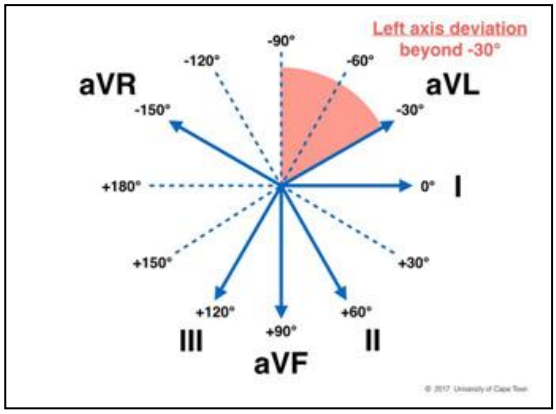
- A **QRS width** of **≥ 120ms**
- The **QRS axis** can be **normal, left** or **right**
- The **QRS morphology** has a typical appearance
    - In **V1** or **V2** there is an **rSR' / rsR' / rsr' pattern.** The second R wave (R') is taller than the first.
    - In **V5** or **V6** there is a **qRs pattern with a slurred s wave.** The s wave is wider and smaller than R wave.



Left axis deviation

The causes of left axis deviation are:

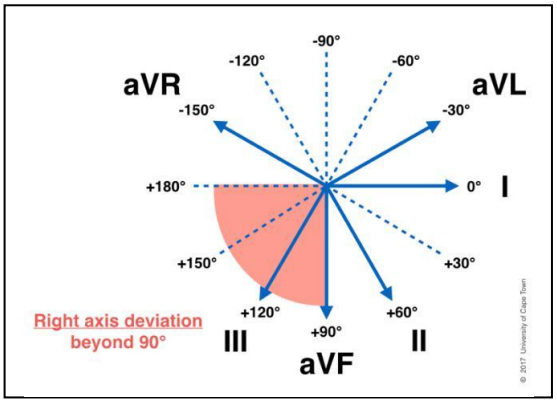
- Left anterior fascicular block
- Inferior myocardial infarction
- Rhythms originating in the ventricles:
    - Ventricular escape rhythms
    - Ventricular tachycardia
- Wolff-Parkinson-White



Right axis deviation

The causes of right axis deviation are:

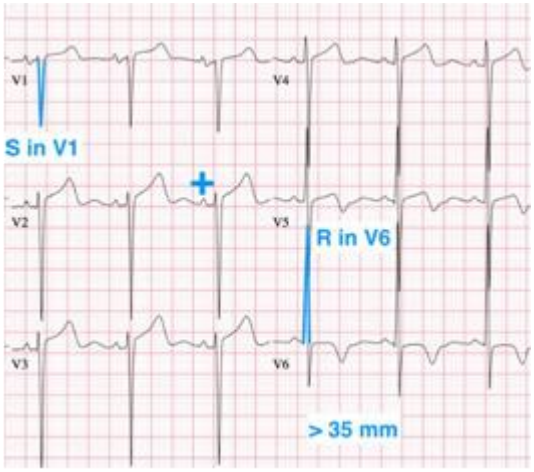
- Right ventricular hypertrophy
- Anterolateral myocardial infarction
- Rhythms originating in the ventricles
    - Ventricular escape rhythm
    - Ventricular tachycardia
- Misplaced limb leads
- Wolff-Parkinson-White
- Dextrocardia
- Left posterior fascicular block



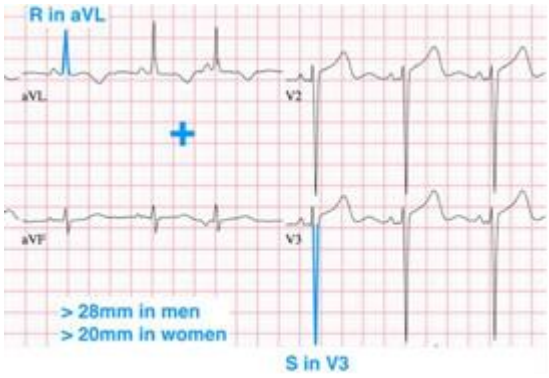
Left ventricular hypertrophy (LVH)

Left ventricular hypertrophy (LVH) is suspected if any of the following criteria is met:

Sokolow-Lyon: S in V1 + R in V5 or V6 (whichever is larger) > 35 mm (Applicable to patients 40 years and older)



Cornell criteria: S in V3 + R in aVL > 28 mm in men or > 20 mm in women



Other criteria

- R in I > 11 mm
- R in aVL > 11 mm
- R in aVF > 20 mm
- R in V5 or V6 > 25 mm
- S in V1 or V2 > 30 mm

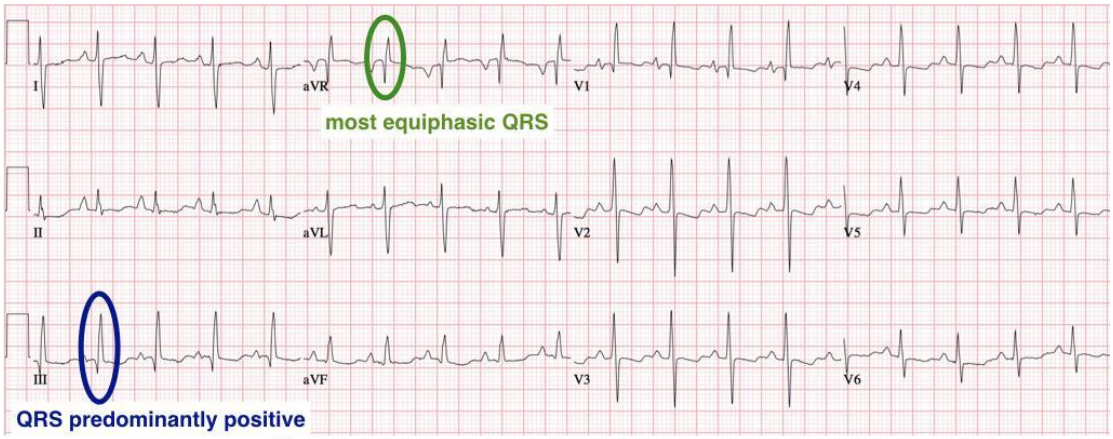
The caveat with the above criteria is that young and thin people often have R and S waves outside of these limits. Echocardiogram remains the gold standard for diagnosis of LVH.

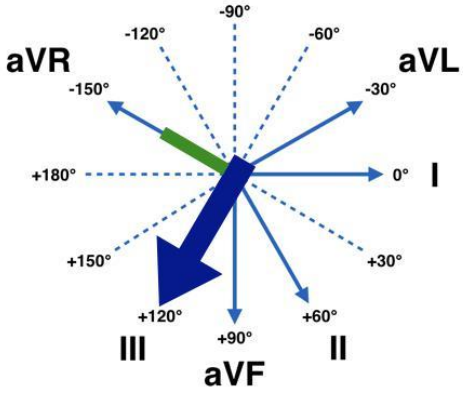
Right ventricular hypertrophy (RVH)

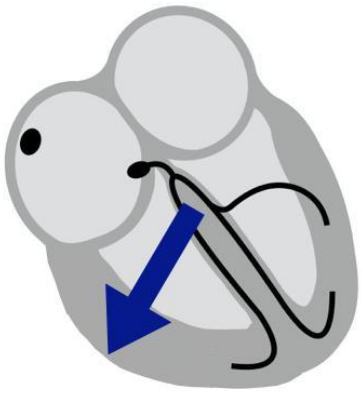
As opposed to left ventricular hypertrophy, which is easily identified by recognizing tall R waves in lateral leads, **right ventricular hypertrophy is not a spot diagnosis, but rather requires systematic analysis of the ECG**. The diagnosis is made in the presence of various ECG features, as discussed below.

ECG features in support of right ventricular hypertrophy:

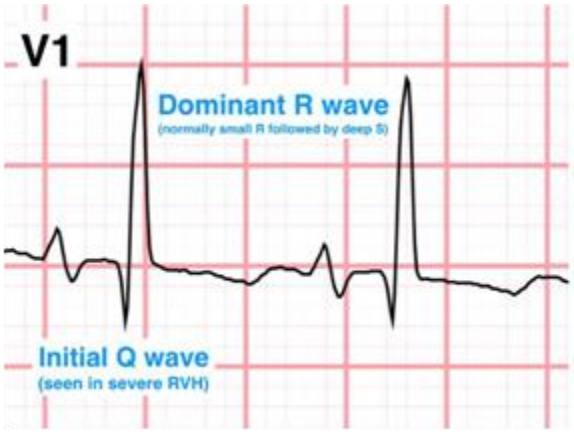
- Right axis deviation





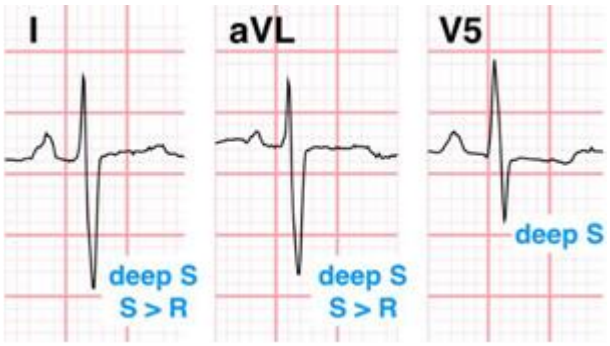


- Dominant R wave in V1 (R wave amplitude > S wave amplitude). The tall R wave in V1 represents the increased muscle mass in the right ventricle, which lies in proximity to the V1 lead. The predominant vector therefore travels towards V1, causing the R wave to be taller than the S wave in V1 (and in V2).



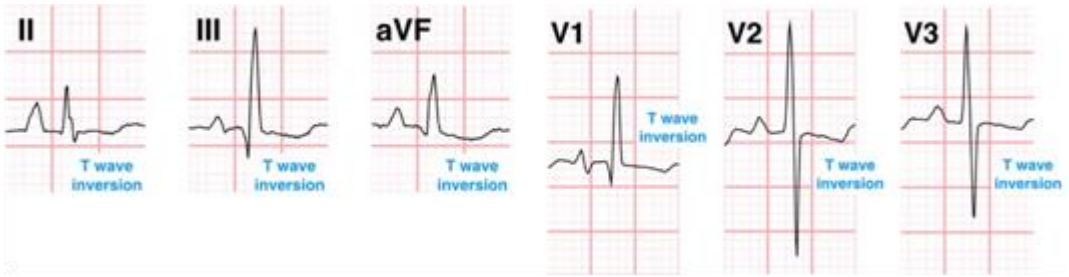
- Initial Q wave in V1 in severe RVH

- Deep S wave in lateral leads (standard lead I, aVL, V5 and V6). The deep S waves in the lateral leads represent the vector forces which are directed towards the right, which is away from the lateral leads, hence the deep S waves.

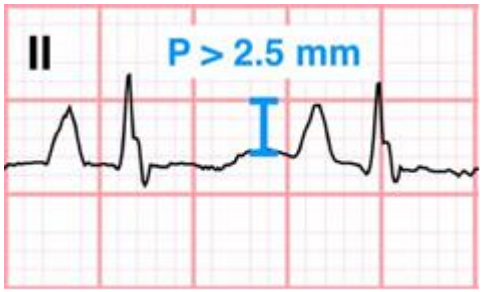


Other supporting ECG features that may accompany right ventricular hypertrophy

- T wave inversion in anterior leads (V1 to V4) and inferior leads (II, III, aVF) These represent secondary repolarization changes that are associated with right ventricular hypertrophy.



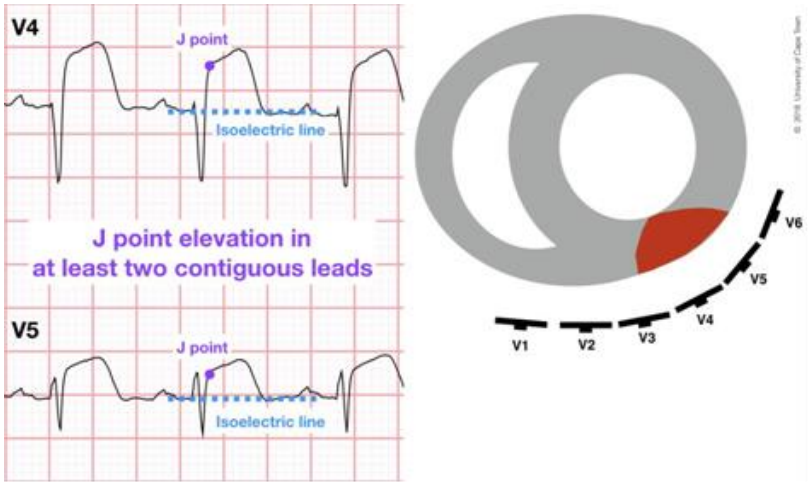
- P pulmonale (tall P waves > 2.5 mm in standard lead II). There is often right atrial enlargement in RVH, due to the higher filling pressures on the right.



ST elevation myocardial infarction

ST segment elevation is present when the J point is deviated upwards from the isoelectric line.

In the right clinical context, the diagnosis of acute coronary occlusion should be sought in the presence of **ST segment elevation** (as measured at the J point) in **at least two contiguous leads**.



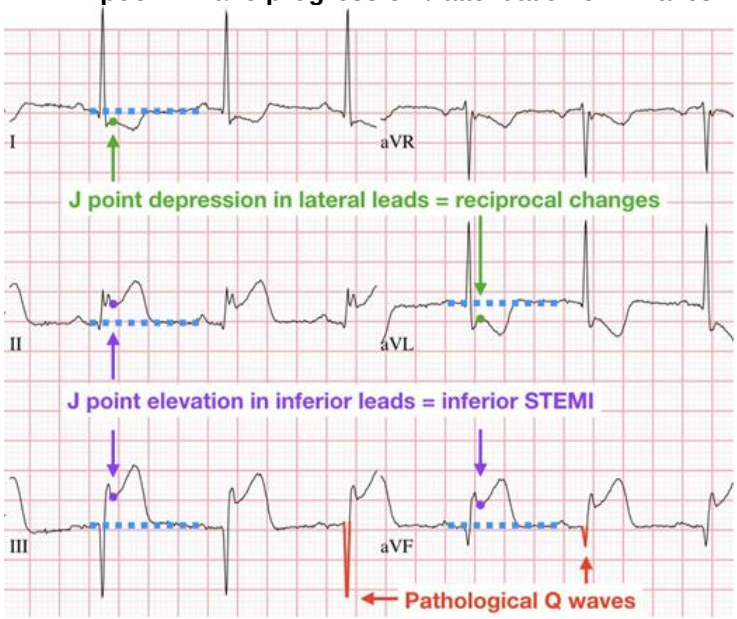
ST segment elevation is caused by the disturbance of current flow across the myocardial cell membrane in the setting of transmural ischaemia that ensues with acute coronary artery occlusion.

Localising **ST segment elevation myocardial infarction:**

V1–V4	Anterior myocardial infarction
I, aVL, V5 – V6	Lateral myocardial infarction
I, aVL, V1 – V6	Antero-lateral myocardial infarction
V1–V3	Antero-septal myocardial infarction
II, III, aVF	Inferior myocardial infarction
I, aVL, V5 – V6, II, III, aVF	Infero-lateral myocardial infarction

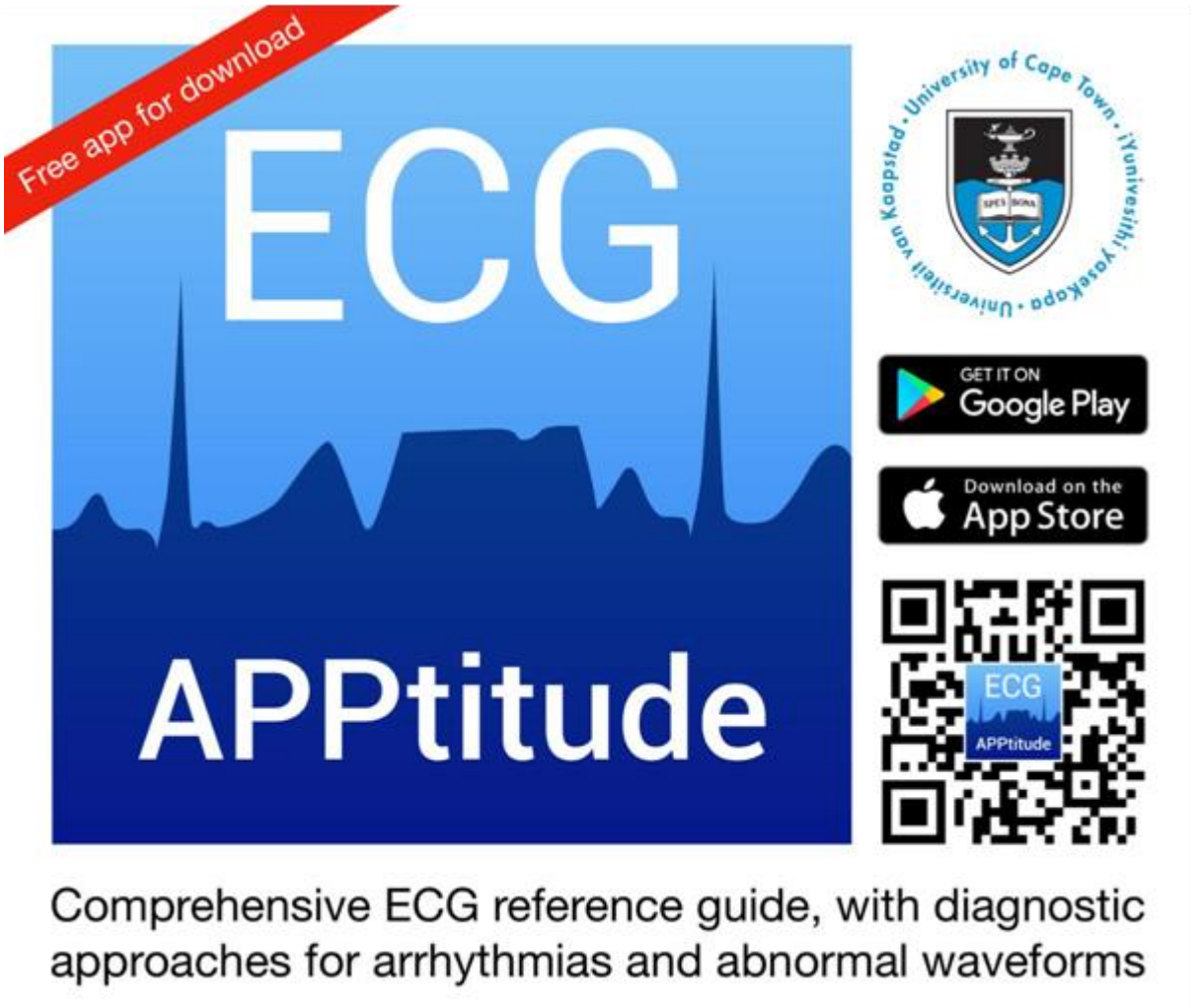
- ECG features **in addition to ST segment elevation**, but not necessarily present, that *support* the diagnosis of STEMI
- **reciprocal ST segment depression** in leads opposite the ST segment elevation; however, also note that:
  - patients with pericarditis can have ST depression in leads aVR or V1 (only)
  - patients with high take off do not have reciprocal ST segment changes

- **evolving Q waves**
- **poor R wave progression** / attenuation of R waves



In the correct clinical context, the diagnosis of ST elevation myocardial infarction (STEMI) should always be sought. Effective revascularization strategies for acute coronary occlusion depend on early recognition of ST segment elevation and diagnosis of STEMI. However, apart from STEMI, the following conditions can also cause ST segment elevation:

- Prinzmetal's angina (coronary vasospasm)
- Left ventricular aneurysm
- Pulmonary embolism
- Pericarditis
- Myocarditis
- High take off
- Hypertrophic cardiomyopathy
- Brugada syndrome
- Hyperkalaemia
- Hypothermia



Hepatorenal Syndrome and Hepatopulmonary Syndrome
Why should we care?

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Hepatorenal Syndrome (HRS)

- Introduction and definition
- Pathophysiology
- Mechanisms involved in AKI in decompensated cirrhosis
- Diagnosis of HRS
- Clinical subtypes of HRS-Type 1 and 2
- ICA Diagnostic criteria for HRS (Old and new) with new classification for HRS type 1 and 2
- An algorithm developed for the diagnosis and treatment of AKI-HRS for hepatorenal disorders in cirrhosis.
- Treatment
    - Vasoconstrictors
    - Albumin
    - Renal replacement therapy
    - TIPS procedure
    - Experimental agents
    - Liver Transplant

Hepatopulmonary Syndrome (HPS)

- Introduction
- Signs and symptoms and diagnosis
- Pathogenesis
- Diagnostic criteria and staging
- Clinical workup
- Therapeutic options
    - Pharmacologic Options
    - TIPS procedure
    - Embolotherapy
- Principles of Management
    - Liver transplant
    - Intraoperative Management
    - Postoperative Management
    - Post-operative treatment algorithm suggested for patients with severe, refractory hypoxemia following liver transplant.

Hepatorenal Syndrome (HRS)

Definition

Hepatorenal syndrome (HRS) is the development of renal failure in patients with severe liver disease (acute or chronic) in the absence of any other identifiable cause of renal pathology.

Up to 20.0% of acute kidney failure in cirrhotics is due to type 1 HRS, and 6.6% is due to type 2 HRS. It is estimated that about 20% of individuals with cirrhosis and ascites will develop HRS within one year of their diagnosis with cirrhosis, and 40% of these individuals will develop HRS within five years of diagnosis.

An association between advanced liver disease, ascites, and renal failure was first described 1861. Helvig and Schutz named this Hepatorenal syndrome in 1932. Shortly thereafter, HRS was found to

be a functional form of renal failure without renal histologic changes. The assumed absence of renal parenchymal damage, has been substantiated mainly based on:

a) renal dysfunction in cirrhosis usually occurs in the absence of significant renal histological changes as seen in post-mortem examinations,
b) classical images of HRS showing extreme but reversible renal vasoconstriction,
c) reversibility of renal dysfunction by liver transplant alone and
d) the ability to use kidneys from patients with HRS as grafts for renal transplantation.

Risk factors for renal parenchymal damage (septic shock, treatment with nephrotoxic drugs) or evidence of such damage (significant proteinuria, haematuria, abnormal renal ultrasonography) should be excluded before the diagnosis of HRS can be established.

Advanced cirrhosis is a condition characterized by impaired liver function, portal hypertension, increased splanchnic blood volume, a hyperdynamic state with increased cardiac output, systemic vasodilatation, a state of decreased central blood volume, and a systemic inflammatory response.

AKI (Acute Kidney Injury), is one of the most severe complications of cirrhosis, occurring in up to 30-50% of hospitalized patients, and has been associated with higher mortality, which increases with severity of AKI. Hepatorenal syndrome is now considered one of the phenotypes of AKI that occurs in patients with advanced cirrhosis and is **characterized by decreased kidney blood flow that is unresponsive to volume expansion**. Refinements in the definitions have helped in the diagnosis of hepatorenal syndrome at an earlier stage during the course of cirrhosis and recent advances in understanding the pathophysiology of hepatorenal syndrome suggest the involvement of systemic inflammation and circulatory changes in the kidney, in parallel with systemic and splanchnic circulatory changes. Although treatment of hepatorenal syndrome with the use of vasoconstrictive agents in combination with albumin has improved outcomes, prognosis remains poor without liver transplantation.

Pathophysiology

Four primary factors are involved in the pathophysiology of HRS:

1. Systemic vasodilation leads to a moderate lowering of blood pressure

2. Activation of the sympathetic nervous system leads to renal vasoconstriction and altered renal autoregulation, such that renal blood flow is much more dependent on mean arterial pressure

3. There is a relative impairment of cardiac function such that, although cardiac output may increase, it cannot increase adequately to maintain blood pressure. In cirrhosis, this is termed cirrhotic cardiomyopathy

4. There is an imbalance between the activity of renal vasoconstrictor systems and the renal production of vasodilators.

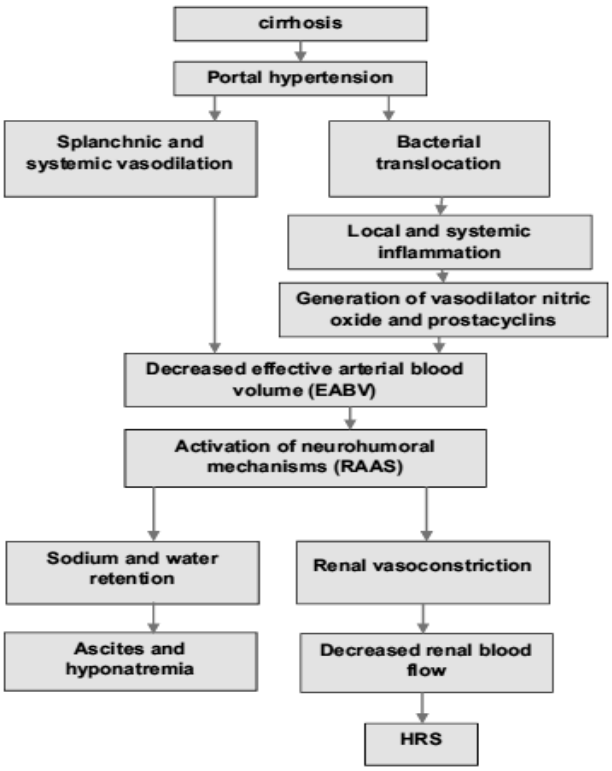

Figure 1. Pathophysiological basis of HRS (RAAS renin angiotensin aldosterone system)

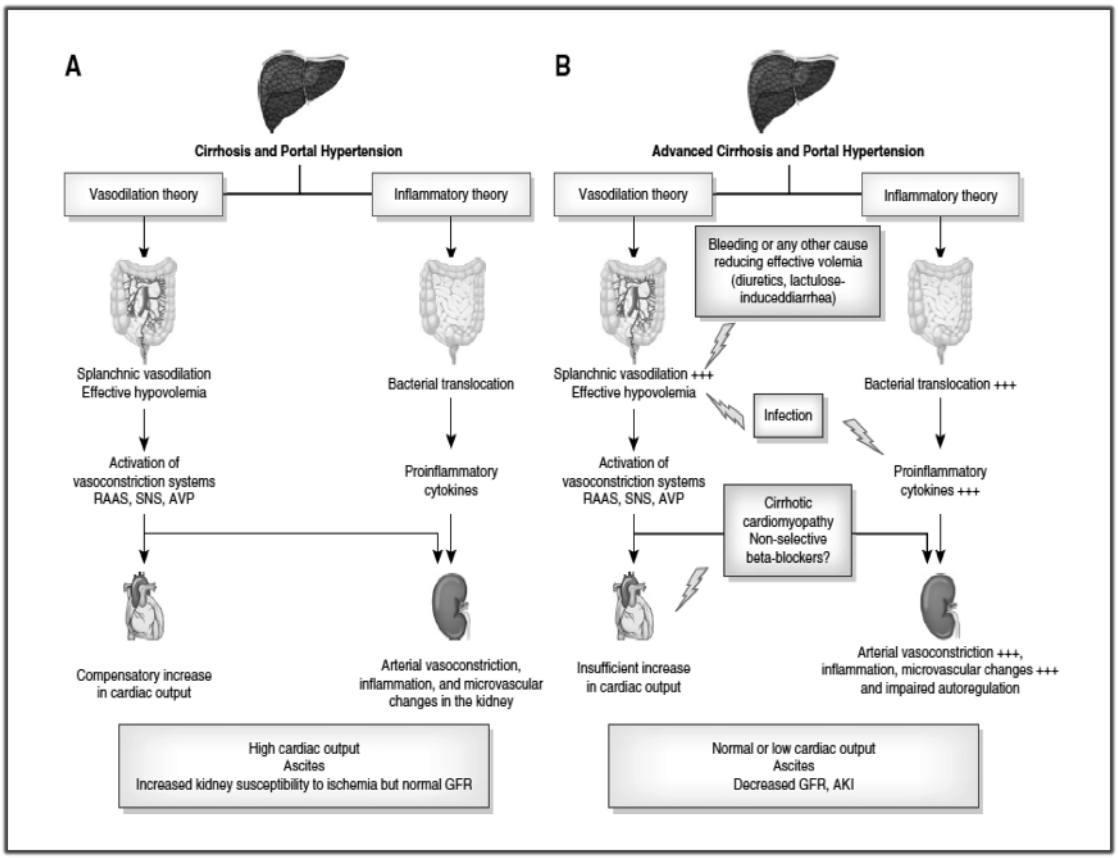

Figure 2. Mechanisms involved in AKI in decompensated cirrhosis (AVP, arginine vasopressin; RAAS, renin-angiotensin- aldosterone system; SNS, sympathetic nervous system.

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(A) In decompensated cirrhosis, both vasodilation secondary to portal hypertension and systemic inflammation induced by gut bacterial translocation tend to induce kidney arterial vasoconstriction because of the activation of vasoconstrictive systems in response to decreased effective blood volume and inflammation in the kidney inducing microvascular changes. These changes result in a hyperdynamic state characterized by increased cardiac output, ascites, and normal GFR, but increase susceptibility of the kidney to AKI.

(B) Development of HRS represents the terminal phase of the disease with an intense kidney vasoconstriction and impaired kidney autoregulation leading to a decrease in GFR. Any event further causing hypovolemia is a risk factor for the onset of HRS

Risk factors:

- Large volume paracentesis >5l without adequate albumin substitution.
- Bleeding e.g. from oesophageal varices
- Diuretics overdose,
- Nephrotoxic drugs such as NSAIDs
- Lactulose-induced diarrhoea
- Decreased cardiac output (e.g., cirrhotic cardiomyopathy, non-selective β-blockers)
- Systemic inflammation, with or without overt sepsis (subacute bacterial peritonitis - SBP)

Although extreme stimulation of the renin-angiotensin and sympathetic nervous systems in cirrhosis may be the primary cause of HRS, other mechanisms such as systemic inflammation and circulatory changes in the kidney are supported by the finding that urinary excretion of renal prostaglandins is decreased in patients with HRS, indicating that renal production of these substances is reduced. There is increased formation of renal vasoconstrictors such as thromboxane A_2, endothelin-1 and leukotrienes, although their exact role in the pathogenesis of HRS is unclear.

Renal failure in HRS might therefore be the consequence of an imbalance between the activity of vasoconstrictor systems and the renal production of vasodilators. This theory is supported by the fact that HRS can be reproduced in non-azotemic, hyper-reninemic, cirrhotic patients with ascites by introducing NSAIDs (anti prostaglandins).

Diagnosis

To diagnose HRS demonstration of a reduced GFR is needed. This is difficult in advanced cirrhosis because of the limitations in the use of creatinine levels alone to estimate GFR. Multiple factors contribute to low serum creatinine levels in cirrhosis. Decreased muscle mass, decreased creatine production, which is a precursor for creatinine means that serum creatinine concentration can be normal despite having a very low GFR. Decreased urea synthesis due to hepatic insufficiency means failure to appropriately diagnosis HRS is relatively common.

Other methods i.e. measuring GFR (inulin clearance) are either time consuming and expensive or impractical in sick cirrhotic oliguric patients (24 hour urine collection for creatinine clearance). Other methods to calculate GFR are constantly being devised. The most recent promising development is the Cr Cystatin C GFR Equation for Cirrhosis.

Clinical Types of HRS

HRS is sub-divided into type 1 and type 2 HRS.

Type 1

- Acute kidney injury that is rapidly progressive with doubling of initial serum creatinine to a value of more than **221 micromole/L (2.5 mg/dL) in less than 2 weeks**
- May appear spontaneously, but often develops after a precipitating event, especially spontaneous bacterial peritonitis (SBP)
- Associated with impaired cardiac and liver functions as well as encephalopathy
- Poor prognosis

Type 2

- Moderate renal failure, not meeting type 1 criteria, which tends to fluctuate over time and may convert to type 1 HRS if there is a further insult such as the development of SBP
- Associated with refractory or diuretic resistant ascites
- Steady or slowly progressive course.

HRS type 1 is severe, rapidly progressive and defined by doubling of the serum creatinine concentration in less than 2 weeks. There is often a precipitating factor, superimposed on cirrhosis. Liver failure progresses rapidly to multi-organ failure. HRS type 1 is the complication of cirrhosis with the poorest prognosis, with a 2-week median survival.

HRS type 2 is characterized by a moderate, steady decrease in renal function (serum creatinine < 2.5 mg/dL)(220umol/l). Patients with HRS type 2 show signs of liver failure and arterial hypotension but to a lesser degree than patients with HRS type 1. **The dominant clinical feature is refractory ascites** (severe ascites with poor or no response to diuretics). Patients with HRS type 2 are predisposed to develop HRS type 1 after infections or other precipitating events. The median survival of patients with HRS type 2 is 6 months.

A major limitation of these criteria is that it does not allow for the co-existence of other forms of acute or chronic kidney disease often present in patients with liver disease. In addition the definition for HRS type 1 includes a time interval (2 weeks) over which serum creatinine must double to a value >2.5mg/dL for the diagnosis to be made. This does not allow physicians to initiate treatment, specifically vasoconstrictors and albumin, timeously. In patients with type 1 HRS, a higher serum creatinine at the beginning of treatment leads to a lower probability of response to terlipressin and albumin, the most investigated and effective treatment of type 1 HRS. The definition of AKI and hepatorenal syndrome in cirrhosis has undergone significant changes over the past years as definitions now use **dynamic and relative changes in serum creatinine** from a baseline serum creatinine instead of absolute cut-offs (e.g.1.5 mg/dl).

Oliguria is not included in the current definition of AKI in patients with cirrhosis, but urine output is a sensitive and early marker for AKI in cirrhotic critically ill patients and is associated with adverse outcomes. Therefore, regardless of any rise in serum creatinine, decrease in urine output or development of anuria should be considered as AKI in patients with cirrhosis until proven otherwise.

Diagnostic criteria for HRS have evolved from these older criteria:

International Club of Ascites (ICA) Criteria for the diagnosis of hepatorenal syndrome:

- Cirrhosis with ascites
- **Serum creatinine >133 micromol/L (>1.5 mg/dL)**
- Absence of shock
- Absence of hypovolaemia as defined by no sustained improvement of renal function **(creatinine decreasing to <133 micromol/L [<1.5 mg/dL])** following at least 2 days of diuretic withdrawal (if on diuretics), and volume expansion with albumin at 1 g/kg/day up to a maximum of 100 g/day
- No current or recent treatment with nephrotoxic drugs
- Absence of parenchymal renal disease as defined by proteinuria <0.5 g/day, no microhaematuria (<50 red cells/high powered field), and normal renal ultrasonography.

Absolute creatinine levels as a diagnostic criterion has been removed for the diagnosis of HRS. Dynamic creatinine values allow for more practical assessment and management of cirrhotic patients with AKI. This aids early diagnosis and treatment of those patients with HRS that would respond to medical management.

Newly proposed ICA Diagnostic Criteria for HRS AKI:

- Cirrhosis with ascites
- **Diagnosis of AKI according to ICA AKI diagnostic criteria**
- Absence of shock

- **No response at 48 hours of plasma volume expansion using albumin 1g/kg of body weight and withdrawal of diuretics.**
- No current or recent treatment with nephrotoxic drugs
- Absence of parenchymal renal disease as defined by proteinuria <0.5 g/day, no microhaematuria (<50 red cells/high powered field), and normal renal ultrasonography
- Normal renal ultrasound

The above ICA classification of HRS –AKI is informed by the Acute Kidney Injury Network, Acute Dialysis Quality Initiative (ADQI) and the Kidney Disease Improving Global Outcomes clinical practice guidelines for AKI. The HRS classification has been altered to accommodate this new approach

Table 1. New classification of HRS subtypes.

Old classification	New classification		Criteria
HRS-1 #	HRS-AKI		• a) Absolute increase in sCr ≥0.3 mg/dl within 48 h *and/or* • b) Urinary output ≤ 0.5 ml/kg B.W. ≥6 h * *or* • **c) Percent increase in sCr ≥50% using the last available value of outpatient sCr within 3 months as the baseline value**
HRS-2 #	HRS-NAKI	HRS-AKD	• a) eGFR <60 ml/min per 1.73 m ^{2} for <3 months in the absence of other (structural) causes • b) Percent increase in sCr <50% using the last available value of outpatient sCr within 3 months as the baseline value
		HRS-CKD	• a) eGFR <60 ml/min per 1.73 m ^{2} for ≥3 months in the absence of other (structural) causes

AKD, acute kidney disease; AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HRS, hepatorenal syndrome; sCr, serum creatinine; CKD, chronic kidney disease.

As such, hepatorenal syndrome type 1 is categorized as a specific type of AKI and **hepatorenal syndrome type 2 is categorized as a form of AKD or CKD.**

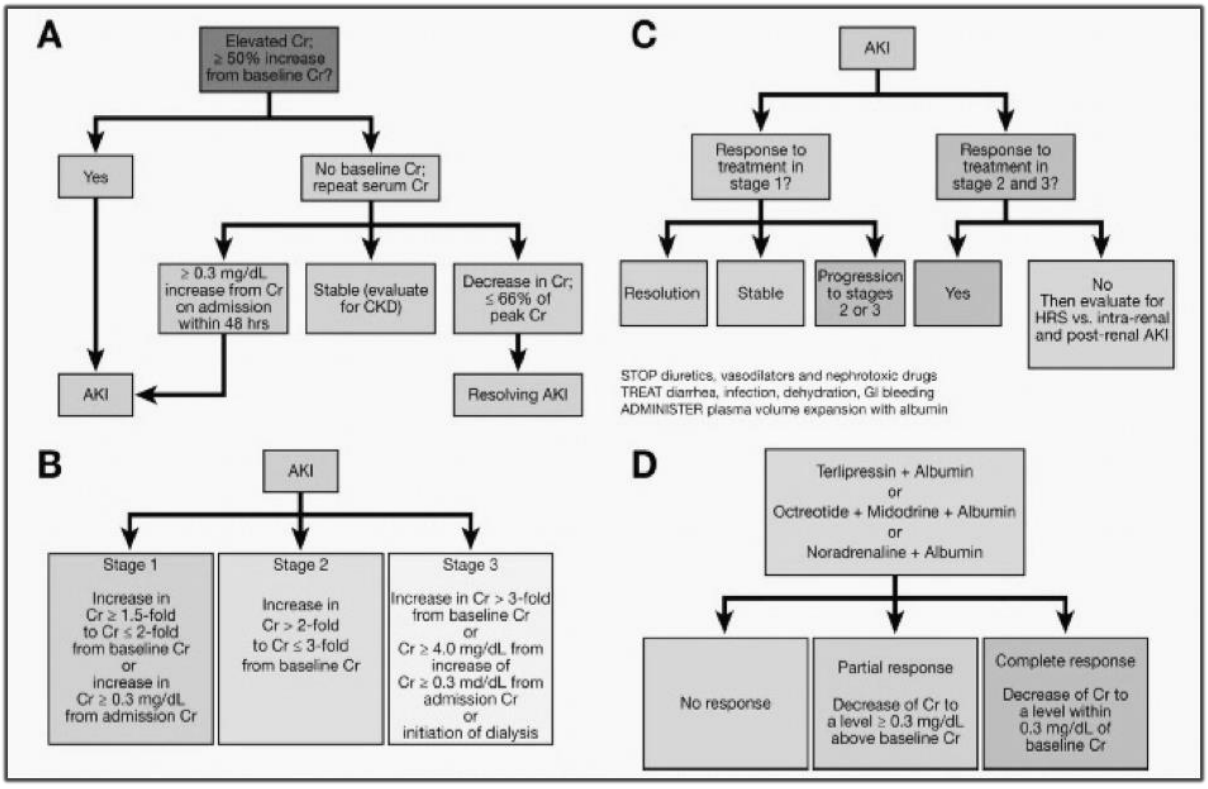


Figure 3. An algorithm developed for the diagnosis and treatment of AKI-HRS for hepatorenal disorders in cirrhosis. AKI Acute kidney injury; Cr serum creatinine; CKD chronic kidney disease; HRS hepatorenal syndrome

Figure 3 A: An algorithm developed for the diagnosis and treatment of AKI-HRS for hepatorenal disorders in cirrhosis.

