PART II ANAESTHESIA REFRESHER COURSE

2019

DEPARTMENT OF ANAESTHESIA
AND PERIOPERATIVE MEDICINE
UNIVERSITY OF CAPE TOWN

ACKNOWLEDGEMENTS

The committee extends its sincere gratitude to the following companies for their generous financial assistance:

- Adcock Ingram
- Fresenius Kabi
- Intersurgical RSA (Pty) Ltd
- Medhold Trade
- Mundi Pharma
- Pharma Dynamics
- Safeline Pharmaceuticals
- SSEM Mthembu Medical
- Teleflex Medical (Pty) Ltd
- Viking Critical Care

Special thanks go to Adcock Ingram **for sponsoring the production of this book.**

COMMITTEE

Prof J Swanevelder	-	Head of Department
Dr M Nejthardt	-	Chairman/ Programme/ Trade
Dr R Llewellyn	-	Treasurer
Mrs Z Carlse	-	Secretary
Dr R Duys	-	Educational input/ Programme
Dr R Haylett	-	Programme/ Book compilation
Dr M Miller	-	Committee member
Dr K Timmerman	-	Website/ Printing
Dr D van Dyk		Programme/ Book compilation

This course is held under the auspices of, and supported by, the

Colleges of Medicine of South Africa

Index of lectures

01.	***Acute Ischaemic Stroke- Implications for anaesthesia in 2019***	*Dr Kerry Timmerman*
02.	***Thoracic Surgery- Lung Resection***	*Dr Ollie Smith*
03.	**Liver Resection**	*Dr Ollie Smith*
04.	**Consent**	*Dr Gareth Davies*
05.	**Cardiopulmonary Bypass**	*Professor Justiaan Swanevelder*
06.	**Anticoagulation & Bridging in Obstetric Anaesthesia**	*Dr Dominique van Dyk*
07.	**The Anaesthetist's Role in Metabolic Surgery**	*Dr Leon du Toit*
08.	**Ventilation- From the OR to ICU and back**	*Dr Ollie Smith*
09.	**Metabolic syndrome controversies**	*Dr Estie Cloete*
10.	**Cardiac Risk Mitigation for Non-cardiac Surgery**	*Dr Christella Alphonsus*
11.	**Perioperative Acute Kidney Injury**	*Dr Ollie Smith*
12.	**The How and Why of Awake Craniotomy**	*Dr Brigid Brennan*
13.	**Antibiotics**	*Dr Jenna piercy*
14.	**Anaesthesia for Tracheal Resection**	*Dr Richard Llewellyn*
15.	**Anaesthesia for Shoulder Surgery**	*Dr Felipe Montoya-Pelaez*
16.	**Haemodynamic Monitoring- Assessing fluid responsiveness**	*Dr Malcolm Miller*
17.	**Anaesthesia for the Patient with Traumatic Brain Injury**	*Drs Anthony Reed & Karen van der Spuy*
18.	**Care of the Organ Donor**	*Dr Adri Vorster*
19.	**Anaesthesia in Patients with Platelet and Inherited Coagulation Disorders**	*Dr Graeme Wilson*
20.	**MINS - Myocardial Injury after Non-cardiac Surgery**	*Dr Marcelle Jagga*
21.	**ERAS – Enhanced Recovery After Surgery**	*Dr Matthew Gibbs*
22.	**Anaesthetic and Perioperative Management of Severe Preeclampsia**	*Professor Robert Dyer*
23.	**Major Obstetric Haemorrhage- Implications for anaesthesia**	*Dr Rowan Duys*
24.	**The Impaired Practitioner**	*Dr Adalbert Ernst*
25.	**Perioperative Management of Total Hip and Knee Arthroplasty Patients**	*Dr Ulla Plenge*
26.	**Anaesthesia for Scoliosis Surgery**	*Dr Noshina Khan*
27.	**Update on the Management of Predicted Difficult Airways**	*Professor Ross Hofmeyr*
28.	**Perioperative Analgesia in Children Recent Controversies**	*Dr Karmen Kep*
29.	**Quality Improvement**	*Dr Gareth Kantor*
30.	**Pain workshop**	*Drs Janieke van Nugteren, Rowan Duys, Tory Madden, Prof Romy Parker*
31.	**Paper 3 questions**	*Drs Ettienne Coetzee, Adriaan Myburgh, Alma de Vaal, Mariesa Nock & Nicole Fernandes*
32.	**SBA questions**	*UCT specialist anaesthetists*
33.	**SBA answers**	*UCT specialist anaesthetists*

Acute Ischaemic Stroke
Implications for anaesthesia in 2019

Dr Kerry Timmerman

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Acute ischaemic stroke (AIS) was covered in detail in the 2016 UCT Anaesthetic Refresher Course, so I urge you to read that in conjunction with these updated notes.

This lecture aims to build on the controversies facing anaesthetists when managing patients with AIS presenting for mechanical thrombectomy in specialised centres equipped with interventional neuroradiology suites.

What we already know about AIS:

1. We know that stroke is a leading cause of death and disability worldwide, with massive associated economic burden. In South Africa, stroke is responsible for about 25 000 deaths annually.

2. When it comes to pathophysiology, we know that acute ischaemic stroke (AIS) accounts for around 60 to 80% of strokes. The remainder are haemorrhagic (either intracranial or subarachnoid bleeds). Reperfusion of the fragile ischaemic penumbra within a critical time frame can significantly improve functional outcome; “time is brain”. Reperfusion of infarcted tissue may however be complicated by haemorrhage into the affected area.

3. We also know that, in select suitable cases of proximal large-vessel occlusion (terminal internal carotid, middle cerebral and anterior cerebral arteries), reperfusion is most successfully achieved by intra-arterial mechanical clot retrieval or endovascular thrombectomy (EVT) which aims to rapidly reperfuse the affected ischaemic brain by removing clot from cerebral vessels. In 2016 the HERMES meta-analysis of 5 randomised trials (Highly Effective Reperfusion Evaluated Multiple Endovascular Stroke Trials) confirmed the impressive efficacy of thrombectomy for patients with AIS caused by occlusion of proximal anterior circulation, irrespective of patient characteristics or geographical location. To summarise the treatment benefits of this meta-analysis: outcomes with thrombectomy are far better than what was seen with best medical therapy alone (intravenous thrombolysis), with the number needed to treat (NNT) to reduce disability by at least 1 point on the modified Rankin scale (mRS) being 2.6; and increases in functional independence of between 19 and 35%. The best results occurred if the clot was retrieved within 6 hours of symptom onset.
   Subsequent RCTs have further confirmed benefit, namely THRACE (mechanical thrombectomy after intravenous alteplase versus alteplase alone alone after stroke), THERAPY (The Randomized, Concurrent Controlled Trial to Assess the Penumbra System’s Safety and Effectiveness in the Treatment of Acute Stroke), PISTE (Pragmatic Ischemic Stroke Thrombectomy Evaluation), and EASI (Endovascular Acute Stroke Intervention). All this information has led to updated practice guidelines in countries such as the USA, Canada, Europe and the UK.

   Inclusion criteria for mechanical thrombectomy based current evidence include:
   - Patients of all ages with anterior circulation stroke
   - Presentation <6 h of symptom onset
   - Inadequate response or contraindications to intravenous thrombolysis
   - Proximal vessel occlusion (internal carotid/M1/M2 segments of MCA) on imaging
   - No new ischaemic changes present on CT/MRI brain
   - Significant new disability (NIHSS>5) ***Appendix A***
   - Previously independent in ADL (mRS<3) ***Appendix A***

   A select group of patients benefit from thrombectomy after 6 hours as evidenced by the DAWN trial. This was a prospective, multicenter RCT comparing mechanical thrombectomy *and* medical treatment with medical treatment alone. In cases of delayed presentation, or in

cases where patients wake up with a stroke, advanced imaging may help determine who might benefit from thrombectomy up to 24 hours after AIS.

What mechanical thrombectomy entails:

For mechanical thrombectomy to be an effective therapeutic option for AIS, systems must be in place to expedite both assessment and intervention. Patients need to get to the correct facilities within the recommended time frames for maximum benefit. This requires streamlined co-ordination of services, including early assessment, appropriate baseline diagnostics and management, and timeous transfer to stroke centres.
After diagnosis of acute ischaemic stroke, intravenous thrombolysis (alteplase) should be administered within 4,5 hours in eligible patients. The actual thrombectomy procedure is then carried out in an adequately equipped neuroradiology suite within 6 hours after careful selection by stroke neurologists or physicians. Vascular access is usually via the femoral artery, from where a guidewire is passed into the internal carotid artery. A device of choice is then navigated to the affected artery in the brain to extract the clot. With the ongoing development of more effective devices, vessels can be successfully reopened in up to 85% of patients.

Mechanical thrombectomy is not without risk, but luckily complications are infrequent in experienced hands. Most radiology suites are remote from operating theatres, which poses additional logistical problems.

Anaesthesia for mechanical thrombectomy in 2019:

1. Sedation versus general anaesthesia for mechanical thrombectomy

This is a topic of ongoing debate. Unfortunately, current available data are not yet strong enough to clearly guide anaesthetic management.

- Early consensus based on retrospective reviews reported that outcomes were worse following general anaesthesia (GA) for thrombectomy. The problem with these reviews was that there was little consensus on what actually constituted general anaesthesia for these cases, and there was no standardization of anaesthetic technique. Selection bias also complicated the picture with sicker patients, having suffered more severe strokes, most often receiving GA. Unfortunately, poorer outcomes in these sicker patients was interpreted to mean that GA was harmful.
  A meta-analysis of 7 RCT's published by Campbell in 2018 found that patients do worse under GA, maintaining that GA should be avoided whenever possible. Again, evidence mostly came from studies not primarily designed to answer the GA vs sedation question. This meta-analysis did not include data from any of the three randomized controlled trials discussed below.
- Three recent prospective randomized controlled studies have shown no differences in outcomes between sedation and GA, or a tendency to better outcomes with GA.
  - The Sedation vs Intubation for Endovascular Stroke Treatment (SIESTA) trial in 2016 failed to show an advantage of conscious sedation over GA, with long term outcome at 90 days in favour of GA;
  - The Anaesthesia During Stroke (AnStroke) trial in 2017 randomized patients to standardized GA or sedation with strict haemodynamic control, normal ventilation and normoglycaemia. There were no differences in early neurological recovery, infarct volume, or anaesthetic or neurointerventional complications.
  - Published in 2016, the General Or Local Anaesthesia in IntraArterial Therapy (GOLIATH) study randomized patients in a similar fashion to the AnStroke trial, and found no difference in infarct volume size, but a trend towards better outcomes in the GA group.
- The bottom line is, regardless of what is best, GA is often unavoidable in certain circumstances including restless patients, failed sedation, excessive sedation, threatened airway, or low GCS. As such, anaesthetists should know how to optimally provide either sedation or GA for patients presenting for thrombectomy for AIS, and pay careful attention to all the many variables (discussed below) which may impact on patient outcome.

The latest recommendation from the AHA and American Stroke Association is that it is reasonable to select an anaesthetic technique based on an individualized assessment of patient risk factors, as well as technical performance of the procedure.

General anaesthesia	**Local anaesthesia**
Pros: • Immobility • Pain control • Airway protection	Pros: • Smoother haemodynamics • Neurological examination during procedure
Cons: • Haemodynamic changes • Additional workforce • Potential time delay	Cons: • Lack of airway protection • Potential for movement • Uncontrolled pain and agitation • Prolonged procedure time

Table: pros and cons of general anaesthesia and local anaesthesia for thrombectomy for AIS

2.Optimal care under sedation or general anaesthesia for thrombectomy

Remember that preoperative assessment needs to be focused and there is little time to request additional tests. This is all covered in the 2016 lecture.

- **Local anaesthesia and Sedation**

If patients are extremely co-operative, then the procedure may be done under local anaesthesia alone, but groin puncture, contrast injection, and clot retrieval may be painful and require small doses of intravenous fentanyl (25ug boluses as required).
Sedation can be tricky in an already neurologically compromised patient, combined with the fact that the airway (and entire patient) is relatively inaccessible. There is a fine line between oversedation and undersedation, and the possibility of stroke evolution during the procedure can change the clinical picture rapidly and significantly.
The use of short-acting agents that provide sedation and analgesia would be favourable, such as target controlled infusions of remifentanil and propofol, or dexmedetomidine.
Intraprocedural conversion to GA is associated with significantly worse outcome. It is argued that a skilled anaesthetist should administer sedation for all thrombectomy cases.

- **General anaesthesia**

There is no single “anaesthetic” for AIS, and there is currently no evidence to support one agent over another. The use of institutional protocols can help deliver safe care within the limited time frame available to maximize outcome.
All patients receiving GA should be intubated for the procedure (RSI if any doubt about starvation status). Suitable options for anaesthesia include target controlled infusions of propofol and remifentanil, or inhalational agents. Regardless of the type of agents used for GA, the key is maintaining physiological targets. Research suggestions include the following:

- *Blood pressure control*
  - It is probably safe to target SBP 140-180mmHg, or <10% decrease in MAP from baseline.
  - There is currently no consensus on agents used to control BP.
  - Remember the BP may surge up significantly with intubation (increasing the risk of haemorrhagic transformation), or drop precipitously after induction (with significant risk of further reducing perfusion to the critically ischaemic penumbra), and you should be prepared for both hyper- and hypotension.
  - BP control is further complicated by the lack of understanding of the influence of recanalization on cerebral autoregulation – most likely there is loss of cerebral autoregulation in the territory of the affected vessel, and blood flow is therefore pressure passive with increased risk of haemorrhagic complications with uncontrolled hypertension.

- *Respiratory control*
  - Maintain saturation >94%
  - Currently no evidence for hyperoxia
  - Maintain $PaCO_2$ 4,5-5kPa
  - There is also a paucity of information about the effect of PaO_2 and $PaCO_2$ on vascular tone in the affected vascular bed

- *Temperature control*
  - Maintain normothermia
  - Currently no evidence for cooling

- *Glucose control*
  - Maintain normoglycaemia (7,8-10 mmol/l)
  - Hyper- and hypoglycaemia are detrimental

- *Monitoring*
  - Standard of care for general anaesthesia is ECG, pulse oximetry, end tidal CO_2 and intra-arterial BP monitoring.
  - Do not delay the procedure to place a difficult arterial line as, although it is preferable to have it in situ to monitor and control BP at induction, we do not want to unnecessarily delay reperfusion. Measurements can be obtained from the femoral sheath once inserted by the interventional neuroradiologists if necessary.
  - There is currently no evidence for neurological monitoring.

3.Intra-procedural anticoagulation

There is currently no consensus on intra-procedural anticoagulation. Some centers will ask for a single dose of heparin to minimalise the risk of catheter-related embolism. If a stent is going to be deployed and left in-situ, then dual antiplatelet therapy will likely be needed for 3 to 6 months after the procedure, but there is no consensus on when to start as it may increase the chance of haemorrhagic transformation. All patients will be started on aspirin within 24-48 hours after the procedure.

4.Post-operative care

No specific data exists regarding patient management following thrombectomy. What is certain is that all patients need input from a specialized multidisciplinary stroke team. Placement would be guided by institutional protocol and patient condition.
What is important is:

- Haemodynamic and neurological monitoring, particularly for haemorrhagic transformation of the infarcted tissue
- BP control after reperfusion – it is suggested to maintain BP <180/105. Again, no specific agents are advocated and use would be based on local preference, protocol and availability. Reasonable options for BP control include labetalol, nicardipine, and nitroprusside.
- Pain management (groin pain and/or headache are common) – simple analgesics usually suffice
- Commencement of aspirin
- Initiation of secondary prevention and rehabilitation

To end off:

Mechanical thrombectomy is changing the face of AIS globally. Thrombectomy centres require immediate access to interventional neuroradiologists, anaesthetists, skilled anaesthetic support, appropriately trained nurses, and radiographers. Practical implementation of 24/7 thrombectomy services presents many challenges, and has certainly placed strain on our already overburdened emergency anaesthesia service at GSH. What is clear is that comprehensive stroke units with appropriate referral pathways are essential to improve patient outcomes.

Specific anaesthetic concerns include time-dependent provision of sedation or anaesthesia to often critically ill patients at a remote location by an adequately experienced anaesthetist. It is crucial that anaesthetists involved in sedation or anaesthesia for these cases pay careful attention to physiologic targets to help optimize patient outcome, acting as part of a multidisciplinary team.

APPENDIX A

The National Institutes of Health Stroke Scale (NIHSS) is a systematic assessment tool that provides a quantitative measure of stroke-related neurologic deficit. The NIHSS was originally designed as a research tool to measure baseline data on patients in acute stroke clinical trials. Now, the scale is also widely used as a clinical assessment tool to evaluate acuity of stroke patients, determine appropriate treatment, and predict patient outcome. The scale is designed to be a simple, valid, and reliable tool that can be administered at the bedside consistently by physicians, nurses or therapists. The NIHSS is composed of 11 items and is used to evaluate the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss. A trained observer rates the patent's ability to answer questions and perform activities. Ratings for each item are scored with 3 to 5 grades with 0 as normal, and there is an allowance for untestable items. The single patient assessment requires less than 10 minutes to complete.

For a comprehensive copy of the NIHSS go to ninds.nih.gov/doctors/NIH_Stroke_Scale.pdf

Score [3]	Stroke Severity
0	No Stroke Symptoms
1-4	Minor Stroke
5-15	Moderate Stroke
16-20	Moderate to Severe Stroke
21-42	Severe Stroke

The Modified Rankin Scale (mRS) is used for measuring the degree of disability or dependence following stroke.
The scale runs from 0-6, running from perfect health without symptoms to death.

- 0 - No symptoms.
- 1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3 - Moderate disability. Requires some help, but able to walk unassisted.
- 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- 6 - Dead.

References

1. J Dinsmore, M Elwishi, P Kailainathan. Anaesthesia for endovascular thrombectomy. BJA Education 2018; vol 18, No 10: 291-299
2. Venema AM, Uyttenboogaart M, Absalom AR. Land of confusion: anaesthetic management during thrombectomy for acute ischaemic stroke. *British Journal of Anaesthesia*, 2019, 22 (3): 300-304
3. Taylor A, le Feuvre D, et al. Advances in stroke treatment are within reach. *SAMJ* 1026;106(5):454-455
4. Taylor A. Evolving concepts of stroke and stroke management in South Africa: Quo vadis? SAMJ 2019, Vol 109, No. 2
5. M Goyal, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomized trials. Lancet 2016; 387: 1723-31 (HERMES meta-analysis)
6. Harrichandparsad R. Mechanical thrombectomy for acute ischaemic stroke. *SAMJ* 2019, Vol. 109, No. 2
7. Nogueira RG, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378(1): 11-21 (DAWN trial)
8. Campbell BC, et al. Endovascular stent thrombectomy: The new standard of care for large vessel ischaemic stroke. *Lancet Neurol* 2015; 14(8):846-854
9. Schonenberger S, et al. Effect of conscious sedation vs general anaesthesia on early neurological improvement among patients with ischaemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. JAMA 2016; 316: 1986-96
   (SIESTA)
10. Lowhagen Henden PL, et al. General anaesthesia versus conscious sedation for endovascular treatment of acute ischaemic stroke: The AnStroke trial (anaesthesia during stroke). *Stroke* 2017;48(6):1601-1607
11. Simonsen CZ, et al. Anaesthetic strategy during endovascular therapy: General anaesthesia or conscious sedation? (GOLIATH – general or local anaesthesia in intra arterial therapy) A single-center randomized trial. Int J Stroke 2016;11(9):1045-1052
12. Powers WJ, et al. 2018 Guidelines for the early management of patients with acute ischaemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2018; 49: e1-65

Thoracic Surgery
Lung resection

Dr Ollie Smith

Department of Anaesthesia
Charlotte Maxeke Johannesburg Academic Hospital

Introduction

This note is not designed to be a re-publication of existing work, but rather to point out some of the areas of controversy and maybe clarify some misunderstandings.

Patients presenting for lung resection (lobectomy, bi-lobectomy, pneumonectomy and wedge resections) can broadly speaking be divided into either oncological (primary and secondary) and non-oncological (bronchiectasis, abscess, mycetoma, hydatid, haemoptysis, etc)

There are often marked physiological differences between the two groups. While there may be a greater preponderance of the infective type in our local population, data from North America and Europe shows that lung cancer is one of their leading causes of death. With a growing smoking population in Africa- this will become a greater reality for us too. This particular patient phenotype has likely got other smoking related morbidity: COPD, IHD etc. We therefore contemplate surgical resection in patients with abnormal underlying lung function and other cardiovascular disease placing them at increased risk for perioperative morbidity and mortality.

For the majority of these patients, the surgical resection, with or without adjuvant therapy, represents their greatest chance of cure…this fact must not be taken lightly. With the greatest morbidity and mortality related to pulmonary and cardiovascular events, the question has always been how to decide who can be safely resected, with reasonable balancing of the risk of perioperative morbidity/ mortality vs overall survival. The trick then is to find the limit of pulmonary function where the risk of resection is prohibitive in order to provide the best chance for as many patients as possible. As simple as this sounds, their risk assessment remains complex

Preoperative evaluation and preparation is thus the cornerstone of a good program.
Risk to the patient is not only for short-term perioperative morbidity and mortality relating to cardiopulmonary complications, and long-term pulmonary disability - but balanced against risk of reduced survival if a suboptimal oncological treatment plan is provided. Our task is thus to identify the patients at increased risk of both the short and long term complications.

Preoperative evaluation

It is important to remember that these patients are being evaluated by a multidisciplinary team consisting of physician/pulmonologist, thoracic surgeon, oncologist/radiation oncologist and anaesthetist. This must put into perspective, that risk in the marginal candidate has been considered by others, as well as alternative treatment options, and outcomes before presentation for surgical resection. Anaesthetists do not hold the sole rights to patient safety advocacy… the whole team is invested in a good outcome.

It is no surprise then that there is an improved quality of care and survival benefit in patients managed in such a multidisciplinary team (ranging from improved outcome in some cohorts, to increased resection rates in other cohorts, without increased mortality)

Always discuss your patient within the team!

Traditional risk factors to consider:

1) Age
2) Nutritional state
3) Smoking
4) CVS comorbidity

5) Pulmonary mechanics
6) Gas exchange
7) Exercise capacity

The last 3 being the most investigated and used in the assessment of suitability. All 3 should always be considered together

Pulmonary mechanics

Assessment of pulmonary mechanics in the form of spirometry (FEV1 and in particular predicted post operative FEV1) has been the mainstay of assessment. There is a good body of evidence showing that reduced FEV1 and ppoFEV1 are associated with poorer outcome, with a preoperative FEV 1 < 60% predicted being associated with increased risk of perioperative complications. How poor the outcome relative to the reduction has been the subject of debate and research dating back to the 1950's.

There are a few threshold values often reported

FEV1 > 2L (>80% predicted): generally suitable for anatomical resection up to pneumonectomy
FEV1 > 1.5L: generally suitable for lobectomy

These on their own should not be used as the sole discriminators for success. Current recommendations from the major societies (BTS/ ERS/ ESTS/ ACCP) are in rough agreement as to a reasonable approach.

Always consider the lung volume to be resected and its contribution to overall function. Also consider the worst-case scenario - will the same patient tolerate extension of procedure to bi-lobectomy or pneumonectomy if the situation arises?

It is important to assess every patient adequately. Calculate the ppoFEV1.

For pneumonectomy this is based on consideration of the perfused fraction of the lung to be resected (calculated based on the VQ scan)

ppoFEV1 = preoperative FEV1 x (1 – fraction of total perfusion in the resected lung)

For lobectomy this is based on the anatomical method (usually 19 segments)

There are 10 bronchopulmonary segments in the right lung (3 in upper lobe, 2 in middle lobe, 5 in lower lobe) and 9 segments on the left (4 in upper lobe, 5 in lower lobe).

$$\text{ppoFEV1} = \text{FEV1} \times \left(1 - \frac{\text{functional segments to be removed}}{\text{(total no of functional segments)}}\right)$$

Patients can then be divided into 3 groups based on the results:

ppoFEV1 >60% (of predicted preoperative FEV1)
ppoFEV1 30% - 60% predicted
ppoFEV1 <30% predicted

Gas exchange

Resting blood gas: traditionally a resting $PaCO_2$ of >45mmHg/ 6kPa has been considered an exclusion criteria for resection. There are numerous case series that have shown no increased mortality with hypercapnia, and very little to show it is an independent risk factor. In some cases it may be that the presence of hypercapnia is a contraindication, but this is usually in conjunction with a markedly reduced FEV1.

Measurement of DLCO has an equal, if not greater predictive value than the FEV1 in terms of predicting morbidity, mortality, long-term survival and quality of life. Correlation between DLCO and the FEV1 has not proved to be great, but each has predictive value in outcome. DLCO is important to

measure as there are a subset of patients with FEV1 >80% with significantly reduced DLCO, which is then a strong predictor of complications.

As such there is consensus that DLCO is to be measured in all patients, irrespective of the FEV1.

These are then converted into ppoDLCO values using the same above equations.

Once again 3 groups result:

ppoDLCO >60% (of predicted preoperative DLCO)
ppoDLCO 30% - 60% predicted
ppoDLCO <30% predicted

Exercise Capacity

This represents a comprehensive physiologic test as it is dependent on the interaction between lungs and CVS for delivery of O_2 as well as utilization by peripheral tissues. Testing ranges from low tech (stair climbing/ISWT/6min walk test) to formal CPET testing (treadmill/Cycle/arm ergometer)

VO_2 peak as measured in formal CPET testing has consistently shown good correlation with outcome and complications at the extremes, but becomes difficult to interpret as we approach the lower limits. Part of the reason for this is the lack of robust datasets taken from large population groups, and hence insufficient data to generate ROC curves for VO_2 and morbidity/ mortality in this group. Based on the VO_2 these patients are grouped as follows:

Low Risk: VO_2 >20ml/kg/min (>75% predicted) unsurprisingly is associated in all cohorts with very low morbidity and mortality for any type of resection

Very High Risk: VO_2 <10ml/kg/min (<35% predicted) is consistently associated with very high perioperative complication rate and mortality for anatomical resections via thoracotomy! Many would consider risk here to be prohibitive for anatomical resection and another treatment plan should be formulated.

Moderate risk: VO_2 10 - 20ml/kg/min- considered moderate risk, however the variation in individual risk within their group is massive, with VO_2 <12ml/kg/min reported in some series to have mortalities in excess of 15%.

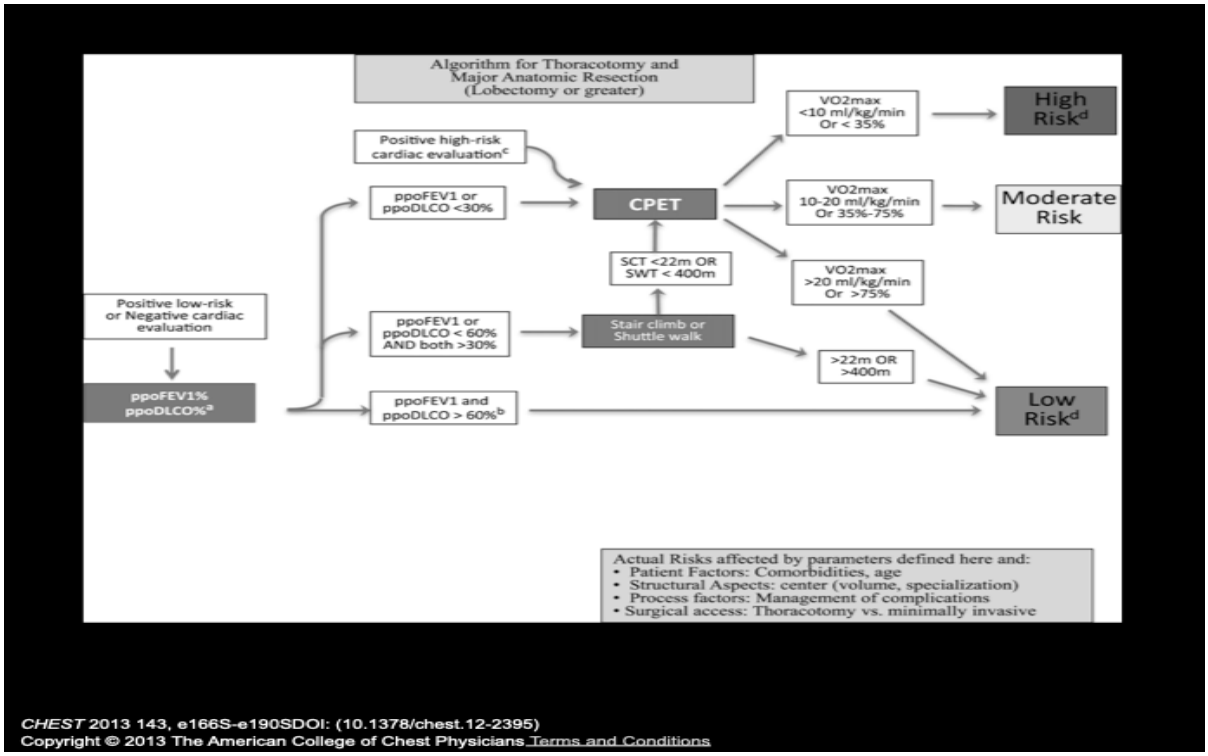
Realistically this group should be divided into 15-20ml/kg/min in whom the risk is relatively low, and a 10-15ml/kg/min group where there is significant but not prohibitive risk.

While there is definite agreement across the big pond between societies that exercise testing is essential in the workup- there is a difference in the timing and utilization of testing in the workup. My preference for simplicity is the ACCP functional approach.

Stair climbing - the altitude achieved, has a reasonably good correlation with VO_2peak. Vertical height of greater than 22m (>7 flights) correlates well with a VO_2>15ml/kg/min, whereas <12m (3 flights) was accompanied by a 50% complication rate and 10-20% mortality for open anatomical resection.

Similarly the SWT: > 25 shuttles and distance >400m correlates with a VO_2 peak > 15ml/kg/min.

The algorithm below from the ACCP is a neat and logical integration of the discussed tests.



There has been some recent work suggesting that ppoVO_2 <10ml/kg/min (<35% predicated) may be the lower limit threshold in terms of risk for anatomical resections. It is a neat concept, and so far seems to predict the highest risk group.

Where a patient has ppoFEV1 and ppoDLCO results that fall within two groups the lower of the two should be used to risk stratify i.e. ppoFEV1 >60% but ppoDLCO 35%.

Scoring systems

A brief note on this: Many composite scoring systems have been proposed in the past (some even included into national body guidelines); however, their predictive power for post operative complications remains poor and adds little to the physiological components already considered. Examples of these are the THORACOSCORE and the ESOS score.

One area that must however be considered is the patients risk of MACE. The group of patients presenting for oncological resection are generally older, have more advanced underlying comorbidity, smoking related illness, and a significantly higher cardiac risk. Equally, the procedures that they will undergo, place them at higher risk than the traditional RCRI can predict. While previous versions of the guidelines have recommended the RCRI score, some more recent work has proposed a modification called the ThRCRI (thoracic RCRI) which is a minor modification and recalibration of the RCRI (which tends to underestimate the risk of MACE).

The important consideration here is the higher risk of MACE and hence due consideration must be given to appropriate evaluation of the CVS and monitoring post op.

The score is composed of 4 components:

- IHD - 1.5 points
- Cerebrovascular disease - 1.5 points
- Creatinine > 177ummol/l - 1.0 point
- Pneumonectomy - 1.5 points

Distribution of Patients in Each Class of the Recalibrated Revised Cardiac Risk Index

Table 3 Distribution of Patients in Each Class of the Recalibrated Revised Cardiac Risk Index

ThRCRI Score	Risk Class	Number of Cases	Major Cardiac Complications
0	A	1,173	18 (1.5%)
1–1.5	B	468	27 (5.8%)
2–2.5	C	16	3 (19%)
>2.5	D	39	9 (23%)

ThRCRI = thoracic revised cardiac risk index.

Comparison of Traditional and Thoracic Revised Cardiac Risk Index

Table 4 Comparison of Traditional and Thoracic Revised Cardiac Risk Index

Risk Classes	Traditional RCRI	ThRCRI
A	…	1.5%
B	2.3%	5.8%
C	6%	19%
D	7.5%	23%
p value	0.001	<0.0001
c index	0.62 (0.55–0.68)	0.72 (0.65–0.78)a

RCRI = revised cardiac risk index; ThRCRI = recalibrated thoracic revised cardiac risk index.

"ThRCRI > 1.5 or any cardiac condition requiring medication or a newly suspected cardiac condition or limited exercise tolerance (inability to climb two flights of stairs) should be referred for a cardiac consultation."

The assessment of these patients can thus prove challenging, especially in those patients with values approaching the lower limits where we know the complication rate rises. Assessment according to the above process, and managing the patient within team will more often than not lead to an adequate plan with some mitigation of risk.

The next few headings are mentioned as a guide to a structured approach and for completeness sake, but will not be elaborated on here save for some brief notes on ventilatory strategies. The rest will be touched on during the lecture.

Considerations for the anaesthetic plan:

1) Surgical technique planned
2) Analgesic plan
3) Isolation techniques
4) ***Management of One Lung Ventilation***
5) Monitoring options/ fluid management strategies
6) Postoperative plan

Ventilation Strategy

As much as the literature base increases exponentially, agreement on many things becomes less clear. There are still current texts that refer to what we would consider large tidal volume ventilation as being appropriate! This piece represents my personal practice and opinion, which in the end is both supported and refuted by literature, depending on which you choose to read.

The purpose of the OLV is to allow surgical exposure on the operative side, and to hopefully ensure adequate ventilation and oxygenation via the non-operative lung…all the while minimizing risk from lung injury that may occur from soiling, and from mechanical trauma during ventilation. Conduct of OLV should also take into account its effect on cardiac performance and hence cardiac output.

Lung injury is the leading cause of morbidity and mortality post lung resection. Its development is related not only to the fact that lung is being resected, but a complex pathophysiology where injury in the lungs is demonstrated in patients undergoing OLV even without any resection. It is a profoundly unphysiological intervention.

Causative mechanisms include:
Ventilated lung is exposed to physical strain (driving pressure, cyclic derecruitment, overdistention), capillary shear from hyperperfusion, oxidative stress (abnormally high FiO_2 and ischemia reperfusion- from the collapsed lung), inflammatory mediated injury from manipulation and surgical trauma to the operative lung, exacerbated by inappropriate use of too much IV fluid. As such it is imperative that the conduct of ventilation on one lung produces as little injury as possible. The ventilation plan chosen makes a difference.

For each patient, it is important to have at least considered the type of lung that will be ventilated, as well as the nature of the lung to be isolated/ resected. Essentially there are 3 broad types: the COAD type lung, the restrictive type, and the normal type. Interrogation of the preoperative full lung function, as well as the CT scan gives a very good indication of where the patient will fall within these types. As they behave slightly differently, each will have a slightly different strategy, which should have been decided on before the patient even gets to the OR.

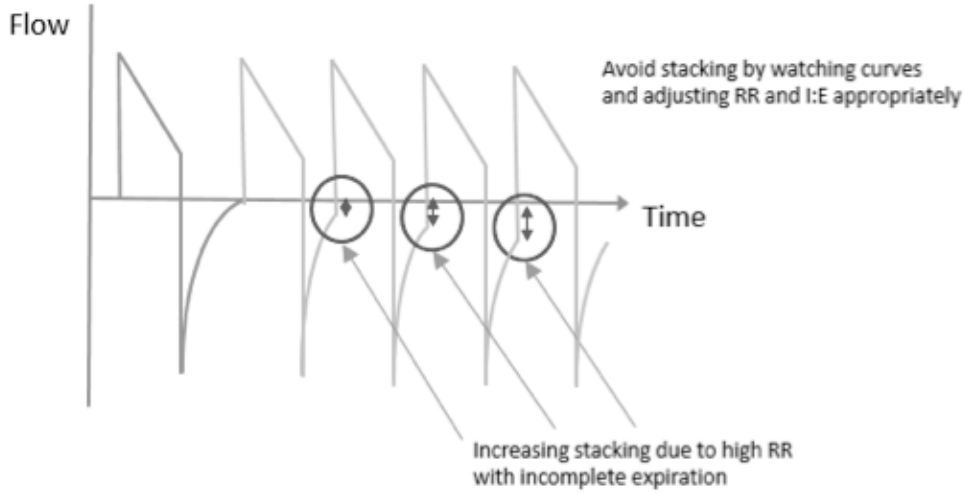
Once the isolation technique has been decided upon, and separation achieved, there is a transition from two-lung ventilation to one lung. This will usually be done in a patient in the lateral position. My preference - once in the lateral position, is to confirm DLT/BB position again visually with bronchoscopy. Bronchial cuffs can be inflated under vision, and patency of the bronchus to be ventilated can be confirmed. Once satisfied, initial ventilation can be as follows:

1) **TV**: while traditional texts advocated for nearly same TV on one and two lungs, this has no bearing on what is physiologically appropriate. The years have seen slow acceptance in anaesthesia of principles used in the critical care environment. If we use 6-8ml/kg IBW on two lungs, it follows that on one lung it should be less. If there is roughly 1.5 -2ml/kg dead space, and half of that dead space is subcarinal, that leaves approximately 1ml/kg conserved dead space. There is then 4-6ml/kg alveolar volume that for simplicity can be split equally between L and R. The result of this is that on one lung, TV should be approximately 3-4ml/kg IBW. There is a bit of wiggle room here, as there must be some consideration taken to the added dead space from the DLT and HME. The simplest way to take this into account, is to do the pre use test with the HME and a catheter mount connected such that this equipment dead space is somewhat taken into account as compressible volume. Current practice should accept TV up to 5ml/kg IBW. It is important to remember that during OLV there is a significant worsening in the Vd/Vt, the implication of which is that even with a preserved minute ventilation $PaCO_2$ will likely rise.

2) **PEEP:** This debate rages on…There is, in my humble opinion, no such thing as high or low peep. Each individual, based on their baseline lung mechanics and body habitus, will have an individual extrinsic peep requirement to prevent de-recruitment. Since peep does not recruit, its application requires the performance of a recruitment maneuver prior to its application at the optimal pressure for that patient. If well recruited, that lung should be closest to its optimum FRC, at which PVR should be lowest- (this is particularly helpful during OLV) and the driving pressure required to distend to the desired TV will be at its lowest. This is extremely important, since high driving pressures (plateau- peep) in excess of 14cmH20 are one of the greatest predictors of lung injury from the ventilator! A word of caution in patients with more than mild obstruction- be careful with recruitment maneuvers- these lungs have excellent compliance, can be easily over distended and require very little peep if any to remain inflated.

3) **Respiratory rate and I:E:** Considering a change in TV from 6 to 4ml/kg (30% reduction) a compensatory increase in rate by 50% would be required to maintain same minute ventilation. The caveat here is that the kinetics of said lung needs to be able to tolerate the increased rate to be able to empty. Dynamic hyperinflation will create over distention, worsen Vd/VT and shunt and have hemodynamic repercussions. This is best done by using the flow - time curve allowing

calculation of the minimum expiratory time to empty completely as well as what maximum rate can be tolerated…. it must always come back to baseline. In general, patients with underlying COAD will require longer expiratory times, tolerate lower maximum rates, and will accumulate more CO_2. Hypercarbia is a common accompaniment to OLV - attempts to overcome it often lead to more harm than good. Mild hypercarbia is well tolerated by most.



Flow time curve for PCV during inappropriately high respiratory rate

4) **FiO_2:** The minimum O_2 required to maintain reasonable SaO_2 is what should be chosen. The hypoxemia occurring during OLV in the vast majority of cases is related to shunt and altered cardiac output - neither of which is corrected by higher inspired O_2 fractions. Using the lowest possible FiO_2 should always be the aim, and SaO_2 as low as 88-90% are considered acceptable.

5) **Pressure limits:** These are a consequence of the above. The aim is to keep driving pressure <14cmH_2O and ideally plateau pressures <25cmH_2O

Adherence to the above principles of low TV, titrated peep post recruitment maneuvers, low driving pressure and low FiO2 are demonstrating a reduction in the degree of lung injury associated with OLV. In this high risk group where perioperative pulmonary complications are common and potentially devastating- simple measures such as the above reduce strain and mechanical injury, with improved ability to maintain oxygenation as seen with a lower incidence of hypoxemia on one lung than is reported in older texts. While the evolution of the lung injury is complex and multifactorial, any means to try to reduce it must be applied. By employing good isolation, thoughtful ventilation, and avoidance of fluid overload- the anaesthetist may meaningfully contribute to reduced perioperative pulmonary morbidity.

Recommended reading

1. Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013; 143:e166S.
2. Lohser J, Slinger P. Lung Injury After One-Lung Ventilation: A Review of the Pathophysiologic Mechanisms Affecting the Ventilated and the Collapsed Lung. Anesth Analg. 2015; 121(2): 302-318
3. Bradley A, Marshall A, Abdelaziz M, Hussain K, Agostini P, Bishay E, et al. Thoracoscore fails to predict complications following elective lung resection. Eur Respir J 2012 Dec 1;40(6):1496-1501.
4. ERS/ESTS CLINICAL GUIDELINES ON FITNESS FOR RADICAL THERAPY IN LUNG CANCER PATIENTS (SURGERY AND CHEMO-RADIOTHERAPY)". A. BRUNELLI, A. CHARLOUX, C.T. BOLLIGER, G. ROCCO, J-P. SCULIER, G. VARELA, M. LICKER, M.K. FERGUSON, C. FAIVRE-FINN, R.M. HUBER, E.M. CLINI, T. WIN, D. DE RUYSSCHER AND L. GOLDMAN ON BEHALF OF THE EUROPEAN RESPIRATORY SOCIETY AND EUROPEAN SOCIETY OF THORACIC SURGEONS JOINT TASK FORCE ON FITNESS FOR RADICAL THERAPY. EUR RESPIR Jour 2009; 34: 17–41.
5. Brunelli A, Varela G, Salati M, Jimenez MF, Pompili C, Novoa N, et al. Recalibration of the Revised Cardiac Risk Index in Lung Resection Candidates. Ann Thorac Surg 2010 Jul 1;90(1):199–203.
6. MiHye Park, M.D.; Hyun Joo Ahn, M.D., Ph.D.; Jie Ae Kim, M.D., Ph.D.; Mikyung Yang, M.D., Ph.D. et al. Driving Pressure During Thoracic Surgery. Anesthesiology. 2019; 130(3): 385-393
7. Fogg, K. J. (2014). Principles and practice of thoracic anaesthesia. Anaesthesia & Intensive Care Medicine, 15(11), 491–494.

Liver Resection

Dr Ollie Smith

Department of Anaesthesia
Charlotte Maxeke Johannesburg Academic Hospital

Notes

Consent

Dr G.L. Davies

HOD, Department of Anaesthesia
Paarl Hospital

The essential components of valid informed consent are:

- Competence
- Information
    - Disclosure
    - Understanding and appreciation of information disclosed
- Voluntariness in decision making
- Ability to express a choice

Therefore, informed consent can be defined as the process which has occurred when a competent person has received thorough disclosure, understands and appreciates the disclosure, acts voluntarily and consents to the intervention.

Competence

Competence refers to the ability to perform a task – which is task and context-specific, changing over time. The key elements determining competence are age and decisional capacity.

Age

The age of full legal capacity in South Africa is 18. Legally, children of 12 or older may consent to a proposed treatment on their own behalf if they have the maturity to understand the implications of the proposed treatment. If the treatment is surgical, the child's consent must be accompanied by a parent or guardian's written assent.

Decisional Capacity

The 2 overriding principles of decisional capacity are:

- Adults are presumed to be competent to make decisions – a lack of capacity must thus be demonstrated and documented
- Minors are presumed to lack decisional capacity – maturity to make a decision must be demonstrated and documented.

When evaluating decisional capacity, the health care provider must ensure that the patient understands the information provided, appreciates the consequences of the treatment and is able to reason about the treatment. Patients with cognitive impairment should always be encouraged and supported to express their decisional capacity. Similarly, patients that lack decisional capacity should still be involved, as far as possible, in decisions affecting their well-being. Should the decisional compromise be temporary or reversible, the healthcare practitioner may wait for decisional capacity to be regained, if feasible,

Should an adult lack decisional capacity, the surrogate hierarchy for obtaining consent is as follows:

- Advance directive, if appropriate to the situation
- A proxy mandated in writing by the patient to make decisions on his/her behalf
- A person authorized by law or a court order
- The patient's spouse or partner
- Parent
- Grandparent
- Adult child
- Brother or sister

If none of these surrogates exist, the healthcare provider may proceed with the intervention in using the "best interests" principle. The National Health Act allows for **emergency treatment** to prevent either death or irreversible damage to a patient's health, provided the patient has not previously refused such treatment (or implied that he/she would refuse it). In these circumstances, the superintendent of the hospital, clinical manager or the person in charge should be informed and may grant permission for the procedure to occur in the hospital without consent.

The "best interests" principle dictates that healthcare providers should take into account all clinical options which are indicated, considering the patient's previously expressed preferences, knowledge of their background, third party contributions and which option least restricts future choices (including non-treatment). The South African Constitution states that a child's bests interests are paramount in every matter concerning a child.

Should conflict exist between the healthcare provider's opinion and a proxy's opinion, legal advice should be obtained with a view of applying for a court order.

It is imperative that all reasons for providing treatment are documented in patients with impaired decisional capacity.

Children and young people

The key considerations in children and young people undergoing surgical treatment are as follows:

- Children aged 12 or over with maturity to understand the benefits, risks, social and other implications of surgical treatment, may consent on their own behalf, with parental / guardian assent ("duly assisted by his/her parent or guardian").
- **In an emergency,** should a person with parental responsibility not be available to provide consent, treatment may proceed with the consent of the superintendent of the hospital, clinical manager or the person in charge. If none of these are available, the healthcare provider may treat the child in the "child's best interest". In non-urgent situations an application should be made to the Minister, who is empowered to give consent in lieu of the child's parent or guardian.
- In circumstances where parental decisions may affect a child adversely, the healthcare team should refer the matter to the hospital legal team, who may petition for a court ruling or to the Minister of Health.
- Children of all ages should be involved in the decision-making process, even if they lack the decisional capacity.

Table 1: Legal framework for the clinical treatment of minors

Circumstance	**Age at which patient can consent**	**Relevant Act**	**Comments**
Medical treatment	12	Section 129 of the Children's Act 2005	A child of 12 or older may consent to medical treatment.
Surgical treatment	12	Section 129 of the Children's Act 2005	A child of 12 or older may consent with a parent's or guardian's assent
Hiv test	12	Section 130 of the Children's Act 2005	Consent for an HIV test may be given by a child of 12 or older, or by a younger child with sufficient maturity to understand the implications of the test.
Termination of pregnancy	no lower age limit.	Section 5 of the Choice on Termination of Pregnancy Act 92 of 1996	"no consent other than that of the pregnant woman shall be required for the termination of a pregnancy." for the purposes of this Act, "woman" means any female person of any age.
Request for contraception	12	Section 134 of the Children's Act 2005	Came into force in July 2007.
Virginity test	16	Section 12 of the Children's Act 2005	It is illegal to carry out a virginity test on someone under the age of 16. if they are 16 or older, a test may be carried out only with their written consent.
Circumcision	16 (males only)	Section 12 of the Children's Act 2005	Female circumcision is illegal at any age. Male circumcision is permissible under specific circumstances
Sexual intercourse	16	Sections 1, 15, 16 & 57 of the Criminal law (Sexual offences and related Matters) Amendment Act 32 of 2007	Section 54 of the Act places an obligation on anyone with knowledge (or a reasonable suspicion) of a sexual offence against a child to report it to the police. There are harsh penalties for failure to report.
Minor with parental responsibility for a child	12	Section 129 of the Children's Act 2005.	A child-parent of sufficient maturity may consent to medical or surgical treatment on her child's behalf.
Sterilisation	18	The Sterilisation Act 44 of 1998 and the Sterilisation Amendment Act 3 of 2005.	

The biological mother of a child automatically has full parental rights and responsibilities. If she herself is a minor, and neither she nor the child's biological father has guardianship of the child, the biological mother's guardian is also the guardian of the child.

A child's biological father has full parental rights if:

- He is married to the child's mother; or was married to her when the child was conceived; or was married to her at any time between conception and birth.
- He was living with the mother in a permanent life partnership when the child was born
- He has consented to be identified as the child's father AND contributes to its upkeep.
- A court order has conferred full parental rights and responsibilities to him.

A person with full rights and responsibilities for a child (e.g. parent or guardian) may confer parental rights and responsibilities to another person who has an interest in the child's care, wellbeing and development. This agreement must be made formally and registered with a family advocate.

A child's caregiver (a person who cares for the child on a voluntary basis without formal parental rights and responsibilities) may consent to medical, but not surgical treatment on a child's behalf.

Information

According to the National Health Act 2003 it is an offence to provide a health service to a user without the user's **informed** consent, thus a patient must have full knowledge of his/her treatment. Every healthcare provider must inform the patient (user) of:

a) The user's health status except in circumstances where there is substantial evidence that the disclosure of the user's health status would be contrary to the best interests of the user;
b) The range of diagnostic procedures and treatment options generally available to the user;
c) The benefits, risks, costs and consequences generally associated with each option; and
d) The user's right to refuse health services and an explanation of the implications, risks and obligations of such refusal.

The healthcare provider must (where possible) inform the user in a language that the user understands and in a manner which takes into account the user's level of literacy.

The HPCSA has indicated the following as the minimum information a patient requires before they are in a position to provide informed consent:

- Details of the diagnosis, and prognosis, and the likely prognosis if the condition is left untreated.
- Uncertainties about the diagnosis, including options for further investigation prior to treatment.
- Options for treatment or management of the condition, including the option not to treat.
- The purpose of a proposed investigation or treatment; details of the procedures or therapies involved, including subsidiary treatment such as methods of pain relief; how the patient should prepare for the procedure; and details of what the patient might experience during or after the procedure, including common and serious side effects.
- For each option, explanations of the likely benefits and the probabilities of success; and discussion of any serious or frequently occurring risks, and of any lifestyle changes which may be caused or necessitated by the treatment.
- Advice about whether a proposed treatment is experimental.
- How and when the patient's condition and any side effects will be monitored or re-assessed.
- The name of the doctor who will have overall responsibility for the treatment and, where appropriate, names of the senior members of his or her team.
- Whether students will be involved, and the extent to which students may be involved in an investigation or treatment.
- A reminder that patients can change their minds about a decision at any time.
- A reminder that patients have a right to seek a second opinion.
- Where applicable, details of costs or charges which the patient may have to meet.

Voluntariness

Any coercion in obtaining consent, whether overt or covert, invalidates the informed consent process. All patients should be asked whether they have any misgivings about their treatment, before proceeding. Patients that are detained by police or immigration services, or are incarcerated, may be particularly vulnerable, and should be informed that they may refuse treatment if they so wish.

Under the Mental Health Act 2002, involuntary and assisted mental health care patients do not lose their right to consent to treatment for illnesses other than mental illnesses, except where "a mental health care practitioner deems a user to be incapable of consenting to treatment or an operation due to mental illness or intellectual disability". In these cases, a court-appointed curator or a family member may consent on the patient's behalf. If none of these people are available, the head of the institution may grant consent.

Furthermore, treatment for mental illness may only be given without the patient's consent if authorised by a court or a Review Board, or in an emergency where failure to treat would result in death or irreversible harm to the patient or in the patient inflicting serious harm to himself or others or property. Psychosurgery may never be performed on a patient without the patient's consent.

References

1. CHILDREN'S ACT NO. 38 OF 2005.
2. Earp BD. In defence of genital autonomy for children. *Journal of Medical Ethics*. 2016;42(3):158-163.
3. Ganya W, Kling S, Moodley K. Autonomy of the child in the South African context: is a 12-year-old of sufficient maturity to consent to medical treatment? *BMC Medical Ethics*. 2016;17(1).
4. Health Professions Council of South Africa. Seeking patients' informed consent: the ethical considerations. 2008.
5. Lundgren C. Consent…who gives it for anaesthesia for children? *Southern African Journal of Anaesthesia and Analgesia*. 2013;19(6):280-1.
6. McMath A. Infant male circumcision and the autonomy of the child: two ethical questions. *Journal of Medical Ethics*. 2015;41(8):687-690.
7. Medical Protection Society. Consent to Medical Treatment in South Africa. 2012.
8. Ogunbanjo G. The rights and wrongs of children's rights. *South African Family Practice*. 2010;52(6):S13-S18.
9. Strode A, Slack C, Essack Z. Child consent in South African law: implications for researchers, service providers and policy-makers. *SAMJ*. 2010;100(4):247-49.

Cardiopulmonary Bypass

Professor Justiaan Swanevelder

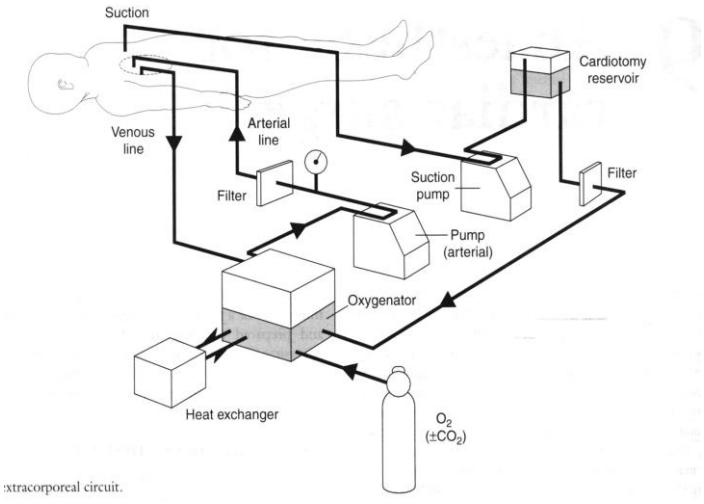
Dept of Anaesthesia & Perioperative Medicine
Groote Schuur and Red Cross War Memorial Children's Hospitals
University of Cape Town

The cardiorespiratory system is responsible for maintenance of adequate oxygen delivery (DO_2) to the cells to meet ongoing oxygen demands (VO_2) during health and disease conditions. During majority of cardiac surgery procedures, cardiopulmonary bypass (CPB) is used to replace the function of the heart and lungs by diverting blood from the patient's venous system towards a pump (supporting the circulation), after which an artificial lung (oxygenator) is oxygenating the blood and removing excess CO_2, therefore replacing the lungs. A standard CPB circuit includes venous drainage cannulae, a venous blood reservoir ("cardiotomy"), a pump, an oxygenator, an arterial line filter, and an arterial return cannula. A system of tubes connects the various components of the CPB circuit. The CPB system is assembled, primed and ready before the start of the procedure.

An adult CPB system typically requires about 1500 ml of prime volume. The exact mix is institution-dependent, but usually consists of isotonic crystalloid and colloid fluid, with or without blood added depending on the patient's starting haemoglobin (Hb). Calcium, Magnesium and mannitol may be added for organ protection. Heparin (5000u) added to the prime prevents clotting when it gets in contact with the patient blood.

Before cannulation of the aorta and initiation of CPB, the anaesthetist will administer intravenous unfractionated heparin (300-400u/kg or 3-4mg/kg) to the patient. A point of care (POC) anticoagulation monitor, the activated coagulation time (ACT), is used to provide an objective measure of the adequacy of anticoagulation. The ACT is a general measure of the end of coagulation. Confirmation of adequate anticoagulation (> 300 seconds) must be obtained before use of the cardiotomy/pump suction, which salvages blood from the operation site back into the CPB circuit. An ACT of more than 480 seconds is required before initiation of CPB, to prevent the formation of micro-thrombi. Throughout the procedure, the ACT should regularly be measured. Additional heparin will be added to the pump to keep the ACT above 480 seconds, and therefore prevent thrombus formation. After the end of the procedure and after separation of the patient from CPB, protamine (3-4 mg/kg) is given to the patient to achieve the starting pre-operative ACT (around 90-110 seconds).

Some patients may have resistance to heparin because of antithrombin III deficiency. This is often because they have been on a heparin infusion before the procedure, which may have depleted their antithrombin III levels. Additional doses of heparin or antithrombin III (concentrate or fresh frozen plasma) may be needed to take the ACT above the required threshold.



:xtracorporeal circuit.

CPB circuit

Depending on the type of the surgical operation, one or two venous cannulae may be used to drain the systemic venous return from the right atrium. Operations requiring direct access to the right or left atrium, such as mitral valve, tricuspid valve atrial, or atrial septal defect closure surgery, require two venous cannulae. These cannulae are placed and snared inside the inferior and superior vena cava, so preventing systemic venous blood entering the cardiac chambers. After oxygenation the patient's blood is returned into the arterial system (aorta), therefore bypassing the heart and lungs. The cardiac procedure is undertaken with or without arresting the heart. For some cardiac procedures like coronary artery bypass graft (CABG) surgery, it is possible to perform the procedure without CPB. This is called "off-pump coronary artery bypass" surgery, or OPCAB.

The venous cardiotomy reservoir may be either a collapsible bag or a hard shell container. When a collapsible bag is used, venous blood is drained passively by gravity. This is affected by the height of the operating table and tubing diameter. When a hard reservoir is used in the circuit, negative vacuum-assisted drainage can be applied, which improves venous drainage.

The CPB pump actively pumps the deoxygenated blood from the venous reservoir through the oxygenator. This CPB pump replaces the role of the human heart as a pump. Either roller- or centrifugal CPB pumps can be used, although the roller-pump is more commonly used for routine cases at most institutions. A simple calculation is used to estimate the total "pump flow" (litre/minute) needed for a specific patient, which is then displayed on a digital monitor. Pump flows are based on patient body-surface-area and temperature. The pump speed (revolutions per minute-rpm) is one of the determinants of pump flow, which represents the cardiac output. A flow transducer is usually used on the arterial cannula to provide a direct measure of pump blood flow. A centrifugal pump is safer in longer CPB cases, because it causes less red blood cell and platelet damage.

The oxygenator (membrane-) is an artificial lung that oxygenates the systemic venous blood, and also removes CO_2. This therefore fulfils the role of the patient's lung. Similar to the human lung, gas transfer depends on Fick's Law (membrane surface area, permeability and thickness). O_2 and CO_2 transfer across the membrane follow partial pressure gradients. CO_2 removal is very efficient across an oxygenator due to its high solubility. The $PaCO_2$ can be adjusted by increasing or decreasing the fresh gas flow (FGF in litre/minute) through the oxygenator. This FGF is also called the "sweep flow". Ventilation of the lungs can therefore be stopped when the patient is "on full CPB flow". Mechanical ventilation should be restarted at the end of the procedure before termination of CPB.

Temperature is controlled (hypothermia or required temperature, as well as rewarming) by a heat-exchanging system connected to the oxygenator. The patient's blood in the CPB circuit does not come in contact with the non-sterile water that flows countercurrent within the heat-exchanger.

Hypothermic CPB is used for congenital cardiac repair procedures in neonates and smaller children by most pediatric centers.

It is usually advocated that hypothermia

- decreases some damaging effects of CPB
- provides a better protection of organs (brain, heart, kidney)
- provides flexibility in CPB management and duration
- provides a safety margin

But

Hypothermia has well-known side-effects :

- microcirculation dysfunction
- endothelial function impairment with capillary leakage
- myocardial contractility impairment
- coagulation disorders with increased bleeding
- inflammatory response is delayed, but not decreased
- rewarming is potentially dangerous
  (brain, kidney, splanchnic organs)

Routine use of inline arterial filters (usually 40 µm) are important to filter microthrombi, fat, or any other debris from the CPB circuit before the blood is returned to the ascending aorta via the arterial return cannula. This is a safety measure to prevent gaseous, as well as particulate embolism to the brain and splanchnic bed.

During CPB some de-oxygenated blood from arterial bronchial blood flow drains into the heart. This fills the left heart chambers that lead to unfavourable surgical conditions and increased ventricular wall tension. The left ventricle is kept empty with a left-heart venting cannula, to assist protection of the myocardium and optimize bloodless operating conditions. This vented blood is drained back into the CPB circuit. Such left heart venting may be achieved through the double-lumen cardioplegia cannula in the ascending aorta, or by placing a vent directly through a pulmonary vein into the left atrium or left ventricle (through the mitral valve).

In routine CPB the arterial cannula returns oxygenated blood into the ascending aorta, back to the systemic circulation. Arterial (aortic) cannulation always precedes venous cannulation. Excessive hypertension should be avoided during aortic cannulation to prevent iatrogenic aortic dissection. Femoral or subclavian arteries may occasionally be used for arterial cannulation in specific situations like major aortic surgery.

All the above CPB techniques require opening of the chest with direct access to the heart. In specific situations indirect venous cannulation may be achieved through the femoral or right internal jugular veins. In such a case the cannulae are placed percutaneously or by surgical cut-down with direct exposure of the femoral vein. This, together with femoral artery cannulation, is used to establish CPB before opening the chest in high-risk cases e.g. re-do CABG procedures where coronary grafts may be at risk. This may also be the approach for minimally invasive cardiac surgery through mini-thoracotomy incisions.

To initiate CPB, the perfusionist releases the arterial line clamp and slowly start to increase pump flow. At the same time the surgeon and perfusionist release the venous line clamp to allow drainage of the venous return into the cardiotomy reservoir. “AVID” is a useful mnemonic for key considerations at the start of CPB.

A – Arterial inflow to patient (blood oxygenated, cannula position, dissection?)
V – Venous inflow to pump (venous drainage, SVC obstruction?)
I – Incomplete CPB (pulsatile arterial trace, AR, target CPB flow reached?)
D – Drugs (vasoactive drugs, anaesthesia administration?)

Although it is outside the scope of this presentation to discuss physiology, pathophysiology and physics in detail, it is assumed that the Part 2 FCA exam candidate will have a good understanding of the following CPB principles and equations, and where they are applied:

- VA (alveolar ventilation) = $VCO_2/PaCO_2$ x K
- $PiO_2 = FiO_2$ X (PB - PH_2O)
  (PiO_2 = 20.93/100 X (760 - 47) = 149 mmHg)
- Alveolar Gas Equation: $PAO_2 = PiO_2 - PACO_2/R + F$
  (where F is a small correction fraction and R = VCO_2/VO_2, also called respiratory quotient, with a normal value of 0.8)
- Fick’s Law of Diffusion: Vgas = A/T x D x (P1-P2) (D = sol/mw)
- Shunt equation: $QS/QT = CcO_2 - CaO_2/CcO_2 - CvO_2$
  Shunt vs Dead Space (cardiac, respiratory - diffusion, filters, oxygen supply and demand, monitoring), also during CPB
- Ventilation-perfusion mismatch, venous admixture and Henry’s Law
- The structure of haemoglobin, and how it carries oxygen.
  O_2Hb-Dissociation curve, P50
- O_2 content of blood: $CaO_2 = (1.39 \times Hb \times Saturation/100)+(0.003 \times PaO_2)$
- Bohr effect, Hamburger effect
- Oxygen supply and demand during CPB: $DO_2 = CO \times CaO_2$
- Fick Principle, oxygen consumption: $VO_2 = CO \times (CaO_2 - CvO_2)$

- Hagen-Poiseuille equation (flow through airways, tubes and tubing/vessels):

$$V = \frac{P\pi r^4}{8nl} \qquad P = Q \times R \text{ (Ohm)}$$

$$R = \frac{8nl}{\pi r^4}$$

Also important, but not covered in this lecture:

- Starling Law and compliance (cardiac function/mechanics, lung physiology, renal function)
- La Place (wall tension, preload, resistance, afterload, oxygen consumption)
- Bernoulli (flow hydraulics, ultrasound-Doppler, pressure drop/flow across tube narrowing)

During cardiac surgery both the surgeon and the anaesthetist can actively contribute to myocardial protection. Patients undergoing cardiac surgery are at risk of acute global myocardial ischemic reperfusion injury. When the aorta is "cross-clamped" after going onto CPB, the heart is subjected to acute ischemia. When the crossclamp is then removed after completion of the procedure, acute myocardial reperfusion injury may occur.

Cardioplegic diastolic arrest, left ventricular venting and hypothermia currently form the foundation of myocardial protective practice for on-pump cardiac surgery. The ideal recipe of cardioplegic solutions to be used during cardiac surgery continues to be the subject of intensive research, and is beyond the scope of this discussion.

For years the maintenance of a favourable myocardial oxygen supply/demand ratio has been the cornerstone of perioperative myocardial protective strategies. Increasing evidence over the last 15 years is indicating that anaesthesists may have additional ways available to protect the vulnerable myocardium in the perioperative period. There is evidence that volatile anaesthetic agents (Halothane, Isoflurane, Desflurane, Sevoflurane) have a direct cardioprotective effect independent of its effects on myocardial O_2 balance. The heart possesses remarkable plasticity, which enables it to overcome ischaemia-reperfusion injury. In recent years the potential clinical application of ischemic and pharmacological preconditioning, ischemic and pharmacological postconditioning, and remote inter-organ ischemic pre- and post-conditioning as perioperative organ protection strategies has been confirmed in the laboratory setting. However, these techniques need further validation and refinement in the clinical setting.

Clear communication between the different members of the cardiac team (surgeon, anaesthetist, perfusionist, and nursing) is crucial before, and continuously during a heart operation. All members of the team must understand the procedure, and must constantly be updated on what is being done, and what is happening to the patient. This is essential to the safe conduct of CPB.

Special issues in the practice of cardiopulmonary bypass will be discussed during this refresher course session:

- Team communication
- Anticoagulation for CPB, and standard point-of-care (POC) anticoagulation monitoring
- Cannulation
- Initiation of CPB ("AVID")
- Physiological considerations during CPB. Managing and monitoring quality of CPB and adequacy of pump flow
- Anaesthesia during CPB
- Haemodilution, haematocrit/Hb
- Cardioplegia
- Optimal CPB perfusion pressure
- Biocompatibility of CPB material, blood activation and inflammation
- Metabolic and glycaemic control, ultrafiltration
- Carbon dioxide insufflation, "De-airing"
- Defibrillation, pacing
- "Weaning" of patient from CPB, also difficult separation ("TAHVR")
- Cardiorespiratory function, monitoring

- Decannulation, protamine, hemostasis
- Chest closure, transfer to ICU
- CPB emergencies, re-opening

Cardiac surgery/anaesthesia can be complex, and requires a solid understanding of cardiovascular physiology, pathophysiology, and pharmacology. Anaesthetising patients with cardiac disease also requires a thorough understanding of CV monitoring and CPB management, which remains a key aspect in the present setting of cardiac surgery. The ability to integrate transoesophageal echocardiography knowledge into the procedure, adds value to improved patient outcomes.

References

1. Alston RP, Myles PS, Ranucci M. Oxford Textbook of cardiothoracic anaesthesia. First Edition, Oxford University Press 2015.
2. Mackay JH, Arrowsmith JE. Core Topics in Cardiac Anesthesia. Second Edition, Cambridge University Press 2012.
3. Gravlee GP, Davis RF, Hammon JW, Kussman BD. Cardiopulmonary bypass and mechanical support. Fourth Edition Wolters Kluwer 2016.

Notes

Anticoagulation & Bridging in Obstetric Anaesthesia

How to handle it

Dr Dominique van Dyk

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Various local and international obstetric bodies have issued guidance recently, expanding the use of thromboprophylaxis in obstetric patients. For example, the National Partnership for Maternal Safety, an American multidisciplinary working group, published its "*Consensus Bundle on Venous Thromboembolism"* in 2016. "*Recommendations for thromboprophylaxis in obstetrics and gynaecology"* were published in SAJOG in May 2018[1]. The impact of such guidance will be felt by anaesthetists, as we will have to make more frequent decisions as to whether patients on anticoagulant therapy can receive neuraxial anaesthesia safely, without undue risk of vertebral canal haematomas. Neuraxial techniques are, of course, favoured for labour analgesia, operative vaginal delivery, caesarean section, other obstetric surgeries and postoperative analgesia in obstetric patients, for reasons which are well-established.

We also encounter pregnant women on *full anticoagulation* because of prosthetic heart valves or for treatment of a new DVT or pulmonary embolism. Here, we need to know about bridging therapy around the time of delivery, so as to minimize the dual risks these patients face: anticoagulant-associated maternal haemorrhage vs valve thrombosis/ repeat venous thromboembolism (VTE). Knowledge of how to reverse the anticoagulant drug effect is necessary when faced with an anticoagulated parturient who is bleeding or must undergo emergency surgery.

Most of these patients will be on **unfractionated heparin** (UFH) or **low molecular weight heparin** (LMWH) by the time delivery approaches. Occasionally, there is the need for unforeseen delivery prior to 36/40, and then one may encounter a gravid patient on **warfarin**.