This classification disregards the cause of AKI and the diagnosis of AKI precedes the diagnosis of HRS**.** The diagnosis of AKI is followed by identifying the stage: 1, 2 or 3**.**

Figure 3 B: Progression through these stages has higher mortality rates in cirrhosis. HRS is a diagnosis of exclusion so stop diuretics, vasodilators and nephrotoxic drugs, **treat any** precipitating factors and give albumin for volume expansion**.**

Figure 3 C: Those patients not responding to volume expansion must be assessed for HRS vs Intrarenal AKI and Postrenal AKI

- Intrarenal AKI. ATN, glomerular or interstitial nephritis (exclude ATN-granular casts in urine sediment, decreased concentrating ability, look for proteinuria and microhaematuria for nephritis)
- Postrenal AKI. Renal ultrasound for size of kidneys, presence of obstruction

Renal biopsy may be indicated to establish the diagnosis but clotting abnormalities in these advanced cirrhotics may prohibit this investigation. In addition, HRS can be superimposed on pre-renal azotemia, other forms of AKI or CKD and HRS can progress to ATN**. As of yet no specific renal biomarkers exist to detect HRS imposed on AKI.**

This is relevant as liver transplant is the only definitive treatment for HRS. In an era of scarcity of donor organs the need to predict HRS and renal recovery, post transplantation to avoid unnecessary combined liver kidney transplant is paramount.

Figure 3 D: Treating the underlying aetiology with liver or combined liver-kidney transplant is the goal of therapy. Given the pathophysiology of extreme renal vasoconstriction, splanchnic vasodilation, and decreased cardiac output, many vasoactive drugs have been evaluated as therapeutic agents to reverse HRS. No single therapeutic agent has been found to permanently reverse HRS. Current goals in treatment are as a bridge to hepatic transplantation and possibly improved long-term survival.

Vasoconstrictor drug treatment options

1. Terlipressin (a vasopressin analogue) plus albumin:

This is the first-line therapeutic approach for type 1 HRS in countries where it is licensed for use. Terlipressin is a V1 agonist of the receptors expressed on vascular smooth muscle cells in the splanchnic circulation. The vasoconstrictive effect of terlipressin corrects the circulatory dysfunction typical of end-stage liver disease, indirectly rebalancing intrarenal vasoconstriction, lowering levels of renin, noradrenaline and serum creatinine. Terlipressin also reduces portal venous flow and porto-systemic pressure with an increase in hepatic arterial blood flow and an improved hepatocellular oxygenation. However, terlipressin is more commonly associated with diarrhoea, abdominal pain, peripheral ischemia, angina pectoris, and circulatory overload. Continuous-infusion terlipressin reduces side effects.

Two meta-analyses suggest that terlipressin plus albumin may reverse type 1 HRS. Terlipressin is administered as an intravenous bolus and the dose increased if the serum creatinine does not decrease by at least 25% after 3 days. Terlipressin is administered at a dose of 0.5 to 1 mg intravenous (IV) bolus, every 4 to 6 hours; the dose can be increased to 2 mg IV bolus every 4 to 6 hours. Terlipressin should be discontinued after a maximum of 14 days if there is no improvement in renal function. Over 50% of HRS-1 patients show a complete response to terlipressin plus albumin. Retreatment of recurrences is usually effective. In patients with type 2 HRS, recurrence of HRS is common and there is no difference in terms of post liver transplantation (LT) outcomes in patients treated or not with terlipressin. Therefore HRS-2, now termed HRS-NAKI, is not an indication for terlipressin plus albumin even in patients who are on the waiting list for Liver transplant.

2. Noradrenaline plus albumin:

Cardiac monitoring in an intensive care unit is required. Noradrenaline is administered at 0.5 to 3 mg/h continuous IV infusion, titrating dosing to achieve an increase of 10 mm Hg in mean arterial pressure.

3. Combination medical therapy with midodrine, octreotide, and albumin:

This is a temporary measure until liver transplantation is available as it rarely reverses the condition. It does improve glomerular filtration rate in patients with HRS, and it may improve survival, particularly in type 1 HRS. Octreotide dosage is 100 to 200 µg subcutaneously every 8 hours. Midodrine dose is 7.5-12.5 mg orally 3 times a day; the dose should be titrated to achieve an increase of 15 mm Hg in mean arterial pressure Midodrine is a vasoconstrictor, while octreotide inhibits release of endogenous vasodilators. These drugs work synergistically to improve renal haemodynamics.

4. Vasopressin plus albumin

Albumin

Albumin should be given in combination with any vasoconstrictor drug regimens as it is crucial for the effectiveness of the treatment of HRS. One possible explanation is that a fall in cardiac output, which is a crucial event in the pathophysiology of HRS, could be exacerbated by the effect of terlipressin while albumin maintains or increases the CO even in advanced phases of liver disease. Albumin is given at a dose of 1mg/kg/day for 2 days then 20–40 g/day .The increase in CO and SVR with albumin are mainly related to its non-oncotic, anti-oxidant and anti-inflammatory actions

Other treatment modalities include:

Renal replacement therapy (RRT)

The effect of renal replacement therapy (RRT) is controversial in the management of HRS AKI, as studies show little difference in survival compared with non−RRT-treated patients. The Acute Dialysis Quality Initiative group recommended renal support for patients with HRS AKI only if there was an acute potentially reversible event, or liver transplantation planned,

Transjugular intrahepatic portosystemic shunting

The TIPS procedure involves angiographic insertion of a low resistance expandable metal stent between the hepatic vein and the intrahepatic portion of the portal vein. It is useful in life threatening complications of portal hypertension, such as variceal bleeding, by temporarily reducing the portal pressure. TIPS is an option for treatment of HRS AKI, especially if a patient is failing to respond to pharmacologic treatment, or has frequent relapses. TIPS increases the effective renal blood flow by decreasing portal pressure and redistributing regional vascular resistance. It also reduces the potent renal vasoconstrictor endothelin-1, reduces intrarenal pressure and increases diastolic blood flow. A meta-analysis reported on the efficacy and safety of TIPS for the treatment of HRS AKI showed that serum creatinine, sodium, blood urea nitrogen, urinary sodium excretion, and urine volume significantly improved after TIPS. **However, the higher incidence of hepatic encephalopathy limits the standard use of TIPS as a routine therapeutic option for HRS.**

Experimental agents

There is a clinical need to develop agents to reverse HRS-AKI:

- Serelaxin (a recombinant human relaxin-2) increases renal perfusion by reducing renal vascular resistance in rats.
- Nebivolol is a non-selective vasodilator β-blocker shows renoprotective and hepatoprotective effects in rats with induced HRS.
- Pentoxifylline is used for treatment of alcoholic hepatitis, reducing inflammation by decreasing pro-inflammatory cytokines, such as IL-6, TNF and endotoxins.

Liver transplantation

Liver transplantation is the treatment of choice in HRS patients even though its mortality rate is particularly high in patients with type I HRS, many of whom die while waiting for transplant. Recovery of renal function is not universal (complete recovery of kidney function in 58% of transplanted patients, partial recovery in 15% and no recovery in 25%). Renal sodium excretion, serum creatinine and neuro-hormonal levels may normalize within a month whereas renovascular resistance may take more than a year to return to normal after transplantation. Organ allocation is mainly based on the MELD score, considering all liver transplant recipients, those with HRS are more exposed to post-transplant complications, at greater risk of developing CKD and have a shorter overall survival. Those patients who fail to recover renal function and need to continue haemodialysis have an even worse survival rate (70% mortality at one year).

RRT prior to liver transplant for more than eight weeks indicates a markedly reduced probability of renal recovery and a combined liver-kidney transplant is recommended in these cases.

There are no specific recommendations as to post-transplant immunosuppressive therapy, but it may be advisable to delay the start of cyclosporine or tacrolimus to 48-72 h after transplantation to enhance renal recovery.

Hepatopulmonary Syndrome (HPS)

HPS occurs in 10–32% of patients with advanced liver disease resulting in significant morbidity and mortality in the absence of liver transplant. The first recorded description of hypoxemia with liver dysfunction was by Flückiger in 1884. The characteristic intrapulmonary vascular dilation (IPVD) of HPS was identified in 1966 following post-mortem study of cirrhotic patients in the UK. This condition was termed “hepatopulmonary syndrome” by Kennedy and Knudson in 1977 and applied to patients with liver disease and severe hypoxemia unexplained by other causes. HPS most commonly occurs in patients with cirrhosis and portal hypertension, but it can present in non-cirrhotic patients with presinusoidal and postsinusoidal portal hypertension, such as Budd Chiari syndrome, as well as patients with ischemic hepatitis.

Type I HPS is the most common and is caused by widespread pulmonary capillary dilatation, while type II HPS involves true arteriovenous pulmonary fistulas.

Signs and symptoms

HPS is usually asymptomatic with 80% of patients presenting with features of liver disease. The most frequent symptoms of HPS are progressive dyspnoea and cyanosis. Diagnosis is often delayed as dyspnoea is common in all cirrhotics. In the majority of patients, dyspnoea and hypoxemia progress over time despite stable liver function. Platypnea is more specific, breathlessness experienced in the upright position improved when supine. This correlates to the objective finding of orthodeoxia, a drop of $\geq$ 4mmHg (0.54 kPa) in PaO_2 or $\geq$ 5% in saturation when moving from the supine to the standing position.

Other clinical manifestations of HPS include: spider angiomata (likelihood of HPS 21%), clubbing (likelihood of HPS 78%), cyanosis (likelihood of HPS 100%)

No specific aetiology or severity of cirrhosis has been found to be correlated with the incidence or severity of HPS.

Pathogenesis

The pathophysiologic basis of HPS is still not fully understood. Pathologic evaluation reveals dilated pulmonary vessels. The hyperdynamic circulation commonly seen in liver disease results in over-perfusion of alveoli, and the dilated pulmonary capillaries increase the distance between the alveolar wall and red blood cells; both result in **incomplete gas exchange**. In addition, the development of pleural and intrapulmonary **arteriovenous shunts** result in systemic hypoxemia. Shunting is worse in the lower lobes. Therefore gravitational pulmonary blood flow redistribution when sitting up worsens hypoxemia (orthodeoxia) that is characteristic of HPS. The pulmonary vascular dilatation that results in

HPS appears to be caused by a decreased vascular reactivity to vasoconstrictors, an increased response to vasodilators as well as to an impairment of hypoxic pulmonary vasoconstriction (HPV). The abnormal production of vasodilatory mediators in the diseased liver is in response to tissue ischemia. One of the mediators responsible for the vascular dilatation is nitric oxide. Thus, increased exhaled nitric oxide is found in patients with HPS and decreases with the disappearance of HPS following OLT.
These vasodilatory and pro-angiogenic factors including endothelin-1 (ET-1) enter the pulmonary circulation. ET-1 is overproduced by cirrhotic cholangiocytes and binds to endothelin-B receptors which also increase in expression on pulmonary endothelial cells, releasing nitric oxide via endothelial nitric oxide synthase (eNOS). Hepatic ischemia also increases production of TNF-α and vascular endothelial growth factor (VEGF) which promote pulmonary angiogenesis, resulting in vascular proliferation and increased arteriovenous shunting.

NO is also released through other pathways, including through inflammation caused by gut bacterial translocation. This leads to recruitment of macrophages to the pulmonary blood vessels, where they produce and release NO via iNOS (inducible nitric oxide synthase) and carbon monoxide (CO).

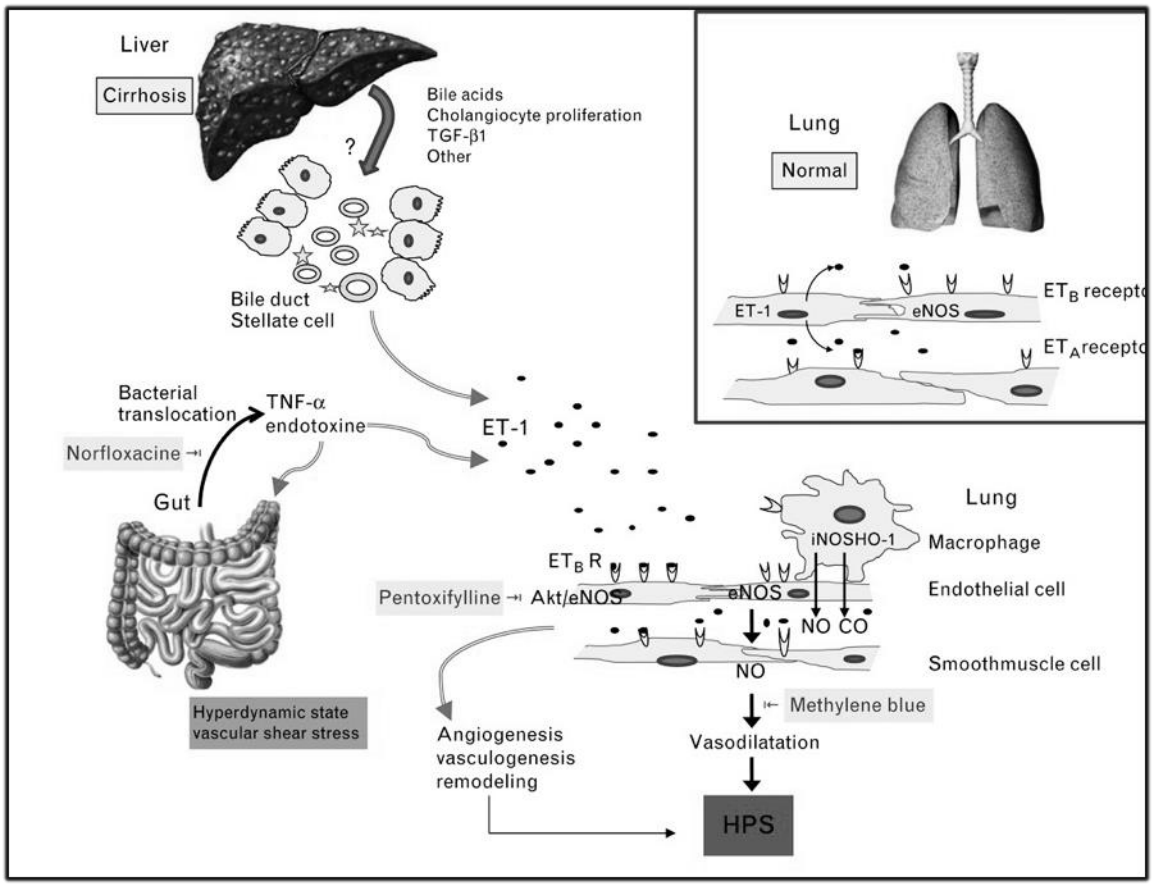


Figure 4. HPS: Main findings in experimental and clinical trials.

Diagnosis

All patients with cirrhosis should be screened for the presence of HPS or other pulmonary pathology with pulse oximetry. Patients with room air pulse oximetry saturation (SpO_2) < 96 % or dyspnoea should undergo room air arterial blood gas (ABG) testing and chest radiography. ABG should be performed only after 15 to 20 minutes at rest in the sitting position. Serial SpO_2 measurements are also useful for monitoring impaired oxygenation over time in HPS patients. Chest X-ray and thoracic CT scanning are often unremarkable.

Consider HPS in patients with liver disease and an unexplained oxygen saturation of < 96%, and/or any of the following: platypnea, orthodeoxia, clubbing, or cyanosis. After pulmonary evaluation, any patient with a PaO_2 < 80 mmHg (10.7 kPa) or alveolar-arterial oxygen gradient ($AaDO_2$) ≥ 15 mmHg

(2kPa) that cannot be fully explained by other diagnoses should be referred for a diagnostic workup for possible HPS.

Clinical testing and work-up

Pulmonary function tests in HPS show normal flows and lung volumes. Patients may have reduced lung volumes (ascites/pleural effusions). Diffusion impairment is common in HPS, however this finding is frequent in people with cirrhosis who do not have HPS as well. However HPS subjects have been noted to have more profound reductions in diffusion capacity, with a mean DLCO of 55% predicted versus a mean of 72% predicted in people with cirrhosis who do not have HPS.

Six Minute Walk Test/ Oxygen Titration study
If a patient desaturates to below 88% with exertion, an oxygen titration study should be performed to identify and match oxygen requirements.

Liver Function Tests
Includes abdominal ultrasound and/or CT scan and blood tests to determine the severity of the liver disease.

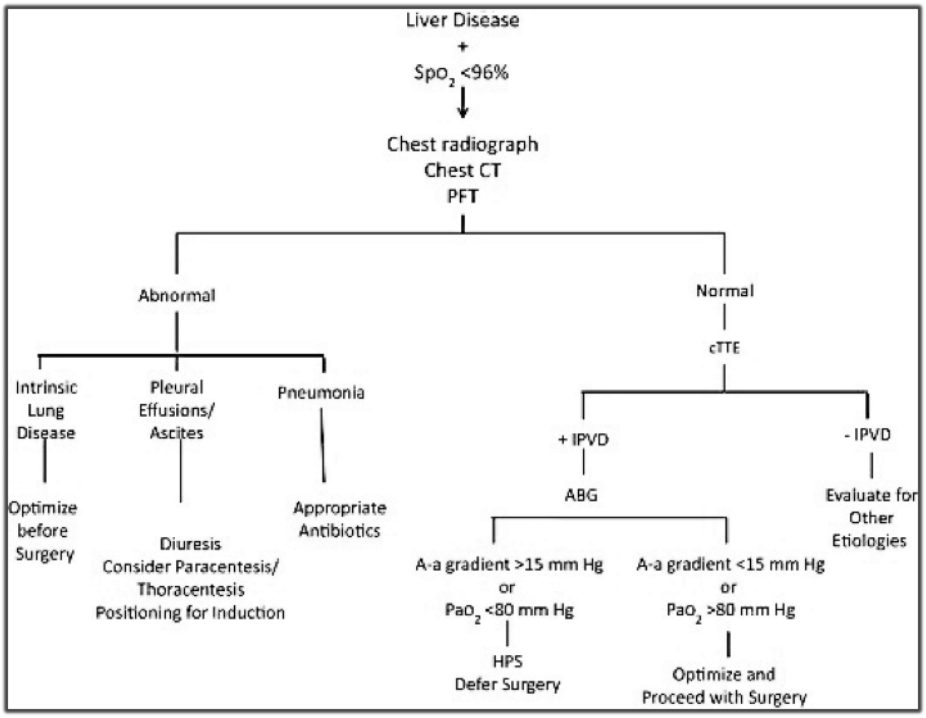


Figure 5

Echocardiogram (contrast enhanced Transthoracic echocardiography CTEE)
2-D transthoracic agitated saline contrast echocardiography (CTEE) has become the test of choice for identifying IPVDs. Saline microbubbles are created by mixing 10 ml of normal saline with 10 ml air, and are injected intravenously during normal transthoracic echocardiography. Within seconds, these bubbles appear in the right-sided heart chambers, and in the absence of IPVDs, become trapped in the pulmonary capillary bed, and are eventually absorbed. In HPS, IPVDs allow bubbles to pass through the pulmonary vascular bed, resulting in detectable bubbles in the left-sided heart chambers. Since an intracardiac shunt could have the same effect, the timing of left-sided bubble appearance is closely monitored, and the shunt is likely to be intracardiac if bubbles appear within 1-3 beats, and intrapulmonary if they appear after 3 beats (usually within 4-6 heartbeats). If contrast-enhanced echocardiography is negative, HPS is excluded and no follow-up is necessary. If hypoxaemia is mild-to-moderate ($AaPO_2$ ≥2 kPa and/or PaO_2 ≥8 to <10.7 kPa), periodic follow-up is recommended by the European Respiratory Society (ERS), with a yearly assessment of lung function, including pulse oximetry and/or arterial blood gas levels if necessary.

Macroaggregated Albumin Lung Perfusion Scan
[MAA] with brain uptake imaging is another method for detecting and quantifying IPVD. In this technique, radio-isotope labelled aggregates of albumin ranging between 20-60 µm in diameter are injected into the venous circulation. The MAA lung-brain perfusion scan is normal in non-HPS causes of hypoxemia. However, the lung perfusion scan does not distinguish intracardiac and intrapulmonary shunting and has inferior sensitivity compared to CEE for detection of mild or moderate HPS in adults. In HPS patients with concomitant lung problems (chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, or hepatic hydrothorax), abnormal brain uptake of 99mTcMAA after lung perfusion (uptake > 6%) helps to distinguish the degree of hypoxemia caused by IPVD versus hypoxemia due to nonvascular lung parenchymal abnormalities. An MAA ratio of 20% has a greater correlation with ”severe post-transplant hypoxemia”.

CT Scan of the chest is done to evaluate for other abnormalities that may be contributing to abnormal oxygenation. The CT scan does not distinguish patients with liver disease and HPS from those without HPS

In patients with HPS, pulmonary angiography should be performed only when hypoxaemia is severe (PaO_2 <8 kPa) and poorly responsive to the administration of 100% oxygen, and when there is a strong suspicion (on the basis of a chest computed tomography scan) of direct arteriovenous communication that would be amenable to embolization.

Follow-up whilst awaiting liver transplant includes pulmonary function tests, a six-minute walk test, an oxygen titration study, and an arterial blood gas to monitor disease progression.

Prognosis

HPS results in significant morbidity and mortality that exceeds that of patients with end-stage liver disease (ESLD) alone. Patients with HPS have an expected decline in PaO_2 of 5.2 mmHg and nearly a threefold increase in mortality at 5 years when compared with ESLD patients without HPS.

Diagnostic Criteria of hepatopulmonary syndrome

1	Presence of liver disease and/or portal hypertension
2	Elevated room air alveolar-arteriole oxygen gradient $P(A\text{-}a)O_2$ gradient >15 mmHg (2 kPa) or >20 mmHg (2.66 kPa) when >65 years
3	Evidence of Intrapulmonary vascular dilation (IPVD)

Staging of HPS

Mild	PaO_2 >80 mmHg	PaO_2 >10.7 kPa
Moderate	PaO_2 60-79 mmHg	PaO_2 8-10.7 kPa
Severe	PaO_2 50-59 mmHg	PaO_2 6.7-8.0 mmHg
Very severe	PaO_2 <50 mmHg	PaO_2 <6.7mmHg

Therapeutic options

Organ donor shortage and the high peri-operative mortality associated with liver transplantation in HPS leads to a continued search for effective medical therapies. Thus far however none have been found to be effective.

Pharmacologic options

Unsuccessful trials have used octreotide to inhibit angiogenesis, norfloxacin to decrease bacterial production of endotoxin, NO (nitric oxide) production inhibitors such as inhaled L-NAME, N(G)-nitro-L-arginine methylester and pentoxifyline which inhibits TNF-α .

There is limited data supporting the use of methylene blue which blocks NO-mediated vasodilation through inhibition of soluble guanylate cyclase stimulation, but this requires intravenous administration at 3 mg/kg IV every 2 hours and so is impractical as a long-term treatment.
In some studies, garlic has shown potential.

TIPS

The use of TIPS as a possible treatment in HPS shows varied results but TIPS placement does not appear to worsen oxygenation in patients with HPS and can be used for the treatment of sequelae of portal hypertension when clinically indicated.

Embolotherapy (coiling) has been shown to improve hypoxemia pre- and post-LTx in type II HPS by occlusion of the arterio-venous pulmonary fistulas, but has had limited success in type I HPS.

Principles of Management

Management of HPS is supportive as no medical therapies exist. Supplemental oxygen is to maintain O_2 saturation above 88% is advised although it has not consistently been shown to reduce dyspnoea or improve quality of life. In patients with PaO2 less than 60 mmHg (8.0Kpa) at rest or with exertion, the administration of supplemental oxygen is appropriate because chronic hypoxemia may contribute to the mortality of HPS. It should be considered during periods of sleep and exercise in all HPS patients and there may be a role for pre-and post-operative pulmonary rehabilitation.

General anesthesia for any surgery other than LT in patients with HPS is associated with very high perioperative risk. HPS is often underappreciated in patients with ESLD with abnormal gas exchange and should be suspected in any patient with a low SpO_2 . If suspected, a screening transthoracic agitated saline contrast echocardiography or intraoperative transesophageal echocardiography (TEE) can be used to confirm the diagnosis. When recognized, aggressive weaning of mechanical ventilation to extubate as early as possible in the postoperative period is advised. Non-invasive positive pressure ventilation (NPPV) immediately following extubation to augment oxygenation can be very useful.

Liver transplantation is the only known effective therapy for HPS, with significant improvement in oxygenation observed in the majority of patients within one year of transplantation. It has been clearly shown that HPS patients with a $PaO_2 \leq 60$ mmHg (8KPa) have significantly better 5-year survival rates with liver transplantation, when compared to supportive therapy. OLT for HPS is indicated only in severe hypoxaemia (PaO_2 <8 kPa).

Whilst perioperative management and care can be challenging, outcome after LTx for HPS now approximates that of other conditions. This is the justification for the current UNOS policy providing MELD exception points for candidates with HPS subjects with PaO2 < 8kPa, and a goal of transplantation within 3 months of listing. HPS patients should be listed for transplantation as early as possible as hypoxemia is progressive in HPS, and perioperative prognosis and surgical outcomes are closely linked to the severity of hypoxemia. Some still consider very severe HPS (PaO_2 < 6.7kPa) to be a contraindication for LTx as case series suggest worse outcomes in this group.

Patients require close assessment and follow-up before and after transplant.

Intraoperative Issues

The major issue in managing HPS patients during LT is maintaining satisfactory arterial oxygenation. Even in the setting of severe HPS (PaO_2< 50 mmHg), most patients can significantly improve PaO_2 with 100% inspired oxygen. Monitoring mixed venous oxygen saturation (SvO_2) is potentially important. SvO_2 monitoring may guide the need to initiate veno-venous bypass (if SvO_2 drops below 65%). Veno-venous bypass may reduce right ventricular overload, reducing further vasodilation in the pulmonary vascular beds.

Transoesophageal echocardiography is used to evaluate for other causes of hypoxemia such as pulmonary embolism, pericardial or pleural effusion, or myocardial dysfunction and used in conjunction with cardiac output monitoring (CO, SVR, SVV) to facilitate goal-directed resuscitation.
Hepatopulmonary syndrome patients are usually orally intubated and mechanically ventilated with lung protective ventilation (tidal volumes, 6-8 mL/kg). Of unique interest in HPS is the characteristic of orthodeoxia (worsening PaO_2 in the upright position/better than PaO_2 supine). Therefore, supine patient positioning in the operating room may be favoured by the existence of HPS. There are no established cut-offs regarding degree of pre-LT arterial oxygenation that dictates cancellation of a

case. There is no significant difference in oxygenation between patients anesthetized with inhalational compared with intravenous anaesthetics. Prolonged ventilator support is commonly needed in patients with HPS as LTx can acutely worsen VQ mismatching, due to the abrupt decrease in the release of vasodilatory mediators following removal of the cirrhotic liver. It has been postulated, though not confirmed, that the removal of vasodilators contributes to reactive vasoconstriction which has a greater impact on the normal (non-dilated) pulmonary vessels, increasing shunting via enlarged, remodelled vessels, and transiently worsening hypoxemia. **This effect may be greater in patients with severe HPS pre-transplant or in patients with a greater MAA shunt fraction and can explain refractory hypoxaemia postoperatively.**

For patients with severe intraoperative hypoxemia inhaled nitric oxide or epoprostenol **may** result in improved blood flow to alveoli that are better ventilated, reducing shunting through poorly aerated dependent lung.

Inhaled vasodilators

Inhaled nitric oxide (up to 40 ppm, ranging from 2 to 14 days) is the most widely reported agent used for severe post-transplant hypoxemia but can theoretically be used intra-operatively. It may mitigate the transient vasoconstriction in the normal pulmonary vessels following recipient hepatectomy. (Practically however, it is difficult to administer). Nitric oxide may be the primary vasodilator responsible for HPS. Paradoxically however in ‘‘severe post-transplant hypoxemia,’’ inhaled NO likely acts by mitigating the postoperative pulmonary vasoconstriction of normal vessels that causes shunting through the maximally dilated basilar vessels. In addition, by preferentially vasodilating normal vessels in the mid and upper portions of the lung, it may effectively divert pulmonary blood flow away from the dilated basilar vessels that are responsible for hypoxemia.

Inhaled eprostenol - (inhaled prostaglandin) - similar effect but less widely used.

Inhaled vasodilator plus intravenous methylene blue

Preferentially vasodilates normal vessels in well-ventilated areas, and vasoconstricts IPVDs in poorly ventilated areas with impaired hypoxic vasoconstriction.

In refractory cases, inhaled agents may be combined with intravenous methylene blue that reduces NO driven vasodilation globally. This results in vasoconstriction of IPVDs in the dependent lung, particularly in areas of impaired hypoxic vasoconstriction that receives less ventilation during mechanical ventilation and consequently less inhaled agent, preferentially directing pulmonary blood flow to better oxygenated segments with fewer abnormal vessels. In patients receiving methylene blue, epoprostenol is preferred to inhaled NO as it produces vasodilation by increasing cyclic AMP rather than cyclic GMP, and so is not blocked by the effects of the methylene blue.

ECMO

Can be considered as a salvage therapy to provide oxygenation and ventilation in patients with refractory intraoperative hypoxemia

Although liver transplantation (LT) is curative in HPS, these patients have an elevated **postoperative complication rate.**

1. Severe post-transplant hypoxemia with prolonged mechanical ventilation and innovative techniques to manage hypoxemia
2. Increased post-operative infections and anastomotic bile duct leaks from delayed wound healing due to hypoxemia.
3. Early post-operative thrombosis (including portal vein and hepatic artery) due to polycythemia from chronic hypoxemia
4. Post-transplant recurrence of HPS due to graft dysfunction from liver inflammation, NASH, or recurrent hepatitis C.
5. Post-transplant resolution of hypoxemia followed by the development of progressive pulmonary hypertension.
6. Finally, decreased diffusing capacity of the lungs (DLCO) in HPS does not improve post-transplant, despite an improvement in oxygenation.

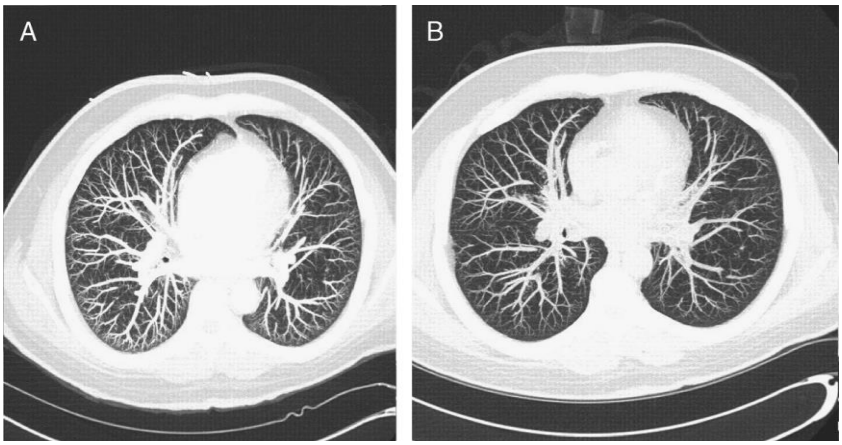
Post-Operative Management

Early extubation should be accomplished to prevent ventilator-associated pneumonia. This can be facilitated when accompanied with high-flow oxygen.

100% inspired oxygen via face mask/non-invasive ventilation/nasal oxygen should be used to maintain O_2 saturation >= 85%

Goal directed fluid therapy should be conducted to avoid fluid overload and pulmonary congestion Patients should be kept flat or even in Trendelenburg position to reduce shunting in the dependent lung. Care should be taken to ensure adequate gastric drainage to reduce the risk of aspiration. Ventilated patients may benefit from rotation into the prone position to improve recruitment of poorly ventilated dependent lung fields.

Most patients do well after transplant with supplementary oxygen and progressively improve over weeks to months. Supplemental oxygen should be discontinued when O_2 saturation remains greater than 88% (rest, exercise, and sleep).



Computed tomography scan of the chest with maximum-intensity projection images performed during the first month following transplantation (A) and a year later (B).

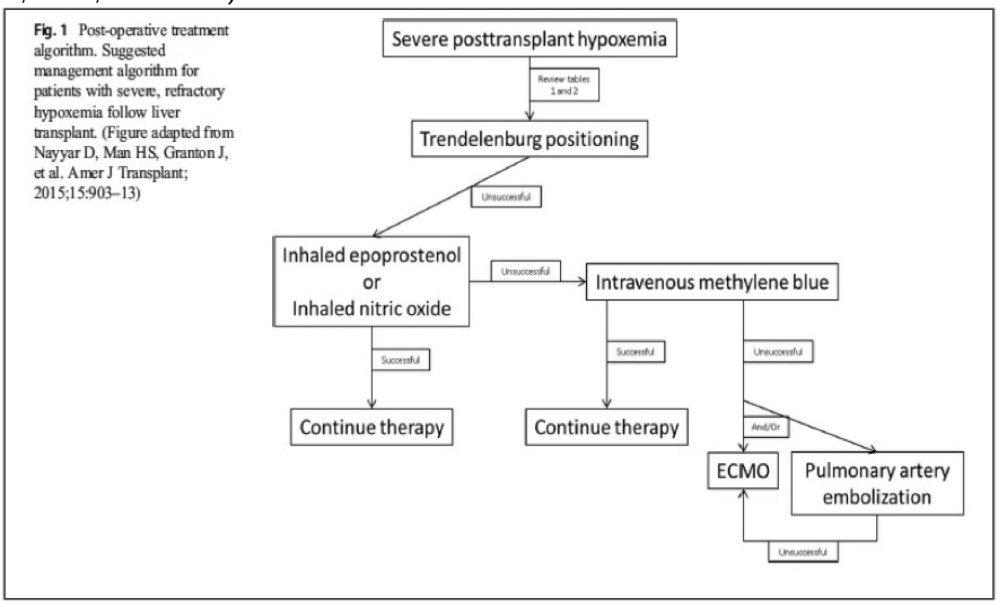
However, a subset of HPS patients develop refractory hypoxemia. The development of “severe post-transplant hypoxemia” has been defined by Nayyer and colleagues as the requirement for 100% FIO_2 to maintain an oxygen saturation of ≥ 85% in the absence of other contributing factors. It occurs early in the postoperative period (usually within 24 h of LT). It affects up to 20% of HPS patients and carries a mortality of 45%. The incidence varies with severity of pre-transplant hypoxemia. It is more likely to occur with severe HPS and in patients with measured MAA shunt fraction > 20%.

Patients with severe post-transplant hypoxemia should be maintained in the Trendelenburg or prone position and may benefit from early use of adjunctive therapies including inhaled vasodilators and methylene blue. ECMO is warranted for refractory cases and has been demonstrated to result in long-term survival.

Treatment modalities for severe hypoxemia after liver transplant in patients with HPS:

- Positional: Trendelenburg positioning /Prone positioning
- Pharmacologic: Inhaled nitric oxide/ Inhaled epoprostenol/ Intravenous methylene blue
- Invasive: Trans-tracheal oxygenation/Pulmonary artery embolization/Extracorporeal membrane oxygenation. Patients can be maintained on ECMO for days to weeks until lung function is adequate to support oxygenation

Post-operative treatment algorithm suggested for patients with severe, refractory hypoxemia following liver transplant. (Figure adapted from Nayyar D, Man HS, Granton J, et al. Amer J Transplant; 2015;15:903–13)



Rationale and considerations for included therapies:

- **Trendelenburg positioning**
  Onset and peak effect in minutes. IPVDs are predominantly basilar. Gravitational redistribution of blood flow to upper and mid lung zones decreases flow through intrapulmonary vascular dilatations.

- **Inhalational vasodilators** and **Methylene blue** are discussed above.

- **Embolization of lower lobar pulmonary vessels**
  This redistributes blood flow away from intrapulmonary vascular dilatations, to mid and upper lung zones. However the response is unpredictable, and transporting a severely hypoxemic patient to a fluoroscopic procedure suite is high risk so embolization is a ‘‘last resort’’ approach. Access is limited to specialized centres.

- **Extracorporeal life support**
  ECLS sustains tissue oxygenation until intrapulmonary vascular dilatations begin to reverse and pulmonary gas exchange improves.

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Informed Consent
Protecting yourself by protecting the patient

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Anaesthesiologists are the specialty which generate the most complaints at the HPCSA. The majority of the complaints concern billing and inadequate preoperative assessments (and hence informed consent) from the patient. Mamojee and Alli did a study published in SAJAA in 2018 and found that Wits anaesthetists demonstrated an inadequate knowledge of the laws governing informed consent in South Africa. It would be reasonable to assume this is true of the anaesthetists in other areas of the country.