Fortunately, the oral direct thrombin inhibitor **dabigatran** and oral direct factor Xa inhibitors **rivaroxaban**, **apixaban**, and **edoxaban** are not used during pregnancy because of absence of information on efficacy and fetal safety. Rivaroxaban, dabigatran and edoxaban are classified US FDA Category C-"*animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks*"- and apixaban falls in category B, as animal studies did not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Coagulation changes in pregnancy

Pregnancy is a hypercoagulable state. The concentrations of the thrombogenic clotting factors, including fibrinogen, von Willebrand factor and factors VII, VIII, IX, X, XII and XIII, increase progressively as pregnancy advances. There is reduced endogenous anticoagulant activity, mediated by an increased resistance to activated protein C and decreased free protein S levels. After the first trimester, there is an increase in platelet aggregation.
At the same time, the enlarging uterus progressively compresses the abdominal IVC, causing venous stasis in the pelvis and lower limbs. While the majority of pregnancy-associated deep vein thromboses occur during the first 20 weeks of pregnancy, the thrombotic risk is greatest in the immediate postpartum period, with almost ⅔ of episodes of pregnancy-associated pulmonary thromboembolism occurring after delivery. The vascular trauma induced by vaginal, and more especially, caesarean delivery, and the reduction in fibrinolytic activity in the first 48 hours after delivery, undoubtedly play a role. Clotting factors levels remain elevated, gradually returning to non-pregnant levels by 8-12 weeks post-delivery.
The hypercoagulability of pregnancy may make neuraxial techniques safer in normal healthy parturients than in non-pregnant patients.

Pharmacokinetic changes in pregnancy

↑ maternal plasma volume → ↑ volume of distribution for water soluble drugs, and ↓ peak and steady-state drug concentrations.
↑ renal blood flow and GFR by the second trimester → enhanced clearance of renal-excreted drugs
↓ albumin concentration and altered drug metabolism → ↑ free fraction of highly protein-bound drugs

In term pregnancy, the activated partial thromboplastin time (aPTT) response to, and the duration of action of UFH is ↓ due to ↑ FVIII and fibrinogen, and ↑ nonspecific protein binding, when compared with non-pregnant patients. Similarly, for LMWH, peak anti‑factor Xa levels, duration of action, and the total exposure to the drug over time are lower in obstetric patients compared with non-pregnant or postpartum patients

Spinal epidural haematoma risk in obstetric patients[2]

Compared with the estimated risk of spinal epidural haematoma (SEH) in elderly orthopaedic patients (1:3,600), the overall incidence of this condition is much, much lower in obstetric patients, at 1:200,000 to 1:250,000. What makes this low incidence remarkable is that bloody taps occur with 3% of obstetric epidural insertions. Various factors may be protective against symptomatic SEH in obstetric patients, including (1) their hypercoagulability, (2) their highly compliant epidural spaces which may allow for a greater volume of blood to collect before symptoms arise, and (3) their relative freedom from the osteoporosis, degenerative spinal changes and vascular disease that together cause a reduction in the epidural volume of elderly people. The true incidence of spinal epidural haematoma in obstetric patients receiving anticoagulant and antithrobotic treatment remains unknown.

What guidelines are available to guide the use of neuraxial anaesthesia?

There are a number of published guidelines which address the use of regional/ neuraxial anaesthesia in patients on anticoagulant and antithrombotic medication. Until the publication of the *SOAP Consensus Statement,* not one of the available guidelines had addressed this issue from a purely obstetric perspective:

1) The review article, "*Nordic guidelines for neuraxial blocks in disturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine",* was published in *Acta Anaesthesiologica Scandinavica* in January 2010[3]. The Scandinavian group considered the type of neuraxial procedure being performed (i.e., single-shot spinal versus epidural), as well as the impact of neuraxial anaesthesia on maternal morbidity and mortality, in producing its recommendations.

2) The **ESA** (European Society of Anaesthesiology) last published guidance in December 2010, entitled *Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology".*[4] It had no recommendations specific to obstetric patients on anticoagulation therapy.

3) The **AAGBI** (Association of Anaesthetists of Great Britain & Ireland) guideline, "*Regional anaesthesia and patients with abnormalities of coagulation"*, was published in *Anaesthesia* in 2013.[5] It included a table indicating the relative risks of performing neuraxial blocks in obstetric patients on various anticoagulant drug dosing regimens:

Risk factor	Normal risk	Increased risk	High risk	Very high risk
LMWH- prophylactic dose	>12 h	6-12 h	< 6 h	< 6 h
LMWH- therapeutic dose	>24 h	12-24 h	6-12 h	
UFH- infusion	Stopped > 4 h and aPTTR ≤ 1.4			aPPTR above normal range
UFH- prophylactic bolus dose	Last given > 4 h	Last given < 4 h		
NSAID + aspirin	Without LMWH	With LMWH dose 12-24 h	With LMWH dose < 12 h	
Warfarin	INR ≤ 1.4	INR 1.4 – 1.7	INR 1.7 – 2.0	INR > 2.0
General anaesthesia	Starved, not in labour, antacids given		Full stomach or in labour	

This guideline highlighted the fact that for caesarean delivery (CD), the alternative to neuraxial anaesthesia is general anaesthesia (GA), with its own serious risks, including hypoxaemia related to difficult intubation, awareness and pulmonary aspiration. The choice of anaesthetic technique for caesarean section thus always entails a risk–benefit comparison.

4) The American Society of Regional Anesthesia and Pain Medicine (**ASRA**) published the fourth edition of its evidence-based guideline "*Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy*" in the April 2018 issue of *Regional Anesthesia and Pain Medicine.*[6] This is regarded by many as the authoritative guideline to guide safe neuraxial blockade. It gives specific consideration to the obstetric patient on antithrombotic therapy.

ASRA recommendations for neuraxial blockade in the presence of antithrombotic therapy or higher dose anticoagulants (2017):

Subcutaneous unfractionated heparin	**Intravenous unfractionated heparin**	**Low molecular weight heparin**	**Warfarin**	**Aspirin and NSAIDS**
Prophylactic low-dose SC UFH (≤5000 U in a single dose BD or TDS and ≤15,000 U in 24 h): -Wait 4–6 h before NB/CR ***Prophylactic higher dose SC UFH*** (>5000 U and ≤10,000 U in a single dose or >15,000 U in 24 h): -Wait 12 h before NB/CR and assess coagulation status. ***Therapeutic SC UFH*** (>10,000 U in a single dose or >20,000 U in 24 h): -Wait 8–12 h before NB/CR and check coagulation status before NB/CR. -Subsequent (prophylactic or therapeutic) SC UFH dose may be administered 1 h after NB/CR For any dosing regimen of SC UFH administered >4 d, check platelet count before NB/CR	Normalization of coagulation before NB/CR (usually 4–6 h) Delay heparinization for 1 h after NB/CR If administered >4 d, check platelet count before NB/CR	***Prophylactic LMWH*** (eg, dalteparin 5000 U once daily, enoxaparin 30 mg twice daily, or enoxaparin 40 mg once daily): -Any amount greater than prophylactic dosing is considered "therapeutic dosing" -Wait 12 h before NB/CR -No twice daily dosing with indwelling catheter -Avoid concomitant use of other drugs affecting haemostasis -The first postpartum LMWH dose should be administered at least 12 h after NB or 4 h after CR, whichever is greater ***Therapeutic LMWH*** (e.g., dalteparin 120 U/kg BD or 200 U/kg once daily, enoxaparin 1 mg/kg BD, enoxaparin 1.5 mg/kg once daily, tinzaparin 175 U/kg once daily): -Wait 24 h before NB -The first postpartum LMWH dose should be administered 24 h after NB or 4 h after CR, whichever is greater	-Discontinue 4–5 d and check INR. Normal INR for NB. -Warfarin may be administered with the presence of an indwelling epidural catheter, however, remove catheter before INR >1.4. -INR >1.5 but <3, indwelling catheters may be maintained with caution, based on INR and duration of warfarin therapy. -INR >3, hold warfarin, consider reversal to allow CR. Factor levels may be helpful	No contraindications when used alone Avoid NB in patients on other anticoagulants along with ASA/NSAID No contraindications for COX-2 inhibitors

NB = neuraxial block; CR = catheter removal

As in previous editions, the committee recommends that the general ASRA guidelines be applied to parturients (LOE grade 2C). The reasons for not differentiating between pregnant women and other groups include: limited pharmacologic data on antithrombotic agents in pregnancy, and the absence in the literature of large series of pregnant patients receiving neuraxial techniques whilst on prophylaxis or treatment for VTE.

A *new recommendation* in the 4th edition states that *exceptions/modifications to the ASRA guidelines may be appropriate in circumstances involving select high-risk parturients receiving VTE prophylaxis and requiring urgent interventions for maternal or fetal indications, where the risk of general anesthesia may be greater than neuraxial anesthesia.* (LOE grade 2C).

5) The ***SASA Guidelines for Regional Anaesthesia in South Africa 2016*** predate the publication of the 4th edition of the ASRA guidelines; they advise following the ASRA guidelines.

6) The ***SOAP Consensus Statement***[7]: In the presence of so many subtly differing guidelines, none of which have a purely obstetric focus, the need for a consensus statement on the anaesthetic management of obstetric patients receiving thromboprophylaxis or higher dose anticoagulants was identified in North America. In March 2018, the members of the Society for Obstetric Anesthesia and Perinatology *VTE Taskforce* published a special article in *Anesthesia and Analgesia*. It included a practical guide to appropriately identifying, preparing, and managing women receiving thromboprophylaxis or higher dose anticoagulants during the ante-, intra-, and postpartum periods. These are summarized as follows:

Antepartum guidelines:
Early planning is crucial! An outpatient anaesthesia consultation with the pregnant woman on thromboprophylaxis or higher dose anticoagulants should occur at 36/40, or earlier if preterm delivery is anticipated. This is particularly important where there are other concerns, e.g. additional medical or obstetric morbidity, obesity, difficult airway. At this consultation, the patient and her obstetrician can be fully informed of the indications and timing of neuraxial anesthesia for labour and delivery. Alternative anaesthetic options in case of persistent anticoagulant effects during the peripartum and early postpartum periods should be discussed. Where there is concern about the safety of potentially long periods of anticoagulant treatment interruption, a haematologist's opinion should be sought.

Obstetricians should consciously employ antepartum thromboprophylactic regimens that facilitate neuraxial procedures: Antepartum outpatients requiring thromboprophylaxis can be converted from LMWH to low-dose UFH 5000 U SC twice daily, at 36 weeks of gestation or earlier, particularly in women with additional comorbidities, or in women at a high risk for urgent caesarean or preterm labour.
Alternately, if the plan is to continue low, intermediate, or high LMWH beyond 36 weeks of gestation, then the need to withhold LMWH must be anticipated (see *Intrapartum Guidelines*). The same holds true if delivery or another procedure (e.g., external cephalic version) is planned.

Robust systems must be in place to ensure that the patient is flagged once admitted to hospital, and that details of her drug dose(s), dosing intervals and the time of last administration are clearly documented and available. If anything happens to increase the risk of imminent or high-risk delivery, this must be promptly shared with the on-duty anaesthetist and the nursing team by the obstetricians. The nursing team should know to withhold the next anticoagulant dose, pending obstetric evaluation of the patient.
Mechanical thromboprophylaxis or low-dose UFH (e.g., 5000 U SC bd), rather than LMWH or higher dose UFH, should be considered for antepartum inpatients requiring thromboprophylaxis.
All women who have received UFH for >4 days should have their platelet counts checked before any neuraxial procedure, to rule out heparin-induced thrombocytopaenia (HIT).

Intrapartum guidelines:
The aim is, of course, to minimize the risk of the parturient being unable to receive a labour epidural or neuraxial anaesthetic safely, due to the recent administration of her thromboprophylaxis or higher dose anticoagulants.
In well-functioning delivery units, the admission for delivery of a woman receiving thromboprophylaxis or higher dose anticoagulants should trigger an instruction to withhold the anticoagulant and obtain an obstetric evaluation and a clear-cut plan for further management. Units should have clear guidelines of when women are eligible for neuraxial techniques after cessation of their anticoagulant medication.

Elective obstetric procedures (e.g., cerclage, induction of labour, planned caesarean delivery, ECV, or postpartum BTL):
The size of the dose and the cumulative daily dose help to inform the recommended time intervals between the last dose of anticoagulant and the performance of a neuraxial procedure, or the removal

of an epidural catheter. All recommendations assume the absence of other contraindications to neuraxial anesthesia, renal insufficiency, or body weight <40 kg.

Unfractionated Heparin:

Low-dose UFH thromboprophylaxis *(i.e., 5000 U SC BD or TDS):* -Consider holding the dose for 4–6 hours before placing neuraxial anaesthetic or assessing coagulation status as per ASRA recommendations.	***Intermediate-dose UFH thromboprophylaxis****, (e.g., 7500 U SC BD or 10,000 U SC BD):* -Consider holding the dose for 12 hours and assessing coagulation status before placing a neuraxial anaesthetic	***High-dose UFH*** *(e.g., individual dose >10,000 U SC per dose, or >20,000 U SC total daily dose:* -Consider holding the dose for 24 hours before placing a neuraxial anaesthetic and assessing coagulation status to help guide anaesthetic management

IV Heparin: The recommendation is to stop the infusion for 4‑6 hours and then assess the coagulation status, before placing a neuraxial anaesthetic.

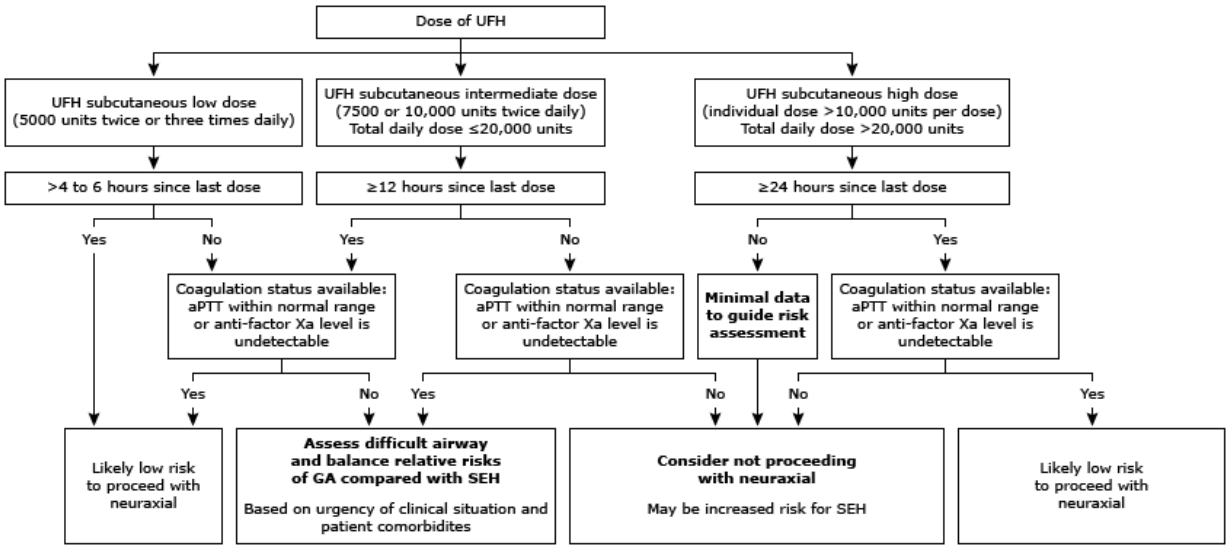
Low Molecular Weight Heparin:

Low-dose LMWH thromboprophylaxis *(e.g.,enoxaparin ≤40 mg SC once daily or 30 mg SC twice daily, or dalteparin 5000 U SC once daily):* -Consider holding the dose ≥12 hours before placing a neuraxial anaesthetic	***Intermediate-dose LMWH thromboprophylaxis*** *(e.g., enoxaparin >40 mg SC once daily or 30 mg SC twice daily and <1 mg/kg SC twice daily or 1.5 mg/kg SC once daily; dalteparin >5000 U SC once daily and <120 U/kg SC twice daily or 200 U/kg SC once daily)*: -Insufficient published data to recommend a specific interval between 12 and 24 hours to wait before proceeding with neuraxial anaesthesia	***Higher dose LMWH*** *(e.g., enoxaparin 1 mg/kg SC twice daily or 1.5 mg/kg SC once daily; dalteparin 120 U/kg SC twice daily or 200 U/kg SC once daily):* -Consider holding the dose ≥24 hours before placing a neuraxial anaesthetic

Urgent and Emergent Obstetric Procedures

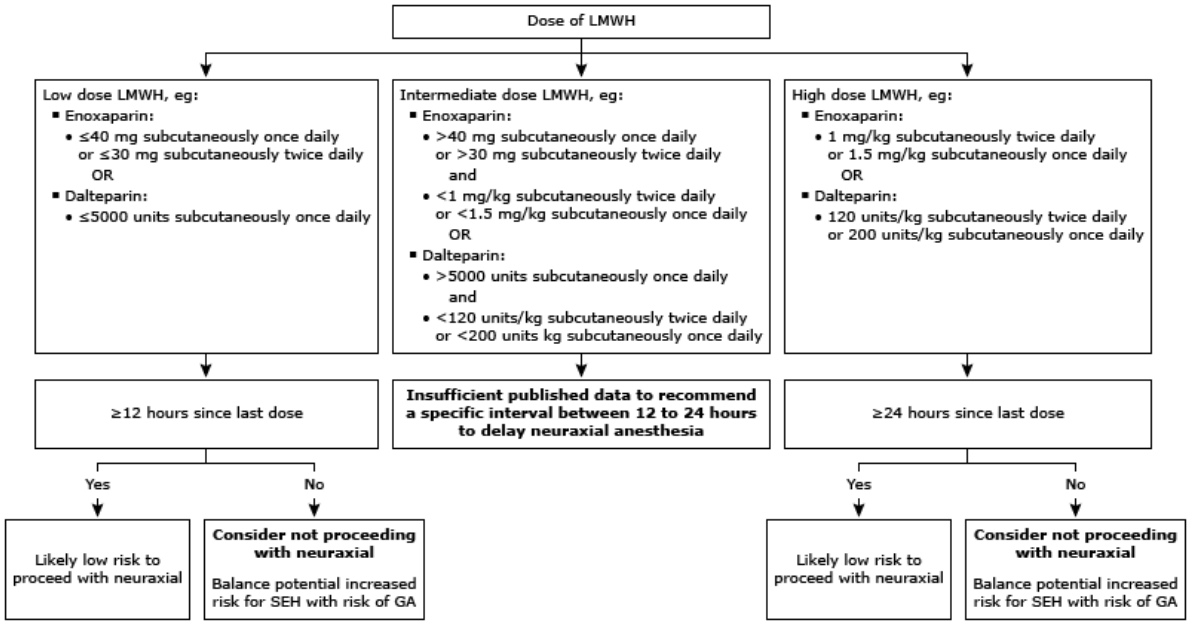
Patient education is crucial- the pregnant woman must know to withhold her UFH or LMWH dose if she suspects that she is in labour, has rupture of membranes, and/or if she has vaginal bleeding, until she has spoken to her obstetrician.
The SOAP VTE taskforce has created Decision Aids to make anaesthetic decisions in urgent or emergent situations easier. These aids integrate the ASRA guidelines and anticoagulant pharmacokinetics in pregnancy, and try to balance the risks of GA against fetal well-being.

SOAP Decision Aid for urgent or emergent neuraxial procedures in the obstetric patient receiving UFH. Assume normal renal function, body weight >40 kg, and no other contraindications to neuraxial anaesthesia. *For all women on UFH for >4 days, check platelet count before neuraxial procedure to rule out HIT.*



Protamine to Reverse Anticoagulation with UFH: The use of protamine sulphate to reverse UFH fully, so as to allow for safe obstetric neuraxial anaesthesia, has not been studied.

SOAP decision aid for urgent or emergency neuraxial procedures in the obstetric patient receiving LMWH. Assume normal renal function, body weight >40 kg, and no other contraindications to neuraxial anaesthesia.



Protamine to Reverse Anticoagulation with LMWH: Protamine sulphate can only achieve 60%–80% reversal of the anti-Xa activity of LMWH. There has been no work done looking at any potential use of protamine to facilitate obstetric neuraxial anaesthesia.

Considerations for the Use of Peripheral Blocks (not considered in SOAP consensus; included here for completeness)

The use of transversus abdominis plane (TAP) and quadratus lumborum (QL) blocks to provide analgesia after caesarean delivery is growing, particularly when long-acting intrathecal opioids are contraindicated or not available. There is a paucity of research into the frequency and severity of bleeding complications after peripheral blocks in anticoagulated patients. Whilst bleeding into the tissue surrounding local anaesthetic placement for TAP or QL blocks is unlikely to lead to any permanent neurological deficit, it could result in a significant drop in the haematocrit which could trigger relook surgery. A TAP block performed under ultrasound guidance can probably be considered a superficial block, and the ASRA guidelines suggest that in an anticoagulated patient the management (performance, catheter maintenance, and catheter removal) should be "based on site compressibility, vascularity, and consequences of bleeding". A QL block should probably be regarded as a deep block, and there ASRA recommends that the guidelines regarding neuraxial techniques should be similarly applied.

Postpartum guidelines:
The anaesthetic management plan *must* incorporate a plan for resuming (or commencing, where indicated) anticoagulation after delivery. The priority in the early postpartum period is ensuring that haemostasis is adequate and the bleeding risk is decreased; until then, administration of thromboprophylaxis is delayed for between 6 and 24 hours typically.
It is reasonable, if the bleeding risk is considered not to be high, to commence/recommence prophylactic LMWH 6 to 12 hours after delivery and no sooner than 4 hours after removal of an epidural catheter (whichever is later). Therapeutic LMWH may be given 24 hours after delivery, if haemostasis is certain.

The time intervals for epidural catheter removal relative to the administration of UFH or LMWH are the same as those in the non-obstetric patient. Monitoring the anti-factor Xa activity before catheter removal is currently not recommended, if the GFR is normal.

There is no literature to guide commencement of anticoagulation after there has been a "bloody tap", i.e. blood during needle and/or catheter placement when a neuraxial block has been performed. The following guidance is based on personal communication with Professor Brendan Carvalho. The reason for anticoagulation should be considered- if there is a low risk of thrombosis, one could either choose

to (1) forgo pharmacoprophylaxis and use mechanical VTE prophylaxis or (2) commence pharmacoprophylaxis once at least 24 hours have elapsed since the bloody tap. If the risk of thrombosis is high, one could justify starting pharmacoprophylaxis sooner than 24 hours after the bloody tap; a solid clot should have formed by 12 hours after the vascular puncture.

Subcutaneous UFH	Intravenous UFH	LMWH
For SC UFH thromboprophylaxis (regardless of dose): • Wait ≥1 h after NB (if no signs of PPH) and after CR before initiating or restarting UFH • Indwelling catheters can be maintained with low dose UFH (specifically 5000 U SC BD): -CR can occur ≥4–6 h after a dose of UFH and subsequent UFH dosing should occur ≥1 h after CR • Consider holding NSAIDs (including aspirin), but not paracetamol, until CR if receiving thromboprophylaxis.	Wait ≥1 h after NB (if no signs of PPH)before initiating or restarting anticoagulation.	**For low-dose LMWH thromboprophylaxis** (e.g., enoxaparin <40 mg SC once daily or 30 mg SC BD; or dalteparin 5000 U SC once daily) • Wait ≥ 12 h after NB and ≥4 h after CR before initiating or restarting LMWH thromboprophylaxis • Indwelling catheters can be maintained with low-dose LMWH: -CR can occur ≥12 h after a LMWH dose and subsequent LMWH dosing should occur ≥4 h after CR • Consider holding NSAIDs (including aspirin), until CR if receiving thromboprophylaxis **For higher dose LMWH** (e.g., enoxaparin 1 mg/kg SC BD or 1.5 mg/kg SC once daily; dalteparin 120 U/kg SC BD or 200 U/kg SC once daily) • Consider waiting ≥24 h after NB and ≥4 h after CR before initiating or restarting LMWH thromboprophylaxis.

An alternative to starting LMWH postpartum is to bridge with UFH 5000 U SC (BD or TDS), as the latter has a shorter duration of action and can be restarted sooner than LMWH (1 vs 4 hours). The unusual circumstances when this may be considered include where there is:
1. the requirement for early thromboprophylaxis after caesarean (<12 hours after surgery)
2. a heightened risk of PPH after caesarean delivery
3. postpartum surgery (e.g., tubal ligation) and/or a neuraxial procedure (e.g., epidural blood patch) planned
4. an indwelling epidural catheter present, to facilitate its removal

NSAIDs are an essential part of post-caesarean multimodal analgesia. Once any epidural catheter has been removed, a parturient who had a neuraxial procedure and no longer has an epidural catheter in situ should receive NSAIDs, even if she will be receiving low-dose thromboprophylactic UFH or LMWH doses. Obviously, there should be no other contraindications to NSAIDS.

Elective peripartum management of anticoagulation therapy in pregnant women with prosthetic heart valves

There exists a variety of opinions on how this clinical situation should be managed, depending on how maternal and fetal outcomes are weighted, and whether the risks of valve thrombosis and/or systemic embolism are thought to outweigh the risk of maternal haemorrhage at delivery.[9,10]

Some approaches for planned delivery: These patients are usually delivered at around 38 weeks, with the mode of delivery determined by obstetric factors and maternal stability.
Anticoagulant therapy may be managed as follows in the peripartum period:

●At approximately 36 weeks, i.e. two weeks before the planned delivery, warfarin is stopped and the woman switched to dose-adjusted subcutaneous (SC) low-molecular weight heparin (LMWH) administered at least twice daily (target anti-Xa activity 1.0 to 1.2 units/mL for mitral valve replacement and 0.8 to 1.0 units/mL for aortic valve replacement at four to six hours post-dose; consider checking the trough activity as well). Dose-adjusted continuous infusion of UFH (maintaining the aPTT at 2 to 2.5 times control) should only be offered if LMWH is unavailable. Stopping warfarin at this time allows for the fetal INR to normalize, reducing an otherwise substantial risk of intracranial haemorrhage at delivery. Some patients are maintained on low-dose aspirin until delivery, which along with early postpartum anticoagulation may increase the risk of SEH if neuraxial analgesia is used.

●The last dose of dose-adjusted SC LMWH is administered 24 hours before planned induction of labour or caesarean delivery if the mother has normal renal function. This is to facilitate use of neuraxial analgesia/anaesthesia and minimize the risk of bleeding at delivery. The various options for peripartum bridging anticoagulation thereafter include:

1. *Use of dose-adjusted IV UFH* (target aPTT at least twice control):
   Twelve hours after cessation of LMWH, IV UFH is commenced with no loading dose at 1000 to 1250 units/hour (±18 units/kg/hour) and the infusion rate adjusted at six hourly intervals to achieve an aPTT that is twice control. The IV UFH is stopped prior to delivery. The timing of the cessation of IV UFH can be difficult when the woman is induced. IV UFH should be discontinued four to six hours prior to initiation of neuraxial anesthesia or analgesia. A neuraxial catheter can be placed once the aPTT has returned to normal.
2. *Use of intermittent prophylactic doses of LMWH* (e.g. enoxaparin 40 mg SC once daily). Initiation of neuraxial anaesthesia or analgesia should be delayed for at least 10 to 12 hours after the last dose of prophylactic LMWH. Caesarean delivery is performed 24 hours after the last dose of LMWH.
3. Induction of labour is commenced 24 hours after the last therapeutic dose of LMWH, and an early epidural catheter is sited. At least six to eight hours after atraumatic (at least 24 hours after traumatic) epidural catheter placement, a prophylactic dose of LMWH is given if the woman is not in active labour and repeated every 24 hours until the woman is in active labour.
4. After stopping the LMWH at least 24 hours prior to the planned delivery, serial anti-Xa levels are performed, starting 12 hours after the last dose of LMWH. This done in order to plan the timing of delivery. It is considered safe, in terms of the bleeding risk, to deliver vaginally or by caesarean section when the anti-Xa level is 0.2 - 0.5 U/mL. Following induction of labour, caesarean delivery is recommended if the anti-Xa level is <0.5 U/mL and the patient is not in the active phase of labour. (This last option is the 2015 recommendation of the South African Society of Thrombosis and Haemostasis).

Postpartum management: The timing of resuming anticoagulation requires yet another risk analysis: the risk of PPH, versus the risk of prosthetic valve thrombosis or thromboembolic complications.

Four to six hours after uncomplicated vaginal delivery, or 6-12 hours after uncomplicated caesarean delivery, an intravenous UFH infusion should be restarted, without a bolus, at expected maintenance infusion rates. This should be increased, over 24–48 hours if a NVD or 48-72 hours if a caesarean delivery, to target an aPTT 2-3 times normal. The use of IV UFH may be associated with fewer bleeding complications whilst warfarin is being restarted, than is the use of therapeutic LMWH.

An alternative to IV UFH is to start with a prophylactic dose of SC LMWH initially, and then 12 hours later prescribe half a therapeutic dose (e.g., enoxaparin 0.75 mg/kg) based upon the patient's postpartum weight; this is then continued as twice-daily dosing (i.e., enoxaparin 0.75 mg/kg every 12 hours). The SA Society of Thrombosis and Haemostasis suggests a post-delivery LMWH regimen guided by the anti-Xa levels, as follows: The timing and dosing of LMWH is guided by the anti-Xa level at the time of delivery. After delivery, LMWH should be restarted at half the pre-delivery dose for the next 24 hours. The anti-Xa level should be monitored 3 - 4 hours after a therapeutic dose, and the dose adjusted to achieve an anti-Xa level of 0.8 - 1.0 U/mL.

The literature varies on when in the postnatal period to restart warfarin. Some authors recommend that if delivery via the vaginal route was uncomplicated, warfarin should be restarted on day 1 postpartum; otherwise, warfarin is recommenced on day 2-3 after caesarean section or if there were any haemorrhagic complications. The South African Society of Thrombosis and Haemostasis recommends "delaying" warfarin resumption, yet confusingly it suggests administering it at the prenatal dose simultaneously with LMWH. Those who are particularly wary of the heightened haemorrhagic risk when UFH or LMWH therapy is overlapped with warfarin in the early postpartum period, advocate that warfarin should not be reintroduced until day 5 to 7.

The UFH infusion or the LMWH is stopped once the INR is in the therapeutic range (2.5-3.5), although some guidelines suggest continuing heparin until the INR has been therapeutic for 24 to 48 hours.

It is safe to remove an epidural catheter at least 12 hours after the last dose of prophylactic low molecular weight heparin (LMWH), and before resumption of full anticoagulant therapy.

Management of the therapeutically anticoagulated patient who requires unscheduled delivery

Whether the urgent, unscheduled delivery is to be vaginal or by caesarean section, full reversal of anticoagulation is not mandatory, unless the woman is suffering from significant, life-threatening haemorrhage. If the woman is taking warfarin, however, it is usual to give vitamin K for reversal, in order to reduce the high risk of fetal intracranial haemorrhage to some extent.

There are 3 possible scenarios:

1. *Warfarin treatment* (INR therapeutic or supratherapeutic)
   -The long plasma half-life of 40 hours is problematic in terms of the bleeding risk.
   -Caesarean delivery is indicated, to reduce the risk of fetal trauma and bleeding, as the fetus is therapeutically anticoagulated too. Assisted vaginal delivery is contraindicated.
   -Warfarin must be stopped.
   -Prothrombin complex concentrate (Haemosolvex Factor IX®) should be administered to target an INR of 2.0. This contains factor IX and the vitamin K-dependent clotting factors II, VII and X. The required initial dosage is determined using the following formula:
   Required units (IU) = Body weight (kg) x (30% desired factor increase) x 1.2
   -If no Haemosolvex® is available, the less desirable alternative is FFP (initial dose, 15 to 30 mL/kg); its utility is limited by the time required to infuse such a large volume.
   -Small doses (e.g., 1-2 mg) of oral or IV vitamin K are given, which reverse the maternal INR in ± six hours. This does not fully normalize the fetal INR, however, and postnatal vitamin K will still need to be given to the neonate.
2. *Therapeutic LMWH treatment*
   -LMWH must be stopped
   -Protamine reversal should be considered, at a dose of 1 mg protamine IV over 10 minutes, per 1 mg enoxaparin (Clexane®) given in the previous 8 hours. The maximum recommended single dose is 50 mg.) As previously explained, this can only achieve partial reversal.
3. *Intravenous unfractionated heparin infusion*
   -Stopping the infusion rapidly restores normal coagulation status because the plasma half-life is so short (1-2 hours), and so protamine is not usually given unless there is major obstetric haemorrhage.
   -1 mg IV protamine is required for reversal of heparinisation per 90-100 units heparin given in the previous 2-3 hours (e.g., 25-35 mg if 1000-1250 units/hour heparin infusion).The maximum recommended single dose is 50 mg protamine.

Any substantial remaining anticoagulant effect at the time of labour or delivery will of course preclude the use of neuraxial analgesia or anaesthesia.

Selected references

1. Schapkaitz E, de Jong P, Jacobson B, Buller H. Recommendations for thromboprophylaxis in obstetrics and gynaecology. *S Afr J Obstet Gynaecol.* 2018;24(1):27-31.

2. Leffert L, Dubois H,Butwick A, Carvalho B, Houle T, Landau R. Neuraxial Anesthesia in Obstetric Patients Receiving Thromboprophylaxis With Unfractionated or Low-Molecular-Weight Heparin: A Systematic Review of Spinal Epidural Hematoma *Anesth Analg* 2017;125:223–31.

3. Breivik H, Bang U, Jalonen J, Vigfusson G, Alahuhta S,Lagerkranser M. Nordic guidelines for neuraxial blocks indisturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine. *Acta Anaesthesiol Scand*. 2010;54:16‐41.

4. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM; European Society of Anaesthesiology. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2010;27:999‐1015.

5. Working Party; Association of Anaesthetists of Great Britain & Ireland; Obstetric Anaesthetists Association; Regional Anaesthesia UK. Regional anaesthesia and patients with abnormalities of coagulation. *Anaesthesia*. 2013;68:966‐972.

6. Horlocker T, Vandermeulen E, Kopp S, Gogarten W, Leffert L, Benzon H. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). *Reg Anesth Pain Med*. 2018;43:263-309.

7. Leffert L, Butwick A, Carvalho B, et al. The Society for Obstetric Anesthesia and Perinatology consensus statement on the anesthetic management of pregnant and postpartum women receiving thromboprophylaxis or higher dose anticoagulants. *Anesth Analg*. 2018;126:928‐944.

8. Banayan M, Scavone B, Mhyre J. Consensus Statement on Pregnant Women Receiving Thromboprophylaxis: An Essential Tool to Guide Our Management. *Anesth Analg.* 2018;126:754-756

9. Elkayam U. Anticoagulation Therapy for Pregnant Women With Mechanical Prosthetic Heart Valves- How to Improve Safety? *JACC.* 2017;69:2692-2695.

10. Schapkaitz E, Jacobson B, Manga P, Chitsike R, Benade E, Jackson S, Haas S, Buller H; The South African Society of Thrombosis and Haemostasis. Recommendations for the anticoagulation of pregnant patients with mechanical heart valves. *S Afr Med J* 2015;105:733-738.

11. Butwick A, Carvalho B. Anticoagulant and antithrombotic drugs in pregnancy: What are the anesthetic implications for labor and cesarean delivery? *J Perinatol* 2011;31:73–84.

12. Nelson-Piercy C. Management of antithrombotic therapy for a prosthetic heart valve during pregnancy. *UpToDate.* Accessed April 2019. Available at https://www.uptodate.com/contents/management-of-antithrombotic-therapy-for-a-prosthetic-heart-valve-during-pregnancy?source=history_widget#H1774597690

The Anaesthetist's Role in Metabolic Surgery

Dr Leon du Toit

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Metabolic surgery is also known as bariatric surgery and weight loss surgery.

Anaesthesia for surgery in the obese patient is part of routine anaesthesia practice. The principles of anaesthesia for metabolic surgery also apply to other obese patients undergoing anaesthesia. In preoperative evaluation of the metabolic surgery patient we consider the comorbidities association with obesity. Breathing disorders related to sleeping are the main concern. Metabolic surgery should exclusively take place in the context of an established multidisciplinary team. In South Africa a functioning multidisciplinary team is a requirement for accreditation of metabolic surgery programs by SASSO.

Metabolic surgery acts via calorie restriction: i) volume restriction and ii) malabsorption; iii) it also produces instant neuroendocrine changes. Changes in Leptin/Ghrelin signalling and Incretins contribute to the beneficial effects of metabolic surgery, but calorie restriction is likely the main mechanism for weight loss and improvement in comorbid conditions.

The main types of metabolic surgery procedures are:

- Adjustable Gastric Banding ("banding")
- Roux-en-Y Gastric Bypass (RYGB)
- Sleeve Gastrectomy ("sleeve")
- Biliopancreatic Diversion with Duodenal Switch (BPD-DS)
- Single Anastomosis Duodenal Ileostomy (SADI).

Apart from banding, which only acts via volume restriction, the other types of surgery act via a combination of the three listed mechanisms. Sleeve gastrectomy is an inferior procedure on its own, but is nowadays used as bridge to a later BPD or SADI. Type 2 diabetes (T2DM) is cured (HBA1C < 6%) in 84% of patients after RYGB and sleeve gastrectomy, and 99% after BPD. The change in insulin and glycaemic profile is almost instantaneous.

Antidiabetic medication should be discontinued before surgery and blood glucose tracked carefully both intra- and postoperatively. Involvement of the endocrinologist / internist is important for planning perioperative glycaemic control in the patient with insulin dependent T2DM.

The main complications after metabolic surgery are:

1. Stomal ulceration (Typically within the first 3 months after RYGB. After RYGB patients get PPIs and surveillance gastroscopy.)
2. Vitamin deficiency (B1, B12, A, D, E, K)
3. Mineral deficiency (Fe, Folate, Calcium, Magnesium)
4. Anastomotic leak
5. Obstruction at the anastomosis site
6. Internal herniation (bowel herniating through a mesenteric defect presents a surgical emergency.)
7. Dumping syndrome (rapid emptying of the stomach content into the duodenum causes distention of the bowel with discomfort and nausea. It also produces osmotic diarrhoea.)
8. Protein malabsorption (associated with the BPD procedure.)
9. Residual stomach gastritis (the unused portion of stomach after RYGB is not readily accessible by gastroscopy, making this a difficult entity to diagnose.)
10. Chronic nausea syndrome (associated with BPD; responds to TPN.)
11. Alcoholism (RYGB is associated with increased inebriation with alcohol use. Reversal of the bypass may be considered to treat alcohol addiction.)

12. Breakdown of relationships (divorce is an acknowledge complication; the person undergoing metabolic surgery also undergoes a personality change and is in many respects not the same person they were before the surgery.)

Metabolic surgery as a bridge to other procedures

Metabolic surgery itself is being investigated as a means to optimise obese patients prior to other surgery. Improved outcomes have been reported when renal transplant and cardiac surgery is preceded by metabolic surgery. Metabolic surgery as a bridge to orthopaedic surgery has mixed results in literature.[1]

Definition of obesity

Obesity is defined as body fat composition ≥ 25% in men and ≥ 35% in women. Fat composition is not easily measure; body mass index (BMI) is used to grade obesity according to the World Health Organization system (and the National Institutes of Health in the USA).

- BMI 25-29.9 is considered overweight
- BMI 30-34.9 is grade I obesity
- BMI 35-39.9 is grade II obesity
- BMI 40+ is grade III obesity (also referred to as morbid obesity)

BMI > 50, > 60, and > 70 (or > 200kg) have been referred to as super-obesity (or grade IV obesity), super-super-obesity (or grade V obesity) and ultra-obesity.[2]

Consider the type of obesity. Central obesity (android, the classic obese male), which is associated with intra-abdominal fat deposition, is associated with more cardiovascular and respiratory morbidity than obesity distributed to the buttocks and limbs (the classic obese female). For this reason, other measures like the waist-hip ratio may be a more appropriate measurement of obesity. A waist hip ratio > 0.85 in women and > 0.90 in men are used to identify central obesity.[2]

Preoperative evaluation and preparation

Metabolic surgery should always take place within the setting of a multidisciplinary team. Use of a "green light" system is common, whereby every member of the team (surgeon, anaesthetist, psychologist, endocrinologist, dietician, and physiotherapist) must give the "green light" in order to proceed to surgery. Any member of the team can at any stage delay or call off the surgery if they discover a contraindication.

Respiratory evaluation
Central obesity causes upward displacement of the diaphragm. Along with increased chest wall mass, this leads to decreased residual volume and increased work of breathing. Obese patients are at risk of obstructive sleep apnoea (OSA) and obesity hypoventilation syndrome.

Most patients qualifying for metabolic surgery will have OSA (60 to 70% prevalence, compared to 9 to 25% prevalence in the general population).[1] Most cases of OSA are undiagnosed. Definitive diagnosis is based on polysomnography (gold standard test). It requires 5 recorded events of apnoea (lasting ≥ 10 seconds) or other obstructive breathing events per hour with one of the following i) sleep interruption, ii) day time symptoms, or iii) OSA related morbidity (mood disorder, cognitive dysfunction, cardiovascular disease). The diagnosis can also be made when ≥ 15 events occur per hour regardless of the other features. The number of obstructive breathing events per hour is referred to as the apnoea hypopnoea index (AHI). Obstructive breathing events lead to:[1]

- Intermittent hypoxia
- Sleep arousal and sleep fragmentation
- Increased work of breathing
- Sympathetic activation
- Daytime hypersomnolence
- Memory loss and cognitive dysfunction

- Psychomotor retardation

Obesity hypoventilation syndrome (OHS) is an entity distinct from OSA with significant overlap. 90% of patients with OHS will also have OSA and 9 to 20% of patients with OSA will have OHS. OHS consists of the triad of i) sleep disordered breathing, ii) obesity (typically morbidly obese), and iii) daytime hypoventilation ($PCO_2 \geq 45$ mmHg | 6 kPa or $HCO_3 \geq 28$ mmol L^{-1}) with or without hypoxaemia ($PO_2 \leq$ 70 mmHg | 9.3 kPa). Patients with OHS are hypersensitive to opioids. They are regularly misclassified as having COPD with respiratory failure.[1] OSA and OHS are associated with increased postoperative morbidity, mortality, length of stay and cost of care. Of these patients, those with OHS have the worst outcomes. Pulmonary hypertension is more commonly attributed to OHS; it is rarely attributed to OSA alone.

Preoperative screening of OSA is the recommended standard for all obese patients. Various screening tools exist, but the STOP-BANG score is the most validated tool.[1]

STOP-BANG risk factors:

S – Snoring loud enough to be heard through closed doors

T – Tiredness causing one to fall asleep during daytime activities on most days (hypersomnolence)

O – Observed apnoea events lasting ≥ 10 seconds

P – Pressure (hypertension)

B – BMI ≥ 35

A – Age ≥ 50 years

N – Neck circumference ≥ 40 cm

G – Gender (male)

A STOP-BANG score:

- 0-2 → Low risk
- 3-4 → Intermediate risk
- 5-8 → High risk

Perioperative *high risk* patients are managed as having OSA.

A STOP-BANG score ≥ 5 has a sensitivity of 83.6% and a specificity of 56.3% for diagnosing OSA. Sensitivity increases with increased disease severity.[1]

One modification of the STOP-BANG tool adds serum HCO_3 testing for those with a STOP-BANG score ≥ 3. Serum $HCO_3 \geq 28$ mmol L^{-1} in these patients, reclassifies them as *high risk*. This modification increases the specificity of the STOP-BANG tool to 85.2%.[1]

Polysomnography is not easily accessible. Acceptable alternative tests for diagnosing OSA are peripheral artery tonometry-based ambulatory devices and devices measuring mean overnight blood oxygen saturation along with the oxygen desaturation index.[1]

Ideally patients with OSA should be started on home CPAP prior to elective surgery. Poor compliance with home CPAP may be one reason for inconsistent results from trials investigating the benefit of preoperative CPAP for reducing perioperative complications.[1] Clinical improvements may only become significant after 3 months of using CPAP.[2]

Short term perioperative CPAP for OSA patients do not reliably confer benefit, for this reason it is not advisable to postpone surgery to get polysomnography or for initiation of preoperative CPAP. The patient should be managed as *high risk* and CPAP should be used in-hospital if clinically indicated.

Metabolic surgery is an effective treatment of OSA.[1]

Cardiovascular evaluation

Obesity is associated with cardiovascular diseases, but also with improved cardiovascular outcomes;

this is part of the *obesity paradox.* Nonetheless, obesity predisposes patients to heart failure, dysrhythmias, and hypertension.[1]

The pathophysiology of *obesity cardiomyopathy,* a cause of heart failure in the obese, is incompletely understood. Increased blood volume combined with increased systemic vascular resistance produces increased left ventricular work which causes remodelling and dysfunction. Respiratory changes promote pulmonary arterial hypertension with right ventricular remodelling and dysfunction. Patients should be evaluated for symptoms and signs of heart failure, and those who cannot be adequately evaluated clinically should undergo special investigation.[1] BNP testing and echocardiography should be considered (guidelines are not consistent as evidence is lacking in this area; compare AHA/ACC[3] versus CCS[4] perioperative guidelines for management of patients with cardiac disease undergoing non-cardiac surgery). Patients with elevated preoperative natriuretic peptides (NT-proBNP ≥ 300 ng L^{-1} or BNP ≥ 92 mg L^{-1}) and patients with LVEF ≤ 40% (HFrEF) are at increased risk of perioperative complications and death. These patients with heart failure should be medically optimised (anti-failure therapy). Referral to cardiology for cardiac resynchronisation therapy prior to elective surgery is indicated for those with clinical features of heart failure despite optimal medical therapy.

Primary hypertension is more common in obese patients. This is attributed to activation of the renin-angiotensin-aldosterone system and altered sodium metabolism. Angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists and diuretics are appropriate therapies. Thiazides, although effective for treating hypertension, promote dyslipidaemia and insulin resistance and should be used with caution. The Association for Anaesthetists of Great Britain and Ireland (AAGBI) recommend that elective surgery be postposed when preoperative systolic BP is ≥ 180 mmHg or diastolic BP is ≥ 110 mmHg. Omission of ACE inhibitors and ARBs on the day of surgery is controversial.[1] The author of these notes generally omits these on the day of metabolic surgery because of the steep head-up position during surgery and the clear association these agents have with intraoperative hypotension.

Metabolic and nutritional evaluation
Obesity is a risk factor for type 2 diabetes mellitus. The author reviews the perioperative approach to type 2 diabetes mellitus elsewhere.[5] The AABGI recommends that elective surgery be postponed for patients with an HBA_1C ≥ 8.5% | 69 mmol mol^{-1}, because it is associated with worse perioperative outcomes compared to those with lower HBA_1C values.[1]

Obesity is a form of malnutrition. Patients typically have micronutrient deficiencies and are more likely to be anaemic. Prior to metabolic surgery micronutrient deficiencies should be corrected by dietary supplementation.[1]

In preparation for metabolic surgery patients undertake an intense calorie restricting diet during the last two weeks (range 1 – 6 weeks) before surgery. This causes reduction in intraabdominal fat and liver size (by depleting hepatic energy stores). These changes make the surgery easier and may reduce perioperative complications.[1]

Intraoperative management

Positioning
These patients are best managed in a seated or 30-40 degrees head-up position. This position improves ventilation as gravity moves abdominal content caudally. The associated increase in residual volume improves preoxygenation prior to induction, affording a longer apnoeic time without desaturation. Allowing the patient to self-position in the desired location on the operating table prior induction of anaesthesia reduces the need to move the patient under general anaesthesia. This in turn reduces the risk of injury for both the patient and healthcare provider. Intubating the patient in a seated or head-up position also reduces risk of passive regurgitation of stomach contents and facilitates alignment of the visual axes for intubation. These benefits should be weighed against the risk of cardiovascular compromise associated with induction of general anaesthesia in a seated or head-up position. Patients with ventricular dysfunction may not tolerate the simultaneous reduction in preload and contractility. Co-loading the patient with 500 to 1000 ml intravenous fluid upon induction of anaesthesia improves preload immediately after induction of anaesthesia.

Ensure adequate padding of pressure points and secure limbs with nonconstrictive straps or

bandages. Rhabdomyolysis, peripheral nerve injuries and pressure sores are more common in the obese surgical patient. The use of memory foam mattresses, gel pads, and bean bags along with meticulous attention to detail can prevent most of these injuries.

A commonly used position for metabolic surgery is seated 30-40 degrees head-up with hips abducted and extended to increase spinal lordosis. A bean bag or similar device may be placed under the lumber spine to increase lordosis. The knees are either straight with feet against foot plates or flexed with the feet not bearing weight. This position allows the surgeon to stand between the patient's legs while operating. The patient's arms are abducted, supported by arm boards. The arms must not carry weight and must not be abducted beyond 90 degrees in any plane, so as to avoid injury to the brachial plexus.

Vascular access
It may be difficult to establish venous cannulation. Ultrasound is helpful to find veins that are not visible, however, short cannulas placed in deep veins are prone to displacement as the tissue planes slide over one another with small movements like rotation of the arm. Use longer cannulas for veins that are located deep subcutaneously. On occasion central venous access may be necessary because peripheral access cannot be obtained.

Monitoring
Arterial and central venous access is not routinely indicated for metabolic surgery. Those with significant cardiovascular comorbidity (for example, heart failure) and those in whom non-invasive measurement is not possible due to a poorly fitting NIBP cuff should have invasive arterial blood pressure monitored. When non-invasive cuffs do not fit well on the upper arm, the forearm is an acceptable measuring site and may provide a more reliable measure; the forearms are kept at the level of the heart (abducted) throughout the procedure. New generation, non-invasive BP monitoring devices show promise in small observational studies (e.g. the ClearSight).

Neuromuscular monitoring using a peripheral nerve stimulator with automated quantitative Train-of-Four and Post-Tetanic Count measurement is essential when using deep neuromuscular blockade; it is also necessary to documentation full reversal prior to arousal and extubation.

The author recommends the use of depth of anaesthesia monitoring (e.g. BIS or Entropy). The anaesthesia management of the metabolic surgery patient uses multiple agents that reduce effective MAC, so that we typically end up using ~0.7 times normal MAC during the case. Although large studies in awareness during metabolic surgery have not been done, the combination of i) low end tidal anaesthetic agent concentration, ii) deep muscle relaxation, and iii) altered pharmacokinetics of the obese patient, represents known risk factors for awareness under anaesthesia. The same concern holds when a TIVA approach is used.

Airway management
Endotracheal intubation is necessary to manage intraoperative ventilation during metabolic surgery. This protects against aspiration and allows for higher ventilatory pressures needed during pneumoperitoneum. As part of the surgical work-up these patients all have gastroscopic evaluation prior to metabolic surgery. Those without a diagnosis of gastro-oesophageal reflux disease or hiatus hernia do <u>not</u> require a strict rapid sequence induction and intubation. Intubation is not more difficult than in the non-obese population, but mask ventilation may be nearly impossible in those with OSA. The Head Elevated Laryngoscopy Position (HELP or ramp) must be used. The time between initiation of induction and placement of the endotracheal tube should be kept as brief as possible to minimise the period of hypoventilation. When video laryngoscopy is not used as the first option for laryngoscopy, it should be on stand-by in theatre. Apnoeic oxygenation appears less effective in the obese population. Use of CPAP before induction improves preoxygenation. Consider extubating to CPAP in patient with home CPAP. Patients are encouraged to bring their own CPAP device to theatre, but the anaesthetist must ensure that the patient demonstrates to them how the device works before putting the patient to sleep.

Ventilation
Obese patients have decreased lung compliance. This is improved by the head-up position and spinal lordosis. Compliance can be significantly reduced during pneumoperitoneum. This is managed by adequate muscle relaxation, lung recruitment and optimising the ventilation strategy. PEEP between

10-15 cmH_2O is typically optimal from the respiratory point of view.

Gastric tubes and gastric bougies
Immediately after intubation a naso- or orogastric tube is inserted and the stomach deflated. For a Roux-Y-Gastric Bypass (RYGB) procedure a normal calibre nasogratric tube is adequate. The tube must be measured preoperatively and withdrawn into the oesophagus (25 cm at the nares, or 22 cm at the lips) to ensure the tube is not stapled into the new gastric pouch. Loosely secure the gastric tube. Double check the gastric tube depth before the surgeon staples the stomach. At the end of the procedure a leak test is performed. The anaesthetist must carefully re-advance the gastric tube into the new stomach pouch. This should be done under vision (i.e. while looking at the laparoscopic screen) while communicating with the surgeon. Once in the new stomach pouch 50 – 100 ml dye solution is injected reasonably fast to test the anastomosis. The dye may run out of the mouth or nares at this stage. After successful leak testing the dye and any blood in the stomach should be aspirated so that the stomach pouch is empty. Any residual blood in the stomach is a potent emetogenic. The gastric tube is typically completely removed at this stage while gently aspirating. Take care not to pull back on the gastric tube when aspiration is blocked. This suggests that the tip of the gastric tube is stuck against the mucosal surface and traction may compromise the anastomosis.

For sleeve gastrectomy procedures a gastric bougie or large bore gastric lavage tube is pass into the stomach after intubation. This forms a guide for the surgeon when stapling the stomach. A leak test is not usually performed for a sleeve gastrectomy procedure because it is technically difficult to instil sufficient volume (~ 200 ml) dye into the stomach over a short enough period of time. It is worth attempting to aspirate residual blood out of the stomach at the end of the procedure, as it is a potent emetogenic. However, do this in discussion with the surgeon who might not want any tubes advanced into the stomach which risks the anastomosis.

Arousal and extubation
Patients should be seated or head-up 30-40 degrees for arousal and extubation. Document complete reversal of neuromuscular blockade. Patients should be counselled preoperatively about awake extubation. Extubation only takes place when the patient is fully awake and clearly indicating that they can maintain their own airway.

General considerations

Venous thromboembolic prophylaxis
Obese patients are at increased risk of venous thromboembolic events (DVT and PE). Chemoprophylaxis is started the day before surgery and immediately continued postoperatively. Dose adjustment is necessary (refer to following section on adjustment of drug doses).[6] Intraoperative mechanical DVT prophylaxis (calf compressors) is recommended.[2]

Ambulatory surgery
Although obesity per se is not a contraindication to day-case surgery, it is not acceptable to perform metabolic surgery as day case surgery (apart from adjustable gastric banding.) This is due to the type of surgery (abdominal as opposed to peripheral) and the common comorbidities (sleep disordered breathing, diabetes and hypertension).[2]

Opiate free and opiate sparing anaesthesia
Metabolic surgery should always be done laparoscopically. Pain after laparoscopic RYGB can be managed with minimal to no opioids. Avoiding or minimizing opioid use reduces risk of respiratory events.

An opioid-free anaesthesia recipe is described by Jan Mulier:

- Instant premedication: 0.25mcg/kg Dexmedetomidine (max 20mcg) when monitors are applied.
- Opioid-free mixture (OFA mix): Dexmedetomidine 50mcg + Ketamine 50mg + Lignocaine 500mg diluted to 50mL with normal saline (0.9% NaCl)
- Induction: OFA mix 0.1mL/kg LBW PLUS Propofol to effect PLUS Rocuronium. Give Dexamethasone (if not done before induction) and MgSO4 40mg/kg LBW.
- Maintenance: OFA mix 0.1mL/kg LBW/hr infusion PLUS Propofol infusion or volatile. Consider repeating induction bolus of OFA mix if patient remains tachycardic before skin incision. Consider additional 25mcg Ketamine before skin incision. Decrease OFA mix to 0.05ml/kg

LBW/hr 15min before end of surgery.

Opioid sparing anaesthesia is always indicated when, opioid-free anaesthesia is not attainable. This is typically the case where Dexmedetomidine is not available. The author uses a loading dose of Fentanyl 200mcg PLUS infusion of Ketamine (0.2mg/kg ABW loading dose and 0.1mg/kg ABW/hr) PLUS Lignocaine (100mg loading dose and 1mg/kg ABW/hr) PLUS Remifentanil (0.1-0.15mcg/kg ABW/min)(Sufentanil is also used with success) along with Paracetamol 2g, Parecoxib 40mg (when not contraindicated), Dexamethasone 8mg and skin infiltration with Bupivacaine prior to port placement. (Bupivacaine and Lignocaine doses are not additive.) The author avoids the combination of MgSO4 and Rocuronium when Sugammadex is not available for reversal of neuromuscular blockage. With this recipe the patients typically requires one or two boluses of fentanyl (25mcg) in the recovery area. Opioid requirements are minimal after RYGB. It is the authors impression that Sleeve Gastrectomy patients require more analgesia postoperatively, even though it is a much shorter procedure.

Muscle relaxation
The use of deep neuromuscular blockage (PTC 1-2) is controversial. Those who use the technique swear by it, but there is no convincing evidence of improved patient outcomes. In theory deep muscle relaxation provides an improved visual field (increased intraperitoneal space) at lower insufflation pressures. This facilitates the surgeon's work and reduces pneumoperitoneum pressures as well as ventilatory pressures. Not all successful metabolic surgery centres use deep muscle relaxation, and some operate on the other extreme – surgery without any muscle relaxation (TIVA only). The author cautions against deep muscle relaxation when Sugammadex is not available for reversal, as the risks of residual muscle relaxation compromising the airway and respiratory system postoperatively outweighs purported benefits of the technique. When deep muscle relaxation is used, the anaesthetist should be meticulous in recording the baseline train-of-four ratio after induction, prior to administration of Rocuronium. In all cases train-of-four ratio should return to >90% (aim for 100%) before the patient is woken and extubated. Maintain a high index of suspicion so as not to miss residual muscle relaxation and recurarization in the recovery area.

Post-Operative Nausea and Vomiting (PONV)
PONV prophylaxis is an important part of anaesthesia for metabolic surgery. The standard approach is triple therapy with i) Dexamethasone (8 mg 30-60 minutes before induction of anaesthesia), ii) Droperidol 0.01mg/kg ABW towards the end of surgery, and iii) Ondansetron 4mg towards the end of surgery. Other $5HT_3$ antagonists like granisetron and palonosetron may be considered instead of ondansetron. Rescue analgesia should be provided with a drug from a different class than already used. Promethazine 6.25mg (0.1mg/kg ABW) is effective for rescue, but is very sedating. Either Promethazine or Ondansetron are prescribed routinely in the first 24-hour postoperative period. Changing from an opioid to a multimodal postoperative analgesia strategy reduces PONV but the risk remains significant (20 to 30% after RYGB surgery and 60% after Sleeve Gastrectomy). The choice of intraoperative maintenance and postoperative analgesia affect the risk of PONV. Use of opioid free TIVA (Propofol + Dexmedetomindine + Ketamine) has been show superior to triple prophylaxis for prevention of PONV.[7] Avoidance of Neostigmine by using Sugammadex for reversal of neuromuscular blockade may reduce the risk of PONV; such benefit is not empirically proven. Some centres completely avoid the use of muscle relaxant (see section on Muscle Relaxation).

Adjustment of drug doses[6]
Obesity affects i) volume of distribution, ii) clearance, and iii) elimination. The Janmahasatian equation for Lean Body Weight (LBW) is appropriate for water soluble agents. Dose propofol at ABW. TCI models are not validated in morbidly obese patients. The Eleveld model for Propofol performs better than the Marsh and Schnider models in obese patients.

	Men	Women
LBW (Janmahasatian)	9270 x TBW / (6680 + 216 x BMI)	9270 x TBW / (8780 + 244 x BMI)
IBW (Divine)	49.9 + 0.89 x [height (cm) – 152.4]	45.4 x 0.89 [height (cm) – 152.4]
ABW	IBW (Devine) + 0.4 (TBW – IBW)	

Antibiotic: 2g Cefazolin IV within 60 minutes before skin incision is adequate. Some centres use 3g, but this is not evidence based. A top-up dose is recommended after 3hr (twice the half-life of Cefazolin) or after 4hr (based on pharmacokinetic studies). The top-up dose should be 2g. That said, a top-up dose is rarely required as metabolic surgery does not normally exceed 3-4 hours.

Paracetamol: A loading dose of 2g followed by 1g six hourly produces safe plasma levels in the morbidly obese population (>100kg).

Neuromuscular blocking agents: Suxamethonium should be dosed at TBW. Non-depolarising muscle relaxants can be dosed at LBW, but use 1.2mg/kg Rocuronium for intubation to avoid prolonged period of hypoventilation.

VTE prophylaxis: Enoxaparin is started the day before surgery. The morning of surgery dose is omitted. Enoxaparin is restarted day 0 postoperatively. Recommended dose adjustment for below[6]

Weight	<50 kg	50-100kg	100-150kg	>150kg
Dose	20mg daily	40mg daily	40mg twice daily	60mg twice daily

www.SOBAuk.com The Society for Obesity and Bariatric Anaesthesia in the UK provides a simple 1-page guideline for management of patients with a BMI > 35.

References

1. Lukosiute A, Karmali A, Cousins JM. Anaesthetic Preparation of Obese Patients: Current Status on Optimal Work-up. *Current obesity reports* 2017; **6**: 229-37

2. Sinha AC, Singh PM. Controversies in perioperative anesthetic management of the morbidly obese: I am a surgeon, why should I care? *Obesity surgery* 2015; **25**: 879-87

3. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology* 2014; **64**: e77-e137

4. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. *Canadian Journal of Cardiology* 2017; **33**: 17-32

5. Du Toit L, Biesman-Simons T, Levy N, Dave J. A practical approach to managing diabetes in the perioperative period. *South African Medical Journal* 2018; **108**: 369-75

6. De Baerdemaeker L, Margarson M. Best anaesthetic drug strategy for morbidly obese patients. *Current Opinion in Anesthesiology* 2016; **29**: 119-28

7. Ziemann-Gimmel P, Goldfarb A, Koppman J, Marema R. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. *British journal of anaesthesia* 2014; **112**: 906-11

Ventilation
From the OR to ICU and back

Dr Ollie Smith

Department of Anaesthesia
Charlotte Maxeke Johannesburg Academic Hospital

This is a topic that continues to receive significant attention in the critical care literature and anesthetic literature, where the question being asked is whether the "protective" strategies employed for the patient in ICU should be employed in the OR for the surgical patent? This begs the question: if we are not ventilating in a protective/ physiological manner in the OR, how are we ventilating our patients?…Is it a "lung harming" strategy? The argument often put forward is that the patient coming for a surgical procedure has relatively normal lungs, and hence does not require a "lung protective strategy", and the literature to date also does not give clear answers. There are increasing numbers of publications on this topic, many of which I feel miss the point… Doing a trial where all patients have low TV and low driving pressure, irrespective of peep level, with and without recruitment (when we did not know if recruitment was necessary) will always fail to show a difference.

High peep/ low peep/ open lung/ standard treatment…this is an illogical argument as I see it. Perioperative pulmonary complications remain a significant cause of in hospital morbidity and mortality, so clearly the above hypothesis is incorrect…. either the lungs we are ventilating are not normal, or we are doing harm! Probably it's both! Yes this is an oversimplification of the problem, as the etiology and pathogenesis of the PPC's is complex, and includes the inflammatory response initiated by the surgical procedure, as well as any ventilator induced injury. There is enough evidence out there that mechanical ventilation itself represents a direct injury to the lung, even more so when done poorly. Volutrauma, Barotrauma, Atelectrauma, Biotrauma… these are all familiar terms, and for good reason. Their presence is associated with poorer outcome and should be avoided at all costs.

The final ventilation strategy should be tailored to the actual kinetics of that lung with its unique tidal volume, peep and inspiratory/ expiratory times. The approach described should achieve all those targets within the prescripts of a non-injurious strategy.

To my mind there is thus no difference between these groups of patients (surgical vs those in ICU), they are merely the same patients at different temporal points on a disease spectrum. How we manage that patient early on will have an impact on how far they travel down that spectrum… and one of our interventions happens to be ventilation. Whether initiated in the OR or in ICU, the principles remain the same.

This text will try to provide a simple approach to the anaesthesia machine as a ventilator, how the mode works and initiation of ventilation on a patient. Some basic trouble-shooting will be included in the lecture.

" Air must go in and out and blood must go round and round"

So, we must get the air (correct TV) **in and out**, ideally at the **lowest possible pressures**, and with as much alveolar ventilation as possible (alveolar recruitment/ limitation of Vd/Vt), where it can be exposed to the greatest capillary surface area (lowest shunt) and circulate round and round (adequate CO).

Understanding your equipment

Anaesthesia Machine vs ICU ventilator:

These are two very different beasts in most cases. As an anaesthesia machine is designed to introduce volatile agents into the system, and allow for the rebreathing of expired gas, it must have a significant internal volume to act as a reservoir for this gas. This represents compressible volume/ machine compliance (plus the circuit). Modern machines, by way of regulation are all required to perform a self check where compressible volume and hence machine compliance is calculated. This is

usually displayed for you to see. Newer machines should have automatic compliance compensation- something that is very important to know- as it needs to be compensated for. This becomes extremely relevant the smaller the TV is, and the higher the pressure is. These machines are also designed to perform at a wide range of fresh gas flows, which can also have significant effect on the delivered TV (concept of Fresh Gas Coupling/ Decoupling) with discrepancies of up to 15% from set volume reported in some bench studies between higher and lower flows and with altered resistive and compliance settings. In a speciality where precision counts, we should be more aware of the potential shortcomings in our equipment.

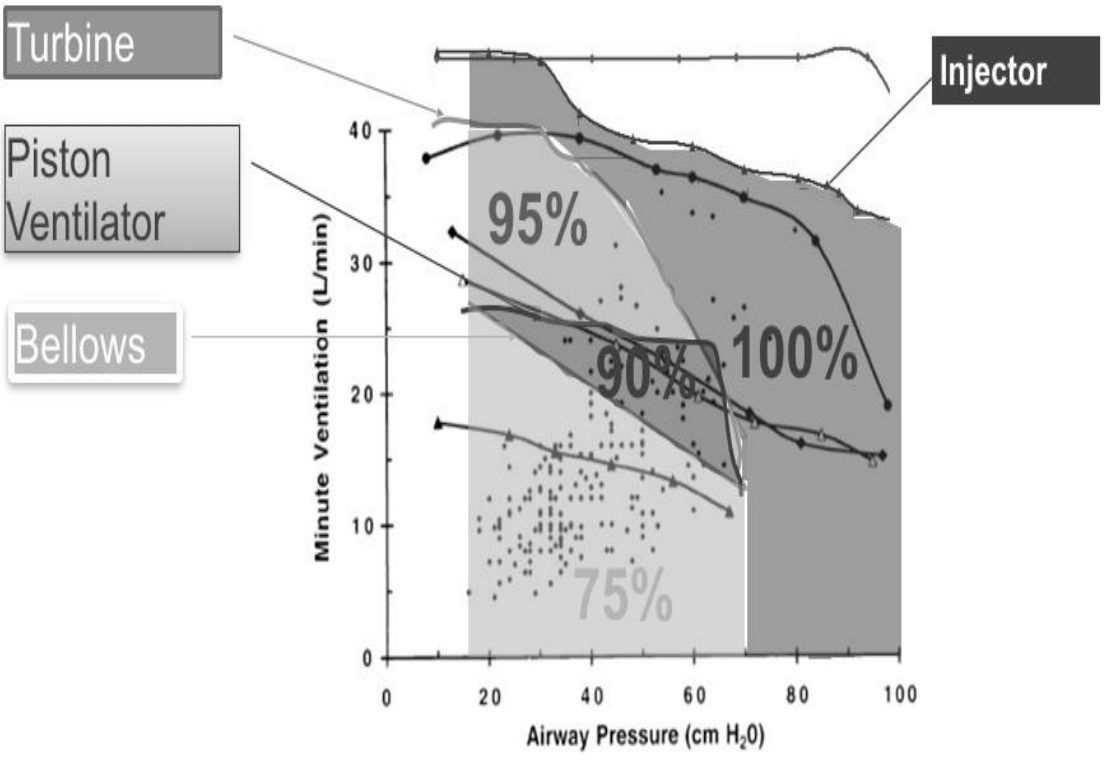
With newer software algorithms governing the ventilator, feedback systems and better flow sensors, there is definitely some movement towards correction of these problems.

Leak compensation: Anaesthesia machines, traditionally are not designed to compensate for leaks within the system, which means that in the presence of a leak without the corrective increase in FGF- ventilation will inevitably cease. This is especially true of the bellows, piston and turbine types currently available to us. There is a newer injector type anaesthesia ventilator that does have leak compensation independent of the set FGF.

ICU ventilators, by contrast, have very little compressible volume, that is actively compensated for, work at high flows, as well as have the ability to compensate for leaks. This has significant impact on the ventilatory power and precision. Typically, power of insufflation is dependent on the type of flow generation, with Injector >turbine > piston > bellows.

It is important to take machine performance into account, as for patients requiring very small precise volumes (neonates), those requiring far higher pressures (e.g. morbidly obese, severe bronchospasm, very poor compliance- typical ICU patient) or even those with significant leaks, a typical anaesthesia ventilator may not be sufficient, and may in fact be dangerous for the patient. In these instances it may be best to arrange an ICU ventilator for such a case.

The below is an adaptation of work done by Katz on ventilator power/ power of insufflation, illustrating graphically the comparison between the different anaesthesia flow generators.



Mode: Volume vs Pressure

Currently there is no evidence to support one mode of ventilation over another.

Understanding of the basic differences between a volume based mode and a pressure based one is essential in order to realise full advantage of each. Confusion is often created by industry as they coin different names for their various modes of ventilation. While this may seem confusing, it can be simplified.

A breath is delivered in one of two ways: a fixed flow for a defined inspiratory time (volume mode- volume is primary and pressure achieved a consequence of the resistive and compliance issues) or a fixed pressure for a defined inspiratory time where the flow and hence volume delivered is dependent on the dynamic and static compliance of the lung (pressure mode- pressure is primary and flow achieved and hence volume secondary). Thus, interrogation of the flow time curve will always tell you how the mode works! **See diagrams below**

A *volume based mode* is defined by its constant flow pattern – tidal volume and inspiratory time is set and the ventilator determines the flow required to meet that target. The flow is always constant regardless of compliance or airway resistance. This constancy with the addition of an inspiratory pause (T_{plat}) *allows* us to discriminate easily where the respiratory issues in the lung lie (compliance vs resistance). However this constant flow also makes this mode less dynamic and less suited for a spontaneously breathing patient to synchronize with.

Advantages of this mode are:

1) Where compliance changes may occur suddenly and frequently, e.g. during surgical procedures

2) Acute bronchospasm where the fixed volume ensures a guaranteed TV provided pressure limit is not breached, and avoids sudden over distention if the bronchospasm breaks.

3) Assists in discerning resistive vs compliance issues by looking at the peak- plateau pressure difference. This requires a pause time to get a true Plateau pressure

A *pressure based mode* uses a rapidly accelerating flow that then decelerates ensuring a constant pressure. The amount of flow delivered to the patient is determined by the inspiratory time and more importantly the pressure target, patient's compliance and airway resistance. If there is high resistance or low compliance then the flow delivered and consequent volume will be less. This mode is more dynamic for spontaneously breathing patients, and in general allows better flow distribution with the lung than a fixed flow pattern.

Advantages here include:

1) Easier limitation of pressure

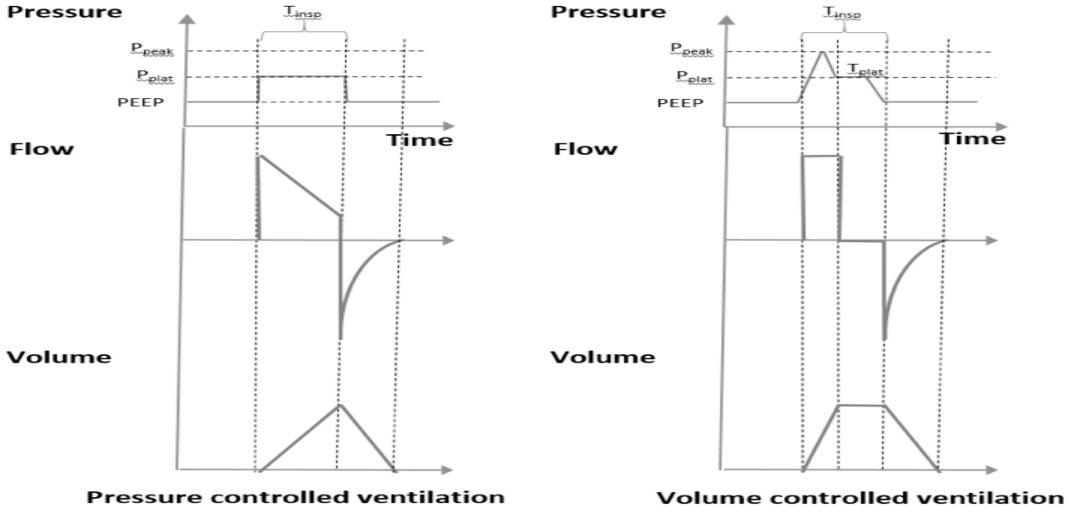
2) Greater TV for any given pressure when compared with volume control

3) Greater patient comfort and synchrony during spontaneous ventilation.

What we do not control- we must monitor!

If we use a volume based mode we must monitor the pressures and be aware of its rigidity while if we use a pressure based mode we must monitor the volumes delivered due to its dynamic reaction to compliance changes and airway resistance.

These fundamental modes can be further discriminated by modes not allowing for patient spontaneity -the control modes (e.g., VCV- volume controlled ventilation or PCV- pressure controlled ventilation); hybrid modes (e.g. SIMV – synchronised intermittent mandatory ventilation, Assist control) and full spontaneous modes with allowance for apnea backup (e.g. PSV- pressure support ventilation, APRV/ BiVent).



The specifics of the various modes of ventilation and their pros, and cons are beyond the scope of these notes. However, there is one mode that is quite useful since it represents a combination of pressure and Volume: PCV- VG/ PRVC. This is a pressure based mode (decelerating flow) that varies its driving pressure to target a set volume. On initiation, it will deliver 2 to 3 VC breaths to assess plateau pressure and compliance, and use that as the baseline pressure required for the volume to be delivered.

Initiation

Now that there is some clarity on the different modes of flow generation and performance, it is time to discuss the initiation of ventilation.

Here the aim is to prevent further harm.

Ventilator induced lung injury is defined as a dysregulated inflammatory response that occurs as a consequence of **excessive volume/pressure load (volu- and barotrauma)** in the aerated lung along with the **cyclic opening and closing (cyclic derecruitment) of** flooded or collapsed alveoli during tidal ventilation (atelectrauma). So our ventilatory strategy must be targeted to the following limits:

- **TV 6ml/kg IBW**
- **Plateau pressure <30cmH2O**
- **Driving Pressure (Plat-PEEP) < 14cmH2O**

This is the cyclic distending pressure for the aerated lung, and consistently is a predictor of lung injury as it increases in magnitude above 14cmH2O.

Plateau pressure and driving pressure are our surrogate targets to reduce the true transpulmonary pressure (airway pressure - pleural pressure) which represents the actual alveolar distending pressure.

- **Lowest inspired O2 fraction** to maintain required oxygenation- prevent excess oxidative stress.

- **Tidal volume**:

There is now little debate, that over distention is harmful, and that the 6ml/kg IBW represents a physiological TV. It meets the tidal requirement for CO2 elimination and for most preserves the Vd/Vt < 30% which ensures adequate CO2 removal. There is obviously some room for volume to go up or down slightly based on the pressure limits discussed.

- **Lung recruitment and setting PEEP**:

Each individual, based on their baseline lung mechanics and body habitus, will have an individual extrinsic peep requirement to prevent de-recruitment. Since peep does not recruit, its application requires the performance of a recruitment maneuver prior to its application at the optimal pressure for that patient.

Of note here is that there must be recruitable lung in order to justify recruitment, else we are performing a maneuver that will have no benefit and potentially create harm. Not all lungs will have recruitable areas e.g. a pneumonia- overzealous attempts in such a patient will only over-distend already well aerated areas and create more problems. Typically, secondary ARDS, atelectasis pulmonary oedema etc. will be recruitable, whereas primary type lung injuries will not. Having said that- any lung may have coexisting atelectasis that can be recruited.

Predicting recruitability classically is done after review of a lung CT (not so practical) or can be done clinically in two simple ways-1) after passing the ET tube and confirming position, ventilate the patient on FiO2 of 21%. Provided the hemodynamics are preserved, if the O2 saturation is lower than pre induction- then shunt has been created and we have atelectasis to reverse. 2) The second test is related to change in end-expired lung volume (release volume) with reduction in PEEP. If it is greater than 30% of the set TV it predicts recruitable lung. More accurately: is the change in volume with reduced peep predicted by (delta PEEP X compliance at lower PEEP) - if yes, no recruitability, if no- then there is chance of recruit ability.

There have been many recruitment maneuvers described. Regardless of which one is chosen, it will require an alveolar opening pressure of 40-45cmH2O in most adults. Even then there will be some who require higher pressures. Most commonly it is done on a pressure control mode, with fixed driving pressure and a sequential increase in peep till peak reached, followed by decremental PEEP and monitoring the change in dynamic compliance. Peak dynamic compliance (at the respective peep) represents optimal peep. Worsening of compliance below this peep confirms de-recruitment and affirms that that the previous peep level was optimal.

NB: these maneuvers can have a significant effect on haemodynamics- don't do in an unstable patient/ cardiovascularly fragile or hypovolemic patient, someone who's lung dynamics are already described as obstructive or has bullae, and avoid in patients with raised intracranial pressure.
Once well recruited, that lung should be closest to its optimum FRC, at which compliance should be at its best, PVR should be lowest and the driving pressure required to distend to the desired TV will be at its lowest (meets all our above requirements) This should also be a scenario with the least amount of shunt, allowing the lowest FiO2 possible for oxygenation.

A word of caution in patients with more than mild obstruction- be careful with recruitment maneuvers- these lungs have excellent compliance, can be easily over distended and require very little peep if any to remain inflated.

Once the correct peep has been determined, the driving pressure is then reduced until the TV is at the 6ml/kg IBW mark.

- **Inspiratory and expiratory times (I:E)**

Interrogation of the flow time curve at this point will also allow defining of the optimal inspiratory time (inspiratory flow reduced to 0 before cycling to expiration) as well as the optimal expiratory time (expiratory flow must return to baseline before cycling to inspiration again) These times based on

inspection of the curve should then allow defining of the maximum allowable rate to prevent stacking and dynamic hyperinflation (very NB in COAD/ acute bronchospasm etc.) as well as the optimal inspiratory time for those with poorly compliant lungs. The diagram below gives reference.

The choice of mode hereafter is at the clinician's discretion. If available the hybrid PCV-Vg or PRVC type modes are great. If not, then for abdominal and thoracic procedures, where compliance changes occur frequently- a volume controlled mode may be best. But so long as you monitor what you don't control- there is really little difference between them.

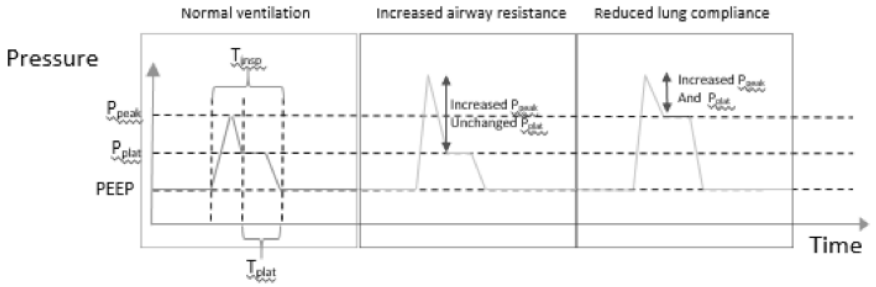
Lastly, once each of the above parameters has been set, FiO2 can be weaned according to SaO2 such that the lowest inspiratory fraction required is used!

Following an approach such as the above, will allow for a sensible initial ventilation strategy, for any type of lung- as each step takes into account the individual lung kinetics with the lowest possible distending pressures, avoiding cyclic derecruitment, and allowing maximal oxygenation with the lowest allowable FiO2.

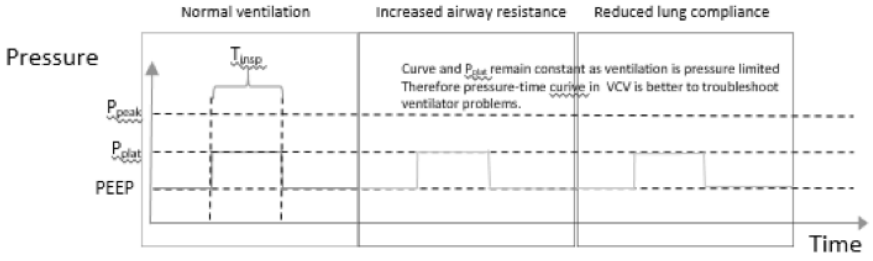
Transport

On a practical note with respect to movement of ventilated patients: based on the time, effort and thought that has often been expended in getting the patient well-ventilated, and taking into account the entire clinical need for keeping them ventilated, it seems very poor practice to then transition them onto a manual self-inflating bag (Ambu-bag) for transport! The pressures and volumes generated during manual breaths delivered with such a device are staggering…. this contradicts everything we understand and try to practice relating to a non-injurious ventilatory strategy. These patients are best moved with a transport ventilator that allows continued ventilation as per their requirement, which prevents the de recruitments that inevitably occur with multiple connections and disconnections.

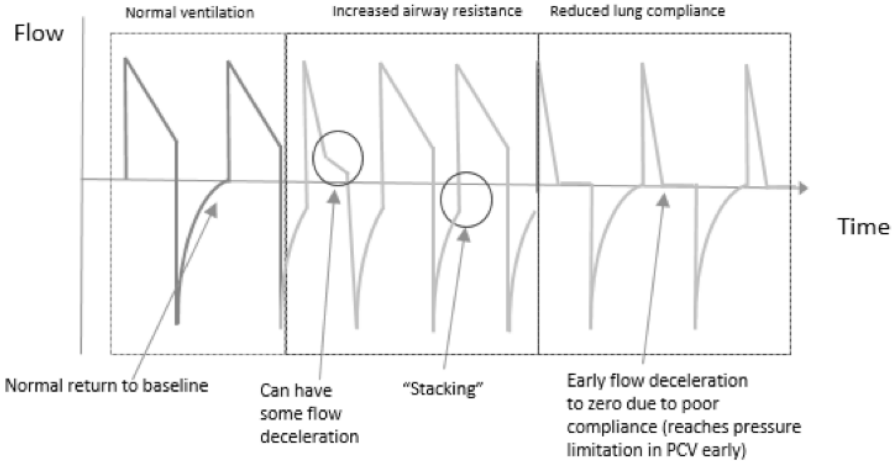
Where an Ambu-bag has been used, with or without a PEEP valve, it is important to recognize that careful re recruitment will be required at the destination when put back onto a ventilator in order to return them to the pre transport state.



Pressure time curve for VCV during different pathology



Pressure time curve for PCV during different pathology



Flow time curve for PCV during different pathology

Recommended reading:

1) Grieco DL, Chen L, Brochard L. Transpulmonary pressure: importance and limits. *Ann Transl Med*. 2017 Jul;5(14):285.

2) Robert M. Kacmarek, Jesús Villar; Lung-protective Ventilation in the Operating Room: Individualized Positive End-expiratory Pressure Is Needed!. *Anesthesiology* 2018;129(6):1057-1059.

3) Schultz, M. J., Neto, A. S., Pelosi, P., & de Abreu, M. G. (2018). Should the lungs be rested or open during anaesthesia to prevent postoperative complications? The Lancet Respiratory Medicine, 6(3), 163–165.

4) Soro, Megmerio, Francisco Javier Belda, María Luisa García-Pérez and Gerardo Aguilar. "Functional characteristics of anesthesia machines with circle breathing system. Current Anaesthesia and Critical Care 2010; 21(5):239-243.

5) Hedenstierna, Lennart Edmark, Mechanisms of atelectasis in the perioperative period.Best Practice & Research Clinical Anaesthesiology 2010; 24(2), 157-169

6) Raquel S Santos, Pedro L Silva, Paolo Pelosi, Patricia RM Rocco. Recruitment maneuvers in ARDS: the safe way is the best way. *World J Crit Care Med* 2015 November 4; 4(4): 278-286

7) O'gara B, Talmor D. Perioperative Lung Protective Ventilation. *BMJ* 2018;362:k3030

8) Kallet RH, Lipnick MS. Is there still a role for alveolar recruitment maneuvers in acute respiratory distress syndrome? J Thorac Dis. 2018; 10(1): 85–90

9) Goligher EC, Hodgson CL, Adhikari NKJ, Meade MO, Wunsch H, Uleryk E et al. Lung recruitment maneuvers for adult patients with acute respiratory distress syndrome. Ann Am Thorac Soc 2017;14:S304-11

Metabolic syndrome controversies

Dr Estie Cloete

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Please read these notes in conjunction with L. du Toit on Bariatric surgery as topics related will be not be covered in detail in these notes: OSA, Physiological changes, Drug dosing, positioning and opioid free anaesthesia

I will discuss here current controversies and updates. Please see references at the end for good review articles on the different topics.

The population is becoming more obese and as the advantages of ambulatory surgery is also increasing, we will have more obese patients for ambulatory surgery. These notes are looking at specific controversies regarding these matters.

Outline of discussion

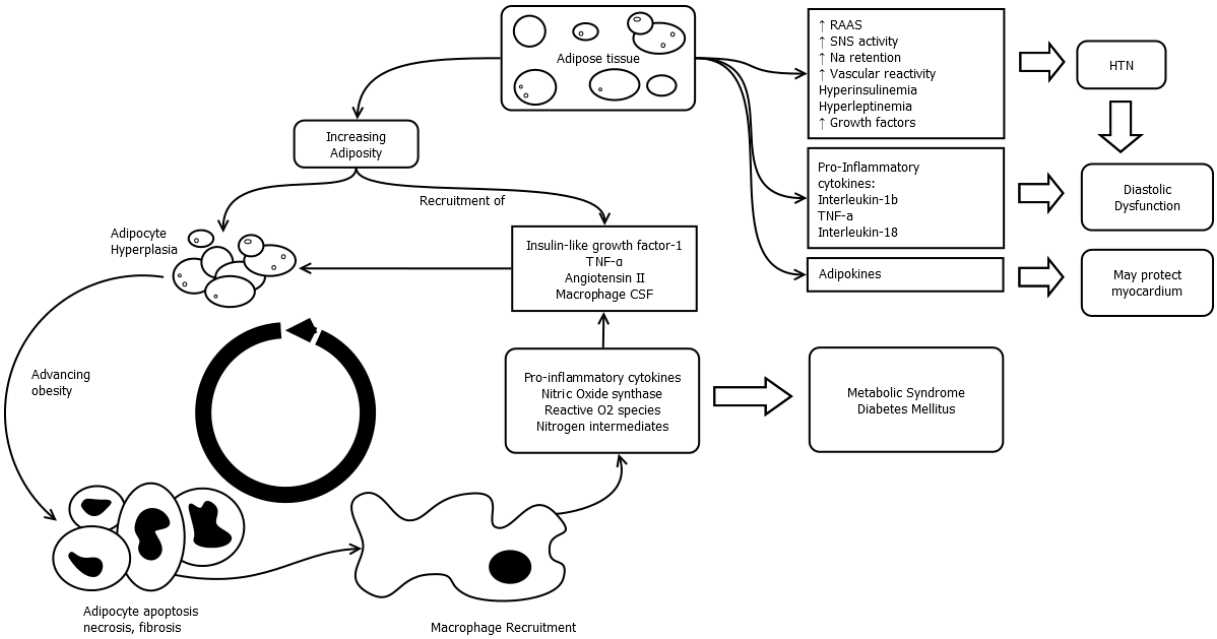
- Challenges with ambulatory surgery in the metabolic syndrome
- Regional/Neuraxial for ambulatory surgery
- Physiological changes post bariatric surgery

Metabolic syndrome is a cluster of diseases that increase the incidence of cardiovascular, cerebrovascular disease and diabetes. The incidence is increased at an alarming rate. Metabolic syndrome leads to increased risk of perioperative complications.

Common Definitions for Metabolic Syndrome

Criterion	NCEP ATP III (3 or more criteria)
Abdominal obesity	Waist circumference
Men	>40 inches (>102 cm)
Women	>35 inches (>88 cm)
Hypertriglyceridemia	>150 mg/dl (≥1.7 mmol/L)
Low HDL	
Men	<40 mg/dl (<1.03 mmol/L)
Women	<50 mg/dl (<1.30 mmol/L)
Hypertension	≥130/85 mm Hg or on antihypertensive medication
Impaired fasting glucose or diabetes	>100 mg/dl (5.6 mmol/L) or taking insulin or hypoglycemic medication

Metabolic syndrome is clinical pathological entities paired together due to the associated with insulin resistance. Insulin resistance is due to diminished physiological response to insulin the result of excess abdominal adipose tissue, increased secretion of free fatty acids and inflammatory factors like tumor necrosis factor alpha (TNFa), IL-6 and others. This results in a defective glucose transport and abnormal metabolism of lipids. The result is the development of metabolic disorders such as obesity, arterial hypertension, dyslipidemia, and diabetes mellitus.



Similar to the metabolic syndrome, the perioperative period is a a state of insulin resistance marked by hyperglycemia and with triggers other metabolic disorders, have negative impact on organ function.

Ambulatory surgery in diabetic patients remains a challenge. There are a few goals in the preoperative visit of any diabetic patient. These may include the target organ complications of micro as well as macrovascular origin, to manage any episodes of hypoglycemia and specific focus should be to evaluate the pharmacological regimen and development of a clear plan for the perioperative period for (pharmacologic as well as nonpharmacologic),

When considering these patients for ambulatory surgery, there are a few things to take into consideration such as the stability and control of their disease. Specific care should be taken with the undiagnosed diabetic patient as they are at increased risk of morbidity and mortality.

Discussion of this topic is topic on its own. For the latest updates I refer you to the updates published in June 2019 in Current Opinion in Anesthesiology in References. [10]

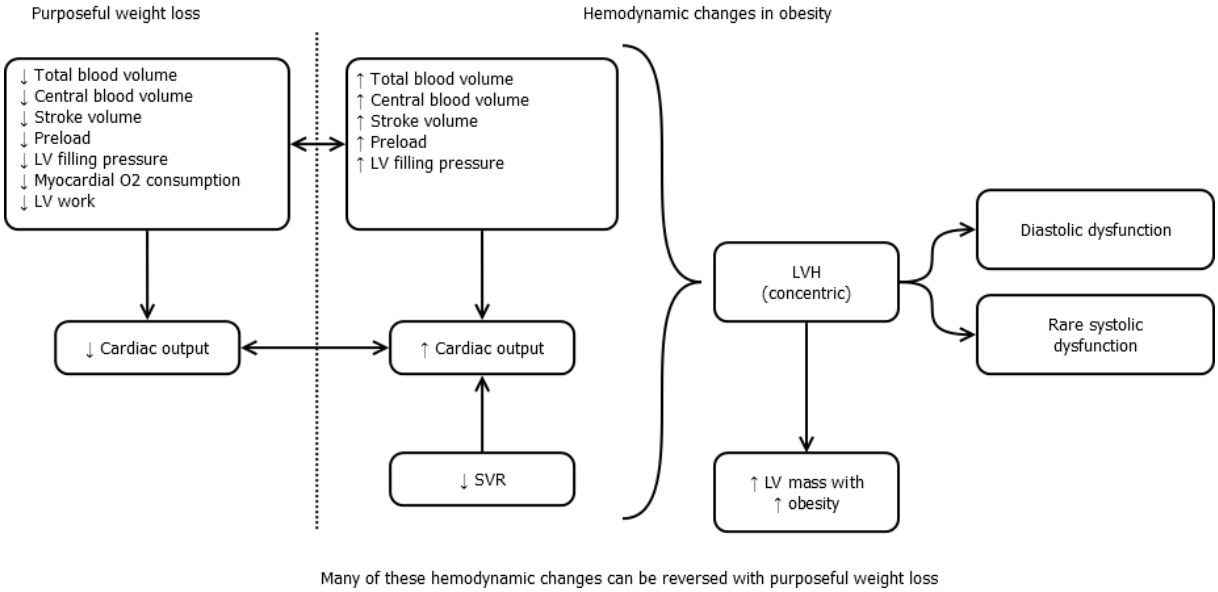
Ambulatory surgery in metabolic syndrome

The WHO (World Health Organization) classification of obesity according to BMI (kg/m2) is

Class 1: 30-35; Class 2 = 35-40 and Class 3: ≥ 40 kg/m^2 (also known as extreme, severe or morbid obesity)

BMI alone should not be the only determinant of ambulatory surgery in the patient with metabolic syndrome. Other factors like invasiveness of the surgery, surgical experience and anaesthetic technique can all influence the outcome. Patients that is super obese (BMI>50) have higher risk for perioperative complications and readmission rate and should be carefully selected for ambulatory surgery. Ambulatory surgery seems to be safe in patients with a BMI of <40 but between 40-50, a thorough preoperative assessment should focus on comorbidities e.g. OSA, pulmonary hypertension, coronary artery disease and cardiac failure. These comorbidities may not be suitable for ambulatory surgery.

During the preoperative assessment of obese patients for ambulatory surgery, specific attention should be focused on the cardiovascular comorbidities. Ambulatory surgeries usually have a low risk for cardiovascular complications, but in the face of obesity and specifically patients with a BMI >40 can have cardiomyopathy without coronary artery disease. The presence of a Left Bundle Branch Block and Right Ventricular Hypertrophy on the ECG can respectively indicate underlying heart disease and pulmonary hypertension.



Ambulatory surgery and OSA

Obesity alone is not a contraindication to ambulatory surgery. However, in patients with BMI of 41-50 OSA should also be taken into consideration as more than 70% of patients with a BMI over 40 have got OSA. The STOP BANG questionnaire is a validated tool accepted by the Society for Ambulatory Anesthesia and the Society of Anesthesia and Sleep Medicine (SASM). The STOP-Bang score is not only useful for identifying the presence of OSA, but it
is also predictive of its severity.
Patients known with OSA should have access to CPAP after discharge and have all their comorbidities optimized. Currently there is no evidence to suggest delay of surgery for a sleep study and initiation of CPAP to improve perioperative outcome.

In the consensus statement of the ASA, the guideline has been recommended for which procedures may be safely performed on an outpatient basis for patients with OSA

Sedation and Obesity

Some ambulatory surgeries can be done with analgosedation. However, in the obese patient extreme caution need to be taken with especially type of drug, dosing as interindividual variation take place (As mentioned above, dosing will be discussed in other notes). Propofol caused hypoxic events during sedation specifically with patients with OSA, male, ASA 3, increased age. Careful titration of any drug is recommended. Ketamine in addition to Propofol might be a safer alternative than Propofol alone in this population. Other agents and combinations have been studied in ambulatory surgery for the obese population. Dexmedetomidine has got a favorable respiratory and cardiovascular profile but combined with Propofol a longer induction and recovery times. The combination of ketamine and dexmedetomidine has not been adequately studied in the obese and OSA populations. It is of utmost importance if sedation is chosen, to monitor capnography as this will allow early detection of respiratory events like apnoea and hypoxia. The use of CPAP during sedation has been studied, but there is limited evidence to support an improved outcome.

Airway challenges and controversies

Major airway complications were twice as likely in the obese patient according to NAP4. This led to permanent hypoxic brain injury or death and in the morbid obese the risk was increased fourfold. Issues that was identified includes lack of planning/recognition and difficult mask ventilation (BMV) and emergency cricothyrotomy difficulty especially in obstructive sleep apnoea (OSA) and high Mallampati patients. Inappropriate SGA that lead to airway failure/aspiration and failure of AFOI when indicated

was further contributing factors to morbidity and mortality. Regarding SGA according to NAP4 recommendations and the UK society for Obesity and Anaesthesia, SGA should not be used in pts with a BMI >35. They also recommend that regional anaesthesia should be used where indicated to avoid the need for general anaesthesia and airway issues.

Do obese patients have a difficult airway?

We know that we frequently encounter difficult face mask ventilation in the obese patient, but is obesity on its own a risk for difficult intubation? In higher body weights, difficult direct laryngoscopy (DL) is more frequently encountered than in more lean patients, where difficulty in DL is defined as requiring more than one attempt at DL. In a recent study, the degree of obesity was not associated with more than one intubation attempt.

Should Video laryngoscopy (VL) rather be the routine approach to intubation in these patients or should we use conventional DL?

Does VL reduce the number of failed intubations and improve the view and reduce the airway trauma? In a recent Cochrane review that compared VL vs DL, VL was shown to improve the view of laryngoscope and reduce difficulty intubation. However failed intubations were reduced with increased operator experience as familiarity with VL is important before the clinical situation arise.
The ASA Guidelines for Management of the Difficult Airway and the Difficult Airway Society (DAS) guidelines suggest VL as the default procedure for an anticipated difficult intubation as this will lead to the best chance of intubation on first attempt.

Is VL better than AFOI in the morbid obese?

Both of these techniques have got equal success in recent studies, despite difficulty due to airway narrowing by fatty tissue. According to NAP4, a high rate of failure with AFOI was due to airway obstruction, excessive sedation and lack of skill. It is predicted that VL will replace AFOI as first choice for awake intubation.

What if conventional methods fail to secure the airway?

Front of neck access in the morbid obese might be difficult or impossible. NAP4 identified the following causes for failure: decision-making delays, equipment or technical failures and lack of knowledge. The inability to palpate the cricothyroid membrane and inability to extend the neck is 2 factors which can be identified pre-operatively. The cricothyroid membrane should be identified by using ultrasonography pre-operatively.

The safe apneic period (SAP) in obese patients differ markedly in obese vs non-obese patients. In the obese this time between muscle paralysis and apnea till SpO2 drop to extreme low levels is 203 min in the obese vs 8-10 min in patients of normal weight.
Recent developments focus on increasing the SAP. The apneic time with difficult airways and the obese patients can be extended with THRIVE (transnasal humidified rapid-insufflation ventilatory exchange. THRIVE not only oxygenate during the apneic period but also allow CPAP continuous positive airway pressure but also gas exchange through flow-dependent flushing of the dead space. It a recent study where THRIVE was used during IV induction and paralysis; the median apnea time has been extended to 14 minutes without a decrease in spo2 of <90%.

Do obese patients have an increased risk of aspiration?

Should you still do an RSI in your obese patient? In fasted obese patient's vs fasted lean patients coming for elective surgery, there appears to be similar incidence of perioperative aspiration and a recent consensus states that RSI is not necessary in every obese patient. IF they have another reason for increase aspiration, like reflux

Of note regarding drugs used in RSI: in a recent manuscript the following recommendation regarding drugs for RSI: suxamethonium 1 mg/kg of total body weight, and rocuronium
>0.9mg/kg of lean body weight. Keeping in mind that fasciculations will increase oxygen consumption and the FRC might be reduced by muscle contraction which will both reduce the SAP. Rocuronium can potentially be rapidly antagonized with sugammadex if needed for a failed intubation.

Should cricoid pressure be used?

Cricoid pressure is controversial between different medical disciplines but mostly used as standard technique in most anaesthesia settings. What makes it controversial? First of all, badly applied cricoid pressure causes laryngeal displacement and airway obstruction and is frequently the cause of failed intubations. During BMV with cricoid pressures, the inspiratory pressures might be increased together with a reduction in tidal volumes. Some studies showed that due to the reduction in lower oesophageal sphincter
And leads potentially to increase reflux risk.
In conclusion: The incidence of difficult laryngoscopy is similar to the non-obese but when it occurs a 'cannot intubate can't oxygenate' CICO scenario can rapidly develop. Plans for airway rescue must be known and well-rehearsed

Regional anaesthesia in obese

Although regional and neuraxial anaesthesia pose a significant and unique challenges with a high failure rate in the obese, it has many advantages and is still supported by recent evidence even in ambulatory setting.

Some of the known advantages include minimal or no airway manipulation, avoidance of cardiopulmonary depression by drugs, reduced PONV and better pain control perioperatively.

Technical difficulties in performing peripheral blocks was especially experienced in a case series in patients with a BMI >25 with an increased failure rate in this population. Blocks with the highest failure rates include epidural, superficial cervical plexus block, paravertebral and supraclavicular (continuous) block.

Ultrasound guided techniques and adjustment of the local anaesthetic dose esp. for neuraxial anaesthesia is recommended.

Obesity is a known risk factor for perioperative respiratory complications. For thoracic and upper abdominal surgery, an epidural will decrease the rate of pulmonary complications, lead to earlier extubation and minimize the need for opioid use.

The use of regional anaesthesia in ambulatory surgery

As mentioned above regional has got many advantages despite the challenges in the obese population. With careful selection for ambulatory surgery and clear guidelines, obese patients receiving regional anaesthesia will have many benefits such as decreased hospital stay and reduced PAHCU use.

In a series done on regional anaesthesia for ambulatory surgery, obese patients (30%) had similar opioid requirements, PONV, length of stay and unplanned hospital admissions than patients with normal weight. However, the rate of block failure and complications was significantly higher than the non-obese. Acute block complications include pneumothorax, seizure, subdural block and epidural spread of a paravertebral and lumbar plexus block.

Post bariatric surgery challenges

Table 26.3 Incidence of comorbidity remission 2 years after bariatric surgery

Comorbidity	Remission at 2 years (%)
Type 2 diabetes mellitus	85
Hypertention	66
Sleep apnea	40
Obesity-hypoventilation syndrome	76

What to expect after bariatric surgery?

The anaesthesiologist needs to be familiar with the physiological and metabolic changes after bariatric surgery.

The cardiovascular system is impacted by patient hypertension, metabolic disorders and increased blood volume as well as impaired aortic function and OSA than leads to arterial stiffness. These changes might be reversed after weight reduction and a reduction in the inflammatory mediators restore nitric oxide system, improve the endothelial function and decrease hypertension. Three months after surgery the heart rate might be decreased due to decrease in the sympathetic tone and there is a reduction in LV hypertrophy between 3-24 months after surgery. Weight loss also lead to improved diastolic function.

With regards to respiratory function, the obese patients can both obstructive or restrictive disorders. Restrictive disorders may be due to fat accumulation in the thorax and abdomen and limit thoracic expansion. Adipose tissue in the upper airway lead to obstructive disease which impairs airflow and lead to gas trapping and prolonged expiration. Although bariatric surgery reduces the AHI (apnea hypopnea index) significantly, the patients still have moderate to severe OSA, which still put them at an increased mortality risk. Only when the AHI is <15/hr (mild OSA) there is improved outcomes in OSA patients. After bariatric procedures most patients still needed the CPAP, but at a lower pressure.

Metabolic changes: after bariatric surgery patient have reduced levels of free fatty acids due to the loss of fat mass and this is associated with improved insulin sensitivity and glucose disposal. Insulin doses is substantially decreased in most patients and some may discontinue their insulin 6 weeks post operatively.

Table 26.2 Major metabolic complications after bariatric surgery

Nutritional deficiencies		Clinical manifestation
Protein-calorie malnutrition		Altered healing processes, edema
Fat malabsorption		Steatorrhea
Iron deficiency		Microcytic anemia
Vitamin deficiencies	B12	Macrocytic anemia
		Paresthesias, peripheral neuropathy
	A	Night blindness, conjunctival xerosis, diffuse keratitis, corneal scarring
	K	Prolonged prothrombin time
	D	Osteoporosis
Calcium deficiency/ hypocalcemia		Paresthesias, confusion, laryngospasm, Trousseau's sing, Chvostek's sing, seizures, arrhythmias
Folate deficiency		Macrocytic anemia
Thiamine deficiency		Paresthesiae, lower extremity weakness, sensory impairments, Wernicke encephalopathy

Drug dosing after bariatric surgery remains a challenge. Many of the comorbidities improve but patients may still remain clinically obese and regain the weight. Malabsorption of drugs is a problem as most oral agents needs to be absorbed in the small intestine, which is bypassed in bariatric surgery. Other factors that may impair drug absorption is delayed gastric emptying, decreased mucosal exposure, changes in the intestinal pH. Drugs with a narrow therapeutic index is of specific concern and patients need to be monitored carefully.

Regional anaesthesia post-bariatric surgery

These procedures are increasing in frequency and thus it is important for the anaesthetist to be familiar with these challenges. Post bariatric procedures might lead to nutrient malabsorption and deficiencies. Important deficiencies we need to aware of includes vitamin K, B12 and folate.

Vitamin K deficiency may be encountered in 50-68% even in patients taking medicine to prevent this. Coagulation disorders should be kept in mind when considering neuraxial anesthesia in these patients. Vitamin B12 and folate also occurring in a significant incidence of 6-10% can manifest as peripheral neuropathy and demyelination as well as neuronal death. The associated loss of motor function and weakness should be documented and risk/benefits of neuraxial anaesthesia considered when encountering these patients.

Weight loss after bariatric surgery correlate with an increased risk of peroneal nerve injury and other peripheral nerves during anaesthesia as the fat pads are decreased with weight loss.

In conclusion, patients should reach a stable weight after bariatric procedures before alternative elective procedures should be considered. This is recommended to be only 6 months post bariatric surgery. A focused exam of the airway and respiratory function, changes in cardiac function and altered metabolic disease should be done. Many of the comorbidities of obesity may still remain after the surgery.

References

1. Joshi GP, Ahmad S, Riad W, et al. Selection of obese patients undergoing ambulatory surgery: a systematic review of the literature. Anesth Analg 2013; 117:1082–1091
2. Brodsky JB. Recent advances in anesthesia of the obese patient [version 1; referees: 2 approved] F1000Research 2018, 7(F1000 Faculty Rev):1195 (doi: 10.12688/f1000research.15093.1)
3. Lewis SR, Butler AR, Parker J, et al.: Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation. Cochrane Database Syst Rev. 2016; 11: CD011136.
3. Moon TS, Joshi GP. Are morbidly obese patients suitable for ambulatory surgery? Curr Opin Anesthesiol 2016, 29:141–145
4. Chung F, Liao P, Farney R. Correlation between the STOP-Bang score and the severity of obstructive sleep apnea. Anesthesiology 2015; 122:1436–1437.
5. American Society of Anesthesiologists Task Force on Management of the Obstructive Sleep Apnea: Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea. Anesthesiology 2006; 104:1081–93
6. American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 2014; 120:268–286.
7.Sreedharan R, Abdelmalak R. Diabetes Mellitus. Anesthesiology Clinics 2018; 36(4): 581-597
8. Simha V, Shah P. Perioperative Glucose Control in Patients With Diabetes Undergoing Elective Surgery. *JAMA.* 2019;321(4):399–400. doi:10.1001/jama.2018.20922
9. Godoroja D, Sorbello M, Margarson M, Airway management in obese patients: The need for lean strategies, Trends in Anaesthesia and Critical Care (2019), doi: https:// doi.org/10.1016/j.tacc.2019.04.003.
10. Kuzulugila D, Papeixb G, Luua J, Kerridge RK. Recent advances in diabetes treatments and their perioperative implications, Curr Opin Anesthesiol 2019, 32:398–404
11. Ingrande J, Brodsky JB, Lemmens HJM. Regional anesthesia and obesity,Curr Opin Anaesthesiol 2009,22:683–686
12. Brodsky J.B. (2013) Can Morbidly Obese Patients Safely Undergo Surgery at an Outpatient Surgery Center?. In: Leykin Y., Brodsky J. (eds) Controversies in the Anesthetic Management of the Obese Surgical Patient. Springer, Milano

The following great articles in press at Anaesthesiology Clinics

1. Grewal G, Joshi GP. Obesity and Obstructive Sleep Apnea in the Ambulatory Patient
2. Okocha O , Gerlach RM , Sweitzer B. Preoperative Evaluation for ambulatory anesthesia
3. Ardon A et.al. Regional Anesthesia for the Ambulatory Anesthesiologist

Cardiac Risk Mitigation for Non-cardiac Surgery

Dr Christella Alphonsus

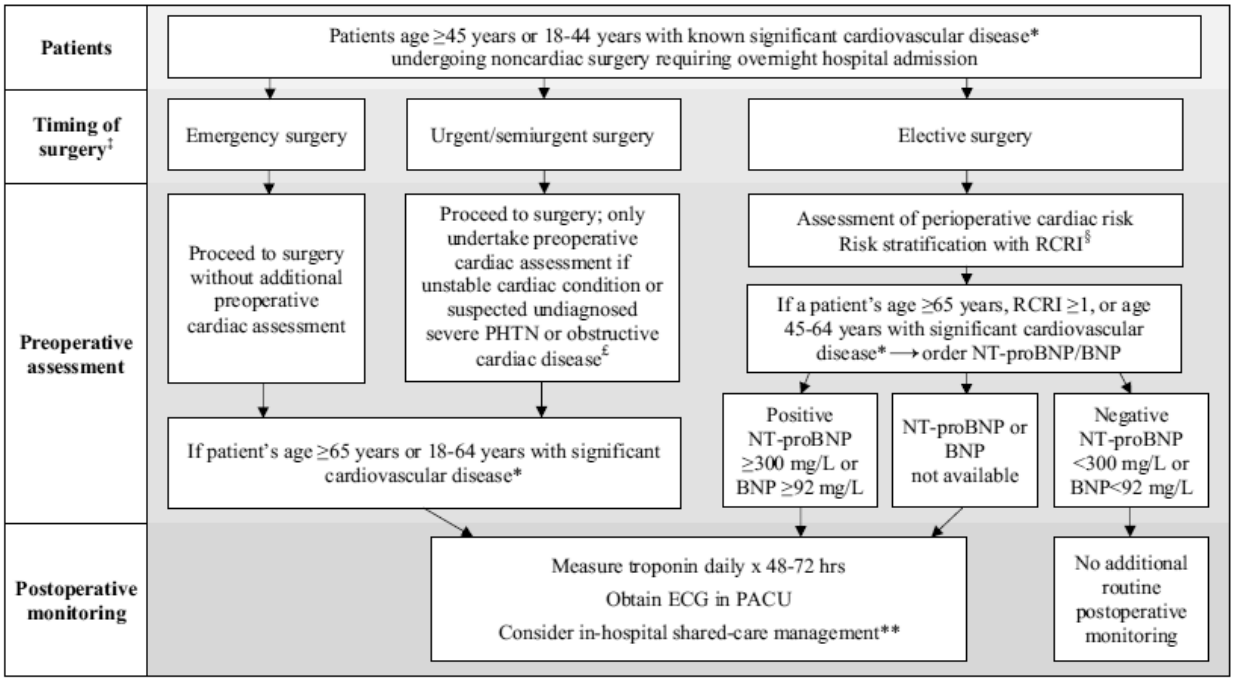
Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Over 200 million adults undergo surgical procedures annually. About one in 20 patients suffer myocardial injury/infarction or cardiac arrest or death within 30 days of major non-cardiac surgery. Peri-operative cardiac complications account for one third of all peri-operative deaths.[3]

Cardiac risk mitigation is a continuum that begins in the preoperative period and extends into the intraoperative and postoperative period.

Preoperative Period

CCS guidelines[4]



Type of patient

Current evidence suggests the following patients warrant further assessment:

- 45 years and older + significant cardiovascular disease
- intermediate to high risk surgery

Risk assessment

Commonly used risk assessment tools have limitations. When a risk assessment tool is used, careful consideration is required in the conclusions that are drawn.

i) Clinical risk indices

- Revised cardiac risk index (RCRI): This is the most validated risk assessment tool. However, the RCRI only has a moderate ability to discriminate **especially for patients in class 2 and 3.** Rodseth and colleagues showed in their meta-analysis in vascular surgical patients, that 60% of patients who have adverse cardiac events are derived from this "intermediate" group.[6]

- American College of Surgeons, National Surgical Quality Improvement Program (ACS NSQIP)[7]

This risk index was derived from large datasets from one country and has not undergone external validation. It is an on-line tool that is useful for explaining risk to patients. It may underestimate cardiovascular risk due to a lack of troponin screening. More than half of all perioperative myocardial infarctions are not detected without troponin screening.[8]

ii) Exercise capacity and exercise testing

Self-reported functional capacity is neither a good predictor of peak oxygen consumption (i.e. METS) nor of postoperative cardiac events.[9] The recently completed prospective observational METS study also shows that cardiopulmonary exercise testing is also a poor predictor of postoperative cardiac events.[10]

iii) Cardiac biomarkers

An individual patient data meta-analysis included 2179 patients from 18 studies and showed that a preoperative NT-proBNP ≥300ng/ml or BNP ≥ 92ng/ml was independently associated death or nonfatal myocardial infarction at 30 days after noncardiac surgery (adjusted OR, 3.40; 95% CI, 2.57-4.47; P < 0.001).[2]

Natriuretic peptide screening should be restricted to patients ≥65 or 45-64 years of age with known cardiovascular disease. These patients have a baseline risk > 5% for postoperative cardiac complications at 30 days after surgery (patients without these characteristics have a ≤ 2.0% risk).[4]

Test result	Risk estimate, %	95% CI for the risk estimate
NT-proBNP < 300 ng/L or BNP < 92 mg/L	4.9	3.9%-6.1%
NT-proBNP value ≥ 300 ng/L or BNP ≥ 92 mg/L	21.8	19.0%-24.8%

BNP, brain natriuretic peptide; CI, confidence interval; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Risk of death or myocardial infarction at 30 days after non-cardiac surgery, based on patient's natriuretic peptide result[2]

iv) Resting echocardiography

The prognostic ability of echocardiography is not as strong as natriuretic peptide testing. It should not be used routinely to predict risk.[11] But echocardiography can be used if there is a clinical suspicion of obstructive intracardiac abnormality, cardiomyopathy or pulmonary hypertension, as this would assist with planning for surgery and anaesthesia.

Optimising pre-existing conditions

i) Hypertension

It is recommended that elective surgery should proceed in patients with blood pressures up to systolic BP of 180mmhg and diastolic BP of 110mmHg.[12] A prospective, observational study of seven hospitals in the Western Cape showed over half of patients presenting for surgery in one week were hypertensive and 38% were poorly controlled. This was mostly related to compliance to medication.[13] Patients with poorly controlled hypertension tend to have greater cardiovascular lability intraoperatively[14]although this does not necessary independently predict increased cardiovascular complications in the perioperative period.[15]

Poorly controlled hypertension is not directly linked to adverse perioperative outcomes but has implications for longer term morbidity and mortality relating to end-organ damage and presents a greater public health issue. Thus, the perioperative period provides an opportunity for education and surveillance. If time permits, newly diagnosed or poorly controlled hypertensive patients should be further assessed and have their medication optimised before surgery.

ii) Cardiac failure

Patients with stable or decompensated heart failure have higher risk of peri-operative complications.[16] Patients with stable cardiac failure need not be delayed for surgery but the risk of cardiovascular complications needs to be explained in relation to intermediate or high-risk surgery. Surgery and anaesthesia need to be tailored to reduce risk of complications.

Patients in decompensated heart failure need to be assessed as to the risk/benefit of surgery. If surgery can be delayed patients should be referred for further optimisation.

Diagnosis of heart failure:

Type of HF	HFrEF	HFmrEF	HFpEF
Criteria			
1	Symptoms ± signs[a]	Symptoms ± signs[a]	Symptoms ± signs[a]
2	LVEF < 40%	LVEF 40–49%	LVEF > 50%
3	–	1 Elevated levels of natriuretic peptides; 2 At least one additional criterion: a A relevant structural heart disease (LVH and/or LAE) Diastolic dysfunction	1 Elevated levels of natriuretic peptides; 2 At least one additional criterion: a A relevant structural heart disease (LVH and/or LAE) Diastolic dysfunction

HF, heart failure; HFrEF, heart failure with a reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with a preserved ejection fraction; LAE, left atrial enlargement; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction.
[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

iii) Anaemia

Both anaemia and blood transfusions lead to higher perioperative complications. This puts greater emphasis on diagnosis and treatment of anaemia before surgery. A one-week prospective observational South African study showed that 48% of patients presenting for surgery were anaemic and this was independently associated with an increased risk of in-hospital mortality and admission to the intensive care unit.[17]

Medication

It is important that chronic medication is continued in the perioperative period with some notable exceptions.

In patients with ischaemic heart disease it is important that B-blockers and statins are continued. Results from the POISE II study showed aspirin should be stopped at least 3 days before non-cardiac surgery and restarted 8-10days after.[18] The exception is in patients who have had recent coronary artery stenting and carotid endarterectomy.

Risk of procedure	Examples
High (> 5%)	Aortic and major vascular surgery, peripheral vascular surgery
Intermediate (1–5%)	Intraperitoneal and intrathoracic surgery, carotid endarterectomy, head and neck surgery, orthopaedic surgery, prostate surgery
Low (< 1%)	Endoscopic procedures, superficial procedures, cataract surgery, breast surgery, ambulatory surgery

'Cardiac risk' denotes combined incidence of cardiac death and nonfatal myocardial infarction.

Cardiac risk related to surgical procedures[1]

Angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker should be withheld 24 hours before high to intermediate risk non-cardiac surgery and restarted postoperatively when the patient is haemodynamically stable.[19]

Intraoperative Period

Haemodynamic goals

Oxygen supply-demand imbalance is a proposed pathophysiological cause of myocardial ischaemia in non-cardiac surgery. The relationship between the surgical procedure and postoperative cardiac complications is therefore dependent on the duration of surgery, haemodynamic instability, perioperative bleeding and the need for transfusion, and the associated inflammatory response.[20]

Intraoperative tachycardia can lead to supply-demand imbalance, and hypotension is associated with perioperative adverse cardiac outcomes.[21]

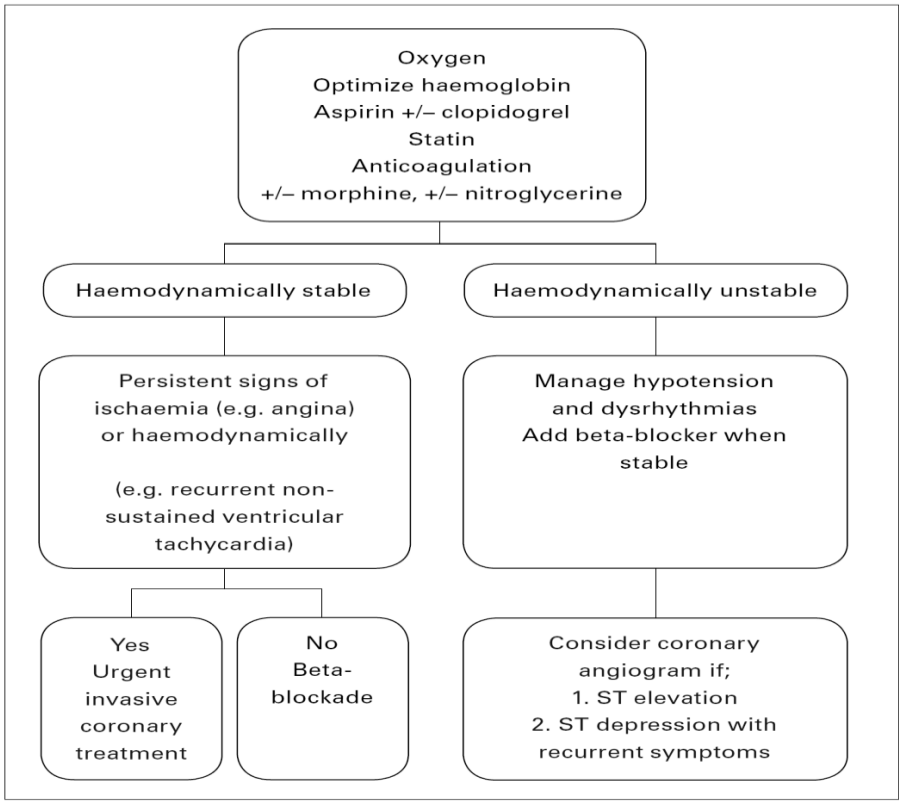
Postoperative Period

Postoperative troponin surveillance to detect Myocardial Injury after non-cardiac Surgery (MINS)[4]

Daily troponin measurements for 48-72 hours after noncardiac surgery recommended in patients:

- Baseline risk > 5% for cardiovascular death or nonfatal myocardial infarction at 30 days after surgery,
- An elevated NT-proBNP/BNP measurement before surgery or,
- A RCRI score ≥1, age 45-64 years with significant cardiovascular disease
- Age 65 years or older

Management of MINS[22]



Proposed management algorithm for perioperative myocardial infarction

Anticoagulation

Postoperative patients are at risk for vascular complications. The MANAGE trial, the first intervention trial in patients with MINS used Dabigatran postoperatively and showed a reduction in vascular events (primary outcome: composite of vascular mortality and nonfatal MI, non-haemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic VTE). Dabigatran provides another avenue for treatment of MINS.[23]

References

1. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 2014; **64:** e77-137.
2. Rodseth RN, Biccard BM, Le Manach Y, et al. The prognostic value of pre-operative and post-operative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. *J Am Coll Cardiol* 2014; **63:** 170-80.
3. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation Study I, Devereaux PJ, Chan MT, et al. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; **307:** 2295-304.
4. Duceppe E, Parlow J, MacDonald P, et al. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery. *Can J Cardiol* 2017; **33:** 17-32.
5. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *Rev Esp Cardiol (Engl Ed)* 2016; **69:** 1167.
6. Rodseth RN, Lurati Buse GA, Bolliger D, et al. The predictive ability of pre-operative B-type natriuretic peptide in vascular patients for major adverse cardiac events: an individual patient data meta-analysis. *J Am Coll Cardiol* 2011; **58:** 522-9.
7. Gupta PK, Gupta H, Sundaram A, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation* 2011; **124:** 381-7.
8. Writing Committee for the VSI, Devereaux PJ, Biccard BM, et al. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA* 2017; **317:** 1642-51.
9. Shulman MA, Cuthbertson BH, Wijeysundera DN, et al. Using the 6-minute walk test to predict disability-free survival after major surgery. *Br J Anaesth* 2019; **122:** 111-9.
10. Wijeysundera DN, Pearse RM, Shulman MA, et al. Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet* 2018; **391:** 2631-40.
11. Park SJ, Choi JH, Cho SJ, et al. Comparison of transthoracic echocardiography with N-terminal pro-brain natriuretic Peptide as a tool for risk stratification of patients undergoing major noncardiac surgery. *Korean Circ J* 2011; **41:** 505-11.
12. Hartle A, McCormack T, Carlisle J, et al. The measurement of adult blood pressure and management of hypertension before elective surgery: Joint Guidelines from the Association of Anaesthetists of Great Britain and Ireland and the British Hypertension Society. *Anaesthesia* 2016; **71:** 326-37.
13. Van der Spuy K, Crowther M, Nejthardt M, et al. A multicentre, cross-sectional study investigating the prevalence of hypertensive disease in patients presenting for elective surgery in the Western Cape Province, South Africa. *S Afr Med J* 2018; **108:** 590-5.
14. Lee LKK, Tsai PNW, Ip KY, Irwin MG Pre-operative cardiac optimisation: a directed review. *Anaesthesia* 2019; **74 Suppl 1:** 67-79.
15. Crowther M, van der Spuy K, Roodt F, et al. The relationship between pre-operative hypertension and intra-operative haemodynamic changes known to be associated with postoperative morbidity. *Anaesthesia* 2018; **73:** 812-8.
16. Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100:** 1043-9.
17. Marsicano D, Hauser N, Roodt F, et al. Preoperative anaemia and clinical outcomes in the South African Surgical Outcomes Study. *S Afr Med J* 2018; **108:** 839-46.
18. Devereaux PJ, Mrkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370:** 1494-503.
19. Roshanov PS, Rochwerg B, Patel A, et al. Withholding versus Continuing Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Blockers before Noncardiac Surgery: An Analysis of the Vascular events In noncardiac Surgery patIents cOhort evaluatioN Prospective Cohort. *Anesthesiology* 2017; **126:** 16-27.
20. Devereaux PJ, Sessler DI, Leslie K, et al. Clonidine in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370:** 1504-13.
21. Walsh M, Devereaux PJ, Garg AX, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. *Anesthesiology* 2013; **119:** 507-15.
22. Biccard BM Detection and management of perioperative myocardial ischemia. *Curr Opin Anaesthesiol* 2014; **27:** 336-43.
23. Devereaux PJ, Duceppe E, Guyatt G, et al. Dabigatran in patients with myocardial injury after non-cardiac surgery (MANAGE): an international, randomised, placebo-controlled trial. *Lancet* 2018; **391:** 2325-34.

Notes

Perioperative Acute Kidney Injury

Dr Ollie Smith

Department of Anaesthesia
Charlotte Maxeke Johannesburg Academic Hospital

Notes

The How and Why of Awake Craniotomy

Dr Brigid Brennan

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Anaesthesia for awake craniotomy essentially means the anaesthetic management of a patient who is required to be awake and co-operative for some period of time during a craniotomy for resection of a lesion (Tumour/Epilepsy) in or close to the eloquent cortex, to allow for functional testing of the eloquent cortex. The eloquent cortex is that part of the brain responsible for speech, language, memory, motor and sensory function. Awake functional testing allows for maximum resection of the lesion while minimizing damage to functional brain tissue.

Awake craniotomy was originally introduced for the surgical management of epilepsy. It is now more commonly indicated for the resection of supratentorial brain tumours or AV malformations near the eloquent cortex. Functional neurosurgery for DBS placement for movement disorders such as Parkinson's disease does not require craniotomy per se but does require the patient to be awake and co-operative throughout.

In the context of neuro-oncology the aim of the modern neurosurgeon is to have a positive impact on disease progression and hopefully survival while maintaining or even improving quality of life. This means avoiding devastating neurological dysfunction (aphasia/hemiparesis) but also preserving higher neuro-cognitive functions for the enjoyment of life. The aim of tumour surgery is often not curative but rather to reduce the bulk of the tumour, relieve symptoms, buy time and optimize efficacy of chemo/radio therapy. An optimal excision results in maximal removal of tumour mass with minimal functional consequences. Awake craniotomy allows for intraoperative cortical mapping of functional brain tissue allowing maximum resection with maximum preservation of function.

For tumour resection, awake craniotomy offers significant advantages in terms of patient outcome, including extent of tumour resection, survival and length of hospital stay.
A recent meta-analysis comparing outcomes in glioma resection in adults with and without intraoperative mapping in >8000 patients showed that intraoperative mapping allowed a significant increase in resection with a significant decrease in permanent severe neurological deficits.

Despite numerous advances in surgical technique and neurophysiological monitoring, awake craniotomy remains the gold standard for tumour surgery in close proximity to the eloquent cortex. It allows real time assessment of functional areas of the brain, including the subcortical tracts. Awake Mapping

Awake Mapping

Cortical mapping has shown that there is wide inter-individual variability in the location of areas controlling speech, memory, motor and sensory function (eloquent cortex).

Awake Mapping involves direct cortical electrical stimulation using a bipolar probe, while the patient is awake and able to attempt to perform a relevant task to determine if the stimulus impacts on the execution of the task.

By doing this the surgeon literally creates a map on the cortex that correlates anatomical location with function, so called functional mapping, allowing the surgeon to find the balance between completeness of tumour resection and preservation of function.

The type of mapping required obviously depends on tumour location. Ideally awake testing should be performed by a speech therapist, neuropsychologist or neurophysiologist but if such a person is not available this task may fall to the anaesthetist.

Speech and language mapping: Naming objects, counting, reading, repeating complex sentences. Monitored for language deficits such as speech arrest, expressive/receptive aphasia. Direct stimulation of speech/language cortex can result in slurring/slowing/inhibition of speech.
Motor mapping: Observe the patient for involuntary movements or interruptions in voluntary movements in the contralateral face, arm and leg.

Sensory mapping: The patient is asked to report abnormal sensations.

Visual mapping: Monitoring for abnormal visual phenomena or visual field defects.

Motor and sensory mapping can be done during craniotomy in a patient who is not awake using motor evoked and somatosensory evoked potentials (MEPS, SSEPS). Advantages of this are that mapping is independent of patient cooperation and effort. The disadvantage is that only those functions can be mapped. For language mapping awake surgery is absolutely the gold standard.

Positive mapping allows the identification of areas serving motor/language function and allows avoidance/preservation of these areas.
Negative mapping allows more aggressive resection with the assurance that the operative corridor/tumour did not affect eloquent areas.

When an awake procedure is contraindicated or fails, alternative modalities to delineate the eloquent areas of the brain would include functional MRI, diffusion tensor imaging, image guided resections and extra operative functional mapping using surface and depth electrodes. The end result would most likely be a more conservative resection than would have been possible with an awake technique.

Anaesthetic Management

The anaesthetic management of patients undergoing awake craniotomy has been extensively reviewed. Many different anaesthetic approaches have been suggested, differing mainly in drug choices and drug delivery as well as airway management. Neuroanaesthetists involved in these procedures have usually developed a preferred technique.

Preoperative preparation:

For an awake procedure psychological preparation of the patient is key. The success of the procedure and therefore patient outcome requires a calm co-operative patient.
The patient will meet with the surgeon, anaesthetist and speech/language therapist, neuropsychologist or neurophysiologist in the week leading up to surgery. These pre-op visits allow a valuable opportunity for the multidisciplinary team to create a rapport with the patient and encourage trust and familiarity. The person doing the testing will go through all the tests with the patient beforehand , both to allay patient anxiety and also to get a baseline measurement of the patients function as there may already be memory/speech/language/motor deficit as a result of the lesion. They must be counselled on what to expect with the testing e.g. involuntary movements /aphasia during speech testing, and that if this happens it is temporary and a necessary part of the procedure.
The patient must be informed of all potential risks, safety measures and stages of the procedure. The patient must be prepared for the wake-up including expected discomforts, in particular the urinary catheter and the fact that they cannot move their head/neck. They must be told what to expect with regards to noises in theatre (suction, alarms, drapes, lights). They must be counselled on potential complications that may occur while they are awake which may necessitate conversion to GA.

Physiological preoperative assessment:

A routine thorough anaesthetic pre-op assessment must be performed. Look for any anaesthetic contra-indications to the procedure.

Absolute Contraindications:

- Patient Refusal
- Inability to lie still
- Inability to co-operate

Relative contra-indications:

- Respiratory pathology. E.g. uncontrolled asthma, Severe COPD, chronic cough, respiratory tract infection, pulmonary hypertension.
- Severe OSA
- Difficult Airway
- Aspiration risk
- Language barriers
- Inability to lie supine
- Young age

Pay particular attention to the following during the pre-op visit:

1. Airway: Predictors of a difficult airway. Obstructive and central apnoea risk. Have a plan for elective and emergent airway management.
2. Epilepsy: Take anti-epileptics on morning of surgery. Interestingly though patients with symptomatic epilepsy do not appear to have a higher risk of intraoperative stimulation-associated seizures than patients without symptomatic epilepsy.
3. Tumour features: Intracranial pressures and haemorrhage risk.
4. Neurological deficits that may impact on testing. Document any pre-existing neurology.

Pharmacological premedication:

Clonidine 2-3ug/kg 1hr pre-op provides anxiolysis and stable haemodynamics without the risk of disinhibition, respiratory depression or delayed waking that may be seen with Midazolam. If Clonidine is not available and the patient requires an anxiolytic then Midazolam can be used.

Anaesthetic technique:

The anaesthetist's role is to make the operation safe and effective (facilitating surgery and mapping) while at the same time minimizing psychological and physical distress.
Choice of technique is influenced by a number of factors including local expertise and experience, patient factors, duration of procedure, pathology, etc. The main decision that needs to be made is whether the phases of the operation before and after mapping are to be performed under local anaesthesia alone, sedation or GA.
In the history of anaesthesia for awake craniotomies multiple techniques/drugs have been used but modern anaesthetic techniques for awake craniotomy can generally be classified as follows:

General Anaesthesia: 'Asleep/Awake+/-Asleep'

This technique is most commonly used in our institution for tumour surgery. The patient is under general anaesthesia for the first phase of the procedure, mechanically ventilated via LMA. This avoids the risk of oversedation and resultant airway obstruction as well as hypertension during this uncomfortable phase. It also allows for controlled mechanical ventilation and control of EtCO2. The patient is woken during the procedure and LMA removed once airway reflexes have returned but before coughing occurs. Functional testing follows. The patient may remain awake or sedated for the resection and completion of the procedure or GA can be re-commenced and LMA re-inserted.

Monitored anaesthesia care/Sedation:

Patient is sedated, spontaneously breathing with their natural airway. The level of sedation is varied during the different phases of the procedure. If the level of sedation is not titrated correctly, there are risks of airway obstruction which can lead to hypercapnia, hypoxia, and increased intracranial pressure with a 'tight' brain, or conversely a patient who is not adequately sedated will be uncomfortable and anxious. The advantages of this technique are the avoidance of airway manipulation and its inherent risks.

Awake throughout:

Uncommon. Local anaesthetic only, outpatient procedures <4hours duration.

A Meta-analysis and systematic review published in 2016 comparing complication rates in patients undergoing awake craniotomy with MAC vs. SAS showed no significant difference in complication rates (failure AC, conversion to GA, seizures, permanent neurological deficit).
What all techniques have in common are these specific aims:

- Maintaining patient co-operation, ensuring they are comfortable and awake during the mapping phase.
- Maintaining Physiological homeostasis: As for craniotomy in general, essentially ensuring a soft, slack brain during resection while maintaining cerebral perfusion.
- Prevention of nausea and vomiting.
- Minimizing interference with cortical mapping. Using drugs/techniques that do not interfere with electrophysiological recordings (epilepsy)/electrical stimulation used for functional mapping.

It is vital that communication between the anaesthetist and surgeon is effective and that the operative plan has been discussed in detail.

Positioning and theater ergonomics:

Positioning is usually supine/semi-lateral. It is often a compromise between surgical access, patient visibility, patient comfort, airway access, adequate ventilation. A useful addition would be closed circuit TV/microphone to enable the surgeon to hear and see the patient optimally during testing.

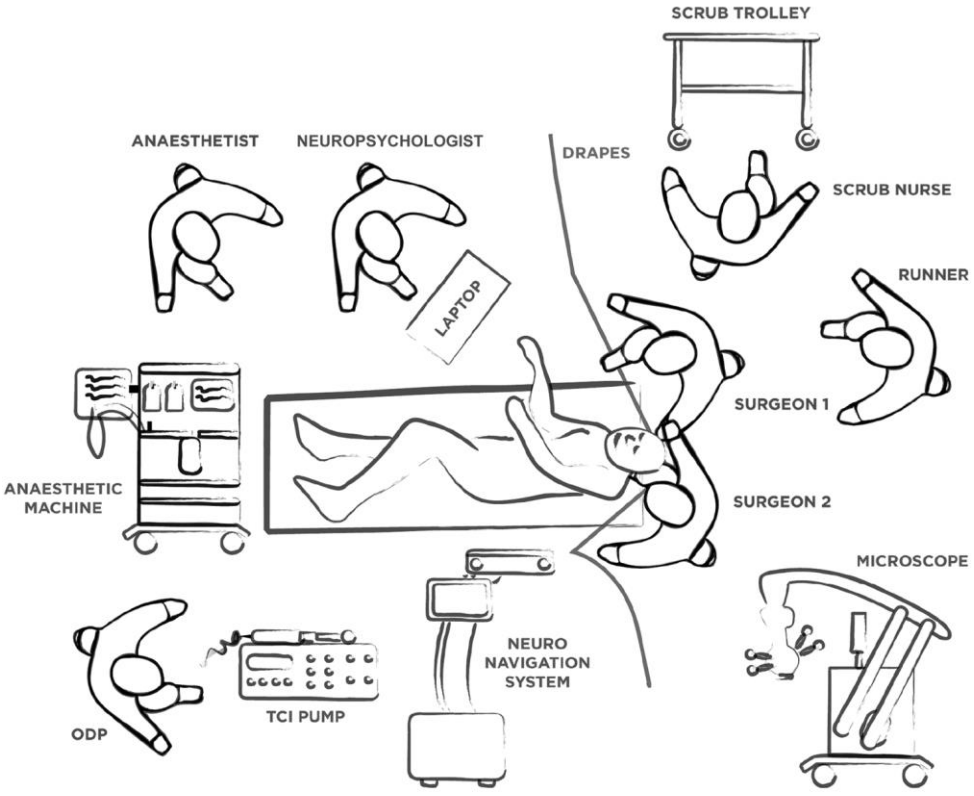


Figure 1: Theatre layout for an awake craniotomy (CEACCP Vol 14, Issue 1, Feb 2014, Pages 6-11)

Analgesia:

Along with appropriate psychological preparation, analgesia is key to a successful awake procedure. A patient is unlikely to be co-operative if they are experiencing pain/discomfort. Painful parts of the procedure are placement of the Mayfield clamp, craniotomy and dural opening.

Scalp blocks are performed after induction of GA in Asleep-Awake-Asleep procedures.

Scalp blocks are performed on every patient undergoing an awake procedure. This involves targeted administration of local anaesthetic to block the nerves supplying the scalp. For tumour or epilepsy

surgery unilateral blocks on the side of surgery suffice. This will be supplemented by the surgeon with incision line infiltration, pin site infiltration and dural infiltration. It is important to remain vigilant and to communicate and document the dose of local anaesthetic to ensure it does not exceed toxic levels. For DBS surgery bilateral blocks are required.

Scalp blocks:

The scalp is innervated by branches of the trigeminal nerve and spinal nerves. Innervation to the forehead and anterior scalp is supplied by the supraorbital and supratrochlear nerves. Temple sensory innervation is provided by the zygomaticotemporal and auriculotemporal nerves. The posterior scalp gets its nerve supply from the greater occipital nerve with the lesser occipital nerve supplying the skin behind the ear. A unilateral block therefore involves blocking 4 anterior nerves and 2 posterior nerves. Analgesic duration = 8hours.

How to:

Landmark technique. Bupivacaine 0.25% with 1:400 000 adrenalin. Aseptic. 22/23G needle.

1. Supraorbital nerve: Needle perpendicular to skin just above the supraorbital notch. LA just superficial to periosteum. Volume 1-2ml.
2. Supratrochlear nerve: Needle perpendicular to skin. 1cm medial to supraorbital injection, above eyebrow line. Volume 1-2ml.
3. Zygomaticotemporal nerve: Emerges from the temporalis fascia near the lateral border of the orbit, but many small deep branches ramify within the muscle. Field infiltration just above the zygoma through the muscle and down to the periosteum of the temporal bone with medial and lateral infiltration between the lateral edge of the supraorbital margin and the distal aspect of the zygomatic arch. Deep block. Volume: 5ml.
4. Auriculotemporal nerve: At level of auditory meatus, above TMJ, just posterior to superficial temporal artery. Injection is superficial and subcutaneous. Too deep an injection risks a facial nerve block. Volume: 1-2ml.
5. Greater occipital and lesser occipital: Divide line between external occipital protruberance and mastoid process into 3rds. Inject 45' to skin onto the superior nuchal ridge at point between middle and lateral 3rd (lesser occipital) and middle and medial third (greater occipital). Beware vessels. Volume: 5ml. Alternatively for the greater occipital nerve palpate the occipital artery, which is found about 3–4 cm lateral to the external occipital protuberance along the superior nuchal line and then inject the local anaesthetic medial to the occipital artery.