Surgeons have always traditionally been the ones to routinely get consent for their own procedures. Many patients assume this covers the anaesthetic too. This was confirmed by a study done by Naidu and Gopalan on patients using public hospitals in the eThekwini area. However, after a discussion, 56% of the patients surveyed felt that specific separate written consent should be taken for the anaesthetic.

The National Health Act (NHA) of 2003 states "a health service may not be provided to a user without the user's informed consent". Therefore, we are mandated by law to take our own consent for anaesthesia, and not rely on the surgeon's consent for their procedure. The NHA furthermore emphasizes that the consent taking process should be a DISCUSSION. This is your opportunity to not only get consent for your anaesthetic and the procedures associated therewith, but also to get to know your patient and their desires and wishes. The NHA encourages us to regard taking consent as a communication process, not a once off event. When we take consent we should not follow a prescriptive, paternalistic approach but encourage the patient to take part in the decisions regarding their own health. We have similar guidelines to the UK where informed consent is a patient-centered event with a shared decision making model.

The exceptions to providing medical care without informed consent are the following:

- an emergency where delay would result in death or serious harm
- treatment is mandated by law/ a court order (e.g. treatment of a drug mule)
- failure to treat would result in a serious risk to public health (e.g. quarantine in a Covid 19 positive patient)

When taking informed consent there are two areas that must be satisfied. Firstly, the **moral requirements** (bioethics), and secondly the **legal requirements**.

Moral Requirements

There are 4 primary principles of bioethics as set out by Beauchamp and Childress:

1) Autonomy - the right of self-determination or free choice
2) Beneficence - to act in the best interests of the patient
3) Non Maleficence - do no harm
4) Justice - ensure the benefits and burdens of the management are distributed equally (i.e. a favourable risk/benefit ratio)

Other principles of bioethics that are important are:

5) Dignity - treating the patient with respect and ethically
6) Truthfulness and honesty - regarding what we do and don't know

Legal Requirements

The legal requirements are set out in several documents. The most important of these are the NHA of 2003, the Children's Act of 2005 and the Patient's Right Charter. They are supplemented by the guidelines issued in the HPCSA booklet 4 and, for our profession, the SASA practice guidelines.

As a summary of all of these documents I would highly recommend reading the booklet issued by the MPS regarding consent.

We follow a model similar to the UK where emphasis is placed on shared decision making between the healthcare practitioner and the patient.

Three core considerations are important to the consent taking process:

1) Decisional capacity - is the patient fit to take the decision?
2) Information - what is the relevant information to be shared with the patient?
3) Voluntariness - was the decision made by the patient done so freely and without coercion?

I will consider them in greater detail.

Capacity

The first thing to consider under decisional capacity is **age**. As a general rule, adults are presumed competent and we must only intervene if they lack capacity. Minors (younger than 18) are presumed to lack decisional capacity and we must only intervene if we feel they have the maturity.

The Children's Act of 2005 defines this in more detail. It should be noted that this act places great emphasis the **best interests** of the child. Throughout the decision making process it is important to always act in the best interests of the child.

1) Children over the age of 12 with sufficient maturity and mental capacity to understand the benefits, risks, social and other implications may:

- consent to *medical* treatment
- consent to *surgical* treatment but this must be accompanied by written assent of the parent/guardian. The assent must be recorded on form 34. If the child's parents are themselves minors form 35 must be used.

2) Children under the age of 12, or over the age of 12 *but* with insufficient maturity or unable to understand the benefits, risks, social and other implications of the treatment, may not consent to either medical or surgical treatment. The consent for medical treatment then needs to be obtained from the legal guardian, parent or caregiver. Note that only a legal guardian or a parent may consent to surgery, not a caregiver.

3) In an emergency with no time to contact/trace the parents or legal guardian, the superintendent of the hospital may consent to medical or surgical treatment if it is necessary to preserve life, or to save the child from lasting physical injury or disability, and so urgent it cannot be deferred. If the superintendent is unavailable the person in charge of the hospital can consent. If neither are available, the HPCSA guidelines suggest the healthcare practitioner may treat the child if it is in the child's best interests. The treatment must be limited to what is reasonably necessary at the time of the emergency. Careful and meticulous documentation of efforts to locate parents, clinical managers etc. is required. Also document the child's clinical status throughout.

4) In non-urgent cases the Minister of Social Development may consent to medical or surgical treatment of the child. In non-urgent cases the Minister can also consent if the child unreasonably refuses, or the parent or guardian unreasonably refuses, is incapable, not readily traceable or deceased. This process can be started by contacting a social worker. Alternatively seek legal advice with the view to seeking consent from either the High Court or the Children's Court.
If either the child of the parents/guardian refuse, discussion with them must be initiated to try to get to the root of the refusal. We may be able to address fears once we know what they are.

5) In the case of an emergency with an unreasonable refusal by the child or parents, the medical superintendent must be contacted.

How does one decide whether a child over 12 is mature enough to consent to a procedure? Legal opinion says we have to be able to answer the following questions:

- does the patient must be able to understand the nature, purpose and possible consequences of the proposed investigation or treatment?
- does the patient understand the consequences of non-treatment?
- does the patient have adequate knowledge of the risk or harm of the treatment?
- can the patient appreciate and understand the risk or harm?
- can the patient assume the risk or harm associated with the treatment?
- The consent must be comprehensive

Special Notes:

ALWAYS involve the child in the decision making, whether they are over or under 12, whether they are mature enough to consent or not. Children need to know what is wrong with them and what treatment they will be having. Younger children can make other decisions such as what toy to accompany them to theatre and which parent should be there during induction of anaesthesia. The responsibility falls on the healthcare worker to communicate the relevant information to the child in such a way that it makes sense to them.

Consent and assent must always be WRITTEN. Record this on the anaesthetic chart and include details such as discussed details of the procedure, risks, regional anaesthesia, insertion of rectal suppositories and invasive lines. Note any questions asked and answered.

Parents

The biological mother automatically has full parental rights and responsibilities. If she is a "child parent" (under the age of 18) she has guardianship of the child and may consent to medical treatment. For surgical treatment she must be assisted by her legal guardian or parent, unless she is married.

The biological father only has rights if:

- married to the mother during pregnancy or after birth
- in a permanent life partnership with the mother during pregnancy or after birth
- he consented to be identified as the father and contributes to the child's upkeep
- court ordered

When both have full rights and responsibilities, either can consent to medical or surgical treatment or research without consulting the other. However it is advisable for them to discuss major decisions with each other and this should be encouraged even though it is not legally necessary.

Special Circumstances

TOP: a female of any age may consent to the termination of her own pregnancy

RESEARCH: parental or guardian consent is required under the age of 18. Over the age of 7 this must be accompanied by the child's assent. Caregivers cannot give consent to research.

VIRGINITY TESTING: forbidden under the age of 16. Over 16 it may only be done with the child's consent and accompanied by counseling. The results may not be disclosed without the consent of the child

CIRCUMCISION: female circumcision is always prohibited, regardless of age. Male children may refuse circumcision. It may only be performed under the age of 16 if necessary for religious or medical reasons.
The second thing to consider under capacity is the **Decisional Capacity** of the patient. In other words, is your adult patient capable of making or communicating a decision regarding their own care?

As previously mentioned, adults are presumed competent and we are only to intervene if we feel they lack capacity. There are 3 important components to decisional capacity:

1) Do they understand the relevant information?
2) Can the patient appreciate the consequences of the situation?
3) Can the patient reason with you regarding the proposed treatment?

If you are in doubt about the patient's decisional capacity pause and assess it. Give them information, discuss it and then ask open-ended questions to gauge understanding. It is important that we must focus on their reasoning rather than the actual decision reached. If the reasoning is sound we cannot interfere with a decision that we do not agree with. Great effort must be made to get the patient to make the decision. If the patient has a fluctuating level of consciousness taking consent at a different time of day may be effective. If the patient has cognitive impairment adjust your delivery of information. If the patient has communication issues use speech therapists, translators and other professionals to assist in the discussion. Some patients may require a less intimidating environment.

Incapacity has not yet legally been defined, but a bill has been tabled in parliament and it demonstrates principles of good practice. As a general rule the adult must be unable to either **communicate or make** the decision. To be unable to make the decision means that the patient cannot understand or retain the information, or practically make an informed rational decision based on the information given. The information must be conveyed in broad terms in simple language, taking the patient's home language and level of literacy into account. All practical steps must have been taken without success.

Even if the adult lacks the decisional capacity to consent, try to get their assent and include it in the final decision making process. Also include past decisions, views of the family and carers and results of the formal functional tests. DOCUMENT all of this carefully in the patient record.

In the case of compromised decisional capacity **surrogates** can be used to achieve informed consent in the following order:

1) The presence of an advanced directive must be honoured. If you doubt its validity or applicability, provide care in the best interest of the patient until the issue is resolved. Use the courts if necessary.
2) Person authorised by law or court order
3) Family member (first spouse or partner, then parent, then grandparent, then adult child, then sibling)
4) Healthcare professional using the "best interests" principles
   - available medical options
   - previously expressed preferences
   - patient's cultural, religious and employment background
   - third party view of patient's preferences
   - which option restricts the patient's future choices (including non-treatment)

If the patient has never been competent and the patient's beliefs, values or preferences are unknown, then choose the option a reasonable person would prefer.

In an emergency situation where treatment is required to prevent death or irreversible injury, the healthcare practitioner may go ahead providing the patient hasn't previously refused it.

If a conflict exists between the clinician and the proxy regarding the best interests of the patient, seek legal advice with the view to applying for a court order. In an emergency situation where time is of the essence the NHA makes provision for the healthcare worker to intervene to prevent death or irreversible damage to the health of the patient. If however there is a strong likelihood of complications arising that can result in conflict with the patient's wishes, it is important to explore the options beforehand. *(For example a Jehovah's Witness patient with a major placenta praevia presenting for a C/Section - discuss the options for blood transfusion ahead of the procedure.)*

If you are unsure of the way forward, consult with the patient's family or your colleagues or seek legal advice.

DOCUMENT all steps of the process, including consultations with family and colleagues.

Information

I can highly recommend '*What should I tell my patient? Disclosure in anaesthesiology: difficulties, requirements, guidelines and suggestions'* by M de Roubaix in SAJAA 2018

I will use the example of obtaining consent for a spinal anaesthetic.

The health status of the patient must be disclosed to the patient, especially when it regards your medical decision-making. For example if a pregnant patient has tight mitral stenosis this will influence your choice of anaesthetic for the C/Section and the patient must understand that. They should also be told if it will influence the risks and complications of the procedure and whether it will require further pre- or postoperative management (e.g. ICU admission).

The available treatment options must be disclosed, which of those is appropriate for the patient and the implications thereof. For us that usually means we must explain the options of GA vs neuraxial vs regional vs infiltration +/- sedation. The majority of our uncomplicated C/Sections occur under spinal anaesthetic because the studies support this and that must be explained to the patient. Likewise if another technique is indicated the patient needs to understand why. In some cases this may even mean we need to discuss our airway technique if appropriate (e.g. awake fiberoptic technique in severe scoliosis) or drug choice (e.g. if TIVA or TCI).

If appropriate other procedures (e.g. arterial lines and CVP's) and monitoring also need to be discussed.

The benefits, risks and costs implications of each option must be disclosed. There has always been a discussion around the scope of the disclosure to the patient. Full disclosure around an option might involve a discussion of a few hours long that is clearly not possible and will probably overwhelm the patient.

The NHA clearly states that the validity of the informed consent is confined to what has been disclosed to, and discussed by the patient. To confuse the issue the law also says that the extent of the discussion is subject to patient preference. In which case a patient may tell you he doesn't want to know about any complications. Experts in this area advise us that if we are unsure we should err on the safe side.

The complications around each option are often numerous and we need guidance on what to tell the patient. Traditionally complications are only mentioned if there is a 1% incidence or greater, and exotic complications are only mentioned if they are serious. But this may not be enough for patients. Legal opinions state that we should tell the patient what a reasonable person would want to know or disclose something if it would induce them to decide against an option (e.g. a rugby player would want to know of the risk of brachial plexus injury with an interscalene block). The courts will normally seek expert opinion regarding what should have been disclosed.

To make the complications more understandable it is advisable to break them up into common (but usually less severe) and rare (but often more serious) complications. Try to relate them in an understandable way. For example, a spinal anaesthetic has common complications of hypotension and shivering, whereas a post-spinal headache is less common, and anaphylaxis and neurological damage is rare. This information should be conveyed in a way that is relatable to the patient. It is also helpful to convey the information in such a way as to empower the patient and emphasise your ability to deal with it. For example, hypotension after a spinal anaesthetic is very common so "I have drugs ready to manage it. From your side if you suddenly feel very tired or nauseous please let me know so that I can immediately check your BP and treat it so you can feel better." The SASA practice guidelines state that the goal is to allay fears and provide reassurance.

It can be helpful to include a scale like Calman's verbal scale where incidences are ranked as:

Very high - risk > 1:10 (e.g. sore throat, PONV with a GA)
High – risk 1:10 to 1:99 (e.g. hypotension after a spinal anaesthetic)
Moderate - risk 1:100 - 1:999 (the risk of being in a car accident in South Africa or your spinal anaesthetic failing)
Low - risk 1:1 000 - 1: 9 999 (e.g. anaphylaxis)

Very low - risk 1:10 000 - 1:99 999
Minimal - risk 1:100 000 - 1:999 999
Negligible - risk < 1: 1 000 000 (risk of dying in a lightning strike)

Right to refuse treatment/ procedures:
"Competent patients have the right to refuse treatment, even when the refusal will result in disability or death." In addition, once given the consent can be withdrawn by the patient at **any** time. We must however explain the potential consequences of the refusal i.e. the refusal also needs to be an informed refusal. If the patient does refuse do make an effort to find out why, you may be able to allay their fears without coercing consent (e.g. pain as a reason to refuse a spinal anaesthetic). The patient once again has the right to change their mind about refusal too.

Details of the treatment team and the role of each member are important. If students are involved that must be explained too.

Other:
The HPCSA booklet emphasises that we must make an effort to find out about the patient's individual needs and priorities. We must not make assumptions. The information should be presented in a language that the patient understands. Aids may need to be used such as videos. The discussion must take the patient's level of understanding into account and questions should be asked to determine what they understand. Give the patient opportunity to ask questions themselves. The presence of a friend or relative is advised.

Voluntariness

Informed consent is only valid if it is freely given.

In the case of mentally ill patients who have been involuntarily committed according to the Mental Health Act of 2002, only treatment for the mental illness may be given. No psychosurgery may be performed without consent. If they have other coexisting diagnoses that need treatment we are to check their decisional capacity. If they do not have decisional capacity then consent may be sought from a court appointed curator, if none then a family member, if none then the head of the institution.

Details of the consent taking process

Written consent is preferred to verbal consent. Verbal consent is valid, but your memory fades and the patient's recall is often inaccurate. If the courts are ever involved the process may take many years.

Implied consent is invalid (i.e. just because the patient signed a consent form for surgery and then proceeds to lie down on the theatre table does not mean they consented to anaesthesia). Express consent is preferred.

Leaflets and pre-printed consent forms are valid. Be careful that they are not too voluminous and allow space for written notes and individualisation of consent. It is important to still discuss the content of the leaflet with the patient however.

The presence of severe pain, opiates or sedatives does not invalidate consent, but recall of the information is then low. It is doubly important in this scenario to have a relative or friend present.

Timing of the consent taking for elective surgery is controversial. Patients are often seen in a suboptimal environment shortly before surgery, and may be sick or high risk. This is not the ideal time to take an un-coerced consent and discuss fees. However medical aids will often not pay if the patients are admitted the night before. Pre-operative assessment clinics are good places to discuss consent, but these clinics may take place so long before the procedure that patient recall drops or additional questions arise. In that case, consent should be reviewed before the procedure.

The person who takes consent should be the person best able to provide all the relevant information. As such the healthcare practitioner who will provide that aspect of the patient's care is in the best position to take the consent. They may delegate the task, but it should be to a suitably trained and qualified person with sufficient knowledge of the patient and the procedure and they should comply

with the HPCSA's guidance on the topic. The actual service provider however accepts ultimate responsibility for the consent (i.e. the surgeon cannot take the anaesthetist's consent).

Negligence

To prove neglect 4 essential elements must be proven:

1) presence of duty - establishing the standard of care
2) breach of duty - standard of care was not met
3) causation - failure to meet the standard of care resulted in the injury
4) proof of damage - injury resulted

Negligence can apply if the informed consent was incorrect. Thus if there was insufficient disclosure and injury occurred negligence can be proven. This can also be applied if the injury was foreseeable and a treatment error did not occur. It is therefore critical that your informed consent taking process is above board.

Documentation

I have emphasised throughout that documentation of your consent is important. It does not need to be on a separate form (although that is also fine), but can be on the anaesthetic record too. It must include the relevant clinical findings, points of discussion between you and the patient, and with a multidisciplinary team if that occurred, details of their treatment, and details of other significant factors that may affect future care.

Conclusion

For details about other special circumstances surrounding consent such as clinical trials, HIV testing, communicable diseases, end of life decisions and DNR orders I can recommend reading the MPS booklet about consent.

Throughout the above article I have emphasised two things: the first is that consent taking is a discussion between yourself and the practitioner, and the second that this should be documented. By improving our communication with the patient we will not only improve our consent taking, but our patients will also go into theatre having built a better relationship with you which will go a long way to allaying their fears.

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Intra-operative Use of the EEG

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What are we talking about?

There are several techniques used for intraoperative neurophysiological monitoring, and they can be classified into 2 types:

- Detection of spontaneous activity, such as:
    - Electroencephalography (EEG)
    - Electromyography (EMG)

- Measurement of evoked responses from a specific neural pathway. Such as:
    - Somatosensory evoked potential (SSEP)
    - Motor evoked potential (MEP)
    - Brainstem auditory evoked potential

The EEG monitors the changes in electrical activity at baseline neurological states, and different levels of sleep and anaesthesia. Typically this is done in the superficial frontal cortex for commercial, processed electroencephalogram (EEG) in “anaesthesia systems”, or over the whole cortex, as a formal EEG, as in neurophysiological intraoperative monitoring(IOM)

The processed EEG monitors (BIS, Entropy, SEDLine etc) first extract, then amplify and then filter frontal cortical activity. Following signal acquisition, they perform a Fourier analysis, and then the deconstructed signal is typically projected in the frequency domain (by individual frequencies with time on the x-axis, amplitude on the y-axis). These commercial monitors show both the EEG trace, as well as a calculated value produced using various proprietary “tools” to measure differences including the amplitude (called the “power”), of the various frequencies alone, in frequency aliquots, and in power ratios (eg median and spectral edge frequencies); and in coherence of the waves of different frequencies.

The interpretation of these electrical signals, have been correlated with large groups of patients thought to be demonstrating “adequate” anaesthesia, and are then given alpha-numeric values based on complex algorithms, thought to describe a particular state, or “depth” of anaesthesia.

Any interpretation of these monitors needs to recognise that there is no evidence that either the state of “consciousness”, or of “general anaesthesia” is explained by the state of the superficial frontal cortex. Indeed there is little evidence that this superficial region of the brain is either responsible for the “state of anaesthesia”, or is the particular site of anaesthesia induced changes.

However, a significant portion of the immobility and CNS state produced by anaesthesia is manifest through the drugs’ action on the spinal cord. Cranial EEG analysis may therefore not be a particularly good way to measure the effects of anaesthetic drugs on the spinal cord, and hence is not a particularly reliable method for predicting whether patients will move during surgery.

Unequivocally, changes in frequency, amplitude and phase relationship between frequencies do occur in the frontal cortex, but there is no evidence that these changes account for the state of altered consciousness, or of general anaesthesia induced by anaesthetic drugs. These changes may be best described as frontal lobe correlations, with the state of general anaesthesia, much as the MAC measurement measures/describes the state of spinal cord suppression by an end-tidal concentration of an inhalational agent. So just like the MAC value, it gives us a measure to assess the degree of altered consciousness, induced by general anaesthesia. However there is one big difference, the MAC value is an absolute measure value of that particular drug, whereas the processed EEG attempts to provide a measure of the summation of the effects of many different agents, and combination of

agents. It is not as simple as that, because it tends to predominantly measure changes brought by GABAergic transmission in the frontal cortex, and is silent to the hypnotic agent lowering effects of the opiates, regional or neuroaxial anaesthesia, of all the NMDA antagonists etc.

Principles of processed EEG measurement

Frequency

Different areas of the brain are able to generate frequencies between 0.5 and 500 Hz. Clinically relevant frequencies are mostly between 0.5 and 60Hz, and with the essential clinical ones in **bold**, include:

- **3 Hz or less (Delta waves)**
    - Have a large amplitude
    - Seen in deep sleep
    - Are abnormal in the awake adult.

- **3.5-7.5 Hz (Theta waves)**
    - Theta waves normally are seen in sleep at any age. In awake adults, these waves are abnormal if they occur in excess

- **8-13 Hz (Alpha waves)**
    - Occur particularly in the posterior part of the cortex
    - Prominent when the eyes are closed, with subject in a relaxed state.
    - Alpha activity disappears normally with attention to a subject or a task
    - Usually Alpha waves are regarded as a normal waveform

- **13Hz and faster (Beta waves)**
    - Usually small amplitude, symmetric and especially anterior part of cortex
    - Augmented by drugs, such as barbiturates and benzodiazepines

- **Sleep spindles**
    - Are groupings of waves that occur during many sleep stages, but especially in stage 2 sleep.
    - Their frequencies are between 5 and 15 Hz
    - They last for a second or less, initially they increase in amplitude, followed by a decreasing amplitude. The resultant waveform complex resembles a spindle.
    - Usually are symmetric, most obvious in the parasagittal regions.

Effects of anaesthesia on the EEG

The cortical EEG in an awake and conscious patient is typically one with a flat baseline and high frequency, low amplitude waves. With sleep and the administration of most, but not all, anaesthetic drugs; the initial change is increased wave amplitude, followed at larger doses by decreased frequency and increased regularity.

The pathognomonic features of the state of surgical anaesthesia are the development of sleep spindles (they look not dissimilar to the Torsade pattern on an ECG) and the entrance of the deep Delta waves.

Finally, at very deep levels, periods of isoelectric (flat) EEG interspersed with bursts of undulating EEG activity (burst suppression). However there are some individual differences in the EEG effects of various anaesthetic drugs.

So, in practise what do we see?

1. Awake patient, baseline, we see:
    a. Flat baseline
    b. Fine ‘saw-tooth” oscillations with high frequency and small amplitude, sometimes so dense that it looks like a thick, dark line

   c. When patient blinks, see broad, and high amplitude waves (almost look like Delta waves)

2. Light sedation
   a. Increasing amplitude
   b. Often blinking is lost
   c. May see slight slowing of frequency
   d. Baseline usually flat

3. Deeper sedation
   a. Increasing amplitude
   b. Frequency slowing and start seeing individual waves better
   c. May start to see wavy baseline

4. Light anaesthesia
   a. Increase amplitude
   b. Slower frequency
   c. Sleep spindles (torsade like crescendo, de-crescendo amplitudes)
   d. Baseline drift

5. Surgical anaesthesia
   a. Sleep spindles
   b. Wavy baseline
   c. Delta waves (1-2Hz) large oscillations

6. Deep anaesthesia
   a. Dominant Delta waves
   b. May have occasional sleep spindles

7. Overdose (Burst suppression)
   a. Approaching isoelectric state
   b. Flat line, with occasional wave-activity

8. Isoelectric
   a. Flat line, with no “bursts”

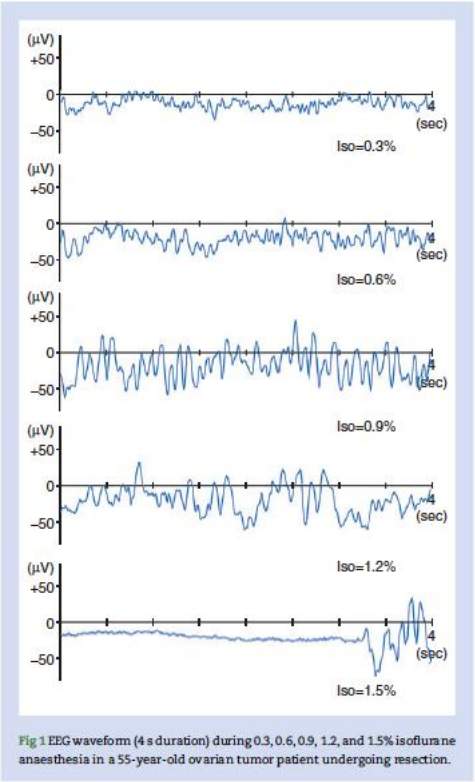
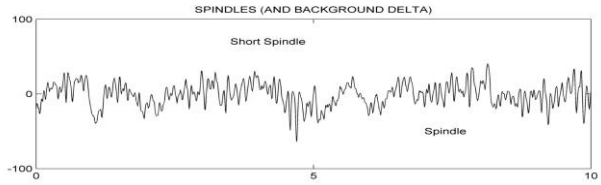


Fig 1 EEG waveform (4 s duration) during 0.3, 0.6, 0.9, 1.2, and 1.5% isoflurane anaesthesia in a 55-year-old ovarian tumor patient undergoing resection.

While raw EEG patterns have elements that are anaesthetic-agent specific; concentration related changes in EEG waveforms are actually quite similar among different agents that potentiate gamma-aminobutyric acid type-A (GABAA) receptors.

In addition to changes in frequency dominance, and the amplitudes of each frequency, the EEG also demonstrates increased synchronization of the raw EEG waveforms with increasing concentrations of anaesthetic agents. When the sine waves are consistently in phase with each other, the EEG may be described as synchronized and anaesthetics tend to increase the degree of synchronization in a dose related manner. This is properly called the bicoherence value, and quantifies the extent of phase coupling in a signal. It is also known as bispectral coherency but in EEG processing is termed the "bispectral analysis".



What we know about BIS

BIS appears to analyse changes in the 11-20Hz and 30-47Hz bands, as well as looking at the sum of the power (or amplitude for that frequency) in the 0.5-47Hz frequency aliquot and comparing that to the sum of the power in the 40-47Hz aliquot. Advanced analysis of the EEG signal and processing time is an important limitation with all computerized EEG interpretation, processing time is substantial, requiring some seconds, although usually less than a minute, and can be easily observed clinically when administering a bolus of an intravenous induction agent to an awake patient. Time delays of 14 to 155 seconds are reported for all of the devices. For a sudden transition from ''general anaesthesia'' to ''awake,'' the delays were 15, 30 and 65 seconds for CSM, BIS and Narcotrend, respectively. Recent work published using volunteer anaesthesiologists who received neuromuscular blockade (with no hypnotic agents) with both suxamethonium and rocuronium suggests that the time constant may really be closer to 4 minutes.

Other commercial processed EEG DoA monitors include:

Like the BIS, the other commercial monitors have proprietary algorithms, so the exact contribution of their known analytics of the EEG, is not known, except for Entropy (GE) which seems to have the most open source software.

- Entropy (GE Healthcare): State (0.8Hz-32Hz) and Response Entropy (0.8-47hz) evaluate changes in the shape of the power spectrum, and use signal theory to calculate the degree of predictability of the signal. In addition in partially or unparalysed patients, Response Entropy analyses the higher frequency activity, and if the RE is greater than SE, then is thought to reflect requirement for more analgesia, as frontalis muscle activity "signals" that through high frequency muscular signals. SE and RE should not differ in fully paralysed patients.

- Cerebral State Index (CSI) (Danmeter, IoC (Morpheus Medical), or qCON (Quantium Medical) use ratios of EEG band power. The interpretation is projected as a unit-less scale between 0 and 100.

- Narcotrend (Narcotrend) utilizes information from the spectral domain as well from autoregressive modeling in the time domain. There is almost no recent literature mentioning the Narcotrend monitor.

- The PSI from the SEDLine monitor (Masimo) processes spectral power from different frequency bands, interhemispheric power gradients and synchrony, and a measure of the spectral array (similar to spectral edge frequency analysis, but it is not clear what the power of spectral edge is).

- Brain Anesthesia Response (BAR) monitor generates its index by modeling EEG dynamics, and includes a “cortical input” algorithm that attempts to measure analgesic requirements.

Evidence to support BIS/ processed EEG DoA monitoring

A meta-analysis of 11 randomized controlled trials of BIS monitoring for ambulatory surgery, comprising 1380 patients, found that the use of BIS monitoring reduced anaesthetic consumption by 19%, reduced the incidence of nausea and vomiting to 32% from 38%, and reduced recovery room stay by 4 minutes.

The four large trials assessing the utility, and efficacy of BIS monitoring in preventing Awareness Associated with General Anaesthesia (AAGA) are the:

- B-AWARE (Myles 2004) trial
    - Multicentre, randomly assigned, adult patients BIS vs Standard anaesthesia (not defined) in high risk patients, showed that BIS decreased awareness in high risk adult patients.

- B-UNAWARE (Avidan 2008) and BAG-RECALL (Avidan 2011) trials
    - Demonstrated that targeted ET AA of 0.7 MAC (control group alert set at 1.3-0.7 MAC) was as good or better than BIS (intervention group alert set at 40-60) in high risk patients

- Mashour (2012) trial
    - Is largest RCT, and was performed in low risk patients unlike the B-AWARE, B-UNAWARE and BAG-RECALL trial
    - Demonstrated that BIS is better than clinical signs in preventing explicit recall, but not better than 0.5 times the age-adjusted MAC in patients under general anaesthesia.

GABA-ergic relationship

The algorithms have been derived using the common drugs as propofol, midazolam, and isoflurane that are largely GABA-ergic. Nitrous oxide produces EEG effects that are distinct from the potent inhalational agents, and in most studies nitrous oxide has produced little or no change in BIS or entropy index values. Nitrous is a relatively weak hypnotic, but a good analgesic, and the effects seem similar to that of the opioids, that have relatively little effect on the EEG.

Ketamine is an unusual intravenous anaesthetic because it produces EEG activation, an increase in high frequency activity in the EEG, which often paradoxically increases the BIS index or other EEG-derived indexes, depending upon the dose used. Smaller doses of ketamine may not have a noticeable effect on the BIS index.

Essentially, BIS seems “blind” to agents that are thought to be dominant at non-GABA-ergic neurones, such as nitrous oxide and ketamine, despite both being established to add to the state of anaesthesia. The addition of ketamine to a standard anaesthetic can even result in an increase in the BIS value, when most would agree that the additional analgesic and hypnotic effects should decrease BIS. Similarly the effect of opiates is also “not seen” by BIS- so the MAC sparing effect of opiates is not detected.

The effects of etomidate and dexmedetomidine on the EEG are not well studied, but the BIS index does appear to track the effects of these drugs.

Challenges with drugs with alternative mechanisms, dementia, opiates, spinal anaesthesia

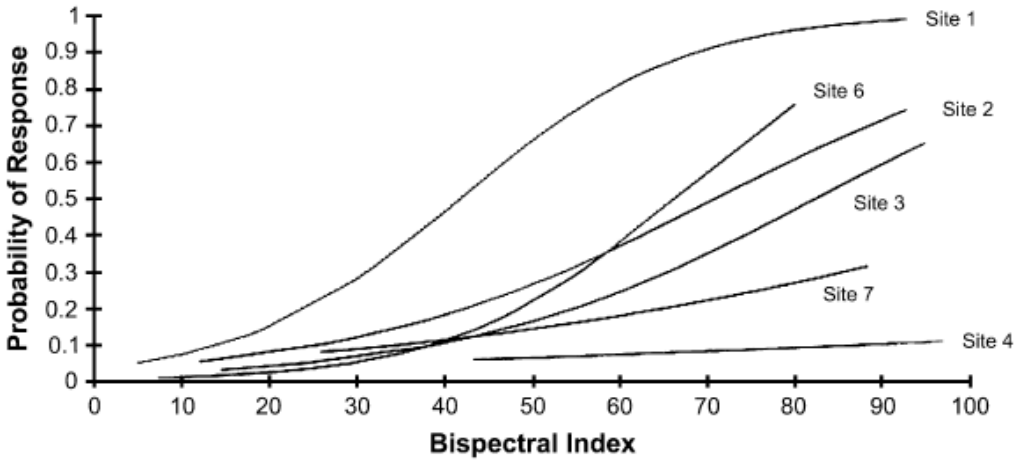


Fig. 1. The probability of movement in response to a surgical stimulus versus BIS index (bispectral index) for seven centers in a multicenter study. Each center employed a different anaesthetic technique, and variable amounts of opioid were used. When isoflurane was the sole anesthetic agent, there was a sigmoid-shaped relationship with a probability of movement of about 50% at a BIS index of 40 (Site 1). For the other six centers in which varying amounts of opioid were combined with isoflurane, propofol, or nitrous oxide, the probability of movement at a BIS index of 40 was reduced to around 10% or less. Site 5 had no movement in response to a surgical stimulus, thus, a relationship to BIS could not be determined.
(From Sebel PS, Lang E, Rampil IJ, et al. A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. Anesth Analg 1997;84:896; with permission.)

Some clinical situations can significantly influence the BIS value and render it completely unrepresentative. These include:

- Influence of muscle tone (EMG) from the forehead muscles, body motion and sustained eye movements
    - The BIS monitor evaluates the presence of EMG or other high-frequency noise and lights up an EMG signal-strength indicator on the monitor screen alerting the user that the BIS index may be influenced by artifacts
    - Administration of a muscle relaxant (Usually only a small dose is required.) will usually eliminate the EMG activity and restore conditions for reliable EEG signal acquisition. The true BIS index value can then be ascertained.
    - The BIS index value typically falls following administration of a muscle relaxant when an EMG artifact is present, since the EMG activity usually elevates the BIS index value.

- Potential artifacts may be caused by
    - Poor skin contact (high impedance), muscle activity or rigidity
    - Head and body motion, sustained eye movements,
    - Improper sensor placement
    - Unusual or excessive electrical or mechanical interference caused through
        - Electro-cautery
        - Cardiac atrial pacing
        - Vibrations from forced air warmers

- BIS values should be interpreted cautiously with certain anaesthetic combinations, such as those relying primarily on either ketamine or nitrous oxide/narcotics to produce unconsciousness.

- In some instances high doses of opioids can cause a paradoxical increase in the processed EEG, while low doses of ketamine can result in increased high frequency EEG activity.

- Because the BIS algorithm was developed using healthy volunteers with normal EEG patterns, any pre-existing neurologic disorder that exhibits abnormal EEG waveforms can affect the BIS.

  - Patients with Alzheimer's or vascular dementia can show an increase in the slow wave activity of the EEG, associated with a lower mean awake BIS.
  - Patients with cerebral vascular disease may have cerebral ischaemia leading to cortical inactivation leading to EEG slowing or a decrease in the BIS

- Some serious clinical conditions such as profound hypotension and severe hypothermia (hypothermia reduces the BIS by approximately one BIS unit per degree Celsius)

Cost effectiveness

Cost saving could come from two sources- less drugs, shorter theatre and recovery time; and litigation savings if risk of awareness is decreased. One study showed that the costs savings in drugs and recovery time was the equivalent of 0.18 Euro/min, and the costs of the BIS consumables was 14.01 Euros.

Other studies have shown similar outcomes - costs are increased with BIS monitoring and the potential savings do not overcome the additional cost. Currently it cannot be said that BIS is cost-effective.

Concerns

MAC for anaesthetic agents is a measure of the ED_{50} for awake, movement or BAR and is a measure of equivalence for all agents in terms of the desired clinical effect. This has been described as "normalising" the population response between different inhalational agents. So, for MAC there is shared probability of 50% of patients not responding/moving in response to the specified stimulus. If a DoA monitor shared this accuracy then for a given value for all anaesthetic agents, it should match the MAC value. This does not hold true so that the BIS value is different for MAC with each inhalational agent, varying as much as BIS =35 for some agents and BIS=60 for others.

The differences between inhalational agents, and TIVA with propofol, are even more stark, with the probability of unconsciousness at a BIS value of 70 being 50% with isoflurane and only 15% with propofol.

Because healthy adult EEG data were used to authenticate the BIS algorithm, it cannot automatically be extrapolated to young children, as the paediatric EEG only approaches the adult pattern by about 5 years of age. However, it does appear that BIS may be valid in children older than 1 year of age.

Current status of processed EEG DoA monitoring

Product monologue from manufacturers states:

> "Reliance on BIS values alone for intraoperative anesthetic management is not recommended"

The UK National Institute of Heath Research Health Technology Assessment performed a Technology Assessment Report (2012) on EEG based monitors and concluded that:

> "The available evidence on the impact of the technologies on reducing the likelihood of intraoperative awareness is limited. Overall, [EEG-base monitors are] not associated with a statistically significant reduction in intra-operative awareness in patients classified as at higher risk."

Current Opinion in Anesthesiology (2016)

> "Current research suggests that processed EEG monitors may be most useful in specific patient populations, such as TIVAs and in patients with hemodynamic compromise that requires the clinician to minimize the concentration of the vaporized agents. Alternatively, measuring ETAC and maintaining it greater than 0.7 age-adjusted MAC can prevent awareness while being most cost-conscious."

A 2014 Cochrane review found that

> "Four studies in 7761 patients, that used clinical signs as a guide to anaesthetic administration in standard practice, as the control group, demonstrated a significant reduction in the risk of awareness with BIS monitoring.
> Four studies with a total of 26,530 patients, compared BIS monitoring with end tidal anaesthetic gas (ETAG) monitoring as a guide to management of anaesthesia and they did not demonstrate any difference in terms of intraoperative awareness"

A 2014 editorial in the Anaesthesia

> "Each anaesthetic agent appears to act via its own unique spectrum of affinity/ efficacy for different channel receptors. The resulting effect is not just related to effect of dose on one receptor system, but also to the spectrum of receptors on which the agents act at a given dose. Since these receptors are unevenly distributed in different parts of the brain, this suggests that each agent acts on its own unique set of brain regions. And since brain function is localised by region, this suggests in turn that each anaesthetic drug may induce anaesthesia by its own unique mechanism involving different, specific brain functions.
> These conclusions are in view that there must a singular, binary mechanism by which all anaesthetics induce anaesthesia. Furthermore, there is an emerging consensus that accidental awareness during anaesthesia is also a spectrum of brain states, some of which are in fact broadly acceptable to patients (even though they involve a degree of awareness of surroundings, which may be surprising or unanticipated at the time)

Indications for intra-operative EEG monitoring

UK National Institute for Clinical Excellence (NICE) Recommendations (2016)

- "Is recommended as an option during any type of general anaesthesia in patients considered at higher risk of adverse outcomes. This includes (1)patients at higher risk of unintended awareness and patients at (2) higher risk of excessively deep anaesthesia."
- "Also recommended as an option in all patients (3) receiving total intravenous anaesthesia."
- "Greater uncertainty of clinical benefit for the E-Entropy and Narcotrend-Compact M depth of anaesthesia monitors than for the BIS monitor, the Committee concluded that the E-Entropy and Narcotrend-Compact M monitors are broadly equivalent to BIS. These monitors are therefore recommended as options"
- "Anaesthetists using EEG-based depth of anaesthesia monitors should have appropriate training and experience with these monitors and understand the potential limitations of their use in clinical practice."

In addition to the above three DoA indications:

- Processed EEG to limit adverse outcomes
    - Prevention of excessive anaesthesia depth, to minimize post-op delirium. Monitors were not designed with algorithms that target associations with post-operative outcomes, so are limited in their utility.
    - Alpha-band (8-12Hz) activity or power (amplitude) shows a shift from posterior regions to anterior regions under most general anaesthesia, but elderly patients demonstrate less frontilisation of EEG alpha-band activity, and work is exploring whether this could correlate with poorer cognitive outcomes. However this is not currently standard clinical practice.
    - Understanding anaesthetic emergence better, in the hope of limiting "emergence phenomena". It seems that patients who abruptly transition from EEG patterns of unconsciousness to awake EEG patterns, may be more vulnerable to pain and delirium in early recovery phases.
    - Mortality has been related to low intraoperative BIS values, and recent work suggests that patient frailty may well account for this observed correlation. Concern remains, and this is an area of active work.

- Anaesthesia “quality”
    - The 8-12Hz alpha power, shift from the posterior regions towards the anterior regions, seems to possibly correlate with changes in a thalamocortical loop, involved in the state of general anaesthesia. There is some work suggesting that the alpha peak demonstrates better “quality” anaesthesia, and that less frontal alpha activity could suggest a state of arousal, or of inadequate analgesia.

There is a movement developing that suggests that rather than provide processed EEG data, that anaesthetists should rather have knowledge of changes in the raw EEG during anaesthesia, and that this it could better help them judge the adequacy of EEG indices and enable them to respond more rapidly and confidently in circumstances where equipment algorithms provide misleading indications. There is developing evidence that after just one or two weeks training, it seems likely that most anaesthetists should be able to reliably judge and interpret the effects, and the state of anaesthesia on the raw EEG.

Paper III Session: Radiology
Interpreting imaging of the chest and mediastinum

Prof. Sally Candy

Associate Professor (Emeritus)
Division of Diagnostic Radiology
University of Cape Town

An imprecise tool!

Only five different densities are detectable on plain films: (if you exclude the odd bullet / knife /stent etc)

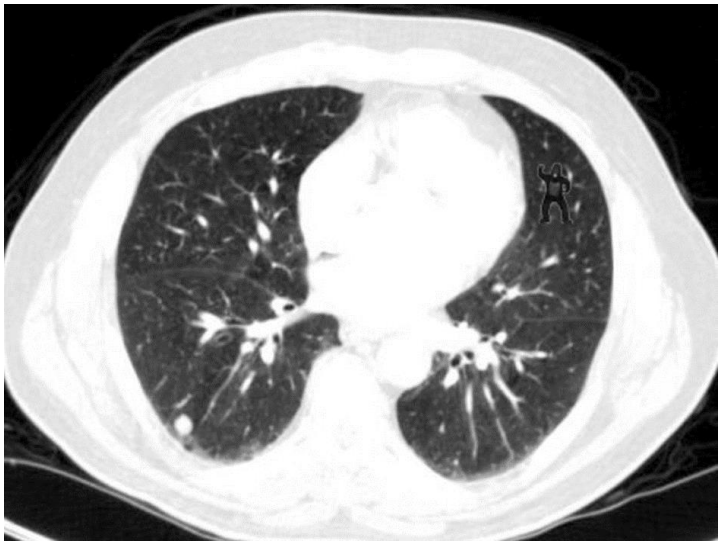
- Air, fat, soft tissue, calcium and contrast (barium, iodine).

An optimistic claim!

Is has been said (no doubt by a radiologist), “Expert radiologists not only perceive abnormalities that non-experts do not, but they also better understand what to attend to and what to ignore” (Gunderman and Patel, 2019).

An interesting statistic!

So in that case…



…why did 83% of radiologists not notice the gorilla in the top right of this image when scrolling through five chest CT scans looking for lung nodules?!

A poor excuse!

This is explained by a phenomenon known as ‘inattention blindness’:

“….when engaged in a demanding task, we may fail to perceive an unexpected stimulus that is in plain sight….”

The error rate in reading radiological images has not improved in the last seven decades!

The implications of getting it wrong!

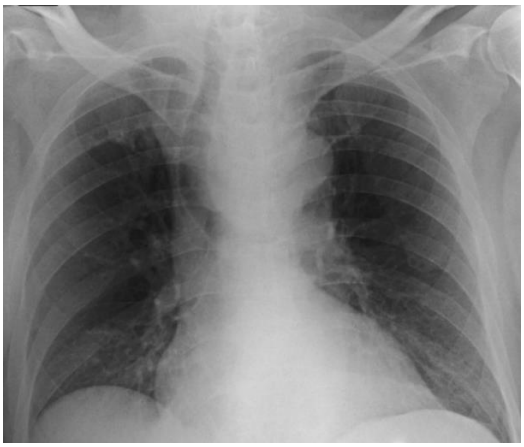
It goes without saying that false negatives and false positives may be equally disastrous for the patient and that you cannot see what you do not know.

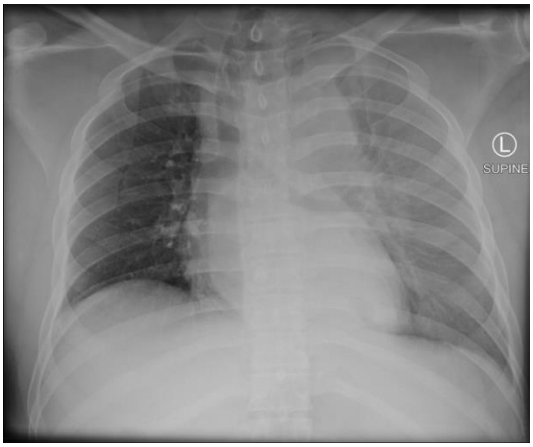
So how should we approach the interpretation of a CXR?

Armed with:

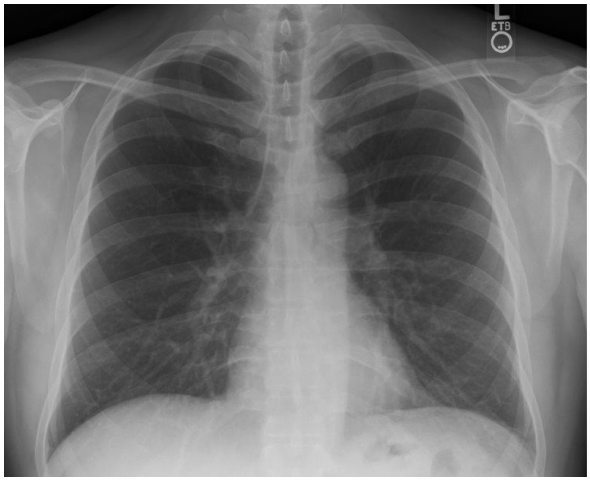
- a knowledge of the clinical scenario
- a little knowledge of 3D anatomy
- a very good idea of what is normal
- an educated guess as to what you might expect to see
- extreme caution!

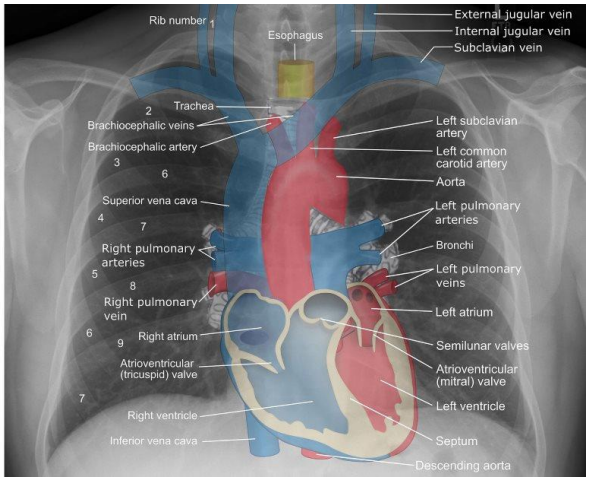
Compare these CXR's with similar features: Can you make the diagnosis in each?

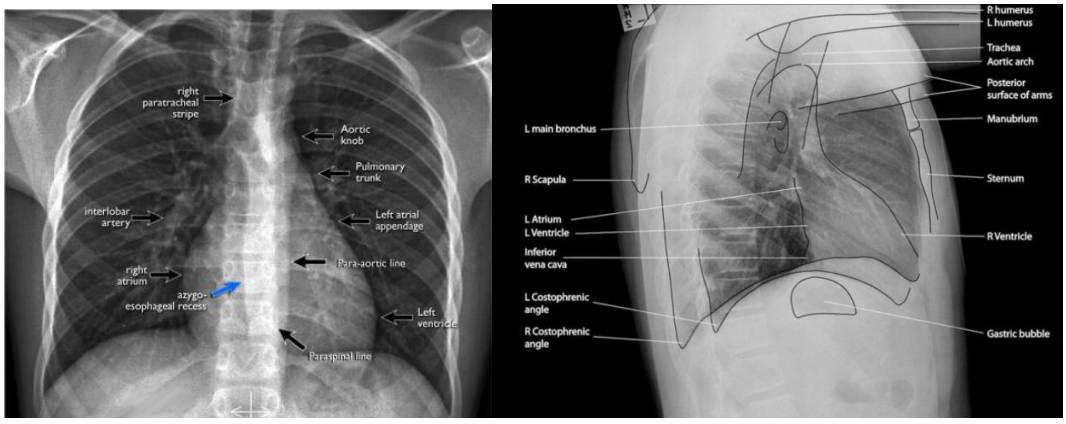




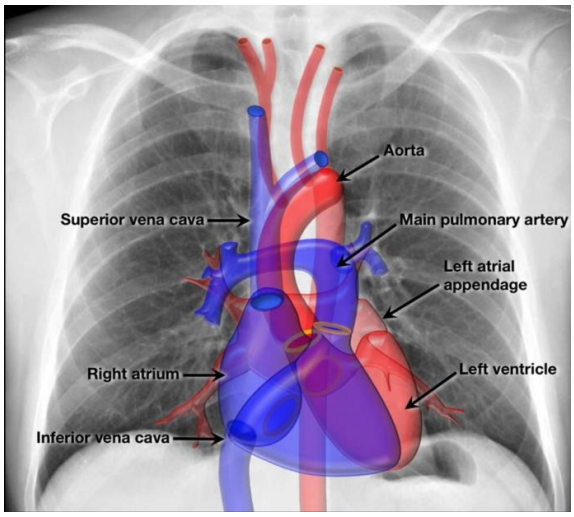
Back to basics – the normal chest radiograph /plain film:

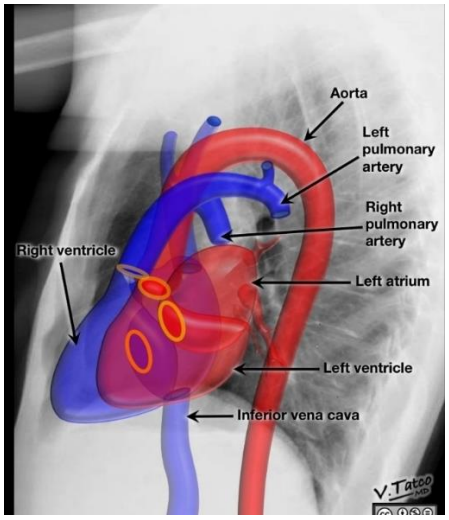






And here is the artist's rendition (with a little help from the computer)



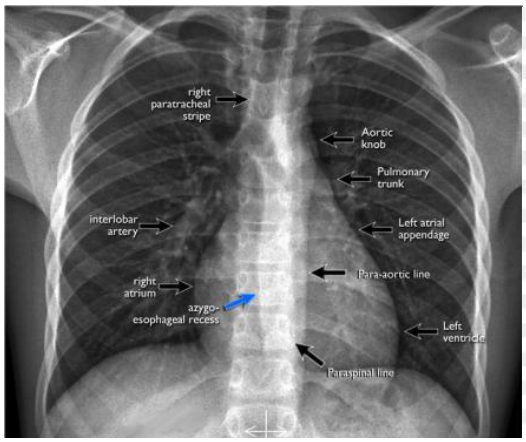


Case courtesy of Dr Vincent Tatco, Radiopaedia.org. From the case rID: 46331

Sadly, most of our radiographs do not come with "augmented reality" but in a few shades of black and white. They are often technically suboptimal – a challenge to even the most experienced viewer. An anatomic distance of roughly 20 cm is collapsed into one dimension, incorporating all anatomy, pathology and any incidental overlying foreign body e.g. sheet fold, hair braid, buttons, catheters and tubing etc. This applies equally to both the PA and Lateral; having both views adds significantly to the interpretation.

Outlines and edges seen on plain radiographs depend on *differential density.*

Two structures of similar density will be distinguishable only if they are separated by air (the silhouette). This applies both to normal anatomical structures (e.g. the right and left ventricles) and to an abnormal structure or process lying adjacent to a normal bit of the anatomy (e.g. left lower lobe consolidation and the left hemidiaphragm).



Assessing the image

1. Does this radiograph belong to the patient you want to review?
   Correct name, age, sex

2. How was the film taken?
   Erect /supine /semi-erect /PA /AP/inspiration/expiration?
   NB mobiles are AP - easy to miss pleural effusions and pneumothoraces

3. Is the left /right marker correct?

4. Is the film rotated?
   Beware the rotated film – over-call pulmonary artery prominence/ adenopathy.
   Distorts or obscures mediastinal pathology
   False impression of differential translucency between the lungs

5. Is the image adequately penetrated?
   The intervertebral disc spaces should be more visible than the outlines of the vertebral bodies.
   Penetration is less of a problem with digital imaging (answer to a radiographer's prayer), salvage possible.

6. Is the entire chest visible? Apices and CP angles fully visible?

7. Are the radiographic silhouettes maintained? Beware the right middle lobe and lingual

8. Develop a routine and stick to it. Start centrally and move peripherally scanning and re-scanning continually. This is particularly important when there is one glaring abnormality that will detract from others.

ABC: AIRWAY / BONES / CARDIAC / DIAPHRAGM (PLEURA) / EFFUSIONS / GIZMOS

REVIEW SITES: APICES / BEHIND THE HEART / BENEATH THE DIAPHRAGM / BONES

AIRWAY

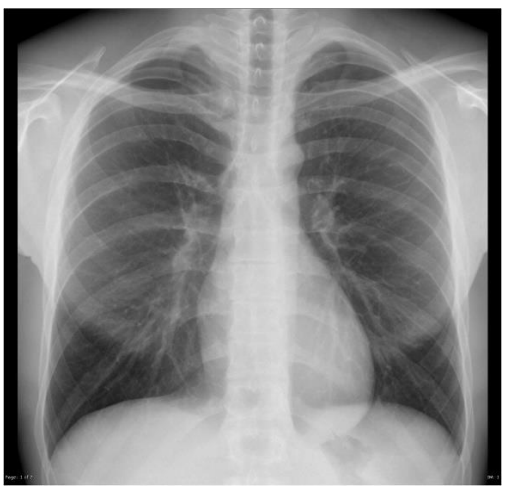
Is there an endotracheal tube in situ? Is the position adequate? Between the clavicular head and the carina (3-4cm above carina)
Is the trachea central?
Are both main bronchi visible?
Is the angle of the carina normal? (60 to 100 degrees)
Is there any foreign body? e.g. tooth often dislodged during intubation?

MEDIASTINUM

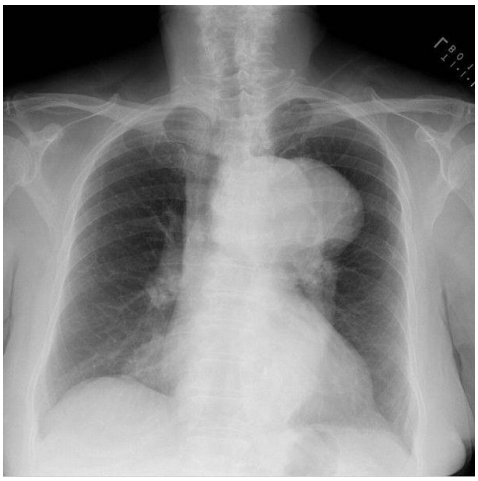
Measure at the arch
Is it widened (max allowed on a supine film 8cm, erect film, 6cm)?
Is the aortic knuckle normally positioned?
Is the aortic knuckle crisp? NB most sensitive sign of mediastinal haematoma on CXR
Beware the right-sided arch
Beware the small aortic knuckle
Beware the big arch
Beware the 'Figure 3' arch
Aortic arch calcification (interrupted – dissection with imminent arch rupture)

Diagnoses A B C and D?

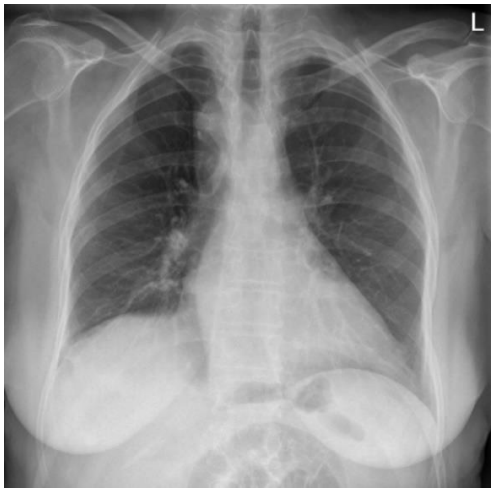
A



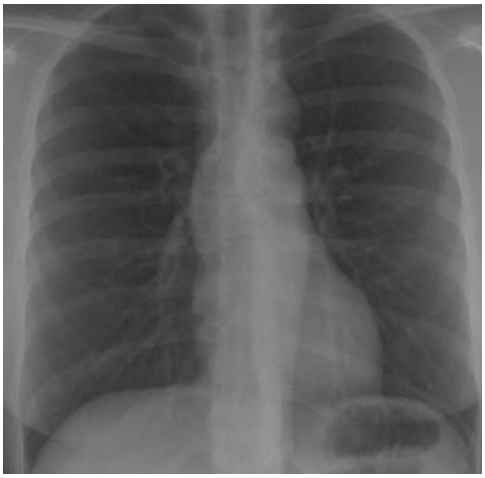
B



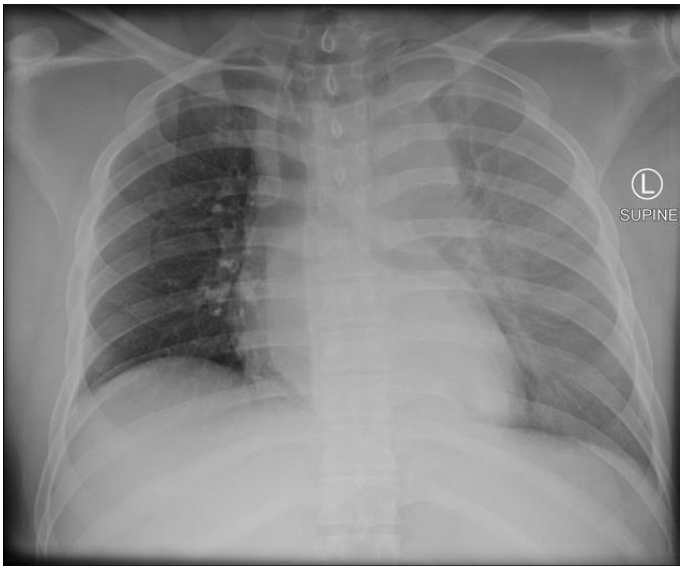
C



D



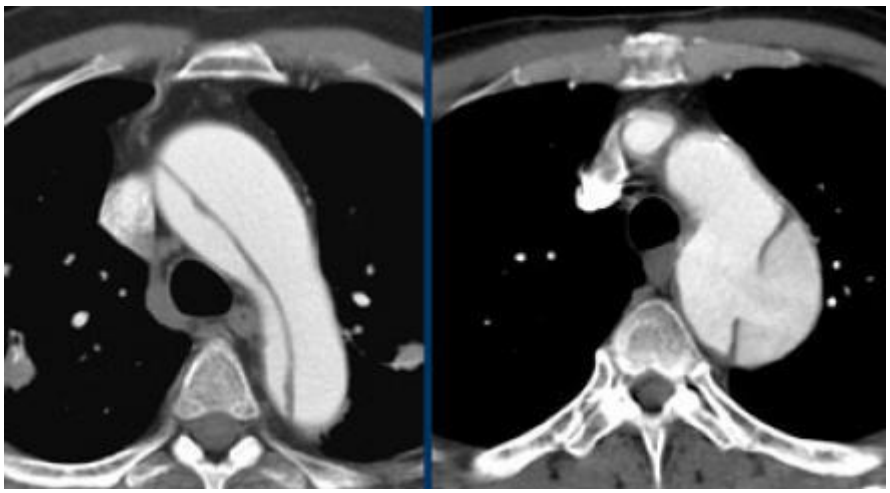
Describe the abnormalities visible on the following CXR:



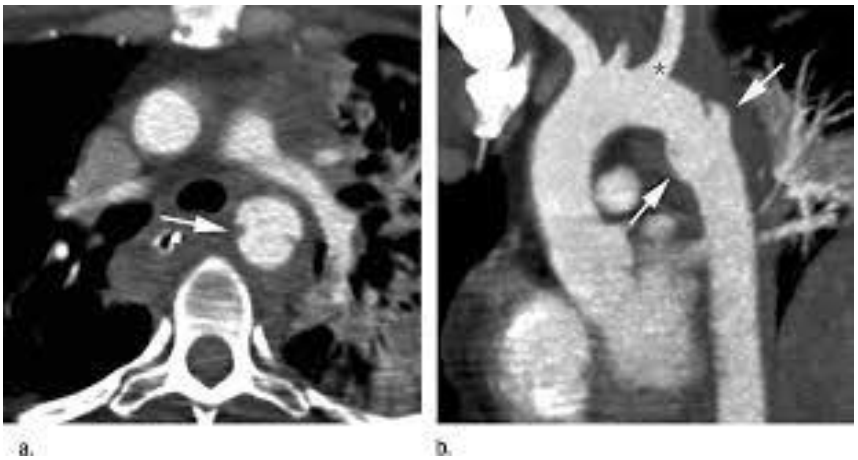
- widened mediastinum >8 cm when supine>6 cm when erect
- indistinct or abnormal aortic contour
- deviation of trachea or NGT to the right
- depression of left main bronchus
- loss of the aorto-pulmonary window
- widened paraspinal stripe
- widened paratracheal stripe
- left apical pleural cap
- large left haemothorax (note difference in radiolucency)

- **Features of traumatic aortic rupture**

CT Angiography takes away the guesswork:



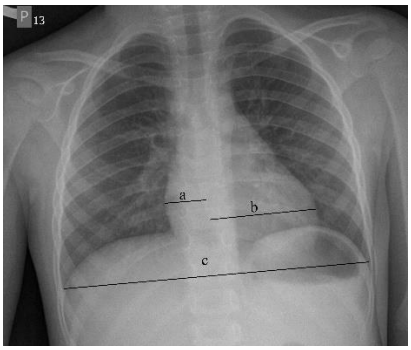
Stanford Type A dissection **Type B dissection**



- **Traumatic aortic rupture mediastinal haematoma and dissection flap shown on axial and oblique cor recons**

THE HEART

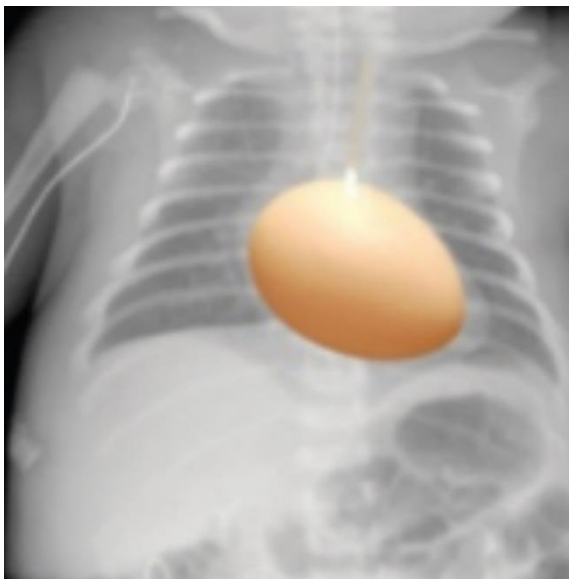
Size: Adults PA heart <50%
Paediatric AP heart < 60% transverse diameter of the chest wall

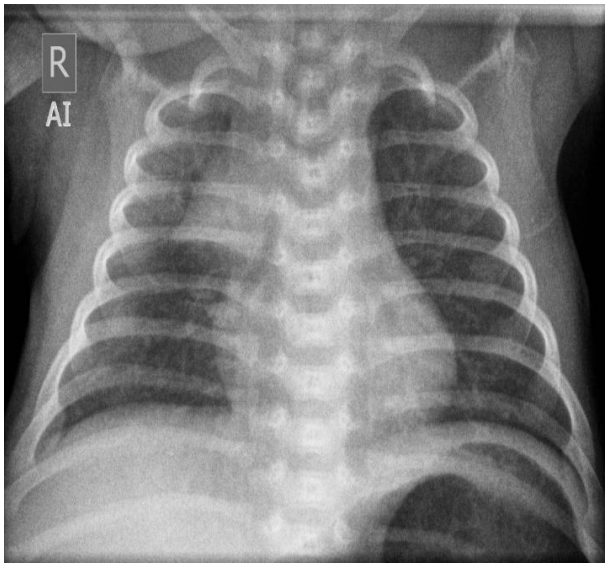


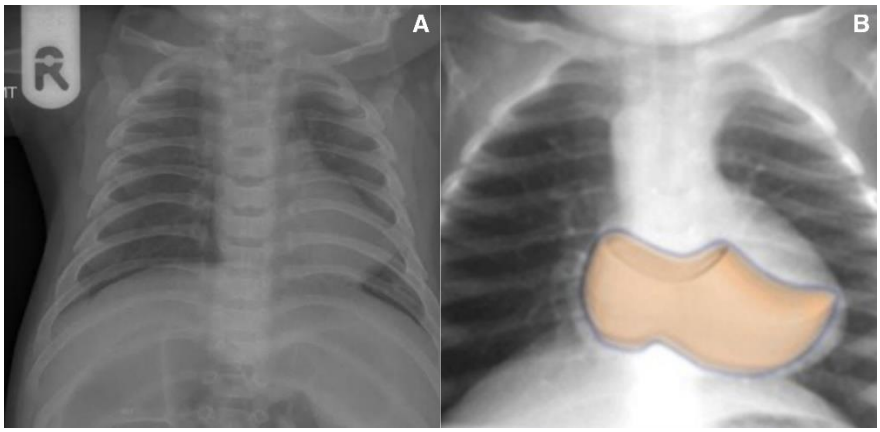
Shape: Remarkably constant in normal adults.
Thymus messes with the mediastinal contour in young children.
If the heart is enlarged, then which chamber(s) are affected? Use your PA and Lateral for clues.
Shapes: You know the common ones.

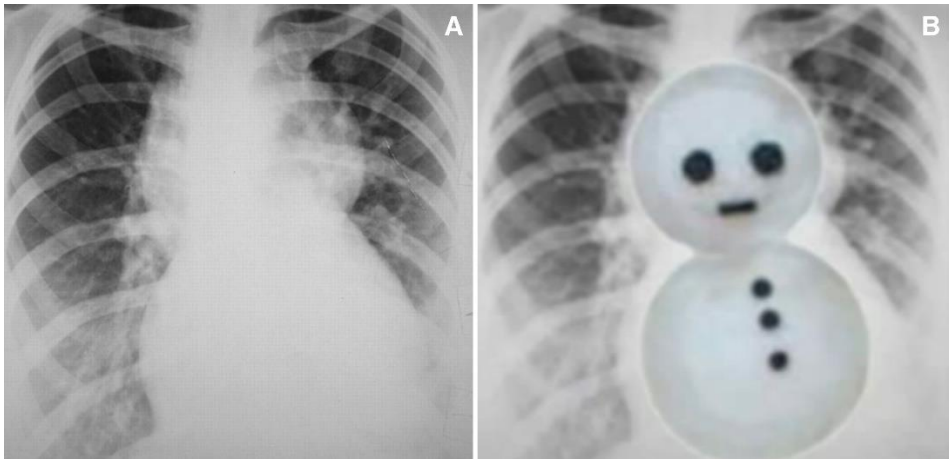
Match the pairs:

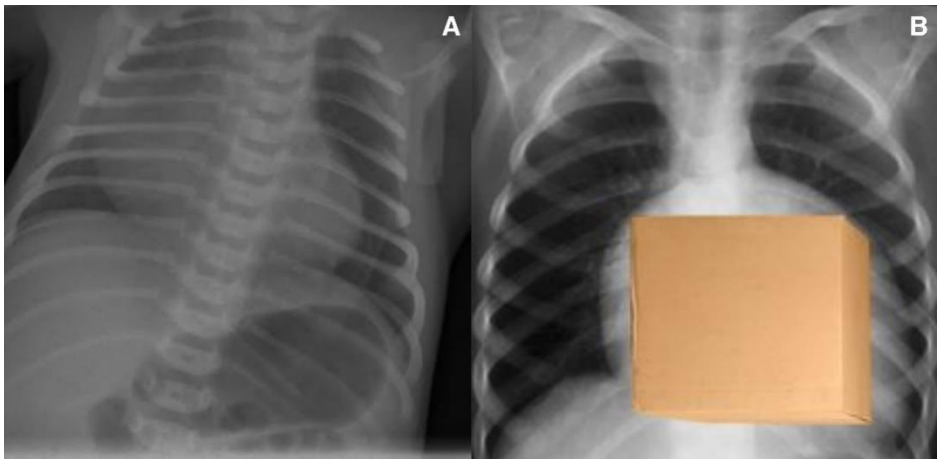
Tetralogy of Fallot
Transposition of the great vessels
Coarctation of the aorta
Epstein Anomaly
Normal thymus









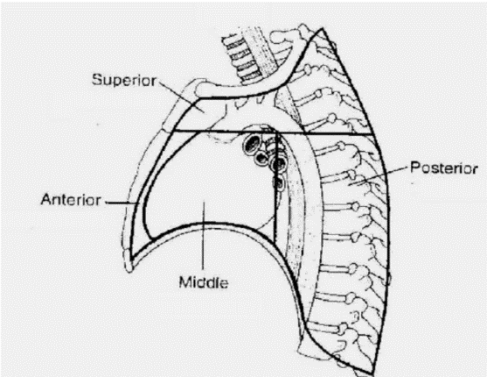


Reference: Department of Radiology Dankst University Poland. The tell-tale heart. Chest x-ray revisited in children with congenital heart disease. Pictorial essay. ECR 2018

RESOLVING THE MADDENING MYSTERY OF THE MEDIASTINUM – ITMIG

based on multi-detector CT with multi-planar reformatting

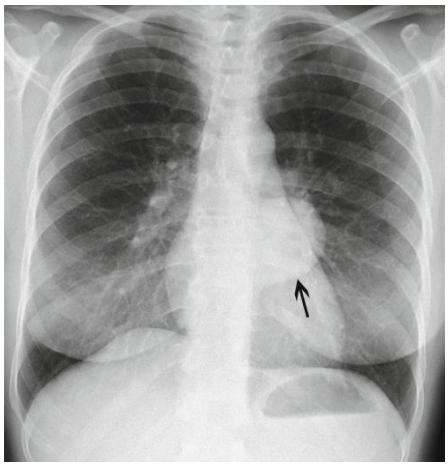
Old Classification of compartments based on lateral radiograph:
(Reference: Swanevelder CME 2007!)



- **Middle**: Heart and pericardium, tracheal bifurcation and main bronchi, the lung hila, phrenic nerve, thoracic duct, lymphatics and lymph nodes.
- **Anterior**: Between anterior pericardial reflection and the sternum
- **Posterior**: Between the posterior pericardial reflection and the vertebral column. Descending aorta, oesophagus, vagus nerve, sympathetic chain.
- **Anterosuperior**: Thymus, aortic arch and its branches, SVC, nodes. thoracic duct, azygos and hemiazygos veins and paravertebral lymph nodes.

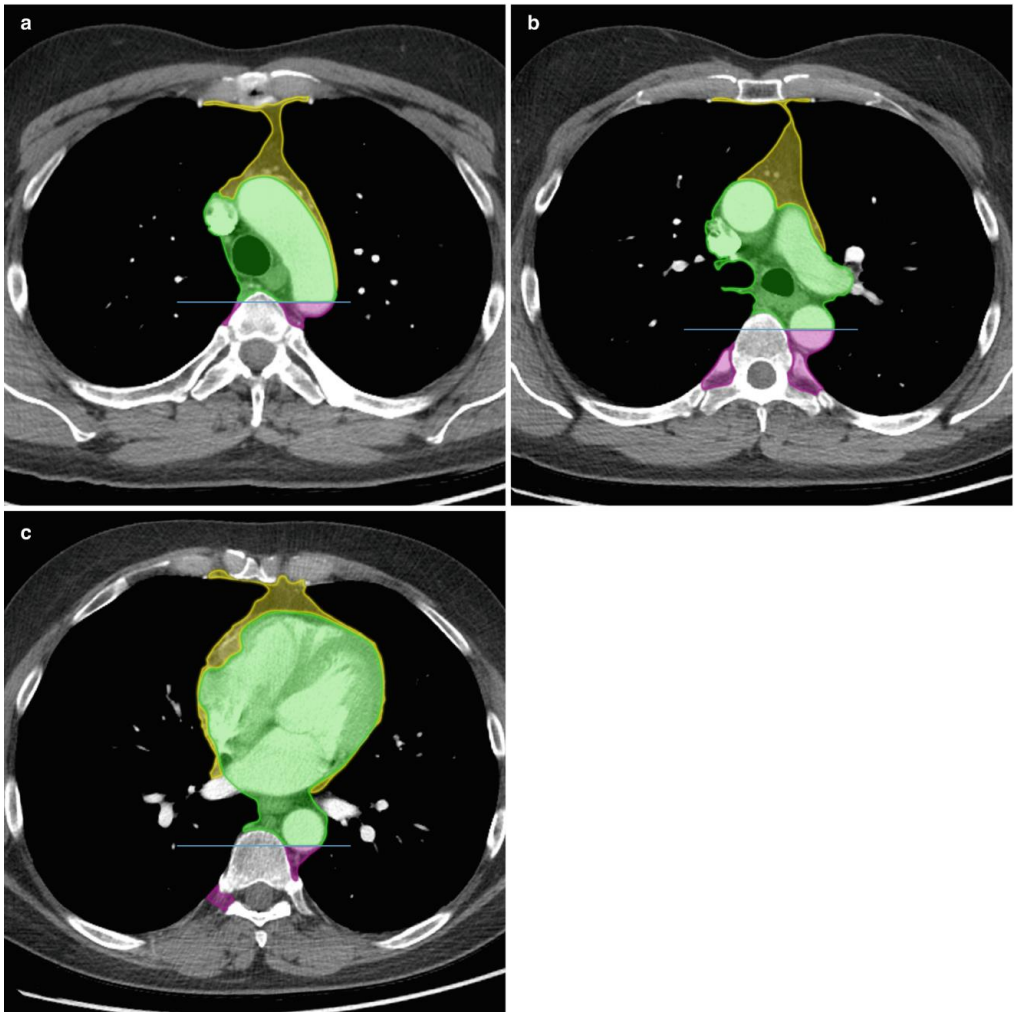
So, let's see how far our approach takes us on this CXR:

Is the cardiac silhouette maintained?
In which compartment is the lesion NOT located?
What is the location and likely diagnosis?



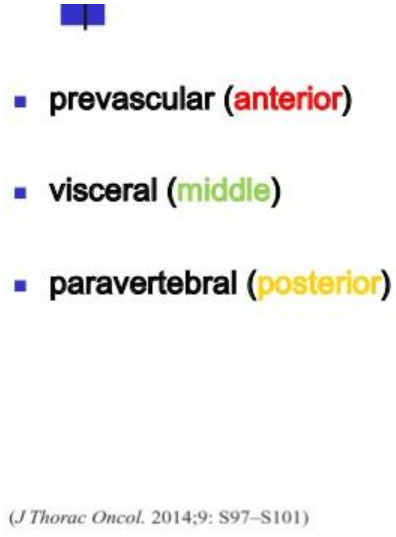
ITMIG (INTERNATIONAL THYMIC MALIGNANCY INTEREST GROUP) IS BASED ON CT (AXIAL IMAGING)

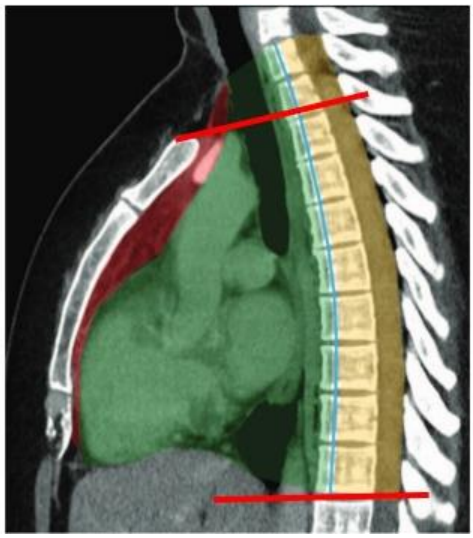
Axial CECT Chest

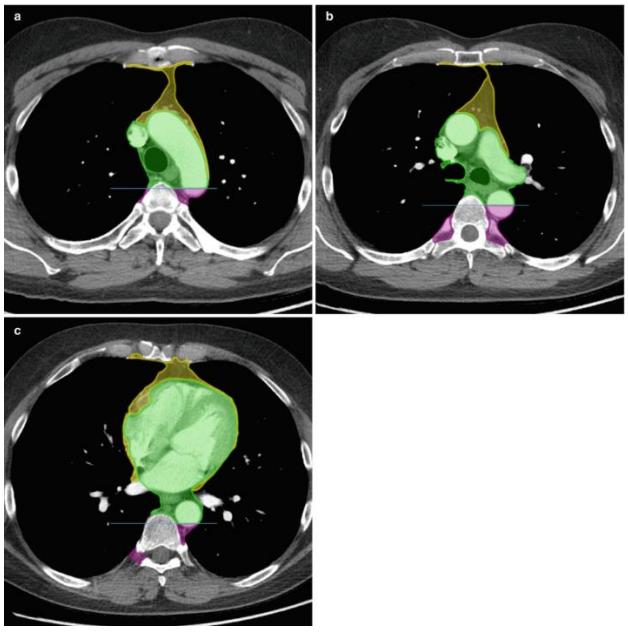


ITMIG mediastinal compartments on corresponding axial CT levels:

a) aortic arch
b) left pulmonary artery
c) heart







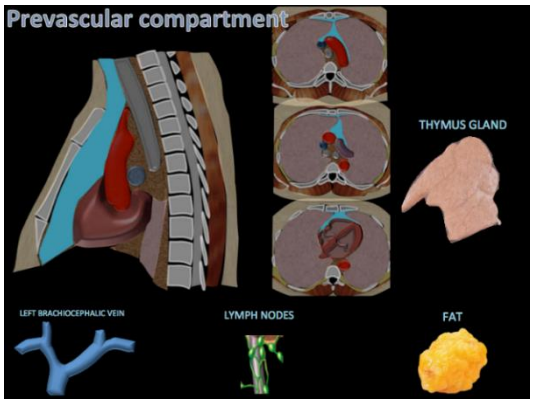
The pre-vascular compartment is anterior or peripheral to the pericardium
The paravertebral compartment is separated from the visceral compartment
by a line 1 cm posterior to the anterior vertebral body border

1. ANTERIOR / PREVASCULAR SPACE:

BORDERS

- Superiorly: Thoracic inlet.
- Inferiorly: Diaphragm.
- Anteriorly: Posterior border of sternum.
- Laterally: Parietal mediastinal pleura.
- Posteriorly: Anterior aspect of the pericardium as it wraps around the heart.