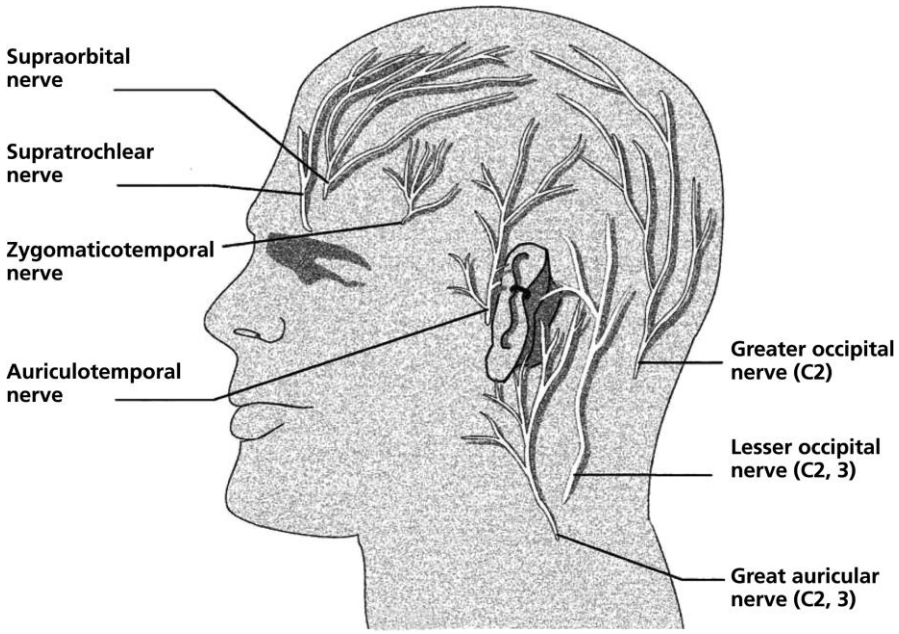


Figure 2: Scalp innervation. (CEACCP Vol 14, Issue 1, Feb 2014, Pages 6-11)

Airway:

There are a large number of airway techniques described in the literature for awake craniotomy. However, the majority of anaesthetists use an LMA for these procedures. In a UK survey about 10% of anaesthetists opt to use an ETT. Once the airway is placed the patient is ventilated to allow control of EtCO2. With positioning of the patient for surgery the LMA may become displaced. It is important to spend time ensuring that your airway is adequate. Positioning of the head may need to be a compromise between surgical requirements and a reliable, secure airway.

Monitoring:

In addition to standard monitoring most anaesthetists would insert an arterial-line. Depth of anaesthesia monitors are often used. EEG based monitors of depth of anaesthesia, despite their known limitations, are a useful measure of the clinical effects of the drugs, and can be used to guide drug dosing and improve the speed and quality of intraoperative wakening. Having said this clinical observation of vital signs and sedation scores can be used instead. The use of capnography while the patient is sedated/awake is also common practice to confirm ventilation.

Drug choice and anaesthetic technique:

The ideal anaesthetic agent would be rapidly titrateable with no major haemodynamic effects, no respiratory depression and would not interfere with electrocorticography or functional brain mapping.

For general anaesthesia TIVA/TCI with Propofol and Remifentanil is most commonly used. TCI infusion systems allow better drug titration while avoiding oversedation and respiratory depression. A Dexmedetomidine infusion may be used from the start or for anxiolysis/analgesia when the patient is awake. Sedation regimes also include Propofol/Remifentanil TCI or Dexmedetomidine.

It is important to appreciate the potential impact of your drug choices on the functional testing:
Propofol: Anticonvulsant. This is beneficial for tumour surgery but may impact on testing in epilepsy surgery. If the infusion is stopped 15-20mins before testing it does not interfere with ECOG or cortical mapping. Propofol, compared with volatile anaesthesia, increases cerebral perfusion pressure, decreases neurophysiologic monitoring interference and is antiemetic.

Remifentanil: There is an increase in epileptiform activity seen with remifentanil and other opioids. Localisation of an epileptogenic zone may be facilitated by Remi but this property is less desirable for tumour surgery.

Dexmedetomidine: Provides rousable sleep-like sedation, some analgesia and no respiratory depression. Effects of dexmedetomidine on ECOG, EEG and cortical mapping are not well delineated. While it seems to have minimal effect on the EEG there is conflicting evidence regarding its impact on the seizure threshold but most clinical literature seems to support its use in awake surgery.
Before the patient wakes up perfalgan, dexamethasone and ondansetron must have been administered. Glycopyrolate 5ug/kg can be considered to reduce secretions and theoretically reduce the risk of laryngospasm.

Once the highly sensitive dura has been infiltrated the patient is woken up and the LMA removed. The dura is only opened once full cognitive ability has been regained. Appropriate intraoperative testing can then be performed. Once the surgeon is satisfied with the mapped area the patient can either be put back to sleep (LMA re-inserted) or remain awake with sedation/analgesia as required.

Intraoperative complications:

1. Seizures. Seizures are triggered by the electrical stimulation of the cortex by the surgeon during mapping. 12 % of patients undergoing awake surgery will have intra-operative seizures resulting in 18% of these patients failing the procedure. The post-ictal state combined with any medication used to terminate the seizure can cause sedation thereby either changing the anaesthetic management or delaying testing. Ice cold saline must be available for the surgeon to apply to the brain should a seizure occur, this is usually effective in terminating the seizure. If it does not, midazolam, propofol or general anaesthesia may be required.
2. Airway obstruction. This can lead to hypoxia, hypoventilation, and hypercapnia. Suctioning, NPA, LMA, ETT. If intubation is required the surgeon de-clamps the head, covers surgical site with sterile drape and keeps head in appropriate position for intubation. Excellent communication between surgeon and anaesthetist is required as well as having all equipment ready for airway management.
3. Anxiety/Agitation. Causes may include pain, catheter, temperature etc. Reassurance, excellent pre-op preparation and full theatre staff support is mandatory.
4. Pain. A common complaint is the discomfort of the urinary catheter as well as neck stiffness from the fixed position. Remifentanil/Dexmedetomidine is usually sufficient to overcome this.
5. Hypertension. Often seen in patients with chronic hypertension. Exacerbated by pain/anxiety. Treat with remifentanil, labetalol, esmolol, verapamil as required. MgSO4 not well tolerated as a bolus in an awake patient.
6. Nausea and Bradycardia. Usually associated with deep cortical resections close to the midline. Administering anticholinergics rather than antiemetics may be more effective in this situation. Communicate closely with surgeon.

Deep Brain Stimulation (DBS)

DBS electrode implants are used in the treatment of medically refractory movement disorders such as Parkinson's disease, essential tremor, dystonia as well as severe depression and obsessive compulsive disorder. For micro-electrode reading one needs an awake, alert, attentive and co-operative patient.

Anatomical planning includes MRI/CT and 3D computer mapping transposition. This required the patient to have a stereotactic frame attached with pins to their head to provide unchanging reference points. This requires bilateral scalp blocks. DBS can be an extremely long procedure (6hrs).

The literature is vague in its recommendations for the best method of anaesthesia for DBS. Most authors hesitate to advocate for the use of sedation in patients requiring microelectrode recordings and some surgeons request termination of the dexmedetomidine infusion if cognition and arousal are at all affected. Anti-hypertensive medication may be required because of the release of Dopamine and Noradrenalin on electrode stimulation. Intra-operative hypertension must be promptly managed as it may predispose to intracranial haemorrhage.

Conclusion

Awake craniotomy for tumour resection involving functional areas is a surgical approach that offers great advantages in terms of patient outcome. Most patients can be guided through an awake procedure without much anxiety and most will later admit that the difficulties were less severe than anticipated. International studies demonstrate that awake craniotomy is generally well tolerated and only moderately burdened by intraoperative complications. This type of surgery requires a multidisciplinary approach with excellent communication between all involved in order to optimize patient outcome.

References:

1. Lobo FA, Wagemakers M, Absalom AR. Anaesthesia for Awake Craniotomy. Editorial. British Journal of Anaesthesia. 2016; 116 (6): 744-746
2. Burnand C, Sebastian J. Anaesthesia for Awake Craniotomy. Continuing education in Anaesthesia, Critical Care and Pain. 2014. Volume 14. Issue 1: 6-11.
3. Meyersfeld ND. Awake Craniotomy. Part 2 Anaesthesia Refresher Course 2015. Cape Town.

Antibiotics

Dr Jenna Piercy

Dept of Anaesthesia & Perioperative Medicine
Division of Critical Care
University of Cape Town

It's hard to know where to start to tackle such a huge subject. I have tried to include sections to cover:

- Commonly asked questions from registrars,
- Important topics for exams,
- And most importantly…topics which will (hopefully) make you a better doctor and give your patients a better outcome!

1. Classes of antibiotics and when to use them

This is something registrars (and consultants) ***always*** ask – which antimicrobials cover which bugs … often something that is very difficult to answer, and a huge section in its own right. Below is a brief overview of some of the commonly used antibiotics in clinical practice in South Africa.

1.1. Drugs which inhibit cell wall synthesis

These include the ß-lactams and glycopeptides.

1.1.1. ß-lactams

ß-lactams are antibiotics which include a ß-lactam ring in their chemical structure. They are the most commonly used class of antibiotic and have hydrophilic properties (the importance of this is covered in the section of dosing in the critically ill patient). ß-lactam antibiotics include: *Penicillins* and *penicillin derivatives* (e.g. *amoxicillin, piperacillin*), c*ephalosporins*, *monobactams* and *carbapenems.* All the ß-lactams are excreted in the urine.

ß-lactam antibiotics exert their bacteriocidal effects through binding to penicillin binding proteins (PBP). PBPs are bacterial enzymes which are responsible for cross-linking of peptidoglycans and are necessary to maintain the integrity of the bacterial cell wall. ß-lactam antibiotics therefore inhibit PBPs, which weakens the peptidoglycan layer, causing the cell to lyse due to osmotic pressure. Because ß-lactams interfere with bacterial cell wall synthesis, they are ineffective against bacteria which do not possess a cell wall (such as *Mycoplasma*). Being hydrophilic, they are also ineffective against intracellular pathogens (such as *Chlamydia*, *Brucella* or *Legionella*) and pathogens with impenetrable cell walls (such as *Mycobacteria*).

- *Penicillins*

The natural penicillins (e.g. benzylpenicillin / penicillin G, and phenoxymethylpenicillin / penicillin V) have a narrow spectrum of activity and resistance is common. Penicillin derivatives have been developed to improve features such as spectrum of activity, bioavailability, stability etc. The first major development was that of ampicillin in 1961 followed by ß-lactamase-resistant penicillins (e.g. methicillin, flucloxacillin) and antipseudomonal penicillins (e.g. piperacillin), which have a broader coverage against Gram-negative organisms.

(Note: Piptazobactam is a combination of piperacillin and tazobactam, it has good activity against Gram-positive, Gram-negative and anaerobic microorganisms). See Table 1.

- *Cephalosporins*

These ß-lactam antibiotics are frequently grouped into "generations" depending on their antimicrobial effects, although exact categorisation may vary between countries.
By and large, each subsequent generation of cephalosporin has greater Gram-negative cover than the preceding generation, and *usually* less activity against Gram-positive organisms (see Table 2.)

Table 1. Classification and spectrum of antimicrobial activity of penicillins

Penicillin	Category	Spectrum of activity
Penicillin G / V	Natural penicillin	Gram-positive bacteria
Cloxacillin, oxacillin	Semi-synthetic, ß-lactamase resistant	Gram-positive bacteria
Amoximcillin, ampicillin	Semi-synthetic, amino penicillin	Gram-positive bacteria e.g. *Listeria monocytogenes* Gram-negatives including *Escherichia coli, Proteus mirabilis*
Piperacillin	Semi-synthetic, ureido penicillin	Gram-positive bacteria Improved Gram-negative coverage including *Klebsiella* spp. and *Pseudomonas*

Table 2. Classification and spectrum of antimicrobial activity of cephalosporins

Generation	Examples	Spectrum of activity
First	Cefazolin Cefadroxil	G+ (no activity against Methicillin-resistant *Staphylococcus aureus - MRSA*) G- some *Proteus mirabilis*, *E. coli* and *Klebsiella pneumonia* (PEcK). No effect against *Pseudomonas, Enterobacter, Serratia, Acinetobacter*
Second	Cefuroxime Cefoxitin	Less G+ effect than 1st generation More G- effect than 1st generation (e.g. against *Haemophilus influenza, Enterobacter* spp.) Cefoxitin has anaerobic effects
Third	Ceftriaxone Cefotaxime	Less G+ effect (compared to 1st and 2nd generation cephalosporins) More G- effect, including nosocomial sepsis (no effect against Extended-spectrum ß-lactamases) Penetrate central nervous system No activity against anaerobic organisms
Fourth	Cefepime	G+ effect similar to 1st generation cephalosporins G- antipseudomonal effects; more resistant to ß-lactamases than 3rd generation No activity against anaerobic organisms
Fifth	Ceftobiprole Ceftaroline	Ceftobiprole has good effect against *Pseudomonas* spp. and Vancomycin Resistant Enterococci (VRE) Ceftaroline has activity against MRSA but no antipseudomonal or VRE effect

- *Monobactams*

e.g. Aztreonam
Possess activity against Gram-negative organisms only.

- *Carbapenems*

Carbapenems are ß-lactam antibiotics with a broad spectrum of activity, and are usually reserved for nosocomial or multidrug resistant pathogens. They are particularly effective against Gram-negative organisms, (but their Gram-positive effects are slightly narrower) and they possess anaerobic activity. In addition to the spectrum of activity highlighted in table 3, the carbapenems do not have activity against atypical microorganisms (e.g. *Chlamydia, Legionella, Mycoplasma*).

Carbapenems are divided into 3 groups according to their spectrum of activity (see Table 3).

The carbapenems diffuse poorly through the Gram-negative outer cell membrane so are reliant upon porins (outer membrane proteins) to facilitate their passage through the cell wall. Once inside the bacteria, carbapenems bind to PBPs and weaken peptidoglycans, rendering the cell wall less resistant to osmotic stress.
Imipenem is deactivated in the kidneys by the enzyme dehydropeptidase-1 (DHP-1), to overcome this deactivation, it is administered with the DHP-1 inhibitor, cilastatin. Imipenem is frequently described as having the potential to induce seizures, but bear in mind that this is not only a side-effect of

imipenem – all the ß-lactam antibiotics can cause seizures, especially when administered in high doses.

Imipenem has slightly better activity against Gram-positive bacteria compared to meropenem; meropenem is slightly more effective against Gram-negative organisms compared to imipenem. Ertapenem has a more limited spectrum of activity than the Group 2 carbapenems as it is ineffective against *Pseudomonas aeruginosa* and *Enterococcus* spp.

Side effects of the ß-lactams include neurotoxicity (seizures, spasms, hallucinations) as well as the well-known hypersensitivity reactions.

Table 3. Classification of carbapenems and spectrum of activity

Group	Examples	Spectrum of activity
1	Ertapenem	Broad spectrum Limited activity against non-fermentative Gram-negative bacilli (e.g. *Acinetobacter, Pseudomonas, Burkholderia, Stenotrophomonas*) No activity against MRSA or *Enterococcus* spp. Half-life 4 hours
2	Imipenem Meropenem Doripenem	Broad spectrum. Activity against non-fermentative Gram-negative bacilli. No activity against MRSA. Half-life ±1 hour
3	None currently licensed for clinical use	Broad spectrum MRSA activity

1.1.2. Glycopeptides

e.g. Vancomycin and Teicoplanin

Their activity is against Gram-positive organisms as they are such a large molecule, and thus are unable to penetrate the outer membrane of the Gram-negative organisms. Like the ß-lactams, they interfere with cell-wall synthesis, although the glycopeptides act at an earlier stage of synthesis than the ß-lactams.

Resistance to the glycopeptides is also well described, especially in *Enterococci species* (*Enterococcus faecium* and *faecalis*), Vancomycin-resistant Enterococci (VRE) and Coagulase-negative staphylococci (CNS). Coagulase-positive staphylococci (e.g. *Staphylococcus aureus*) may also demonstrate reduced susceptibility to the glycopepetides (e.g. Vancomycin-Intermediate Staphylococcus Aureus (VISA) and Glycopeptide-Intermediate Staphylococcus Aureus (GISA)).

Side effects of the glycopeptides include ototoxicity and nephrotoxicity (although the renal toxic effects of vancomycin are over-exaggerated; however, vancomycin accumulates in renal failure and serum drug level monitoring is recommended). Rapid infusion of vancomycin can cause histamine release, resulting in “red-man syndrome”.

1.2. Antibiotics which inhibit protein synthesis

These include the aminoglycosides, tetracyclines, chloramphenicol, macrolides, lincosamides, streptogramins, oxazolidinones and fusidic acid….I will only deal with the most clinically relevant ones, otherwise I’ll be here forever!

1.2.1. Aminoglyosides

e.g. Gentamycin, Amikacin, Tobramycin

This important group of antibiotics is administered via the intravenous route, since these drugs are poorly absorbed from the gut. Importantly, they have poor tissue and lung penetration so are not very good for treating pneumonia. However, the use of nebulized aminoglycosides (**in addition to** targeted intravenous therapy) is finding favour due to the extremely high concentration of antibiotic in the alveolar fluids which this mode of delivery yields. The aminoglycosides are an important defence against Gram-negative organisms. They have no activity against anaerobes or streptococci, but have good activity against Staphylococci.

Aminoglycoside-modifying enzymes (AME) are an important mechanism of resistance to this class of antibiotics. The enzymes inactivate the drug by altering the structure of the aminoglycoside (see section on mechanisms of resistance).

Side-effects of aminoglycosides include nephro- and oto-toxicity. They have a narrow therapeutic window.

1.2.2. Macrolides

e.g. Erythromycin, Clarithromycin, Azithromycin
Erythromycin deserves a mention here; not for its antimicrobial use in ICU, but for its increasing use as a prokinetic to facilitate enteral feeding. The dose for prokinesis is much smaller than that used for treatment of microbial infections (250mg 6 hourly, intravenously); its antimicrobial action is against Gram-positive organisms (and is often used in patients who are allergic to penicillin compounds).

Clarithromycin and azithromycin (as well as erythromycin) have excellent activity against atypical microorganisms (*Legionella, Chlamydia, Rickettsia, Brucella*) and have an important role in the treatment of severe community acquired pneumonia.

1.2.3. Lincosamides

e.g. Clindamycin
Clindamycin has a similar spectrum of activity as erythromycin, but has better anaerobic cover. It has excellent penetration into the bone and soft tissue, but received bad press as it was the first antibiotic to be implicated in causing pseudomembranous colitis.

1.2.4. Oxazolidinones

e.g. Linezolid
Linezolid is a bacteriostatic antibiotic with activity against a wide-range of Gram-positive bacteria (including MRSA and *Enterococcus faecium*). Linezolid may be associated with a worse outcome (compared to Daptomycin) when used to treat blood stream infections caused by Vancomycin-resistant enterococci (VRE).

1.3. Antibiotics which inhibit nucleic acid synthesis

1.3.1. Quinolones

e.g. Nalidixic acid, Ciprofloxacin, Moxifloxacin, Levofloxacin
The quinolones interfere with the replication of the bacterial chromosome. They have Gram-positive and good Gram-negative activity. Moxifloxacin and levofloxacin have some activity against anaerobes. Side effects include neurotoxicity and photosensitivity; caution is advised in the use of quinolones during pregnancy and in children due to their adverse effect on cartilage development. Quinolone-associated tendinitis and tendon rupture is more likely in the elderly, as well as in patients with renal impairment, solid organ transplants and those taking corticosteroids. A recent safety warning has emerged with the recognition of quinolones being associated with aortic aneurysm and dissection.

1.3.2. Rifamycins

e.g. Rifampicin
Rifampicin blocks the synthesis of bacterial mRNA. It is primarily used for the treatment of Mycobacterial infections. Side-effects includes hepatic dysfunction and skin rashes. In our setting, rifampicin is seldom used other than for the treatment of tuberculosis, due to the increased risk of collateral damage with the development of rifampicin-resistant-TB, in a setting where TB prevalence is very high.

1.4. Antibiotics which inhibit metabolic pathways

1.4.1. Sulfonamides

e.g. Sulfamethoxazole is a bacteriostatic antibiotic which competes with *para*-aminobenzoic acid (PABA), an enzyme involved in the catalysis of tetrahydrofolic acid (THFA) (which is required for the synthesis of purines and pyrimidines). Sulfonamides may cause Stevens-Johnson syndrome.

Trimethoprim prevents synthesis of THFA, but does so at a later stage of the pathway than sulfamethoxazole. Trimethoprim has activity against Gram-negative bacteria (but no activity against *Pseudomonas* spp).

Sulfamethoxazole and trimethoprim are often administered as the combination agent co-trimoxazole. The combination of the 2 drug is synergistic and is valuable in the treatment of *Pneumocystis jirovecii* and *Nocardia*.

1.5. Other commonly used antibiotics

1.5.1. Nitroimidazoles

e.g. Metronidazole. For metronidazole to destroy bacterial DNA, the parent compound must enter the bacterial cell, which requires activation by reduction. Anaerobic organisms have the ability to produce a low redox potential for the reduction and activation of metronidazole. As such, metronidazole has activity against anaerobic organisms, and no activity against aerobic bacteria. Metronidazole also has anti-parasitic effects; it is used in high doses for the treatment of amoebic liver abscesses.

1.5.2. Polymixins

e.g. Colistin (Polymixin E).
The polymixins disrupt the cell membrane and have good activity against Gram-negative bacteria. *Proteus* spp. is inherently resistant to the polymixins. In our clinical setting Colistin is commonly used for infections due to pan-drug-resistant *Acinetobacter baumanii*. Side effects include nephrotoxicity and neurotoxicity.

2. Mechanisms of resistance

Bacteria can be innately resistant to certain classes of antibiotics (e.g. *Serratia* spp., *Burkholderia* spp. and *Proteus* spp. are intrinsically resistant to Colistin, *Enterococci* spp. are intrinsically resistant to cephalosporins) or they may develop or acquire resistance (after having been previously susceptible).

Acquired resistance may arise from:

- Single spontaneous chromosomal mutation
- Multiple spontaneous chromosomal mutations
- Transfer of resistant genes on plasmids, transposons or cassettes which become inserted into the bacteria's DNA.

The mechanisms by which resistance occurs is divided into 3 main types:

1. Alteration of the target site where the antibiotic acts; e.g. alteration of structure of the Penicillin Binding Protein (PBP). This means that the antibiotics are unable to bind effectively to the PBP and don't effectively interrupt cell wall synthesis. Methicillin-resistant *Staphyloccus aureus* (MRSA) is an example of a bacteria which uses this mode of resistance.
2. Alteration of antibiotic access to the target site (altered uptake or increased elimination of the drug)
    a. Modification of porin channels or cell wall permeability may impede entry of the antibiotic into the cell. Porin channels in the outer membrane permit entry of the antibiotic into Gram-negative bacteria. Mutations in the porin gene causes repression of porin channels which decreases the permeability of the outer membrane to the antibiotic, rendering the antibiotic ineffective as it is unable to gain access into the bacteria.
    b. Insertion of efflux pumps in the cell wall which pump the antibiotic out of the cell. This is an important mechanism of resistance to tetracylines as well as carbapenems.
3. Production of enzymes which inactivate the antibiotic agent
    a. ß-lactamases and Extended-Spectrum ß-lactamases (ESBLs)
    b. Aminoglycoside modifying enzymes (AME)
    c. Carbapenemases

ß-lactamases deserve a special mention as they are the commonest mechanism of bacterial resistance against ß-lactam antibiotics.

- ß-lactamase enzymes hydrolyse the ß-lactam ring and render the antibiotic ineffective. Some ß-lactamases are specific and target specific compounds (e.g. penicillins).
- Inducible ß-lactamases (IBL) are cephalosporinases. In IBL producing organisms (such as *Enterobacter* spp*., Serratia* spp*., Pseudomonas aeruginosa)* the expression of ß-lactamase is usually repressed, but in the presence of selected ß-lactam antibiotics (particularly 3rd generation cephalosporins) the production of the enzyme is greatly increased. This can lead to the rapid emergence of resistance to multiple ß-lactam antibiotics. ß-lactamase inhibitors (e.g. clavulanic acid, sulbactam, tazobactam) are molecules which contain a ß-lactam ring but have little bactericidal activity. When combined with a ß-lactam antibiotic they act as "suicide inhibitors" by binding to the ß-lactamase enzyme and preventing the ß-lactam antibiotic from being hydrolysed and destroyed. For example, Co-amoxyclav is made up of amoxicillin (the ß-lactam antibiotic) and clavulanic acid (a ß-lactamase inhibitor) which prevents amoxicillin being inactivated by the ß-lactamase enzyme. Similarly, piperacillin-tazobactam combines the ß-lactam antibiotic piperacillin, with tazobactam (a ß-lactamase inhibitor).
- Extended-spectrum ß-lactamases are ß-lactamases produced by *Enterobacteriacae,* which confer resistance to many ß-lactam antibiotics (penicillins, cephalopsporins and monobactams) but not against carbapenems. Carbapenems are the antibiotic of choice if the bacteria produce ESBLs; ertapenem is recommended as it has the narrowest spectrum of activity, but some ertapenem-resistant isolates have been reported. Although (occasionally) some of the later generation cephalosporins may appear to be effective against such organisms *in vitro*, the use of these antibiotics is associated with a high treatment failure rate *in vivo*.
- Carbapenemases have activity against the penicillins, cephalosporins and carbapenems. The carbapenems have been the "go-to" class of antibiotics for nosocomial sepsis for many years as they are relatively resistant to hydrolysis by most ß-lactamases. However, in recent years, the emergence of enzymes which destroy the carbapenems (carbapenemases) threatens their successful antimicrobial profile, especially against Enterobacteriacae - termed *Carbapenem-resistant Enterobacteriacae* (CRE). KPC (*Klebsiella pneumoniae* carbapenemase), OXAs (oxacillinase), VIM (Verona integron encoded metallo-ß-lactamase) and NDM-1 (New Delhi metallo-ß-lactamase) are all examples of enzymes which destroy carbapenems and are spread by plasmids across a wide spectrum of bacteria.

[Plasmids are molecules of DNA which exist outside of the chromosomal DNA. They are readily passed between bacteria, and frequently express enzymes which confer resistance to more than 1 antibiotic].

Risk factors for developing resistant infections (e.g. CREs) include cumulative antibiotic exposure – this includes not only the number of previous exposures to antibiotics, but also increasing duration of treatments.

3. Microbiological speak

Deciding on which antibiotic to use against which microbe depends on many factors:

- Susceptibility of the organism to the antibiotic
- Effect site concentration
- Collateral damage and side effects
- Pharmacokinetic and pharmacodynamic (PKPD) principles

3.1. Susceptibility of the organism to the antibiotic

The ***minimum inhibitory concentration*** ***(MIC)*** **is the lowest concentration of an antibiotic (in µg/mL) that inhibits the growth of a strain of bacteria.** Quantifying the result can help to determine which antibiotic is most effective against the bacteria (the lower the MIC, the more likely an organism is likely to be susceptible to a particular antibiotic). However, the MIC must be compared to the **breakpoint** (see below) to describe whether the bacteria is Resistant, Sensitive or Intermediate when the antibiotic is administered in "usual doses".

The MIC for one antibiotic cannot be compared to an MIC for another antibiotic, as this relies on other information such as the antibiotic ***breakpoint*** and the site of infection etc. The **breakpoint is a previously agreed upon concentration of antibiotic which defines whether a species of bacteria is susceptible or resistant to the antibiotic** i.e. where bacteria begin to show resistance. If the MIC is less than, or equal to the breakpoint, then the bacterial isolate is reported as being susceptible / sensitive to the antibiotic. Breakpoints are predetermined by national organisations (e.g. EUCAST in Europe and CLSI in the USA). These are published and updated annually. By way of example: a strain of *Klebsiella pneumonia* has MICs of 2µg/mL for piptazobactam, 2µg/mL for cefepime and 2µg/mL for gentamycin. Although the MICs are the same, it does not necessarily mean that the *Klebsiella pneumonia* will be equally susceptible to all three agents. The closer the MIC is to the breakpoint, the less susceptible the organism. If, in the above example the MIC breakpoint for piptazobactam is 8, cefepime is 1 and gentamycin is 2, then the *Klebsiella* will be most susceptible to the piptazobactam and will be least susceptible to cefepime.

Resistant implies that "normally" achievable serum drug levels are inadequate to inhibit bacterial growth. Intermediate implies that organisms are likely to be inhibited only if maximally recommended doses are used to achieve serum concentrations. Organisms which are resistant or have intermediate sensitivities may still be susceptible if high concentrations of the antibiotic are achieved.

Mutant Prevention Concentrations (MPC) is a pharmacodynamic concept which highlights the importance of achieving high levels of antibiotic to prevent the development of microbial mutations and the emergence of resistant organisms. MPC is defined as the concentration of antibiotic that prevents the growth of single step mutations. This means that, above the MPC, microbes need to mutate more than once to develop resistance (i.e. makes the development of resistance more difficult). Dosing in the concentration window between the MIC and the MPC encourages mutations and selects for resistant organisms. This is termed the Mutant Selection Window (MSW) and is the difference between the MPC and MIC. See Figure 1.

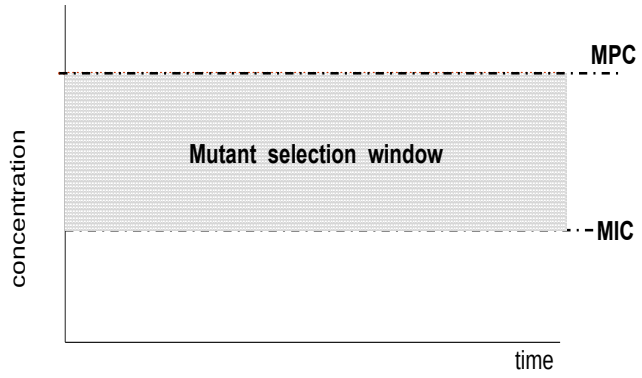


Figure 1. Graph to demonstrate the relationship between MIC, MPC and MSW.

3.2. Effect site concentration

It is not possible to measure the drug level at a microbe level, so surrogate levels of the drugs are used instead, i.e. the concentration of the drug in serum or in tissue. Some knowledge about the penetration of the antibiotic at the site of infection is important when prescribing such agents. For example, some drugs (e.g. the aminoglycosides) have poor penetration in to the lung parenchyma and alveolar fluid, and are unsuitable for treating pneumonia. However, if aminoglycosides are delivered by nebulisation, the extremely high doses generated in alveolar fluid may be sufficient to kill the bacteria, even those which are relatively resistant. Similarly, large doses of ceftriaxone and meropenem have good penetration into cerebrospinal fluid (CSF), whereas ertapenem and vancomycin have poor penetration and are unsuitable for systemic use in infections of the central nervous system (CNS). See Table 4.

Table 4. Target tissue penetration by commonly used antibiotics (taken from South African Antibiotic Stewardship Programme: A pocket guide to antibiotic prescribing for adults in South Africa 2015. Wasserman, Boyles and Mendelson)

Antibiotic	CSF	Lung	Soft tissue	Urinary tract
Co-amoxyclav	Poor	Good	Good	Fair
Ceftriaxone	Good (in high dose)	Good	Good	Good
Aminoglycosides	Poor	Poor	Fair	Good
Co-trimoxazole	Good	Good	Good	Good
Ertapenem	Poor	Good	Good	Good
Meropenem	Good (in high doses)	Good	Good	Good
Imipenem	Good	Good	Good	Good
Vancomycin	Poor	Fair	Poor	Good

Therapeutic drug monitoring (TDM) is the measurement of specific drugs (in this case antibiotics) at designated time intervals to optimise individual dosing regimens, and achieve required PK/PD targets. However, most TDM measures serum / blood concentrations, which may not reflect the concentration at the effect site.

3.3. Collateral damage

Collateral damage is the term describing unintended adverse effects on the ecology due to antibiotic use which manifests as the selecting out of, and development of colonization with, multi-drug resistant (MDR) pathogens. In particular, the use of broad spectrum agents such as third generation cephalosporins and quinolones have been linked to the development of bacterial resistance. Quinolones have been linked to the development of methicillin-resistant *Staphylcoccus aureus* (MRSA) and an increase in the resistance of *Pseudomonas aeruginosa* to quinolones; 3rd generation cephalosporins are linked to the development of subsequent infections with *Clostridium difficile*, vancomycin-resistant enterococci (VRE), resistant *Acinetobacter baumanii* and extended-spectrum ß-lactamase-producing (ESBL) *Klebsiella pneumoniae.*

Clearly, one must also be cognisant of the side effects of the antibiotics as well as the patient's clinical condition, for example: avoiding nephrotoxic agents in patients with renal dysfunction.

3.4. Pharmacokinetic / pharmacodynamic properties

Antibiotics exhibit optimal antibacterial effects based on pharmacokinetic (PK) and pharmacodynamics (PD) principles; the dose and dosing interval of the antimicrobial is determined by these PKPD relationships. Antibiotics are broadly classified into one or more of the following categories in terms of the relationship between dose and concentration (See Figure 2 – this will be explained fully later in the text):

a) time-dependent (t >MIC)
b) concentration dependent (C_{max}/MIC)
c) a combination of a and b, expressed as the area under the concentration-time curve (AUC_{0-24h}/MIC).

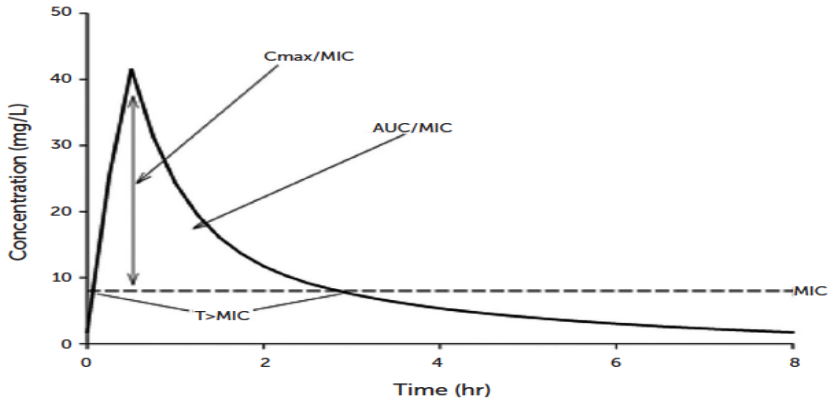


Figure 2. Summary of pharmacodynamic parameters over a concentration time profile

Examples of which antibiotics belong to which PKPD class are given in Table 5 (adapted from Blot SI et al. Advanced drug delivery reviews 2014; 77:3-11).

Table 5. Pharmacokinetic and pharmacodynamic properties of commonly used antibiotics

	Time-dependent (t>MIC)	Concentration-dependent (C_{max}/MIC)	Concentration AND time dependent (AUC_{0-24h}/MIC)
Objective	Maximise duration of exposure	Maximise concentration	Maximise amount of drug exposure
Antibiotic	Penicillins	Aminoglycosides	Vancomycin
	Cephalosporins	Metronidazole	Clindamycin
	Carbapenems	(Fluoroquinolones)	(Fluoroquinolones)
	(Linezolid)		(Linezolid)
			Azithromycin

3.4.1. Time-dependent (see Figure 3)
Classes of antibiotics which exhibit optimal antimicrobial effect by time-dependency (also referred to as non-concentration dependent antibiotics) exert their effects by the length of duration the concentration exceeds the MIC over a 24h period. Further increasing the concentration above the MIC probably leads to better killing rates: current recommendations are that a drug exposure of ≥4-8x MIC could improve outcomes in patients treated with ß-lactam antibiotics. Antibiotic effect is ineffective if the concentration is below the MIC. The ß-lactams are typically time-dependent antimicrobials.

Previous recommendations suggested that optimal effects occur when the concentration of the antibiotic remains above the MIC for ≥40-75% of the dosing interval. However, current recommendations suggest that the t>MIC (for ß-lactams especially) should be as close to 100% of the dosing interval to achieve optimal effects. This is particularly true in critically ill patients who, due to their altered physiology (see below), frequently fail to achieve desirable antibiotic concentrations. In order to achieve a prolonged period above the MIC, these drugs are sometimes administered as a continuous infusion (***AFTER A LOADING DOSE***), or as an extended infusion. Extended infusions are often used with imipenem and meropenem as they are not stable in solution for long time periods. Continuous / prolonged infusions with ß-lactam antibiotics seem to be of greatest value in critically ill patients, especially those infected with relatively resistant organisms (e.g. those with higher MICs).

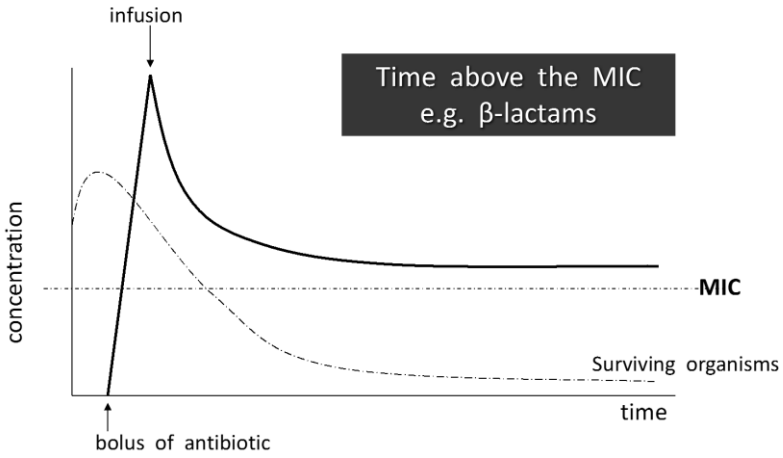


Figure 3. Graph to illustrate time-dependent killing

3.4.2. Concentration dependent (See Figure 4)
Antimicrobials which work in this way rely on a high peak concentration (C_{max}) in relation to the MIC; this is how aminoglycosides act (although, in fact, aminoglycosides also fit into the AUC/MIC category as well and have some degree of time-dependence too…but their concentration-dependence is paramount!). For the aminoglycosides, it should be mandatory to measure a peak concentration 30 minutes after the infusion is completed. ***The peak level of aminoglycosides should be taken after the FIRST DOSE (I cannot emphasise this enough…..as there is this widespread, outdated belief that levels should only be taken on day 3….and it drives me NUTS and gives me grey hair – don't be that person!!!).*** Measuring a peak level after the first dose is crucial, as under-dosing is extremely common and you **MUST!!!!** give an adequate dose from the get-go. Under-dosing exposes the patient to the side-effects of a drug, without the effective therapeutic benefit. The best recommendation is to achieve a concentration of ≥10-12x above the MIC for that organism at the site of infection. Aminoglycosides are usually given as a once daily dose, yet they continue to have a clinical effect even when their concentration falls. This is due to their ***POST-ANTIBIOTIC EFFECT*** *(PAE)*, and is seen because the antibiotic is taken up into the organism and continues to exert its effects from within, even though the serum concentration has fallen. Metronidazole also demonstrates a PAE.

Trough levels should be taken on day 3, immediately before the dose is administered. ***T***rough levels relate to the ***T***oxicity of the aminoglycosides (ototoxicity, nephrotoxicity) since uptake of aminoglycosides by the inner ear and renal cortex is most marked at sustained levels. To minimise trough levels, the aminoglycosides are administered by ***extended interval dosing***, usually as a once daily dose.

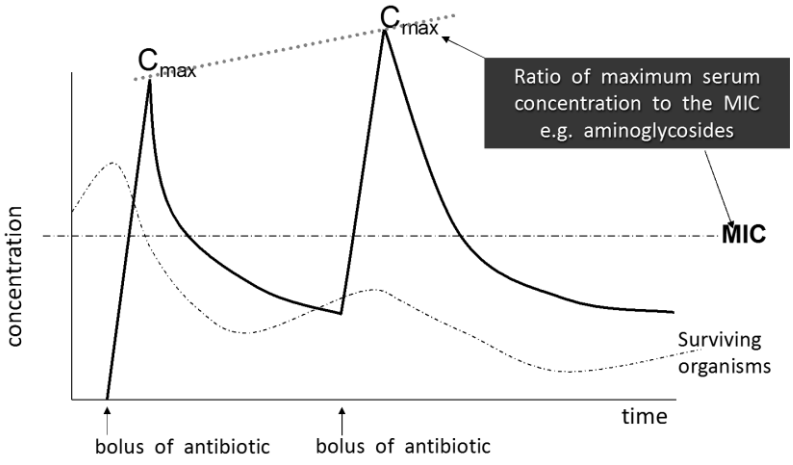


Figure 4. Graph to illustrate concentration-dependent killing

Some antibiotics demonstrate both time and concentration dependent killing. For Gram-positive cocci with an MIC <1µ/mL vancomycin demonstrates time dependent killing kinetics, but if the MIC >1µ/mL, it demonstrates concentration dependent killing.

3.4.3. A combination of concentration-dependent with time-dependency (See Figure 5)
Mathematically, this is expressed by the area subtended by the concentration-time curve and is expressed as $AUC_{0\text{-}24h}$/MIC. Specific values for the $AUC_{0\text{-}24h}$/MIC depend on the particular antimicrobial.

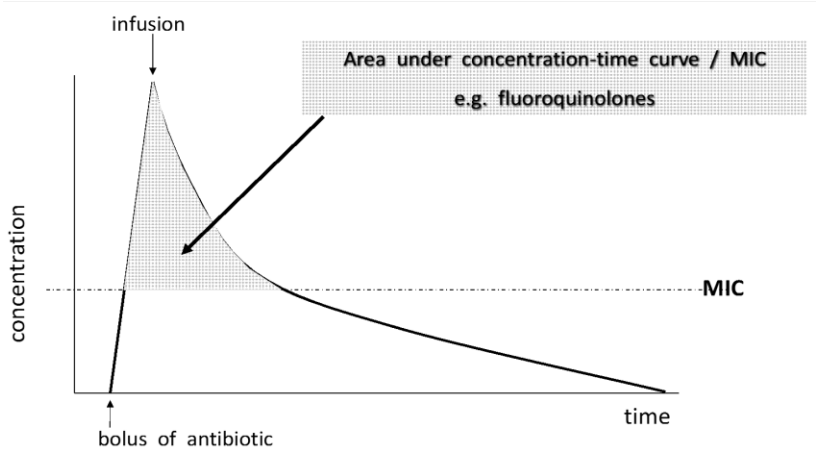


Figure 5. Graph to illustrate antimicrobial killing by $AUC_{0\text{-}24}$/MIC

4. Dosing

This is such an important area and we are cocking it up royally!!
The literature shows that we are under-dosing antimicrobials WAAAAAY more often than we are over-dosing. Under-dosing leads to:

- Inefficient antimicrobial killing
- Compromised clinical outcome
- The development of multi-drug resistant organisms.

Most antimicrobials in clinical practice are hydrophilic (e.g. ß-lactams, aminoglycosides and glycopeptides). Lipophilic antibiotics include the fluoroquinolones and macrolides; these are easier to administer to septic patients as they tend to have intracellular accumulation and hepatic clearance, so are only need their maintenance doses to be adjusted in the case of severe hepatic failure. The hydrophilic antibiotics are prone to failure in septic patients due to the volume of distribution and renal clearance often being greatly enhanced…and here's why.

4.1. Increased volume of distribution (Vd)

Septic patients have circulating endotoxins and exotoxins which damage capillaries and cause capillary leak. This causes fluid to shift from the intravascular space to the interstitial space, taking with it hydrophilic molecules (importantly, antibiotics!!) which hugely increases their Vd and therefore reduces the serum concentration of the hydrophilic antimicrobials. In addition, vasodilatation and hypotension frequently require fluid resuscitation which, over hours, further expands the interstitium and further increases the Vd. It is important to recognise that the increase in Vd is only of relevance for hydrophilic antibiotics (the majority of antibiotics used in clinical practice), and not those which are lipophilic.

4.2. Increased renal clearance

The amount of hydrophilic antibiotic that remains behind in the intravascular space is also "under threat". Sepsis is frequently associated with a hyperdynamic cardiovascular system and an increased cardiac output, which in turn translates to an increased renal blood flow…and thus increased clearance of renally eliminated drugs. Antimicrobial clearance is proportional to creatinine clearance (see below in the section of augmented renal clearance).
In addition, septic patients are likely to have hypoalbuminaemia. Low albumin is associated with an increase in free fraction of the drug, although this may be advantageous initially, can lead to low concentrations later in the dosing interval. This occurs because the unbound form is a smaller molecule than the bound form, and is therefore more efficiently filtered by the kidney; thus, more

antibiotic is eliminated in the urine. Hypoalbuminaemia is more clinically relevant when the antibiotics are both highly protein bound and predominantly cleared by glomerular filtration (such as ertapenem and ceftriaxone). Optimisation of dosing schedules in such scenarios should include the use of loading doses and higher-than-usual maintenance doses.

4.2.1 Augmented renal clearance

Augmented renal clearance (ARC) is a phenomenon that has only been recognised in the past decade, but is of great importance as it probably leads to faster elimination of drugs (including antibiotics), which in turn leads to sub-therapeutic concentrations and likely poor clinical outcomes (see Figure 6). ARC occurs when the urinary clearance of creatinine (CrCl) exceeds 130mL/min/1.73m^2 (normal values approximately 88-125 mL/min/1.73m^2 - with women having slightly lower levels than men). The exact mechanism remains unclear, but is, in part, related to: inflammation, increased renal blood flow, increased cardiac output, increased atrial natriuretic peptide and fluid resuscitation. ARC is estimated to occur in up to 65% of critically ill patients, and often occurs even in the setting of a normal serum creatinine. Young patients with polytrauma, burns, traumatic brain injury and lower severity of illness are particularly at risk of developing ARC. ARC is associated with sub-therapeutic antibiotic plasma concentrations of ***time-dependent antibiotics***, especially vancomycin and the ß-lactams. Recommendations are emerging that continuous infusions (or extended infusions) be used for these drugs, to maximise the duration of time that bacteria are exposed to adequate concentrations of antibiotics. Concentration-dependent antibiotics are **minimally affected** by ARC as their mode of action depends primarily on the peak concentration and volume of distribution, and not on the clearance of the drug.

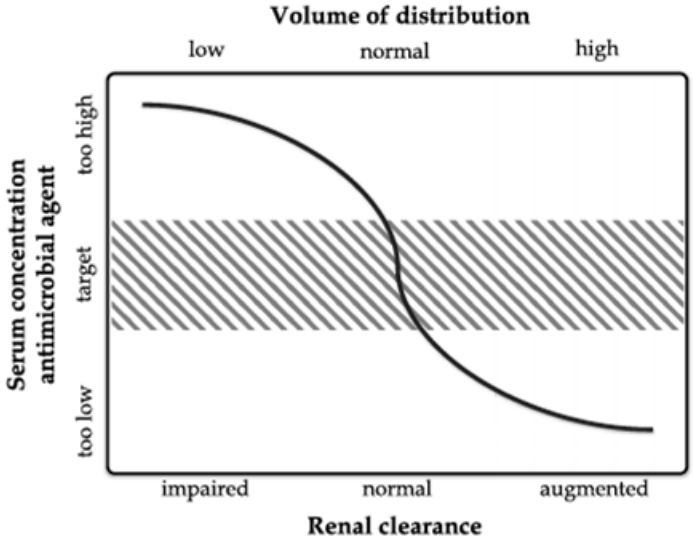


Figure 6. Graphical depiction of the effects of volume of distribution and renal function on serum concentration of hydrophilic antimicrobials.

4.3. Recommended doses

There has been an increase in the recommended doses of antimicrobials in the past few years. To summarise the above section: time-dependent and concentration-dependent antibiotics both require an increase in dose due to the increased volume of distribution seen in critically ill patients. In the setting of ARC, time-dependent antibiotics should be administered at higher doses (or continuous / prolonged infusions), whereas ARC does not have a big impact on concentration dependent antimicrobials (which depend on the C_{max}/MIC). See Table 6 for recent recommendations of doses and dosing schedules.

Table 6. Dosing schedule for some common antimicrobials

Drug	Recommended dose
Amikacin	25-30mg/kg daily **(N.B. not 1g!!!!!!!)**
Cefepime	2g bolus and 6g daily over 24h
Ceftazidime	2g bolus and 6g over 24h
Cloxacillin	2g 6-hourly, or 3g 6-hourly in staphyloccal bacteraemia
Colistin	9-12mU loading dose then 3mU 8-hourly or 4.5mU 12-hourly
Ertapenem	1g 12 hourly
Gentamycin	7-9mg/kg daily **(N.B. not 320 or 400mg!!!!!)**
Imipenem	1g 6-8 hourly
Meropenem	1-2g 8 hourly
Piptazobactam	4.5g 6 hourly (or 4.5g bolus then 18g over the following 24h as a continuous infusion)

4.4. Dosing in acute kidney injury

Since many hydrophilic antibiotics are renally eliminated, a knee-jerk reaction is to automatically reduce the dose of (all) antimicrobials as soon as they are initiated. The rationale behind this is that this will limit the toxicity from accumulation of the drug. This rationale is somewhat flawed however, since the initial standard loading dose is likely to reach suboptimal serum concentrations due to the increased Vd (which initially is independent of renal function). Of course, with time, there will be accumulation of renally cleared (hydrophilic) antibiotics, but in the initial period this is not a concern. The literature does not have firm evidence as when to cut back on the standard doses of renally eliminated drugs, but recommendations are emerging to probably continue the usual doses for 24-72h before reducing the dose, to prevent accumulation and toxicity. However, there are a couple of important exceptions which need to be noted:

a) Drugs which are not eliminated by the kidneys are unlikely to pose such a problem
b) There may be compensatory elimination by alternative pathways. For example, ciprofloxacin is almost completely cleared by the kidneys, but in renal failure ciprofloxacin doesn't not accumulate, as there is compensatory elimination by alternative pathways such as hepatic and trans-intestinal elimination.

Therefore, please consider carefully your rationale for reduction the dose of your antibiotic….there's a very good chance you may be ***WRONG***!!

4.5. What about in renal replacement therapy?

This is too detailed a topic to go into here, since the clearance of antimicrobial depends not only on factors such as Vd, plasma protein concentration and compensatory elimination, but also on the mode and dose of renal replacement therapy (RRT) as well as factors such as blood flow rate, dialysis filter material, and surface area. Although therapeutic drug monitoring may provide some clue, this is not widely available for all antibiotics and, in addition, only reflects plasma concentration and not necessarily effect site concentration.

4.6. Dosing in hepatic failure

Also not as straightforward as you might think!! Although the Child-Pugh score has previously been used to guide dosing, so far, the only antibiotics which need adjustment for Child-Pugh class C are metronidazole and tigecycline. Hepatic failure is associated with hypoproteinaemia, and thus an increase in unbound fraction of many drugs; however, it is estimated that a reduction in hepatic function by 90% is required before drug clearance is affected. In addition, hepatic blood flow is frequently increased in critically ill patients and this may compensate for the reduction in liver enzyme activity in drugs which have a high extraction ratio.

My advice……always go big. In septic patients, time is of the essence and achieving high effect site concentrations as soon as possible is paramount. The literature supports that we are under-dosing far more commonly than overdosing. Give big doses, as least for the first 48h….and probably for longer!

However…there is a phenomenon called the Eagle effect, whereby when bacteria and fungi are exposed to high concentrations of antimicrobial (above the MIC, or minimum bactericidal concentration - MBC); paradoxically there is an improved bacterial survival and decreased rate of bacterial cell death. Although this is fascinating and thought provoking, it's outside the required depth of knowledge for your examination! I should comment however, that MICs and MBCs are *in vitro* tests, and one cannot often be certain of the effect site concentration in clinical practice. Similarly, most of the examples of the Eagle effect have been demonstrated *in vitro* with only 2 case reports of it in humans (both in the setting of bacterial endocarditis). Again, I reiterate, the literature supports the fact that we are under-dosing far more frequently than we are overdosing.

5. Antimicrobial Stewardship

This is a term which is frequently bandied around and poorly understood, often irritating clinicians by curbing their antibiotic autonomy. Stewardship is ***crucial*** to our survival as human beings and boils down to "minimising antibiotic resistance whilst maximising antibiotic effectiveness". We must protect the antibiotics which we currently have by using them appropriately, to maintain their effectiveness. Overuse, misuse and under-use (such as occurs in under-dosing) all drive the emergence of multi-drug resistant organisms.

I'm not going to go into huge detail, despite the enormous importance of this section, but will give you a few bullet points and principles. www.fidssa.co.za is an excellent source for good articles on stewardship. The list below is modified from South African Antibiotic Stewardship Programme: A pocket guide to antibiotic prescribing for adults in South Africa 2015. Wasserman, Boyles and Mendelson).

- Is an antibiotic necessary?
    - About 50% of all antibiotic use is unnecessary
- Perform cultures before administering antibiotics
    - This helps to guide therapy after the initial empiric antibiotic choice, and makes de-escalation possible
- For empiric antibiotics:
    - Chose the antibiotic which targets the most likely pathogen at the site of infection
    - Consider the likelihood of antimicrobial resistance
    - Consider target site and adequacy of tissue penetration
    - Preferably use monotherapy with the appropriate spectrum of activity
- Ensure correct dose and route of administration
    - Dose according to the PK/PD principles which I have highlighted above
        - Give big doses!
        - Consider ARC (and organ dysfunction)
    - Aim for oral therapy except:
        - In certain infections such as meningitis, osteomyelitis, endocarditis and blood stream infections
        - In patients who are unable to swallow or absorb oral medication
        - In the setting of haemodynamic instability (this may be septic shock, but other shocked states also mean that absorption from the gastrointestinal tract or from intramuscular injections are unreliable)
        - For initial therapy for severe infections (always start with intravenous therapy in critically ill patients)
        - If no appropriate oral antibiotics are available
- Give early in severe infections
- Early and effective source control
- Evaluate appropriateness every day and avoid unnecessarily prolonged courses
- De-escalate as soon as possible.

The WHO essential medicines list has divided antibiotics into 3 categories according to the **AW**a**R**e mnemonic to preserve the effectiveness of "last resort" antimicrobials (see Table 7). This is an attempt to ensure that the correct antibiotics are used for the right infection and to improve prescribing decisions. The categories are:

- **A**ccess – which antimicrobials should be widely available. These tend to be narrow spectrum agents which have a low risk of toxicity. Importantly, it is only from this group that prophylactic antibiotics should be selected.
- **W**atch – first or second line treatment for a small number of infections, or antibiotics which have a higher concern regarding toxicity.
- **R**eserve – which should only be used in severe circumstances as last-resort options and must be tailored to specific patients and clinical circumstances.

Table 7. List of *some of* the antibiotic classified into the AWaRe groups by the WHO

Access	Watch	Reserve
Benzylpenicillins, Phenoxymethylpenicillin	Antipseudomonal penicillins and ß-lactamase inhibitor (e.g. piptazobactam)	Aztreonam
Ampicillin	Carbapenems	4th generation cephalosporins
Amoxicillin	3rd generation cephalosporins	5th generation cephalosporins
Co-amoxyclav	Glycopeptides	Polymixins (e.g. colistin)
Cefalexin or cefazolin	Macrolides	Tigecycline
Cloxacillin	Quinolones and fluoroquinolones	Oxazolidinones (e.g. linezolid)
Doxycycline		
Gentamycin, Amikacin		
Metronidazole		

6. Closing remark

(I think) Antimicrobial therapy is perhaps the most important area of medical therapy, especially given the burden of sepsis and its associated high mortality rates. Unfortunately, it's an enormous area and I have limited space for these notes!! I hope that the notes provide some insight into some of the various intricacies of optimising antimicrobial therapy, and the damage we can do by getting this wrong!!

References

1. Blot SI, Pea F, Lipman J. Advanced drug delivery reviews. 2014; 77:3-11
2. Varghese J, Roberts JA, Lipman J. Current Opinion in Anaesthesiology. 2010; 23:472-478
3. South African Antibiotic Stewardship Programme 2015. Wasserman S, Boyles T and Mendelson M.
4. Prasetyoputri A, Jarrad AM, Cooper MA, Blaskovich MAT. Trends in Microbiology 2019; 27:339-354
5. Cunha CB, Opal SM. Medical Clinics of North America. 2018; 102:831-843
6. Udy AA et al. Crit Care Med 2014; 42:520-527
7. De Waele JJ et al. Int Care Med 2014; 40:1340-1351
8. Richards GA, Joubert IA, Brink AJ. S Afr Med J 2015; 105:419
9. Guilhaumou R et al. Crtitical Care 2019; 23:104

Anaesthesia for Tracheal Resection

Dr Richard Llewellyn

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Introduction

Although there are several management modalities for tracheal stenosis including dilatation with a number of options and laser incision or resection, tracheal resection, together with tracheal transplantation and more recently tracheal non-occlusive balloon dilatation, remains one of the definitive treatment options.

Tracheal resection presents a few challenges to the anaesthetist amongst which are inducing a patient with a compromised airway, sharing the airway with the surgeon and co-ordinating airway management during the excision and anastomotic process, the management of emergence following surgery and the postoperative management.

Anatomy and physiology

Knowledge of the anatomy of the trachea and upper airway including the blood and nerve supply is key to understanding and appreciating the intricacies of anaesthesia and surgical technique for this procedure. The interested reader is referred to reference 1 for an excellent summary of these aspects.

Aetiology

The most common cause of tracheal stenosis remains complications from endotracheal intubation or tracheostomy tubes. It must be emphasised that even a short period of intubation may initiate the inflammatory process resulting in tracheal stenosis. Monitoring of endotracheal cuff pressure should be mandatory in all intubated patients.

Other causes are listed in the Table below: (from Hobai et al. Anesthesiology Clinics 2012)[1]

Table1
Causes of tracheal obstruction

Benign	Malignant	Infectious	Non-infectious

Congenital
• Vascular rings
• Aortic aneurysm
• Tracheogenic cyst
• Congenital tracheal stenosis or malacia
 	
Acquired
• Foreign body
• Blood clots
• Mucus plug
• Post-surgical
  ◦ Lung transplant
  ◦ Sleeve resection (trachea or bronchus)
  ◦ Tracheostomy
• Traumatic
  ◦ Post-intubation
  ◦ Burn/inhalation
  ◦ Airway hematoma
  ◦ Laceration
	Primary tracheal tumors
	• Adenoid carcinoma
	• Squamous cell carcinoma
	• Neurofibroma
	• Chondroma
	• Chondroblastoma
	• Hemangioma
	• Carcinoid
	
	Metastatic tumors (origin)
	• Thyroid
	• Larynx
	• Lung
	• Esophagus
	• Breast
	• Lymphoma
		• Papillomas
		• Tuberculosis
		• Rhinoscleroma
		• Viral tracheobronchitis
		• Bacterial tracheitis
			Inflammatory
			• Amyloidosis
			• Wegener's granulomatosis
			• Relapsing polychondritis
			
			Miscellaneous
			• Aortic aneurysm
			• Retrosternal goiter
			• Mediastinal adenopathy
			• Mediastinal fibrosis

Preoperative evaluation

Critical airway stenosis may be anticipated from preoperative symptoms of orthopnoea, stridor and exercise tolerance. If the latter is impaired with effort this implies a 50% reduction in tracheal diameter and breathing difficulty at rest implies a tracheal diameter of less than 6 mm. Further noteworthy history includes difficulty in breathing related to positional changes and ability to cough and clear secretions.

Traditional airway assessment, neck mobility, mouth opening and prediction of successful mask ventilation should be performed as well always remembering that a reassuring airway examination does not guarantee a successful intubation. Appropriate reserve and emergency equipment must be available. [2]

The symptoms of significant upper airway obstruction, stridor or dyspnoea, correlate with the reduction in intraluminal diameter and resistance to air flow across the area of narrowing. Usually flow is laminar and depends mainly on airway diameter. The Hagen-Poiseuille equation for laminar tube flow is:

$$\text{Airflow} = \text{Pressure Gradient} \times \frac{\pi r^4}{8 \times \eta \times l}$$

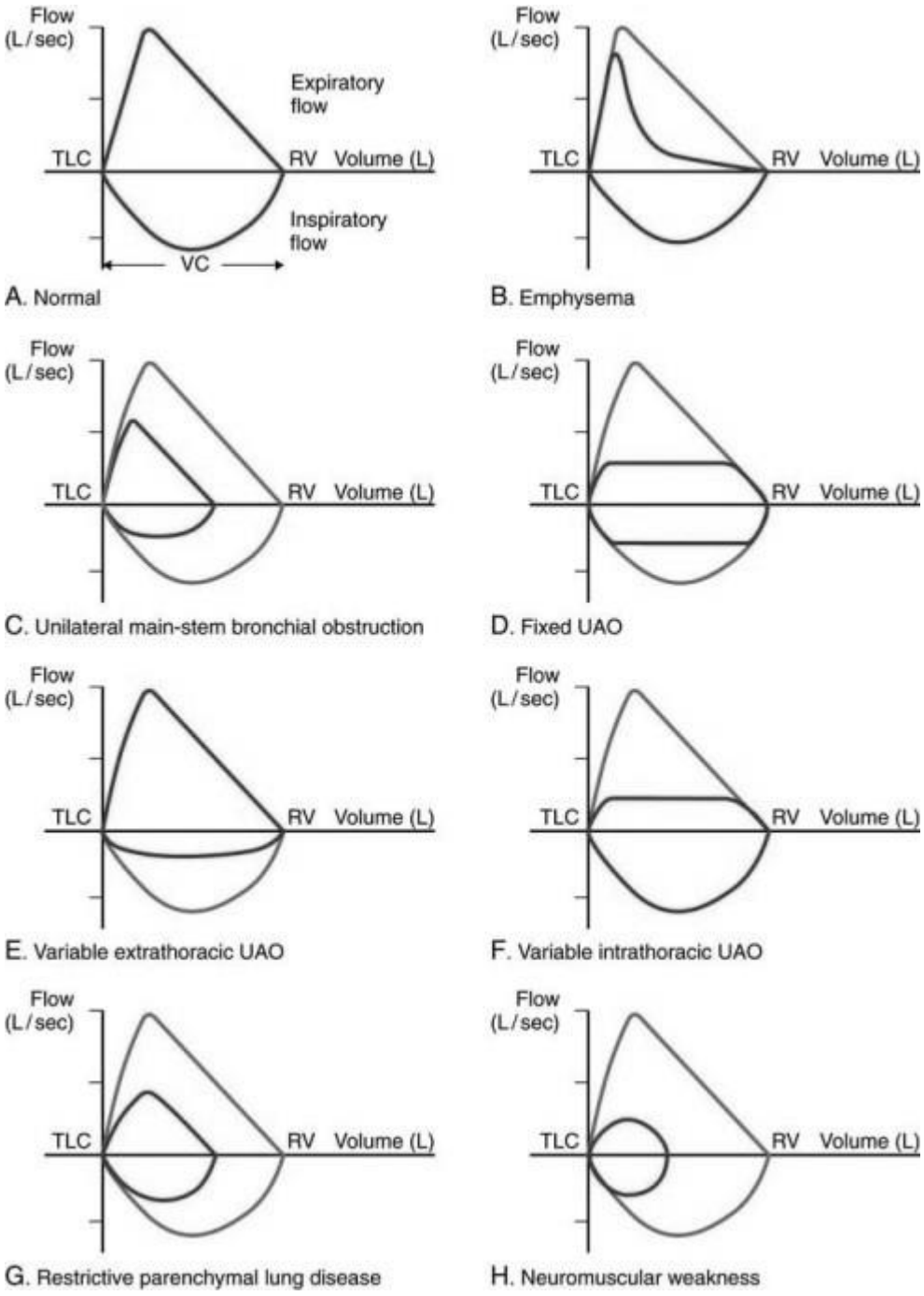
Flow can be increased by increasing the pressure gradient at the expense of increased work of breathing and decreased effort tolerance.

Respiratory symptoms may become apparent with exertion when the internal diameter of the tracheal lumen is reduced to approximately 50 % or 8 mm. Inspiratory stridor appears at rest when the tracheal lumen is further reduced to 5 to 6 mm. [1]

Pulmonary function testing, specifically flow-volume loops, has traditionally been used in the diagnosis and characterization of tracheal pathology. The classical teaching is that fixed stenosis (the more common case) attenuates both inspiratory and expiratory peak flows. Dynamic collapse occurs in different phases depending on the location of the lesion. Extrathoracic compromise occurs in inspiration, when airway pressure is below atmospheric pressure. Intrathoracic compromise occurs in expiration when thoracic pressure is above tracheal pressure. Spontaneous ventilation is better tolerated with intrathoracic lesions because thoracic pressure drops below tracheal pressure during inspiration. In actual practice, the role of flow-volume loops has been de-emphasized.

Imaging has improved and careful clinical observation and questioning can elicit much of the relevant dynamic respiratory components. [1] But remember CT imaging gives a poor functional assessment of the dynamic nature of the pathology.

Classical flow-volume loops are shown overleaf.



From: Dr Michael Thompson – Gold Coast Lung function Laboratory
https: /www.lungfunction.com.au/flow-volume-loops.html

Blood tests will depend on other co-morbidities but should include a baseline haemoglobin.
As mentioned above CT imaging is used for planning. ECG and echocardiography as indicated.

Multi-disciplinary team assessment and communication is critical.

These procedures are mostly elective and preoperative optimisation in terms of smoking cessation, chest physiotherapy, and improved fitness should be part of the preoperative preparation.

Intraoperative management

Good communication with the surgeon about both the anaesthetic and surgical plan is crucial. As mentioned thorough preparation in terms of airway equipment and devices is equally paramount.

Standard monitors are routinely used together with an arterial line. This is usually sited in the left radial artery in case the right innominate is compressed or retracted. It is wise to place the saturation probe on the right hand for early warning should this happen. Depth of anaesthesia monitoring is indicated if using a TIVA technique. If the case is expected to take more than 3 hours, a urinary catheter should be placed.

The patient symptomatology and location and extent of the lesion will largely determine the method of induction of anaesthesia which may range from an intravenous induction with a neuromuscular blocking agent to an inhalational induction. Maintenance of anaesthesia may be either with TIVA or an inhalational agent.

Although maintenance of spontaneous (negative pressure) ventilation via inhalational induction has been classically taught, positive pressure ventilation (PPV) with muscular relaxation and a supraglottic airway may produce superior peak inspiratory and expiratory flows. By maintaining positive intratracheal pressure throughout the respiratory cycle, PPV may prevent the indrawing of mobile tracheal segments and prevent airway collapse.[2]

The location of the lesion will also determine the surgical approach. Upper or mid-tracheal lesions, usually the most common, are typically approached through a cervical transverse collar incision. Lower tracheal or carinal lesions may require a right thoracotomy. The following section relates to the former.[3]

If there are positional symptoms related to breathing the patient is placed in a position of comfort otherwise in the usual supine position.

Following induction, it is usual to perform a rigid bronchoscopy to confirm the location and extent of the lesion to be resected, the health and function of the vocal cords, any areas of inflammation of the trachea, including signs of aspiration, and any areas of tracheomalacia.[1] If a supraglottic device is used flexible endoscopy may be performed.

The patient is then intubated with the largest size endotracheal tube possible. Occasionally very tight stenoses may need to be cored out or dilated to allow endotracheal intubation.[1]

Once the airway is secured for a cervical surgical approach the neck may be extended with the placement of a shoulder or scapular roll. Later on after resection the neck will need to be flexed for the anastomotic part of the procedure.

Surgery starts with dissection and mobilisation of the trachea. The distal trachea is then divided and a sterile ETT and circuit are used to intubate the distal segment, so-called cross-field ventilation as shown below.[4] The ETT from above is withdrawn from the surgical field.