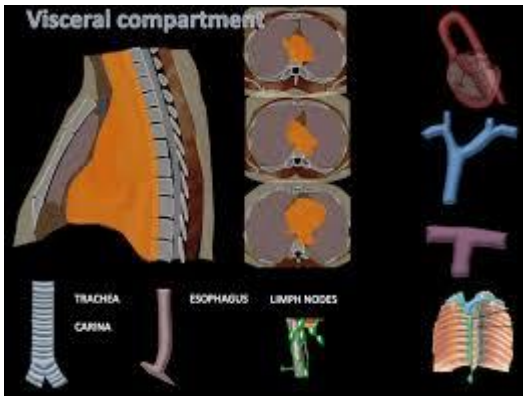
PATHOLOGY



- The four 'T's : Thymus / / Teratoma (Germ Cell Tumor)/Terrible Lymphoma / +_Thyroid
- Morgagni Hernia / Ectopic parathyroid adenoma (rare)

Most masses are thymic in origin (even lymphoma and teratoma)
Look for displacement of trachea (especially on lateral CXR)
Check for fat (black / HU -80) (Teratoma/ thymolipoma/ anterior fat pad/ fat in Morgagni)
Check for fluid/cysts (grey / HU 0-5) (Teratoma/ Pericardial cyst/ cystic thymoma)
Check for soft tissue enhancement (NB vascular! More likely in malignant lesions)
Check for calcification (white HU >100) (aneurysm/ thymoma/ teratoma) NOT lymphoma unless DXRT

2.MIDDLE / VISCERAL SPACE:



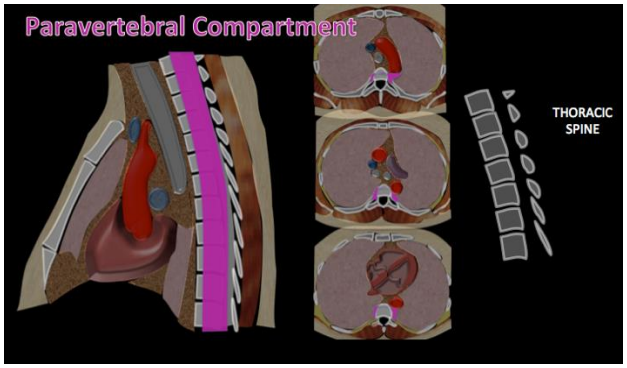
BORDERS

- Superiorly: Thoracic inlet.
- Inferiorly: Diaphragm.
- Anteriorly: Posterior boundaries of the prevascular compartment.
- Laterally: Parietal mediastinal pleura.
- Posteriorly: Vertical line 1 cm posterior to the anterior margin of the spine.

PATHOLOGY

Lymphadenopathy / Duplication cysts (bronchogenic and oesophageal) / Vascular eg aneurysms / Cardiac cardiac chamber enlargement /oesophageal /retrosternal thyroid goitre

3.PARAVERTEBRAL SPACE:



BORDERS

- Superiorly: Thoracic inlet.
- Inferiorly: Diaphragm.
- Anteriorly: Posterior boundaries of the visceral compartment.
- Laterally: Parietal mediastinal pleura.
- Posteriorly: Vertical line along the posterior margins of the chest wall at the lateral aspect of the transverse processes.

PATHOLOGY

Neurogenic neoplasm /discitis / osteomyelitis / bone tumours / haematoma / extramedullary haematopoiesis

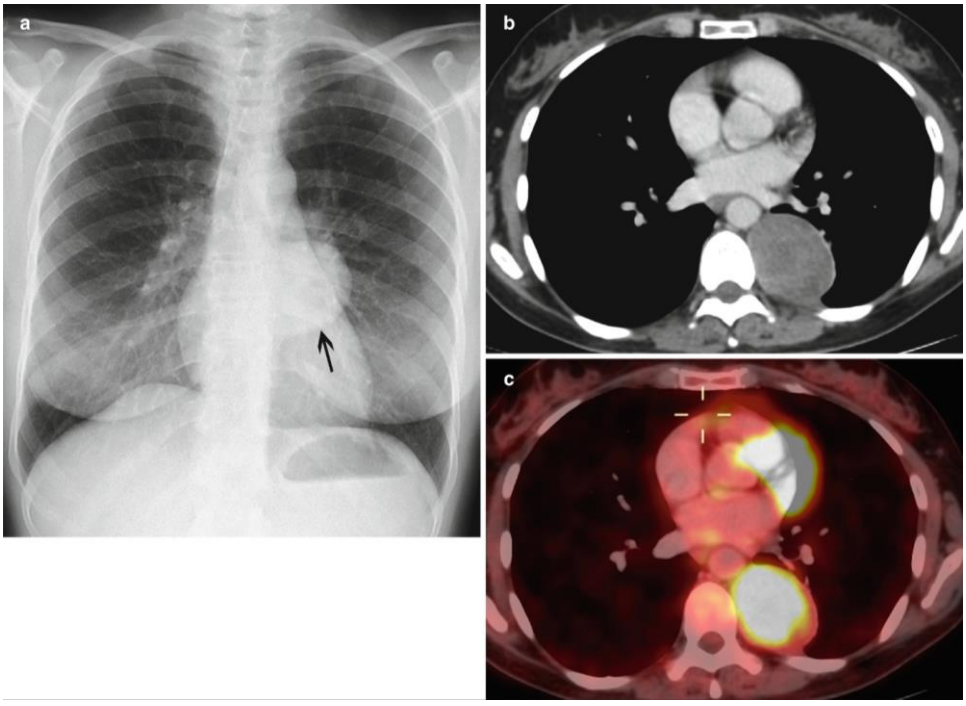
PEARLS

- Cysts may bleed (HU> water /CSF but should NEVER enhance.
- Necrotic nodes may appear cystic but will have peripheral enhancement.
- Calcification in nodes in old TB, sarcoidosis or silicosis and some nodal mets.
- NB Papillary thyroid CA may be largely cystic.
- Hyper-enhancing lesions may be nodes, retrosternal goitre or vascular e.g. enlarged azygous vein / arch anomaly.
- MRI offers better contrast resolution and assessment of water motion within tissue (DWI!!)
- CT offers better spatial resolution
- CECT distinguishes vascular from non-vascular (e.g. nodes from hilar vesssels)
- In imaging as in life, timing is everything (CTPA, systemic arterial, porto-venous phases)
- 'Windowing' important – know what tissue you want to look at e.g. lung vs vessel vs bone vs soft tissue
- PET/CT offers combined anatomical & functional aspects of tissue (sensitive but not specific)

So if we do a CECT we should be able to answer the following questions:

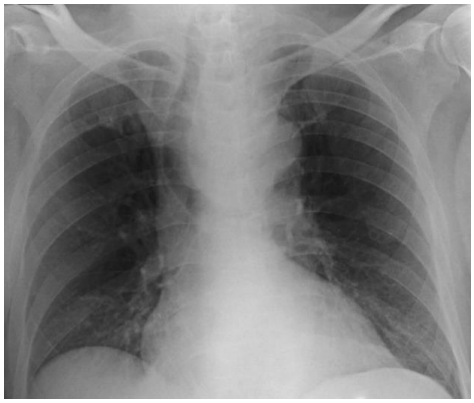
1. Is the lesion as dense as the vessels on CT?
2. Does it have fat or calcification?
3. Is it a simple or complex cyst or is it solid?

If we then superimpose PET on the CT, what further information do we get? Diagnosis?

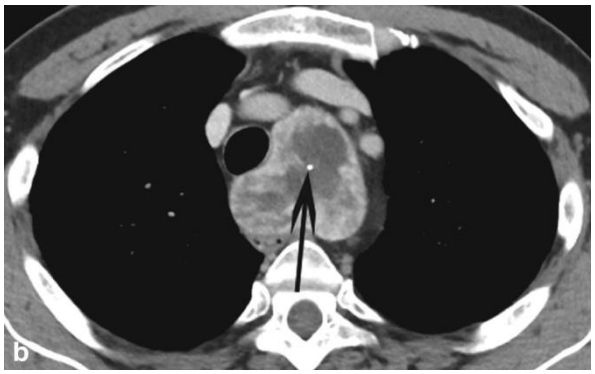


In the following example:

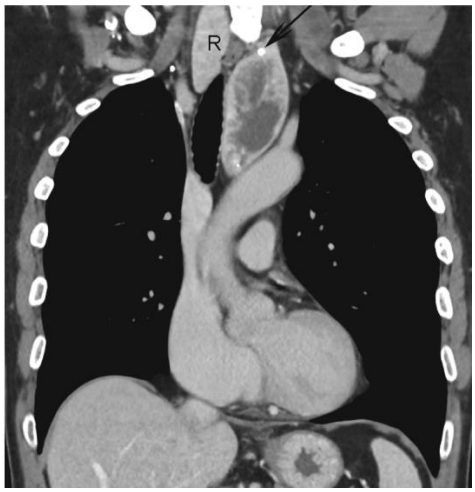
What structure is displaced?
Is the aortic arch silhouette lost?
In which space is the mass?
Is it calcified?
Does it contain fat?
Is it cystic or solid?

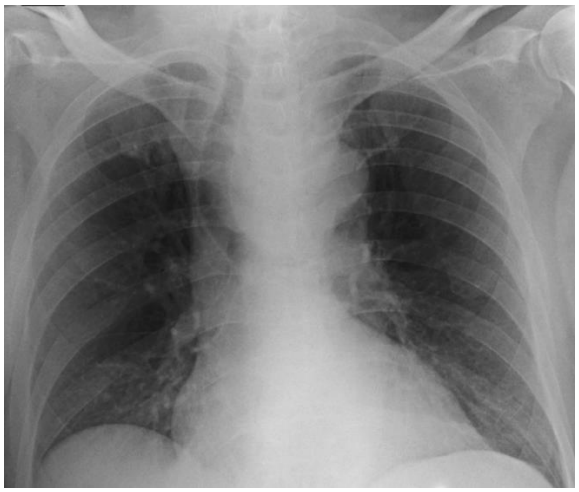


CT enables us to answer these questions more precisely:



Multiplanar reformatting now possible on CT. Compare this coronal recon with the original CXR:





Using the above approach to the chest radiograph and CT, we will spend the last 30 minutes of the session working through a number of examples of relatively common conditions that the anaesthetist / intensivist is likely to encounter.

References

1. Tapia et al [ITMIG classification of medistinal anatomy:exposure through augmented reality. ECR 2018]. http://dx.doi.org/10.1594/ecr2018/C-1392
2. Radiopaedia, Various Images. Editor: Frank Gaillard
3. Acute traumatic aortic injury. Radiology. State of the Art, Steenburg et al.2008
4. Interpreting the normal CXR : https://www.youtube.com/watch?v=L6bnD2wOEmg

Paper III Session
Arterial Blood Gas Analysis

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Introduction

Arterial blood gas analysis is part of the day to day work of anaesthetists in the peri-operative and ICU settings. The subject matter lends itself to practical, problem-based learning. This set of notes will aim to unpack the common disturbances encountered, additional aspects of arterial blood gases which may provide useful information to the clinician, as well as explore the different methods of blood gas analysis employed in clinical practice. These notes will explore some examples and problems. For the theory of arterial blood gas analysis the reader is referred to the list of references.

Basic Principles

Four principle acid-base disturbances exist:

1. Respiratory Acidosis
2. Respiratory Alkalosis
3. Metabolic Acidosis
4. Metabolic Alkalosis

An Acidaemia refers to a blood pH of < 7.35
An Alkalaemia refers to a blood pH of > 7.45

Where pH is defined as the concentration of hydrogen ions expressed as the negative log to base 10.

Blood gas analysis is based on the understanding of the Henderson Hasselbach equation, which describes the relationship between pH, pKa and the concentration of acid and base in the solution.

$$pH = pK_a + \log \frac{base}{acid}$$

In this instance the equation is represented as:

$$pH = 6.1 + \log \frac{[HCO_3^-]}{0.03\ pCO_2}$$

Where: 6.1 is the pKa of the bicarbonate buffer system

Interpreting the ABG

Blood gas analysers only measure pH, pO_2 and pCO_2, All other variables are calculated, including **bicarbonate**. Thus, the bicarbonate value is dependent on the pH and pCO_2 and will as such be affected in both metabolic and respiratory disturbances. This realisation lead to the search for a more robust parameter for the interpretation of blood gas disturbances.

Standard bicarbonate, introduced in 1957, is defined as the bicarbonate concentration under standard conditions: pCO_2 = 40 mmHg (5.3 kPa), temperature of 37C°, and haemoglobin being fully saturated with oxygen. The standardization to normal pCO_2 eliminates any respiratory component to the disturbance and makes standard bicarbonate useful in the interpretation of metabolic disturbances.

Base excess is the quantity of acid or alkali required to return the plasma in-vitro to a normal pH under standard conditions (these being pCO_2 and temperature).

Standard base excess is the base excess value calculated for anaemic blood (Hb = 5 g/dl) on the principle that this closely represents the behaviour of the whole human being. The method predicts the quantity of acid or alkali required to return the plasma in-vivo to a normal pH under standard conditions. Standard base excess is the best measure of a metabolic disturbance in clinical practice.

Whilst the above are useful measures to determine the presence of an acid base disturbance, they offer no insight to the cause of the disturbance. Let's look at an example to further explain possible causes of an abnormal ABG.

Example 1 – Interpreting a metabolic disturbance

A 23 year-old woman was found unconscious at home. She is currently in the emergency department on a 60% oxygen facemask, breathing spontaneously. You have been asked to assess this patient as a candidate for ICU. Her arterial blood gas and blood biochemistry follows. Give a full account of the results.

FiO_2:	0.6	Na:	140 mmol/L
pH:	7.0	K:	5.7 mmol/L
pCO_2:	1.7 kPa (13 mmHg)	Cl:	105 mmol/L
pO_2:	20 kPa (150 mmHg)	Creatinine:	80 µmol/L
HCO_3^-:	5 mmol/L	Urea:	4.8 mmol/L
SaO_2:	97%	Glucose:	8 mmol/L
Lactate:	7.8 mmol/L	Measured osmolality: 340 mOsm/L	

1. Start with the assessment of pH, pCO_2 and SBE. Interpreting a metabolic disturbance is best done through the inspection of SBE, as explained earlier.

   In the example above, the very low pH indicates an acidaemia. Inspection of the BE reveals that this is metabolic in nature. The low pCO_2 might indicate an attempt at compensation (more on this later!)

2. It is then important to note the ANION GAP – Is this high or normal?

   The Anion Gap is calculated as: $(Na^+ + K^+) – (Cl^- + HCO_3^-)$. A normal anion gap is 12 ± 4mEq/L.

   A normal anion gap metabolic acidosis is most likely attributable to a disturbance of chloride concentration.

   The most common causes of a HIGH anion gap metabolic acidosis are:

   - **C -** Carbon monoxide, Cyanide
   - **A -** Aminoglycosides
   - **T -** Toluene (glue sniffing)
   - **M -** Methanol
   - **U -** Uraemia
   - **D -** Diabetic ketoacidosis
   - **P -** Paracetamol
   - **I -** Iron, Isoniazid, Inborn errors of metabolism
   - **L -** Lactic acidosis
   - **E -** Ethanol, ethylene glycol
   - **S -** Salicylates

   In the example provided the Anion Gap is:
   (140 + 5.7) – (105 + 5)
   = 35.7

Thus, it is a HIGH AG metabolic acidosis, and the list of causes above can be consulted. This patient is unlikely to be in DKA (Gluc 8). Potential poisoning should be considered.

3. The Stewart approach is based on the principals of electroneutrality, dissociation and conservation of mass. It assesses the Strong Ion Difference (SID) and Total Weak Acids (A_{TOT}) to further describe the acid base disturbance.

SID is the difference between the sums of concentrations of the strong cations and strong anions:
[SID] = [Na^+] + [K^+] + [Ca^{2+}] + [Mg^{2+}] - [Cl^-] - [Other Strong Anions]

It is important to note that bicarbonate is NOT a strong ion. A normal SID is ± 40 and a change in SID usually equates numerically to the changed in SBE. Lactate is a strong ion and should be considered in the above equation.

[SID] can be changed by two principal methods:

1) Concentration:

Dehydration or over-hydration alters the concentration of the strong ions and therefore increases, or decreases, any difference. The body's normal state is on the alkaline side of neutral. Therefore, dehydration concentrates the alkalinity (contraction alkalosis) and increases [SID]; whereas, overhydration dilutes this alkaline state towards neutral (dilutional acidosis) and decreases [SID].

2) Strong Ion Changes:

If the sodium concentration is normal, alterations in the concentration of other strong ions will affect [SID]: The only strong ion capable of sufficient change is chloride (potassium, calcium and magnesium do not change significantly). An increased Cl^- concentration causes an acidosis and a decreased [SID] – hyperchloraemic acidosis. Because the chloride ions are measured, the anion gap will be normal.

By contrast, if the body accumulates one of the organic acids, e.g. lactate, formate, ketoacids, then the metabolic acidosis is characterized by a normal chloride concentration and an abnormal anion gap because of the presence of the "unmeasured" organic acid.

[ATOT] is the total plasma concentration of the weak non-volatile acids, inorganic phosphate, serum proteins, and albumin.

[ATOT] = [PiTOT] + [PrTOT] + albumin

Proteins provide a significant source of ionisable substrate that is useful in the buffering of acid-base disturbances. A low albumin plays an alkalinizing role from an acid-base perspective.

In the example above, the SID can be calculated as (Na^+ + K^+) – (Cl^- + Lac), giving a result of 32.9. As chloride is normal, the elevated lactate is contributing to the decrease in SID and is thus a significant component of the metabolic disturbance observed.

Albumin is not provided and therefore the contribution of ATOT to the metabolic disturbance cannot be assessed.

4. When provided with a measured osmolality, it is very important to calculate the osmolar gap. The presence of additional osmoles is commonly encountered in some poisonings, specifically the alcohols methanol, ethanol and ethylene glycol. A normal osmolar gap is <10.

Osmolality is calculated as: 2Na + Urea + Glucose
In the above example the calculated osmolality is 292.8
The Osmolar Gap is thus elevated at 47.2.

The above example is best interpreted as being a high anion gap, high osmolar gap metabolic acidosis, likely due to a poisoning with an organic alcohol, with a contributing hyperlactataemia. There is partial respiratory compensation present.

Example 2 – Interpreting a respiratory disturbance

A 64-year-old female patient presents for transurethral fulguration treatment for her recurring bladder carcinoma. She has a poor exercise tolerance for the last 2 years. She was previously a heavy smoker with a 30 pack-year history, but she has not smoked for the past 5 years. She is on no treatment for any medical conditions, is thin and her cardiovascular examination demonstrates a loud second heart sound and a parasternal heave. Her ABG shows:

pH:	7.30	Ca:	1.07 mmol/L
pCO_2:	12.8 kPa (96mmHg)	Lactate:	0.8 mmol/L
pO_2:	8.9 kPa (66.7mmHg)	HCT:	51%
Na:	135 mmol/L	HCO_3^-:	53 mmol/L
K:	4.1 mmol/L	BE:	27.4
Gluc:	11 mmol/L	Hb:	15.7 g/dL

What is your overall interpretation of the blood gas?

The effects of changes of pCO_2 are well understood and produce the expected alterations in $[H^+]$: $CO_2 + H_2O <—> H_2CO_3 <—> HCO_3^- + H^+$

Thus, from the above equation, an increase in pCO_2 will produce an increase in H^+ concentration, reflected as an acidaemia.

From the above it is clear that the patient has an elevated pCO_2, however the pH remains near normal. The BE and bicarbonate are elevated, indicating a degree of chronic renal compensation. The AG cannot be calculated as Cl is not provided, but is likely to be normal. The patient is hypoxic with an elevated haematocrit, indicating chronicity.

This ABG displays a partially compensated respiratory acidosis, with hypoxaemia and polycythaemia, likely due to underlying lung disease and cor pulmonale from longstanding smoking.

Compensation

From the above two examples it is apparent that the concept of compensation is important in the interpretation of the ABG. Compensation for acid-base disturbances is never complete from a mathematical perspective. In other words the pH can never be brought back to 7.4 by physiologic means. Compensation may be complete in that physiology has done all it can to offset the disturbance. At best complete physiologic compensation will lie roughly halfway between full mathematical compensation, and no compensation.

Whilst we know full compensation is not possible, 6 bicarbonate based rules exist as a rough guide for the degree of compensation which can be expected for any given acid base disturbance.

These rules are:

1. **The 1 for 10 Rule for Acute Respiratory Acidosis**
   The $[HCO_3]$ will increase by 1 mmol/l for every 10 mmHg elevation in pCO_2 above 40 mmHg.
   Expected $[HCO_3] = 24 + \{ (\text{Actual } pCO_2 - 40) / 10 \}$

2. **The 4 for 10 Rule for Chronic Respiratory Acidosis**
   The $[HCO_3]$ will increase by 4 mmol/l for every 10 mmHg elevation in pCO_2 above 40 mmHg.
   Expected $[HCO_3] = 24 + 4 \{ (\text{Actual } pCO_2 - 40) / 10 \}$

3. **The 2 for 10 Rule for Acute Respiratory Alkalosis**
   The $[HCO_3]$ will decrease by 2 mmol/l for every 10 mmHg decrease in pCO_2 below 40 mmHg.
   Expected $[HCO_3] = 24 - 2 \{ (40 - \text{Actual } pCO_2) / 10 \}$

4. **The 5 for 10 Rule for a Chronic Respiratory Alkalosis**
   The $[HCO_3]$ will decrease by 5 mmol/l for every 10 mmHg decrease in pCO_2 below 40 mmHg.
   Expected $[HCO_3] = 24 - 5 \{ (40 - \text{Actual } pCO_2) / 10 \}$ (range: +/- 2)

5. **The One & a Half plus 8 Rule - for a Metabolic Acidosis**
   The expected pCO_2 (in mmHg) is calculated from the following formula:
   Expected $pCO_2 = 1.5 \times [HCO_3] + 8$ (range: +/- 2)

6. **The Point Seven plus Twenty Rule - for a Metabolic Alkalosis**
   The expected pCO_2 (in mmHg) is calculated from the following formula:
   Expected $pCO_2 = 0.7 [HCO_3] + 20$ (range: +/- 5)

Conclusion

ABG interpretation is easy when approached in a systematic manner.

1. Identify an acidaemia or alkalaemia
2. Examine the pH, pCO_2 and SBE to determine whether the disturbance is metabolic or respiratory in nature
3. For metabolic disturbances calculate the AG, SID and ATOT for further insight to the cause
4. Apply the rules of compensation – remember full compensation is never possible

References

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2. Sirker AA, Rhodes A, Grounds RM, Bennet ED. Acid-base physiology: The ‘traditional’ and the ‘modern’ methods. Anaesthesia 2002: (57) 348-356.

Evidence Based Medicine

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This Refresher Course summarises the key points from the Evidence-based Medicine book of Guyatt and Colleagues.[1]

1. What is evidence-based medicine?

The 3 fundamental principles of evidence-based medicine

- An awareness of the best available evidence
- The ability to decide the trustworthiness of the evidence
- Consideration of the values and preferences for the patient

2. Evidence-based medicine and the theory of knowledge.

Epistemological principles of evidence-based medicine

- Examine the totality of the evidence
- Understand that not all evidence is equal
- Acknowledge that evidence is necessary but not sufficient. It must include values and preferences in decision making

3. What is the question?

A clinician must be able to;

- Distinguish between ‘background’ versus ‘foreground’ questions

Understand the concepts of ‘aim’, ‘objectives’, ‘hypotheses’ and ‘outcomes’

- ‘Aim’ is a broad summary statement of purpose
    - It is the ‘WHAT?’
    - The aim is to answer the research question
- ‘Objectives’ are the operationalised steps describing how the aim(s) will be reached
    - It is ‘HOW?’
    - It is how we “quantify” or “determine”
- ‘Hypotheses’ are testable opposing statements
- ‘Outcomes’
    - Usually one primary outcome for which the study is powered
    - Secondary outcomes are essentially descriptive or explorative i.e. hypothesis generating for future research

Frame a question in the ‘PICO’ format

- Patients or Population
- Intervention(s) or Exposure(s)

- Comparator
- Outcome

Understand that there are five fundamental types of clinical questions (according to study design)

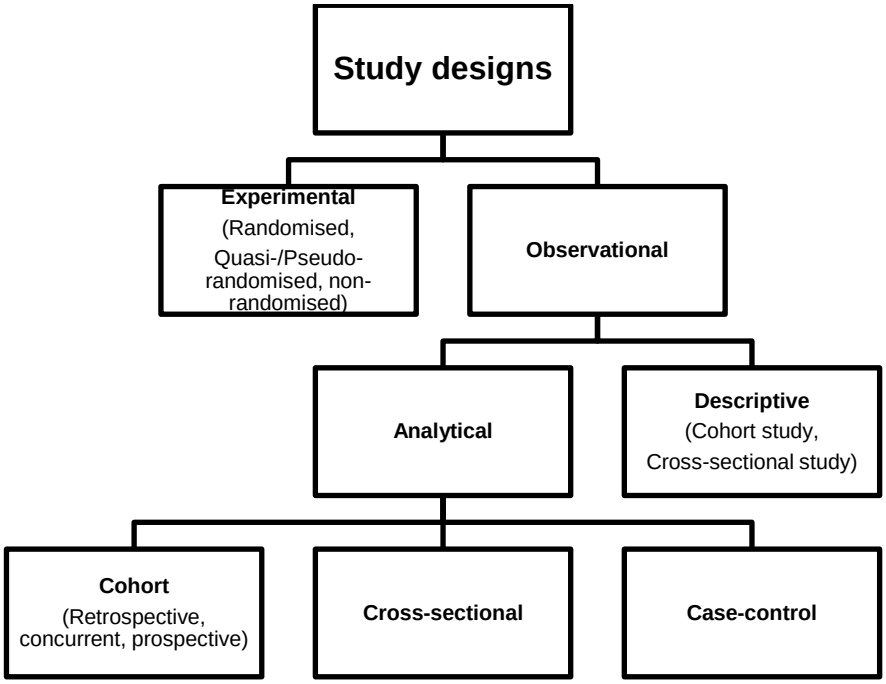
- Therapy
- Harm
- Differential diagnosis
- Diagnosis
- Prognosis

4. Finding current best evidence.

Make the librarian you friend. They have tremendous skills.

Understand the hierarchy of evidence

Summary of study designs



Six basic study designs

Ecological Study	Observational	Retrospective	Occurrence and associations in groups
Case Study / Case Series	Observational	(Usually) Retrospective	Descriptive
Cross-Sectional Study	Observational	Snap Shot*	Descriptive, Analytical, Diagnostic
Case-Control Study	Observational	Retrospective	Analytical (cannot describe occurrence)
Cohort Study	Observational	Longitudinal (Retrospective, concurent, prospective)	Descriptive and Analytical
Randomised Control Trial	Experimental	Prospective	Interventional and Analytical

* Loss of temporal precedence. The exposure and outcome of interest is measured concurrently. Also true for ecological studies.

Bookmarking web resources

To make finding the current best evidence easier, bookmark websites according to levels of evidence as follows;

- Summaries and guidelines
  - https://www.evidence.nhs.uk/
  - https://g-i-n.net/library/international-guidelines-library
  - https://www.ahrq.gov/gam/index.html

    - https://www.uptodate.com/contents/search
    - https://bestpractice.bmj.com/info/
- Pre-appraised resources
    - https://hiru.mcmaster.ca/hiru/HIRU_McMaster_PLUS_Projects.aspx
    - https://www.nyam.org/library/collections-and-resources/databases/
    - https://www.cochrane.org/
    - https://www.crd.york.ac.uk/CRDWeb/
    - https://www.essentialevidenceplus.com/content/poems
- Non pre-appraised resources
    - https://pubmed.ncbi.nlm.nih.gov/
    - https://www.embase.com/login
- Federated resources (these cross all the above resource groups)
    - https://www.accessss.org/
    - https://www.tripdatabase.com/
    - https://hiru.mcmaster.ca/hiru/HIRU_Hedges_MEDLINE_Strategies.aspx
    - https://www.epistemonikos.org/

My personal favourite resources

- Best federated resource: https://www.accessss.org/
- Pubmed
- The HIRU Hedges Filters; https://hiru.mcmaster.ca/hiru/HIRU_Hedges_home.aspx
    - This allows for setting up personalised filters for PubMed
    - This is useful for limiting searches which are prohibitively large

Learn how to do a decent literature search

- Learn how to use MeSH (Medical Subject Headings) in PubMed
    - https://www.ncbi.nlm.nih.gov/
- Learn how to save a search on PubMed
- Learn how to import search ‘hits’ into Endnote[2]
- Learn how to export ‘hits’ from Endnote into Excel, so can screen ‘hits’ for inclusion/ exclusion in review. There are good youtube videos on doing this.

5. Why studies mislead: bias and random error.

How can a study of an intervention be biased?

- Intervention and control groups may be different at the start
- Intervention and control groups become different as the study progresses
- Intervention and control groups differ, independent of treatment at the end of the study

How to reduce bias in studies of therapy and harm

Source of bias	Therapy: strategy to reduce bias	Harm: strategy to reduce bias
Intervention and control groups may be different at the start		
Treatment and control patients differ in prognosis	Randomisation	Statistical adjustment of prognostic factors
	Randomisation with stratification	Matching
Intervention and control groups become different as the study progresses		
Placebo effects	Blinding of patients	Outcomes associated with less subjective effects e.g. mortalty
Cointervention	Blinding of caregivers	Document treatment differences and statistically adjust
Bias in assessment	Blinding of assessors of outcomes	Document treatment and statistically adjust
Intervention and control groups differ, independent of treatment at the end of the study		
Loss to follow up	Ensure complete follow up	Ensure complete follow up
Stop study early because of large effect	Complete study as initially planned	Not applicable
Omitting patients who did not receive assigned treatment	Include all patients in the arm to which they were randomised	Not applicable

Top tip: Learn how to calculate confidence intervals and plug into a simple spreadsheet

6. Confidence intervals: Was the single study or the meta-analysis large enough?

Broad concept of statistical versus clinical importance

- Concept p-value essentially meaningless for clinical significance
- Need to understand two things to determine clinical significance;
    - Need to define what constitutes clinically significance
        - i.e. need to define a clinically significant outcome which would change practice e.g. a 20% relative risk reduction in cardiovascular events
    - Need to determine the fragility of the result i.e. the fragility of the p-value

Concept of fragility[3]

- The fragility index is a measure of the robustness (or fragility) of the results of a clinical trial. The fragility index is a number indicating how many patients would be required to convert a trial from being statistically significant to not significant ($p \geq 0.05$). The larger the fragility index the better (more robust) a trial's data are.
- Examples of fragility in perioperative medicine and critical care studies/ trials[4 5]
- Website to conduct fragility analyses for studies: https://clincalc.com/Stats/FragilityIndex.aspx

Useful statistical website: http://vassarstats.net/

7. Therapy (randomized trials)

How to assess an article about therapy

The 3 areas that one needs to evaluate

- How serious was the risk of bias?
  - Did the intervention and control groups start with the same prognosis
  - Were the patients randomised?
  - Was randomisation concealed?
  - Were patients in the study groups similar with respect to known prognostic factors>
  - Was prognostic balance maintained as the study progressed?
  - To what extent was the study blinded?
  - Were the groups prognostically balanced at the study's completion>
  - Was the follow up complete?
  - Were the patients analysed in the groups to which they were randomised?
  - Was the trial stopped early?

- What are the results?
  - How large was the treatment effect?
  - How precise was the estimate of the treatment effect?

- How can I apply the results to patient care?
  - Were the study patients similar to my patient?
  - Were all patient-important outcomes considered?
  - Are the likely treatment benefits worth the potential harm and costs?

Sample sizes

- Calculate if the sample size is adequate for the primary outcome.
- Useful websites for sample sizes
  - clincalc.com (use the post hoc function)
  - https://www.sealedenvelope.com/

8. Does treatment lower risks? Understanding the results.

Know how to set up a 2x2 table

2x2 Table

Exposure	**Outcome**	
	Yes	**No**
Yes	a	b
No	c	d

Definitions
Risk with exposure=a/(a+b)
Risk without exposure=c/(c+d)

Odds with exposure=a/b
Odds without exposure=c/d

Relative risk= a/(a+b)
---
c/(c+d)
Odds ratio= [a/b] / [c/d] = (a*d)/(c*b)

Absolute risk reduction (ARR) = c/(c+d) – a/(a+b)

Number needed to treat (NNT) = 100/(ARR expressed as a %)

- The importance of absolute risk reduction (ARR), which Guyatt calls risk difference (RD)
    - Higher ARR, lower NNT

Higher grade reference, on calculating CI for 2x2 table[6]

9. Composite end points

Determination of appropriate composite endpoints

Answer the following to ensure that it is appropriate to consider the composite end point

- Are the component end points of the composite end point of similar importance?
- Did the more and less important end points occur with similar frequency?
- Can one be confident that the component end points similar enough that one would expect similar relative risk reductions?
- Are the point estimates of the relative risk reductions similar, and are the confidence intervals sufficiently narrow?
- To the extent that one can answer yes to these questions, one can feel confident using the treatment effect on the combined end point as the basis for decision making.
- To the extent one answers no to these questions, one should look separately at the treatment effect on the component end points as the basis for decision making.

10. Misleading presentation of clinical trial results

How to avoid being misled by clinical trial results

- Read methods and results: bypass the discussion section
- Read the summary structured abstract published in evidence-based secondary publications (i.e. pre-appraised resources)
- Beware large effects in trials with only a few events
- Beware faulty comparators
- Beware small treatment effects and extrapolation to very low-risk patients
- Beware uneven emphasis on benefits and harms
- Wait for the overall results to emerge; do not rush

Reasons for being cautious in adopting new interventions

- Initial studies may be biased by inadequacies in concealment, blinding, loss to follow-up, or stopping early
- Initial studies are susceptible to reporting bias
- Initial studies are susceptible to dissemination bias; markedly positive studies ae likely to receive disproportionate attention
- Initial studies may overestimate effects by chance (particularly if effects are large and the number of events is small)
- There is substantial probability (20%) that serious adverse effects will emerge subsequently
- On rare occasions, research results will prove to have been fraudulent

Faulty comparators

- Comparison with placebo when effective agents are available
- Comparison with less effective agents when more effective comparators are available
- Comparison with too low a dose (or inadequate dose titration) of an otherwise effective comparator, leading to misleading claims of effectiveness

- Comparison with a too high (and thus toxic) dose (or inadequate dose titration) of an otherwise safe comparator, leading to misleading claims of lower toxicity

Strategies for making a treatment effect appear larger than it is

- Use relative rather than absolute risk; a 50% RRR may mean a decrease in risk from 1% to 0.5%
- Express risk during a long period; the reduction in risk from 1% to 0.5% may occur during 10 years
- For visual presentations, make sure the x-axis intersects the y-axis well above 0 if the x-axis intersects the y-axis at 60%, you can make an improvement from 70 to 75% appears as a 33% increase in survival
- Include a few high-risk patients in a trial of predominantly low-risk patients; even though most events occur in high-risk individuals, claim important benefits for a large number of low-risk patients in the general population
- Ignore the lower boundary of the confidence interval; when the lower boundary of the CI around the relative risk reduction approaches 0, declare significance and henceforth focus exclusively on the point estimate
- Focus on statistical significance; when a result achieves statistical significance but both relative and absolute effects are small; highlight the statistical significance and downplay or ignore the magnitude

11. Harm (Observational studies)

The 3 areas that one needs to evaluate for an article about harm

- How serious was the risk of bias?
    - In a cohort study, aside from the exposure of interest, did the exposed and control groups start and finish with the same risk for the outcome?
    - Were the patients similar for prognostic factors that are known to be associated with outcome (or did statistical adjustment address the imbalance)?
    - Were the circumstances and methods for detecting the outcome similar?
    - Was the follow up complete?
    - In case-control study, did the cases and the control group have the same risk for being exposed in the past?
    - Were cases and controls similar with respect to the indication or circumstances that would lead to exposure (or did statistical adjustment address the imbalance)?
    - Were the circumstances and methods for determining exposure similar for cases and controls?

- What are the results?
    - How strong is the association between exposure and outcome?
    - How precise was the estimate of risk?