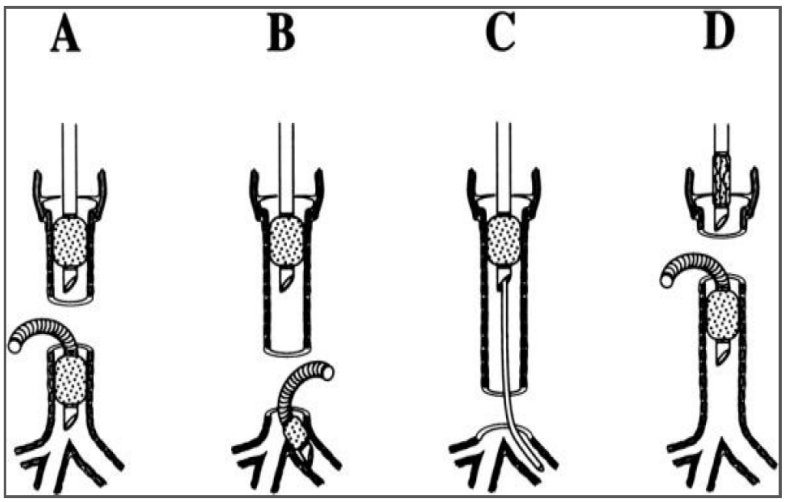


Figure 5. *Ventilatory management of the open airway. In all cases, the open trachea is shown after resection of the lesion. (A) In the technique employed for the vast majority of cases, the oral endotracheal tube (ETT) is pulled back so that the lesion can be easily manipulated, but the cuff is left inflated to protect the airway from above. Intubation of the distal airway is accomplished across the field using sterile equipment. (B) The same arrangement is shown as applied to a low tracheal lesion, with endobronchial intubation. This technique can be used for most low tracheal and carinal resections. (C) Endobronchial ventilation is shown using a jet ventilation catheter placed through the oral ETT. (D) A high tracheal lesion with the oral ETT cuff deflated and the tube pulled back into the larynx is shown. If necessary for surgical exposure, the oral ETT can be removed entirely and the patient reintubated by a retrograde technique. In A, B, and D, ventilation may be intermittent, with the sterile cross-field ETT placed in the airway or moved aside by the surgeon as needed.*

From: Sandberg W. Int Anes Clinics 2000;38(1):55-75 [4]

The segment to be removed is dissected circumferentially and then removed. Sutures are placed through the posterior wall and then the anterior rings. The ETT from above is positioned with the cuff below the distal anastomotic suture line. The distal ETT is removed.

The sutures are tied and after the trachea is closed a test is performed to see that the anastomosis is leak proof. The operative field is flooded with saline and about 30 cm of water pressure is applied to the breathing circuit. If no bubbles are seen the incision is closed. [1]

In order to avoid coughing the usual approach is to extubate these patients deep once breathing spontaneously. In the flexed position this may lead to a degree of obstruction until the patient is fully awake. This is usually resolved by means of a nasopharyngeal airway. An alternative approach is to remove the ETT and replace with a SGA. Whichever approach is used a final endoscopy need to be performed before the patient awakes to check that the airway is clear of secretions and the integrity of the suture lines confirmed. Also to check points 3 and 4 below.

A “guardian” or Grillo suture may or may not be placed over the manubrium to the submental crease to keep the neck flexed. This should not be so tight as to be uncomfortable. The aim is to prevent hyperextension, not force hyperflexion. [1]

Postoperative management

At emergence and extubation the aims and considerations are to:

1. Maintain neck flexion
2. Assess and manage tracheal bleeding and obstruction
3. Check for laryngeal swelling
4. Check for vocal cord dysfunction [1]

Depending on the extent of surgery the patient may be managed in an ICU or HCU.

For cervical incisions pain is usually mild to minimal postoperatively and large doses of opiate analgesia are seldom required.

Early complications include respiratory difficulties from various aetiologies and delayed complications such as dehiscence of the anastomosis and haemoptysis.

Departures from cervical incisions

Less commonly carinal resection may require a right thoracotomy in which case the patient will be positioned in the left lateral position and epidural analgesia may need to be considered. In the event of such resections where airway management may be extremely challenging ECMO has been utilised.

References

1. Hobai IA, Chhangani SV and Alfille PH. Anesthesia for tracheal resection and reconstruction. Anesthesiology Clinics 2012;30:709-730
2. Roman PEF, Battafarano RJ and Grigore AM. Anesthesia for tracheal reconstruction and transplantation. Current Opinion in Anesthesiology 2013;26:1-5
3. Modest VE. Anesthesia for tracheal surgery. UpToDate Last updated 11 July 2018
4. Sandberg W. Anesthesia and airway management for tracheal resection and reconstruction. International Anesthesiology Clinics 2000;38(1):55-75

Further reading

- Daumerie G, Su S and Ochroch EA. Anesthesia for the patient with Tracheal Stenosis Anesthesiology Clinics 2010;28:157-154
- https://openairway.org/

Anaesthesia for Shoulder Surgery

Dr Luis Felipe Montoya-Pelaez

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Introduction

Surgical procedures of the shoulder joint, whether minimally invasive (arthroscopic) or open, are associated with considerable post-operative pain for up to 48 hours and beyond. Regional anaesthesia (RA) techniques, often combined with sedation or general anaesthesia, have become the mainstay of anaesthetic management for shoulder surgery. The most common procedures on the shoulder joint include hemiarthroplasty, total shoulder arthroplasty, arthroscopy, subacromial (SA) decompression, shoulder instability procedures including bankart and laterjet capsule tightening procedures, rotator cuff repair and frozen shoulder manipulations.

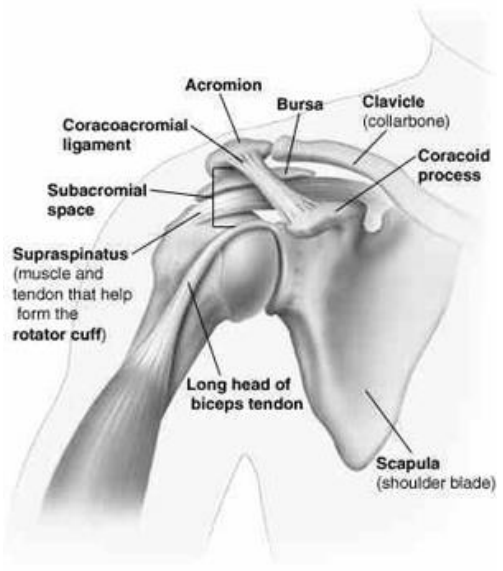
Interscalene brachial plexus blockade (ISB) is the RA technique of choice as it provides excellent and consistent intra and post-operative analgesia with minimal complications in expert hands. The use of RA for shoulder surgery has seen an increase in popularity, especially in ambulatory surgery, where it has shown to have a better profile than other analgesic interventions as regards quality of pain control, earlier discharge from the post-anaesthesia care unit, PONV, improved patient co-operation with rehabilitation and a reduced hospital length of stay.

History

In 1884, Halstead was the first to inject cocaine around the exposed roots of the brachial plexus (BP). But it was not until 1911 that Hirschel and Kulenkampff described a percutaneous approach to the supraclavicular BP. The posterior (paravertebral) approach to the BP at the level of the nerve roots was first described by Kappis in 1912 and subsequently reintroduced by Pippa et al in 1990. In 2003, Boezaart modified this approach to avoid the often painful needle passage through the posterior muscles of the neck. First performed in 1919 by Mulley, the anterior approach to the BP was perfected by Winnie in 1970 also using the transverse process of the 6th cervical vertebra as a reference for needle insertion.

Anatomy and innervation of the shoulder joint

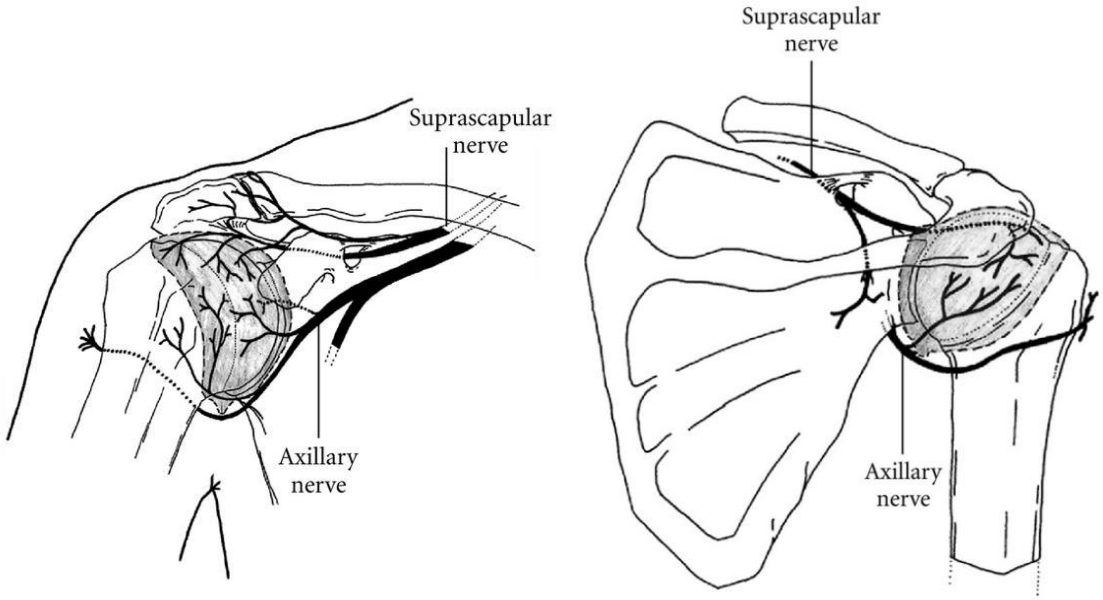
The shoulder girdle consists of three main joints: sternoclavicular, acromioclavicular and glenohumeral joints and the often unmentioned scapulothoracic joint. Static shoulder stability is provided by the labrum, capsule and glenohumeral ligament; dynamic stability by the the rotator cuff, the long head of the biceps tendon and the periscapular muscles.



The shoulder joint is innervated by multiuple peripheral nerves that originate from the trunks and cords of the BP. The anterior aspect of the joint is innervated by the subscapular, axillary and lateral pectoral nerves. The subscapular and axillary nerves originate from the posterior cord of the BP and the lateral pectoral nerve from the lateral cord. The posterior aspect of the shoulder joint is innervated by the suprascapular nerve (SSN) and small branches of the axillary nerve. The SSN originates from the C5 and C6 nerve roots of the superior trunk of the BP with variable contribution from C4.

The SSN is responsible for 70% of the sensory supply to the shoulder joint, the capsule, SA bursa, coracoclavicular ligament and makes variable contributions to the overlying skin. The posterior branch of the axillary nerve teminates as the superior lateral cutaneous nerve that supplies the skin over the deltoid muscle; the anterior branch supplies motor innervation to the deltiod muscle. The supraclavicular nerves (anterior, middle and posterior) arise from the cervical plexus (C3 and C4) and supply the skin from the sternoclavicular joint antero-medially to the shoulder postero-laterally. They can be blocked as the emerge from under the posterior aspect of the sternocleidomastoid muscle.

Innervation of the shoulder joint



Pre-operative considerations

Due to advances in minimally invasive techniques and an increasing confidence in the use of RA by anaesthetists, the benefits of shoulder surgery have been extended to include patients with considerable co-morbidity and frailty. The spectrum of conditions that require surgery to the shoulder joint varies from simple trauma in relatively healthy individuals to shoulder arthroplasty in patients with rheumatoid arthritis that are often on a host of disease modifying and other drugs that may have significant anaesthetic implications. In these patients, a detailed assessment of organ reserve, in particular cardio-respiratory and renal function, should be investigated and optimisation effected as for any other surgical procedure. Severely affected patients may present challenges with IV or intra-arterial cannula placement as well as the performance of a RA block and positioning for surgery. The airway should be examined carefully for potential difficulties that may affect ease of mask ventilation, placement of a supraglottic device or performance of laryngoscopy (e.g. RA affecting cervical spine and TM joints, obesity).

Unless undergoing minor diagnostic arthroscopic procedures or manipulations under anaesthesia, all patients should be offered an anaesthetic that includes a regional technique either as a sole anaesthetic or in combination with sedation or general anaesthesia. The risks and relative benefits of RA and other forms of anaesthesia should be clearly explained so that patients are able to make an informed choice regarding their anaesthetic care.

Anaesthetic options

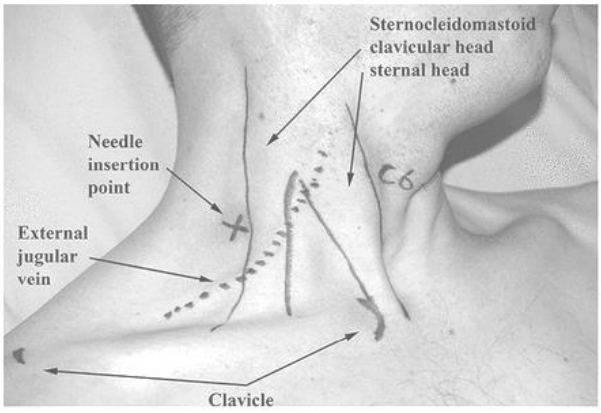
Patients may undergo shoulder surgery under GA alone, RA with or without sedation or a combination of RA and GA. The latter is the most common approach to shoulder surgery although RA with or without a degree of sedation is becoming more popular. RA only anaesthesia is associated with greater patient satisfaction, superior analgesia, less PONV, less cognitive dysfunction and earlier discharge from hospital. In awake shoulder surgery, patient selection is crucial with preparation starting long before the day of surgery. Obstacles to overcome include patient perceptions of RA to practical issues such as proximity of the patient's face to the surgical site (claustrophobia). Patients who are unable to communicate freely, sit still for prolonged periods, have multiple co-morbidities or potential airway problems are not suitable candidates RA only surgery.

It has been stated that an advantage of GA over RA for shoulder surgery is that any anaesthetic approach that incorporates RA takes longer and reduces efficiency. Good communication between anaesthesia, surgeon and nursing staff and a well-organised regional anaesthesia team has been shown to reduce turnover time and improve efficiency.

- **Interscalene block (ISB)**

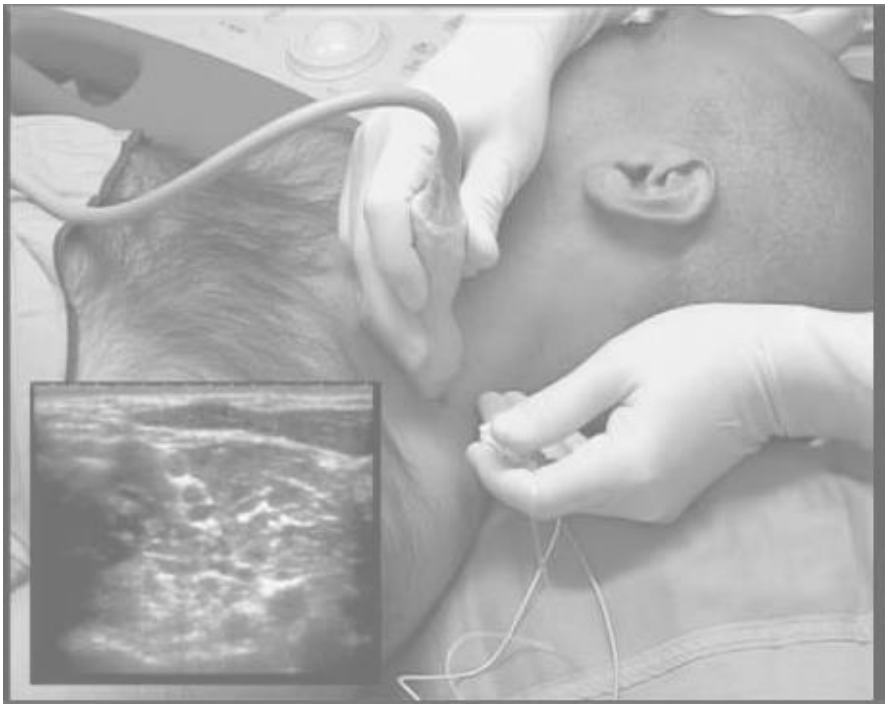
The ISB is considered the gold standard RA technique for shoulder procedures. ISB can be used for procedures involving the shoulder, including the lateral two thirds of the clavicle, proximal humerus and shoulder joint and is widely used both as the primary anaesthetic and as an adjuvant in post-operative pain management. Ulnar sparing (C8) is often seen with this block which limits its usefulness for more distal procedures. The ISB can be performed as a single injection or as a continuous nerve block with the placement of a perineural catheter. Localisation techniques range from 'blind' (paraesthesia and nerve stimulation) to the use of ultrasound guided (USG) nerve localisation and visualisation of LA deposition around nerves. With the ready availability of nerve stimulators and the evolving ubiquity of US machines, no patient should have to undergo ISB (or any other RA block, for that matter) using paraesthesia localisation techniques.

The classic interscalene approach as described by Winne (anterior approach) is still commonly performed, especially for single-injection blocks. Although Winnie used paraesthesia as an end-point for the block, most practitioners now use either NS or USG techniques.



Surface anatomy. The typical needle entry point (x) for an interscalene nerve block is shown in relation to the sternocleidomastoid muscle and its clavicular and sternal heads (solid lines) as well as the course of the external jugular vein (dotted line) and the ends of the clavicle.

Chan used US to directly visualise the nerve roots of the BP in the interscalene groove at the level of the cricoid. The needle can either be inserted using an in-plane or an out-of plane technique. Although the in-plane technique allows better visualisation of the needle, the out-of plane technique provides a shorter path to target tissues.



The use of US for ISB has been shown to have higher success rates than with NS (99,8% vs 91%) with better sensory and motor blockade than with NS. There is also a reduced number of needle passes with USG as compared with NS. In expert hands, ISB using USG or NS is highly effective with no significant difference in complications related to nerve injury.

Posterior approach to ISB: The cervical paravertebral block (CPB)

Over the past decade, the posterior approach to the BP has regained interest. Advantages of the posterior approach include avoidance of the eternal jugular vein, a greater distance between the catheter entry site and the surgical field, and a lower incidence of catheter migration. Disadvantages include pain on passing the needle through the posterior muscles of the neck (hence Boezaart's modification), possible damage to the dorsal scapular and long thoracic nerves, as well as inadvertent needle entry into neuraxial structures.

The technique is performed with the patient either sitting or in the lateral position. After anaesthetizing the skin and subcutaneous tissue, an insulated 17- or 18-gauge Tuohy is inserted at the apex of the "V" formed by the trapezius and levator scapulae muscles at the level of C6 vertebra. The nerve stimulator is attached and the needle is advanced medially and approximately 30° caudally, towards the suprasternal notch until the short transverse processes or the pars intervertralis of C6 is encountered, typically at a depth of 4-6 cm from the skin. The loss-of-resistance syringe is attached to the needle and directed laterally until there is loss of resistance. A motor response of the shoulder muscles should immediately follow as the paravertebral space is entered 0.5 to 1 cm beyond bony contact. Supraclavicular nerve block or local infiltration by the surgeon is required if there is conversion to an open procedure as CPB does not block the superficial cervical plexus. Recently, Antonakakis and Mariano have each described their version of US guided placement of a continuous interscalene perineural catheter using a posterior approach.

Many institutions are discharging patients home with in-situ catheters and pumps with LA solutions with promising results. The cost effectiveness of this approach and potential for misadventure is still a subject for debate.

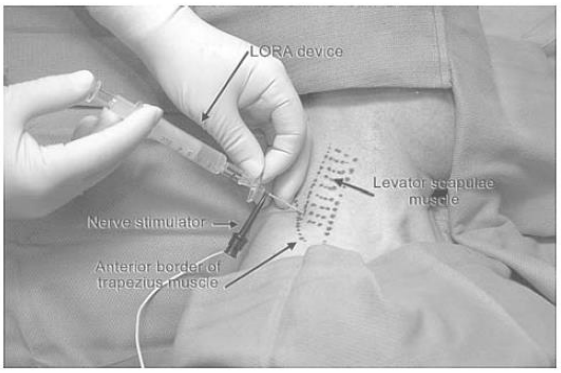


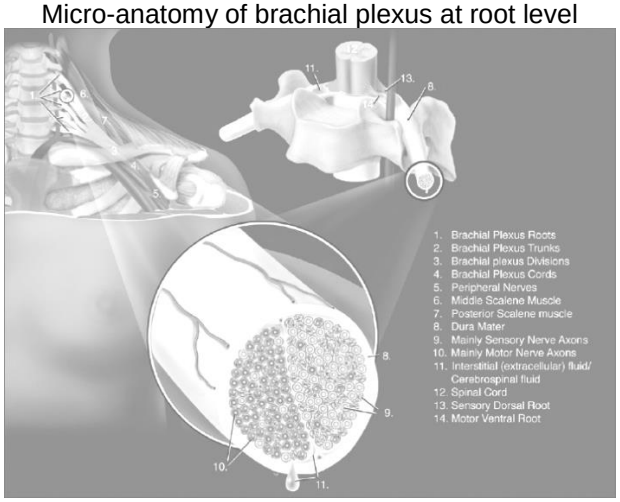
Fig 2. Needle entry. The nerve stimulator and the loss-of-resistance to air syringe (LORA) are applied to the needle. The needle enters in the "V" formed by the levator scapulae muscle anterior and the anterior border of the trapezius muscle posterior. The needle is aimed at the suprasternal notch and, in this way, penetration of the often-sensitive extensor muscles of the neck is avoided. Anterior = right side of figure.

Complications of interscalene block

The complications of ISB include phrenic nerve block (virtually 100%), recurrent laryngeal nerve block, horner's syndrome (stellate ganglion block), intravascular injection of LA, nerve injury,cervical spine injury, neuraxial spread of LA, pneumothorax, haemorrhage and sepsis.

The cervical roots (and possibly trunks in some patients) have *epineurium* that is continuous with the dural sheath of the cervical spinal cord. At this level, nerve fascicles are abundant, compact and easily detached from each other being poorly surrounded by *perineurium*. They appear as hypo-echoic structures, in contrast to peripheral nerves with more perineurium that appear hyper-echoic under US examination. Intra-neural (sub-epineurial but not intra-fascicular) injection of LA will likely track proximally epidurally or into the subarachnoid space resulting in a cervical epidural or cervical (total) spinal anaesthesia. Intra-fascicular injection will not only certainly cause severe nerve damage at the site of injection but also within the substance of the cervical spinal cord as the LA solution, injected under high pressure, tracks proximally. This is likely the mechanism of injury of several reported cases of paraplegia resulting from ISB carried out on patients under GA where diect damage to the spinal cord by the needle was deemed highly unlikely.

Micro-anatomy of brachial plexus at root level



Peripheral nerve injury (PNI) after surgery with ISB has been well described. In a retrospective study involving 1569 patients that underwent total shoulder arthroplasty (TSA) between 1993 and 2007, Sviggum et al reported an incidence of nerve injury of 2.2%, consistent with previous studies looking at nerve injury after TSA. The majority of patients (71%) recovered fully during the follow up period (2,6 years) and a further 26% had partial recovery. Considering that surgery itself can cause PNI due

to positioning or stretching of the BP, they concluded that the use of ISB did not increase the risk for PNI.

Causes of surgery associated nerve injury

Anesthetic	Direct trauma with needle or catheter
	Direct nerve perforation, injury to fascicle and/or perineurium
	Pressure effect of local anesthetic injectate
	Nerve edema and/or hematoma
	Direct toxicity of local anesthetics and adjuvants
	Concentration and time dependent (in-vitro studies)
	Decreased neuronal blood flow
	Needle size and type
	Improper positioning (e.g. elbow flexion)
Patient	Diabetic mellitus, ulnar neuropathy, carpal tunnel syndrome, peripheral neuropathies, chemotherapy, vascular disease, multiple sclerosis, age, proximal nerve root compression, spinal canal stenosis
Surgical	Tourniquet pressure and duration compression, contusion, stretch, transection
	compressive dressings and casts
	Improper positioning (e.g. extreme abduction and external rotation of upper limb)
Other	Inflammatory-immune

Contraindications to ISB

1. Patient refusal
2. Allergy to LA (I have yet to see this)
3. Contralateral phrenic nerve block (realative in some cases, a risk benefit judgement call)
4. Contralateral recurrent laryngral nerve block
5. Sepsis at the site of injection
6. Peripheral neuropathy
7. Anticoagulation (controversial but a consideration if a breach of dural cuff occurs during ISB)

Volume and concentration of LA for ISB

There is no standard for the volume and concentration of LA that is maximally effective for intra and post operative analgesia for ISB. Higher volumes and concentrations are thought to lead to denser blocks and longer durarion of analgesic action (as well as motor block) but with an increased risk of complications (LA toxicty, LA associated nerve toxicity, phrenic nerve blockade etc.). Lower volumes of LA can be used in USG ISB with comparable analgesic effects to high volume techniques. Low volume ISB reduces the incidence of adverse events such as diaphragmatic paresis. In a study by McNaught et al using 0.5% ropivacaine, patients were randomised to receive either GA and ISB with 5 mL LA or 20 mL LA solution. There were no significant differences in pain scores, sleep quality and total morphine consumption for up to 24 hours after surgery. Most RA practitioners will agree that USG ISB rarely requires more than 20 mL of 0.25-0.5% ropivacaine or bupivacaine (the higher concentration if used as a sole anaesthetic)

Adjuvants

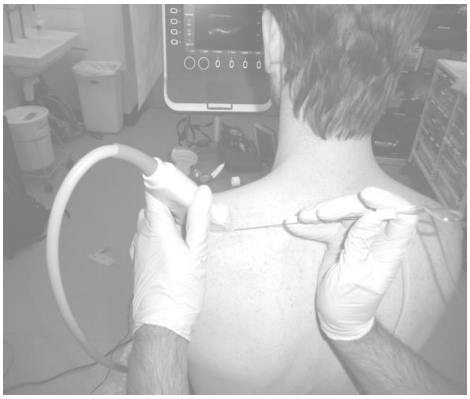
Numerous adjuvants have been used in combination with LA in an attempt to optimise block characteristics and improve clinical outcomes with variable success. Common additons to LA solutions are adrenaline and clonidine, with opiods, midazolam, ketamine and neostigmine also utilised. Recent research has focused on the addition of the glucocorticoid dexamethasone as an adjuvant in RA. Studies have shown that it can significantly prolong (up to 4 times) the duration of analgesia with minimal adverse events. The exact mechanism of action is unknown although it has been suggested that it acts by increasing the activity of potassium channels on nociceptive C-fibers or by causing vasoconstriction via glucocorticoid receptor mediated nuclear transcription modulation. However, recent studies have suggested a systemic effect may be responsible for its clinical effect and IV administartion may give similar results. Dosages range between 4 and 10 mg with 8 mg being the most common dose used.

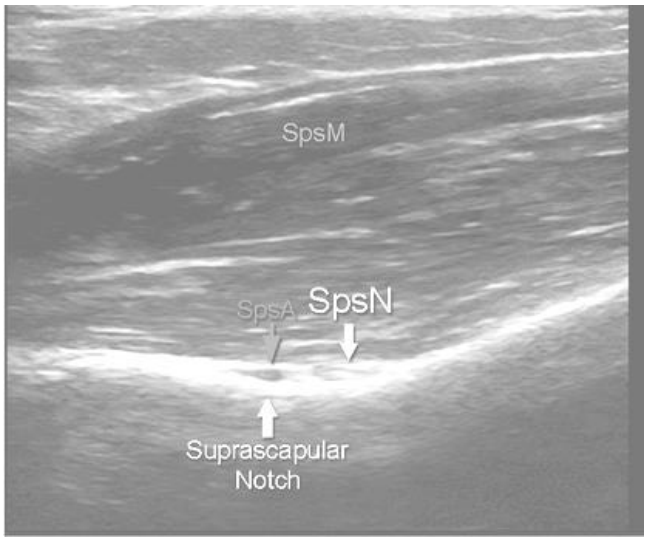
- **Supraclavicular block (SCB)**

SCB is a block at the level of the BP divisions between the anterior and middle scalene muscle and the first rib. USG has increased the popularity of this block as it visualises target tissues and surrounding structures in real time reducing common complications such as pneumothorax. SCBs have not been used for shoulder surgery because of concern that the block is too distal from the cervical nerve trunks and roots to provide satisfactory shoulder anaesthesia. However, anatomic studies with US and CT scanning demonstrate that LA injected for a SCB travels cephalad between the anterior and middle scalene muscles onto the trunks and roots within the paravertebral fascial covering. SCB for shoulder surgery has shown similar success to ISB in a recent study with no evidence of pneumothorax and an incidence of post-operative nerve symptoms at 0.4%. The investigators concluded that USG ISB and SCB are both effective for shoulder surgery.

- **Suprascapular and axillary nerve blocks (shoulder block)**

Patients in whom there is a contraindication to ISB e.g. those who would not tolerate a phrenic nerve block, may benefit from combined suprascapular and axillary nerve blocks for shoulder surgery. Although good intra and post-operative analegesia has been reported with these blocks, they are not comparable to ISB or even SCB and should probably be used as part of a multimodal analgesic approach in combination with GA.





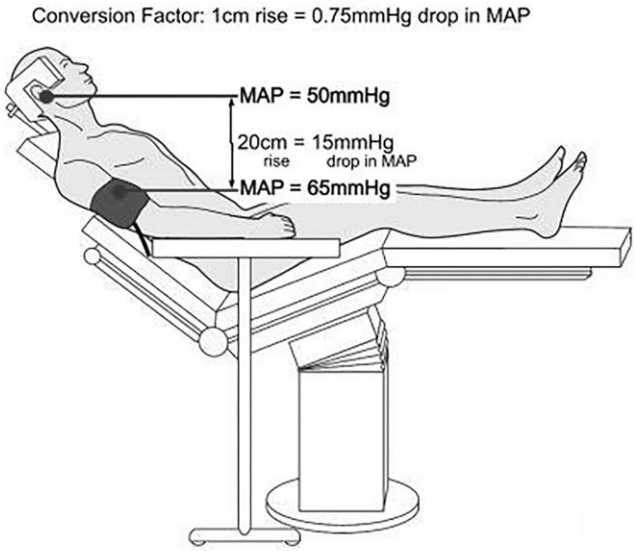
- **Intra-articular infiltration (IA) of LA and sub-acromial block (SAB)**

Many surgeons are enthusiastic proponents of IA and/or SAB for post-operative pain management for a variety of arthroscopic shoulder joint procedures claiming equal efficacy to ISB with a lower incidence of complications. Apart from the avoidance of anaesthesia related delay attributed to the performance of RA blocks, no studies have shown equivalence with ISB as regards quality and duration of post-operative analgesia. IA and SAB with indwelling catheters have been assoiciated with post-arthroscopic glenohumeral chondrolysis, a devastating complication that occurs mainly in young, healthy patients who have received IA boluses and infusions of high concentrations of bupivaciane.

Intra-operative management

On arrival in theatre the patient must be positively identified and asked to indicate the side that is to be operated upon. Hopefully, the surgeons have also made clear, unambiguous markings on the indicated limb. IV access is secured on the contra-lateral arm, or either a foot or ankle vein if none are available in the upper limb. Blood loss during shoulder surgery is not usually significant unless the patient is undergoing a revision arhtroplasty or open reduction of joint or upper humeral fractures. In these instances, a large bore IV cannula must be placed and a blood should be typed and screened if appropriate. RA is carried out in an awake (my preference), lightly sedated patient (a combination of midazolam and fentanyl) who is calm but able to communicate at all times.

Shoulder surgery can be carried out in the supine, lateral decubius position (LDP) or beach-chair position (BCP). Standard monitoring should be employed in all but the most compromised patients, with the NIBP cuff placed in the same arm as the IV in the BCP and the dependent arm or lower leg in the LDP. An NIBP cuff on the leg in the BCP is unacceptable as it falsely overestimates mean blood pressures compared to the upper arm. Mean pressure measurements at the level of the upper arm significantly overestimates that at the level of the carotid bifurcation. It must be noted that mean blood pressures fall 0.75 mmHg per cm rise above the upper arm NIBP cuff. There is no place for hypotensive anaesthesia, especially in elderly or patients with significant co-morbidities.



Invasive arterial monitoring should be considered in patients with significant cardiovascular co-morbidity. The transducer should be elevated to the level of the tragus of the ear as this will more accurately reflect cerebral perfusion pressure than NIBP. Cerebral perfusion monitoring using Near Infra-Red Spectroscopy (NIRS-INVOS) as a measure of regional cerebral oxygen saturation ($rScO_2$) is becoming standard monitoring for patients operated in the BCP under GA and mechanical ventilation.

Once surgery has commenced, it is extremely difficult to have access to the airway should it become compromised, hence most anaesthetists prefer to manage the aiway with an armoured ETT or south facing RAE as this ensures a more sucure airway. Use of LMA- with spontaneous ventilation or IPPV- is equally acceptable provided the patient is appropriately selected and the LMA well secured. The head and neck should be secure while care should be taken throughout the procedure to ensure that excessive stretching of the brachial plexus does not occur as a result of the excessive surgical traction. The eyes should be carefully taped and padded as the head is under drapes and surgeons will often use it as an arm rest during the procedure! Pressure points must be carefully padded (heels, elbows), the legs flexed with a pillow under the knees. An axillary roll must be placed when the patient is in the LDP as this protects the brachial plexus from compression between the rib cage and the head of the humerus. Sequential calf compressors must be utilised, not only to prevent thomboembolism, but to reduce venous pooling, particularly important in the BCP. Forced air warming is recommended as some procedures are lengthy and irrigation fluid used during arthroscopy is often well below body temperature. Antibiotic cover is mandatory for joint surgery and the use of tranexamic acid for more bloody procedures, such as TSA is recommended (1g infused over 20 mins).

Shoulder surgery is associated with grave complications related to positioning, particularly in the BCP. Visual loss as well as stroke and permanent post-operative cognitive dysfunction is an infrequent but devastating complication probably related to cerebral hypoperfusion. Cerebral autoregulation is well maintained in spontaneously breathing patients under GA, but becomes pressure dependent during IPPV, especially in older patients with systemic diseases such as hypertension, diabetes and peripheral vascular disease. All case reports of neurological misadventure in the BCP have occurred in patients under GA who have been mechanically ventilated. However, a recent article has shown that cerebral autoregulation is disordered in patients undergoing surgery in the BCP with no differences in post-operative cognition and brain injury biomarkers compared to the supine position.

Hypotension is a frequent occurrence in patients induced and then elevated into the BCP (elevations range from 30 up to 70 degrees from the horizontal). Mean pressures must be supported with vasopressors (ephedreine>>phenylephrine, or adrenaline) if they fall below 20 to 30% of baseline values. rScO2 values that drop to 20% or below baseline (taken in an awake patient breathing room air) should alert the anaesthetist to pathological cerebral hypoperfusion. Interventions include reducing the angle of elevation, increasing end-tidal CO2 and using vasopressors (probably not phenylephrine as it is a vasoconstrictor that has been shown to decrease rScO2 saturations). The Bezold-Jarisch reflex may be activated during shoulder surgery in the BCP, especially when surgery is performed under interscalene block. This presents as sudden, profound bradycardia and hypotension, which can rapidly progress to cardiac arrest.

The aetiology of nerve injury has already been addressed. Extravasation of irrigation fluid into the subcutaneous tissues of the neck and head may lead to peri-operative airway compromise. Venous air embolism, pneumothorax, pneumomediastinum and sub-cutaneous surgical emphysema has been described.

References on request

Notes

Haemodynamic Monitoring
Assessing fluid responsiveness under anaesthesia

Dr Malcolm Miller

Dept of Anaesthesia & Perioperative Medicine
Division of Critical Care
University of Cape Town

Introduction

Fluid therapy has undergone a paradigm shift in terms of the indications (context) and represents a shift towards a more physiological approach to fluid administration. It has been clearly shown that fluid overload causes harm and fluid administration seems to be at best arbitrary in most circumstances.[1]

Fluid responsiveness

The definition of responsiveness came about following seminal work showing that patients are fluid responsive if their stroke volume (SV) increases by 10% following a fluid challenge (usually 500mls of crystalloid).[2] However, fluid administration will only increase SV if two conditions are met i.e. if the fluid bolus increases the stressed blood volume causing the mean circulating filling pressure to increase greater than the right atrial pressure, thereby increasing the gradient for venous return and if both ventricles are functioning on the steep part of the Frank-Starling curve.[3,4] Therefore, it is critical to demonstrate fluid responsiveness before fluid loading and potentially fluid overload patients which leads to tissue oedema and organ dysfunction.[5,6]

Assessment of fluid responsiveness

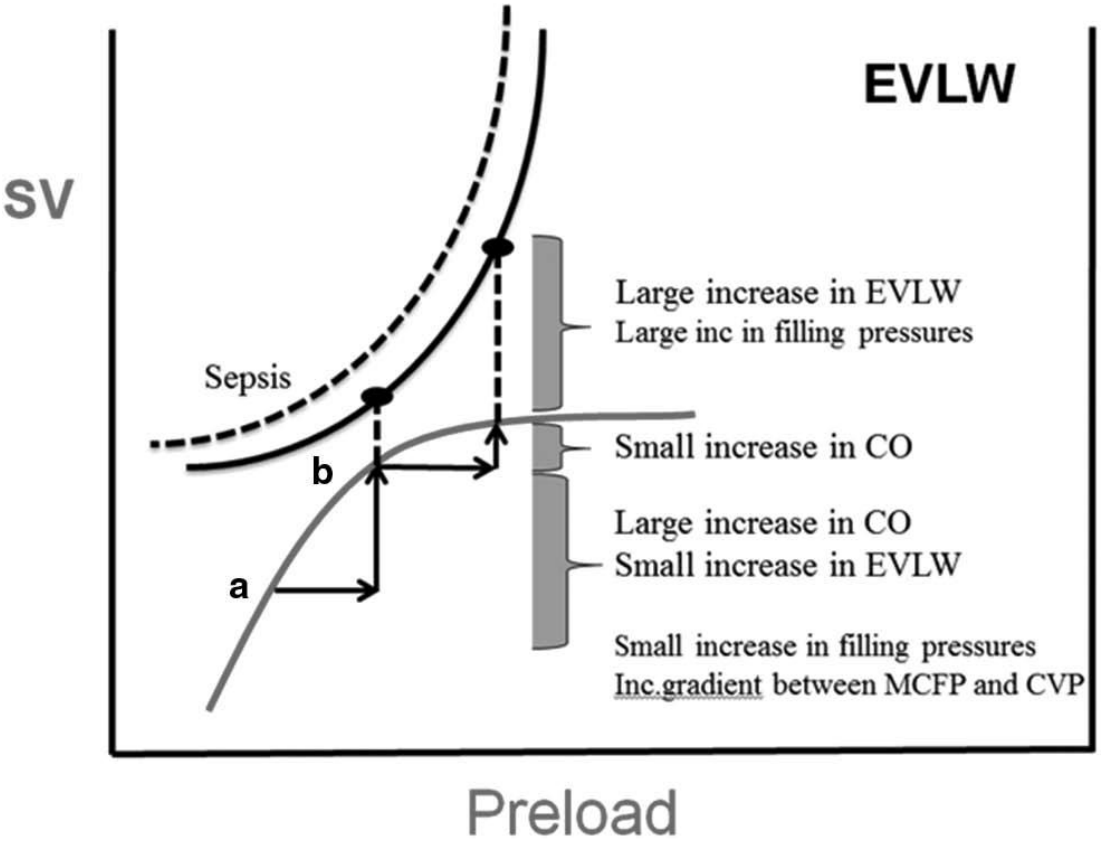
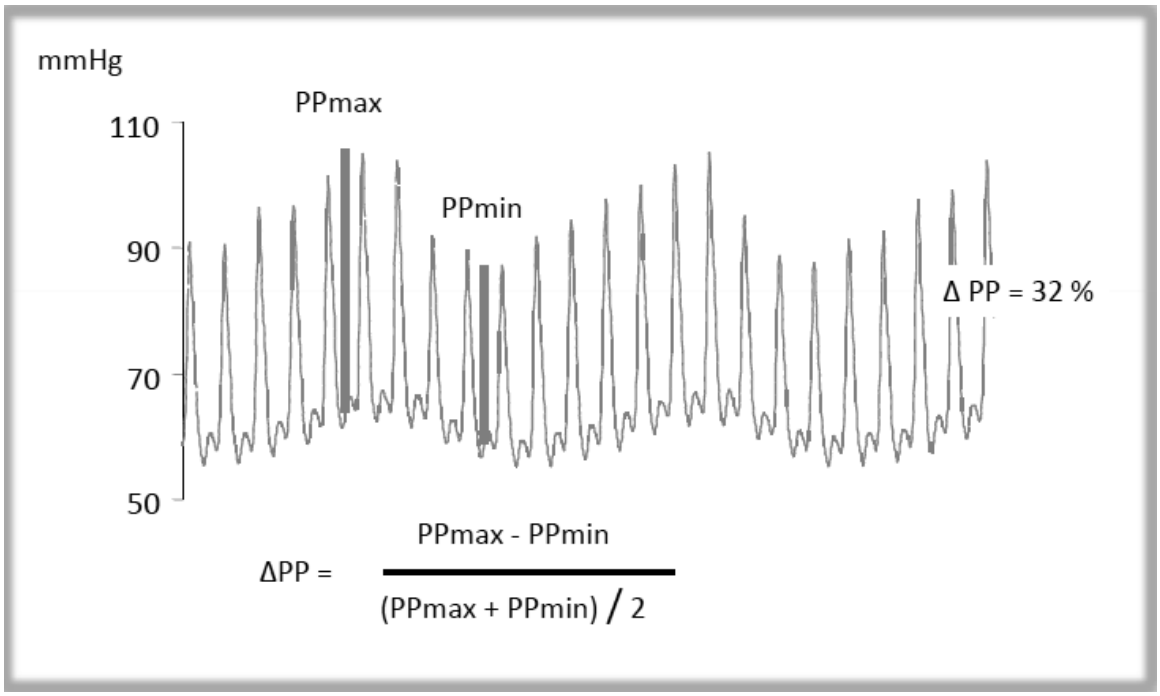


Figure 1. Superimposition of the Frank-Starling and Marik-Phillips curves demonstrating the effects of increasing preload on stroke volume (SV) and lung water in a patient who is preload responsive (a) and nonresponsive (b). With sepsis, the extravascular lung water (EVLW) curve is shifted to the left.
CO = cardiac output, CVP = central venous pressure, MCFP = mean circulating filling pressure.

The most reliable and robust markers of fluid responsiveness are the dynamic markers. These are the following:

- Pulse pressure variation
- Systolic pressure variation
- Stroke volume variation
- Plethysmographic waveform variation
- Passive leg raising

Pulse Pressure Variation



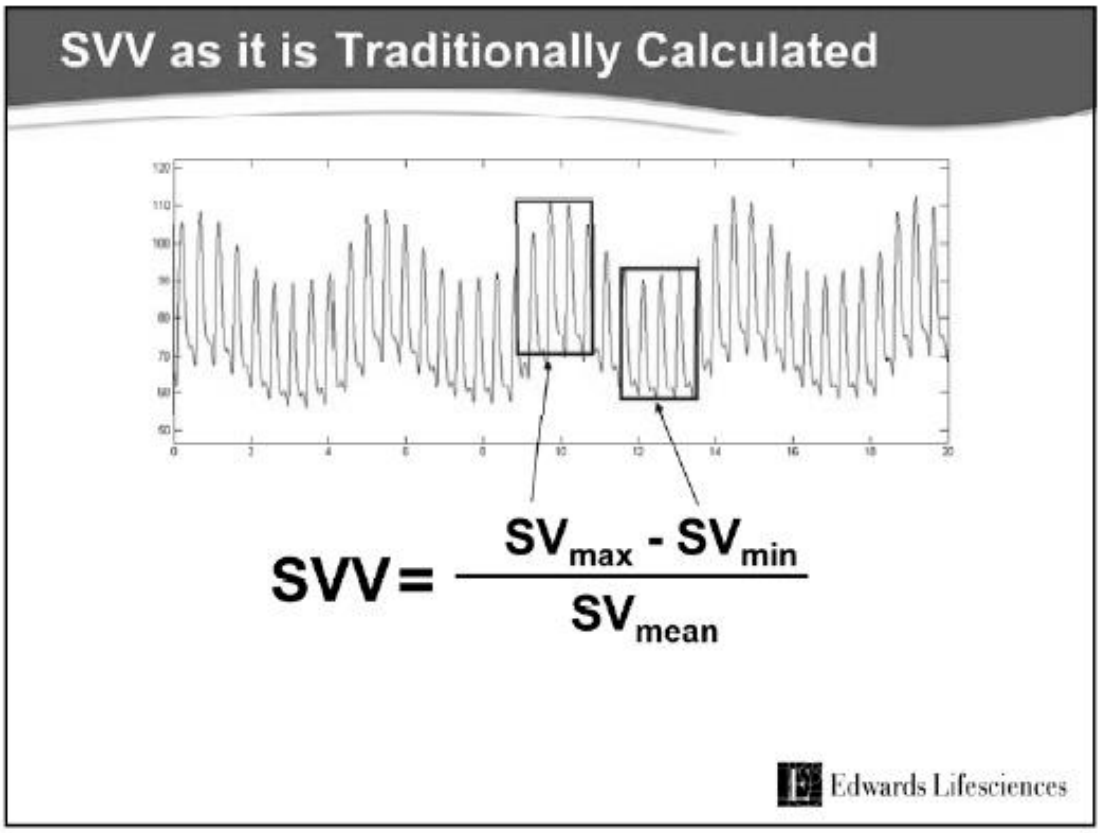
Prof Xavier Monnet – Fluid responsiveness lecture SASA congress 2012

The respiratory variation in systolic pressure or pulse pressure for that matter relates to changes in intra-thoracic blood volume during controlled positive pressure ventilation. Blood is propelled forward during each inspiration towards the left atrium and therefore provides the left atrium with a preload during each mechanical breath. This concept was originally referred to as preload recruitability of the left ventricle. If this variation is exaggerated during mechanical ventilation and the ΔPP is greater than 10% as calculated by the above formula then the patient will benefit from a fluid bolus.

There are pre-requisites for the interpretation of Pulse pressure variation though. The patient must be ventilated with Tidal volumes of 8mls/kg or greater during the manoeuver and the lung compliance should be normal.[7] Secondly, the patient must be in sinus rhythm since any arrhythmia will result in changes in stroke volume which influences arterial pressure. The last absolute contra-indication will be if the patient is breathing spontaneously, since the tidal volume will vary and result in variation in the arterial waveform, purely related to the changes in tidal volume.

Stroke Volume Variation

Another dynamic marker to assess fluid responsiveness is to use pulse contour analysis to calculate stroke volume and to look at stroke volume variation (SVV) to measure fluid responsiveness. This remains the most accurate measure of fluid responsiveness since it assesses changes in SV during mechanical ventilation. The changes in SV mirror the changes in pulse pressure as described above during controlled mechanical ventilation based on the following calculation.



A SVV of greater that 10% is associated with fluid responsiveness. Once again, this method of assessment of intravascular volume is influenced by the following:

- Spontaneously breathing patients
- Arrythmias
- Artefact in arterial waveform tracings or devices like intra-aortic balloon pumps which distort the arterial waveform and makes interpretation of the area under the systolic part of the waveform inaccurate.

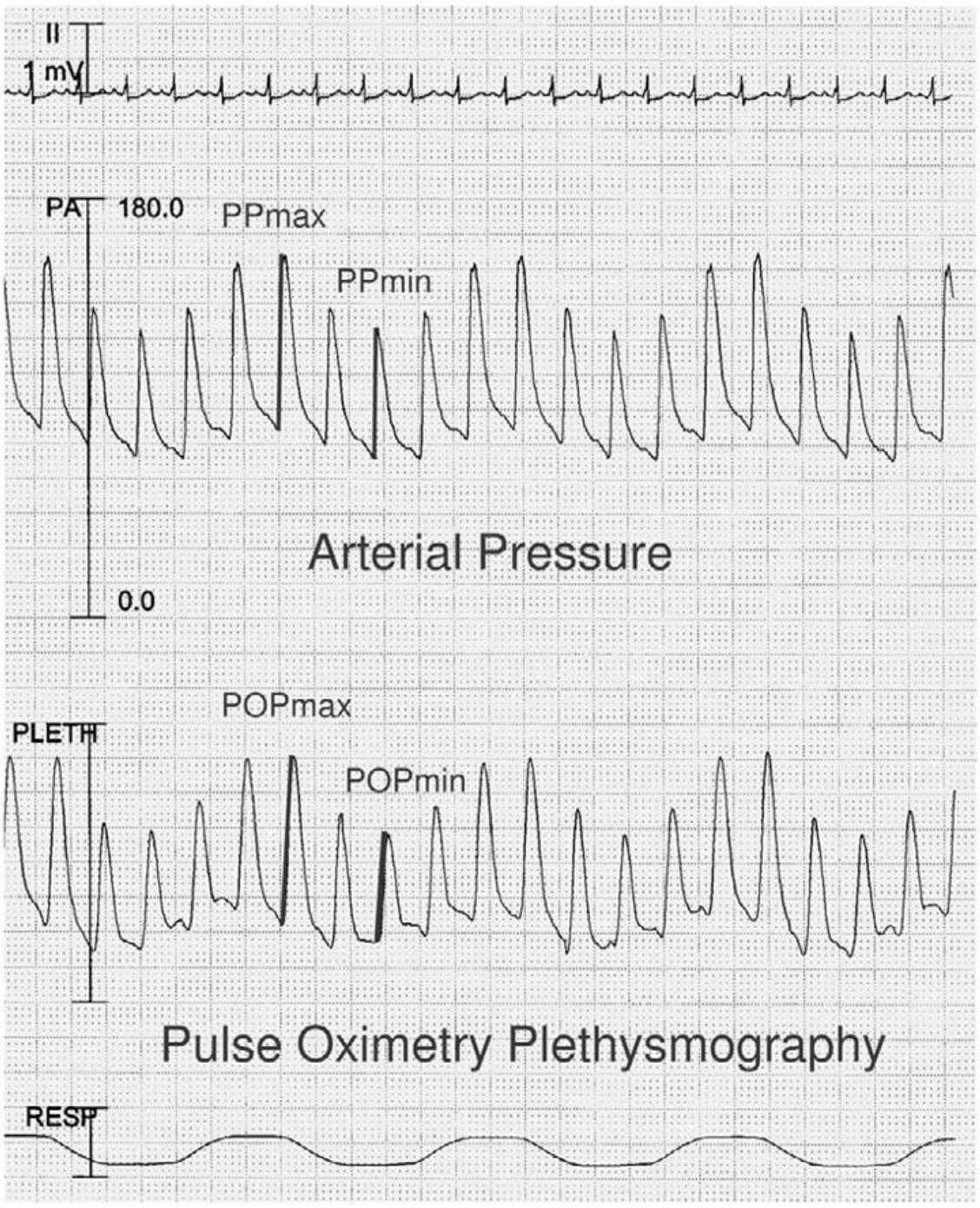
Pulse Plethysmography Analysis

Pulse oximetry plethysmography (POP) demonstrates a pulsatile waveform similar to the arterial waveform and therefore can be used to infer the same information obtained from the arterial pressure tracing to assess volume responsiveness. In a study of patients mechanically ventilated and sedated the correlation between pulse pressure variation and POP showed excellent correlation ($r^2 = 0.83$) in terms of demonstrating fluid responsiveness however, the monitor has not been validated in the setting of volume expansion. It is not clear what the threshold value should be in terms of a cutoff for predicting fluid responsiveness and whether this will be similar to the thresholds for SVV and PPV.[8] This technique represents an attractive alternative to more invasive techniques which require an intra-arterial catheter however, further studies are needed to validate this technique. Furthermore, any artefact in the plethysmographic trace will render the information inaccurate and makes the monitor typically one with a low signal to noise ratio.

The calculation to predict fluid responsiveness is similar to the those described above and is as follows:

$$\Delta POP = [POP_{max} - POP_{min}] / [(POP_{max} + POP_{min}) / 2] \times 100$$

A threshold of 15% has been used to predict fluid responsiveness. See below:



Passive Leg Raising

Possibly the easiest and least invasive test of assessment of intra-vascular volume is to perform a passive leg raise (PLR). This manoeuver requires nothing more than a functioning bed that can be manipulated to raise the legs and ideally a measure of SV to assess response. Mean arterial pressure (MAP) is used in clinical practice as a surrogate of cardiac output but this increases the number of false negative tests reported.[9]

It is important to recognize that the test must be performed in a standardized way to ensure consistent results. The cartoon below demonstrates how the test should be performed.[10]

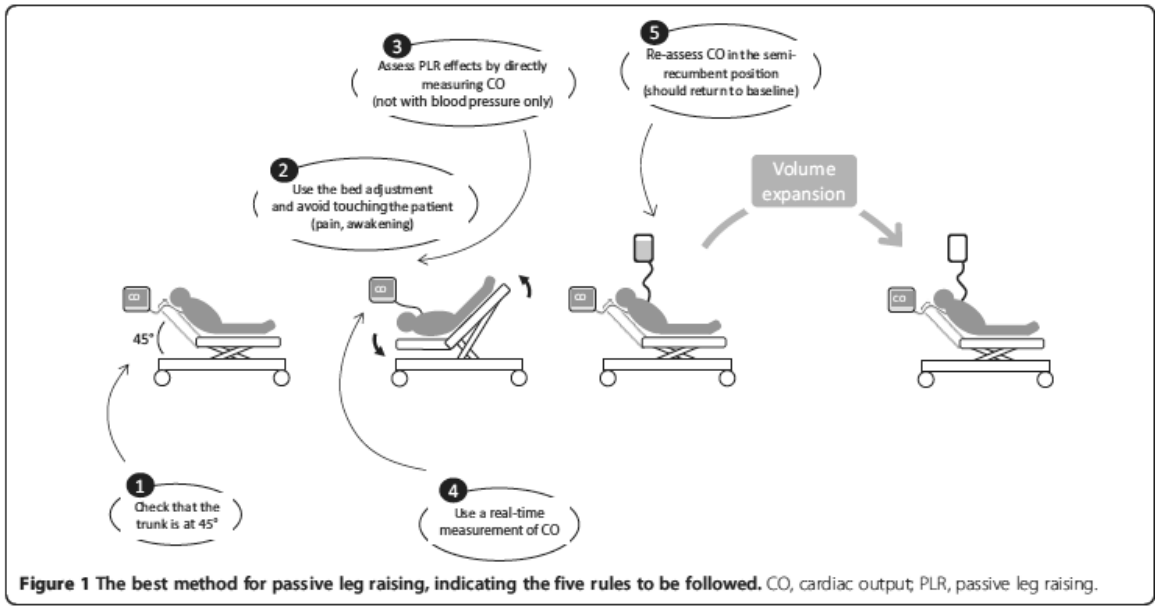


Figure 1 The best method for passive leg raising, indicating the five rules to be followed. CO, cardiac output; PLR, passive leg raising.

It the only test that has been validated in spontaneously breathing patients and is not influenced by cardiac rhythm. This test offers the advantage that no additional fluid is administered to the patient therefore avoiding the risks of fluid overload.

End Expiratory Occlusion Test

This test although not widely used once again relies on the interaction between the cardiac and respiratory system. During inspiration in patients on mechanical ventilation, venous return is impeded and hence cardiac output is decreased. If expiration is paused for approximately 15s, the effects on venous return is inhibited and hence cardiac output increases and hence this phenomenon can be used to assess fluid responsiveness. Therefore, if arterial pressure or stroke volume increases by 5% following an end expiratory occlusion test for at least 15s, the patient would benefit from a bolus of fluid. The advantage of the test is that it remains robust over several cardiac cycles and therefore can be used in patients with cardiac arrhythmias and in patients breathing spontaneously despite being ventilated.[11]

Conclusion

Fluid therapy has evolved and is based on sound physiological principles governing cardio-respiratory interaction. The concept of fluid challenges should be replaced by these more physiological and less harmful tests of fluid responsiveness.

Patients who are volume responsive should only receive fluid if they are likely to benefit from a bolus of fluid and if the benefits of the fluid outweigh the risks associated with fluid overload. Patients should NOT receive fluid until they are no longer fluid responsive.[12]

Some haemodynamic variables to remember

CI	**CO/BSA**	2.8-4.2 litres/min/m^2
SVR	$\frac{\text{MAP – CVP}}{\text{CO}} \times 80$	900-1400 dyne.s.cm^{-5} 11-17.5 Wood units
PVR	$\frac{\text{PAP - PAOP}}{\text{CO}} \times 80$	150-250 dyne.s.cm^{-5} 2-4 Wood units
SI	$\frac{\text{SV} \times 100}{\text{BSA}}$	40-60 ml/m^2
LVSWI	$\frac{1.36 \times (\text{MAP-PAOP}) \times \text{SI}}{100}$	45-60 g-m/m^2
RVSWI	$\frac{1.36 \times (\text{MPAP-PAOP}) \times \text{SI}}{100}$	5-10 g-m/m^2

References

1. Cecconi M, Hofer C, Teboul JL, Pettila V, Wilkman E, Molnar Z, et al. Fluid challenges in intensive care: the FENICE study: A global inception cohort study. Intensive care medicine. 2015;41(9):1529-37.
2. Marik PE, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. Ann Intensive Care. 2011;1(1):1.
3. Guyton AC. Determination of cardiac output by equating venous return curves with cardiac response curves. Physiol Rev. 1955;35(1):123-9.
4. Marik PE, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Critical care medicine. 2013;41(7):1774-81.
5. Marik PE. Iatrogenic salt water drowning and the hazards of a high central venous pressure. Ann Intensive Care. 2014;4:21.
6. Kelm DJ, Perrin JT, Cartin-Ceba R, Gajic O, Schenck L, Kennedy CC. Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. Shock (Augusta, Ga. 2015;43(1):68-73.
7. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. Intensive Care Med. 2005;31(4):517-23.
8. Cannesson M, Besnard C, Durand PG, Bohe J, Jacques D. Relation between respiratory variations in pulse oximetry plethysmographic waveform amplitude and arterial pulse pressure in ventilated patients. Critical care (London, England). 2005;9(5):R562-8.
9. Monnet X, Rienzo M, Osman D, Anguel N, Richard C, Pinsky MR, et al. Passive leg raising predicts fluid responsiveness in the critically ill. Critical care medicine. 2006;34(5):1402-7.
10. Monnet X, Teboul JL. Passive leg raising: five rules, not a drop of fluid! Critical care (London, England). 2015;19:18.
11. Monnet X, Teboul JL. Assessment of volume responsiveness during mechanical ventilation: recent advances. Critical care (London, England). 2013;17(2):217.
12. Marik PE. Fluid Responsiveness and the Six Guiding Principles of Fluid Resuscitation. Critical care medicine. 2015.

Anaesthesia for the Patient with Traumatic Brain Injury
Do we influence patient outcome?

Drs Anthony Reed & Karen van der Spuy

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

What is clear is that we cannot influence the primary injury that results in the disruption of neural tissue, pathways, supporting tissue and blood vessels. However it is now clear that the primary injury initiates a set of injurious processes that are not only ongoing, but also render the injured brain susceptible to secondary insults, or "injuries", that in the uninjured brain would just have been physiological variables that occurred with no consequence.

So surgery and anaesthesia post traumatic brain injury (TBI) takes place in the setting of established injuries, and the brain being in a state with many evolving cascades and pathophysiological processes that render it susceptible to insults that anaesthesia could contribute to. Optimal anaesthetic care does require the anaesthesia provider to understand the milieu that anaesthesia is taking place in. Unfortunately we do not fully understand, or have even identified, all the processes and their implications; but we are beginning to understand the complexity of situation that we find the injured brain in.

Unfortunately there are factors that definitely impact the outcome that we cannot control, and these are:

- Age (over 55 years)
- Sex (women do far worse with an equivalent injury than men)
- Genetics (Apo E 4 allele)
- Severity of primary injury

Importantly evidence from the past two decades suggests that the standard of care that patients receive, in the immediate period and through their first few weeks after a traumatic brain injury, can make a significant difference to their final outcome. The difference between centres, even in the developed world, can be as high as a six-fold difference in outcome. So the decisions you make, and the care that you can provide as an anaesthesiologist probably contribute to both mortality and functional outcomes.

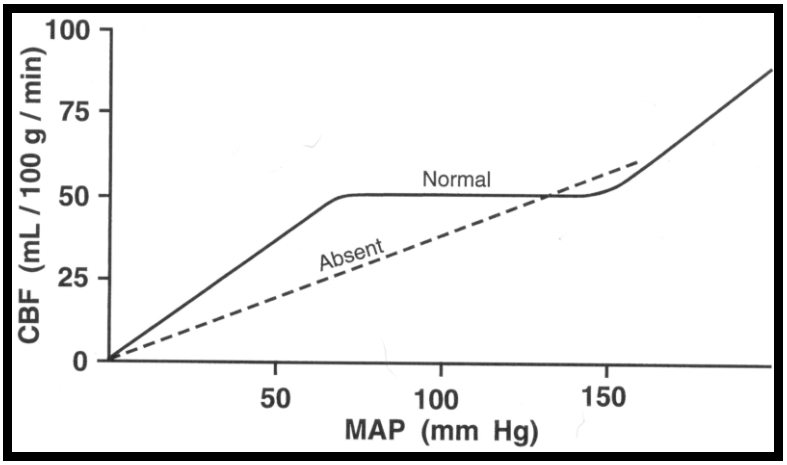
Important components of the pathophysiology of TBI that anaesthesia providers need to be aware of:

- Inflammatory processes
    - Both the primary injury, and secondary insults initiate inflammatory processes including inflammatory cytokines (TNF, interleukin series), prostaglandins, complement and free radical creating peroxidases.
    - These contribute to increased BBB permeability.
    - This process has the ability to mop up destroyed or injured tissue as well as surrounding cells, effectively leaving residual "scar" tissue.

- Oedema formation
    - Two types of oedema occur concurrently after TBI
        - The dominant pathophysiology seems to be **Cytotoxic** oedema secondary to swelling of cells (neurons, astrocytes and microglia). Ischaemic conditions result in anaerobic metabolism and a lack of energy substrates for the cells energy-dependent ionic-pumps. This is the putative target of both perfusion pressure (Rosner therapy) and CBF (Lund therapy) TBI treatment- improving perfusion allows the cells to correct their energy deficiency and re-establish ionic pumping, thereby decreasing cell volume and cerebral oedema caused by this mechanism.
        - Vasogenic oedema is the consequence of a damaged blood-brain barrier (especially the endothelial cell component of the barrier) resulting in ions, colloid-like particles and fluid extravasating into the interstitial space of the brain.

Vasogenic oedema is likely the lesser contributor to clinical picture creating a raised ICP, post a TBI, but may be critical with regards the effects of excitatory neurotransmitters, drugs and fluids in this setting.

- Excitotoxicity follows massive release of excitatory neurotransmitters (glutamine, aspartate) leading to activation of NMDA receptors, AMPA receptors and voltage dependent calcium and sodium channels. The calcium and sodium influx initiates catabolic intracellular processes, mainly through enzyme activation that results in membrane degradation and cellular dysfunction, and pre-lethal programmed cell death.
- Raised ICP, reduced CPP
    - Normal intracranial pressure (ICP) is 10mmHg. There is some debate about exact value when it is raised but some where between 20mmHg and 25mmHg there is agreement that the raise is sufficient enough to warrant ICP reducing therapy. Treatment algorithms typically target attempts to decrease the pressure, failing that then initiating treatment to overcome the perfusion effects of the raised pressure.
    - There is no evidence that ICP reducing treatment improves outcome, but a raised ICP indicates:
        - Presence of significant pathology
        - A brain at risk of hypoperfusion
        - A risk of herniation
        - Single value of no prognostic value, but high values that are unresponsive to treatment may well be an indication of a poor outcome
    - Cerebral perfusion is a measure of ensuring the brain is adequately provided with substrates and flow, in the setting of a raised ICP with or without altered or absent autoregulation. So the principal is that due to an inability to accurately determine the degree of autoregulation and perfusion, that one assumes a straight line relationship between perfusion pressure and flow, thereby ensuring an adequate delivery of blood/substrates to the brain. CPP is calculated simply in the Rosner (CPP driven) paradigm by CPP= MAP-ICP.



Current evidence and guidelines suggest that CPP targets lie between 60 and 70mmHg, with little benefit above 70mmHg and a trend to worse outcome when CPP drops below 60.

- Cerebral autoregulation
    - The ability of the brain to respond rapidly to changes in metabolic requirements, and to fluctuations in systemic perfusion parameters, is a product of the highly effective autoregulation system for CBF.
    - Following traumatic brain injury, autoregulation can be disrupted during the very immediate phase, or it can develop over time(hours to days). Some degree of impairment of autoregulation occurs in every patient after TBI, with some patients experiencing complete disruption of this key flow-metabolism coupling mechanism.
    - The CO_2 response of the cerebral vasculature seems much better preserved than the pressure response, and even in severe injury changes in CO_2 produce rapid changes in vessel calibre and CBF/ICP. This can be a doubled edged sword as discussed later in parameters under anaesthetic control.

- Cerebral blood flow
    - Both hypoperfusion and hyperperfusion occur after TBI, and both are detrimental as they indicate a flow metabolism uncoupling with resultant ischaemia or hyperaemia. The dominant pathophysiology is one of hypoperfusion, and current evidence is the milieu within the neural tissue post TBI, lowers the ischaemic threshold for CBF/100g brain/minute to 15ml, and the threshold appears to be three times higher than the ischaemic threshold in ischaemic stroke(5ml/100g/min), indicating the extreme susceptibility of the brain to "secondary" insults after a traumatic injury, as compared to other serious brain injury states.
    - Hyperperfusion occurs less often, both in the immediate phase after injury and can follow after any subsequent traumatic ischaemia, and is also associated with a worse outcome as it indicates cerebral vasomotor paralysis (and loss of autoregulation), and also because an increase in CBF, beyond metabolic requirements, will raise ICP and decrease CPP, placing the injured brain at risk of further ischaemia.

- Secondary injuries:
    - Systolic BP less than 90mmHg in adult patients has been a key cutoff, associated with an almost doubling of mortality if the BP fell below this threshold for periods as short as two minutes at any time during the first few days post injury. Many guidelines, and more recent work, have suggested that this cut-off systolic pressure should be higher,
        - Currently the Emergency Neurological Life Support (ENLS) guidelines, as well as those from the European brain Injury Consortium(EBIC) and the Brain Trauma Foundation(BTF) all contain a systolic arterial pressure(SAP) >90mmHg before an ICP value is available, after which the CPP becomes the management target (CPP 60-70mmHg).
        - The only anaesthetic specific recommendation comes for the AAGBI in the UK where they target a MAP> 80 during the transfer of patients with a TBI.
        - Children BP targets SAP from the BTF are:
            - Over 10 >90 mmHg
            - 1-10 > 70 + (age x 2) mmHg
            - Infant >70mmHg
            - Neonate >60mmHg
    - Hypoxaemia (PaO_2<8kPa or SPO_2) is the other major secondary insult, carrying a significant mortality effect on its own, and if occurring in the same patient as a hypotensive insult (even if not at the same time) compounds the poor outcome. So whilst the BTF guidelines set 8kPa as the lower limit, EBIC raised this to 10kPa and the AAGBI have this at 13kPa during transfer.
    - Others:
        - Hyper/Hypoglycaemia. Hyperglycaemia is correlated with poor outcomes in TBI, but this appears to be more related to the severity of the injury, and there is no work demonstrating that tight control through the use of insulin improves outcome. Indeed, tighter control introduces the possibility of potentially more deleterious hypoglycaemic episodes. So current consensus is that blood glucose should be regularly monitored during the acute stage, and that blood glucose be kept in the 6-10mmol/L range.
        - Hypo/Hypercarbia (Discussed later under factors under anaesthetic control)
        - Seizures are a potential cause of a rise in ICP, and in any patient with an already raised ICP, further rises can result in cerebral tissue herniation. Preventative anticonvulsants should be prescribed in all patients with a suspected raised ICP post TBI, until the ICP in sure to have returned to normal.

So what should the anaesthetic provider be considering during the peri-operative management?

Firstly do no harm- think of other injuries especially cervical-spine, and consider them if unexplained hypotension, dropping haemoglobin, haemodynamic instability or hypoxaemia occurs during anaesthesia.

The anaesthesia provider is in control of several aspects that impact on outcome, namely:

- Timing of intra-cranial surgery
    - In patients with acute space occupying haematomas – both extradural and subdural, time to surgical evacuation in clinically significant haematomas, is a key determinant of outcome. Key indications would be haematomas more than 10mm thick, or with more than 5mm mid-line shift.
        - Subdural haematomas have the best outcome if evacuated within 4 hours of the injury, and delays beyond eight hours are associated with significant worstening of outcome.
        - Extradural haematomas can present with a more lucid period, but the determinent of outcome is time from neurological deterioration, and is measured in minutes rather than the hours for sub-dural haematomas.
- Timing of non-intracranial surgery
    - **Non-neurological extracranial surgery for the TBI patient**
        - Patients fall into 2 categories:
            - With a life-threatening injury, e.g. solid organ (liver, spleen, kidney) rupture and surgery usual proceeds, some authors even suggesting that the neurosurgical(if required) and other lifesaving surgery could be undertaken simultaneously.
            - With a less serious, non-life-threatening condition, e.g. a long-bone fracture.
        - The timing of surgery depends on:
            - Severity of these injuries
            - Effect on the ability to maintain cerebral protection

        a. A limb-saving vascular procedure may be considered as a matter of urgency in all trauma patients
        b. Long-bone fractures are more controversial
            - Early (<24 h) fixation of long-bone fractures may:
                - Improve outcome
                - Reduce pulmonary complications and mechanical ventilation time
                - Reduce ICU and hospital stay
        - **Head injury with a non-life-threatening extracranial injury**
            - Factors to consider in patients warranting early long-bone stabilisation:
                - Severity of brain injury
                - Pulmonary dysfunction, coagulopathy and hypothermia
                - Evidence of hypotension
                - Risks of delaying surgery
            - Compound fractures:
                - Can be debrided as part of the resuscitative effort
                - Skeletal traction until definitive fracture fixation

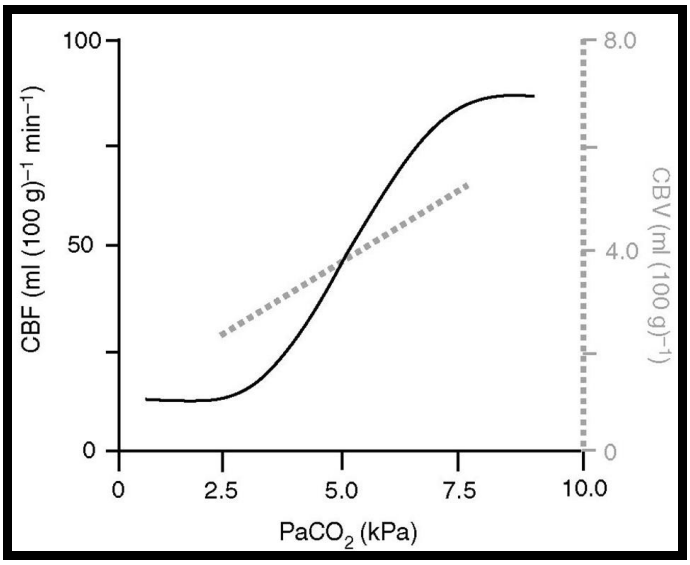
- Airway management: Many severe injuries will be already intubated, but when deciding on best intubation technique one needs to consider the urgency of the situation, the possibility of cervical spine instability, the risk of a full stomach, the possibility of a raised ICP, hypovolaemia or CVS instability and the status of the airway fractures (zygomatic, facial, mandibular), lacerations, bleeding, secretions. In general all patients with a TBI can be assumed to have both a full stomach and the possibility of an unstable c-spine.

    - Consensus that as long as the correct skill-set is available, that general anaesthesia with either RSI or a more elective intubation with a NDMR is preferable, despite concerns about the short-lived affect on ICP during laryngoscopy and intubation.
    - There appears to be no evidence that short-lived ICP rises related to any of the therapeutic manoeuvres, has any effect on outcomes
    - Consider the cervical spine during airway management plans
    - NICE Guidelines from the UK identify the following as adult patients at risk of C-spine injury and needing urgent CT neck scans:
        - GCS less than 13 on initial assessment.
        - The patient has been intubated.

        - Plain X-rays are technically inadequate
        - Plain X-rays are suspicious or definitely abnormal.
        - A definitive diagnosis of cervical spine injury is needed urgently (for example, before surgery).
        - The patient is alert and stable, there is clinical suspicion of cervical spine injury and any of the following apply:
            - Age 65 years or older
            - Dangerous mechanism of injury (fall from a height of greater than 1 metre or 5 stairs; axial load to the head, for example, diving; high-speed motor vehicle
            - Collision; rollover motor accident; ejection from a motor vehicle; accident involving motorised recreational vehicles; bicycle collision)
            - Focal peripheral neurological deficit e.g. paraesthesia in the upper or lower limbs.
    - So whilst there is no evidence that favours any particular technique, a rapid sequence induction with manual in-line-stabilisation(MIS) is the currently accepted standard. Once the cervical spine is secured using MIS the front portion of any hard-collar can be released to allow better mask application to the mandible, as well as allowing increased mandibular movement during laryngoscopy.
    - The ENLS 2014 Guidelines, are the clearest in terms of a recommendation, and state " Rapid sequence intubation is the preferred method of securing the airway in patients with suspected elevated ICP since it provides protection against the reflex responses to laryngoscopy and rises in ICP. The presence of coma should not be interpreted as an indication to proceed without pharmacological agents, or to administer only a neuromuscular blocking agent without a sedative/induction drug. Although the patient may seem unresponsive, laryngoscopy and intubation will provoke reflexes that elevate ICP unless appropriate pretreatment and induction agents are used."

- Blood pressure
    - Fluid administration. The first line management of hypotension is IV fluid administration, and whilst much continues to be written about the fluid choice, we do not have any outcome data suggesting any fluid provides better outcomes that are important to the patient; consensus is that hypotonic fluids, and fluids containing glucose/dextrose should be avoided. Normal saline and the more isotonic balanced electrolyte solutions are all acceptable and are the mainstay of fluid administration.
    - Colloids also have no proven benefit, the use of albumin may be detrimental but the synthetic colloids are possibly best used for volume resuscitation only, as they offer little other benefit to the injured brain, across the blood-brain-barrier.
    - Inotropes/Vasopressors
        - No clear benefit of any one over another
        - Consider patient's age and co-morbidity, young healthy patients can tolerate the pure after-load increasing effects of the α-agonists nor-adrenaline and phenylephrine, but elderly patients or patients with long-standing hypertension may not have the myocardial reserve to cope with the increased cardiac work and they may benefit from an agent with some inotropy, such as dopamine or adrenaline.
        - β-blockers are the mainstay of managing any hypertension, which is not an uncommon occurrence, particularly towards the end of a surgical procedure when the anaesthetic agents are terminated and the patient transferred to the critical care environment. All the direct acting vasodilators (nitrates, calcium channel antagonists) inhibit autoregulation and drop MAP, often taking the CPP to much lower levels, whereas the β-blockers preserve cerebral autoregulation, and act almost entirely on decreasing cardiac output.

- Ventilation
    - CO_2 targets and their effects on CBF and outcomes



        - The normal values for arterial CO_2 are on the steep part of CO_2 response curve, such that small changes in CO_2 have significant effects on CBF and on ICP. The injured brain appears to be rendered rapidly ischaemic if the CO_2 falls suddenly, as cerebral vasoconstriction decreases flow to levels that seem to create a secondary injury. This was first demonstrated to make a difference to outcome in 1991 by Muizelaar, and has subsequently been demonstrated to render injured brain ischaemic and change outcome, despite producing a decrease in ICP.
        - The CBF/ICP reducing effect of a decrease in CO_2 has a very short (few minutes) response time, but the CSF correct the metabolic change rapidly and within 30 minutes the decreased CO_2 effect is lost and more importantly the vasculature appears to be reset at that value, so an increase back to the previous level is now seen as a rise in CO_2 partial pressure and a rise in CBF/ICP occurs. The reverse occurs for rises in CO_2, so that all clinicians ventilating patients after TBI need to be mindful of the acute and detrimental effects on any change in CO_2 partial pressures. Hence the evolving standard of care is for patients to have end-tidal CO_2 measured from initial intubation at the roadside or in the EC, through the patients whole acute care pathway including intensive care ventilation to prevent potential iatrogenic secondary injury through acute CO_2 changes.
        - Current guidelines suggest avoiding hypocapnia (keep greater than 3.3kPa from BTF) and most published opinions and guidelines (AAGBI, ENLS, NICE) target $PaCO_2$ 4.5-5kPa
        - The only role for acute hyperventilation is with imminent brain herniation, when a sudden lowering of the CO_2 can produce a lifesaving drop in ICP, but the anaesthesia provider needs to be aware that this will be successful for a maximum of 30 minutes, so that another management plan must be made to remove the cause of the sudden rise, or to mitigate that rise in another manner.
    - PEEP- has also been considered extensively, but there is no clear role for it, and there is some concern that raising intrathoracic pressure, increases thoracic venous pressures and thereby increases venous drainage pressure from the cranium and is associated with a modest rise in ICP.
        - Whilst there is no evidence that this is detrimental, prophylactic PEEP is not shown to decrease any complications of positive pressure ventilation.
        - So unless PEEP is needed to overcome hypoxaemia, a known cause of secondary to the brain, it may be best avoided in patients with TBI.
        - If PEEP is used, then “modest use” has been described, always less than ICP

- Measures to decrease ICP intraoperatively
    - Head up 10-20°
    - Drain off CSF if there is a ventricular drain in place (20-30ml usually enough)
    - Hyperosmolar therapy
        - Mannitol has been the mainstay of this treatment for decades. Dose 0.25g-1 g per kg body mass. Can be repeated if effective, probably safe for 2-3g/kg total dose over a few days. Early side effects are the diuresis it produces, dropping intravascular volume in the setting of wanting to maintain perfusion pressures. Later side effects are electrolyte abnormalities, and a hyperosmolar renal injury of the plasma osmolality rises above 320mOsm.
        - Hypertonic saline – last 10 years has seen much published, various concentrations used (2.5, 5 and 7.5% are common) and it would appear that it is a useful alternative to mannitol, but the is little or no evidence that it could be better. Certainly no patient-important outcome(functional outcome improvement or survival) data that supports its use over mannitol. Current literature suggests that mannitol probably still more widely used.
    - Decrease CMR
        - Analgesia if possibility that pain an issue (ceiling, or more lie a “floor” effect once pain is controlled)
    - Hyperventilation (mentioned in ventilation section)
    - Removal of mass occupying lesion if not neurosurgical procedure

- Temperature
    - Hypothermia
        - It has become clear that there is currently no role for the use of induced hypothermia in TBI. Despite an unequivocal effect to decrease ICP, and much experimental work suggesting a role, we now have the 2 large USA studies (NABISH I and II), EUROTHERM, a systematic review and a Cochrane review all demonstrating no neurological benefit, and several of the trials have been terminated early because of outcome and safety concerns for the hypothermia groups.
    - Hyperthermia
        - Avoid hyperthermia, and target temperature in the 36° to 36.5°. Fever can be a manifestation of a severe TBI and the use of paracetamol, and active cooling can be considered although there is currently no evidence for these treatments.

- Haemoglobin management
    - Physiology of decreasing haemoglobin
        - Demonstrates an increased CBF as Hb drops below 10g/dl, and there have been arguments for this suggesting improved rheology and flow, and hence improving perfusion and oxygen delivery. However it would appear that this effect is rather as a consequence of the high oxygen extraction requirements, so that when oxygen delivery is decreased by a decreased haemoglobin, that the majority of the available oxygen is extracted early in capillary beds, resulting in low oxygen tension/availability later in the capillary and autoregulation therefore ensures vasodilatation to improve flow, and hence the effect is protective physiology, rather than a super-normal delivery secondary to viscosity improvements.
        - Brain hypoxia and dysfunction usual appears with acute haemodilution below 6-7g/dl.
    - Pathophysiology of decreasing haemoglobin in TBI patients
        - The acutely injured brain appears susceptible to reduced oxygenation with hypotension and hypoxaemia being the dominant secondary injuries. In addition retrospective data suggested that patients in large TBI data bases and clinical trials (CRASH and IMPACT) with lower admission haemoglobins, had a worse outcome. The data seemed to suggest a cut-off point around 9g/dl, similar to the cut-off for experimental work demonstrating evidence of cellular distress.
        - However it is not clear whether this is merely a marker of a seriously injured patient, or whether this is an indication where Red Cell transfusion would

improve outcome.
        - The notion that red cell transfusion will improve cerebral tissue oxygenation is attractive and several studies have demonstrated this effect, but it would appear that in a percentage of patients (between 21-46 %) that cerebral tissue oxygenation actually falls.
        - The most recent work (Robertson JAMA 2014) is a prospective trial comparing transfusion triggers of 7 or 10, and also including a arm with erythropoeitin, which was previously explored as a neuroprotective agent in TBI following exciting animal work. This work showed no benefit to either a higher transfusion trigger or erythroeitin, but the 10g/dl group had a significantly increased incidence of thrombotyic complications during the follow-up period.
    - In prospective clinical trials there is no clear data that suggests that transfusing patients to a Hb>11 is better than an Hb>7. So current guidelines and expert opinion recommend only transfusing if anaemia is believed to be symptomatic.

- Coagulopathy
    - Often reported to be present in up to a third of patients with TBI, and associated with increased morbidity and mortality
        - Our experience is that a coagulopathy caused by the TBI is much less common
    - What is much more of a problem is patients on anti-coagulants.
        - Warfarin use associated with increased frequency and severity of head injury, together with greater likelihood of death.
            - Estimated that pick-up rate for intracranial lesions may be as high as 1:4 in these patients, and liberal scanning policy may result in 2% increase in scanner workload
            - Whether warfarin should be reversed with FFP or PT Complex is unclear, however a lower threshold to scan/rescan patients is probably warranted.
        - For patients on anti-platelet drugs the evidence is less clear

- Drugs
    - Drug choice for anaesthesia, has not been shown to make a difference to outcome, but based on first principles there are drug factors that are considered important:
        - Inhalational agents- all the currently used agents (isoflurane, sevoflurane and desflurane) decrease $CMRO_2$ but may cause vasodilatation especially above 1 MAC. Carbon dioxide reactivity is preserved as is pressure autoregulation at normocapnia. The volatiles may be used in ventilated patients at concentrations up to 1 MAC.
        - Intravenous agent choice needs to consider that thiopentone, propofol and etomidate all decrease CMR and hence in injured brains with enough autoregulation intact, they will decrease ICP. Propofol and thiopentone will result in a larger expected drop in BP than etomidate after an induction dose, but etomidate does have the potential problem of adrenal insufficiency. Ketamine may have the least cardiovascular depression but is still currently contraindicated due to concerns about its effect to increase CBF and ICP.
        - In a rapid sequence induction it is thought that suxemethonium may be the drug of choice, the brief rise in ICP thought to be of no consequence, but the risks of hypercarbia and hypoxia with difficult conditions, or failed airway management with modified rapid-sequence utilizing rocuronium being the alternative.
        - Analgesics
            - Analgesics have no ICP reducing effect unless the patient is experiencing significant pain or agitation, but once the small benefit of analgesia/sedation is achieved there is a ‘ceiling” effect resulting no further metabolic sparing or ICP decreasing effect.
            - Opioids have no direct effects on cerebral haemodymanics if ventilation controlled and if administered such that MAP does not change. If administered as a bolus that result sin a significant fall in MAP, then cerebral autoregulation causes vasodilatation to try and

maintain flow and CBF and ICP rise
- Paracetamol- analgesic and antipyretic of choice
- NSAIDS- because of their antiplatelet effect are not first line drugs, and should probably be avoided despite the lack of clear evidence.

- Anaesthetic monitoring choices
    - Arterial line provides beat-to-beat measurement of arterial pressure, and for arterial blood gas and blood sugar analysis
    - Central line is useful in polytrauma patients, and should be placed in all patients receiving an ICP monitor to allow the safe infusion of inotropes for CPP driven treatment.
    - Pupillary size and reactivity is the earliest monitor of tentorial herniation in the sedated and ventilated patient
    - ICP monitors are valuable in the TBI patient undergoing extensive surgery or surgery at multiple sites. If such surgery is deemed necessary the patient may need to be referred to a unit where ICP monitoring can be instituted

- Access to neurocritical care
    - Close to two decades of work has demonstrated the improved outcome in patients with TBI admitted to a critical care unit that is dedicated to the neurological monitoring and management of TBI patients
    - In addition improved outcomes are demonstrable if the unit is staffed by full-time neurointensivists and then further improvements can be obtained through both the implementation of protocols, but also from protocol adherence projects in units that already have established protocols.
    - So planning the post-anaesthetic care to be provided by the highest level of neurointensive care available, may be a the final decision that the anaesthesia provider can contribute to, that makes a meaningful difference to the patients outcome following a traumatic brain injury.

SUMMARY
- The injured brain is susceptible to insults that, under physiological conditions, would not cause damage
- Prevention of hypoxia, hypotension, seizures and the rapid evacuation of intracranial haematomas offer the best advantages
- Hypothermia, routine hyperventilation and steroids offer no benefit
- Life-saving surgery may take priority over the TBI
- Non-life-saving surgery should be delayed until the TBI has stabilised, ideally 48--72 hours or more after injury
- If used carefully most anaesthetic techniques and drugs are suitable, with a few exceptions
- Attention to the general principles of care, especially avoiding hypotension, is key to maximising the neurological outcome

References

1. Traumatic brain injury: Changing concepts and approaches. Maas A. Chin J Traumatol. 2016 1;19(1):3-6.
2. Pathophysiology of traumatic brain injury. C Werner, K Engelhard. Br J Anaesth 2007; 99: 4–9
3. B.E. Masel, D.S. DeWitt, Traumatic brain injury: a disease process, not an event. J Neurotrauma, 27 (2010), pp. 1529–1540.
4. Cell Death Mechanisms and Modulation in Traumatic Brain Injury. BA. Stoica and AI Faden. Neurotherapeutics. 2010; 7(1): 3–12.
5. Mechanisms of cerebral edema in traumatic brain injury: therapeutic developments. Donkin JJ, Vink R. Curr Opin Neurol. 2010;23(3):293-9.
6. Systemic complications of traumatic brain injury. Wijayatilake DS, Sherren PB, Jigajinni SV. Curr Opin Anaesthesiol. 2015;28(5):525-31
7. What's new in the surgical management of traumatic brain injury? Patel K, Kolias AG, Hutchinson PJ. J Neurol. 2015;262(1):235-8. Review.
8. The International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a list of recommendations and additional conclusions: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. Le Roux P, Menon DK, Citerio G, Vespa P, et al. Neurocrit Care. 2014;21 Suppl 2:S282-96. Review.
9. Transfusion strategies in patients with traumatic brain injury: which is the optimal hemoglobin target? Lelubre C, Taccone FS. Minerva Anestesiol. 2016;82(1):112-6.
10. Effect of erythropoietin and transfusion threshold on neurological recovery after traumatic brain injury: a randomized clinical trial. Robertson CS et al. JAMA 2014; 312(1): 36-47
11. Haemoglobin management in acute brain injury. LeRoux P. Curr Opin Crit Care. 2013;19(2):83-91. Review.
12. The effect of red blood cell transfusion on cerebral oxygenation and metabolism after severe traumatic brain injury. Zygun D et al. Crit Care Med. 2009.
13. The effect of blood transfusion on brain oxygenation in children with severe traumatic brain injury. Figaji A, et al. Pediatr Crit Care Med. 2010
14. Transfusion of red blood cells in patients with a prehospital Glasgow Coma Scale score of 8 or less and no evidence of shock is associated with worse outcomes. Elterman J, Brasel et al Resuscitation Outcomes Consortium Investigators. J Trauma Acute Care Surg. 2013;75(1):8-14.
15. Head Injury: Triage, Assessment, Investigation and Early Management of Head Injury in Children, Young People and Adults. National Clinical Guideline Centre (UK). London: National Institute for Health and Care Excellence (UK); 2014 Jan.
16. Perioperative management of adult traumatic brain injury. Sharma D, Vavilala MS. Anesthesiol Clin. 2012;30(2):333-46. Review.
17. Traumatic brain injury: physiological targets for clinical practice in the prehospital setting and on the Neuro-ICU. Dhuleep S. Wijayatilake Suyogi V. Jigajinni, and Peter B. Sherren. Curr Opin Anesthesiol 2015, 28:517–524
18. Improving outcome in severe trauma: what's new in ABC? Imaging, bleeding and brain injury. Harris T, Davenport R, Hurst T, Hunt P, Fotheringham T, Jones J. Postgrad Med J. 2012;88(1044):595-603. Review.
19. Management of severe head injury: Institutional variations in care and effect on outcome. EM Bulger, AB Nathens. Crit Care Med 2002; 30:1870 –1876.
20. Large Between-Center Differences in Outcome After Moderate and Severe Traumatic Brain Injury in the International Mission on Prognosis and Clinical Trial Design in Traumatic Brain Injury (IMPACT) Study. HF Lingsma, B Roozenbeek. Neurosurgery 2011; 68:601–608.
21. Recommendations for the use of multimodal monitoring in the neurointensive care unit. Citerio G, Oddo M, Taccone FS. Curr Opin Crit Care. 2015;21(2):113-9. Review.
22. Glucose control in acute brain injury: does it matter? D A Godoy, R Behrouz, M Di Napoli. Curr Opin Crit Care 2016, 22:120–127
23. Delivering neurocritical care in resource-challenged environments. Gentle S. Shrestha, Alberto Goffi and Diptesh Aryal. Curr Opin Crit Care 2016, 22:100–105
24. Hypothermia for Intracranial Hypertension after Traumatic Brain Injury. P Andrews, H. Sinclair, A Rodriguez. NEJM; 2015: 373(25)2403-12

Care of the Organ Donor

Dr Adri Vorster

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Worldwide the number of patients requiring organ transplantation continues to be far greater than the number of organs available for transplant. In South Africa the annual number of solid organs transplanted is actually decreasing, despite a growing number of patients awaiting organ transplant. The cause for our low deceased donor rate is multi-factorial, but limited national guidelines and staff education may play a role, affecting the process of referral and subsequent care of the organ donor. Organs for transplantation may be retrieved from living or deceased donors. Only 1% of deceased patients can be considered for potential organ donation, therefore early identification of a suitable donor is an important part of the process. Due to the scarcity of appropriate patients diagnosed with brain death alternative strategies are increasingly being used, for example expanded criteria donors, donation after circulatory determination of death and in-vivo or ex-vivo mechanical organ support. These strategies add complexity to the ethical considerations surrounding organ transplant, and clear and appropriate guidelines should be implemented.

Intensive management following the diagnosis of brain death and consent for donation increases the number of suitable donors and improves the quality of the donor organs.
The objective is to retrieve organs for transplantation within 24 hours of the diagnosis of brain death. During this period it is very important to aggressively manage all physiological derangements and correct any reversible conditions.

Physiological changes following brain death
Brain death is associated with complex physiological derangements that can lead to serious complications for the potential donor, including loss of viability of organs for transplantation. Frequently occurring complications are listed in Table 1.

Cardiovascular	Respiratory	Neurological	Endocrine & Metabolic	Haematological & Immunological	Renal
Myocardial injury Hypotension Arrhythmias	Neurogenic pulmonary oedema ARDS	Autonomic dysfunction	Diabetes insipidus Hyperglycaemia Hypothermia Lactic acidaemia	Thrombocytopaenia DIC SIRS	AKI

Table 1

Monitoring and investigations
Routine Intensive Care monitoring is used, including heart rate and rhythm, oxygen saturation, blood pressure, temperature and urine output. Placement of an arterial line and central venous catheter (CVC) allows the ability to monitor blood pressure, pulse pressure variation, systolic pressure variation and central venous pressure. It is also used for blood sampling and vasopressor administration. Pulmonary artery catheters (PAC) can be used in selected patients.
Laboratory tests for all patients include blood and tissue compatibility testing and viral serology. Also full blood count, renal and hepatic function, electrolytes, serum lactate, serum glucose, acid base status and coagulation monitoring. Serum troponin and brain natriuretic peptide levels are also commonly done. Septic screens on blood, urine and sputum should be performed. These tests are repeated as appropriate.
Recommended imaging techniques include a chest x-ray, electrocardiogram and cardiac echocardiography. Certain patients may require cardiac angiography and bronchoscopy. Liver and kidney imaging and biopsies may also be indicated in selected patients.
Advanced investigations may differ according to the organs planned for retrieval and guidelines from the transplant team.

Haemodynamic and pulmonary support

Brain death often results in significant autonomic dysfunction that can manifest as a massive sympathetic discharge or "storm". This leads to hypertension, tachycardia, arrhythmias and myocardial ischaemia. It should be managed if severe and prolonged, but preferably with short-acting agents like esmolol, as it is inevitably followed by significant hypotension. This can be attributed to hypovolaemia, especially if diabetes insipidus (DI) is present, myocardial dysfunction and vasodilatation. Initial management is fluid administration, but ultimately 97% of patients will require vasopressor or inotropic therapy.

Fluid management can be particularly challenging, as a fluid restrictive regimen is beneficial for the heart, lungs, liver, pancreas and intestine, but if too strict may be detrimental to renal function. The aim is to achieve a urine output >0.5 mL/kg/hr and a MAP >60 mmHg. Other commonly used targets are a CVP of 4-10 mmHg, SPV <10 and PPV <12 mmHg. Pulse contour analysis, PAC or echocardiography can also be used to guide fluid and vasopressor therapy.

The administration of a balanced crystalloid solution is appropriate, albumin or blood products are used when indicated. The use of hydroxyethyl starch is not currently recommended due to an association with renal impairment. Patients with DI usually require treatment with vasopressin or desmopressin in addition to fluid replacement. Blood products are transfused as required, with individualised triggers, but haemoglobin should be maintained >7 g/dL. The choice of vasopressor or inotrope will depend on the pulse pressure, ventricular function and presence of DI. Vasopressin is often used as the incidence of DI is high.

Lung protective ventilator strategies should be used, with a tidal volume of 6 to 8 mL/kg of predicted body weight and PEEP of 5 to 10 cm H_2O. The aim is for peak airway pressure to be <30 cmH2O and plateau pressure <25 cmH2O. Inspired oxygen concentration should be titrated to the lowest concentration that will achieve adequate oxygenation.

Strategies to minimise the risk of acquiring ventilator-associated pneumonia is recommended, for example head elevation, suctioning and good hygiene practice.

Extracorporeal Membrane Oxygenation (ECMO) is increasingly being used in the intensive care setting to support the critically ill patient. Some patients are diagnosed with brain death while receiving ECMO support and this can be continued until the retrieval procedure in appropriate patients to improve organ perfusion. There are case reports of ECMO being started for this purpose after the diagnosis for brain death has already been made, with some success, usually for liver transplants. The use of ECMO after circulatory death is a controversial ethical topic.

Temperature regulation

Following brain death normal hypothalamic thermoregulatory function ceases, leading to progressive hypothermia in all patients. Temperature monitoring is essential, appropriate sites for monitoring includes the nasopharynx, oesophagus, tympanic membrane and pulmonary artery catheter. The use of the rectum, axilla or oral cavity is not recommended.

The objective is to maintain the temperature between 35 and 37.5˚C. There is some evidence that mild hypothermia (34-35˚C) may offer organ protection, but more research is required. Fluid warmers and warming blankets can be used, water immersion and warm fluid infusions into bladder, stomach or body cavities should be avoided. Heat and moisture exchange filters should be used during mechanical ventilation.

Endocrine, metabolic and electrolyte management

Brain death is associated with hypothalamic and pituitary dysfunction, leading to decreased circulating levels of adrenocorticotropic hormone, thyroid stimulating hormone and antidiuretic hormone, resulting in endocrine and metabolic dysfunction, and electrolyte imbalances. DI is common, causing hypovolaemia and hypernatraemia. Hyperglycaemia is also very prevalent.

Hormone treatment with a combination of thyroid hormone (T3 or T4), corticosteroid (Methylprednisolone), antidiuretic hormone (Vasopressin, Desmopressin) and Insulin is most frequently used in patients who present with abnormalities. Steroids should never be given until blood and tissue compatibility tests have been completed as it can interfere with results.

Electrolyte derangements should be corrected.

Coagulation and inflammation management

Brain death causes the activation of leukocytes and a pronounced systemic inflammatory response, leading to elevated levels of cytokines such as interleukin-6 and tumor necrosis factor. This response is reduced by good haemodynamic management, and the administration of corticosteroids, although the evidence for the use of steroids is limited.

Thrombocytopaenia and coagulopathy may occur and is treated with appropriate products.

Infection control
Existing infections should be treated appropriately and new infections avoided by following strict preventative guidelines, as the recipient will be extremely vulnerable to any acquired infection. Empiric antibiotics may be given, depending on the organ being transplanted.

Ex-vivo organ perfusion
The approximate acceptable post retrieval ischaemic times for solid organs are listed in Table 2.

Heart	Lungs	Liver	Intestine	Pancreas	Kidneys
4 hours	4-6 hours	6-10 hours	6-12 hours	12-18 hours	24 hours

Table 2

Instead of utilising the traditional method of organ preservation solution and cooling, ex-vivo organ perfusion is increasingly being used following organ retrieval to preserve organs prior to transplant. These portable devices offers the following benefits compared to the traditional approach:

- Continuous circulation and preservation of the microcirculation
- Metabolic demands met by continuous nutrient and oxygen delivery
- Removal of metabolic waste products
- Opportunity to assess organ viability by direct assessment, biochemical analysis and imaging techniques
- Improved condition of borderline organs
- Prolonged preservation times

Current studies also suggest improved graft survival rates and economic benefit in using ex-vivo preservation, but more research is required.

Considerations during organ retrieval
Intra-operative management of the donor is a continuation of the supportive care provided in the Intensive Care Unit, following the same principles, while also providing appropriate anaesthesia. The live donor will be managed with standard anaesthesia care, individualised according to the health status of the patient and the organ they are donating.
In the brain dead donor standard preparation for theatre is followed. The consent should be verified carefully. The patient should have adequate vascular access, with cross matched blood available. Vasopressors and inotropes are continued if already in use, otherwise it should be readily available. When preparing resuscitation drugs keep in mind that Atropine will be ineffective in the brain dead patient. Temperature and glucose regulation is continued. Prophylactic antibiotics and steroids are given according to transplant team instructions. Fluid management should be guided by monitoring, and electrolyte and acid-base abnormalities corrected.
The patient is positioned supine and anaesthesia initiated. As spinal cord function is still intact sympathetic stimulation will trigger reflexes. This is attenuated with the use of opiates, volatile anaesthetic agents (1 MAC) and neuromuscular blockers. Heparin (350 IU/kg) should be given and Activated Clotting Time measured prior to aortic cross clamping. The role of the anaesthetist is limited after cross clamping, but ventilation should be continued until the lungs are removed.
When the retrieval procedure is planned for donation after circulatory determination of death, the preparation is adjusted. This is someone who does not meet the criteria for brain death, but has another condition that will lead to death and a decision has been made to with draw life support. Death should be expected to occur rapidly following withdrawal. In this case the patient will be kept in a location close to the operating theatre, where life support is withdrawn. The family is allowed to be present if they wish to be, and only the primary health care staff is involved. Adequate patient comfort should be ensured. Once the patient is declared dead using standard criteria and the family has left, the transplant team will take over management and reinstate life support measures. The patient is then taken to theatre and the retrieval procedure started. The predicted warm ischaemic time should be less than 60 minutes from withdrawal to organ cooling (120 minutes still acceptable for kidneys). If death does not occur rapidly following withdrawal, the patient is returned to the Intensive Care Unit. Mechanical organ support may allow a longer interval between withdrawal and retrieval, but this requires more research. It is also ethically very complex, and may therefore only be applicable in very specific situations.

Take home message

- The care of the organ donor can be difficult and complex
- Aggressive and meticulous management of physiological derangements leads to better outcomes for the recipient(s)
- Organ donation is a selfless and generous act at a terrible time and every step should be handled with great empathy

References

1. The Organ Donor Foundation. Transplant Statistics, https://www.odf.org.za.
2. Muller E. Management of the Potential Organ Donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement. Transplantation 2015; 99:1743
3. G.A. Westphal, M. Caldeira Filho, A et al: Guidelines for Maintenance of Adult Patients with Brain Death and Potential for Multiple Organ Donations: The Task Force of the Brazilian Association of Intensive Medicine the Brazilian Association of Organs Transplantation, and the Transplantation Center of Santa Catarina. Transplantation Proceedings, 44, 2260–2267
4. Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement. Crit Care Med 2015; 43:1291
5. Wood KE, Becker BN, McCartney JG, et al. Care of the potential organ donor. N Engl J Med 2004; 351:2730
6. Patel MS, Zatarain J, De La Cruz S, et al. The impact of meeting donor management goals on the number of organs transplanted per expanded criteria donor: a prospective study from the UNOS Region 5 Donor Management Goals Workgroup. JAMA Surg 2014; 149:969
7. Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. Transplantation 2014; 97:258
8. Dalle Ave AL, Shaw DM, Bernat JL. Ethical Issues in the Use of Extracorporeal Membrane Oxygenation in Controlled Donation After Circulatory Determination of Death. Am J Transplant 2016; 16:2293
9. Monbaliu D, Brassil J: Machine perfusion of the liver: past, present and future. Curr Opin Organ Transplant 2010;15:160-166
10. Ciubotaru A, Haverich A: Ex vivo approach to treat failing organs: Expanding the limits. Eur Surg Res 2015;54:64-74

Anaesthetic Considerations in Patients with Platelet and Inherited Coagulation Disorders

Dr Graeme Wilson

Dept of Anaesthesia & Perioperative Medicine
Red Cross War Memorial Children's Hospital
University of Cape Town

It is estimated that up to 1% of the general population has a congenital bleeding disorder. With this level of disease burden, it is likely that anaesthetists will have to occasionally manage these patients. Congenital haemophilia, both A and B, von Willebrand's disease, and inherited qualitative platelet defects, constitute the bulk of these disorders, with the rest distributed between much rarer conditions. Blood is a necessary component of the human body, and the loss of it may be life-threatening. Blood is generated via haematopoiesis and ultimately becomes the delivery method for oxygen to the tissues and cells. The human body protects against loss of blood through the clotting mechanism. Vascular mechanisms, platelets, coagulation factors, prostaglandins, enzymes, and proteins are the contributors to the clotting mechanism which act together to form clots and stop a loss of blood. Through vasoconstriction, adhesion, activation, and aggregation, the contributors form a transient plug to act as the cork to the leaking blood flow. Soon after, fibrin, the functioning form of fibrinogen, stabilizes this weak platelet plug. Haemostasis depends on an adequate number of functional platelets, together with an intact coagulation (clotting factor) system.

Vascular Spasm

When the wall of a vessel is damaged, vascular spasm occurs. In vascular spasm, the smooth muscle in the walls of the vessel contracts dramatically. Smooth muscle is arranged in circular layers as well as longitudinal layers in larger vessels. The circular layers tend to constrict the flow of blood, whereas the longitudinal layers, when present, draw the vessel back into the surrounding tissue. The vascular spasm response is believed to be triggered by several chemicals - endothelins that are released by vessel-lining cells and by pain receptors in response to vessel injury. This phenomenon typically lasts for up to 30 minutes, although it can last for hours.

Formation of the Platelet Plug

Platelets are circulating anucleate disc-shaped cells, responsible for initiation of the haemostatic mechanisms that repair injury to the vascular endothelium. The four major platelet functions include the following

- Platelet adherence
- Platelet activation and secretion
- Platelet aggregation
- Interaction with coagulation factors

Platelets are not usually exposed to the subendothelial matrix. However, if the integrity of the endothelium is compromised, platelets will be exposed to collagen fibres and will subsequently interact with collagen and the platelets will adhere and become activated. In vessels with low or moderate shear stress Glycoprotein Ia/IIa serves as an initial anchor for platelets to attach to exposed collagen.

Under high arterial shear conditions, the platelet glycoprotein complex GPIb/V/IX predominantly mediates the first contact to the matrix-absorbed plasma protein von Willebrand factor (vWF). Platelet interactions with collagen not only provide a surface for platelet adhesion, but also serve as a strong stimulus for platelet activation. This results in signalling pathways that induce platelets to change their shape, spreading along the collagen fibrils and to secrete thromboxane A2 (TXA2) and Adenosine diphosphate (ADP) into the circulation. The released TXA2 and ADP stimulate neighbouring platelets, causing them to become activated and in turn to secrete additional TXA2 and ADP. ADP is stored in platelet dense granules and released upon platelet activation. ADP interacts with two G-protein-coupled platelet receptors, P2Y1 and P2Y12

Activated platelets bind directly to circulating fibrinogen, via the platelet integrin glycoprotein (GPIIb/IIIa). Fibrinogen can simultaneously bind two GPIIb/IIIa receptors and can link two platelets together. Each platelet has up to 80,000 GPIIb/IIIa receptors on its surface and can assemble large aggregates at the site of platelet activation.

In addition to collagen, ADP and TXA2, other agonists can activate platelets at sites of vascular injury. Tissue factor, which is expressed on all subendothelial cells, is exposed upon disruption of the protective endothelial layer. Tissue factor interacts with factor VIIa to start local coagulation, and the generation of thrombin, which is the most potent of the platelet agonists. Platelets facilitate this process by providing procoagulant phospholipids that accelerate thrombin generation. Consequently, platelet activation and fibrin deposition are intimately linked, maximizing the growth and strength of the haemostatic plug.

Coagulation

Coagulation is the production of a gelatinous but robust clot made up of a mesh of fibrin—an insoluble filamentous protein derived from fibrinogen, the plasma protein introduced earlier—in which platelets and blood cells are trapped. Instead of the older views of two pathways, extrinsic and intrinsic, both converging on a common pathway, it is more physiologically correct to think of macromolecular complexes of coagulation factors interacting with cellular components ultimately causing fibrin generation – the so-called cell-based model of coagulation.

The cell-based model of coagulation

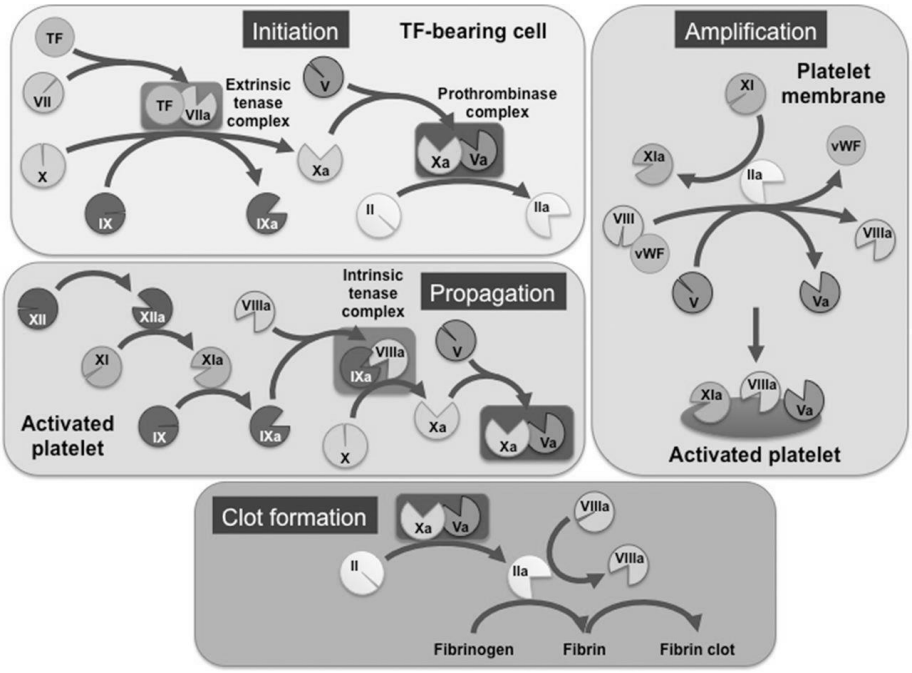
The cell-based model explains the mechanism of haemostasis in vivo and includes the important interactions between cells directly involved in haemostasis (i.e. tissue factor [TF]-bearing cells and platelets) and coagulation factors. This model more accurately represents the interaction between cellular activity and coagulation proteins that leads to thrombus formation and haemostasis. The cell-based model identifies the membranes of TF-bearing cells and platelets as the sites where activation of specific coagulation factors occurs. This model is described in a three-phase process:

Initiation
All evidence to date indicates that the sole relevant initiator of coagulation in vivo is TF. Cells expressing TF are generally localized outside the vasculature, which prevents initiation of coagulation under normal flow circumstances with an intact endothelium. Once an injury occurs and the flowing blood is exposed to a TF-bearing cell, FVIIa rapidly binds to the exposed TF. FVIIa is the only coagulation protein that routinely circulates in the blood in its active enzyme form, with approximately 1% of total FVII circulating as FVIIa. The TF-FVIIa complex then activates additional FVII to FVIIa, allowing for even more TF-FVIIa complex activity, which then activates small amounts of FIX and FX. FV can be activated directly by FXa. The FXa generated by TF-FVIIa binds to the few generated molecules of its cofactor FVa to form the prothrombinase complex, which subsequently cleaves prothrombin and generates a small amount of thrombin. Due to rapid inactivation by antithrombin the FXa generated is effectively restricted to the surface of the TF-bearing cell on which it was generated. However, the FIXa generated can dissociate and move to the surface of nearby platelets or other cells.

Amplification
Once a small amount of thrombin has been generated on the surface of a TF-bearing cell (the initiation phase), that thrombin diffuses away from the TF-bearing cell and is available for activation of platelets at the site of injury. Binding of thrombin to platelet surface receptors causes rapid changes in the surface of the platelet, resulting in shape change, reorganisation of membrane phospholipids to create a procoagulant membrane surface, and release of granule contents that provide additional fuel for the reaction. The thrombin generated in the initiation phase also cleaves FXI to FXIa and activates FV to FVa on the platelet surface. Furthermore, thrombin cleaves von Willebrand factor off FVIII (they circulate bound together), releasing it to mediate platelet adhesion and aggregation. the released FVIII is subsequently activated by thrombin to FVIIIa.

Propagation
The propagation phase occurs on the surface of the activated platelets. FIXa that was generated by TF-FVIIa in the initiation phase can bind to FVIIIa (generated in the amplification phase) on the platelet surface. The intrinsic tenase complex (FIXa– FVIIIa) on the activated platelet surface rapidly begins to

generate FXa on the platelet. The FXa generated on platelets then rapidly binds to FVa (generated by thrombin in the amplification phase) and cleaves prothrombin to thrombin. This prothrombinase activity results in a burst of thrombin generation leading to cleavage of fibrinopeptide A from fibrinogen. When enough thrombin is generated with enough speed to result in a critical mass of fibrin, these soluble fibrin molecules will spontaneously polymerize into fibrin strands, resulting in an insoluble fibrin matrix. Thrombin also activates Factor XIII, which stabilizes the thrombus by cross-linking fibrin. The resulting fibrin mesh traps and holds cellular components of the thrombus (platelets and red blood cells).



Fibrinolysis

The stabilized clot is acted upon by contractile proteins within the platelets. As these proteins contract, they pull on the fibrin threads, bringing the edges of the clot more tightly together, akin to tightening loose shoelaces. This process also wrings out of the clot a small amount of serum, which is devoid of clotting factors.
To restore normal blood flow as the vessel heals, the clot must eventually be removed. Fibrinolysis is the gradual degradation of the clot. Again, there is a complicated series of reactions that involves factor XII and protein-catabolizing enzymes. During this process, the inactive protein plasminogen is converted into the active plasmin, which gradually breaks down the fibrin of the clot. Additionally, bradykinin, a vasodilator, is released, reversing the effects of the serotonin and prostaglandins from the platelets. This allows the smooth muscle in the walls of the vessels to relax and helps to restore circulation.

Inherited and Acquired Disorders of Platelet Function

Platelet function defects are caused by rare congenital or, more frequently, by acquired disorders. They may lead to bleeding or thrombotic tendencies despite of normal platelet counts. The corresponding symptoms are often quite heterogeneous.

Acquired Platelet Disorders

Liver disease

Liver disease may lead to impairment of haemostasis by a variety of mechanisms, not simply due to decreased production of clotting factors. Both quantitative and qualitative platelet disorders are a consequence of chronic and acute liver damage. Thrombocytopenia can be a manifestation of acute hepatitis. Chronic liver disease with cirrhosis often manifests as modest thrombocytopenia due to

portal hypertension and splenic sequestration of platelets. Dysfunctional platelets in the absence thrombocytopenia may also contribute to bleeding risk in patients with liver disease.

Cardiopulmonary bypass

Mechanical trauma, interaction of platelets with the negatively charged plastic surface components, hypothermia, complement activation, release of cytokines, and thrombin generation may also contribute to significant platelet dysfunction during CPB. Thrombocytopenia is also commonly seen due to haemodilution from the prime and adherence of platelets to artificial surfaces.

Uraemia

Uraemia associated with chronic renal failure has long been associated with increased clinical bleeding and reflects underlying platelet dysfunction. Platelet dysfunction is due to both decreased platelet aggregation and impaired platelet adhesiveness. The impairment in platelet adhesiveness results from intrinsic dysfunction of glycoprotein IIb/IIIa, and adhesion by its interaction with fibrinogen and von Willebrand factor There is no deficiency in von Willebrand factor levels in uremic patients. Studies in uremic patients have shown that platelet NO synthesis is increased, and that uremic plasma stimulates NO production by cultured endothelial cells. Nitric oxide is an inhibitor of platelet aggregation.

Inherited disorders of platelet function

Bernard-Soulier Syndrome

Bernard-Soulier syndrome (BSS) is an inherited platelet function disorder caused by an abnormality in the receptor for von Willebrand factor - the GpIb/V/IX receptor. Since the VWF receptor is absent or dysfunctional, the platelets do not adhere to the collagen. Bernard-Soulier syndrome is an autosomal recessive disorder and affects both males and females. BSS is a giant platelet disorder, characterized by abnormally large platelets. Clinical manifestations usually include purpura, epistaxis, gingival bleeding and menorrhagia, and more rarely gastrointestinal bleeding and haematuria. Severe bleeding episodes are associated with surgery, dental extraction, menses, delivery, or accidents.

Glanzmann Thrombasthenia

Glanzmann thrombasthenia is an inherited platelet function disorder caused by an abnormality in the GpIIb/IIIa receptor. It can also be acquired as an autoimmune disorder. Glanzmann thrombasthenia is an autosomal recessive disorder. Haemorrhagic symptoms, such as mucocutaneous bleeding with epistaxis and purpura, gingival bleeding and menorrhagia, occur only in homozygous patients. Platelet numbers and morphology are normal. The bleeding tendency in Glanzmann's thrombasthenia is variable.

Storage Pool Disorders

Storage pool disorders are a group of inherited disorders caused by abnormalities with platelet storage granules. The contents of granules are released during the activation phase of platelet activation, to recruit platelets and other cells to the site of injury. There are two main types of granules: alpha granules and dense granules. Some storage pool deficiencies are caused by a lack of granules or contents, the most common defects are caused by a failure of the platelets to release their contents.

- Release defects are a diverse group of disorders caused by an abnormality in the secretion mechanism. Even though the granules are present within the platelets, their contents are not secreted properly.
- Delta storage pool deficiency is a platelet function disorder caused by a lack of dense granules. The dense granules contain adenosine diphosphate (ADP), adenosine triphosphate (ATP), ionized calcium and serotonin. Examples include conditions such as Hermansky-Pudlak and Chediak-Higashi syndromes.
- Gray platelet syndrome (GPS) is a very rare platelet function disorder caused by a lack of alpha granules. Contents of alpha granules include insulin-like growth factor 1, platelet-derived growth factors, TGFβ, platelet factor 4, thrombospondin, fibronectin, factor V, and von Willebrand

factor. GPS is characterized by thrombocytopenia, and abnormally large agranular platelets in peripheral blood smears. The defect in GPS is the failure of megakaryocytes to package secretory proteins into alpha-granules. Patients with the GPS are affected by mild to moderate bleeding tendencies.

Prophylaxis and Treatment of Bleeding in Patients with Platelet Disorders

There are a limited number of therapeutic options available if specific treatment is required to correct platelet dysfunction. This is especially true for most of the inherited platelet disorders, in which there is little evidence from randomized trials upon which to base recommendations for management.

Systemic Antifibrinolytic Therapy

Antifibrinolytic agents, such as tranexamic acid, are effective in the management of bleeding in patients with thrombocytopathy or thrombocytopenia. Oral tranexamic acid should be commenced the day before the elective surgery and continued for 5–7 days.

Desmopressin

Desmopressin (DDAVP) is commonly used to correct the haemostatic defect in von Willebrand disease. In the case of VWD, DDAVP releases endogenous VWF from the endothelium. DDAVP shortens the bleeding time in storage pool deficiencies but is not effective in patients with receptor defects.

Its use has also been used in patients with acquired platelet dysfunction. One study demonstrated correction of an abnormal bleeding time in seven of nine patients with acquired platelet dysfunction. This correction did not correlate with changes in VWF levels and interestingly, there was no improvement in tests of in vitro platelet aggregation. Similarly, DDAVP can shorten the bleeding time in patients with cirrhosis or uraemia, although this correction does not necessarily correlate with a decline in bleeding risk.

In patients undergoing cardiopulmonary bypass, two well-designed studies came to opposite conclusions in two different patient populations concerning the value of this agent for treatment of the bleeding diathesis that often complicates open-heart surgery:

- In a double-blind, randomized, placebo-controlled trial 150 consecutive patients undergoing primary coronary-artery bypass grafting received intravenous DDAVP or placebo. The median amount of postoperative blood loss within the first 24 hours after operation was similar in the two groups as was the postoperative use of blood replacement products. The authors concluded that most patients who undergo elective cardiac surgery do not benefit from the use of DDAVP.
- A second double-blind, randomized study included 70 patients. Unlike the above study, patients undergoing uncomplicated primary coronary-artery bypass grafting were not included. DDAVP significantly reduced mean operative and early postoperative blood loss. Plasma levels of von Willebrand factor were higher after desmopressin administration than following placebo.

Oestrogens

Conjugated oestrogens have been used, most commonly for uremic bleeding or in patients with mild to moderate type 1 von Willebrand disease. Intravenous oestrogen 0.6 mg/kg per day for four to five days, oral oestrogen 50 mg/kg per day, or transdermal estradiol 50 to 100 mcg/24 hours applied as a patch twice weekly have been shown to be effective, particularly for gastrointestinal bleeding. Onset of action is slow which limits the usefulness of oestrogen therapy in the acute setting.

Platelet transfusion

Transfusion of platelets may be required in patients with disordered platelet function. Platelet transfusions are particularly indicated in cases of severe, uncontrolled bleeding, when prior treatments (e.g., DDAVP, oestrogen) have been unsuccessful, and/or in the presence of, or anticipation of,

excessive traumatic or surgical bleeding. One unit of platelets (2–4 × 1011 platelets) would be expected to increase the platelet count of an adult patient (70 kg) by 20,000–30,000/μl. Young children and infants should receive 10 ml/kg body weight. Specific indications for platelet transfusions are: i) bleeding complications in inherited platelet disorders (e.g. GT, BSS); ii) emergency therapy of thrombocytopenic/-pathic bleeding in patients with disorders of megakaryopoiesis or increased platelet turnover (e.g. ITP, liver disease, or DIC); iii) thrombocytopenia after massive transfusion; iv) prophylaxis in thrombocytopenia/-pathy and bleeding risk as well as preoperatively. Immunological or non-immunological refractoriness may be the cause of a reduced increase in platelet count after transfusion. Immunological refractoriness is primarily caused by HLA antibody-mediated destruction of transfused platelets. In such a case not only ABO, but also HLA-compatible platelets should be given. Patients with GT have a particularly high risk for alloimmunization. Prevention is best accomplished by using leukocyte-depleted blood products. Use of platelets matched via HLA is a further attempt to prevent platelet alloimmunization.

Refractoriness to platelet transfusion therapy

Patients who cannot receive platelet transfusions because of alloimmunization or antibody formation to the absent platelet glycoprotein (e.g., Glanzmann thrombasthenia and Bernard-Soulier syndrome) may benefit from rFVIIa.

Recombinant Activated Factor VIIa (rFVIIa)

rFVIIa is often used in thrombocytopathic/-penic patients suffering from bleeding that cannot be stopped by conventional treatments. Best reported data concerning the efficacy of rFVIIa is documented in thrombasthenic patients. Prophylaxis with rFVIIa in 29 out of 31 Glanzmann thrombasthenia patients undergoing surgery was effective and it has also been used for the treatment of severe bleeding complications in patients with BSS, storage pool diseases, and several acquired thrombocytopathies. The use of rFVIIa in thrombocytopenia should be limited to life-threatening or conservative non-treatable bleeding complications. To increase the effect of rFVIIa, a prompt transfusion of platelets should be considered considering the risk-benefit ratio**.** rFVIIa is approved in Europe for use in patients with Glanzmann thrombasthenia refractory to platelet transfusions. Benefits of rFVIIa must be balanced against the risk of thrombosis.

Inherited disorders of coagulation

Hereditary bleeding disorders are a diverse group of diseases that include abnormalities of primary and secondary haemostasis. Perioperative management of these uncommon conditions can be challenging. The most common congenital bleeding disorders include:

- von Willebrand disease
- Haemophilia A (factor VIII deficiency)
- Haemophilia B (factor IX deficiency)

Haemophilia

Haemophilia can be classified as haemophilia A, B, or C depending on the deficiency of the coagulation factors VIII, IX, or XI respectively. Haemophilia A and B are inherited as X-linked recessive (XLR) disorders due to mutation in the long arm of chromosome X at F8 and F9 genes, respectively.1 As with any XLR disorder, males are affected, and females are carriers. One-third of the patients presenting with haemophilia have no family history and are probably due to de novo gene mutations.

Haemophilia A

Classic haemophilia or haemophilia A is an X-linked recessive hereditary disorder characterized by defective or deficient clotting factor VIII (FVIII) which affects the male offspring. The incidence is 1/5000 male live births. The affected individual may present with spontaneous haemorrhage specifically into the joint cavities or uncontrollable bleeding even after minimal injury. Haemophilia A is characterized by intra-articular and intramuscular bleeding. There are numerous different mutations, which cause haemophilia A. Due to differences in the gene involved (and the subsequent resulting

protein), patients with haemophilia have varying levels of factor VIII clotting activity. Individuals with less than 1% FVIII clotting activity are classified as having 'severe' haemophilia, those with 1–5% as 'moderate', and those with between 5-40% as mild. Most severe haemophilia patients require regular supplementation with intravenous recombinant or plasma derived Factor VIII concentrate.

Haemophilia B

Haemophilia B is a disease with an estimated incidence of 1 in 25,000 males and perioperative management of such patients can often be challenging. The most common symptoms at presentation relate to bleeding into the joints with inflammation leading to deformities. The management of bleeding mainly involves use of factor concentrates, whole blood and plasma but the use of antifibrinolytics, factor VIIa and immunoglobulins have also been described.

Von Willebrand's disease

VWD is the most common inherited bleeding disorder. The prevalence of vWD is one in 100 but is asymptomatic in most patients and is clinically significant in only one in 10 000 patients. Most cases of VWD are transmitted as an autosomal dominant trait. vWD is caused by either a quantitative or qualitative defect in von Willebrand's factor. VWD is classified on quantitative or qualitative defect of VWF into three types.

Type 1 is due to a quantitative reduction in vWD protein.

Type 2 is due to dysfunctional vWD.

Type 3 is due to absent or severely reduced vWD.

Treatment of Bleeding in Patients with inherited coagulation disorders

For individuals with inherited coagulopathies who are undergoing elective surgery, collaboration between the surgeon, anaesthesiologist, haematologist, and laboratory and transfusion medicine services should occur, with enough time to allow a smooth surgical course in which factor levels can be monitored and replacement therapy administered on time. The specific factor dosing schedule and appropriate target factor levels depend on the individual patient and procedure being performed; some individuals may be able to use products other than clotting factor (e.g. DDAVP for mild haemophilia A).

Factor concentrates VIII and IX

Recombinant factors VIII and IX used in haemophilia A and B respectively. Commercial preparations of factors VIII and IX as lyophilized powder are available. It is free from the risk of disease transmission as seen with blood products. Intermediate and high purity factor VIII concentrates: plasma derived, can have other non-factor VIII proteins, alternative when recombinant factors are not available.

Patients with severe and moderate haemophilia A must be treated with factor VIII (FVIII) concentrates before intubation, because there is a high risk of haemorrhagic complications, such as haematoma of the epiglottis and trauma induced bleeding from the upper respiratory tract.

Desmopressin

DDAVP is generally reserved for minor bleeding or minor invasive procedures in individuals with mild haemophilia A or vWD types 1 and 2. Severe, life-threatening bleeding should be treated with factor infusion because the response to DDAVP is not immediate and may not raise the factor levels for optimal haemostasis. Individuals with moderate to severe haemophilia A (factor VIII level <5 percent) are unlikely to derive benefit from DDAVP because the incremental increase in factor VIII level would be insufficient for haemostasis. Mild haemophilia patients do not necessarily require FVIII concentrates before intubation or surgery. Most mild haemophilia patients respond very well to DDAVP, which can raise FVIII and von Willebrand factor levels 3-5 times above baseline levels. DDAVP is the haemostatic agent of choice for mild haemophilia, Not FVIII concentrate. Drug selection will also depend on the volume and type of surgery. Haemophilia A patients with inhibitors must be treated with Recombinant FVIIa or FEIBA before intubation.

Prothrombin complex concentrates

Prothrombin complex concentrate (PCC) is a combination of blood clotting factors II, VII, IX, and X. Although the current main indication of PCC is for emergency reversal of warfarin therapy, PCC were initially developed for treatment of haemophilia B; they have been sparingly used after the development of highly purified and recombinant factors. Its thrombogenic calculated units are based on factor IX levels. The dosage is 15–50 units kg−1 (maximum 5000 units stat). Factor eight inhibitor bypassing activity (FEIBA, or anti-inhibitor coagulant complex) is an activated PCC (aPCC). FEIBA is licensed for use in patients with inhibitors to factor VIII and IX. Commercially available as Haemosolvex in South Africa.

rVIIa

Recombinant factor VIIa binds to the surface of activated platelets, thereby directly activating factor X and leading to an improved generation of thrombin. rFVIIa has been shown to be effective in achieving haemostasis in haemophilia patients with inhibitors in about 80% of cases. The thrombogenic activity of rFVIIa is optimized when fibrinogen levels and pH are within the normal range

Cryoprecipitate

Cryoprecipitate has an unpredictable effect with a high risk of transmissible infections. Its use should be reserved for the emergency scenario where replacement factors are not available. One unit of Cryoprecipitate contains the following proteins in a volume of approximately 5 to 20 mL:

●Fibrinogen – >150 mg of fibrinogen (range: 150 to 250 mg); half-life: 100 to 150 hours

●Factor VIII – >80 international units (range: 80 to 150 units); half-life: 12 hours

●Factor XIII – 50 to 75 units; half-life of 150 to 300 hours

●von Willebrand factor – 100 to 150 units; half-life: 24 hours

VWF preparations

Several products are available that contain VWF in high concentration, including "intermediate purity" (plasma-derived) factor VIII concentrates (which also contain VWF), more highly purified VWF concentrates, and a recombinant VWF product.

Most cases of VWD do not need blood components to control haemorrhage, pharmacological management would suffice. In type 3 VWD, it is recommended that the vWF level is maintained at about 100 IU dl−1 perioperatively and >50 IU dl−1 in the immediate postoperative period. The FVIII plasma concentration should be above 100 IU dl−1 to cover major surgery and sustained above 50 IU dl−1 in the postoperative period. Major surgery requires treatment for 7–14 days and minor surgery for 1–5 days.

SBAs

What receptor does adenosine diphosphate bind to during platelet activation?

A. P2Y12
B. Gp IIb/IIIa
C. Gp Ib-Ix
D. Von Willebrand Factor

Where is von Willebrand factor synthesized?

A. Megakaryocytes
B. Leukocytes
C. Erythrocytes
D. Endothelium

What is the primary mediator for vasoconstriction to occur in primary hemostasis?

A. Renin-angiotensin-aldosterone-system
B. Endothelin-1
C. Von Willebrand factor
D. Subendothelial collagen exposure

Which of the following proteins binds to tissue factor to initiate clotting?

A. Factor V
B. Factor VII
C. Factor X
D. Prothrombin

What serum factor is involved in the cross-linking of newly formed fibrin threads of a blood clot?

A. Fibrinogen
B. Tissue factor
C. Factor XIII
D. Calcium

Notes

MINS - Myocardial Injury after Non-cardiac Surgery

Dr Marcelle Jagga

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Background

Global surgery accounts for more than 300 million procedures annually. Cardiovascular complications account for one third major peri-operative morbidity and mortality after non-cardiac surgery.

Recent data suggests non-cardiac surgery in the age group older than 45, account for more than 100 million procedures annually. In the Vascular events in Non-cardiac surgery patient's cohort evaluation (VISION) trial, 7% experienced Myocardial injury after non-cardiac surgery (MINS). The incidence of major adverse cardiac events (Cardiac death, nonfatal myocardial injury, heart failure) in patients ≥ 45 years of age after having non cardiac surgery was 1 in 20 (5%). Myocardial infarction and ischaemia account for 39% of all deaths after non-cardiac surgery. These deaths are equally distributed between myocardial infarction and ischaemia.

According to the 2018 Joint Task Force of the European Society of Cardiology, American college of Cardiology Foundation (ACC), American Heart Association (AHA) and World Health Federation, Myocardial infarction (MI) is defined as a clinical event in the setting of myocardial ischemia in which there is evidence of myocardial injury.

Classification of myocardial injury and infarction is according to international consensus.

Myocardial infarction (MI) is differentiated from myocardial injury by meeting criteria of the fourth universal definition. To be classified as an myocardial infarction a detection on rise/ or fall in cardiac biomarker levels with at least one level above the 99th centile and at least one of the following criteria 1) new ST elevation or new Left bundle branch block on Electrocardiogram (ECG), 2) symptoms in keeping with myocardial infarction, 3) pathological Q-waves on ECG, 4) imaging showing loss of viable myocardium or new regional wall motion abnormalities, 5) identification of intracoronary thrombus by angiography or autopsy.

Although a clear definition is still required, myocardial injury after non cardiac surgery (MINS) is currently defined as myocardial cell injury within 30 days after non-cardiac surgery due to an ischemic aetiology. MINS include MI (both symptomatic and non-symptomatic that meet criteria in the fourth universal definition for myocardial infarctions) as well as patients with isolated elevations in troponins (that **do not** meet the criteria in the fourth universal definition for myocardial infarctions).

Patients who have a rise in troponins, caused by ischemia, after non-cardiac surgery in absence of symptoms or ECG changes are labelled as having myocardial ischaemia.

Non-ischaemic causes for a rise in troponins most commonly include:

- sepsis
- pulmonary embolism
- atrial fibrillation
- chronic troponin elevation
- acute kidney injury

Pathophysiology

Arteriosclerosis

Arteriosclerosis is a chronic inflammatory fibro-proliferative disease mostly noted in the medium and large conduit arteries. The most prominent risk factors are hyperlipidaemia, diabetes mellitus, hypertension, smoking and genetic predisposition. The entire systemic vasculature is exposed to systemic risk factors for atherogenic formation. Plaques form at specific regions of the arterial tree, these are in the vicinity of branch points, at the outer wall of bifurcations, at the inner wall of curvatures and where turbulent flow occurs. Hemodynamic forces play a major role in localization of atherosclerosis. Local vascular factors that play the most significant role is flow generated endothelial shear stress and to a lesser extent blood pressure derived tensile stress. Atherosclerotic lesions occur in larger coronary vessels (1.5 – 4mm).

Coronaries

Coronaries receive 5% of cardiac output during resting conditions. With exercise this can increase 3-4 times to accommodate the increase in myocardial oxygen demand. Under normal circumstances this increase is almost linear. This is necessary due to the fact that oxygen extraction is near complete under basal conditions, coronary sinus saturation being 25%. In contrast other muscle groups have physiological reserve with the ability to increase arteriovenous oxygen gradient by increasing oxygen extraction. Coronary blood flow to the left ventricle occurs predominantly during diastole, with flow determined by aortic diastolic pressure, resistance inside the coronary vessels (Tone of the walls and compressive force of the myocardium) and the left ventricular end diastolic pressure. Tone within the resistance vessel play a significant role and accounts for a large part of variability during angina. Unluckily no coronary selective vasodilator drug exists.

Two main components exist within the model for coronary resistance.

Larger vessels (100 – 350µm)
- Display myogenic and neurogenic responsiveness.
- Likely where nitric oxide mediated vasodilation occurs.

Smaller vessels (<100µm)
- Where metabolic regulation occurs.
- Possible oxygen sensing, response to carbon dioxide and adenosine release from cardiac myocytes.

Resistance vessels are responsible for two phenomena

- Autoregulation during a wide variation of perfusion pressure
- Increase in coronary blood flow during exercise.

Main determinants of myocardial oxygen consumption are

- Myocardial mass
- Myocardial work (HR, Pressure, Volume)
- Pre-contractile tension
- Inotropic status

Coronary reserve is the difference between basal autoregulated flow and maximal coronary flow.

Coronary flow and shear stress

Mechanical shear stress

Normal mechanical shear stress is when force is applied at 90 degrees to the vessel wall. Fluid movement induces shear stress parallel to the face of the vessel.

Factors influencing the severity of the shear stress are blood viscosity (Ƞ) and shear rate.

Shear rate is the change in blood velocity ($v_1 – v_2$) over distance(h).
Shear stress = Ƞ x ($v_1 – v_2$)/h

When the diameter of the vessel stays constant, shear rate is proportional to velocity.

Flow

As fluid interacts with the vessel wall, its velocity rapidly approaches zero. A thin layer of fluid, known as the boundary layer, is the layer where fluid shows reduction in velocity next to the vessel wall. The boundary layer will follow the contour of the vessel leading to formation of new stream lines or flow patterns. This happens with an intrusion, such as a coronary plaque, into the lumen of a cylinder(vessel wall).

Boundary layer separation occurs when the streamline separates/detaches from the wall.

As the fluid separates from the wall an area of low pressure develops behind the stenosis leading to reverse flow or recirculation.

Turbulent flow imparts more energy on the boundary layer. Describing the probability of turbulence is the Reynolds formula, with turbulence very likely to occur at a number greater than 2000. Due to the higher energy, flow separation happening at a point further down the vessel.

Re = ρ(Density) x V(Velocity) x D (diameter)/ Ƞ(Viscosity)

Poiseuille equation calculates blood flow volume

$Q = \pi r^4(P1 – P2)/8\eta l$
V (Velocity) = Q (Flow) / πr^2 (area)
Velocity = r^2 (P1-P2)/8Ƞl

Blood flow velocity (Q) is directly proportional to pressure gradient (P1-P2), if the vessel diameter, length (l) and viscosity (Ƞ) stay constant. (r=radius)

We can extrapolate that shear stress and flow patterns are proportional to pressure gradient.

Troponins

Cardiac troponin testing is the only recommended biomarker for the detection of myocardial necrosis. The majority of cardiac troponins are found intracellular, and more than 90% of the isoforms are found within the sarcomere. The mechanisms of release into the circulation are thought to include myocardial necrosis, apoptosis, formation and release of membranous blebs, increased membrane permeability and release of proteolytic troponin degradation products.

Troponin release can be found outside the context of cardiac myocyte ischaemia and necrosis. These mechanisms include:

- Myocardial stretch in response to increased pressure or volume, causing activation of intracellular proteases associated with degradation of troponin.
- Tachycardia stimulating stress responsive integrins leading to release of troponin I from the cardiac myocyte in absence of necrosis
- Release of troponins during reversible ischaemia as noted during stress testing

Ultra-sensitive cardiac troponin with single molecule counting technology found change in cardiac troponin concentration matched the extent of myocardial ischaemia.

For diagnosing acute myocardial injury/infarction

- Any peak above the 99th centile or
- Increase/decrease ≥ 20% if baseline levels above the 99th centile

For diagnosing **clinically significant MINS** (High sensitivity Troponin)

- **≥ 20ng/L and rise/fall (>5ng/L or 20%) or**
- **≥ 65**

Biomarkers 99th centile

- 4th generation Troponin = 30 ng/L (0.03ug/L)
- 5th generation Troponin(High sensitivity) = 14 ng/L

Mechanism of ischaemia

After 15 – 20 seconds after inadequate perfusion, anaerobic glycolysis supervenes as the only new source of new high-energy phosphate.

This is only sufficient to meet the most basic demand of the cardiac myocyte. This is depleted within 60 – 90 minutes of ischaemia.

Physiological stressors

Perfusion pressure, velocity and coagulation may play a pivotal role.

Thrombus formation is classically demonstrated by a low flow state, increased platelet activation and endothelial damage forming Virchow's triad. In the first 5 days post operatively these 3 factors create an optimal condition for thrombus formation.
In the absence of plaque rupture post-stenotic blood flow stasis and platelet activation is likely to play a key role.

Sympathetic induced hemodynamic changes

Catecholamines, cortisol and other stress hormones increase post operatively and remain elevated for several days. This leads to a profound increase in myocardial work while compromising supply.
Some correlation has been found between catecholamine levels and graft occlusion after vascular surgery.

Plaque rupture and thrombi formation

Hypertension and tachycardia are prominent contributors to increased shear stress/rate. Leading to either outward remodelling with thin fibrous caps, high circumferential tensile stress or inward remodelling with erosion of endothelium due to high velocities around plaque.

Increased shear stress can precipitate peri-operative plaque rupture. Despite this we can see from post-mortem studies that the suspected increased in plaque rupture, due to the increased blood velocity, was not significantly present in the post-operative period.

It is more likely that relative **hypotension** and reduced **blood velocity**, due to a lower pressure gradient, is more important. During periods of low blood velocity, the low energy laminar flow result in flow reversal and stagnation post stenosis. Larger degrees of stasis have been noted where multiple stenotic lesions are present. This is ideal for thrombus formation.

Despite this few thrombi, in absence of plaque rupture, have been found during post-mortem studies. It is possible that thrombolysis, as occurs just prior to death, accounts for this discrepancy although this is still unproven.