- How can I apply the results to patient care?
    - Were the study patients similar to my patient?
    - Was follow up sufficiently long?
    - Is the exposure similar to what might occur in my patient?
    - What is the magnitude of the risk?
    - Are the any benefits that are known to be associated with the exposure?

12. Prognosis

The 3 areas that one needs to evaluate for an article about prognosis

- How serious is the risk of bias?
    - Was the sample of patients representative?
    - Were the patients classified in prognostically homogenous groups?
    - Was follow up sufficiently complete?
    - Were outcome criteria objective and unbiased?
- What are the results?
    - How likely are the outcomes over time?
    - How precise are the estimates of likelihood?
- How can I apply the results to patient care?
    - Were the study patients and their management similar to those in my practice?
    - Was follow-up sufficiently long?
    - Can I use the results in the management of patients in my practice?

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Single Best Answer (SBA) Practice Questions

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Domain 1: Fundamentals of anaesthesia and pain management

1.1 Regarding medical gas cylinders:

a. The pin index system ensures that cylinders do not require a seal between the cylinder valve outlet and the yoke.
b. On anaesthesia machines the size B cylinder is most commonly used as a reserve cylinder.
c. Nitrous oxide and carbon dioxide are stored as liquefied gases employing filling ratios.
d. An international colour code to identify gas cylinders was adopted globally in 1949.

1.2 During normal laminar airflow, resistance is dependent upon which characteristic of oxygen?

a. Density
b. Viscosity
c. Molecular weight
d. Vapour pressure

1.3 After an otherwise uneventful surgical procedure under general anaesthesia, a patient is noted to have a burn at the site of the plate electrode. What is the most likely cause of this burn?

a. Inadequate application of the plate electrode.
b. Prolonged usage of high voltage cutting diathermy.
c. Using diathermy in the presence of saline wash.
d. Increased current density due to the channelling effect.

1.4 A patient scheduled for an elective lymph node biopsy has a family history of haemophilia. Which would be the most appropriate screening tests for haemophilia in this patient?

a. Activated clotting time and thrombin time.
b. Activated partial thromboplastin time and prothrombin time.
c. Prothrombin time and fibrinogen levels
d. Thrombin time and bleeding time.

1.5 A patient under general anaesthesia displays the following changes on electrocardiogram: prolonged PR interval, flattened T wave and a J wave. What is the most likely cause?

a. Hypokalaemia.
b. Hypocalcaemia.
c. Hypothermia.
d. Hypotension.

1.6 Which substance may increase the effect of warfarin?

a. Co-enzyme Q10
b. Garlic
c. Milk thistle
d. St John's wort

1.7 Withholding blood products in a bleeding Jehovah's Witness is ethically justified by which principle?

a. Fidelity
b. Non-maleficence
c. Patient autonomy
d. Social justice

1.8 Accurate end-tidal oxygen concentration measurement is possible using which one of the following?

a. Clark electrode
b. electro-galvanic fuel cell
c. infrared spectroscopy
d. paramagnetic cell

1.9 The first step during unanticipated difficult tracheal intubation is:

a. Call for help
b. External laryngeal manipulation
c. Maintain oxygenation
d. Optimise head position

1.10 The most sensitive electrode to detect myocardial ischaemia during perioperative ECG is:

a. aVL
b. II
c. V1
d. V4

Domain 2: Anaesthesia for major and trauma surgery

(Q2.1 – Q2.2)
A 27-year-old male arrives to the operating room with laryngo-tracheal injuries stemming from a motorcycle collision. He presents with hoarseness and dyspnea while sitting but is unable to lie flat due to worsening dyspnea. He is unable to swallow and is drooling/spitting moderately bloodstained sputum. His anterior neck is diffusely swollen and exquisitely tender with notable subcutaneous emphysema. Oxygen saturation is 100% with supplemental oxygen via facemask. Review of imaging reveals a thyroid cartilage fracture horizontally and crossing the midline.

2.1 The most appropriate approach to his airway management is:

a. Tracheostomy
b. Laryngeal mask airway
c. Nasotracheal intubation
d. Cricothyroidotomy

2.2 His injury would be consistent with trauma to this zone of his neck:

a. Zone I
b. Zone II
c. Zone III
d. Zone IV

2.3 In a three-year-old patient with hot water burns, the best assessment of total body surface area is via:

a. Lund-Brower burn diagram
b. Rule of 9’s
c. Palm size area
d. Parkland chart

2.4 The most important element of damage control resuscitation is to:

a. Aggressively target systolic blood pressures >110 mmHg
b. Limit the use of crystalloid with early use of blood and blood products
c. Delay giving tranexamic acid until after the initial resuscitation phase
d. Correct serum electrolytes, particularly calcium

2.5 A massive blood transfusion is defined by:

a. The loss of one blood volume over 48 hours
b. Blood loss at >150 ml/min
c. 20% blood volume loss in six hours
d. Any trauma patient requiring >4 units packed red cells within three hours

2.6 In flame burns, the most common cause of death within the first hour is due to:

a. Smoke inhalation and subsequent hypoxaemia
b. Shock due to capillary leak and dehydration
c. Overwhelming sepsis due to translocation of bacteria
d. Stroke secondary to venous thrombosis

2.7 During a right hemi-hepatectomy, the most important way to decrease blood loss is by:

a. Placing the patient head down
b. Increasing the PEEP
c. Maintaining the CVP at 10 cmH_2O
d. Conservative fluid therapy

2.8 A 65-year-old man is booked for a laparoscopic right hemi-colectomy for carcinoma in the hepatic flexure. He presented with a three-month history of increasing shortness of breath on exertion and occasional palpitations, despite previously being able to exercise strenuously. His haemoglobin is 7.6 g/dL with normal electrolytes and an ECG showing a sinus rhythm at a rate of 97 beats per minute with non-specific ST-T changes and no features suggestive of LVH. He has taken only 80 mg Aspirin daily for the last ten years, on the recommendation of his GP. The most useful evaluation of this patient's risk for post-operative cardiac complications is:

a. Pre-operative levels of cardiac biomarkers (BNP, Troponins)
b. Rest echocardiography
c. Premorbid Duke Activity Status Index (DASI)
d. Pharmacologic myocardial imaging stress testing

2.9 A 40-year-old woman with a three-month history of fatigue, intermittent difficulty in swallowing and nocturnal diplopia presents for a mediastinoscopy and biopsy. Computed Tomography reveals a mass in the anterior mediastinum with no abnormalities detected in her lung parenchyma and no compression of the heart, great vessels or tracheo-bronchial tree. She has a 10-pack year history of smoking. Perioperative considerations include:

a. Pre-operative echocardiography is mandatory
b. Antibodies against pre-synaptic Voltage Gated Calcium Channels are detected in her blood
c. Pulse oximetry and blood pressure monitoring should be placed on her left arm
d. Sugammadex is indicated for rocuronium induced neuromuscular blockade

2.10 A 62-year-old male patient is booked for excision of a carcinoid tumour of the lung. He presented with nausea and recurrent bronchospasm. Urine 5-HIAA was elevated. Which of the following statements is most accurate this scenario?

a. The symptoms described are likely caused by the secretion of histamine
b. 10% of carcinoid tumours produce mediators, and these patients benefit from perioperative treatment with Octreotide
c. Intraoperative insulin infusion will be useful in this patient
d. Sympathectomy caused by neuraxial anaesthesia may precipitate a carcinoid crisis and should therefore be avoided

Domain 3: Obstetric anaesthesia and analgesia

3.1 Compared to Oxytocin, Carbetocin:

a. Causes more nausea and vomiting
b. Has no significant difference in estimated blood loss, need for transfusion or drop in haemoglobin
c. Should be used with caution in epileptics
d. Causes less pronounced hypotension

3.2 Regarding the inadvertent injection of Tranexamic acid during spinal anaesthesia for caesarean section:

a. Toxic effects of spinal tranexamic acid are reduced by reducing the CSF concentration by concomitant or subsequent administration of local anaesthetic
b. Massive sympathetic stimulation frequently seen leads to ventricular fibrillation.
c. The immediate backache and lower limb pain are due to the direct local effect on the dorsal horn of the spinal cord.
d. Intrathecal TXA is a potent neurotoxin and neurological sequelae dominate the clinical presentation, usually with refractory seizures.

3.3 Regarding postoperative pain control after caesarean section:

a. Dexmedetomidine showed reduced 24-h pain scores and rescue analgesia requirements
b. Posterior Quadratus Lumborum block and NSAIDs are particularly effective in the treatment of the visceral pain
c. TAP blocks and parenteral morphine had similar pain scores 24 hrs post-operatively
d. The opioid-sparing effect of intravenous lidocaine is well-established in open and laparoscopic abdominal surgery, as well as in caesarean delivery

3.4 The use of Tranexamic acid for the prevention of PPH during caesarean section:

a. The dose should be adjusted in the obese patient
b. A repeat dose can be given if bleeding continues within 30 min of the initial dose or when bleeding restarts within 24 hours of the first dose.
c. Consideration should be given to storing TXA out of theatre, provided that the drug will be available immediately when requested to prevent drug errors
d. The intravenous lethal dose of tranexamic acid is approximately 0.5–1.0 g/kg body weight

3.5 Intrathecal opioids for pain control after caesarean section:

a. 3 mg epidural morphine in labour epidural analgesia prior to surgery provides better analgesia than parenteral opioids and has similar analgesic efficacy to intrathecal morphine.
b. Ultra-low dose intrathecal morphine (≤50 μg) and epidural morphine (≤1 mg) may provide safer alternatives in otherwise healthy women in resource limited settings
c. Intrathecal opioids are currently recommended as the gold standard for postoperative analgesia following spinal anaesthesia
d. Cognitive modalities such as music therapy lower pain scores and reduce opioid consumption in the immediate postoperative period

3.6 Unintentional subdural placement of an epidural catheter for labour analgesia classically results in:

a. A negative aspiration test and a positive test dose, resulting in the rapid onset of typical spinal blockade
b. A delayed onset of an unexpected high block with moderate to severe hypotension, weakness of the upper limbs, and respiratory difficulty
c. A negative aspiration test and a negative test dose, followed by total spinal blockade on activating the “epidural”
d. Permanent neurologic sequelae

3.7 Pruritus caused by epidural morphine administration for post-caesarean analgesia:

a. Is commonest over the chest and shoulders
b. Can be prevented by low dose propofol infusion and 5HT3 antagonists
c. Is genetically determined and independent of morphine dose
d. Occurs more commonly in parturients than in non-obstetric surgical patients

3.8 Regarding maternal morbid obesity:

a. Aorto-caval compression syndrome is chiefly due to fetal macrosomia.
b. Low molecular weight heparin for post-caesarean thromboprophylaxis is best dosed according to ideal rather than lean body weight.
c. Epidural catheter dislodgement occurs more frequently, due to the sliding of the skin over subcutaneous tissue.
d. The local anaesthetic dose for caesarean single-shot spinal should be reduced to avoid high spinal blockade.

3.9 In a patient undergoing caesarean hysterectomy for placenta accreta, with expected major haemorrhage:

a. Fibrinogen levels should be maintained above 4 g/L during ongoing haemorrhage.
b. Prophylactic placement of balloon catheters in the internal iliac arteries reliably reduces blood loss with minor complications reported.
c. Combined spinal-epidural anaesthesia is the preferred anaesthetic technique in a patient with a known difficult airway.
d. Autologous cell-saver technology is a safe option with current filtering techniques available.

3.10 The use of spinal anaesthesia for caesarean delivery at 28/40 gestation in *severe* early-onset preeclampsia:

a. Mandates the administration of a 10 mL/kg colloid preload.
b. Is contraindicated when abruptio placentae is suspected.
c. May provide inadequate anaesthesia if a standard spinal local anaesthetic dose is given.
d. Induces hypotension with the same incidence as in normotensive patients.

Domain 4: Anaesthesia for cardiac, thoracic and vascular surgery

4.1 A 75-year-old woman with a history of congestive cardiac failure and ischaemic heart disease is currently stable on medication and undergoes a right total hip replacement after a hip fracture. She has a high risk of myocardial injury after non-cardiac surgery (MINS). Which postoperative test will you do to detect MINS?

a. Postoperative electrocardiogram
b. Postoperative troponin screening
c. Postoperative NT-proBNP screening
d. Postoperative stress testing

4.2 A 31-year-old female patient presents for a thymectomy due to myasthenia gravis. In terms of the use of muscle relaxants during anaesthesia, these patients tend to:

a. Be resistant to depolarizing muscle relaxants and sensitive to non-depolarising muscle relaxants.
b. Be resistant to non-depolarising muscle relaxants and sensitive to depolarizing muscle relaxants.
c. Be resistant to opioid analgesics.
d. Be resistant to volatile anaesthetic agents.

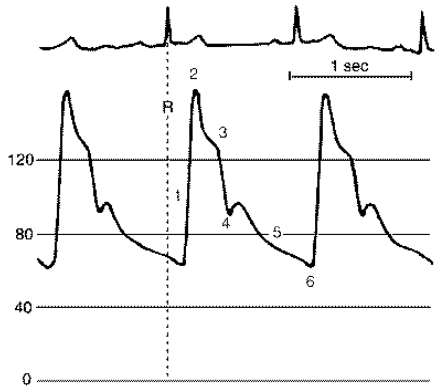
4.3 A 33-year-old presents with dyspnoea and he also gets syncope and angina. What are you expecting to hear on auscultation?

a. diastolic murmur over the apex radiating to the axilla
b. systolic murmur over the apex radiating to the axilla
c. diastolic murmur over the aortic area radiating to the neck
d. systolic murmur over the aortic area radiating to the neck

4.4 Patients with hypertrophic obstructive cardiomyopathy have:

a. Pericardial effusion
b. Septal hypertrophy
c. Pulmonary artery stenosis
d. Ventricular septal defect

4.5 You have decided to place a radial arterial line for intraoperative monitoring, and you see the following trace. Event number 4 is the dicrotic notch. This shows:



a. Peripheral vascular resistance
b. Opening of the aortic valve
c. Closure of the aortic valve
d. Stroke volume output

4.6 A patient for coronary bypass surgery has a hypokinetic inferior wall of the left ventricle. The most likely artery that is under supplying the area is:

a. Circumflex artery
b. Left coronary artery
c. Obtuse marginal 3
d. Right coronary artery

4.7 In a patient with bilateral broncho-pleural fistula, following multiple stab wounds, the best anaesthesia/airway option is:

a. Intermittent positive pressure ventilation and double lumen tube
b. Intermittent positive pressure ventilation high tidal volumes
c. Spontaneous ventilation single lumen tube and bronchial blocker
d. Spontaneous ventilation, supraglottic device

4.8 Following the release of the supra-celiac clamp in a patient that had an abdominal aorta aneurysm repair, the blood pressure drops considerably. The most probable cause is:

a. Active bleeding
b. Reperfusion injury
c. Sepsis
d. Spinal cord hypoperfusion

4.9 The tricuspid regurgitant jet velocity on continuous wave doppler is 3 m/s. The pulmonary artery pressure is therefore at least:

a. 36mm Hg
b. 36mm Hg + Left atrial pressure
c. 36mm Hg – Jugular venous pressure
d. 36 mm Hg + Jugular venous pressure

4.10 A patient is anaesthetised for a mitral valve replacement. After the administration of 300 IU/kg body weight Heparin, the ACT is 360 seconds. The most appropriate action is to:

a. Administer fresh frozen plasma
b. Administer 5000 U of heparin
c. Administer the same dose of heparin again
d. Repeat the test

4.11 A 58-year-old man undergoes three-vessel coronary artery bypass grafting under cardiopulmonary bypass (CPB). Aortic cross clamp time totaled 160 minutes and CPB time 190 minutes. Despite good quality grafts reported by the surgeon, post bypass trans-oesophageal echocardiography shows a left ventricular ejection fraction of less than 35% with global hypokinesia. The most likely mechanism for this clinical scenario is:

a. Myocardial hibernation with decreased VO_2 due to impaired blood flow resulting in reduced contractility
b. Myocardial stunning with normal myocardial blood flow and energy metabolism accompanied by reduced contractility
c. Myocardial damage due to release of reactive oxygen radicals during reperfusion
d. Hypocalcaemia

4.12 An 83-year-old man with longstanding hypertension and a 50-pack year smoking history presents to his GP with a two-month history of intermittent abdominal pain that radiates to his back. Abdominal examination reveals a pulsatile mass. A CT scan confirms a 7.4 cm juxta-renal abdominal aortic aneurysm with no signs of rupture. He is referred to a vascular surgeon who plans an endovascular aneurysm repair with a stent (EVAR). Concerning perioperative management of this patient:

a. The risk of aneurysm rupture is 20% to 50% per annum
b. Pre-operative risk assessment guidelines may be curtailed in this patient
c. EVAR under regional anaesthesia is advised based on the patient's age and co-morbidity
d. N-acetylcysteine is indicated for the primary prevention of contrast induced nephrotoxicity

4.13 You are called to the cardiac catheterisation lab to evaluate a 53-year-old woman with stage IV pulmonary sarcoidosis (severe pulmonary fibrosis) who is scheduled for a full heart study as part of her evaluation for lung transplantation. Trans-thoracic echocardiography suggests a high probability of pulmonary hypertension. She is lying supine on supplemental oxygen via nasal cannulae with an oxygen saturation of 87%. Your anaesthetic plan for this patient will include:

a. Invasive arterial monitoring
b. General anaesthesia with endotracheal intubation
c. Sedation with a propofol/ketamine TIVA technique
d. Sedation with TCI propofol/opioid technique

4.14 A patient requires deep hypothermic circulatory arrest for aortic arch surgery. Choose the best answer related to the physiological effects and safety of DHCA.

a. Electrolyte disturbances are common, the most dangerous of which is hyperkalaemia
b. Cerebral metabolic rate decrease with decreasing temperature in a linear fashion
c. Volatile agents such as Isoflurane, Sevoflurane and Nitrous oxide may confer a degree of preconditioning and is recommended as part of a balanced anaesthetic technique
d. Neuronal injury may continue for several weeks following the use of DHCA

4.15 A 54-year-old female patient is booked for an ablation procedure for atrial fibrillation, which statement most accurately describe the perioperative course?

a. A preoperative transthoracic echocardiogram is performed to exclude an intra-atrial thrombus
b. Trans-septal puncture is used during the procedure and carries a risk of cardiac tamponade
c. Pulmonary artery mapping is achieved with the use of contrast injection
d. The procedure carries a 5% risk of CVA

4.16 In patients infected with SARS-CoV-2, cardiac involvement may be present. Select the statement that is most appropriate to describe this.

a. ACE2 receptors in alveolar epithelial cells may be responsible for direct lung injury, but myocardial injury is likely a secondary event
b. Patients taking ACE inhibitors should discontinue its use due to the increased severity of disease observed in these patients
c. Fulminant myocarditis is the commonest cardiac complication in patients with underlying cardiovascular disease
d. Increased serum Lactate dehydrogenase may indicate myocardial injury

Domain 5: Anaesthesia for neurosurgery

5.1 Which of the following statements about commonly used induction agents for electroconvulsive therapy is most accurate:

a. Propofol results in the shortest seizure duration but has good cardiovascular stability and favourable time to emergence
b. Etomidate increases the seizure threshold and is associated with a more pronounced hyperdynamic response when compared with propofol
c. Ketamine results in the longest seizure duration and is the only known intravenous induction agent that may reduce the seizure threshold
d. Thiopental results in the longest seizure duration and is associated with an increased risk of dysrhythmias

5.2 Regarding the use of hyperosmolar fluids for the management of elevated intracranial pressure, which of the following statements is incorrect:

a. It is reasonable to use hypertonic lactate as the first-line osmotic solution for reducing increased intracranial pressure
b. The use of mannitol or hypertonic saline is recognised as appropriate treatment for reducing increased intracranial pressure
c. It is recommended that a combination of neurological worsening and intracranial pressure of > 25 mmHg are appropriate triggers for starting osmotherapy to treat elevated intracranial pressure
d. It is acceptable to use an intracranial pressure threshold of > 25 mmHg independent of other variables as a trigger for starting osmotherapy to reduce intracranial pressure

5.3 Compared with craniotomy under general anaesthesia, awake craniotomy has been associated with all the following, except:

a. Greater extent of tumour resection
b. Fewer late neurological defects
c. Shorter length of hospital stay
d. Higher postoperative analgesic requirements

5.4 Considering the anaesthetic management of thrombectomy for acute ischaemic stroke, which of the following statements is most inaccurate:

a. Guidelines suggest that endovascular thrombectomy should occur within 6 hours of symptom onset if the thrombus produces an anterior large vessel occlusion
b. Perfusion imaging can be used to extent the treatment window of endovascular thrombectomy beyond 6 hours in select patients
c. Endovascular thrombectomy should preferentially be done under sedation rather than general anaesthesia so that the procedure can be expedited, and the patients' neurologic status can be assessed as soon as possible after clot removal
d. The haemodynamic goals are to avoid pre-thrombectomy hypoperfusion (generally systolic blood pressure 140 – 180 mmHg) and post-thrombectomy hyperperfusion

5.5 When considering perioperative stroke (defined as 'a brain infarction of ischaemic or haemorrhagic aetiology that occurs during surgery or within 30 days after surgery'), which of the following statements is least accurate?

a. Patients at high risk of perioperative stroke should be identified preoperatively by the presence of risk factors including advanced age, female sex, renal failure, history of stroke, and cardiac disease
b. The identification of risk factors is important to inform patients about their risk of perioperative stroke so that an informed risk-benefit analysis can be made for their particular surgery
c. It is prudent to wait at least 12 months before elective surgery following a major stroke to reduce the risk of a major adverse cardiovascular event in the perioperative period
d. Recognition of stroke following surgery is a challenging problem because signs are often obscured by the residual effects of anaesthesia

5.6 A 4-month-old child is undergoing a craniectomy for craniosynostosis under general anaesthesia. Suddenly the systolic BP drops from 75 mmHg to 30 mmHg and the $EtCO_2$ decreases from 35 to 6 mmHg. Which of the following manoeuvres is LEAST likely to have a beneficial effect?

a. Application of PEEP
b. Fluid bolus 10ml/kg
c. Administration of a vasopressor
d. Aspiration from the central venous catheter

5.7 Scalp blocks for awake craniotomy anaesthetise all the following nerves EXCEPT:

a. Auriculotemporal nerve
b. Branches of C4 cervical nerve root
c. Supratrochlear nerve
d. Branches of the ophthalmic division of the trigeminal nerve

5.8 A 25-year-old male sustains a cervical spine injury and concussion during a rugby match. He has partial neurological fall-out below the level of the injury and is drowsy. His CT brain is normal. He arrives in theatre in a cervical collar. He has a normal BMI and no facial injuries. The most appropriate airway management would be:

a. Awake fibreoptic intubation with assessment of neurology post intubation, pre-induction.
b. Rapid sequence induction with manual-in-line stabilisation of the cervical spine.
c. Video-laryngoscopy and nasal intubation.
d. Intubation with a flexible scope through an intubating LMA after induction of anaesthesia.

5.9 A 30-year-old otherwise healthy male patient is booked on the emergency list for the placement of an ICP monitor. He was involved in an MVA that day and has a traumatic brain injury with multiple skull fracture and cerebral oedema but no intracranial haematoma. He also has a lung contusion with multiple rib fractures. The procedure is underway. The ICP monitor is placed. ICP 25mmHg.
Other vitals at this point:

Sats 91% on FiO_2 0.6, PaO_2 9 kPa (70 mmHg), $PaCO_2$ 4.2 kPa (32 mmHg).
SBP 130 mmHg, MAP 80 mmHg

In order to maintain cerebral perfusion pressure and avoid secondary brain injury your next action should be:

a. Administer Mannitol 0.5 g/kg over 15 minutes
b. Start a noradrenaline infusion to target a CPP of 70 mmHg
c. Hyperventilate the patient to maintain a target $PaCO_2$ 20 mmHg (2.5 kPa)
d. Administer Dexamethasone 10 mg IVI

5.10 A patient undergoes trans-sphenoidal resection of a pituitary adenoma. Twelve hours later in the neurosurgical HCU the patient becomes restless. Lab results show the following:

Hb 9 g/dL
Na 130 mmol/L
K 4 mmol/L
Glu 15 mmol/L
Urinary Na 40 mEq/L
Urine output 0.8 ml/kg/hour

The likely diagnosis is:

a. Diabetes Insipidus
b. SIADH
c. Cerebral salt wasting syndrome
d. Excess administration of 5% dextrose maintenance solution

5.11 A 65-year-old male is undergoing surgery for medulloblastoma in the posterior fossa of the brain. Approximately one hour into surgery you notice a supraventricular tachycardia (SVT) arrhythmia on the monitor. The next step will be:

a. Inform the surgeon
b. Give β-blockers
c. Administer lignocaine
d. Give 100% oxygen

5.12 The effect of ischaemia on somatosensory-evoked potentials (SSEPs) is:

a. Decreased latency, decreased amplitude
b. Increased latency, increased amplitude
c. Decreased latency, increased amplitude
d. Increased latency, decreased amplitude

5.13 A patient with a spinal cord injury, sustained 3 hours ago, comes to the operating theatre for an exploratory laparotomy. Anaesthetic management of the patient includes which of the following?

a. Rapid-sequence induction with succinylcholine
b. Hypothermia for better neurologic outcome
c. Managing autonomic hyperreflexia
d. Avoiding corticosteroids

Domain 6: Anaesthesia for ENT, eye, dental, maxillofacial and head and neck surgery, including airway management

6.1 When considering your anaesthetic technique to optimise the surgical field for functional endoscopic surgery (FESS), it is fair to say:

a. Systematic reviews on this subject conclude that TIVA provides a better surgical field than when an inhalational agent is used.
b. A Cochrane review found less blood loss when a TIVA technique was employed.
c. More randomised controlled trials with greater power are needed to elucidate whether TIVA is superior to utilising an inhalational agent.
d. Nitrous oxide is relatively contraindicated in FESS.

6.2 The afferent and efferent limbs respectively of the oculo-cardiac reflex are:

a. The short and long ciliary nerves
b. Oculomotor and vagus nerves
c. Trigeminal and vagus nerves
d. Vagus and oculomotor nerves

6.3 A patient with severe Haemophilia A is scheduled for wisdom teeth extraction under GA. Which of the following are NOT considered to be essential to the management of this patient?

a. Recombinant factor 9
b. Local haemostatic measures
c. Infiltration with local anaesthetic and vasoconstrictor
d. Tranexamic acid oral mouth wash

6.4 If deep sedation is planned for a procedure:

a. Fasting is recommended but not mandatory
b. Clear fluids may be given up to 2 hours before the procedure
c. Standard anaesthetic fasting guidelines are recommended
d. Solid food may be given up to 6 hours prior to the procedure

6.5 In anaesthesia for free flap surgery, the best available evidence suggests:

a. Maintain core body temperature > 35° C at all times
b. Maintain crystalloid administration in the range 7 – 10 ml/kg/hr in the first 24-hour perioperative period
c. Vasopressors significantly increase flap failure rates
d. Intraoperative heparin significantly decreases microvascular complications

6.6 The most accurate statement regarding absorption of topically administered ophthalmic drugs is that they are absorbed:

a. Slower than subcutaneous absorption
b. Faster than intravenous absorption
c. Similar to oral absorption
d. Slower than intravenous absorption

6.7 Drainage of aqueous humour occurs at all these sites, except:

a. Canal of Schlemm
b. Trabecular network
c. Episcleral venous system
d. Tear ducts

6.8 The normal intraocular pressure (IOP) is_____(mmHg):

a. 5
b. 10
c. 25
d. 30

6.9 Correct consequence of respiratory variables on intraocular pressure (IOP) is:

a. Decrease in PaO_2 will decrease IOP
b. Increase in PaO_2 will decrease IOP
c. Decrease in $PaCO_2$ will increase IOP
d. Increase in $PaCO_2$ will increase IOP

6.10 All of the following will serve to decrease intraocular pressure (IOP), except:

a. Nitrous oxide
b. Acidosis
c. Morphine
d. Vecuronium

(Q6.11 - Q615)
A 22-month-old 14.5 kg “preemie” is undergoing strabismus repair under general endotracheal anaesthetic. Following an uneventful inhaled induction with sevoflurane, peripheral IV was obtained, and by oversight, the patient was given 20 mg of succinylcholine prior to intubation. Masseter spasm was noted moments later.

6.11 What parameter is considered the earliest sign and symptom of an ensuing hypermetabolic state following succinylcholine administration?

a. Hyperthermia
b. Hypotension
c. $EtCO_2$ increase
d. Low oxygen saturation

6.12 Midway through the surgery, when surgical traction in the operative field is applied, patient’s heart rate plummets from 110 bpm down to 55b pm. The pairing that accurately reflects the afferent and efferent limbs, respectively, of this reflex is:

a. Trigeminal nerve - vagus nerve
b. Optic nerve - vagus nerve
c. Vagus nerve - trigeminal nerve
d. Trochlear nerve – optic nerve

6.13 The most appropriate first step in the management of this hemodynamic instability is:

a. Adrenaline
b. Atropine
c. Remove traction
d. Phenylephrine

6.14 The true statement regarding an oculocardiac reflex is:

a. It does not occur in enucleated patients
b. Incidence is increased in the setting of hypercarbia
c. Intensity increases with repeated stimulation
d. Suppressed by general anaesthesia

6.15 At the conclusion of the surgery, postoperative nausea and vomiting should be anticipated and can be minimized by all the following, except:

a. Serotonin ($5\text{-}HT_3$) antagonist
b. Propofol infusion
c. Limiting opioids
d. Deep extubation

6.16 True statement regarding laryngospasm is:

a. Associated risk of pulmonary oedema
b. The false vocal cords do not spasm
c. Mediated through the recurrent laryngeal nerve
d. Increased risk of aspiration

6.17 A patient in the intensive care unit (ICU) with pulmonary failure requires tracheal intubation. Compared with nasotracheal intubation, oral tracheal intubation carries a higher incidence of:

a. Patient discomfort
b. Maxillary sinusitis
c. Transient bacteraemia
d. Otitis media

6.18 When compared to an adult, the airway anatomy of a 6-week-old infant reveals:

a. Tongue is smaller and floppy
b. Airway is narrowest at the glottic opening
c. Position of the larynx is more anterior in the neck
d. Epiglottis is flat and firm

(Q6.19 – Q6.20)
A 3-year-old patient arrives for rescheduled tonsillectomy and adenoidectomy with another acute upper respiratory tract infection (URTI). Her initial surgery was postponed 3 weeks ago as she had a URI at that time as well. Examination reveals a runny nose with greenish-yellow discharge with an intermittent wet cough. She is afebrile with normal vital signs.

6.19 Postponement of surgery will reduce the risk of:

a. Laryngospasm
b. Haemorrhage
c. Difficult intubation
d. Gastroesophageal reflux

6.20 Surgery proceeded without incident; however, 2 hours later in the recovery room, she vomits a large blood clot followed by ongoing bleeding. She appears pale and anxious. Vitals reveal heart rate = 130 bpm, respiratory rate = 25 bpm, and blood pressure = 77/35 mmHg. Her capillary refill time is 4 seconds. The most appropriate next step in management is:

a. Insertion of orogastric tube to empty the stomach of blood.
b. Emergent return to the operating theatre
c. Administer anxiolytic medication
d. Provide liberal fluid resuscitation

(Q6.21 – Q6.23)
A 65-year-old male requires trans-oral laser microsurgery to address his laryngeal webs. His medical history reveals remote tobacco smoking and recreational drug use at university.

6.21 Minimizing airway fire hazards associated with laser surgery can be accomplished by use of all the following, except:

a. Intermittent mode laser remissions
b. An air/oxygen anaesthetic technique
c. A polyvinylchloride (PVC) endotracheal tube
d. Saline-soaked sponges over exposed tissues

6.22 Ten minutes later, the surgeon yells “FIRE!” The most appropriate next step is to:

a. Ventilate with air
b. Increase FiO_2 to 1.0
c. Instil saline down the endotracheal tube lumen
d. Remove the endotracheal tube

6.23 One hour later while recovering in recovery, the patient is noted to have stridor and difficulty breathing. The most appropriate next step in his airway management includes:

a. Administration of aerosolized adrenaline
b. Endotracheal intubation
c. Administration of helium and oxygen
d. Intravenous injection of dexamethasone

(Q6.24 – Q6.28)
A 35-year-old male with a toxic multinodular goitre presents for thyroidectomy with radical neck dissection. He denies any other significant medical history. Review of systems reveals orthopnoea and dysphagia with a recent change in the calibre of his voice.

6.24 True statements about this patient include the all following, except:

a. A flow–volume loop on spirometry can evaluate tracheal compression
b. The airway may obstruct with sedation
c. The trachea may collapse postoperatively
d. An abnormally low forced expiratory volume in 1 second (FEV_1) would be diagnostic of an upper airway obstruction

6.25 To attenuate risk of a “cannot ventilate, cannot intubate” scenario, an awake airway intubation is discussed. The neural structure that does not need to be blocked in order to provide adequate airway analgesia for a nasal intubation is:

a. Hypoglossal nerve
b. Sphenopalatine ganglion
c. Superior laryngeal nerve
d. Recurrent laryngeal nerve

6.26 At the conclusion of a complicated 4-hour resection, the patient is extubated and brought to the recovery room. One hour after extubation, the patient complains of dyspnoea with stridorous respiration. Initial steps include all the following, except:

a. Intravenous administration of calcium
b. Nebulized racemic epinephrine
c. Inspection of the surgical site
d. Direct laryngoscopy

6.27 If bilateral recurrent laryngeal nerves were unintentionally severed, the likely finding on direct laryngoscopy would be:

a. Paralysis of the crico-thyroid muscles
b. Intermediate position of the cords
c. Midline, closed position of the cords
d. Pure adductor vocal cord paralysis

6.28 Instead, postoperative direct laryngoscopy reveals normal position of the cords at rest, widely open glottis opening at maximal inspiration, and symmetrically moving cords during quiet breathing but with weak phonation and inability to speak loudly or shout. The most likely aetiology is:

a. Recurrent laryngeal nerve paralysis
b. Superior laryngeal nerve (SLN) paralysis
c. External airway compression
d. Vagus nerve paralysis

Domain 7: Paediatric anaesthesia

7.1 The dose of Bupivacaine should be reduced in neonates and premature neonates due to the following reasons, except:

a. Reduced protein binding of Bupivacaine in neonates
b. Decreased hepatic metabolism
c. Decreased volume of distribution
d. Increased bilirubin displacement with risk of kernicterus

7.2 A 9-month-old infant is having laparoscopic surgery for a Nissen fundoplication. Ten minutes after insufflation the $ETCO_2$ reading is 8,1 kPa. Your management includes the following, except:

a. Ask surgical team to release all insufflation pressure while you increase inspiratory pressure to blow off CO_2
b. Check that endotracheal tube has not migrated down one bronchus
c. Increase respiratory rate and increase inspiratory pressure slightly
d. Confirm adequate neuromuscular blockade and decrease insufflation pressure below 10cmH_2O

7.3 A 4-day-old neonate presents for repair of a congenital diaphragmatic hernia. Your management includes:

a. Increased inotropic and ventilatory requirements signals deterioration of the child's condition, and transfer to theatre should be expedited.
b. Perform a recruitment manoeuvre and ventilate with higher pressures after removal of abdominal contents to expand the atelectatic lung
c. Prepare inhaled nitric oxide (noxbox) for the management of pulmonary hypertension post-operatively
d. Reverse patient and aim for early extubation post-surgery to avoid barotrauma to the underdeveloped lung

7.4 A 9-month-old with craniosynostosis presents for a fronto-orbital advancement. Your main consideration as an anaesthetist is:

a. difficulty securing the airway
b. associated syndromes
c. bleeding
d. need for postoperative ventilation

7.5 A one-day-old baby with gastroschisis presents for repair. The most correct statement concerning associated conditions is:

a. Associated with VACTERL syndrome
b. Associated with VSD or ASD
c. Does not frequently have associated conditions
d. Often associated conditions but surgery is too urgent to delay for investigations

7.6 A 3kg term neonate presents for laparotomy for bowel obstruction. His starting Hb is 13g/dl. Regarding maximum allowable blood loss:

a. $\frac{\text{Initial Hb – lowest acceptable Hb}}{\text{Lowest acceptable Hb}}$ x wgt x blood volume (ml/kg)
b. Blood volume for this baby is likely 70ml/kg
c. $\frac{\text{Initial Hb – lowest acceptable Hb}}{\text{Initial Hb}}$ x wgt x blood volume (ml/kg)
d. $\frac{\text{Initial Hb – lowest acceptable Hb}}{\text{Lowest acceptable Hb}}$ x $\frac{\text{blood volume (ml/kg)}}{\text{wgt}}$

7.7 A child with Down Syndrome requires a general anaesthetic. The most likely reason for difficult airway management is:

a. Large, floppy tongue
b. Low tone causing pharyngeal collapse
c. Congenital subglottic or tracheal stenosis
d. Tonsillar hypertrophy

7.8 Regarding adenotonsillectomy, which statement is most true:

a. Patients should be extubated awake to avoid airway obstruction in the recovery room
b. Adenotonsillectomy does not help reverse the neurocognitive side effects of obstructive sleep apnoea
c. Large tonsils frequently complicate intubation
d. Maintaining spontaneous ventilation may help guide analgesic requirements, which can vary greatly in children

Domain 8: Intensive care medicine

8.1 Critically ill patients experience significantly altered physiological processes. During sepsis a large proportion have augmented renal clearance. Concerning augmented renal clearance, which of the following is most correct:

a. Increased volume of distribution is the main reason for this phenomenon
b. Antibiotic dose needs to be decreased to accommodate this phenomenon
c. Creatinine clearance is increased to more than 130ml/min/1.73m^2
d. Antibiotics can be reliable adjusted without the need to monitor levels

8.2 The broad spectrum antimicrobial Ertapenem usually provides adequate cover for the following bacterial infections except:

a. Klebsiella pneumonia
b. Pseudomonas Aeruginosa
c. Enterobacterium feacium
d. Escherichia Coli

8.3 Post-endovascular repair of thoracic aortic aneurysm spinal cord protection in high-risk cases, the following is recommended:

a. Spinal cord perfusion pressure should be kept at a minimum of 50 mmHg
b. Lumber drain drainage pressure should be set at a maximum of 12 mmHg for least 48 hours
c. Sensory evoked potential monitoring is the most accurate means of assessing the spinal cord function on ICU
d. Patients require elective imaging on day 3 post operatively to exclude spinal cord hematoma after lumber drain removal

Domain 9: Pain medicine

9.1 A 23-year-old lady presents to the day hospital unit for tonsillectomy due to recurrent tonsillitis. She weighs 60kg. A reasonable intra-operative approach with the aim of decreasing her post-operative pain would include:

a. Intra-operative IVI Paracetamol 20 mg/kg, NSAID and Morphine 0.1 mg/kg
b. Intra-operative infiltration of surgical field with lignocaine, Dexamethasone 4 mg, Morphine 0.1 mg/kg and Paracetamol 20 mg/kg
c. Pre-operative Gabapentin 600 mg p.o. with intra-operative intravenous Dexamethasone 6 mg, Morphine 0.05 mg/kg, Paracetamol 20 mg/kg
d. Intra-operative intravenous Dexamethasone 6 mg, Paracetamol 20 mg/kg, NSAID and Ketamine 0.5 mg/kg

9.2 A 46-year-old male presents for a forearm amputation after a crush injury to his arm at work. During pre-operative consultation he appears very agitated and angry. He asks you to please make sure he doesn't have as much pain after the surgery as he had a few years ago when he fractured his ankle. To this day he still has pain in his ankle every day. He asks how long you think it will be before he can return to work, since his family is dependent on his income. He is a smoker and heavy alcohol user. He also uses cannabis oil for sleep. The factors in his history that put him at increased risk of persistent post-surgical pain are:

a. Male, anxious, workman compensation case, addictive tendencies
b. The accident occurring at work, social environment, being a smoker and heavy alcohol user.
c. Male, previous negative experiences with the healthcare system, amputation
d. Young, anxious, workman compensation, unpleasant past experience with pain, social environment, amputation

9.3 A paediatric surgeon has a 9-year-old child in the ward who needs a chest drain inserted for a pleural effusion suspected to be an empyema. The child had a thoracotomy 5 days ago for excision of a pulmonary hydatid cyst. He had an epidural catheter placed for post-op pain relief, but this was removed on day 3 post-op. The child is currently pyrexial (Temp 38.4 degrees Celsius) with mild tachypnoea (30 breaths per minute) but maintaining an oxygen saturation of 94% on room air. He hasn't had anything to eat for 6 hours and his last clear fluid intake was 2 hours ago. His parents have consented for the procedure. The best way to proceed would be to:

a. Discuss the risks and benefits of general anaesthesia vs a sedation and local anaesthetic technique with the child and parents and proceed with either once informed consent is obtained.
b. Perform a sedation for the patient in theatre, with full monitoring, using a combined technique of intravenous Ketamine and Fentanyl as well as local anaesthetic infiltration by the surgeon.
c. Ask the surgeon to bring the child to theatre for the procedure and perform a general anaesthetic with an endotracheal tube.
d. Perform a sedation in the ward using a combined technique of intravenous Ketamine and Fentanyl as well as local anaesthetic infiltration by surgeon.