A positive correlation has been found between markers for fibrinolysis and myocardial ischaemia in the early post-operative period. In absence of myocardial ischaemia, markers of fibrinolysis are noted later post operatively. (≥ 24 hours)

Platelet activation

Platelet activation is mediated either by direct mechanical force or von Willebrand factor interaction. Platelet activation and inter-platelet interaction increases exponentially. This can occur during high or low shear stress conditions. Areas that experience peak shear rates are at the apex of the stenosis, this is where platelet and fibrin deposition occur. Thus, it can be seen that tachycardia potentially increases the activation. Activated platelets that do not adhere at the areas of high shear stress, are primed for thrombus formation when in contact with platelet agonists. These activated platelets now move into areas of low shear stress and recirculation post stenosis. Here cellular interaction takes place and leads to thrombus formation. Some correlation has been noted between elevation of troponin and platelet activation in the major vascular surgery patients.

Some procoagulants are increased (Fibrinogen, Factor VIII) with a concomitant decrease in anticoagulants (Protein C, antithrombin III).

Red blood cells also play a role in the low shear stress/recirculation zone as they undergo clumping and interact with both platelets and neutrophils, leading to further thrombus formation.

Endothelium substrate

Oscillatory and low shear stress leads to up regulation of pro-inflammatory cytokines and expression of adhesion molecules (Vascular adhesion molecules, intercellular adhesion molecules (I-CAM), and E-selectin) while down regulating endothelial nitric oxide synthetase (eNOS), prostacyclin and tissue plasminogen activator (t-PA).

Endothelium under the region of flow separation is exposed to low shear stress with prothrombotic changes. When the pressure gradient drops, and flow becomes laminar, damaged endothelium is available to interact with activated platelets in the area of stagnation.

Reperfusion

Another major concern lies when reperfusion occurs. Myocardial stunning is shown after reperfusion and is a period of increased oxygen consumption for the given myocardial work. Possible reason for this is rapid recovery of intracellular pH. Mechanism suggested is after initial accumulation of intracellular H^+, when perfusion is restored, H^+ is pumped extracellularly in exchange for Na^+ to normalize pH. This increase in intracellular Na^+ leads to activation of $2NA^+/Ca^+$ exchanger on the sarcolemma, leading to increased intra cellular Ca^+. This increased intracellular cytosolic Ca^+ results in activation of nuclear endonucleases and other enzymes leading to cellular death.

Reperfusion also leads to overshoot fatty acid oxidation, impaired pyruvate oxidation and accelerated anaerobic glycolysis. This leads to uncoupling of glucose oxidation and glycolysis. The net result of which is production of $2H^+$ from every glucose molecule due to pyruvate being converted to lactate. The Mitochondrial permeability transition pore (PTP), a non-selective pore on the inner pore of the mitochondria, becomes critically important. During reperfusion the cellular survival depends on the permeability of the mitochondrial inner membrane.

Surgical population

In contrast to the non-surgical population, clinical features are notoriously absent in the surgical patients. Therefore, diagnosis usually rely on cardiac troponin measurement. More than 93% of patients diagnosed with MINS did not meet the diagnostic criteria for the universal definition of myocardial infarction. Symptoms where present in 7% and only 15% had non-specific ECG changes. Only 50% of the population showed an increase in Troponins in the first 24 hours with the rest occurring later post operatively, thus highlighting the need for serial testing. Important to note that 80% of patients will not demonstrate clinical or ECG changes despite having MINS. Only 13% of the perioperative MI patients had evidence of thrombus as the culprit lesion. Despite this low incidence of a causative thrombus, 60% of perioperative MI patients showed fibroatheroma as the culprit lesion. Large prospective trials have shown that 85% of perioperative elevations in troponins was due myocardial ischaemia rather than non-ischaemic causes.

MI's account for 20-30% of MINS if high sensitivity troponins are used, compared to 40% if non high sensitivity troponins are used (highlighting the increased sensitivity of high sensitivity Troponins to identify myocardial ischemia).

Acute myocardial injury can occur due to a variety of cardiac and non-cardiac causes. Chronic myocardial injury may occur in structural heart disease or non-cardiac illnesses such as chronic renal failure. These might contribute to diagnostic uncertainty. It is important to note that **clinically significant** MINS requires any value above 65 ng/L, in absence of a non-ischemic cause, or any elevation of more than 20% if value between 20 – 65ng/L.
Myocardial Pathophysiology of Myocardial injury in the perioperative period is complex. Our current understanding is based on based on five different investigative approaches.

Post mortem studies
Noted an equal distribution between myocardial supply demand mismatch and plaque rupture. Myocardial oxygen supply demand related mortality has been found to be the predominate cause for mortality during the first 72 hours, with 86% patients who demised within the first 72 hours not having features of plaque rupture. Patients diagnosed with plaque rupture where evenly distributed over the first 3 weeks post operatively. Also, of note is that 46% of the patient documented to have plaque rupture where found to have intra plaque hematoma formation rather than having clear plaque rupture. Importantly fatal myocardial infarctions occur predominately against a background of coronary artery disease. 69% of thrombus where noted in absence of plaque rupture. 89% of thrombus where found at the area of significant stenosis. Total coronary occlusion was only noted in 56% of those found with a thrombus.

Coronary angiography
When patients for vascular surgery where evaluated with pre-operative angiography, the only independent predictor of mortality was the number of coronary lesions with greater than 30% stenosis. 81% of fatal cases had chronic total coronary occlusion.

Inducible myocardial ischaemic testing
From these studies it was described as the test with the lowest negative likelihood ratio (negative likelihood ratio=0.2) for major adverse cardiac events. Suggesting that patients are unluckily to develop peri-operative cardiac complications in absence of inducible myocardial ischaemia. Interesting myocardial infarctions correlated with the site of inducible ischaemia in 81% of patients. Unluckily the positive likelihood (LR=4) for development of adverse cardiac outcome was less accurate.

Holter studies
20% of vascular surgery patients have ST depression post operatively. ST depression was 40 times more prevalent than ST elevation. The majority of the ST depression occurred within the first 72 hours post operatively. This suggest oxygen supply demand mismatch plays a more significant role in the acute post-operative period. ST- elevation occurred in less than 2% of Myocardial injury after non cardiac surgery. Troponins correlated to duration of ST-segment changes, even after period as short as 30 minutes. When using lower cut off levels of troponin (> 0.03 ng/mL) only 32% showed ECG changes, but when higher cut offs are used of (>0.1 ng/mL) 88% of patients showed ECG changes.

Haemodynamic studies

Post-operative ischaemia is more prevalent than pre/intra operative ischaemia. Many studies show an association between increased heart rate and post-operative ischaemia. Prolonged hypotension of more 60min resulted in a significant increase in post-operative adverse cardiac events. A left ventricular mass of more than 270g has been independently shown as a risk factor for coronary plaque rupture.

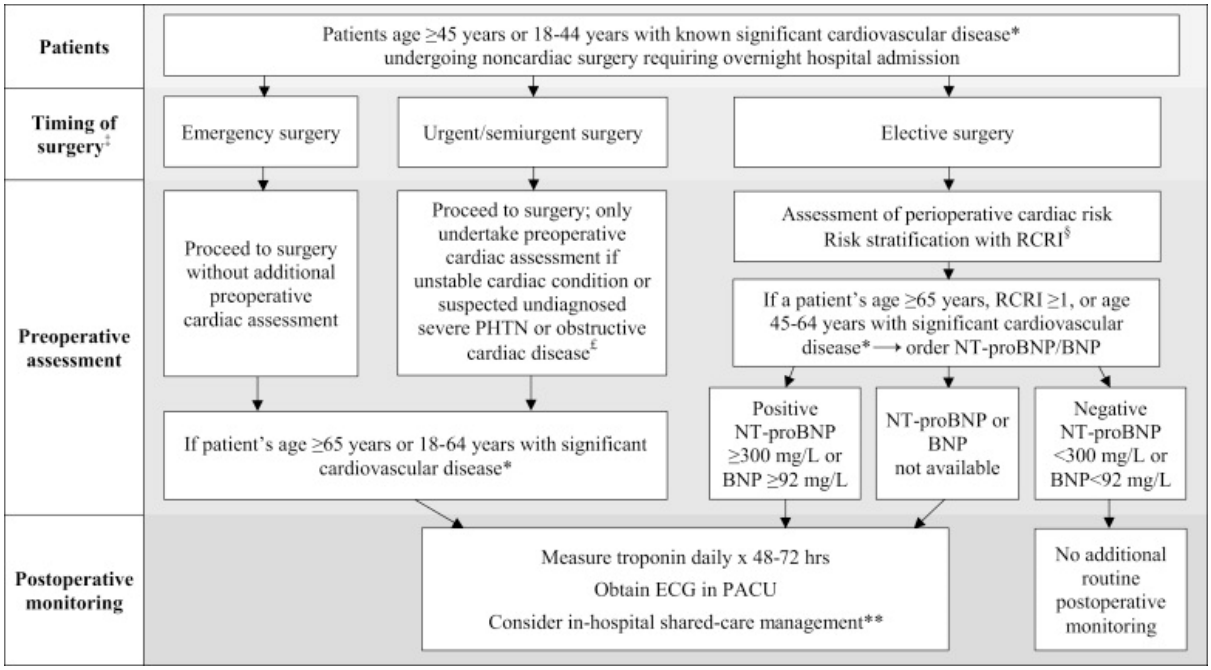
Prediction

Why do we want to assess patients' risk?

- Can be used to assess risk and benefits of specific procedures
- Can be used to guide management decisions
- Guide for monitoring during and after surgery.
  - Especially in limited resource settings, allocates patient that require more intensive strategies.

Which patients should undergo risk assessment?

According to the Canadian Cardiovascular Society guidelines

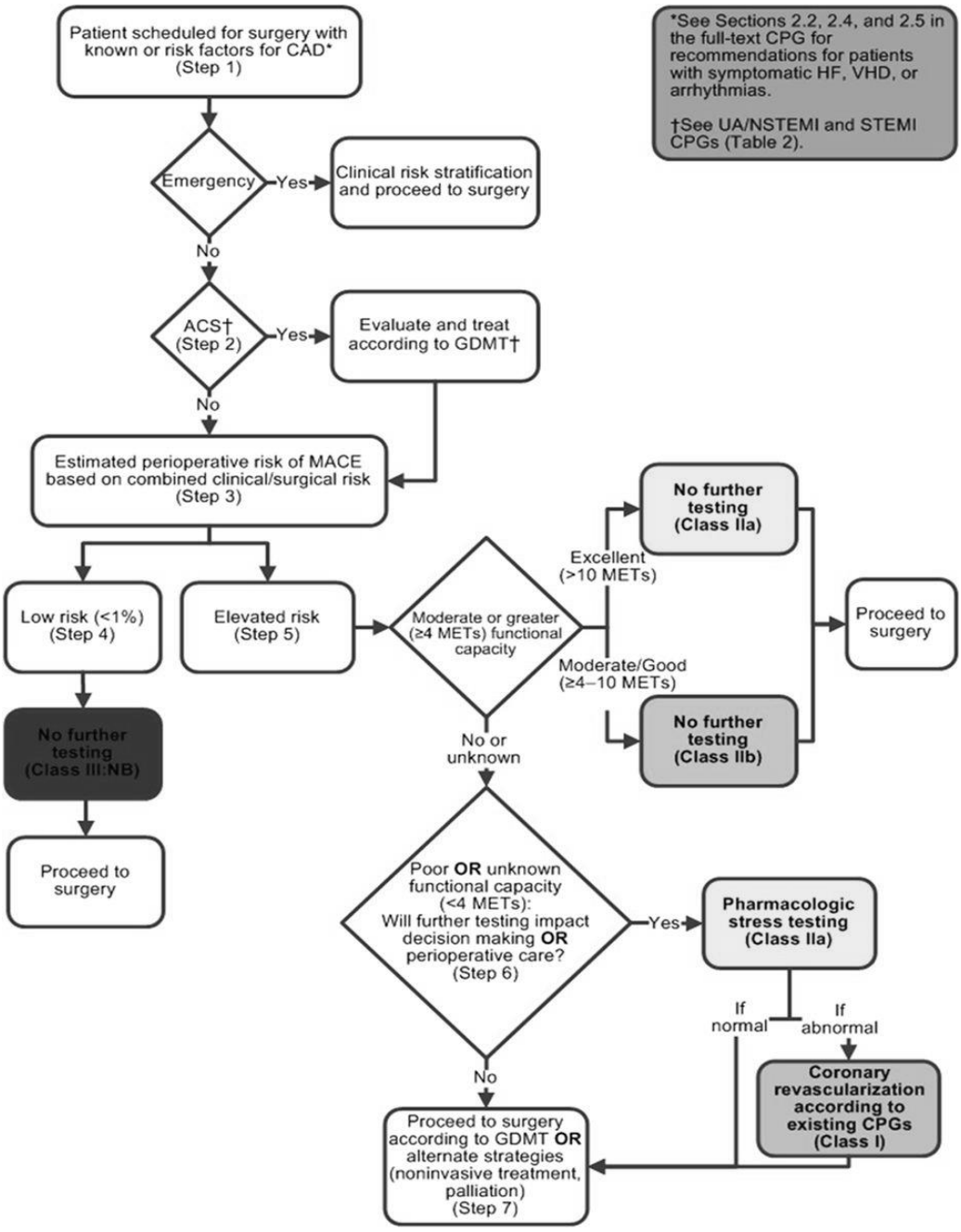


Patients that require overnight stay after surgery

Age

- Patients older than 45 years of age
- Patients between 18 and 44 with significant cardiovascular disease

According to the AHA/ACC



Elevated risk patients

- Patients with high risk cardiovascular pathology
  - Active/Acute myocardial ischaemia
  - Significant structural cardiac disease
    - Severe Valvular lesions
    - Cardiac failure
    - Cardiomyopathies
- Patients with high risk conditions
  - Revised Cardiac Risk Index (RCRI) ≥2
- Patients with decreased functional capacity
  - METS < 4

Elevated risk surgery

- Estimated risk of more than 5% 30-day mortality
- Emergency patients (risk stratify and continue with surgery)

Evaluating risk indices

Revised Cardiac Risk Index (RCRI)

Benefits

Most validated risk indexes
Moderate discrimination to predict major perioperative cardiac complications

Draw back

Some conditions that influence outcome is sometimes missed (Aortic stenosis, pulmonary hypertension, etc.)

Variables used in the RCRI:

Variable	Points
History of ischemic heart disease*	1
History of congestive heart failure†	1
History of cerebrovascular disease‡	1
Use of insulin therapy for diabetes	1
Preoperative serum creatinine > 177 µmol/L (> 2.0 mg/dL)	1
High-risk surgery§	1

Risk estimates per total RCRI points:

Total RCRI points	Risk estimate, %	95% CI for the risk estimate
0	3.9	2.8%-5.4%
1	6.0	4.9%-7.4%
2	10.1	8.1%-12.6%
≥3	15.0	11.1%-20.0%

National Surgical Quality Improvement Program (NSQIP) Myocardial infarction and Cardiac Arrest (MICA) as well as the NSQIP American College of Surgeons (ACS) index:

Benefit

Better discrimination ability when compared to RCRI

Draw back

No external validation
Likely underestimate risk – not all patients received systematic evaluation of their post-operative troponins (Thus up to half of the MINS could go undetected)

Functional capacity

Metabolic equivalents task (METS)

Did not predict perioperative cardiac risk

1999 Reilly et al. assessed self-reported functional capacity and found poor ability to predict perioperative cardiac complications

2001 Wiklund et al. found METS not to be independently predictive of perioperative cardiac complications

2018 Recently published trial looked at assessment of functional capacity prior to major non-cardiac surgery.

- Subjective assessment of metabolic equivalents of tasks (METS) did not correlate to risk of major adverse cardiac events.
- Subjective assessment showed a sensitivity of 19.2% and specificity of 94.7% for identifying the inability to attain four Metabolic equivalents during cardiopulmonary exercise testing.
- Duke activity status index questionnaire showed association with predicting primary outcome (Odds Ratio 0.96)
- NT-proBNP levels did not correlate well with exercise capacity thus indicating better predictive accuracy with using NT-proBNP in addition to other tests.
- NT-proBNP improved prediction for MINS at 30 days and mortality at 1 year.

Cardiac biomarkers

NT-proBNP

- Released from myocardium due to various stimuli, most significantly during increased stretch and ischaemia
- Independently showed to predict the incidence of major adverse cardiac events
- Able to predict patients at low risk of MACE thus able to reallocate patients to either high or low risk groups

30-day risk of Myocardial infarction or death after non-cardiac surgery

Test result	Risk estimate, %	95% CI for the risk estimate
NT-proBNP < 300 ng/L or BNP < 92 mg/L	4.9	3.9%-6.1%
NT-proBNP value ≥ 300 ng/L or BNP ≥ 92 mg/L	21.8	19.0%-24.8%

BNP, brain natriuretic peptide; CI, confidence interval; NT-proBNP, N-terminal pro-brain natriuretic peptide.

CCS guidelines suggest NT-proBNP should be done on all patients at increased risk

- Older than 65 years old
- RCRI ≥ 1
- Age between 45 and 65 with significant cardiovascular disease

Resting Echocardiography

- Has some ability to predict perioperative cardiovascular complication
- Did not improve ability to predict outcomes in addition to NT-proBNP and RCRI
- Scenarios where Resting Echocardiography advised
  - Clinical examination suggests undiagnosed severe intracardiac abnormalities for instance
    - Aortic/mitral stenosis
    - Hypertrophic obstructive cardiomyopathy or other cardiomyopathies
    - Severe pulmonary hypertension

CCS guidelines suggest **against** the routine use of resting echocardiography.

Coronary computed tomographic angiography (CCTA)

- Found to improve risk estimation when compared to RCRI alone
- Also noted to overestimate patients that will undergo MACE

CCS guidelines suggest **against** the use of CCTA to improve MACE prediction

Cardiopulmonary exercise testing

- Despite being on various guidelines limited studies assessing its ability to predict cardiovascular complications
- Poorly validated with studies assessing its prognostic capabilities, finding it to be a weak predictor for long term post-operative mortality
- Cost more than NT-proBNP and is inconvenient to patients

CCS guidelines suggest **against** using CPET to assess risk for perioperative cardiac risk
AHA/ACC guidelines suggest evaluating CPET when

- METS < 4 and
- It will influence care or decision making

Pharmacological stress testing

- Poor quality evidence thus currently not advised by CCS
- AHA/ACC suggest if unable to conduct CPET

Prevention/optimization

Pharmacology

Intervention	Management
Management of medications taken chronically and smoking before noncardiac surgery	
ASA	Withhold at least 3 days before surgery† and restart ASA when the risk of bleeding related to surgery has passed (ie, 8-10 days after major noncardiac surgery)
β-Blocker	Continue the β-blocker during the perioperative period; however, if a patient's systolic blood pressure is low before surgery, physicians should consider decreasing or holding the dose of the β-blocker before surgery
ACEI/ARB	Withhold ACEI/ARB 24 hours before noncardiac surgery and restart ACEI/ARB on day 2 after surgery, if the patient is hemodynamically stable
Statin	Continue the statin during the perioperative period
Smoking	Discuss and facilitate smoking cessation (eg, nicotine replacement therapy), ideally starting ≥ 4 weeks before surgery
Initiation of new medications and coronary revascularization before noncardiac surgery	
ASA	Do not initiate ASA for the prevention of perioperative cardiac events
β-Blocker	Do not initiate a β-blocker within 24 hours before noncardiac surgery
α_2-Agonist	Do not initiate an α_2-agonist for the prevention of perioperative cardiovascular events
Calcium channel blocker	Do not initiate a calcium channel blocker for the prevention of perioperative cardiovascular events
Coronary revascularization	Do not undertake preoperative prophylactic coronary revascularization for patients with stable coronary artery disease

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; ASA, acetylsalicylic acid.

* This applies to patients age 45 years of age or older or 18-44 years of age with known significant cardiovascular disease (ie, history of coronary artery disease, cerebral vascular disease, peripheral vascular disease, congestive heart failure, or a severe obstructive intracardiac abnormality [eg, severe aortic stenosis, severe mitral stenosis, or severe hypertrophic obstructive cardiomyopathy]) undergoing noncardiac surgery requiring hospital admission.

† Except in patients with a recent coronary artery stent and patients undergoing carotid endarterectomy.

Aspirin

- Did not decrease myocardial infarction rates
- Increased risk of major bleeding
- Can consider continuing if patient had recent coronary stent placed and those undergoing carotid endarterectomy

B-Blockers

- If started within 24 hours before surgery
  - Reduced rate of non-fatal myocardial infarction
  - Increased risk of death, non-fatal stroke, hypotension and bradycardia
- Continuing chronic B-Blockers prior to surgery is advised

α_2-Agonist

- Did not show effect on myocardial infarction or death
- Increased risk hypotension, bradycardia and non-fatal cardiac arrest

CCS guidelines advise **against** the use of α_2-Agonist for prevention of cardiovascular complications

Ca-Channel blockers

- Limited evidence
- Current meta-analysis included only small trials with small number of events

CCS guidelines advise **against** the use of initiating Ca-Chanel blockers for prevention of cardiovascular complication

Angiotensin converting enzyme inhibitors

- Is associated with intra-operative hypotension
- Potentially increased risk for death, stroke and myocardial infarction

CCS guidelines advise **stopping** ACE-inhibitor at least 24 hours prior to surgery

Statin

- Reduced number of post-operative myocardial infarctions
- Can consider initiating statins prior to major vascular surgery, evidence still needed for other high-risk groups

CCS guidelines advise **continuing** statins

Coronary artery revascularization prior to non-cardiac surgery

- Is not advised for prophylaxis prior to major surgery
- Should be consider if clinically indicated
    - Patients with left main stem coronary artery disease, acute coronary artery disease, etc.

Stopping smocking prior to surgery

- Highly recommended prior to surgery although high quality evidence lacking

Intraoperative Monitoring

Gold standard for intra operative monitoring has not been established.

Pulmonary artery catheter:

- Routine use not recommended even in patients for elevated risk procedures
- Can be considered where strict hemodynamic monitoring is essential in patients with uncorrected severe cardiac pathology

Transoesophageal echocardiography:

- Routine use for screen of cardiac abnormalities or myocardial ischemia is not recommended.
- Can be considered for specific indications e.g. where severe hemodynamic instability is expected.

ECG:

Based on limited evidence optimal leads used for monitoring for detecting ischaemia

- V4 in isolation 61% sensitivity
- V5 in isolation 75% sensitivity
- Combined lead II and V5 80% sensitivity
- Combined V5 and V4 90% sensitivity
- Combined II, V4 and V5 96% sensitivity

Features of Ischemia

- ST elevation at J-point of at least 1mm
- ST depression of at least 0.5mm/ T-wave inversion of at least 1mm

Risk for MINS

Heart rate

- ≥ 96 beats per minute have been found to significantly increase incidence of MINS
- 88 – 95 an increase in mortality was noted but not increase in MI
- ≥ 83 a slight increase in MINS was noted but no increase in mortality
- ≤ 60 decreased mortality but no additional benefit in decreasing incidence of MINS
- It is important to recognize that acute peri-operative pharmacological treatment required to decrease HR has not shown improve outcomes
    - B-Blockers have shown decrease in MINS but leading to an increase in other adverse effects and no clear improvement in mortality (when initiated immediately pre-operatively at high dose and continues for 30 days post-operatively)
    - α_2-agonist did not improve mortality – increased incidence of bradycardia and hypotension
    - Ca-channel blockers are potent myocardial depressants and not well evaluated

Hypotension

- Intra-operative hypotension has not been clearly defined.
- A recent systematic review found that intra-operative mean arterial blood pressure (MAP) of lower than 80 mm Hg for longer than 10 minutes is associated elevated risk for end organ dysfunction (Relative risk[RR] = 1.02)
- When assessing specific risk for MINS, it also showed that there was an incremental increase in risk with duration of MAP < 65 mm Hg (RR = 1.3) and significant risk with any duration under MAP < 55 (RR = 2.5).

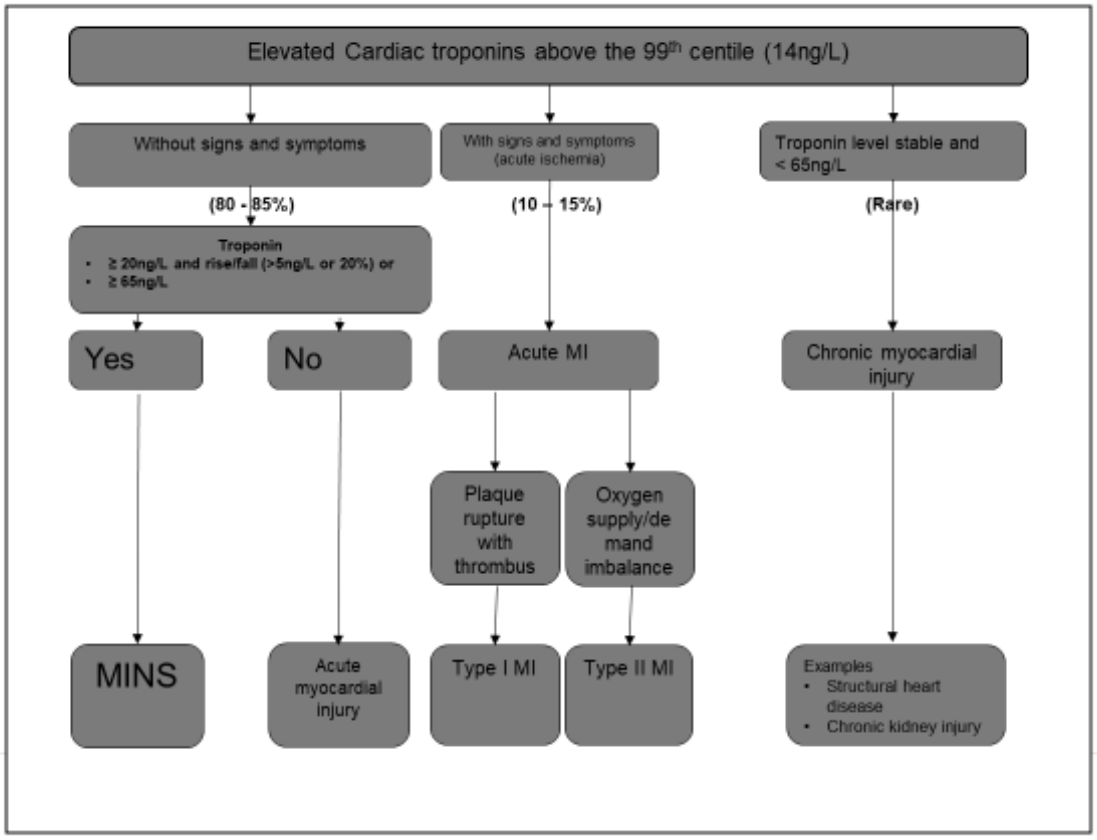
Haemorrhage

- Disabling bleeding or requiring ≥ 2units PRC's where found to be independent predictors of MINS

Temperature

- Not well evaluated in the setting of MINS
- Reasonable to maintain normothermia

Detection



Why is it difficult to detect MINS?

- Analgesia potentially masks symptoms of Myocardial ischaemia, especially in the first 48 hours post operatively
  - In the Poise trial more than 65% of patients with MI's did not have symptoms
- ECG most commonly ordered after detection of elevated Troponins, which is usually at least 6 hours after onset of ischemia. Therefore, ECG changes likely to have resolved.
- If non-high sensitivity troponin testing not used, decreased sensitivity of test to detect small raises
- Patients usually do not have a preoperative troponin to compare changes.

To improve detection

- Elevated risk patients undergoing in-hospital surgery should undergo serial high sensitivity troponin testing (for 72 hours post-operative)
  - Some suggest doing pre-operative troponin testing to be used as comparison
  - 13.8% of patients who had post-operative elevation had elevated baseline values (pre-operative troponin levels)
  - Exclude non-ischaemic causes for elevation
- Patients with signs or symptoms should undergo a 12 lead ECG
  - In the Vision trial only 35% of patients with elevated troponin had ECG changes
  - It is postulated that a higher proportion of patient have ECG changes but that it had resolved at the time the ECG where done.
  - T-wave inversion and ST depression where the most common findings

- Timing of when to conduct post-operative ECG has not been established.
- Concordance between ischaemic changes and elevation of troponins where found to be around 85%.

It is currently unclear if patients with lower risk conditions, i.e. hypertension, diabetes mellitus, smokers, should undergo screening due to the increased morbidity associated with missing the diagnosis.

What do the societies recommend?

American Heart Association(AHA) /American College of Cardiology(ACC) and European Society of Cardiology (ESC) describe high risk patient as someone that undergoes in hospital surgery with one or more risk factors from the revised cardiac risk score.

AHA/ACC (2014)

- Usefulness of conducting of routine post-operative screening still uncertain

ESC (2014)

- Routine screening of high-risk patients with troponins can be considered.

International expert panel compiling the fourth universal definition of Myocardial ischaemia/infarcts

- Recommend conducting routine screening of high-risk patients with perioperative troponin testing for up to 48/72 hours

CCS

- High risk patients described as patient with baseline risk > 5% for MACE.
  - Patients with elevated NT proBNP (≥300mg/L)
  - Patients older or equal to 65
  - Patients between 45 and 65 with significant cardiovascular disease.
  - If no NT proBNP, those patients with Revised cardiac risk index of ≥1

- Recommend conducting daily troponin testing till 72 hours post operatively

Treatment

Early identification is key to appropriate management.

Simple therapeutic interventions could improve outcomes in MINS. The optimal management strategy for diagnosed MINS with or without MI is still mostly unknown due to the lack of data. It should be individualized, considering the mechanism, risk factors, risk of therapy and comorbidities. Multidisciplinary management of these patients are essential. In addition to intensification of therapy, improved monitoring is advised. Hemodynamic support, correction of anaemia, aggressive management of infection and optimizing analgesia are advised to improve myocardial oxygen supply and demand.

Pharmacological interventions

Aspirin and statins seem to be supported in the literature to reduce 30-day mortality.

Other pharmacological interventions include intensification of cardiovascular medications.

Addition of ACE inhibitors, B-Blockers, anti-platelet drugs and statins likely improve outcomes at one year.

Consider oral anticoagulation as soon as bleeding allows.

Oral anticoagulation
Dabigatran in combination with aspirin and statin was found to decrease the following at 16 months

- Vascular mortality
- Non-fatal MI's
- Non – haemorrhagic stroke
- Peripheral arterial thrombosis
- Amputation
- Symptomatic venous thromboembolism

With no difference of life threatening-, major organ bleeding

Low-dose rivaroxaban can be consider in the following

- After acute coronary syndrome
    - Additional benefit when added to dual antiplatelet therapy
- In stable coronary artery disease
    - In addition to aspirin has shown to provide some benefit

Dosing
Atorvastatin
80mg (40mg for those who cannot tolerate higher doses)
Aspirin
81-325mg dly (When bleeding risk minimal)
On discharge Aspirin changed to 75-100mg

Individual conditions

ST elevation MI
Usual STEMI care advised

- Revascularization
    - Urgent Percutaneous coronary intervention usually conducted; thrombolytic therapy usually contra-indicated since they are post-operative
- Aspirin and statin therapy
- Dual antiplatelet therapy started as soon as stent placed
- $P2Y_{12}$ receptor blocker usually started
- (Some have advised starting a $P2Y_{12}$ even if no reperfusion done)

Non-ST elevation MI

- Start aspirin and statin
- Initiate B-Blocker therapy when hemodynamically stable
    - Significant variation has been noted between experts – some suggest only to be given per specific indication where others start it for all patients with Non-STEMI
- If patient hemodynamically unstable with recurrent ischaemia
    - Coronary angiography advised
- If hemodynamically unstable without signs of recurrent ischaemia
    - Risk stratification suggested
        - Non-invasive testing
        - Coronary angiography if it is felt that coronary anatomy will influence decision making

Myocardial injury without MI

- Start aspirin and statin
- Initiating B-Blockers should be individualized
- Cardiac medicine intensification might provide 12-month survival without major cardiac event.
    - aspirin, statin, ACE inhibitor, B-blocker
- Consider starting Dabigatran (when bleeding risk deemed to be minimal)
- Dual antiplatelet therapy not advised
    - Since it is unlikely due to plaque rupture
- Risk stratification is advised when patient is stable.

Prognosis

General population

Comparing type 1 and type 2 myocardial infarction:

In the general population type 2 myocardial infarction and injury is associated with worse outcomes, with up to a third of patients dying at one year. Stein et al found the risk of death between type 1 and type 2 myocardial infarction at 30 days to be 4.9% vs 13.6%, and at one year 8.6% vs 23.9% respectively. Another study by El-Haddad reported mortality to 6.9 times greater in type 2 myocardial infarction.

Comparing myocardial infarction to myocardial injury:

Myocardial injury has a greater risk for mortality at 3.9 year follow up than type 1 myocardial infarction. When comparing myocardial injury to type 2 myocardial infarction outcomes seem equally poor.

It is clinically important to differentiate between type 2 myocardial infarction and injury. Type 2 myocardial infarction is twice as likely to develop type 1 myocardial infarction within a year.

After non-cardiac surgery

MINS carry a significant risk with studies showing 30-day mortality as high as 10%. In addition, 25% of MINS patients develop major cardiovascular complications for instance congestive cardiac failure, non-fatal cardiac arrest and stroke.

Independent factors identified to increase risk in MINS population group are
- Age > 75
- ST – elevation or new LBBB
- Anterior ischaemic changes on ECG

Short- and long-term mortality and is increased in myocardial injury as well as ischaemia.

Increased incidence of long-term risks
- Increased non-fatal cardiac ischaemia
- Increased non-fatal cardiac arrest
- Heart failure
- Rehospitalization within 30 days
- Coronary artery disease requiring revisualization

When comparing mortality of MINS vs non-MINS

30 Day mortality
- 8.9% for those with MINS
- 1.5% for those patients without
- Importantly no difference was noted between isolated troponin elevation and Myocardial infarctions.

Mortality rates for specific hs-TnT levels as compared to less than ≤5ng/l
- 20-65 3%
- 65 – 1000 9.1%
- ≥1000 29.6%

Long term mortality
- One-year mortality was found to be at 22.5% with MINS as compared to 9.3% for those without.

References on request

Notes

ERAS – Enhanced Recovery After Surgery

Dr Matthew Gibbs

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Introduction

Enhanced Recovery after surgery is a multimodal, multidisciplinary approach of caring for a surgical patient. It involves teamwork between, surgeons, anaesthetists, nursing staff, an ERAS coordinator as well as physical therapy, amongst others. ERAS is evidence based, aimed at improving outcomes at a reduced cost and relies on a quality-improvement cycle with regular audits to achieve the goals of the program.[1]

Background

The ERAS protocol was initially developed by a group of surgeons in Europe in 2001 when they formed the ERAS study group. Much of the early work was performed by Kehlet, and although the term *fast-track surgery* had been used, the key emphasis was on the quality, not speed, of recovery. The concept relies on a multidisciplinary team working together for the patient, a multimodal approach to resolving issues that delay recovery and cause complications, and a continuous improvement in practice due to repeated and interactive audit. The approach is now used in multiple surgical specialities, with protocols now published for colonic, gastric and rectal resection, bariatric, liver resection obstetrics, urological, breast reconstruction and pancreaticoduodenectomy, amongst others. Data suggest that ERAS programs can reduce complications by 10 – 20%, with decreased length of stay, and a metanalysis of randomised control trials of colorectal enhanced recovery programs showed reduced nonsurgical complications, morbidity and shortened hospital stay.[2]

Stress response to surgery

ERAS seeks to minimise the effects of trauma and surgery on the patient and subsequent recovery. Surgery and trauma induce complex metabolic, hormonal, haematological and immunological responses in the body and results in activation of the sympathetic nervous system (SNS). Briefly, with the release of interleukin IL-6 and tumour necrosis factor (TNF), alpha-1 adrenoreceptor activation, and the release of multiple hormones, the body is prepared for flight or fight response.[3]

Stress response summary		**Results in:**
Hormones Increased	ACTH Cortisol	Cortisol secretion Anti-inflammatory, peripheral insulin resistance, Hyperglycaemia, , stimulates hepatic glycogen synthesis effects
	Growth hormone, IGF-1,	Inc. GH proportional to severity of injury – protein synthesis, inhibition of protein breakdown: protective mechanism via IGF-1
	ADH Glucagon	Salt/water retention Increased glycogenolysis in liver and muscle Increased lactate concentrations, mobilisation of free fatty acids
Hormones reduced/inappropriately low	Insulin	Do not respond appropriately to hyperglycaemia Insulin resistance in peripheral tissue

Mobilisation of substrates	Glycogenolysis Skeletal muscle breakdown Formation of acute phase proteins Lipolysis	Due to sympathetic nervous system stimulation – alpha-1and beta adrenoreceptor stimulation with increased cardiac contractility, heart rate, metabolic effects
Reduced ability to respond to and control hyperglycaemia	Severity of hyperglycaemia proportional to severity of insult	Utilisation of alternative compounds e.g. ketone bodies, as energy substrates
Haematological **Immunosuppression**	Hypercoagulability Fibrinolysis Leucocytosis Lymphocytosis Due to cortisol secretion	Increased risk VTE Increased risk infection

Potentially harmful effects

- Increased myocardial oxygen demand
- Hypoxaemia
- Splanchnic vasoconstriction (NB: anastomoses)
- Dec. energy , catabolism lean muscle mass
- Impaired wound healing
- Sodium and water retention
- Hypercoagulability

ERAS aims to mitigate this by reducing or pre-empting the metabolic stresses that occur: i.e. preoperative nutritional support for the malnourished patient, carbohydrate loading to minimise postoperative insulin resistance, regional anaesthesia to reduce the endocrine stress response, early feeding to secure energy intake and optimal pain control to avoid stress and insulin resistance

Role-players

These include the patients (via smoking cessation, reduced alcohol consumption and co-operation with optimised medical management, surgeons (via, selection of patients, appropriate surgical options and incisions), anaesthetists (multiple interventions), dedicated nurses, physiotherapists and hospital managers and administrators.

A major difficulty that faces the care of the surgical patient lies during the journey the patient makes through the surgical process: from outpatient clinic, operating room, postoperative recovery and the ward, each with its own set of protocols, personnel and focal areas. The key is team-work and a dedicated co-ordinator. The table below contains the twenty four core elements of ERAS, each with varying amount of evidence. Please refer to the guidelines from the ERAS society for further details – they can be downloaded freely off the website below.

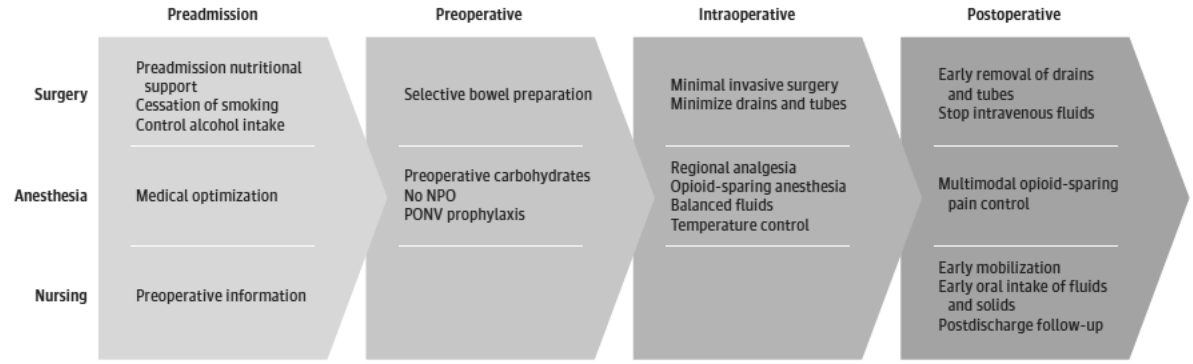
(Source: http://www.erassociety.org)

ERAS Society Guideline Elements for Colonic Resections	
Preadmission - Elements	**Target effect/rationale**
Cessation of smoking and excessive intake of alcohol	Reduce Complications
Preoperative nutritional screening and, as needed, assessment and nutritional support	Reduce Complications
Medical optimization of chronic disease	Reduce Complications
Preoperative	
Structured preoperative information and engagement of the patient and relatives or caretakers	Reduce anxiety, involve the patient to improve compliance with protocol
Preoperative carbohydrate drink	Reduce insulin resistance, improve well-being, possibly faster recovery
Preoperative prophylaxis against infection	Reduce infection rates

Prophylaxis against nausea and vomiting	Minimise nausea and vomiting
Preoperative prophylaxis against thrombosis	Reduce thromboembolic complications
Intraoperative	
Minimal invasive surgical recovery, reduce pain	Reduce complications, faster techniques
Standardized anaesthesia, avoiding long-acting opioids	Avoid or reduce postoperative ileus
Maintaining fluid balance to avoid over- or underhydration, administer vasopressors to support blood pressure control	Reduce complications, reduce postoperative ileus
Epidural anaesthesia for open surgery	Reduce stress response and insulin resistance, basic postoperative pain management
Restrictive use of surgical site drains	Support mobilization, reduce pain and discomfort, no proven benefit of use
Removal of nasogastric tubes before reversal of anaesthesia	Reduce the risk of pneumonia, support oral intake of solids
Control of body temperature using warm air flow blankets and warmed intravenous infusions	Reduce complications
Postoperative	
Early mobilization (day of surgery)	Support return to normal movement
Early intake of oral fluids and solids (offered the day of surgery)	Support energy and protein supply, reduce starvation-induced insulin resistance
Early removal of urinary catheters and intravenous fluids (morning after surgery)	Support ambulation and mobilization
Use of chewing gums and laxatives and peripheral opioid-blocking agents (when using opioids)	Support return of gut function
Intake of protein and energy-rich nutritional supplements	Increase energy and protein intake in addition to normal food
Multimodal approach to opioid-sparing pain control	Pain control reduces insulin resistance, supports mobilization
Multimodal approach to control of nausea and vomiting	Minimize postoperative nausea and vomiting and support energy and protein intake
Prepare for early discharge	Avoid unnecessary delays in discharge
Audit of outcomes and process in a multi-professional, multidisciplinary team on a regular basis	Control of practice (a key to improve outcomes)

Figure 1 illustrates a typical overview flowchart:

Figure 1



It is beyond the remit of these brief notes to detail the evidence base for each step or aspect of the ERAS program. Some important aspects follow.

Preadmission

The focus here is on correcting anaemia, managing diabetes, controlling blood pressure and other chronic medical problems. Smoking cessation and advice on alcohol consumption also play a major role. It is important to fully inform the patient about expectations post-surgery, including early mobilisation, breathing exercises, pain control and to give them joint responsibility for recovery and adherence to the ERAS pathway. Print pamphlets may be helpful.

Preoperative

Features include admission on the day of surgery, bowel preparation avoidance, avoiding prolonged fasting, carbohydrate drinks (usually day before and morning of surgery), avoiding sedative premedication. Early return of bowel function is key, particularly in colo-rectal ERAS programs, and the above measures together with appropriate post-operative nausea and vomiting prophylaxis and analgesia options aim to reduce the incidence of postoperative ileus. Randomised control trials show no benefit from bowel preparation in colorectal surgery, with mixed data for anastomotic leak.

The pre-operative carbohydrate (CHO) drinks aim to minimize the protein catabolism, negative nitrogen balance and insulin resistance, to maintain lean muscle mass. These are usually oral complex CHOs like maltodextrin with a high concentration (12.5%), with 100g (800ml) administered the night before surgery and 50g (400ml) two to three hours prior to surgery.[4] Faster surgical recovery and improved well-being has not been shown however.

Intraoperative

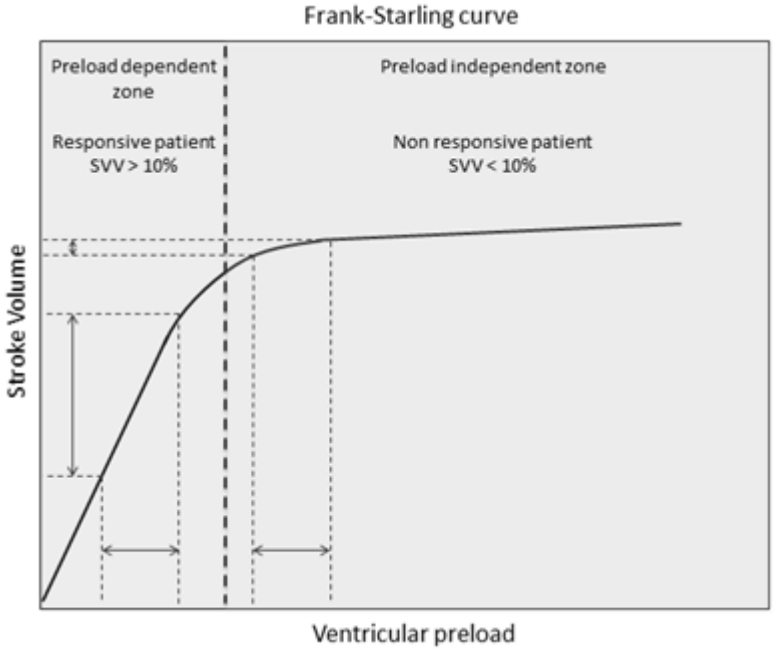
Each patient should be managed individually, with standardised anaesthetic techniques and minimally invasive techniques where possible. Laparoscopic colonic resection results in decreased length-of-stay, decreased initial wound complications and time to return of bowel function. If open techniques are required, transverse incisions are preferred to reduce post-operative pain. Naso-gastric tubes are associated with increased morbidity and delayed return of bowel function and should be therefore be avoided in elective surgeries and certainly removed before discharge to the ward. There is also no benefit to routine wound drainage for most types of colonic surgery. Aggressive post-operative nausea and vomiting prophylaxis is advised, with all patients with one to two risk factors receiving at least two anti-emetics. Opioid-sparing strategies are strongly encouraged.

Fluids

ERAS programs also aim to minimise fluid shifts. Too little fluid can cause a reduction in perfusion and organ dysfunction, especially in combination with the vasodilatory effects of anaesthetics agents and neuraxial anaesthesia. Maintenance of euvolaemia, cardiac output (CO) and the delivery of oxygen and nutrients to vital tissues are imperative. Fluid excess on the other hand may result in decreased stroke volume, cardiac index and inadequate tissue perfusion, with oedema, especially of gut anastomoses, and increased complications. Every litre of excess fluid has been shown to increase length of stay by one day and complications by 32%.

The question really remains ‘which patients are fluid responsive?’ And what does fluid responsive actually mean? The understanding is that an increase in Left Ventricular end diastolic volume (i.e. preload) will result in an increased stroke volume.[5] Static markers such as CVP have long since been debunked, and that neither pressure nor volume markers of cardiac preload can predict fluid responsiveness. A dynamic approach is now advised: as demonstrated in Figure 2, if a patient remains on the steep portion of the Frank-Starling curve, any respiratory variation in stroke volume will be exaggerated (i.e. Stroke Volume Variation) and surrogates thereof, such as Pulse Pressure Variation and Systolic Pressure Variation. The only other measure that has a similar rigorous evidence base is passive leg-raising. The end-expiratory occlusion test or ‘mini’ fluid challenge may also have predictive value.

Figure 2



When using goal-directed fluid therapy, accurate measurements are imperative. Minimally invasive monitoring includes Lidco, Vigileo and CardioQ oesophageal doppler. The OPTIMISE trial by Pearse et al included 734 high risk patients over the age of 50 undergoing major GIT surgery.[6] Patients were randomly assigned to a CO guided (LidCO) haemodynamic algorithm for IV fluids and inotropes (dopexamine) or the usual care. There was no reduction in mortality or secondary measures but when added to an updated meta-analysis of 38 trials, there were fewer complications (relative risk RR 0.77), decreased mortality (but non-significant) and decreased LOS. Other systematic reviews have shown a decrease in renal failure, respiratory complications and wound infections, with 13 out of 100 patients treated expected to avoid complications.

Figure 3 below illustrates the normovolaemic aims of ERAS programs.

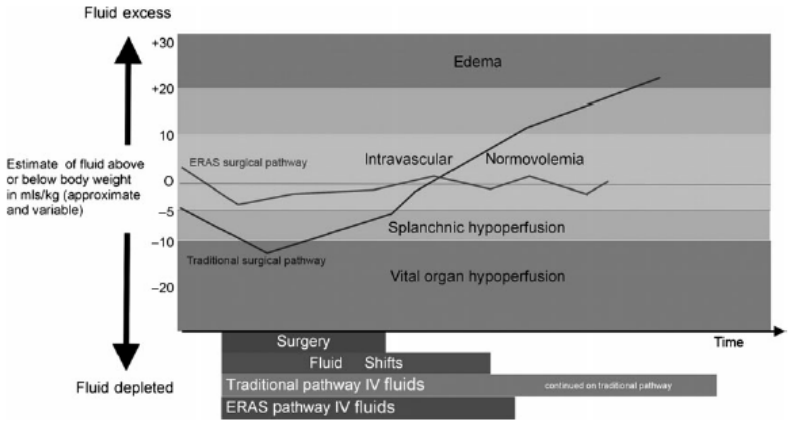


Fig. 2. Perioperative fluid administration with and without an ERAS surgical pathway: risk of perioperative fluid excess and tissue hypoperfusion.[104] Reproduced from Minto G et al. with permission.

Acta Anaesthesiologica Scandinavica **59** (2015) 1212–1231

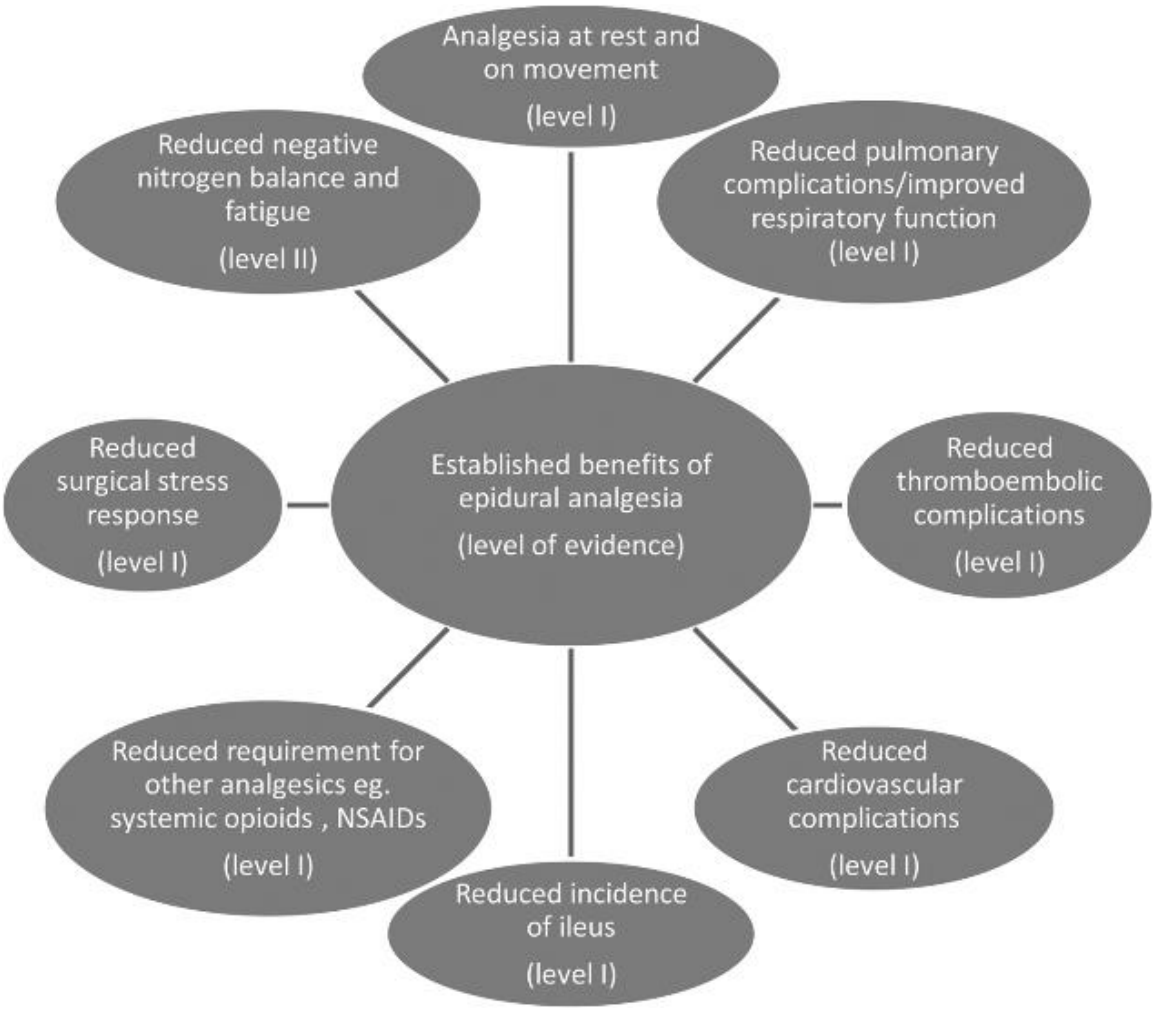
One of the key findings of the multicenter Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery (RELIEF) trial was that patients in the restrictive fluid group had a significantly higher risk of acute kidney injury than those in the liberal fluid group (8.6% vs. 5%, $P < 0.001$).[7] The median duration of surgery was 3.3 h in both groups, and the restrictive regimen led to a median of 1.7 l of fluid administered intraoperatively, compared with 3 l with the liberal regimen. This study used goal-directed fluid therapy to titrate fluids, using appropriate dynamic fluid responsiveness measures like minimally- invasive cardiac output monitoring. There is therefore the implication that many anaesthetists have become too restrictive in the desire to aim for ‘zero-balance’. The authors recommend a crystalloid infusion of 10 – 12 ml/kg/hr during major abdominal surgery.

In contrast the ERAS consensus statement for anaesthetic practice recommends a basal infusion rate of 3-5 ml/kg/hr. It appears that the so-called 'sweet spot' of fluid therapy has yet to be found, and the wise clinician will use all the information at his disposal to direct fluids appropriately in the individual patient, depending on what procedure is being performed or what monitoring is available. An excellent clinical review has been written by Miller in Anesthesiology.[8]

Neuraxial

The standard of care is multimodal, evidence-based and procedure-specific analgesic regimens, aiming to optimise analgesia (and suppressing multi-systemic effects of uncontrolled pain) with minimal side effects, but also allowing early mobilisation and oral feeding.

Thoracic or high lumbar epidural analgesia (TEA) remains the gold standard for post-operative pain control in open abdominal surgery. It is unclear if it improves postoperative outcomes, although impacts cardiovascular and respiratory complications, provides better static and dynamic analgesia for the first 72 hours. However, the associated hypotension, urinary retention and motor blockade are common and troublesome side effects. The benefits of TEA are summarized below.



Truncal blocks like quadratus lumborum, transversus abdominis plane and rectus sheath blocks are associated with decreased opioid consumption with significant analgesia and avoid some of the issues associated with TEA. Intrathecal morphine has a moderate recommendation grade for laparoscopic abdominal surgery. No matter what analgesic regimen, multimodal analgesia including intravenous paracetamol should be used. Non-steroidal anti-inflammatory drugs (NSAIDs) do have role to play, but concern has been raised over the risk of anastomotic leaks. Large randomised control trials are needed to confirm this concern. The gabapentinoids (e.g. pregabalin) have growing role to play, as they too have a beneficial opioid sparing effect.

Other intraoperative goals

Glucose concentrations should be kept as close as possible to normal without compromising safety, and a strong recommendation is to maintain intraoperative normothermia with active warming devices. It is unclear at present whether high concentrations of oxygen protect against the risk of surgical site infections, so current recommendations are to use the lowest concentration of oxygen necessary to produce normal arterial oxygen levels and saturations. Brief periods of hyperoxia are advised at induction to prevent hypoxia if complications arise.

Postoperative phase

Once in the postoperative phase, patients should be encouraged to return to normal activities via early oral nutrition and hydration, early mobilisation with criteria-based rather than time-based discharge criteria. The aim is to reduce skeletal muscle loss and improve respiratory function. Drains and urinary catheters should be removed as early as possible, and excessive opioids should be avoided because of sedation, ileus and respiratory depression. Finally, the ERAS program requires regular audit and regular reviews to ensure compliance with all aspects of the pathway. Appropriate interventions can be then to address the particular needs of the program. Gustafsson demonstrated a 42% decrease in 5-year cancer specific death in patients with >70% adherence to ERAS interventions.[9] Independent predictors of increased survival included avoidance of intravenous fluid overloading and oral intake on the day of operation.

Of course, the financial effects of such a program should also be considered, with the state health care service in Alberta, Canada able to reduce complications by 11% with 8% fewer readmissions and savings of $2800 - $5900 per patient. ERAS pathways can be a key strategy in addressing the issues faced by publicly funded health care systems facing limited funding, increased patient expectations and growing populations.

References

1. Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery. *JAMA Surg* [Internet] 2017; **152**: 292 Available from: http://archsurg.jamanetwork.com/article.aspx?doi=10.1001/jamasurg.2016.4952
2. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. Enhanced Recovery Program in Colorectal Surgery: A Meta-analysis of Randomized Controlled Trials. *World J Surg* [Internet] 2014; **38**: 1531–41 Available from: http://link.springer.com/10.1007/s00268-013-2416-8
3. Matthews C. Enhanced Recovery After Surgery (ERAS). *Anaesth Tutor Week* 2010; **204**: 1–9
4. Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: Consensus statement for anaesthesia practice. Acta Anaesthesiol. Scand. 2016.
5. Guerin L, Monnet X, Teboul J-L. Monitoring volume and fluid responsiveness: from static to dynamic indicators. *Best Pract Res Clin Anaesthesiol* [Internet] Elsevier Ltd; 2013 [cited 2014 Jun 17]; **27**: 177–85 Available from: http://www.ncbi.nlm.nih.gov/pubmed/24012230
6. Pearse RM, Harrison DA, MacDonald N, et al. Effect of a Perioperative, Cardiac Output–Guided Hemodynamic Therapy Algorithm on Outcomes Following Major Gastrointestinal Surgery. *Jama* [Internet] 2014; **311**: 2181 Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2014.5305
7. Myles PS, Bellomo R, Corcoran T, et al. Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery. *N Engl J Med* [Internet] 2018; **378**: 2263–74 Available from: http://www.nejm.org/doi/10.1056/NEJMoa1801601
8. Miller TE, Myles PS. Perioperative Fluid Therapy for Major Surgery. *Anesthesiology* [Internet] 2019; 1 Available from: http://insights.ovid.com/crossref?an=00000542-900000000-96668
9. Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O. Adherence to the ERAS protocol is Associated with 5-Year Survival After Colorectal Cancer Surgery: A Retrospective Cohort Study. *World J Surg* [Internet] 2016; **40**: 1741–7 Available from: http://link.springer.com/10.1007/s00268-016-3460-y

Difficult Obstetric Scenarios
Anaesthetic and Perioperative Management of Severe Preeclampsia

Professor Robert Dyer

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Obstetric practices in preeclampsia are well established. Prompt control of hypertension, fluid restriction, seizure prophylaxis in high-risk groups, and expedited delivery in the presence of severe maternal disease features or fetal compromise, are the core principles.

The establishment of safe regional anaesthesia (RA) for labour and caesarean delivery in preeclampsia is one of the most important developments in the past 25 years in obstetric anaesthesia. Neuraxial anaesthesia offers advantages in preeclampsia in terms of control of hypertension and simplicity of airway management. The indications for general anaesthesia (GA) for caesarean section in preeclamptic women with preserved ejection fraction are eclampsia with altered mentation, coagulopathy, and thrombocytopaenia. Although new evidence is sparse, in HELLP syndrome most anaesthesiologists adhere to an early report which showed that thromboelastographic maximum amplitude decreased once platelet numbers dropped below $75 \times 10^9.L^{-1}$ Abruptio placentae without maternal haemodynamic compromise or cardiotocograph abnormality is not a contraindication to RA. GA introduces problems of difficult tracheal intubation, and the hypertensive response. Therefore, ideal modern management for preeclamptics is early establishment of epidural analgesia in labour, and spinal anaesthesia for caesarean delivery in cases in whom an epidural catheter has not been sited. However, many units around the world still provide routine general anaesthesia.

Only one randomised study has examined fetal acid base status in spinal versus general anaesthesia. The umbilical arterial base deficit was significantly higher in the former group. More of the study vasopressor ephedrine was used in the spinal anaesthesia group, but the median dose pre-delivery was zero. Modern practice employing phenylephrine for closer control of blood pressure would probably eliminate these differences.

Several published observational case series describe anaesthesia in eclampsia. Unless the usual contraindications to regional anaesthesia apply, spinal anaesthesia for caesarean delivery is the method of choice in patients in whom Glasgow Coma Scale (GCS)(79) is ≥ 14, antihypertensive and magnesium sulphate therapy has been administered, and cardiac failure is absent. This includes those in whom a difficult tracheal intubation is anticipated. Patients with persistent decreased level of consciousness who require emergency delivery should receive a general anaesthetic. The occurrence of a seizure during caesarean section in a patient with preeclampsia or eclampsia is very rare, but practitioners should be prepared.

Regional anaesthesia strategies

Concerns about hypotension due to regional anaesthesia in uncomplicated preeclampsia with severe features were based upon the perceived contracted intravascular volume. These have been unfounded, and are the subject of an insightful editorial. Ideally, epidural or combined spinal-epidural (CSE) anaesthesia should be initiated early in labour, allowing extension for operative delivery in urgent cases. CSE has no clear benefits in preeclampsia. If an epidural catheter has not been placed, intrathecal anaesthesia with a small-bore atraumatic needle is appropriate. The ED50 for the spinal component of CSE was found to be similar in normotensive women and those with severe preeclampsia. In early-onset severe preeclampsia where the fetus is small for gestational age, it may be advisable to increase the spinal dose of bupivacaine, particularly in view of the low risk of hypotension.

Control of spinal hypotension

It is well established that spinal hypotension is less severe in preeclampsia, probably as a consequence of the ino-vasoconstrictor state. Spinal anaesthesia induces modest afterload reduction. In preeclampsia, the well preserved or increased inotropy will usually result in effective compensation for vasodilatation. Should significant hypotension occur, this probably points to the absence of severe features of preeclampsia, or the presence of undiagnosed haemorrhage, cardiac failure, or concomitant valvular stenosis. Spinal hypotension is unlikely to be clinically significantly worse than hypotension associated with epidural anaesthesia. Oxytocin causes acute hypotension and should be administered slowly, in small doses. Myocardial infarction has been reported with ergometrine, which should be avoided.

In healthy parturients there is disruption of the endothelial glycocalyx by fluid loading prior to spinal anaesthesia, which may reduce its effectiveness. Recent work demonstrates reduced mRNA transcription resulting in an altered glycocalyx structure in preeclampsia. This correlated with maternal hypertension and neonatal birth weight. Should these changes also be reflected in the pulmonary endothelial glycocalyx, this would give further credence to restrictive fluid management strategies, and preferential use of vasopressors in managing spinal hypotension in preeclampsia.

Preeclamptic patients require less vasopressor for control of spinal hypotension. A randomised trial has shown that phenylephrine 50 µg is more effective than ephedrine 15 mg in restoring systemic vascular resistance after spinal hypotension. Phenylephrine reverses the reduction in systemic vascular resistance induced by spinal anaesthesia, and may be superior to ephedrine for the management of acute spinal hypotension in the absence of systolic heart failure. A further randomised trial has shown that choice of vasopressor does not influence fetal acid-base status in caesarean delivery for a non-reassuring fetal heart trace.

General anaesthesia strategies

Airway management in preeclampsia
The increased incidence of difficult or failed tracheal intubation in obstetric GA is well established. A recent review found that the incidence has not changed significantly from 1970 to the present, remaining at approximately 1 in 440 cases of GA for caesarean section. Some suggest supraglottic airways (SGAs) are safe for elective general anaesthesia for caesarean section. However, this is controversial, particularly in the presence of comorbid disease in pregnancy, and where delivery is urgent and fasting status of concern. Most anaesthesiologists perform endotracheal intubation with rapid sequence induction.

The use of video laryngoscopes in obstetrics has been well summarised. In light of the potential airway swelling in preeclampsia, a channelled laryngoscope such as the KingVision, Pentax AWS or Airtraq may improve the glottic view and ease of guidance of the endotracheal tube.

Where tracheal intubation is not rapidly achieved, the immediate use of a SGA with provision for gastric drainage is essential to allow ongoing oxygenation, as suggested by the guidelines published by the Obstetric Anaesthetists Association (OAA) and Difficult Airway Society (DAS). The selection of an SGA in preeclampsia should take into account the reduction in oropharyngeal cavity dimensions due to oedema or a bitten tongue. The OAA-DAS guidelines include a useful decision matrix to assess whether to wake the patient, or continue the surgery using the SGA. In preeclampsia, where maternal or fetal factors lend urgency to delivery, it will frequently be more desirable to proceed.

Preoxygenation and apnoeic oxygenation
The physiological basis for preoxygenation is well established. Strategies to maintain oxygenation during the apnoeic period of airway management are gaining traction. This is of particular importance in patients with compromised physiological reserves due to increased oxygen consumption (VO_2) in the face of decreased functional residual capacity (FRC), and possible frank or subclinical pulmonary oedema, both of which occur in preeclampsia. Apnoeic mass movement oxygenation (AMMO) using dedicated high flow nasal cannulas to deliver warmed, humidified oxygen is an emerging strategy in this patient population. In the absence of dedicated equipment, high-flow oxygen through standard nasal cannulas may be advantageous.

Obstetric rapid sequence induction
In hypertensive patients with well-preserved ventricular function, tracheal intubation response should be pharmacologically obtunded. A recent narrative review discusses the pharmacology, efficacy, side-effects, and therapeutic range of beta-blockers, opiates, vasodilators and magnesium sulphate used for this purpose. None of these agents are problem-free; maternal beta-blockade may be associated with fetal bradycardia or hypoglycaemia, nitrates may cause precipitous hypotension in volume-depleted patients, hydralazine has a delayed onset time and a prolonged effect, and remifentanil may be associated with respiratory depression in the premature neonate. The authors of the review recommend that bolus magnesium sulphate should be avoided for this purpose, but subsequent correspondence makes strong pharmacokinetic and clinical arguments for its continued use. Preeclamptic women with clinically significant antepartum haemorrhage, or severe heart failure with low ejection fraction, require careful titration of pharmacological agents during induction of general anaesthesia.

Recent airway guidelines discuss the use of sugammadex for reversal of neuromuscular blockade when rocuronium has been used for rapid sequence induction. Magnesium is known to potentiate the effects of rocuronium. Studies in non-pregnant populations showed that peri-induction administration

of 40-60 mg.kg^{-1} of magnesium sulphate did not delay reversal of blockade with sugammadex. There were no cases of recurarisation. These studies do not address the preeclamptic patient who has had magnesium loading doses or continuous infusions, but several case reports of use in preeclampsia with severe features support the contention that magnesium does not influence reversal with sugammadex.

Analgesic strategies

Multimodal analgesia should be employed as in healthy patients. Epidural administration of local anaesthetic agents throughout the labour and delivery process remains a core analgesic strategy. Where epidural is contraindicated, patient-controlled analgesia with intravenous remifentanil has been described in preeclampsia. Non-steroidal analgesics should be avoided in preeclamptic patients with risk of coagulopathy or renal impairment. Of specific interest, a recent retrospective study on pain experience in preeclamptic women after caesarean section showed decreased analgesic requirements.

Haemodynamic monitoring for delivery and critical care

Non-invasive blood pressure monitoring is appropriate in uncomplicated severe preeclampsia. Automated devices may underestimate blood pressure in preeclampsia, necessitating mercury sphygmomanometry. One semi-automated device has recently been found to be sufficiently accurate. Intra-arterial monitoring is warranted in poorly controlled hypertension, haemorrhage, renal failure, and pulmonary oedema. Transoesophageal echocardiography is valuable in the rare event of severe heart failure during caesarean delivery.

Fluid management remains controversial, in the light of a potentially disturbed pulmonary endothelial glycocalyx, and renal glomerulo-endotheliosis. An early meta-analysis found insufficient evidence for reliable estimates of the effect of plasma volume expansion in preeclampsia. In view of the heterogeneity of the disease, best practice is adherence to fluid restriction as recommended by the RCOG guidelines, unless goal-directed fluid administration can be practiced in the individual case. Patients with cardiorespiratory failure, coagulopathy or sepsis should be managed in a critical care unit.

Early recommendations of the American College of Obstetricians and Gynecologists were that the pulmonary artery catheter (PAC) be used to direct fluid management in preeclampsia complicated by pulmonary oedema and/or renal failure. However, pulmonary oedema is probably multifactorial in origin in this condition, arising from a combination of iatrogenic fluid overload, severe diastolic dysfunction, increased pulmonary capillary permeability, hypoalbuminaemia, and occasionally severe systolic dysfunction. Widely varying left ventricular compliance leads to a poor correlation between pulmonary capillary wedge pressure and left ventricular end-diastolic volume. More functional information can be obtained from POC echocardiography. A recent review could not identify any randomised trials evaluating the use of the PAC in fluid management in preeclampsia. The use of a PAC should probably be restricted to the patient with severe multiple organ failure, or in the occasional case in whom there is an acute life-threatening complication when preeclampsia is superimposed upon underlying congenital or valvular heart disease.