9.4 You are asked to review a 48-year-old patient in the ward. He had an above knee amputation one week ago following a gunshot injury that fractured his femur and severed his femoral artery. He has been reporting a lot of pain ever since the surgery. He is currently being treated with regular Paracetamol, Ibuprofen and Tramadol and is receiving 4 hourly intramuscular Morphine injections. During your assessment the patient appears very unhappy and complains of relentless pain. He describes a sharp, aching severe pain in the stump as well as a burning pain that he feels in the absent foot. He also complains of dull back pain. You would like to attempt to assess his pain so that treatment and therapy can be directed and any improvement can be objectively measured. The best tool/s to use for this would be:

a. A Verbal Rating Scale should be used to quantify acute pain. This can be reassessed frequently and any improvement measured.
b. A Numeric Rating Scale should be used to quantify his pain. Treatment should be directed at achieving a minimum of 2 point improvement on the scale.
c. LANSS (Leeds Assessment of Neuropathic Symptoms and Signs) questionnaire should be completed since phantom limb pain is likely neuropathic in nature.
d. A combination of a Visual Analogue Scale and the LANSS questionnaire should be employed to assess and guide treatment.

9.5 You are asked to review a 48-year-old patient in the ward. He had a below knee amputation one week ago following a gunshot injury to his knee. He has been reporting a lot of pain ever since the surgery. He is currently being treated with regular Paracetamol, Ibuprofen and Tramadol and is receiving 4 hourly intramuscular Morphine injections. During your assessment the patient appears very unhappy and complains of relentless pain. He describes a sharp, aching severe pain in the stump as well as a burning pain that he feels in the absent foot. He also complains of dull back pain. After taking a further history and examination you conclude that he is suffering from both acute stump pain as well as phantom limb pain. You don't see any evidence of stump infection currently. The best treatment plan going forward would include:

a. Continue Paracetamol, Tramadol and Ibuprofen. Stop IMI Morphine. Commence Gabapentin orally and change to Morphine and Ketamine PCA. Perform sciatic perineural blockade and continue lignocaine perineural infusion for three days.
b. Continue Paracetamol, Tramadol and Ibuprofen. Stop IMI Morphine. Commence oral Mist Morphine and start an Intravenous Ketamine infusion at 15mg/hr for 72 hours. Start Amitryptilline at night.
c. Continue Paracetamol, Tramadol and Ibuprofen. Stop IMI Morphine. Place epidural catheter, initiate epidural local anaesthetic infusion and continue this for at least 72 hours.
d. Continue Paracetamol, Tramadol and Ibuprofen. Stop IMI Morphine. Commence Gabapentin orally in the morning and Amytriptilline orally at night.

9.6 Which of the following statements regarding the relay of the pain stimulus are correct:

a. Pain is a sensation that has a physical source and the intensity of the stimulus determines the amount of pain
b. Pain is a one-way pathway that transmits painful stimuli from the periphery to the brain through pain pathways
c. Pain is an integrated system with afferent pathways being influenced by efferent modulation from the brain.
d. Pain fibers are controlled by the interneurons of the substantia gelatinosa to control the input of large and small fibers into Lamina V

9.7 Central Sensitization is best described by the following mechanisms or pathways.

a. Secondary hyperalgesia
b. Allodynia
c. Temporal summation
d. All of the above

9.8 The Major excitatory neurotransmitters in the spinal cord are:

a. N-Methyl-D-Aspartate, Nitric Oxide, Aspartate
b. Substance P, Calcitonin Gene Related Peptide and Glutamate
c. Nitric Oxide, Nor-Adrenaline and Serotonin
d. Aspartate, Histamine and Opioids

9.9 Which of these are not goals in managing peri-operative patients known with opioid tolerance?

a. Pre-existing opioid medication has to continue to avoid opioid withdrawal
b. Adequate multimodal analgesia
c. Effective treatment of psychological effective disorders such as anxiety
d. Regional anesthesia should be avoided

9.10 Which of the following facts regarding pregabalin is correct?

a. Pregabalin binds to the alpha2-delta subunit of voltage-sensitive calcium channels and modulates neuronal excitability
b. Pregabalin is FDA approved and registered for use in patients with nociceptive pain, neuralgia's and treatment of anxiety
c. Pregabalin is an alpha-agonist that mainly works in the central nervous system
d. Pregabalin is used as an opioid sparing agent for patients with opioid tolerance

Domains 11, 12 & 13: Education, self-directed learning and research; professionalism and ethics in practice; quality, safety, management & health economics

11.1 An anaesthetic registrar is teaching medical students about the principles of ethics in health care.
She tells them that one of the most important principle to observe while taking care of a patient is to first do no harm. The principle of bioethics that she is describing here is:

a. Beneficence
b. Justice
c. Non-maleficence
d. Respect for autonomy

11.2 A 13-year-old boy presents to theatre for an emergency appendectomy. The theatre nurse expresses her concern about the consent. The boy has signed consent for the procedure – with no parental or guardian consent. Which of the following statements is true?

a. The boy is allowed to give consent for the procedure
b. Only his parents or guardian can give consent for the surgery.
c. Parental / guardian assent is needed together with his consent.
d. It is an emergency so as a minor without parental or guardian consent - hospital superintendent consent is required.

11.3 An 11-year-old girl wants to have a termination of pregnancy (TOP). Which of the following statements is correct?

a. She does not need to give specific consent for the procedure.
b. There is no specific age limit for giving valid consent for a TOP provided she showed maturity and mental capacity.
c. A parent/guardian is required to give consent for this procedure.
d. The patient is not able to give consent for the procedure

11.4 A patient who is a Jehovah's Witness presents in the pre-assessment clinic with an Hb of 8 g/dl. He is undergoing a total knee replacement in 8 weeks. Strategies available to you and acceptable to the patient to optimise their DO_2 include:

a. Controlled hypotension
b. Hypothermia. (Decreases VO_2)
c. Autologous blood transfusion
d. Cell salvage is generally not accepted by Jehovah's Witness patients.

11.5 Your newly appointed anaesthetic colleague comes across as volatile with unpredictable episodes of anger, irritability and hostility which you attribute the difficult divorce he has recently gone through. Although you don't see each other outside work he has confided in you he hardly sees his children anymore and that his social life is non-existing.

One afternoon an anaesthetic nurse informs you that the nursing staff has noticed for a while now that your colleague asks for double the number of ampoules of fentanyl and morphine compared to the other consultants and yet his patients often seems to have inferior postoperative pain management. The nursing staff are now suspicious of the new consultant having a substance abuse. What is your next step?

a. Ask a handful of your consultant colleagues if they are also suspicious of their new colleague being a drug addict
b. Meet with your HOD to inform her of the suspicions raised by the nursing staff
c. Talk face-to-face with your new colleague and confront him with the allegations.
d. Contact your department's wellness health officer/team to guide you how best to deal with the accusation brought forward by the nursing staff.

11.6 You are performing an anaesthetic for total thyroidectomy. As the thyroid gland is being cauterised and lifted off the anterior surface of the trachea towards the end of the procedure, a huge flame emerges on the operative field. As a consequence, your patient is on fire. What is your next immediate step?

a. Pour saline/sterilized water onto the fire
b. Turn off flow of all airway gasses and disconnect the breathing circuit
c. Remove the ETT and pour saline into the airway
d. Remove all burning and burned materials from the patient

11.7 A 58-year-old man presents to the emergency department after collapsing at work. The patient is intubated and has a GCS score of E1, V1, M1. CT-scan reveals intracranial haemorrhage and a probable anterior communicating artery aneurysm. The neurosurgeon states that there are no surgical options and this is a non-survivable event and he meets with the family to discuss organ donation. According to the family, the patient had stated on several occasions he would like to be an organ donor, as he himself would like to receive an organ donation in the event that would be necessary. What is the medical ethical principle which describes 'obligation to respect the decision-making capacity of persons'?

a. Autonomy
b. Beneficence
c. Non-maleficence
d. Justice

11.8 A 65-year-old man is scheduled for elective laparoscopic cholecystectomy. Preoperative assessment reveals a BMI of 42 kg m^{-2}, an inter-incisor distance of 4 cm and a modified Mallampati score of 3. During tracheal intubation using direct laryngoscopy, a single upper incisor tooth is fractured by instrumentation. The fragment is not visible in the mouth. What is your immediate response/primary concern?

a. Further direct laryngoscopy in an attempt to identify the fragment followed by a chest radiograph
b. A dose of metronidazole 500 mg and tetanus booster if the patient has no clear immunisation history
c. Postpone surgery
d. Urgent postoperative dental review and bonding of the fragment to the remaining tooth.

11.9 A 45-year-old female is scheduled for a total knee replacement. She is known with rheumatoid arthritis for which she takes methotrexate, she has no other comorbidities.

Surgical site infection (SSI) following total joint replacement can lead to periprosthetic infection which is a devastating complication. Consequently, a number of perioperative interventions to prevent SSI are considered standard practice in spite of lack of high-quality studies supporting their use. Which intervention to prevent SSI is classified as a 'strong recommendation' in WHO's Global guideline for prevention of surgical site infection 2018?

a. Omit Methotrexate prior to surgery
b. Preoperative bathing using antimicrobial soap rather than plain soap
c. Administration of pre-incisional antibiotic
d. Laminar flow ventilation systems

11.10 While evidence-based medicine (EBM) is now considered the gold standard for good clinical practice, concerns have been raised about its limitations. What is a major ethical limitation of EBM?

a. The data from EBM do not take into account the values of each patient
b. Expert opinion is better suited to make decisions on medical ethics
c. EBM studies population samples and is not patient-centred
d. The data from EBM may conflict with a clinician's individual judgement

11.11 Theoretical knowledge in medical education can be assessed via several methods. You are tasked with setting questions for your department's undergraduate anaesthesia course. Which modality is most robust at assessing your students' theoretical knowledge?

a. Multiple choice questions (classic MCQ) with only one true answer and the rest false
b. Single best answer format (SBA) with other options as plausible alternatives
c. Objective Structured Practical Examination (OSPE) with multiple stations
d. A written paper using classic MCQs, SBAs, short answer questions and True/False items

11.12 The CANMEDS Physician Competency Framework highlights the role of the physician as a Health Advocate. Which scenario best describes a clinician acting in such a role?

a. Being an example to patients by eating a balanced diet, exercising regularly and possessing sober habits
b. Engaging with and partaking in activism to ensure free universal healthcare provided by the state
c. Ensuring equitable access to the healthcare system by taking into account factors such as gender, age, and education
d. Developing a cheaper screening tool for a common preventable disease

Single Best Answer (SBA) Practice
Answers and explanations

Domain 1: Fundamentals of anaesthesia and pain management

1.1 Answer: c

a. False – Pin index cylinders require a seal between cylinder valve outlet and yoke. The seal is called a Bodok washer. It is a gasket with metal rim manufactured from a non-combustible material

Pin index of oxygen cylinder

Bodok seal

b. False - The most common type is E which has a capacity of 660l of oxygen and is the largest commercially available pin index cylinder.

Size	Capacity (L)	Pressure (psi)	Tare Wt. (kg)	Valve type
B	200	1900	2.27	Pin index
D	400	1900	3.4	Pin index
E	660	1900	5.4	Pin index
F	1360	1900	14.5	Bull nose
G	3400	1900	34.5	Bull nose
H	6900	2200	53.2	Bull nose
M	3450	2200	29.0	Bull nose

c. True - Nitrous oxide and carbon-dioxide liquefy at pressures to which cylinders are filled (at ambient temperature) and are therefore stored as liquids. These cylinders are not filled completely, but only up to a filling ratio (weight of gas in a cylinder/weight of water that cylinder can hold at 15° C). The filling ratio of oxygen and nitrous oxide is 0.75, but 0.67 in the tropics. The contents of these cylinders can be accurately measured by weighing the cylinders (1.87 g/L of gas) rather than by pressure gauge.

d. False - An international colour code to aid in identification of gas cylinders was adopted by medical gas industry in 1949. Unfortunately, this has not been adopted by many countries. US uses green and Germany uses blue colour for oxygen cylinders.

Colour coding, pin index and physical state in cylinder of medical gases

	Oxygen	Nitrous oxide	Air	Carbon-dioxide	Entonox	Nitrogen	Helium
Physical state in cylinder	Gas	Gas+Liquid (below 98^0 F)	Gas	Gas+Liquid (below 88^0 F)	Gas	Gas	Gas
Color (India)							
Body	Black	Blue	Black	Gray	Blue	Black	Brown
Shoulder	White	Blue	White/Black	Gray	White/Blue	Black	Brown
International							
Color	White	Blue	Black/White	Gray	Blue/White	Black	Brown
Formula	O_2	N_2O	-	CO_2	-	N_2	He
Pin index	2-5	3-5	1-5	1-6	7	1-4	No pin

1.2 Answer: b

Within the respiratory system both laminar and turbulent flows exist. At low flow rates, the respiratory flow tends to be laminar, like a series of concentric tubes that slide over one another with the centre tubes flowing faster than the more peripheral tubes. Laminar flow is usually inaudible and is dependent on gas viscosity. Turbulent flow tends to be faster flow, is audible and is dependent upon gas density. Gas density can be decreased by using a mixture of helium with oxygen.

1.3 Answer: a

a. True - Burns can occur at the dispersive electrode if it is applied incorrectly or not of enough size, so the site should be well perfused, be distant to any metal implants that may become heated and be free from hair. Burns have also been reported from insulation failure at the active electrode or accidental contact between the active electrode and another conductor.

b. False - The cutting effect is achieved by using a pure continuous sine wave of low voltage. This rapidly produces high temperatures that vaporize tissue fluid causing cells to explode forming a gap in the tissues.

c. False - Heating is as a result of an alternating current that passes between two electrodes. Heating is usually greatest where the current density is highest. Therefore, it is usually the smallest or sharpest electrode that generates the most heat.

d. False - Channeling effect: If the organ to which diathermy is being applied has attachment or pedicle to the body narrower than the diameter of the organ concerned then the passage of the current will concentrate its intensity and coagulation at the narrowest point may occur.

1.4 Answer: b

a. False - The activated clotting time is a non-specific clotting time that is affected by multiple variables.

b. True - Haemophilia A (Factor VIII) deficiency and haemophilia B (Factor IX or Christmas disease) are X-linked recessive disorders. Haemophilia A occurs in 1 to 2 per 10,000 males and haemophilia B occurs in 1 per 100,000 males. Factor V, Factor VII, Factor X, and prothrombin (Factor II) are exceedingly rare autosomal recessive disorders. The PT and the activated partial thromboplastin time (aPTT) are common tests used to evaluate coagulation factors. The PT primarily tests for factor VII in the extrinsic pathway, as well as factors I, II, V, and X of the common pathway. The aPTT primarily tests for factors VIII and IX of the intrinsic pathway, as well as factors I, II, V, and X of the common pathway.

c. False - the PT primarily tests for factor VII in the extrinsic pathway, as well as factors I, II, V, and X of the common pathway. Fibrinogen levels are usually normal in haemophilia.

d. False - Thrombin time is a measure of the ability of thrombin to convert fibrinogen to fibrin. It is prolonged with low amount of fibrinogen, heparin and fibrin degradation products. The bleeding time is a functional test of platelet function.

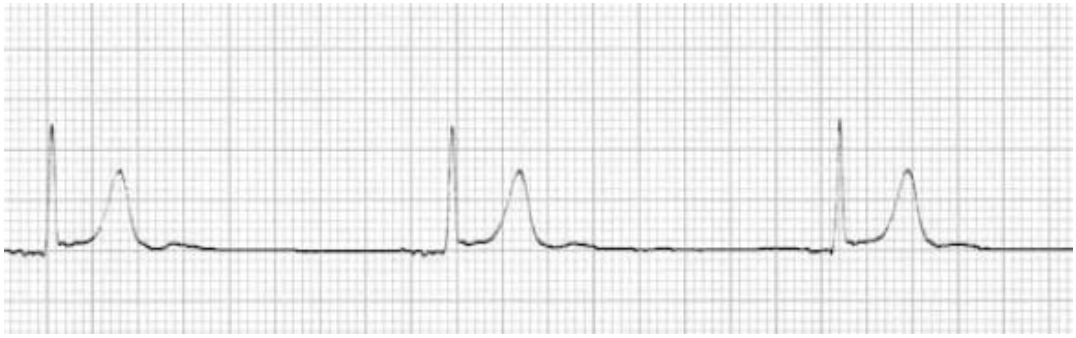
1.5. Answer: c

a. False - in hyperkalaemia the ECG will show a prolonged PR interval, decreased or disappearing P wave, widening of the QRS and an amplified R wave

b. False - hypocalcaemia causes QTc prolongation primarily by prolonging the ST segment. The T-wave is typically left unchanged. Dysrhythmias are uncommon, although atrial fibrillation has been reported. Torsades de pointes may occur, but is much less common than with hypokalaemia or hypomagnesaemia

c. True bradyarrhythmias, Osborne Waves (J waves), prolonged PR, QRS and QT intervals, shivering artefact, ventricular ectopics, cardiac arrest due to VT, VF or asystole

d. False - ECG changes of hypotension will mirror those of myocardial ischaemia. ST segment depression, T wave flattening or inversion, U wave inversion.



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3.https://www.wfsahq.org/components/com_virtual_library/media/abc79fe74461ed182a3d7b59d34129bd-Flow--Update-24-2-2008-.pdf
4. Curry A. Conventional and near-patient tests of coagulation. *Continuing Education in Anaesthesia Critical Care & Pain*, Volume 7, Issue 2, April 2007
5. Barash, Paul G., Cullen, Bruce F.Stoelting, Robert K. (Eds.) (2006) Clinical anesthesia Philadelphia : Lippincott Williams & Wilkins

1.6 Answer: b

CoQ10 decreases warfarin's effect

Milner, Welch. Applied Pharmacology in Anaesthesiology and Critical Care. 1st ed. Medpharm Publications. 2012

1.7 Answer: c

In this scenario, patient autonomy outweighs fidelity and non-maleficence.

1.8 Answer: d

Clark electrode measures arterial O_2, not ETO_2, galvanic cell does not have rapid enough response, O_2 cannot be measured with infrared since it does not absorb infrared light.

Miller RD. Anesthesia. 7th ed. Churchill Livingstone, 2009

1.9 Answer: a

If unanticipated, calling for help should be step one, followed by maintaining O_2 (DAS Guidelines).

1.10 Answer: d

V1 most sensitive for arrythmia detection, V4 most isoelectric.

Miller RD. Anesthesia. 7th ed. Churchill Livingstone, 2009

Domain 2: Anaesthesia for major and trauma surgery

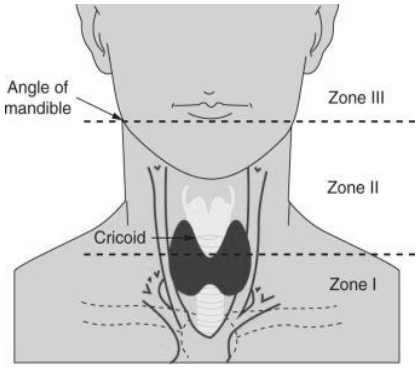
2.1 Answer: a

Blunt-neck trauma is most commonly a result of a motor vehicle collision associated with rapid acceleration or deceleration injuries, which may include crushing injuries of the trachea, oesophagus, vascular structures, and cervical spine. A laryngeal fracture can lead to life-threatening airway obstruction and as such should be treated in an emergent manner. Signs and symptoms of dyspnoea, emphysema, and inability to lie flat reflect a fragile airway. Definitive airway management following

airway trauma is a surgical airway, most commonly a tracheostomy. Cricothyroidotomy is not recommended following laryngo-tracheal injuries, as the landmarks are usually difficult to assess, since the cricoid is often the level of the injury.

2.2 Answer: b

The neck is divided into three zones: zone I, including the thoracic inlet, up to the level of the crico-thyroid membrane, is treated as an upper thoracic injury. Zone III, above the angle of the mandible, is treated as a head injury. In this case, fracture of the thyroid cartilage represents an injury of the neck in zone II. For ease of memory, consider that the cricoid cartilage demarcates the border between zones I and II and the angle of the mandible separates zone II from zone III.



2.3 Answer: a

Wallace rule of 9s is inaccurate in children due to relative size of head and body v limbs. Palm size area (including fingers) equates to about 1% but this is not as accurate as the Lund-Brower burn diagram

Lund C, Browder N. The estimate of areas of burns. Surg Gynecol Obs 1944; 79: 352–8). The Parkland chart only exists in the imagination of the author.
Guilabert P, Usúa G, Martín N, Abarca L, Barret JP, Colomina MJ. Fluid resuscitation management in patients with burns: update. Br J Anaesth [Internet] 2016; 117: 284–96 Available from: https://linkinghub.elsevier.com/retrieve/pii/S0007091217337881

2.4 Answer: b

The main elements of damage control resuscitation are:

- Permissive hypotension
- Early use of blood and blood products
- Early tranexamic acid within 3 hours of trauma
- Damage control surgery
- C>ABC resuscitation
- Correcting the electrolytes is useful but not critical, unless life threatening hyperkalaemia

DCR is defined as: ‘a systematic approach to major trauma combining the <C>ABC paradigm with a series of clinical techniques from point of wounding to definitive treatment in order to minimize blood loss, maximize tissue oxygenation, and optimize outcome’.

2.5 Answer: b

Rationale: Other answers are not sufficient to qualify. Candidate must know a reasonable definition. e.g. More than 10 units red cells in 24 hours/ >1 blood volume in 24 hours/ >50% blood volume in 4 hours/ children: transfusion of more than 40ml/kg

2.6 Answer: a

Most early deaths in flame burns are due to inhalational injuries, toxins released by burning debris and smoke inhalation. The systemic and local effects of burns are only relevant later.

2.7 Answer: d

Decreasing the CVP results in significant decreases in blood loss in liver resections (reduces blood loss from backflow bleeding via the hepatic veins). If fluid restriction is ineffective, drugs like nitroglycerine, diuretics or inhalational agents can be used. Reverse Trendelenburg position, normovolaemic haemodilution and minimising positive end expiratory pressures can also aid in reducing the CVP. Beware the risks of organ hypoperfusion and venous air embolism.

2.8 Answer: c

Cardiac risk stratification in a patient this anaemic would not reflect his true risk profile. He is undergoing an intermediate risk operation and his history suggests that, apart from his age, he has no other risk factors that would require further testing or evaluation prior to surgery. ECG changes are likely reversible once his Hb levels are normalized. His premorbid DASI would confirm his excellent functional capacity. Pre-operative optimization should concentrate on the management of his anaemia. Consultation with the surgical team should inform whether there is time to raise Hb levels using haematinics or else consideration of a pre-op transfusion strategy.

ESA guidelines cardiac for non-cardiac surgery
AHA guidelines cardiac for non-cardiac surgery

2.9 Answer: d

This is a patient that presents with signs and symptoms of myasthenia gravis and a mass in her anterior mediastinum (likely a thymic neoplasm). Due to her smoking history, a differential of carcinoma of the lung with a concomitant Lambert-Eaton Paraneoplastic Syndrome (ELPNS) is reasonable but her age, degree of smoking and clear lung parenchyma on imaging (i.e. no indication of a primary tumour originating in her lung) is against this diagnosis. ELPNS is clinically similar to myasthenia gravis although eye signs are not pathognomonic. Unlike in myasthenia gravis where the abnormality is with post-synaptic acetylcholine receptors, in ELPNS antibodies against pre-synaptic voltage gated calcium channels curtail the release of acetylcholine resulting in abnormalities in muscle contraction. Based on her CT imaging, preoperative echocardiography is not mandatory before proceeding to mediastinoscopy. Because of the likelihood of innominate artery compromise during mediastinoscopy, plethysmography (or, if indicated, invasive arterial blood pressure monitoring) should be placed on the right arm. The use of non-depolarising neuromuscular blockers is generally contraindicated in patients with myasthenia gravis or those with mediastinal tumours that significantly compromise airway and cardiovascular structures. However, the advent of sugammadex has altered this practice.

Ahmed-Nurath A, Swanevelder J. Continuing Education in Anaesthesia Critical Care & Pain, Vol 7, Issue 1, 1 Feb. 2007, pages 6-9
Sungur Ulke Z, Yavru A, Camci E. Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy. Acta Anaesthesiol Scand. 2013 Jul;57(6):745-8

2.10 Answer: c

a. Elevated urine 5-HIAA suggests serotonin secretion. Histamine secretion is common in GI carcinoid tumours.

b. 25% of carcinoid tumours produce mediators.

c. Hyperglycaemia is common in serotonin secreting tumours and should be managed with insulin infusion intraoperatively.

d. General anaesthesia is commonly used, but neuraxial anaesthesia has been used successfully in many cases and may be beneficial for postoperative analgesia.

Domain 3: Obstetric anaesthesia and analgesia

3.1 Answer: c

3.2 Answer: d

3.3 Answer: b

3.4 Answer: b

3.5 Answer: c

3.6 Answer: b

a. This may occur if the test dose given through a catheter placed in the subdural space causes the arachnoid to tear.

b. This is the classic description of inadvertent subdural catheter placement, where the local anaesthetic dose remains in the subdural space.

c. This is rare, but explicable by subdural catheter placement with tearing of the arachnoid only on injection of a *large* volume.

d. This could occur if local anaesthetic trapped in the relatively confined subdural space causes compression of nerve roots and the accompanying radicular arteries, or if a subdural haematoma develops.

Reynolds F & Speedy HM. The subdural space: the third place to go astray. *Anaesthesia* 1990; 45: 120–3.

3.7 Answer: d

a. Pruritus most commonly occurs in facial areas, especially around the eyes and nose, as the trigeminal nerve is rich in opioid receptors.

b. Studies have shown propofol infusions, IV dexamethasone, antihistamines and 5HT3 antagonists to be ineffective; there is some utility in the use of naloxone infusions to prevent neuraxial morphine-induced pruritus.

c. The propensity to develop pruritus is dependent on genetic variation of the mu-opioid receptor gene (OPRM1). There is a higher incidence among parturients carrying the 118AA allele compared with the 118GG and 118AG alleles. However, the incidence of pruritus is clearly dose dependent.

d. Pregnant women are particularly susceptible and show an incidence as high as 60-100%.

Yurashevich M & Habib AS. Monitoring, prevention and treatment of side effects of long-acting neuraxial opioids for post-cesarean analgesia. *IJOA* 2019; 39: 117-128.

3.8 Answer: c

a. Aorto-caval compression syndrome can be grossly exaggerated by the abdominal fat pannus, and this is a well-described cause of maternal cardiac arrest during positioning.

b. LMWH is best dosed according to total body weight, although there is a dearth of data for women weighing more than 130 kg.

c. This is proposed as a major factor in the dislodgment of an initially well-placed epidural catheter and is the rationale for inserting the catheter deeper (6-7 cm) into the epidural space in obese parturients. Also, some experts advise that a seated obese patient be placed in the lateral recumbent position before securing the epidural catheter to the skin, as the catheter may be drawn 1-2.5 cm inward during this manoeuvre.

d. Current guidance is not to reduce the dose of local anaesthetic employed for single-shot spinals in morbidly obese parturients to less than 10 mg hyperbaric bupivacaine. Although a slightly higher block height is achieved than in non-obese caesar patients, the risk of cervical block is acceptably low and the longer duration of block is beneficial, given the typically longer surgical times.

Taylor CR, Dominguez JE & Habib AS. Obesity and Obstetric Anaesthesia: Current Insights. *Local & Regional Anesthesia* 2019;12: 111–124 & Ngaka TC, Coetzee JF, Dyer RA. The influence of body mass index on sensorimotor block and vasopressor requirement during spinal anesthesia for elective cesarean delivery. *Anesth Analg*, 2016; 123:1527-1534.

3.9 Answer: d

a. Current guidelines recommend maintaining the fibrinogen level above 2 g/L during major obstetric haemorrhage. Although normal values for fibrinogen are between 4 and 6 g/L in term pregnant women, there is no further benefit in maintaining the fibrinogen level above 4 g/L during ongoing resuscitation.

b. Small case series have not shown a decrease in blood loss when prophylactic catheters are placed, and the only small randomised control trial showed no benefit in reducing blood loss or the need for peripartum hysterectomy. This may occur because catheters migrate after initial placement, or because the uterus receives a large collateral blood supply from the ovarian arteries. Serious complications include arterial damage, occlusion and infection. Routine use is thus not recommended.

c. Due to the significant risk of massive bleeding complicated by profound hypotension and coagulopathy and a high likelihood of hysterectomy during caesarean delivery, general anaesthesia is generally regarded as the anaesthetic of choice for patients with placenta accreta. It would be undesirable to have to secure a difficult airway midway through a difficult procedure in a haemodynamically unstable patient, when airway oedema from ongoing fluid resuscitation and prolonged supine positioning may further contribute to difficult tracheal intubation.

d. Historically, auto-transfusion was considered contraindicated in the face of maternal haemorrhage because of a fear of inducing amniotic fluid embolism upon reinfusion. Recent data suggests that this fear is unfounded, with several medical societies (including OAA, AAGBI, NICE, ACOG) now recommending that auto-transfusion be used during severe maternal haemorrhage. Auto-transfused blood is equivalent to maternal blood across several parameters when a WBC depletion filter is used, except for fetal haemoglobin, which is higher in auto-transfused blood.

Toledano RD & Leffert LR. Anesthetic and Obstetric Management of Placenta Accreta: Clinical Experience and Available Evidence. *Curr Anesthesiol Rep* 2017; 7:93–102

3.10 Answer: c

a. Alterations in the endothelial glycocalyx limit the response to fluid therapy in severe preeclampsia. Fluid therapy may increase the risk of post-delivery pulmonary oedema before postpartum diuresis can occur. Whilst there is limited high-quality evidence, expert opinion favours fluid restriction. Vasopressors are preferred for the management of spinal hypotension in preeclampsia.

b. Abruptio placentae without maternal haemodynamic compromise or CTG abnormality is not a contraindication to spinal anaesthesia. However, the anaesthetist must be mindful of the time taken to administer the spinal.

c. If the preterm fetus is severely growth restricted, and particularly where the estimated fetal weight is below 1000 g, a larger dose of intrathecal local anaesthetic may be required to achieve adequate (T5 level) sensory and motor block.

d. Spinal-induced hypotension occurs less frequently in severely preeclamptic patients, probably due to the presence of circulating vasoconstrictor substances. The smaller size of the preeclamptic uterus also results in reduced aortocaval compression.

Hofmeyr R, Matjila M & Dyer R. Preeclampsia in 2017: Obstetric and Anaesthesia Management. *Best Pract Res Clin Anaesthesiol* 2017; 125-138

Domain 4: Anaesthesia for cardiac, thoracic and vascular surgery

4.1 Answer: b

MINS is defined by postoperative troponin leak, so troponin screening is the investigation of choice. Most patients with MINS (fewer than 40%) do not have ECG changes.[1] The troponin leak found in MINS has prognostic implications related to postoperative mortality and morbidity that has not been established with NT-proBNP. Rather NT-proBNP is done in the preoperative period to predict which patients are at high risk for MINS. Stress testing is obviously wrong in a postoperative patient.

4.2 Answer: a

Myasthenia gravis is condition where antibodies are formed against post-synaptic acetylcholine receptors that are the site of action for muscle relaxants. The reduction of these receptors results in resistance to suxamethonium that requires adequate depolarization for fasciculations to occur. Sensitivity to non-depolarising muscle relaxants is due to the reduced post-synaptic sites which need to be blocked to prevent muscle activity.

4.3 Answer: d

The symptoms are classically described for aortic stenosis.

4.4 Answer: b

Septal hypertrophy is noted on echocardiogram of HOCM. Pulmonary artery stenosis and VSD are seen in Tetralogy of Fallot.

4.5 Answer: c

The dicrotic notch represents a transient increase in aortic pressure on closure of the aortic valve during diastole.

Botto F, Alonso-Coello P, Chan MT, et al. Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology* 2014; 120(3): 564-78.

4.6 Answer: d

4.7 Answer: c

4.8 Answer: b

4.9 Answer: d

4.10 Answer: c

4.11 Answer: b

The stem of the question alludes to a lengthy aortic cross clamp time and total CPB time which is a risk factor for the development of post CPB low cardiac output syndrome. The most likely explanation for this phenomenon is *myocardial stunning*. It is characterized by increased cytosolic calcium and degradation of contractile proteins resulting from ischaemic injury (by reactive oxygen radicals) in the face of re-established blood flow i.e. a flow-contractility mismatch. *Myocardial hibernation* is a phenomenon related to poor blood flow (demand/supply imbalance) that is reversed by revascularization. Oxygen free radical release due to ischaemia reperfusion is a seminal aetiological factor for the clinical scenario but is not a comprehensive explanation. Hypocalcaemia is a cause of low contractility post bypass and replacement may improve inotropy.

A Dhulki. Myocardial Protection During Cardiac Surgery. Dissertation. Department of Anaesthesia, University of Kwazulu Natal
Scott T, Swanevelder J. Perioperative myocardial protection. Continuing Education in Anaesthesia, Critical Care & Pain j Volume 9 Number 3 2009

4.12 Answer: a

The risk of rupture is 20-50% for aneurysms that are larger than 7.0 cm in diameter, which informs discussions with the surgeon around timing of surgery. All patients undergoing EVAR, unless as an emergency procedure, should be risk assessed and optimized according to the American College of Cardiology/ American Heart Association or European guidelines (**not emergency procedure - distractor 1).** This patient is considered high risk due to age and co-morbidity as well as undergoing a high-risk procedure (complex endovascular aneurysm repair due to juxta-renal position). Although regional anaesthesia is well described for EVAR with many benefits, GA would be preferable due to the likelihood that this complex procedure will last many hours and may require access through one of the subclavian arteries (**distractor 2**). There is no evidence for the use of N-acetylcysteine in the prevention of contrast-induced nephrotoxicity (**distractor 3**).

Kothanda H, Liew Haw Chieh G. *et al*. Annals of Cardiac Anaesthesia. Jan-Mar-2016: Vol 19 Issue 1

4.13 Answer: d

The consideration here is clearly one of anaesthesia/sedation with pulmonary hypertension as the main worry. A full heart study may take up to an hour or more and the patient needs to lie still but be responsive. Invasive monitoring from the anaesthetist's point of view is unnecessary as the cardiologist will cannulate the femoral artery for left heart pressure measurements. This patient is anxious and will require some form of procedural sedation. General anaesthesia with endotracheal intubation is not recommended due to the risk posed by the possibility of severe pulmonary hypertension. There are many ways to skin this cat but a target-controlled infusion using propofol and remifentanil or alfentanil would be the best option. Considerations for not using opiates due to the potential of increasing $PACO_2$ and hence raising pulmonary artery pressures are valid but with these opioids' short half-lives and the ready availability of naloxone this becomes moot in my opinion: it's all about using the appropriate dose range and responding rapidly to changes in the patient's vital signs. Ketamine doses are comparatively low in "ketofol" preparations but, nevertheless, it would not be a drug combination of choice in a patient with severe pulmonary hypertension.

Personal experience with this type of patient in the cath lab
Pilkington SA, Taboada D, Martinez G. Pulmonary hypertension and its management in patients undergoing non-cardiac surgery. Anaesthesia 2015, 70, 56-70.

4.14 Answer: d

a. Hypokalaemia is common

b. CMR decreases in an exponential fashion with decreasing temperature.

c. Volatile agents may confer a degree of preconditioning, but the effect is far less than the effect of temperature or acid base balance. Nitrous oxide is avoided due to cerebral vasodilation and expansion of air emboli.

d. The mechanism of neuronal death is complex, and it may continue for weeks to months. Reperfusion injury, inflammatory changes and impaired autoregulation all play a role.

4.15 Answer: b

Transoesophageal echo is used as transthoracic echo is not sensitive enough to identify a thrombus
Pulmonary veins are mapped
The risk of CVA is 1%

4.16 Answer: d

a. ACE2 receptors are also abundant in myocardial cells and direct myocardial injury is therefore likely. The role of ACE inhibitors is still unclear in these patients. It may play a dual role as it may increase susceptibility to infection due to upregulation of ACE2 receptors, but it may also have a protective effect on the heart and ameliorate lung damage.

b. Due to the well-established benefits of taking these medications in patients who require them stopping medications routinely and abruptly is not recommended at his stage.

c. Acute myocardial injury is most common in this group. Fulminant myocarditis can be seen in previously healthy patients.

d. Increased troponin, CK and LDH is commonly seen in patients with myocardial injury and may be associated with worse outcomes.

Domain 5: Anaesthesia for neurosurgery

5.1 Answer: a

a. True
b. False: Etomidate results in the longest seizure duration, and is the only IV agent induction agent that may reduce the seizure threshold
c. False: unclear seizure quality, may increase or decrease seizure threshold,
d. False: shorter seizure duration

5.2 Answer: a

a. False – here is no recommendation for the use of hypertonic lactate as first-line treatment of raised ICP
b. True – although a weak recommendation
c. True – strong recommendation
d. True – although a weak recommendation

5.3 Answer: d

5.4 Answer: c

There is no consensus on the safest technique, each case should be individualized.

5.5 Answer: c

a. True
b. True – 3 to 4 risk factors carry 0,7% incidence of perioperative stroke. More than 5 risk factors increase the incidence to 1,9%.
c. False – SNACC recommends waiting 30 days, but a Danish Study in 2014 showed that after 9 months, the associated risk appears stable yet still increased compared with patients with no stoke
d. True

5.6 Answer: a

PEEP will increase venous pressure but will also decrease cardiac output, cardiac filling pressure and blood pressure. It may increase the risk of paradoxical air embolism and worsen cardiovascular compromise. Management of suspected venous air embolism:

- Inform the surgeon
- Discontinue Nitrous Oxide, increase oxygen flows
- Surgeon to flood field with saline
- Change patients position head below heart
- Aspirate CVP (atrium R)
- Provide cardiovascular support

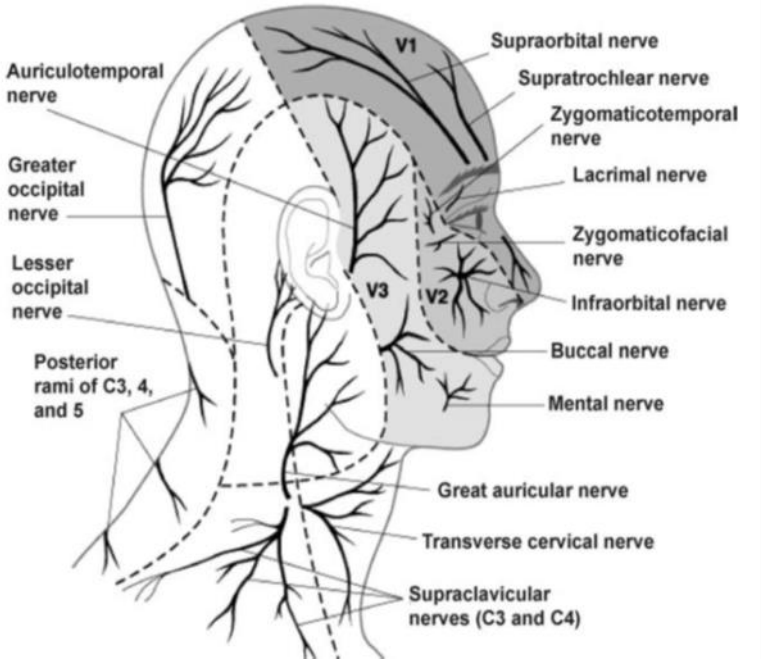
5.7 Answer: b

Greater occipital nerve is a branch of C2 nerve root.
Nerves blocked for scalp block:

- Anterior scalp innervated by divisions of the trigeminal nerve:
- Ophthalmic division (V1): Supraorbital, supratrochlear

- Maxillary division (V2): Zygomaticotemporal
- Mandibular division (V3): Auriculotemporal
- Posterior scalp innervated by branches of C2 nerve root: Greater and lesser occipital nerves.

Osborne et al, "Scalp block" during craniotomy: a classic technique revisited. JNA, 2010;22(3):187-194



5.8 Answer: b

AFOI may be difficult in an emergency, with risk of aspiration and an unco-operative patient in pain. RSI with video-laryngoscope most appropriate with manual in-line stabilisation of the C-spine. AFOI may be indicated if there are other predictors of a difficult airway.

5.9 Answer: a

Avoid aggressive attempts to achieve CPP > 70mmHg. Efforts to optimise CPP should first treat intracranial hypertension.

b. Incorrect: As Above. SBP and MAP already above target. More aggressive attempts can lead to intracranial haemorrhage, cerebral hyperaemia.
   Systolic blood pressure (SBP) ≥100 mmHg for patients 50 to 69 years old
   SBP ≥110 mmHg for patients 15 to 49 or >70 years old
c. Incorrect: $PaCO_2$ target 35 – 38 mmHg. Lower target (25 – 30 mmHg) can be used acutely but can cause cerebral ischaemia. Hypocapnia should not be targeted within first 24 hours as cerebral perfusion already critically low.
d. Incorrect: Glucocorticoid therapy is harmful for patients with moderate to severe TBI.

https://braintrauma.org/uploads/07/04/Guidelines_for_the_Management_of_Severe_Traumatic.97250__2_.pdf
Brain trauma Foundation TBI guidelines

5.10 Answer: b

a. Diabetes Insipidus: Incorrect: Polyuria, dilute urine, hypernatraemia
b. SIADH: Hyponatraemia with hyperosmolar urine
c. Cerebral salt wasting syndrome: Incorrect, causes hyponatraemia and decreased plasma volume, polyuria.
d. Excess administration of 5% dextrose maintenance solution: Incorrect

	CSW	SIADH	Diabetes insipidus
Volume Status	Hypovolemia	Normovolemic or hypervolemia	Hypovolemia
Serum Sodium Concentration	Decreased	Decreased	Increased
Urine Sodium Concentration	Increased	Increased	Decreased
Urine Output	Increased	Normal	Increased
Mechanism	Excess secretion of sodium and water	Water retention due to elevated ADH (vasopresin)	Free water loss due to decreased ADH (vasopresin)

5.11 Answer: a

For posterior fossa tumor resection, the patient is frequently placed in the sitting or prone position. Operations on posterior fossa tumours can injure vital brain-stem respiratory and circulatory nuclei, resulting in haemodynamic fluctuations or depression of ventilation. The surgeon should be informed at the first sign of cardiac arrhythmias.

5.12 Answer: d

SSEPs reflect the integrity of neuronal pathway from the peripheral nerves through the spinal cord (dorsal columns) to the brain. SSEPs are electrical manifestations of the central nervous system response to external stimulation. Intraoperative changes in amplitude or latency or complete loss of waveforms are indicators of compromised sensory pathway integrity. SSEP amplitude loss greater than 50% or a latency increase greater than 10% is considered significant.

5.13 Answer: a

In the early management of acute spinal injury patients, emphasis should be placed on preventing further spinal damage, which may occur during patient movement, airway manipulation, and positioning. High-dose corticosteroids are often administered to help improve neurological outcome. The head and neck should be stabilized using manual inline stabilization. Patients with high cord transections may have impaired airway reflexes, hypotension, and bradycardia and may be prone to hypothermia in view of generalized vasodilation (spinal shock). Succinylcholine can be used safely in the first 24 hours following spinal injury.

Domain 6: Anaesthesia for ENT, eye, dental, maxillofacial and head and neck surgery, including airway management

6.1 Answer: c

There were 3 systematic reviews in 2013 that were not conclusive.
The Cochrane review found no difference in blood loss between the 2 techniques.
Nitrous oxide may be relatively contraindicated in middle ear surgery but its ability to decrease contractility and vasoconstrict is used by some in FESS.

Carlton D and Govindaraj S. Anesthesia for FESS. Curr Opin Otolaryngol Head Neck Surg 2017; 25: 24-29

6.2 Answer: c

Part of the reflex but not the main afferent and efferent limbs
Oculomotor is a red herring owing to its name

6.3 Answer: a

Recombinant factor 9 is incorrect.
Should be factor 8. Factor 9 used for Haemophilia B
The others are all routinely recommended.

6.4 Answer: c

b. and d. are also correct but incomplete
a. applies to minimal and moderate sedation.

South African Society of Anaesthesiologists Sedation Guidelines 2015.
SAJAA 2015; 21(2): S1 – S36

6.5 Answer: a (Level 2b evidence)

b. Should be 3.5 – 6 ml/kg/hr. Level 2b evidence

c. Vasopressor administration after flap anastomosis to treat hypotension does not worsen flap outcome. Level 2b evidence. If infusions are used noradrenaline and dobutamine appear to be the best choices. Level 1b evidence.

d. Administering heparin intraoperatively appears to have no effect on microvascular complications. Level 2b evidence. Either heparin or LMWH should be administered s/c postoperatively. Level 2b evidence

Motakef S et al. Emerging paradigms in perioperative management for microsurgical free tissue transfer: review of the literature. Plastic Reconstructive Surgery. 2015; 135(1): 290-299

6.6 Answer: d

Topically applied drops are quickly absorbed by the mucosal lining of the nasolacrimal duct as well as by blood vessels in the conjunctival sac with a potential to produce systemic effects. Absorption is rapid, faster than oral or subcutaneous administration, but still slower than intravenous.

6.7 Answer: d

Intraocular pressure (IOP) is a reflection of the eye's ability to form and drain aqueous humour. The posterior chamber's ciliary body is the major producer of aqueous humour. Obstruction of the drainage system, whether it is at the canal of Schlemm, the trabecular network, or the episcleral venous system, will elevate IOP. Tear ducts do not contribute to the drainage of aqueous humour.

6.8 Answer: b

Normally, IOP of the eye varies between 10 and 22 mmHg and is generally considered abnormal when >25 mmHg. This pressure is not static, as it can vary by 1 to 2 mmHg with each cardiac contraction. Diurnal variations of up to 5 mmHg also exist, with a higher pressure noted upon awakening.

6.9 Answer: d

Hypoventilation ($\uparrow PaCO_2$) along with hypoxaemia ($\downarrow PaO_2$) will result in increased IOP, whereas hyperventilation ($\downarrow PaCO_2$) will serve to minimize choroidal blood flow to decrease IOP. Hyperoxaemia ($\uparrow PaO_2$) does not affect IOP significantly.

6.10 Answer: b

Inhaled and injected anaesthetics (except for ketamine) along with opioids tend to lower IOP. Non-depolarizing muscle relaxants will decrease IOP, presumably via their relaxant effects on extra-ocular muscles. Hypoventilation ($\uparrow PaCO_2$) results in respiratory acidosis, which will increase IOP.

6.11 Answer: c

Although still quite rare, an increased incidence of malignant hyperthermia (MH) has been reported in patients with strabismus (underlying myopathy) such that a high index of suspicion should be maintained. $EtCO_2$ is considered the earliest indicator of a hypermetabolic state with unexpected increases in CO_2 despite constant minute ventilation. Avoiding known triggers can negate the risk of inducing MH, such that succinylcholine is not recommended during strabismus surgery involving infants and children.

6.12 Answer: a

Trigemino-vagal reflex: the afferent limb of the oculo-cardiac reflex is via the trigeminal nerve (CNV), primarily through the ophthalmic division (V1). The impulse travels along the long and short ciliary nerves (LCN and SCN) to synapse on the ciliary ganglion. The impulse then continues through the trigeminal ganglion arriving at the sensory nucleus of the trigeminal nerve. The convergence between the afferent and efferent limbs is at the motor nucleus of the vagus nerve (CN X) of the brain stem. From here, the efferent limb is via the vagus nerve, which eventually synapses on the sino-atrial node of the heart, resulting in an abrupt bradycardia.

6.13 Answer: c

The oculo-cardiac reflex (OCR) occurs frequently during strabismus surgery. It can occur following traction of the extrinsic eye muscles, or placement of pressure on the globe. The OCR is most commonly manifested as bradycardia, which regresses almost immediately after the stimulus is removed. Bigeminy, ectopy, nodal rhythms, atrioventricular block, and cardiac arrest have also occurred. Traction on any of the extra-ocular muscles can evoke this reflex, but it appears that manipulation of the medial rectus muscle is the most consistent trigger. Though the prophylactic use of an anticholinergic (atropine or glycopyrrolate) before the potential evoking stimulus may be recommended, the most effective treatment is the removal of the stimulus.

6.14 Answer: b

The afferent limb of the oculo-cardiac reflex (OCR) is the trigeminal nerve such that pressures on the globe, conjunctiva, or orbital structures and traction on the extra-ocular muscles are potential triggers. This reflex occurs even with an empty globe. Hypercarbia and hypoxemia are factors believed to augment the incidence and severity of the reflex. This reflex is noted to fatigue with repeated stimulation and is not suppressed by general anaesthesia.

6.15 Answer: d

The incidence of nausea and vomiting following strabismus surgery can be high, ranging anywhere from 48% to 85%. Minimizing the use of opioids, substituting propofol for inhaled anaesthetics, along with the prophylactic use of an antiemetic can reduce nausea and vomiting after surgery. Deep extubation has no impact on postoperative nausea and vomiting and may place patient at risk for aspiration.

6.16 Answer: a

Laryngospasm can complicate any routine airway management and is especially prevalent around the time of extubation. It often occurs during stage 2 — “excitement stage”—of general anaesthesia in combination with an airway irritant such as blood, mucus, laryngoscope blade, suction catheter, surgical debris, or other foreign objects. This protective reflex is mediated by the superior laryngeal nerve and manifested as sustained closure of the glottis. Laryngospasm with complete airway obstruction can be associated with negative pressure pulmonary oedema, as patients can create a significant amount of negative intrathoracic pressure during attempts to breathe against an obstructed upper airway. The management consists of positive pressure ventilation, increasing the depth of anaesthesia, and occasionally a small dose of a muscle relaxant with or without re-intubation.

6.17 Answer: a

Tracheal intubation to facilitate mechanical ventilation is common in ICU patients to appropriately manage failure of adequate spontaneous ventilation and/or oxygenation. Both nasal and oral tracheal

tubes are relatively safe, for at least several weeks, while patients convalesce. When compared with prolonged oral intubation, nasotracheal intubation may be more comfortable for the patient, more secure (fewer occurrences of accidental self-extubations), and less likely to cause laryngeal damage. Nasal intubation, however, has its own significant adverse events, including significant nasal bleeding, transient bacteraemia, sinusitis, and otitis media (from obstruction of the auditory tubes).

6.18 Answer: c

Recognizing the anatomical differences between an adult and a paediatric airway is important. One of the most obvious differences is the tongue itself. The paediatric tongue is larger, in relation to the amount of free space in the oropharynx, when compared to the adult tongue. With regards to the paediatric epiglottis, it tends to be large and floppy with a more oblong configuration, making epiglottis control with a laryngoscope blade more challenging. Additionally, the position of the adult larynx is at about the level C5–C6; the paediatric larynx is more cephalad, at about the level of the C3– C4. This is an important anatomical airway consideration, since the higher larynx tends to be more anterior as well.

6.19 Answer: a

Laryngospasm associated with airway manipulation is more likely to occur in the presence of a URTI such that surgery is typically postponed until resolution of symptoms, typically 1 to 2 weeks. Young children, however, have frequent URIs such that risk: benefit ratio should be considered when determining appropriateness of proceeding versus further postponement.

6.20 Answer: d

Haemorrhage from a bleeding tonsillar bed in the postoperative period is a hazardous complication. Her vitals reveal hypovolaemia and as such, initial management should be to resuscitate the patient prior to returning to the operating room to minimize morbidity associated with anaemia and hypovolaemia in the setting of repeat general anaesthesia. Also assume that patient will now have a difficult airway with a “full stomach.”

6.21 Answer: c

Anaesthesia during laser surgery may be administered with or without an endotracheal tube. If intubation is needed, appropriate laser-resistant endotracheal tubes should be utilized. In this regard, remember that all PVC tubes are flammable and can ignite when contacted by the laser beam. Using the laser intermittently, ventilating the patient with a low concentration of combustible gases, along with protecting adjacent tissues with saline-soaked sponges are all appropriate approaches to minimize the fire hazards.

6.22 Answer: d

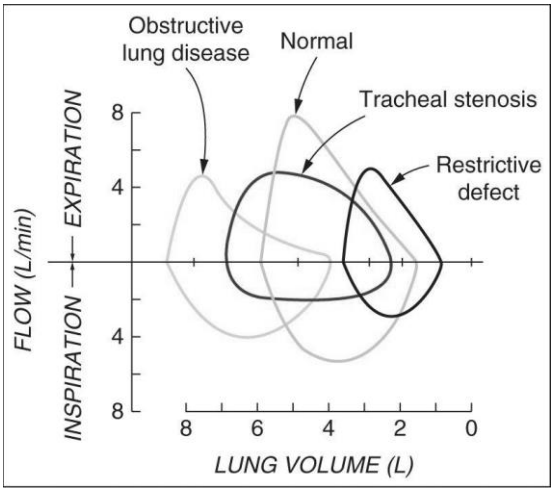
Airway fires are an inherent risk with laser surgery, such that a plan of action should be considered before the case begins. The cuff of the endotracheal tube may be filled with saline, as opposed to air, to minimize flammability should the laser beam rupture the cuff. Inspired oxygen concentration is minimized as tolerated (usually FiO_2 of <0.50), as oxygen readily supports combustion. In the event of an airway fire, the anaesthesia circuit should be immediately disconnected to interrupt further delivery of oxygen, followed by removal of the tube from the patient’s airway. If the flame persists, the field should next be flooded with normal saline.

6.23 Answer: b

Post airway fires, it is most appropriate to leave the patient intubated for continued observation as the presence of laryngeal and pharyngeal oedema can result in failed extubation. Therefore, this patient should be re-intubated with a regular endotracheal tube and monitored for the next 24 hours. Corticosteroids can be considered for severe oedema with absent cuff leak, but generally is not given prophylactically.

6.24 Answer: d

The configuration of the flow–volume curve during spirometry testing can be used to demonstrate abnormalities of the larger central airways (larynx, trachea, and main stem bronchi). The FEV_1/FVC ratio can provide diagnostic value, as disproportionate reduction in the FEV_1 as compared to the FVC is the hallmark of obstructive lung diseases. Concern should be made regarding airway collapse following sedation or induction of anaesthesia when extra thoracic lesions are present. If long-standing, tracheomalacia may leave the trachea weak and collapsible postoperatively.



6.25 Answer: a

Anaesthesia of the nasal mucosa and nasopharynx is achieved via blockade of trigeminal branches, particularly the sphenopalatine ganglion and ethmoid nerves. Blockade of the glossopharyngeal and superior laryngeal nerves provide anaesthesia to the mouth, oropharynx, and base of the tongue. The hypopharynx, larynx, and trachea are innervated via a branch of the vagus nerve (CN X), specifically the recurrent laryngeal nerve, which can be blocked via a trans-tracheal approach. On the other hand, blockade of the hypoglossal nerve (CN XII) will only serve to paralyze the intrinsic muscles of the tongue without adding to anaesthesia of the airway.

6.26 Answer: a

Inspection of the neck is generally considered the first step, as it may reveal a life-threatening and reversible cause of airway obstruction such as a compressing hematoma. Direct visualization of vocal cords may point toward recurrent laryngeal nerve damage contributing to dyspnoea. Though hypocalcaemia due to removal of the parathyroid glands can occur, signs and symptoms will usually present much later in the perioperative course (24–96 hours), and unlikely to be contributing to dyspnea in the PACU. Inhaled racemic epinephrine is commonly used when stridor is present after extubation.

6.27 Answer: b

The recurrent laryngeal nerves provide motor innervation to all the intrinsic muscles of the larynx, except the cricothyroid muscle, which is innervated by the superior laryngeal nerve. Damage to bilateral recurrent laryngeal nerves will affect abduction and adduction of the cords, resulting in both vocal cords adopting an intermediate, or paramedian, position. Patient would also have associated aphonia with risk of airway obstruction with inspiration as the cords flap together. Unilateral damage will present with hoarseness.

6.28 Answer: b

In the case of lesions to the SLNs, adduction and abduction of the vocal cords remain intact. SLN lesions instead lead to weak tensor strength (cricothyroid muscle), leaving the voice hoarse, weak, breathy, and with the inability to scream or shout. Other associated findings would be loss of sensation above the cords, leaving patient vulnerable to inhalation of any material present in the pharynx.

Domain 7: Paediatric anaesthesia

7.1 Answer: c

a. Amide local anesthetics are predominantly bound to plasma alpha$_1$-acid glycoprotein (AAG), and to a minor extent to albumin. The plasma concentration of AAG at birth is approximately 20–50 % of that in adults. During the first 6–9 months of life, it progressively increases to reach adult levels by the end of the first year.

b. Elimination is predominantly dependent on hepatic metabolic activity. The content of both CYP 1A2 and 3A4 is low in infants. Although CYP 3A7 is a major isozyme in the fetus that contributes to the biotransformation of bupivacaine, the clearance of both bupivacaine and ropivacaine is lower in younger children.

c. The volume of distribution is increased in Neonates. It does not play a significant role in Bupivacaine pharmacodynamics as the drug is largely protein-bound.

d. Bilirubin is also bound to plasma alpha$_1$-acid glycoprotein (AAG). Bupivacaine will displace bilirubin and can lead to kernicterus in infants with higher bilirubin levels.

7.2 Answer: a

a. Care should be taken to decrease peak inspiratory pressures when insufflation is terminated, as an unopposed high alveolar pressure will cause high transpulmonary pressures that will lead to lung parenchymal damage. ($P_{tp} = P_{alv} – P_{pl}$)

b. Listen for equal bilateral air entry after insufflation as endotracheal tubes can easily move into a mainstem bronchus with upwards shift of the diaphragm.

c. Minute ventilation must often be increased by up to 25-30% to maintain $ETCO_2$ at an acceptable level.

d. Neuromuscular blockade will decrease pressure with pneumoperitoneum, ease ventilation and improve visualization.

7.3 Answer: c

a. Historically, CDH repair was treated as a surgical emergency. However, the degree of pulmonary hypoplasia is the major influence on prognosis and emergency surgery therefore confers little benefit.

b. Protective lung ventilation should be practiced with small tidal volumes and higher respiratory rates. Permissive hypercapnoea should be practised. Lungs aren't merely compressed but severely underdeveloped and attempt to recruit lungs could cause severe barotrauma.

c. Inhaled nitric oxide should be available in theatre in case of suspected worsening pulmonary hypertension that does not respond to the usual measures of hyperventilation to reduce $PaCO_2$, increasing the FiO_2, management of acidosis, maintenance of adequate warming, and analgesia.

d. The patient will need to be transferred to the neonatal intensive care unit, fully ventilated with ongoing sedation. Compliance and gas exchange tend to deteriorate in the immediate postoperative period.

7.4 Answer: c

Craniosynostosis is frequently associated with craniofacial syndromes but airway management is not typically complicated. Bleeding can be profound and sudden, depending on the extent of the surgery. Blood should be ordered and in theatre prior to starting, and fluid management should be carefully considered. Where possible patients are extubated postoperatively so the neurosurgeons can perform neurological examinations.

7.5 Answer: c

While omphalocoele is associated with other abnormalities in greater than 70% of cases, gastroschisis rarely has other associations. The baby should be resuscitated, and surgery commenced as soon as feasibly possible.

source: BJA education: Exomphalos and gastrochisis 2009 vol 9 Issue 2 pg 48-51

7.6 Answer: c

There are several formulae for maximum allowable blood loss but the most frequently used is c. Approximate blood volumes in ml/kg are:

- Premature neonate: 90-100
- Term neonate: 85
- Infants: 80
- Children: 70-75

7.7 Answer: a

Macroglossia is common in Down Syndrome. Bag mask ventilation can be complicated, and an oropharyngeal airway is often required. Laryngoscopy is thereafter usually straightforward. Congenital subglottic stenosis occurs in less than 1% of cases.

7.8 Answer: d

Asleep extubation is safe as long a recovery is adequately trained and staffed. It may help prevent excessive coughing and subsequent bleeding.
Neurological side effects may be reversed, especially behavioural components.
Tonsils frequently complicate bag mask ventilation, but not intubation.

Chandrakantan, A et al. Pediatric Obstructive Sleep Apnea: Preoperative and Neurocognitive Considerations for Perioperative Management, Pediatric Anaesthesia, March 2020

Domain 8: Intensive care medicine

8.1 Answer: c

Augmented renal clearance is common among critically ill patients with an incidence of up to 80% during sepsis. Understanding augmented clearance has drastic implications for pharmacokinetics in the critically ill and might lead to significant underdosing of drugs for instance antibiotics. The amount of change and when this occurs is very unpredictable and therefore monitoring of levels have been advised.

8.2 Answer: b

Carbapenems are commonly prescribed for nosocomial infections. Ertapenem has a narrower spectrum of cover as compared to meropenem and imipenem. Most significantly it does not adequately cover P. Aeruginosa infections.

8.3 Answer: b

Spinal cord injury occurs in up to 10% of patients undergoing thoracic aortic aneurysm repair. Spinal cord injury is due to compromised perfusion. Perfusion concerns are due to decreased segmental arterial inflow, contributing to this is oedema, increased CSF pressure and decreased venous outflow. It has been advised that CSF drainage should be continued for at least 48 hours but up to 72 hours to maintain an adequate perfusion gradient of 60 mmHg.

Domain 9: Pain medicine

9.1 Answer: c

a. The Morphine dose is potentially too high for outpatient dosage, and Dexamethasone should be included if no contra-indication

b. Local infiltration of lignocaine is not recommended, and the Dexamethasone dose is too low (should be >0.1 mg/kg)

c. Once-off dose Gabapentin has been shown to decrease post-operative pain, nausea and opioid requirements, the Dexamethasone dose is correct and the Morphine dose reasonable

d. Once-off Ketamine has been shown to not be effective in reducing post-op pain.

BJA 2019 Aug; 123(2): e397–e411. Systematic review of analgesics and dexamethasone for post-tonsillectomy pain in adults; **H.K. Tolska**,1,∗ **K. Hamunen**,2 **A. Takala**,1,2 and **V.K. Kontinen**1

9.2 Answer: d

a. Being male doesn't increase risk (females have higher reported pain scores)

b. Substance use not specifically lined to persistent post-surgical pain

c. Male is not specifically a risk factor

d. All of these are correct.

Continuing Education in Anaesthesia Critical Care & Pain, Volume 15, Issue 2, April 2015, Pages 98–102
"Transition from acute to chronic pain " **A Feizerfan, FRCA**, **G Sheh, BHB MBChB FAFRM(RACP) FFPMANZCA**

9.3 Answer: a

a. Correct. Either technique is acceptable, and neither is contraindicated, so involving the parents and patient in the decision is appropriate

b. This is an acceptable technique, although performance in theatre isn't always necessary, it will depend on surgical anticipation of difficulty

c. Performing it under general anaesthesia would be an acceptable option but not necessarily better than under sedation

d. Performing a sedation in the ward is also acceptable, but not better than any of the other options.

SASA South African Acute Pain Guidelines, 2015

9.4 Answer: d

a. The Verbal Rating scale would be appropriate for the acute stump pain but does not adequately assess the phantom limb neuropathic pain

b. A Numeric Rating scale is used in similar context (acute pain) as the verbal rating scale, although not interchangeable

c. LANSS questionnaire is appropriate for assessing the phantom limb pain, but this patient is also complaining of stump pain which is of a more acute nature

d. Correct. Using both the VAS and LANSS questionnaire will enable assessment of both the acute stump pain component and the neuropathic phantom limb pain component of the patient's pain and both questionnaires can be employed to follow-up effectiveness of treatment.

"Assessment of acute and chronic pain"; Green L, Anaesthesia and Intensive Care Medicine 14:11,2013, p 488-490

9.5 Answer: a

a. CORRECT It is reasonable to continue Paracetamol, Ibuprofen and Tramadol as part of multimodal analgesia. IM Morphine is poorly absorbed but can't be abruptly stopped after a week, so PCA is a good way forward. Adding an NMDA antagonist is recommended for both acute stump pain and phantom limb pain, therefore Ketamine IVI PCA is a good option. Regional anaesthesia is the gold standard for treating stump pain. It also decreases the incidence of long-term phantom limb pain.

b. Changing to oral Morphine is not ideal since the patient already has uncontrolled pain with parenteral administration. Adding Intravenous Ketamine infusion is a good option, but since it cannot be continued long term, another agent (like Gabapentin) should be added. Amitryptilline has poor efficacy.

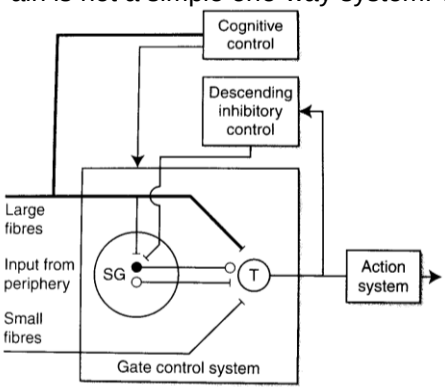
c. Regional anaesthesia is the gold standard treatment for acute stump pain and initial phantom limb pain, but central neuraxial block has not be shown to be more advantageous than perineural block and involves higher risk and more intense monitoring

d. IMI Morphine cannot be abruptly stopped after the patient has been receiving it 4 hourly for 7 days. Amytriptilline has not been shown to have efficacy in acute phantom limb pain, Gabapentin is a good choice, but it will be inadequate to acutely control the patient's pain.

"Pain after amputation"; Neil MJE; BJA Education, 2015, 1-6

9.6 Answer: c

Pain is not a simple one-way system. We like to think if it in terms of a biopsychosocial modal.



Pain is a complex perceptual experience, that together with conveying sensory information also has an intense emotional and cognitive feature. There are no pain fibers and no pain pathways only nociceptors that are stimulated and nociceptive pathways. The experience of pain is the result of processing of multiple complex information.
At any given time, ascending and descending information together with cognitive processes will determine the body's response to threat. Different pain modals have helped our evolved interpretation of nociception and nociceptive pathways.

9.7 Answer: d

Central sensitization is characterized by secondary hyperalgesia, allodynia and temporal summation because of the following:

i. A lowered firing threshold to innocuous or noxious stimuli
ii. Increased responsiveness to innocuous stimuli or noxious stimuli
iii. Increased receptor field size

9.8 Answer: b

A is incorrect as NMDA is a receptor and not a neurotransmitter.
C is incorrect as Nor-Adrenaline and Serotonin usually act as inhibitory neurotransmitters.
D is incorrect as opioids are inhibitory.

9.9 Answer: d

Regional anaesthesia is an excellent alternative in patients with opioid tolerance and provides great analgesia in the consented patient with safety measures taken.

9.10 Answer: a

B is incorrect as pregabalin is registered and approved for neuropathic pain
C is incorrect because it is not an alpha agonist
D is incorrect as it is not indicated for patients with opioid tolerance (this statement is for clonidine or dexmedetomidine)

Domains 11, 12 & 13: Education, self-directed learning and research; professionalism and ethics in practice; quality, safety, management & health economics

11.1 Answer: c

11.2 Answer: d

If they have the maturity to do so, children aged 12 or over may consent to medical treatment on their behalf and to surgical treatment with the assistance/ assent of a parent or guardian.

11.3 Answer: b

According to the Choice of Termination of Pregnancy Act - no specific age limit. The child must be able to give valid consent: meaning the child must have maturity and mental capacity to understand benefits, risk, social and other implications of the TOP.

11.4 Answer: d

a. Incorrect - controlled hypotension may only be considered if physiology allows.
b. Normothermia should always be maintained.
c. Autologous generally not acceptable – since blood is removed from the body and discontinued
d. Cell salvage may be acceptable to Jehovah's Witness patients – especially if the blood circulation remains in continuum.

11.5 Answer: d

10-14% of all doctors will become substance dependent over their lifetime; the incidence of anaesthetists being 2.7 times greater than other physician groups!

Any accusation of substance abuse must be taken seriously and handled professionally. Inform the nurse you will engage with the person/team who is responsible for 'wellness support' in your department (alternative SASA wellness support group) rather than first contacting HOD, anaesthetic colleagues or the colleague in question. The wellness support person/team will help facilitate a truthful investigation if in fact your colleague has a substance abuse and if so, will ensure properly conducted interventions in which irrefutable evidence is presented in a setting of care and concern for the individuals health and well-being. Anaesthetists with substance abuse who have been discovered are at risk for suicide.

https://www.hpcsa-blogs.co.za/assistance-for-impaired-professionals/
Burnett G, Fry RA, Bryson EO. Emerging worldwide trends in substances diverted for personal non-medical use by anaesthetists. BJA Education. 2020 Apr 1;20(4):114-9.

11.6 Answer: b

In fires within the proximity of oxygen, the priority is to stop the flow of oxygen to the field. This action is a priority. Attempts to suppress a fire without reducing the oxygen concentration is likely to be unsuccessful. The vast majority of cases reporting of fire during surgery have been performed in the head, neck or upper chest. Clinicians can reduce the risk of surgical fires by maintaining the local oxygen concentration at less than 30%!

Once a fire is identified, the following tasks should be performed almost simultaneously by all members of the operating room:

- Stop the flow of all airway gases and disconnect the breathing circuit (c).
    - For airway fires, remove the ETT and pour saline in the airway (d).
- Remove all burning and burned materials from the patient (e).
- Extinguish the fire on the burning material (a, b) – only rarely is a fire extinguisher needed.
- Care for the patient.
    - Restore breathing with room air.
    - Consider bronchoscopy if fire involved the airways.

Jones TS, Black IH, Robinson TN, Jones EL. Operating room fires. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2019 Mar 1;130(3):492-501.

11.7 Answer: a

b. Obligation to provide benefits and to balance benefits against risks
c. Obligation to avoid causing harm
d. Obligation of fairness in the distribution of benefits and risks

Farsides B. Respecting wishes and avoiding conflict: understanding the ethical basis for organ donation and retrieval. British journal of anaesthesia. 2012 Jan 1;108(suppl_1):i73-9.

11.8 Answer: a

a. The fragment must be identified and removed from the airway before initiating surgery as aspiration of the fragment into the lower airway could be life-threatening. On the table x-rays may help identify location of fragment(s). Once retrieved, the fragment must be stored in either sterile saline, milk or tissue culture medium.

b. No antibiotics will be required for a dental fracture, although they are sometimes recommended after re-implantation of avulsed teeth. Tetanus booster is only required if an avulsed tooth contacted potentially contaminating external material.

c. Postponing surgery would not be your primary concern but could possibly be a consideration if a large fragment could not be identified despite laryngoscopy, x-rays and help from senior colleagues.

d. This is not your first priority; however, a dental review will determine the degree of damage and suitability for treatment including bonding, if possible while patient is an in-patient. Detailed anaesthetic notes describing the incident and actions taken is mandatory. While information of risk of dental injury should be part of informed consent, such an incident must be accompanied by an apology from the anaesthetist.

Hewson DW, Hardman JG. Physical injuries during anaesthesia. BJA Education. 2018 Oct 1;18(10):310-6.

11.9 Answer: c

a. Very low-quality evidence shows that the perioperative discontinuation of methotrexate might be harmful or have no effect on the risk of SSI compared to its continuation.

b. It's good clinical practice for patients to bathe or shower prior to surgery to reduce the bacterial load, however, there is no evidence that antimicrobial soap is superior to plain soap so either may be used for the purpose.

c. Strong recommendation based on moderate quality evidence supports administration of antibiotics within 120 minutes before incision. Actual timing of administration of antibiotics is poorly investigated but there is consensus that one should aim to ensure adequate tissue concentration of the antibiotics at the time of incision and throughout the procedure. For TJA, where either cefazoline/cefuroxime or clindamycin are most commonly used, antibiotics should be administered within 60 minutes prior to skin incision.

d. Very low-quality evidence shows that in total joint replacement, laminar airflow ventilation has no benefit when compared to conventional ventilation in reducing SSI rate.

https://www.who.int/infection-prevention/publications/ssi-prevention-guidelines/en/

11.10 Answer: a

a. EBM may provide good predictive data but cannot account for a patient's individual preferences and value-system. Strong statistical evidence that a specific treatment prolongs life (e.g. in cancer) does not necessarily translate into increased quality of life.

b. Expert opinion is superior at addressing patient values, but is only one of many modalities used in medical ethics and jurisprudence

c. This simply describes the method by which much of EBM works—translating large data sets into relevant information that can be used to guide clinical practice.

d. This is not necessarily an ethical issue—this distractor highlights that a clinician's "hunches" or insights may sometimes differ from the established evidence and that examining both the evidence and opinion is still sound practice.

https://journalofethics.ama-assn.org/article/limitations-evidence-based-medicine-applying-population-based-recommendations-individual-patients/2011-01

11.11 Answer: b

a. The older "multiple true/false" form of the MCQ did not stipulate a "best" answer, as such, it is easier for candidates to work out the correct answer by a process of elimination. However, most MCQ papers still use a combination of the two.

b. The single best answer (SBA) form of multiple-choice questions is recognised as being superior in assessing higher levels of knowledge, suitable at university level, because distractors are designed as plausible alternatives. As such, candidates are less likely to "guess" the correct answer by looking for obvious wrong answers

c. The OSPE is better at assessing practical skills and clinical practice

d. Classic True/False questions are very underpowered at assessing knowledge and represent a coin toss (50/50) odds of being correct. Using these would decrease the effectivity of the assessment tool/test.

https://www.clinicaloncologyonline.net/article/S0936-6555(08)00261-6/fulltext

11.12 Answer: c

a. This describes a doctor being a role model, but not necessarily a health advocate.

b. Activism is a political act. Health advocacy does not necessary imply political involvement, or pronouncements on the funding of healthcare systems.

c. Improving health of individuals is not limited to mitigating illness or trauma, but also involves promoting health equity, whereby individuals and populations reach their full health potential without being disadvantaged by, for example, race, ethnicity, religion, gender, sexual orientation, age, social class, economic status, or level of education.

d. This describes a tool appropriate for use in health advocacy but is not an example of advocacy itself.

http://canmeds.royalcollege.ca/uploads/en/framework/CanMEDS%202015%20Framework_EN_Reduced.pdf