Fluid management after significant haemorrhage may best be guided by the clinical status, including passive leg raising in combination with an intra-arterial line, and TTE, if available. For cardiac output monitoring, the LiDCO monitor, which employs pulse waveform analysis, has shown acceptable limits of agreement with the PAC.

Anaesthesia for preeclampsia requires an astute assessment of the pathophysiology in the individual case, and whenever possible, the use of regional anaesthesia for labour and caesarean section. Critically ill patients may require general anaesthesia with careful attention to volume and coagulation status, technique for tracheal intubation, assessment and management of cardiac function, and postoperative critical care.

Reference

Hofmeyr R, Matjila M, Dyer RA. Preeclampsia in 2017: Obstetric and Anaesthesia Management. Best Practice and Research Clinical Anaesthesiology 2017; 31: 125 – 138.

Major Obstetric Haemorrhage
Implications for anaesthesia

Dr Rowan Duys

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Justification

In the seventh Saving Mother's Report of the National Committee on Confidential Enquiries into Maternal Deaths (NCCEMD) for the triennial 2014-2016,[1] obstetric haemorrhage was the third most common cause of maternal death accounting for the loss of 624 mothers and contributing 16,9% of all deaths. The NCCEMD reports that a lack of trained doctors and nurses contributed to 50% of these deaths. When the impact on the patient, her children and family, and society as a whole is weighed[2] against the assessment that >85% of these deaths are considered preventable, the scale and urgency of the problem is evident.

The maternal mortality rate in the UK is 9/100 000 live births, and in South Africa it is 134/100 000. 15 times higher, people! That's just crazy. But the institutional maternal mortality rate for mothers who undergo caesarean delivery is even higher, and 3 times as high as those mothers who deliver vaginally.[1]

The picture across the African continent is even more bleak. The mortality rate following caesarean delivery in the ASOS Trial Obstetric sub-study was 50 times higher than the average for high income countries.[3]

The South African data also suggests that deaths due to haemorrhage occur very quickly after the onset of bleeding, and the patients do not survive referral. This necessitates definitive care at the place where the bleeding occurs, which is frequently level one.[1,4]

We have a long way to go. And it's not rocket science. It's about finding ways to deliver what we know is 'safe care', in our resource-constrained environment. And about educating the public about accessing healthcare appropriately. (Delayed healthcare seeking behaviour may contribute to about a third of deaths, but this is a conversation for another time)

I hope this reference note helps guide your learning, but that the figures above also inspire you to invest in the people you train, and the systems you work in, in order to prevent more moms from dying.

I won't do a better job of summarising current thinking on obstetric haemorrhage than Prof Dyer did in his 2014 SAJAA article.[5] Please read it.

Risk of haemorrhage

Identifying the 'at risk' patient is the first step in preventing and treating obstetric haemorrhage. The risk factors are multiple but Dyer suggests the following matrix:

- Tone (uterine atony or inflammation),
- Tissue (placental complications),
- Trauma (physical injury or previous trauma),
- Thrombin (congenital, or more commonly, acquired coagulation abnormalities).[5]

For many obstetric conditions associated with haemorrhage such as uterine atony or evolving placental abruption, the anaesthesia team must respond to the clinical scenario. There is little planning or prevention that can be performed. However with placenta praevia and placenta accreta spectrum, a certain amount of pre-operative decision making may be required.

Placenta Praevia

Placenta Praevia occurs when the placenta lies within the lower segment. It is traditionally a diagnosis made by transabdominal ultrasound scan, but transvaginal scans are now able to more clearly define the relation of the lower edge of the placenta to the internal os of the cervix. To refresh your memory:

	Grade	Description
Placenta Praevia Minor	Grade 1	Within the lower segment
	Grade 2	Touching the internal os
Placenta Praevia Major	Grade 3	Partially covering the internal os
	Grade 4	Completely covering the internal os

Previous caesarean delivery increases the risk of placenta praevia. Thus with rising prevalence of caesarean delivery, rates of placenta praevia are increasing. Other risk factors include prior pregnancy termination, intrauterine surgery, smoking, multifetal gestation, increasing parity, and maternal age

Vaginal delivery is considered possible if the lower edge of the placenta is more than 2cm from the internal os. If closer, patients should be delivered by C/S.

Accreta spectrum

Placenta accreta spectrum is defined as abnormal trophoblast invasion of part or all of the placenta into the myometrium of the uterine wall[6] and the spectrum includes placenta accreta where trophoblastic attachment to the myometrium occurs without intervening decidua, placenta increta where trophoblast invades the myometrium and, placenta percreta where it invades through the myometrium beyond the serosa and into surrounding structures such as the bladder.[7]

Placenta accreta spectrum is more common in placenta praevia, but the major cause of the observed increasing prevalence globally is thought to be increased rates of caesarean delivery. The risk of placenta accreta spectrum rises with each previous caesarean delivery to 3%, 11%, 40%, 61%, and 67% for first, second, third, fourth, and fifth or more caesarean deliveries, respectively.[7]

Placenta accreta spectrum should be sought and excluded in high risk patients, particularly those with placenta praevia and a history of previous caesarean delivery. The mainstay of diagnosis is antenatal ultrasound which some studies suggest demonstrates a very high sensitivity and specificity (>90) with variable importance placed on the need for additional magnetic resonance imaging.[6]

Management decision making

Whatever the diagnosis and potential cause for haemorrhage, we must either make decisions in the **pre-operative period** about how to safely manage patients with potential for major obstetric haemorrhage, or manage patients with **ongoing bleeding**, or care for patients in the **post-operative period** following a large bleed.

I believe the most important or difficult decisions to make are:

- General anaesthesia vs neuraxial blockade
- The use of blood conservation strategies
- How much fluid to transfuse during bleeding
- What type of fluid to transfuse

General Anaesthesia vs Spinal

In the patient that presents to theatre in the midst of a massive post-partum haemorrhage post-vaginal delivery or in an unanticipated post-partum haemorrhage caused by uterine atony at caesarean delivery, there is little controversy that severely shocked patients requiring operative intervention to stop bleeding will end up under general anaesthesia. But it is the patient with an antenatal diagnosis of placenta praevia, at risk of placenta accreta spectrum, presenting for elective caesarean delivery at 36 weeks gestation where decision making around choice of anaesthetic is controversial.

I have not been able to find RCT's pitting general anaesthesia against neuraxial blockade in the presence of abnormal placentation. However some large retrospective analyses do exist suggesting

that a strategy of 'everyone gets a spinal, but some may be converted to general anaesthesia intra-operatively' is acceptable and safe.[8]

This is not our practice. In uncomplicated placenta praevia patients, booked for elective caesarean sections with a history of one or less previous caesarean delivery, and no ultrasound features of placenta accreta spectrum, we would usually consider a neuraxial technique – most commonly single shot spinal. If any other risk factors are present, such as a difficult airway that may make intra-operative conversion to a general anaesthetic difficult, a history of more than one previous caesarean delivery, ongoing bleeding, or pre-operative anaemia, we would strongly consider a general anaesthetic from the outset as it will be easier to control induction, the airway and haemodynamics before surgery begins.

It would also be foolish to make choices about management without an in-depth discussion of the risks with the obstetric and nursing team, and the patient.

Blood conservation strategies

With increasing evidence of the short- and long-term consequences of blood transfusion, strategies to reduce blood loss and transfusion should be considered in the peripartum period:

Treatment of antepartum Iron Deficiency Anaemia
The demand for iron intake is increased during pregnancy because elevated erythrocyte cell mass and expanded plasma volume are required for the developing foetus. The WHO estimates the rate of anaemia (Hb < 11g/dl) in pregnant women to be 38%, with the majority due to iron deficiency.[9]

While oral iron and folate should be prescribed to patients with confirmed iron deficiency anaemia, where they are not well tolerated or do not make an impact, the use of intravenous 'total-dose' iron replacement should be considered. Intravenous iron preparations have become significantly easier to infuse and well tolerated, and the overall cost (approx. R300 per dose), compared to blood transfusion (round R1600 per unit packed cells) and its complications is beginning to make a stronger and stronger argument for more widespread use. Improvements to the Hb can be expected within a few days, with optimal Hb levels reached in 2-6weeks.

While the safety of IV iron infusion is now well established, and its efficacy at improving haemoglobin and reducing red blood cell transfusion rates is also proven,[9] there is no direct evidence yet that it leads to improved mortality outcomes.

Treatment of post-partum anaemia
A small pilot RCT of the use of IV iron vs blood transfusion to treat anaemia in the post-partum period (n = 13 only!) also reports favourable complications profiles and impressive improvements in Hb levels over a sustained period. This is an area for ongoing research and focus.

Cell Salvage
The safety of the use of cell salvage during caesarean delivery is now no-longer considered controversial[10]. Large retrospective analyses[11], and an RCT comparing routine use of cell salvage with usual care in patients deemed 'at high risk' of haemorrhage at caesarean section[12] showed no increased risk of harm although a slight increase in feto-maternal haemorrhage from Rhesus positive babies to their Rhesus negative mothers was noted. The significance of this finding is unclear.

The proposed benefits of cell salvage include reduction of red cell infusions and reduced incidence of coagulopathy, but the RCT by the SALVO group[12] did not show a reduction in transfusion rates and thus recommendation for cell salvage has been removed from the latest Association of Anaesthetists of Great Britain and Ireland guidelines.[13]

Sullivan and Ralph, in their retrospective series of 1170 patients where cell salvage was used routinely for all caesarean sections, report significant improvements in transfusion rates. Their hospital protocol is to wash collected blood with a 'double volume' of saline, as per manufacturer guidelines for cell salvage use in obstetrics, but they no-longer infuse their salvaged blood through a leukocyte depletion filter.[11] However, most other guidelines seem to advocate discarding all suctioned amniotic fluid and blood collected before delivery of the infant, the use of the leukodepleted filter.[10,12,13]

There does not seem to be an association between the transfusion of salvaged blood in obstetrics and 'amniotic fluid embolus' syndrome. In fact, amniotic fluid embolus now seems to be attributed to an anaphylactoid reaction to unknown foetal allergens rather than embolism of foetal squamous cells.[10]

We use cell salvage in obstetric cases with predicted major blood loss in our centre.

Tranexamic Acid
No review of major obstetric haemorrhage would be complete without a review of the results of the WOMAN trial.[14] I recommend these very readable blogs for further analysis:
https://www.thebottomline.org.uk/summaries/icm/woman-trial/
https://broomedocs.com/2017/05/thoughts-woman-trial/

My take is this: a gargantuan effort was executed to perform this RCT in 20 000 patients across 21 countries. The most important data we gain from it is that in the 10 000 women that received tranexamic acid, it appeared safe, although there is some criticism that thromboembolic events were not sought actively. However, while the drug appears safe, its signal for improving outcomes is weak. An absolute risk reduction of 0,4% with a Number Needed to Treat of 267 means that tranexamic acid is probably only going to be making a difference to mortality in a small group of marginal cases. It's safe and relatively cheap, and thus it's hard to justify not using it in the hope that it may make a difference. All our other efforts are likely to make a more important difference to outcome.

How much fluid to transfuse

Decisions around volume of fluid therapy are complex. The purpose of volume therapy, or fluids infused to increase the intravascular volume, must be to increase the delivery of oxygen to the mitochondria of vital organs. There is no intrinsic value in increasing or decreasing intravascular volume. Marik writes eloquently on the subject of fluid responsiveness: "Fundamentally, the only reason to give any patient a fluid challenge is to increase their stroke volume; if this does not happen, the fluid administration serves no useful purpose and is likely to be harmful. Furthermore, the increase in stroke volume (and thus cardiac output) must be judged to be beneficial."[15]

Translating this thinking to the setting of a bleeding obstetric patient means balancing the possible benefit of an increased stroke volume, which may cause an increase in cardiac output, which may increase perfusion, which may increase oxygen delivery to the mitochondria, against the risks of infusion of fluid. The risk of fluid overload and pulmonary oedema, especially in the pre-ecclamptic population, and the adverse effects of fluid therapy on coagulation are paramount. While the dilutional coagulopathy of high dose clear fluid infusion, whether crystalloid or colloid, is established, when lower doses are used, there remains some controversy as to whether they cause hyper- or hypo-coagulable states.[16,17]

Which fluid to infuse

Knowing when to use blood and coagulation products in the bleeding obstetric patient is also tricky. Abiding by conventional haemoglobin transfusion triggers of 6 or 7 g/dl in a patient with ongoing torrential bleeding from a cause like uterine atony that surgeons are unlikely to be able to control quickly, is problematic, in my opinion. *(yes folks, opinion only here)* Equally, the risks of transfusing packed red cells into a patient who has dropped their mean arterial pressures to 55mmHg, and their Hb to 7, but has no evidence of ongoing bleeding, when a single bolus of colloid would suffice, are significant, and a more conservative approach to transfusion in this case would be warranted. (*more opinion!)*

A group from Cardiff relay a compelling journey through multiple studies and quality improvement initiatives that are associated with a reduction in their rates of haemorrhage, rates of transfusion, and improved maternal outcomes.[18] They suggest the mainstay of their approach to be:
1. Risk assessment of all women for post-partum haemorrhage
2. Measurement (rather than estimation) of blood loss with triggers for specific actions at 500, 1000 and 1500ml blood loss
3. Multidisciplinary care with a senior midwife, obstetrician and anaesthetist attending the bedside at 1000 mL blood loss.
4. ROTEM-guided blood product replacement using an algorithm[18]

In the absence of real-time point-of-care coagulation testing, there seems to be little consensus in the ratio of red blood cells to fresh frozen plasma to platelets that is best suited in obstetrics. However 1:1:1 would be considered appropriate. Where fibrinogen levels can be measured, they appear to predict major haemorrhage, as well as track appropriate treatment.[5,9]

Conclusion:

Major obstetric haemorrhage is an important contributor to our devastatingly high maternal mortality rates, and it's of particular importance during caesarean delivery. Most of these deaths are preventable. Predicting at-risk patients, particularly those with placenta praevia or accreta spectrum, allows appropriate planning around choice of anaesthesia technique.

Treating pre-operative anaemia, and deploying other techniques to reduce bleeding during and after delivery, is important. Tranexamic acid is cheap and safe, but will only make a marginal difference.

Dynamic measures of fluid responsiveness coupled with point-of-care testing of coagulation support decision making around how much fluid, of which type, to give to bleeding patients. When point-of-care coagulation tests are not available, consider fibrinogen levels, and an empiric transfusion ratio of 1:1:1 although there is limited evidence for this.

I hope you will have gained some insight into what I believe are the difficult parts of the decision making process around managing obstetric haemorrhage, and that the reference list below is helpful. Good luck with your exams and your practice as you attempt to save moms and their babies.

References

1. NCCEMD. Saving Mothers 2014-2016 : Seventh triennial Report on Confidential Enquiries into Maternal Deaths in South Africa. Heal (San Fr [Internet]. 2018; Available from: http://www.doh.gov.za/docs/reports/2007/savingmothers.pdf
2. Miller S, Belizán JM. The true cost of maternal death: individual tragedy impacts family, community and nations. 2015 [cited 2019 May 13]; Available from: http://whqlibdoc.who.int/publications/2006/
3. Bishop D, Dyer RA, Maswime S, Rodseth RN, van Dyk D, Kluyts H-L, et al. Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. Lancet Glob Heal [Internet]. 2019 Apr 1 [cited 2019 Mar 16];7(4):e513–22. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2214109X19300361
4. Moodley J, Fawcus S, Pattinson R. Improvements in maternal mortality in South Africa. South African Med J. 2018;3(March):S4–8.
5. Dyer R. New trends in management of obstetric haemorrhage . SAJA. 2014.
6. American College of Obstetricians and Gynecologists and Society for the Maternal-Fetal Medicine. Obstetrics Care Consensus: Placenta Accreta Spectrum. Obstet Gynecol [Internet]. 2018;132(6):e259-75. Available from: https://www.acog.org/-/media/Obstetric-Care-Consensus-Series/occ007.pdf?dmc=1&ts=20190116T2002344476
7. Silver RM. Abnormal Placentation: Placenta Previa, Vasa Previa, and Placenta Accreta. Obstet Gynecol [Internet]. 2015 Sep 1 [cited 2019 May 21];126(3):654–68. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26244528
8. Markley JC, Farber MK, Perlman NC, Carusi DA. Neuraxial Anesthesia During Cesarean Delivery for Placenta Previa With Suspected Morbidly Adherent Placenta. Anesth Analg [Internet]. 2018;127(4):930–8. Available from: http://insights.ovid.com/crossref?an=00000539-201810000-00023
9. Neb H, Zacharowski K, Meybohm P. Strategies to reduce blood product utilization in obstetric practice. Curr Opin Anaesthesiol. 2017;30(3):294–9.
10. Goucher H, Wong CA, Patel SK, Toledo P. Cell salvage in obstetrics. Anesth Analg. 2015;121(2):465–8.
11. Sullivan IJ, Ralph CJ. Obstetric intra-operative cell salvage: a review of an established cell salvage service with 1170 re-infused cases. Anaesthesia. 2019;
12. Khan KS, Moore PAS, Wilson MJ, Hooper R, Allard S, Wrench I, et al. Cell salvage and donor blood transfusion during cesarean section: A pragmatic, multicentre randomised controlled trial (SALVO). 2017 [cited 2019 May 21]; Available from: https://doi.org/10.1371/journal.pmed.1002471
13. Klein AA, Bailey CR, Charlton AJ, Evans E, Guckian-Fisher M, McCrossan R, et al. Association of Anaesthetists guidelines: cell salvage for peri-operative blood conservation 2018. Anaesthesia. 2018;73(9):1141–50.
14. Shakur H, Roberts I, Fawole B, Chaudhri R, El-Sheikh M, Akintan A, et al. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet [Internet]. 2017;6736(17):1–12. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0140673617306384

15. Marik PE, Lemson J. Fluid responsiveness: an evolution of our understanding. Br J Anaesth [Internet]. 2014;112(4):617–20. Available from: http://bja.oxfordjournals.org/lookup/doi/10.1093/bja/aet590

16. Roche AM, James MFM, Bennett-Guerrero E, Mythen MG. A head-to-head comparison of the in vitro coagulation effects of saline-based and balanced electrolyte crystalloid and colloid intravenous fluids. Anesth Analg. 2006;102(4):1274–9.

17. Hartog CS, Reuter D, Loesche W, Hofmann M, Reinhart K, Hartog CS, et al. Influence of hydroxyethyl starch (HES) 130/0.4 on hemostasis as measured by viscoelastic device analysis: a systematic review. [cited 2019 May 21]; Available from: http://www.cochrane.com

18. Collins PW, Bell SF, de Lloyd L, Collis RE. Management of postpartum haemorrhage: from research into practice, a narrative review of the literature and the Cardiff experience. Int J Obstet Anesth [Internet]. 2019;37:106–17. Available from: https://doi.org/10.1016/j.ijoa.2018.08.008

The Impaired Practitioner

Dr Adalbert Ernst

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

I have some bad news for you.

There is a fire burning around the edges of our profession. And it is coming towards us all.

It has been burning for quite a while, and many of us have been burned—some of these injuries have been fatal to our colleagues and harmed the patients they care for.

We helped kindle that fire, and some of us are inadvertently feeding that fire as you read this.

We are seeing this conflagration for what it is as of late… hoping that it might not be too late.

What has happened?

As medical practitioners our obligation to *first do no harm* is perhaps the fundamental tenet upon which safe, ethical, and appropriate medical care rests.

Medical practitioners, however, are imperfect human beings who make mistakes. Sometimes not doing harm means recognising when a practitioner is unable to render safe and appropriate care to their patients due to temporary or permanent incapacity on their part.

Unfortunately, the medical profession has historically been loath to admit to its failings, and South Africa is lagging behind the rest of the world in addressing physician impairment (despite official structures ostensibly being in place.)

Anaesthetists are particularly at risk. While our specialty is fascinating, exciting, and rewarding, it is also demanding, taxing, and sometimes downright terrifying. The high rate of both suicide and substance abuse/addiction among our kin is an ugly reminder that our vocation is potentially toxic to our emotional, mental, and even physical well-being.

In his 1942 essay *The Myth of Sisyphus,* the Algerian-French philosopher Albert Camus wrote that "there is but one philosophical problem and that is suicide—judging whether life is worth living amounts to answering the fundamental question of philosophy." [(1)] It is a startling statement, but bleakly fitting given the rate of suicide among anaesthetists. As the following assessment of the darknesses inherent in our vocation hopes to review, we will need to constantly review whether we are fit to practice our profession—and indeed, if our profession is worth practising—if we are to contain the fire.

What is impairment?

At the simplest level, a dictionary definition of impairment refers to the inability to perform a skill competently and adequately, with the connotation that damage has occurred to a previously well-functioning system.

The World Health Organization defines impairment under the umbrella term of "disability", treating it as a "problem in body function or structure" distinct from, but related to "activity limitation" ("difficulty encountered by an individual in executing a task or action") and "participation restriction ("a problem experienced by an individual in involvement in life situations")[(2)].

We are most familiar with clinical impairments in patients. Consider a patient who has loss of physical function such as a hemiparesis or dysarthria following a cerebrovascular event— these are examples

of *impairment* which contribute to the individual's overall *disability*. Appropriate intervention can help minimise the ultimate disability that results—and some cases reverse it.

Impairment amongst medical professionals was only recognised in the literature as a distinct problem in the 1970s.

When considering "adequate" functioning in a healthcare professional, this necessarily implies that the individual is not just performing a set of skills correctly, but also acting *safely, ethically,* and with the patient's *best interests* at heart.

Competence can be thought of the ability to appropriately apply knowledge, skills and attitude while *performance* is the translation of competence into action when managing patient care. These factors may be affected differentially in impaired practitioners.

The Hastings Center Report of 1993 distinguishes between:

a. The impaired doctor who is defined as unable to practise medicine with reasonable skill and safety, because of physical or mental illness, including substance abuse.

b. The unethical doctor, who *knowingly* and *willingly* violates fundamental norms of conduct towards others, especially his/her patients.

c. The incompetent doctor who is ignorant or lacks appropriate skills, but is not ill [(3)].

"Impairment", however, is a loaded word:

- When the term "impaired practitioner" is mentioned, the spectre of substance abuse is almost universally raised, dominating the narrative,
- "Impairment" also conjures up images of a person in an extremely debilitated state, with the connotation that they are "damaged" and not in a position to be rehabilitated.

In reality, the obviously incapacitated physician represents but the tip of the iceberg. Most cases of impairment do not occur overnight.

In an insightful and plangent letter to the editor of SAJAA in 2013, Brannigan and Beeton note that physician impairment typically "is a far more insidious condition characterised by progressive isolation, depersonalisation and unhappiness that manifests as a slow but progressive decline in clinical performance, vigilance and ultimately results in an extremely unsafe state for both patients and the clinician concerned" [(4)].

What is the prevalence of impairment?

We don't know, and this is a problem. Estimates vary—a 2005 estimate suggests up to 1 in 6 may be affected. What we *do* know is that mental illness is much more common among doctors than was previously thought to the point that we may be witnessing the emergence of an epidemic. Dhai et al. attempted to address the scope of the problem in South Africa and quoted alarming statistics [(5)(6)]:

- Psychiatric disorders account for 22% of the global burden of disease
- Depression (ostensibly meeting DSM criteria) is seen in 10-20% of doctors
- 21% of doctors who report work-related stress have contemplated suicide
- The suicide rate in doctors may be up to 50% higher than that of the general population
- The lifetime prevalence of chemical dependency–seemingly the commonest cause of physician impairment—is 10–15%
- Alcohol dependence varies from 8-15%
- Among all doctors, alcohol is the commonest form of dependence, followed by opioids and then benzodiazepines—easily facilitated by self-prescribing. Among anaesthetists, opioids have surpassed alcohol dependency.

Impairment in medical professionals

While substance abuse is most prominently discussed in the literature, we must be mindful that it is only one factor that can lead to impairment.

Common forms of impairment

- Physical impairment—due to physical ill health or injury
- Physiological changes associated with ageing in older practitioners
- Burnout–now reaching epidemic proportions among doctors
- Mental health disorders–the vast majority are mood and anxiety disorders
- Acute adjustment disorders associated with stress due to workload, adverse outcomes with patients
- Social stressors–financial problems, intimate partner violence, family problems
- Substance abuse proper
- Maladaptive process addictions (gambling, sex addiction, internet addiction)

Physical impairment of an individual, whether through injury or disease is relatively easy to understand: the loss or decreased functioning also does not carry the stigma and shame that still clings to mental health and substance abuse. However physical impairment can and does have psychological consequences. Conditions such as rheumatoid arthritis, Parkinson's disease and cerebrovascular incidents can be devastating in rendering a practitioner unable to perform activities of daily living, not to mention their actual profession. Chronic pain conditions are not as visible but can be equally debilitating. The prudent practitioner will recognise that personal disability and "dread disease" insurance from a reputable financial organisation can ensure great peace of mind.

Age-related physical decline is frequently met with embarrassment and practitioners may compensate by relegating practical tasks to more junior staff. Physical decline might render a colleague completely incapable of performing their major skill set. Rheumatoid arthritis rendering a neurosurgeon unable to operate, whereas a psychiatrist would still be able to be able to consult if they were wheelchair-bound.

Significant cognitive decline and early onset dementia are relatively rare among ageing/semi-retired medical professionals, reflecting the protective factor that education seems to have in age-related decline, but should definitely be borne in mind if a senior colleague presents with a pattern of impaired functioning over time.

Mental health disorders remain the chief cause of impairment among doctors. While substance abuse is almost always linked to related to stressors and mental health conditions, it **must** be emphasised that *not all mental health disorders involve substance abuse*, and *not all substance abusers have a background mental health diagnosis.*

- Acute adjustment disorders can be precipitated by a bad outcome with a patient and are often under-reported, particularly in junior colleagues who do not seek debriefing for fear of being perceived as being weak (or, worryingly, have not been made aware that debriefing is available!)

- Burnout is now a near-universal phenomenon among clinicians and a topic in its own right. A detailed discussion is beyond the scope of these notes, but much-needed research into the South African anaesthetic setting has been initiated. A 2015 report revealed high levels of burnout (21%) among anaesthetists working at the academic hospitals of the University of the Witwatersrand (7). It remains to be seen whether unaddressed burnout inevitably leads to clinical depression, but it is safe to assume burnout is a causative and aggravating factor in work-related impairment.

- Major depressive disorder is the most described mental health diagnosis among impaired practitioners, and **the endpoint of untreated depression is suicide.**

- Bipolar disorder is potentially more debilitating than major depressive disorder and should always be managed by a psychiatrist. Of note is that the depressive episodes of this condition

are as a rule more severe than those seen in unipolar depression. Hypomania may easily go unnoticed by both the individual and colleagues and may be a warning symptom of a more severe mood episode (either full mania or a depressive "crash").

- *Medication shaming* persists. Perhaps because of the spectre of substance abuse, doctors may resist taking effective pharmacological treatment because most psychiatric drugs are highly regulated scheduled substances irrespective of their abuse potential.

- Some psychiatric drugs, while not addictive, are however sedative, especially in the beginning of therapy. These pose challenges for the recovering practitioner returning to work. Similarly, practitioners may have to omit a dose of potentially sedative medication whenever they are on call.

- Mood is significantly affected by lack of sleep. Acute lack of sleep tends towards hypomania, while chronic sleep deprivation can trigger depression. Sleep hygiene is notoriously bad among clinicians who do shift work. While this definitely worsens an existing mood disorder, do years and years of disruptive shifts and calls by themselves induce mood disorders?

- Substance abuse is typically a maladaptive coping mechanism in response to ongoing stressors, and can be seen as a symptom of an underlying disorder.

- There is also a difference between *abusing* a substance and being *addicted* to it (whether physically or psychologically). Hines (in the 2002 ASA Refresher Course) puts it succinctly: "Detected addicts are often found comatose, and untreated addicts may be found dead."

- Deaths related to substance abuse in doctors are often erroneously reported as suicides, when in fact a significant number of these deaths were *not* suicide attempts but accidental overdoses (particularly with the respiratory depressant effects of strong opioids).

Aspects particular to anaesthesiology practice that may contribute to impairment

- Shift work impairing sleep patterns
- Lack of exposure to natural light if only working in theatre
- Constant access to scheduled medications coupled with detailed knowledge of how these work
- Interpersonal conflicts with colleagues
- Constant emotional and mental microtrauma (near-misses with patients, adverse events, managing critically ill patients, toll of constant rapid-fire decision making)
- High stakes involved in perioperative care
- The rapid and meteoric development of the specialty on so many fronts (inherently a good thing!) may skew the signal to noise ratio for a busy clinician constantly bombarded with changing guidelines
- Rapid shift in new responsibilities when transitioning from medical officer to registrar to junior consultant to middle management to senior specialist (and/or superspecialties)

Sobering facts

- There is still a worldwide fundamental lack in educating trainees in the inherent risks of their profession, which perpetuates the problem… and South Africa continues to lag behind attempts to improve the situation.

- Anaesthesiologists have almost triple the rate of drug-related deaths than internal medicine specialists (Domino, 2006)

- The British Medical Association (1998) suggested that 1 in 15 doctors in the UK will suffer drug and/or alcohol dependence in their lifetime!

- Shame, denial, and fear of punitive interventions lead to gross underreporting of impairment—as will be seen in discussion of the South African medicolegal framework, the process is *de jure* non-punitive but *de facto* punitive and potentially humiliating.

- The majority of training programmes have no formal systems in place for detecting and managing impairment in practitioners.

- Consider the editorial in SAJAA in 2007 by Lundgren, which asked "The impaired anaesthetist—is this a problem in South Africa?" to Brannigan and Beeton's 2013 clarion call imploring "SASA, CASA, the heads of academic departments countrywide, the HPCSA and clinicians on the ground that this problem is **literally killing our colleagues** at a rate unrivalled by any other 'disease'". They referred specifically to seven deaths of anaesthesia colleagues in South Africa (all of them suicide) in 18 months. As such the 2013 answer to the 2007 question is, unfortunately, an emphatic YES (8) .

- The recognition of burnout has only recently been given attention in the local literature, but severe burnout among South African anaesthetists is **triple the international average**.

- Doctors also deviate from the norm when they fall ill—we frequently self-medicate, rely on our own instincts, avoid seeking advice from colleagues, self-prescribe, and/or simply deny the problem completely.

Medicolegal definitions of impairment in South Africa

To appreciate the South African context, we need to turn back several decades to when the concept of impairment was first given official consideration in legislation.

The **South African Health Professions Act of 1974** forms the basis on which impaired practitioners are managed under the auspices of the Health Professions Council. It does not specifically *define* impairment, but refers to it in Section 51(1) as follows:

"…whenever it appears to the council that a person registered under this Act

(a) has become mentally or physically disabled to such an extent that it would be contrary to the public interest to allow him to continue to practise;
(b) has become unfit to purchase, acquire, keep, use, administer, prescribe, order, supply or possess any scheduled substance;
(c) has used, possessed, prescribed, administered or supplied any substance referred to in paragraph (b) regularly for other than medicinal purposes;
(d) or has become addicted to the use of any substance referred to in paragraph (b),

the council shall cause the matter to be investigated and the council may, if it deems it necessary, hold an inquiry…"

HPCSA Workgroups and Guidelines on Fitness to Practice—Good In Theory

The Health Committee of the HPCSA was established by law in terms of the Health Professions Act. It was tasked with prevention, early identification, treatment and rehabilitation of impaired students and healthcare practitioners. The workgroup on Impairment developed a National Strategy for addressing impaired practitioners. It resolved that the 1974 Act, be appropriately amended to, among other things,

- Specifically define "impairment" in practitioners
- Clearly distinguish between "improper" and "disgraceful" offenses from sequelae / errors resulting from impaired practioners,
- Set up a non-punitive structure to promote health and where possible prevent impairment in practitioners

The council also noted that impairments could be classified as resulting from physical disorders, mental health disorders, substance abuse, or any combination of these, and further added a section dealing with *ethical* misconduct resulting from such impairment.

"One of the most difficult problems is that there is no universal standard of reference, other than consensual agreement of incompetence or substandard performance when we see it. Clearly there are degrees of dysfunctions. So, we need really to look at degrees of dysfunction and to look at particular concepts…"

As at May 2018, 345 impaired practitioners were under the management of the HPCSA's Health Committee, of which 225 were medical practitioners (doctors).

The majority of these impaired practitioners were being managed for substance abuse—nearly half of whom reported use of multiple substances.

Four decades later…

- Theory has not translated into practice: reporting mechanisms in place are still punitive in nature and do not address the causes of the problem
- The HPCSA's management has been criticised. A 2009 SAMJ editorial called the body out for being a "mess in the Health Department's pocket" since practitioners do not have a direct voice on the body—the Department of Health appoints HPCSA members from a list of internal nominees.
- The editorial above acknowledged that the HPCSA is overloaded as many health professions were combined into a single entity.
- The conspiracy of silence (see below) is a potent accelerant of the fire that has been burning for years already
- Practitioners admitted into the existing system have to pay for rehabilitation themselves. This policy has pros and cons—on one hand, avoids a "free ride" for the addict who has no interest in recovery; on the other, this may render care extremely difficult for the vulnerable addict with few resources.

The Conspiracy of Silence and Ethical Issues of Reporting

The "conspiracy of silence" describes the "reluctance or even an unwillingness on the part of colleagues to act in relation to obvious impairment on the part of another colleague". This may be due to:

- Unwillingness to become involved in another person's personal affairs
- Fear of retribution and possible litigation (especially when dealing with senior colleagues)
- Fear of initiating a series of events that may have negative consequences for their colleague (even though maintaining the status quo may be more damaging in the long run)
- The "it won't happen to me" mentality

The HPCSA notes that the silence is unfortunately reinforced by the legal attitude that an individual is not their "brother's keeper" but merely has the obligation "not to harm him".

This contrasts with the physician's ethical obligation to prevent harm to patients *and* to render necessary care to their impaired colleague. It is easy to realise we have a duty to report impaired colleagues, but reluctance dissuades us because of the very real (and probably inevitable) stigmatisation of both the reporter and the reported. Dhai (2006) sums this up succinctly: "Physicians need to feel safe in reporting an impaired colleague and to be assured the impaired practitioner will be *helped* rather than harmed."

The consequences of leaving an impaired practitioner unassisted and unaddressed—the very real harm to patients—greatly outweigh the consequences of going ahead and reporting. As such it is our moral and legal duty to do so.

Physician, Heal Thyself…

The mythology of the "wounded healer" translates into reality when we consider that doctors do not make typical patients:

- At worst, they may not seek help for problems (especially mental health problems) because they do not have insight or are in denial,
- They may recognise there are problems but minimise the severity, avoiding care,
- Many believe they can successfully diagnose and treat themselves
- If seeking care they prefer the advice of colleagues rather than entering the traditional route of health-care
- Presenteeism—the deliberate attending of work even though the practitioner is aware they are ill (physically or mentally)—in an effort either to shrug off their problems, or out of guilt because of an overloaded system and not wanting to burden colleagues.

How do impaired clinicians present?

General Non-Specific Suggestions of Impairment

- Changes in behaviour—especially if a recent stressor is known
- Reports of erratic and unprofessional behaviour
- Distractibility
- Hyperfocus—the individual may appear to be highly engaged or fixed on a specific task to the detriment of others
- Chronic lateness and absenteeism (and/or presenteeism)
- Mood fluctuations
- Increased involvement in interpersonal conflicts
- Pattern of decline in performance seen over time
- Limited social interaction
- "Doing the minimum necessary"

Suspicious Behaviour in Substance Abuse / Addiction

- Consistently signing out unusually high quantities of scheduled drugs
- Inconsistencies in recording drugs
- Unusually high numbers of missing / wasted ampoules
- Wearing long sleeves to conceal needle marks / tracks on arms
- Long working hours and seeking out extra working hours
- Desire to work alone, frequently relieving others, yet refusing relief by others
- Inordinate numbers of patients in recovery in pain despite ostensibly receiving opiates
- Illegible or poorly-filled in patient records
- Altered / erratic behaviour with wide mood swings
- Tremors, pin-point pupils, weight loss
- Bloodshot eyes / reddened conjunctivae (significant differential: allergy / atopy)
- Opioid abuse among anaesthetists may be detected as early as one month with sufentanil, six to twelve months while other opioids such as pethidine may only detected after years.
- Nursing staff are frequently the source of reports

Ethical Responsibilities of Colleagues

The HPCSA's Ethical and Professional Rule 26 legally obliges practitioners to report impairment in colleagues (or themselves) to the Council's appropriate board. This is easier said than done because the rule is non-specific. It does not address that impairment exists on a continuum… in theory, an exhausted registrar after a gruelling call who is struggling to concentrate during handover of a patient

would then require reporting (!). In reality, only the most serious or obviously impaired practitioners end up being reported.

A reasonable framework suggested by Naidoo (2012) includes a stepwise approach combining confidentiality and sensitivity:

- Reflecting whether a worried practitioner is convinced that their colleague is impaired (reflecting the Ethical Rule 2.5 of the Health Professions Act
- Discussing concerns privately with the practitioner concerned first
- Framing the discussion in a non-punitive way—that the concern is directed at both the practitioner's own well-being and their patients'
- Giving the practitioner space to reflect back
- If this is not sufficient, or the concerned practitioner fears negative consequences, they should seek advice from other professional colleagues in a stepwise manner
- If this is not sufficient or feasible, seeking the advice of professional organisations (e.g. MPS and SASA)
- At all times considering whether it is necessary to invoke your duty to the public by bringing concerns directly to the HPCSA. (Complaints may be lodged to the HPCSA on an anonymous basis in writing).
- A stepwise framework is moot if there is obvious evidence of wilful criminal activity and/or gross violation of patient safety… in this case you are legally bound to report fully and urgently.

If a physician is of the opinion that their patient meets the criteria of an impaired practitioner, Section 25 of the Health Professions Act compels them to report them to the HPCSA. The same criteria apply to practitioners who are reasonably convinced of such behaviour in colleagues.

The HPCSA's 2007 guideline on Confidentiality (Protecting and Providing Information) advises that disclosure of personal information without the consent of the impaired practitioner is justified "where failure to do so may expose the patient or others to risk or death or serious harm. Where third parties are exposed to a risk so serious that it outweighs the patient's right to confidentiality, health care practitioners should seek consent to disclosure where practicable. If it is not practicable, they should disclose information promptly to an appropriate person or authority. They should generally inform the patient before disclosing the information."

The Act also implies that where an impaired practitioner is aware of their impairment, they have an obligation to report their impairment to the HPCSA and should be given the opportunity to do so—but this is problematic. No direct mention is made of providing concrete support to the practitioner in a non-punitive way, and an impaired clinician may either be too incapacitated to coherently report themselves, or catastrophise the consequences of self-reporting.

This highlights the urgent need for formalised mentorship programmes and the creation of a culture where clinicians have ready access to debriefing, an open-door policy with senior colleagues, and a confidential and compassionate feedback system. Reflecting Naidoo's suggestions, intervention at an early stage might be as simple as a containing conversation and reassurance after a traumatic event.

What happens if a practitioner is reported to the HPCSA as being impaired?

- The matter is investigated by the Health Committee—note that being reported does not automatically mean immediate removal of the individual from practice.
- Investigations, however, take time!
- After investigation, the Health Committee reports to the Executive Committee of the Council
- If impairment has been established, a continuum of interventions exist, depending on the problem:
    - If mild to moderate impairment has been determined, and substance abuse excluded, the practitioner may be allowed to continue practice in a supervised manner after sick leave, psychiatric appraisal and counselling,
    - Temporary suspension until rehabilitation is complete followed by trial return to practice

    - In cases of established substance abuse, the practitioner must submit to a recognised drug rehabilitation program—unfortunately, this is at their own cost.
- Return to practice requires ongoing attendance of a rehabilitation programme, random screening (blood and/or urine) and a 3–5 year monitoring period.

Getting better

Living with mental illness

- Sadly, only two mental health conditions have prescribed minimum benefit (PMB) cover in South Africa: schizophrenia and bipolar mood disorder. Higher-end medical aids typically have more extensive chronic cover for major depression and certain anxiety disorders.
- Chronic mental health conditions take time to be diagnosed. A single mood episode may resolve with appropriate intervention and never appear again—usually related to a discrete identifiable stressor (compare post-partum depression).
- The *biopsychosocial approach* remains the cornerstone of managing mental illness, with the most positive outcomes seen with an integration of appropriate medication, psychotherapy, and the presence of a support network—this includes not only "the village" of friends, understanding colleagues and family but also engagement with activities such as exercise and constructive self-actualising pursuits and hobbies (such as learning a new language, embarking on an artistic endeavour, or travel).
- A 2015 review in The Lancet questioned the long-term efficacy of antidepressants, suggesting a disappointing effect size of 0.3 due to selective publication [(9)]
- A 2018 systematic review, again in the Lancet, provided reassurance that *all* antidepressants "were more efficacious than placebo" for major depressive disorder [(10)]
- Cognitive behavioural therapy (CBT) has emerged as the most effective counselling-based intervention in the acute phase of a mood or anxiety disorder
- Bipolar disorder may take particularly long to diagnose, especially Bipolar II, which is more common and in which hypomania is difficult to distinguish from a jovial personality type
- Bipolar disorder always requires pharmacological management with a mood-stabiliser and hence specialist supervision
- Many psychiatric medications, while highly efficacious, have significant side-effects that impact overall health: lithium is potentially nephrotoxic; second generation antipsychotics (increasingly used as add-ons in resistant depression and bipolar disorder) tend towards weight-gain or frank dysmetabolic syndrome (quetiapine). These side-effects pose a significant risk to impaired compliance
- The question is raised whether it is prudent that all medical practitioners with a mental health diagnosis should receive long-term specialist management by a psychiatrist. It is sobering to realise that management of the practitioner with mental illness has become a psychiatric subspecialty!

Substance Abuse Rehabilitation

- Domino (2006) notes that the risk of relapse from opioid addiction is highest in the first five years of recovery. Fentanyl is associated with the highest risk of relapse.
- No universal specific rehabilitation programme has been specifically validated for use in substance-addicted medical practitioners.
- The US National Survey on Drug Use and Health identified that as many as half of substance abusers have a *dual diagnosis*—i.e. a co-morbid mental health disorder that can be actively managed on admission
- Immediate treatment of the addict usually involves admission as an inpatient to an accredited recovery and addiction centre. These involve intensive programmes and facilitated step-down management. Rehabilitation centres vary significantly in approach (and cost) but accredited institutions will integrate with psychiatric care.
- Acute withdrawal (especially from opioids) requires close medical supervision with appropriate pharmacological intervention. Stepped down doses of buprenorphine combined with naloxone may be used in the acute setting if naked withdrawal poses a threat to the patient's health.

Benzodiazepines are frequently employed, and clonidine has also been successfully used as an add-on treatment. The recent literature supports the use of medication-assisted withdrawal.

- The majority of medical aids in South Africa will pay for 24 days of inpatient treatment for addiction rehabilitation per year.
- The Twelve Steps model initiated by Alcoholics Anonymous (founded in 1935) was first published in 1939 and forms the core of related successor groups like Narcotics Anonymous (NA, founded 1953). These are the oldest formal recovery programmes and have the advantage of being free of charge. Longitudinal recovery statistics from outside studies suggest that the success of recovery is related to active involvement, prolonged and ongoing attendance of meetings, and checking in daily with a sponsor. The most positive statistics have quoted a 64-5% success rate for motivated individuals. These statistics are limited by self-selection bias. Conversely, randomised controlled trials reveal disappointing statistics showing no statistically significant outcomes related to 12-step programme attendance.
- In *The Sober Truth,* the American psychiatrist Lance Dodes has questioned and criticised the 12-step approach, noting that it could be seen as adopting a shame-based approach (individuals have to acknowledge they are addicts and remain with the label) [11]. He quotes low success rates— 5-8%! He argues an psychotherapeutic approach using psychological and cognitive-based therapeutic approach may be more effective. Psychotherapy, however, is expensive and requires a long-term commitment to form a therapeutic relationship.
- The Talbot Recovery Centre has developed a specific programme for medical professionals and lists three categories for anaesthetists:
    - Those returning to anaesthesia (Group 1)
    - Those possibly returning (Group 2)
    - Those changing specialty (Group 3) or leaving medicine altogether

When Interventions go wrong — and right: the case of Sergé Rachmaninoff

A little detour into the arts and history can shed light on the importance of *appropriate intervention* as opposed to *inappropriate intervention* when considering the case of the temporary psychiatric impairment of the Russian composer, Sergé Rachmaninoff[12]. A rising star in music in late 19th Century Russia, the 1897 concert premiering his Symphony No. 1 ended in disaster when an ill-prepared orchestra gave a shoddy performance under the baton of a drunk conductor. Rachmaninoff was skewered and humiliated by the critics and press. This plunged him into depression that rendered him unable to compose for three years.

- Compare: young medical officer or new registrar in anaesthesia, anxious to impress, is involved in complications with a patient leading to a death on the table that traumatizes them, despite no wrong conduct on their part

A well-meaning colleague organised a meeting with the author Leo Tolstoy in hopes that the famous writer would inspire confidence in the young composer. Unfortunately, upon hearing Rachmaninoff's latest effort, Tolstoy remarked his dislike of the work and suggested he not be so sensitive and try harder. Tolstoy realized he had said the wrong thing and attempted to apologise, but Rachmaninoff was so stung by his remarks that the depression worsened rapidly to suicidal levels.

- Compare: a colleague notices that the young doctor is behaving in an anxious and distracted manner, and suggests they "snap out of it" because "this happens to everyone" and they "shouldn't be so sensitive"—they develop depression, start arriving late for work, have difficulty concentrating, and are distracted to the point that colleagues notice errors and impaired judgement with a few near-misses with patients.

Now desperate, family members intervened and decided that medical attention was necessary—and frog-marched him to the neurologist Nikolai Dahl. Dahl was a contemporary of Sigmund Freud, and was practicing the relatively new disciplines of psychotherapy and hypnotherapy. Although initially distrustful, Rachmaninoff submitted to the intervention and ended up meeting Dr Dahl daily for four months. Little is known of what happened in those sessions apart from the composer's recollections that the therapist acknowledged there was a problem without shaming the patient. The rest is history:

Rachmaninoff went on to compose his Second Piano Concerto, which has become one of the most popular as well as critically-acclaimed pieces of music of all time, securing his place in the musical canon. (The concerto is also the only piece of music known to be dedicated to a medical practitioner.)

- Compare: a discreet intervention is staged where a senior colleague approaches the doctor above in a non-threatening manner in a private environment. Appropriate debriefing is offered, and it is suggested the doctor seek professional help. After evaluation by a psychiatrist and psychologist appropriate medication and therapy is instituted. The doctor recovers, and successfully returns to practice.

While depression periodically visited Rachmaninoff for the rest of his life, Dahl's intervention made such a positive impact on his mental health that he was able to keep track of his moods and seek help timeously in the future. Of note is that the press and critics remained frequently hostile to his compositions throughout his life. Rachmaninoff was however able to develop a *resilience* to this criticism and continue practicing his craft—drawing inspiration from the immense popular acclaim of his work.

Light at the end of the tunnel

- With successful treatment, up to 80% of practitioners with substance abuse return to work—roughly half of these are able to practice as anaesthetists while the rest change to another speciality
- Predictors of successful recovery from substance abuse have been identified:
    - Admission of impairment
    - A strong personal motivation for recovery
    - First instance
    - Early intervention
    - Strong support from family, friends, and colleagues
- Predictors of long-term remission in mood disorders include
    - An active biopsychosocial approach
    - Insight into the condition
    - Discreet disclosure to trusted senior colleagues with the assurance of discreet intervention
    - Adherence to medication, with frequent medication review
    - Long-term psychiatric supervision
    - Long-term psychotherapy with a therapeutic relationship with a psychotherapist (the type of approach is of lesser importance)
    - An active support network of sympathetic colleagues, family and friends
    - Self-actualisation, which includes the achievement of work-life balance, reflection, and the facilitation of the individual's talents and abilities
- The high-functioning practitioner with insight into their condition may in fact be better at managing stressors than colleagues without a diagnosis, and seek help early, with minimal impact on clinical work—this requires collegial support.

How can we make things better?

To switch the metaphor from fire and ice: As of 2019, we have only seen the tip of an iceberg that has hit the trusted *HMS Anaesthesia* that set sail on her maiden voyage from Boston in 1846. Unless we institute some crucial repairs and call for help, we will sink and the body count (of both colleagues and patients) will rise.

No "wellness centres" or platitudes about "open-door policies" will save us unless we abandon another ship of shame.

- We must acknowledge the problem.
- The paternalistic model of "keeping a stiff upper lip" and "I managed to suck it up and therefore so should you" makes for great conflict in an episode of *Grey's Anatomy* but has no place in medical practice. (This is distinct from cultivating either *resilience* or stoicism, the ability to

endure hardship while realising that both good and bad times regress to the mean—traits which emerge with increasing self-actualisation.)

- We need mentorship from our colleagues, and it is clear this needs to be implemented formally.
- Mentorship is required across the board—to mix metaphors, the head of a department wears a heavy crown; the solo practitioner in private walks alone through treacherous woods; the unmentored trainee swims in dangerous currents without nary a life-vest or a lifeguard to keep them safe.
- We need to educate ourselves—especially our junior colleagues embarking on their training—of the risks of our profession.
- We must cultivate a culture of debriefing and openness. This will take time, and effort. For this is so much easier said than done.
- We must be vigilant of warning signs of impairment in both ourselves and our colleagues
- We need to trumpet the message that *asking for help is a sign of strength.*
- The colleague who asks for help must be treated with respect, and discretion—as we would want to be treated.
- Being *kind* is not necessarily the same as being *nice*—intervening for an impaired colleague may not be pleasant for anyone involved but can save lives.
- We must allow our colleagues to play to their strengths. Some of us are experts in specific super-specialties. Some of us are excellent teachers. Some of us are happy at being generalists. Still others are wizards at research and statistics. Expecting a human being to excel on all of these fronts is unrealistic and is a sure recipe for burnout.
- At all times we should recognise that our primary responsibility is to be competent, safe, and ethical in our professional endeavours—and that we have a right to perform these duties in a supportive environment. If we are failing on any of these fronts, we need to take a step back and assess what has gone wrong.
- Not all of us are made for full-time practice (indeed one could argue that as it stands, nobody is made for full-time practice with overtime without suffering some form of collateral damage). More posts, both full and part-time will go a long way to ease the pressure, but often seems like a pipe dream in the limited resource settings many of us work in.

The importance of non-medical pursuits

The noble profession of medicine is a many-splendoured thing, but wounds all healers. Medicine should not consume the practitioner: in our studies we are forced to neglect our other talents that heal and support ourselves. Discovering (or rediscovering) an avocation to practice alongside our vocation will help sustain and nurture both ourselves and our work. It may be CrossFit or birdwatching. It may be writing or art or music or hiking. It does not matter whether we become experts at it; it matters that we find *something else* that we love to do that offers a Fortress of Solitude where we can regenerate and reflect. Quoting the solid body of qualitative evidence that supports the positive impact of hobbies and outside interests on practitioner resilience risks boxing it into one more set of statistics to trundle through—but it is only a PubMed search away.

Finding Help

In 2015, the South African Society of Anaesthesiologists (SASA) established a Wellness in Anaesthesia Support Group that provides 24 hour confidential support for any anaesthetist who may be concerned about themselves or a colleague. Details and resources are freely and publicly available on the sasaweb.com website.

Support Group Practitioners (permission granted to reprint)

Ms Natalie Zimmelman
082 331 7846
ceo@sasaweb.com

Dr Caroline Lee
082 777 2136
dreamdocsa@gmail.com

Dr Allan Hold
082 655 7792
holdfam@iafrica.com

Dr Bhavika Daya
083 787 1177
bhavikadaya@gmail.com

Dr Megan Jaworska
082 371 2383
madzia2908@gmail.com

Other useful resources

- SA Depression and Anxiety Support Group +27 11 262 639 / 24 hour helpline 0800 12 13 13
- SA Suicide Crisis Line 0800 567 567 or SMS 31393 for callback
- Lifeline 0861 322 322 / www.lifelinecounsellor.co.za

Selected References

1. Plant B. Absurdity, Incongruity and Laughter. Philosophy. 2009;
2. WHO. World Report on Disability 2011. World Helath Organ. 2011;
3. My Brother ' s Warden ? 2014;23(3):19–27.
4. L. B, A. B. The impaired clinician and the health and wellness of practitioners in anaesthesia and critical care. South African J Anaesth Analg [Internet]. 2013;19(3):137. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L369208500%0Ahttp://www.sajaa.co.za/index.php/sajaa/article/view/1173/1269%0Ahttp://findit.library.jhu.edu/resolve?sid=EMBASE&issn=22201181&id=doi:&atitle=The+impaired+clinician+and+
5. Dhai A, Szabo CP, Mcquoid-mason DJ. ORIGINAL A RTICLES The impaired practitioner – scope of the problem and ethical challenges. Samj. 2006;96(10):1069–72.
6. Liebenberg AR, Coetzee JF, Conradie HH, Coetzee JF. Burnout among rural hospital doctors in the Western Cape: Comparison with previous South African studies. African J Prim Heal Care Fam Med. 2018;10(1):1–7.
7. N. van der W, J. S, H. P. Burnout among anaesthetists in South Africa. South African J Anaesth Analg [Internet]. 2015;21(6):27–30. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L607371413%5Cnhttp://dx.doi.org/10.1080/22201181.2015.1102798%5Cnhttp://sfx.hul.harvard.edu/sfx_local?sid=EMBASE&issn=22201181&id=doi:10.1080%2F22201181.2015.1102798&atitle=Burnout+a
8. Lundgren C. Editorial. 1998;39–40.
9. Khan A, Brown WA. Antidepressants versus placebo in major depression: An overview. World Psychiatry. 2015;14(3):294–300.
10. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet [Internet]. 2018;391(10128):1357–66. Available from: http://dx.doi.org/10.1016/S0140-6736(17)32802-7
11. Roth JD, Khantzian EJ. Book Review: The Sober Truth: Debunking the Bad Science behind 12-step Programs and the Rehab Industry. J Am Psychoanal Assoc. 2015;
12. Yasser J, Bertensson S, Leyda J. Sergei Rachmaninoff; A Lifetime in Music. Notes. 2006;

Perioperative Management of Total Hip and Knee Arthroplasty Patients

Dr Ulla Plenge

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

In the 1960's the British orthopaedic surgeon Sir John Charnley revolutionized the surgical management of the arthritic hip introducing acrylic cement to fix components to living bone and high-density polyethylene as bearing material and these principles are still key features for total hip and knee arthroplasty today (THA and TKA, respectively).

Total joint arthroplasty (TJA) evolved from being a salvage procedure with poor long-term outcomes for the most infirm patients to one of the most successful and frequently undertaken elective surgeries in high income countries where the demand for TJAs is expected to grow exponentially as a result of a growing elderly population and an increase in obesity. A similar trend is expected in South Africa with an increased demand for joint replacements – hence the importance of this topic!

The majority of the literature for primary, elective TJA is related to end-stage osteoarthritis, however, the principles described in this chapter can be extrapolated to great extend for patients awaiting joint replacement due to avascular necrosis, rheumatic arthritis or revision.

Key concepts covered:

1. **Enhanced recovery protocols for TJA**
2. **Important preoperative interventions**
    a. **Identify high risk profile patients**
    b. **Patient information/education**
3. **Important Intraoperative interventions**
    a. **Choice of anaesthesia**
    b. **Antibiotics**
    c. **PONV**
    d. **Blood conservation techniques**
4. **Important postoperative interventions**
    a. **Postoperative analgesia – what is the evidence?**
        i. **NSAIDs/COX-2 inhibitors & paracetamol**
        ii. **Gabapentinoids**
        iii. **Peripheral nerve blocks**
5. **The importance of a multidisciplinary team**

Enhanced Recovery Pathways for TJA

More than two decades ago, the Danish colorectal surgeon Professor Henrik Kehlet pioneered the concept of Enhanced Recovery Pathways (ERPs), which aims to improve a patient's postoperative recovery trajectory by diminishing the detrimental effects of perioperative surgical stress[1]. The original work applied to colorectal surgery and began as a patient-centred science, based on clear pathophysiological principles to reduce postoperative complications. Standardized, best evidence protocols were implemented by multidisciplinary teams (nurses, physiotherapists, nutritionists, surgeons, physicians and anaesthetists) to ensure a continuum of care throughout a patient's perioperative journey (preoperative, intraoperative and postoperative period).

Today ERPs are well established within most surgical disciplines, but to a wide extent implemented without the scientific rigor (ex. cohort studies vs clinical trials) and with a different scope (length of stay (LOS) in hospital (vs true measures of recovery) than originally intended. The reality is that we still have limited understanding of postoperative pathophysiological mechanisms including systemic inflammatory changes, neurohumeral alterations, volume homeostasis and pain mechanisms. The result is lack of consensus on important postoperative outcomes which consequently leads to protocols differing greatly between institutions.

As a result of these controversies, a 'gold-standard' for best perioperative practice for TJA does not exist. However, the overall impression is that implementation of ERPs improves the immediate postoperative recovery phase decreasing postoperative complication rate without reducing patient satisfaction or increasing readmission rate[2]. Streamlining procedures minimises unnecessary variations and decreases length of stay in hospital, ultimately leading to reduced health care related costs.

Thus, inspired by the concept of ERPs, the following sections describes specific interventions for TJA, where anaesthetists might contribute to improving patient care and patient outcomes. Keep in mind, that the clinical value of each intervention is poorly investigated, and that forming a multidisciplinary team spanning a patient's perioperative journey, possibly is the most important perioperative intervention of them all!

Important preoperative interventions

Identify high-risk patients (what changes outcome)?

Joint replacement aims to provide pain relief, function improvement and patient satisfaction and with the elective nature of primary TJA, modifiable risk factors should be addressed timely reducing risk of postoperative complications. In the following, patient groups at increased risk of persistent postsurgical pain (PPSP) and postsurgical morbidity (other than pain) and mortality, will be considered.

i. Risk profiles for persistent postsurgical pain:

Risk of moderate to severe pain after TJA is high on the first postoperative day (especially for TKA), and acute post-operative pain has increasingly been linked to PPSP[3]. Since pain relief is the most important postoperative outcome for TJA patients, it is disconcerting that up to 13% after THA and 20% after TKA develops PPSP. These results have fuelled substantial efforts investigating which preoperative predictors increase risk of PPSP, to possibly develop preventative strategies[4].

Preoperative risk factors for PPSP

Psychosocial characteristics [5]	Pain catastrophizing – exaggerated fear about pain	Poor coping mechanisms	Mental health (depression/anxiety)
Pre-existing pain[6]	Longstanding severe joint pain	Multiple joint pain	Neuropathic pain-like symptoms*
Medication[7]	Chronic opioid use		

- e.g. burning, shooting, electric shock-like pain, allodynia and hyperalgesia

Ideally 'at risk' patients should be identified early to afford timely presurgical psychological interventions, integrative therapies and preoperative opioid tapering. Once operated, heightened focus on postoperative pain control to reduce time spent in severe pain is a priority. No RCTs exist to guide

postoperative analgesic multimodal techniques, but it is believed these patient groups will benefit substantially from in-hospital and post-discharge follow-up to reduce risk of PPSP.

ii. Risk profiles for increased morbidity and mortality:

Predicting which patients will develop medical and surgical complications after surgery has so far been limited by diverse types of complications and a high NNT[8], as well as lack of high-quality studies with many different perioperative care pathways. Nevertheless, overall consensus exists that the following patient characteristics are associated with increased risk of postoperative morbidity/mortality following TJA why patients presenting with these risk factors should be optimized prior to surgery;

- High comorbidity burden[9]
- Patients with frailty-defining diagnoses, ex. dementia, decubitus ulcer, malnutrition, dependence[10]
- Morbidly obese (BMI≥40)[11]
- Poorly regulated diabetes (HbA_{1c} > 8 % within 4 weeks prior to surgery)[12]
- Anaemia (Female < 12 g/dL, Male < 13 g/dL)[13]

Patient information/education

The preoperative period is a 'window of opportunity' to not only spot 'at risk' patients for poor postoperative outcome, but also to provide preoperative information and education. The aim is to empower patients to play an active role in their recovery process and align patient expectations with realistic surgical short- and long-term outcomes. Whether such efforts improve patient reported outcome measures (ex. pain, satisfaction, function, anxiety) has not been investigated in high quality studies, but the intervention remains a core part of ERPs - not least to assist in shared decision making.

Important Intraoperative interventions

Choice of anaesthesia

In 2000, Rodgers' systematic review was the first to synthesize the evidence for possible benefits of NA vs GA for a broad range of surgical populations[14]. One major critique point was the inclusion of different procedures, as postoperative recovery and risk of morbidity/mortality depends on type of surgery and the associated catabolic and inflammatory response. This appreciation fuelled a multitude of publications specifically addressing choice of anaesthesia for TJA patients and postoperative outcomes. However, as risk of postoperative complications and mortality following TJA is low, we are yet to see a sufficiently powered RCT to inform us if in fact the choice of anaesthesia changes risk of postoperative complications. Instead we are left with:

- Underpowered SRs/MAs of RCTs and prospective observational trials based on outdated modes of anaesthesia and perioperative care[15] – **no difference between NA and GA.**
- Single centre RCTs from 'state of the art' ERP unit showing superiority of GA/TIVA from 2 hours after surgery until discharge (are their results reproducible?)[16, 17] – **favour GA**.
- Retrospective data registry studies with 10.000's and 100.000's patients, documenting rare events but at the cost of detailed patient and perioperative information (results can only suggest associations, never causality as confounders are not measured[9] – **favour NA**.

Interestingly, hardly any studies investigate the fact that NA produces the best immediate postoperative analgesia (unless the surgery outlasts the NA) and whether this is associated with superior recovery trajectory (pain, mobilisation, quality of sleep, PONV, satisfaction/quality of life or PPSP) combined to GA with peripheral nerve block (PNB).

Heterogeneity of study designs from the past 2 decades and their conflicting results prevents a true understanding of whether choice of anaesthesia changes risk for postoperative complications. Rather, identification of signals is the closest we can come to a recommendation:

Odds ratio not affected by choice of anaesthesia = Suggesting no difference in risk	DVT/PE (+ thromboembolic prophylaxis)	Cardiac complications of any kind	30-day mortality
Odds ratio lower for NA = Suggesting less risk with NA (only population-based registry data)	Pulmonary complications of any kind	Combined major complications* in the i. general patient population, ii. OSA-patients, iii. older patients	

*a composite endpoint representing any major complication (coagulopathy, cardiopulmonary, infection, renal, GI, CNS)

In conclusion

- NA provides best immediate postoperative analgesia
- Postoperative complications: NA is not inferior to GA (if no contraindications for NA)
- Subpopulations: Patients with pre-existing i. pulmonary disease, ii. risk of OSA, iii. high risk of acute postoperative pain and iv. old age (and possibly frail) may particularly benefit from NA
- Early in-hospital recovery (pain, mobilisation, PONV): GA/TIVA possibly comparable to NA

Antibiotics - reduce risk of infection

With a prevalence of 1-2 %, periprosthetic joint infection (PJI) is a relatively rare but dreaded complication after primary TJA. Intraoperative antibiotic prophylaxis plays a key role as part of a bundled approach to reduce this risk (ex. no recent infection, nutritional optimisation, diabetic control, preoperative wash, instrument sterilisation, skin decontamination, laminar flow theatres, short surgery time, reduced blood loss etc.). While there are no RCTs available to guide the choice of any particular regimen or ideal timing of such dosing, early administration of first and second generation cephalosporins remains preferred choices, as over half of PJIs are caused by Staphylococcus species - alternatively vancomycin or clindamycin if the patient has beta-lactam allergy[18].

Reduce risk of PONV

The focus on early postoperative functional recovery (eating, drinking, moving) after TJA in ERPs has introduced antiemetics as standard care in many protocols irrespective of a patient's estimated risk for postoperative nausea and vomit (PONV). Corticosteroids have been of interest due to their anti-inflammatory properties in addition to their antiemetic effect but the literature is conflicting and difficult to interpret with respect to clinically meaningful effect on pain scores, morphine consumption, joint swelling, early mobilisation and LOS in hospital (vast heterogeneity of study designs with dexamethasone dosages ranging from 4-40 mg administered in variety of multimodal analgesic protocols). It is possible that TKA patients benefit the most (they also have higher inflammatory response to surgery), and that a systemic dose of 8 mg dexamethasone provides an anti-inflammatory 'spill-over' effect resulting in clinically relevant postoperative pain and morphine reduction in addition to reducing risk of PONV[19]. So far underpowered RCT and retrospective population-based trials have not demonstrated increased risk of neither medical nor surgical complications with use of corticosteroids – particularly wound or periprosthetic infections – but caution is warranted especially for immune compromised patients and for patients with history of diabetes or GI-ulcers/bleed.

Blood conservation strategy

Tranexamic acid (TXA) is an antifibrinolytic agent which exerts its effects by reversibly binding to plasminogen inhibiting activation of plasmin and fibrin degradation. As an integral part of a perioperative Patient Blood Management (PBM) program (preoperative detection and optimization of anaemia, postoperative conservative transfusion triggers), its use has fundamentally changed blood management in TJA making transfusion an infrequent event. A recently published comprehensive review[20] suggest the following:

- No difference between modes of administration (IV, topical, oral, combination of individual formulas) on blood loss and risk of transfusion during the perioperative period.
- High dose intravenous TXA (≥ 20 mg/kg or > 1 g) does not demonstrate additional reduction in blood loss compared with low-dose intravenous TXA (≤ 20 mg/kg or ≤ 1 g).
- Administration of multiple doses intravenous TXA compared with single dose intravenous TXA does not significantly alter blood loss and need for transfusion during the perioperative period.
- Intravenous administration of TXA before incision potentially reduces blood loss and need for transfusion compared with post incision administration (TKA: administer prior to tourniquet).
- In patients without known history of venous thromboembolic event (VTE), intravenous TXA does not increase risk of developing VTE during the perioperative period.
- The existing literature does not suggest increased risk of developing arterial thromboembolic events due to administration of intravenous TXA.
- There is a paucity of RCTs on the risk of adverse effects of TXA in patients with known history of VTE, MI, CVA, TIA and/or vascular stent placement. When considering the possible harm, one must also consider that postoperative cardiovascular complications are associated with anaemia and high blood transfusion rate. The existing high-quality literature regarding administration of TXA in patients of generally higher comorbidity burden, does not suggest increased risk of adverse thromboembolic events during the perioperative period.

Important postoperative interventions

Postoperative analgesia

Drinking, eating and mobilising (DREAMing) are patient- centred outcomes that are consistent with restoration of a normal physiological state and are integral to the road to full recovery. To accomplish DREAMing, postoperative pain control is crucial. **Optimal pain control** after TJA, is best described, as a balance between i. fastest functional recovery (DREAMing) and ii. optimized patient comfort (optimal pain ratings, reduced sleep disruption and improved patient experience) with iii. fewest side effects (nausea, vomiting, sedation, constipation, itching, dizziness)[21].

To achieve this, the main aim is to reduce or eliminate the use of strong opioids, which are recognised to have many disadvantages and unacceptable side-effects. In this regard, multimodal analgesic techniques have received much attention (defined as: a combination of different analgesic drugs to reduce pain through targeting pain pathways at various levels, while decreasing the postoperative use of morphine and associated side-effects). The concept was first described in the mid 1990's as 'balanced analgesia' by Kehlet and Dahl to question the practice of only administering opioids for pain control. Since then, a plethora of studies has been published with a vast variety of combinations of drugs, dosages and techniques, challenging head-to-head comparisons (the reality is we have surprisingly limited understanding of benefit and harm when combining more than two analgesic techniques). Furthermore, only few high-quality studies exist (prospective, RCT, double blinded, sufficiently powered to investigate clinically meaningful outcomes), resulting in lack of globally accepted best practice for postoperative analgesic management after TJA.

The following section is a non-comprehensive overview of current knowledge (or lack thereof) of the most commonly used analgesic techniques for TJA. It is worth noticing that most studies report 24-hour morphine consumption as their primary outcome rather than investigating the impact of analgesic

modes on true measures of in-hospital (ex. early ambulation, functional pain, PONV, sleep quality) and post-discharge (return to work, satisfaction/quality of life) recovery.

i. NSAIDs/COX-2 inhibitors & paracetamol

THA:

- A VERY recent high quality double blinded RCT has finally been published informing us on the morphine sparring, analgesic and harmful effects of analgesic regimens with ibuprofen and/or paracetamol[22]. Combining 1 g paracetamol with 400 mg ibuprofen 6 hourly for 24 hours resulted in clinically meaningful reduction in morphine consumption, pain scores and risk for PONV when compared to 1 g paracetamol 6 hourly for 24 hours. Importantly, 90-day follow-up did not show a statistically significant increase in serious adverse events between the groups receiving only ibuprofen (400 mg 6 hourly) or paracetamol (1 g 6 hourly) for 24 hours.

TKA:

- No studies have evaluated the clinical efficacy of NSAIDs/COX-2 inhibitors combined with paracetamol.
- The literature describes no clinically important differences (morphine sparring/pain scores/side effect profile/functional outcomes) between i. administration of acetaminophen or placebo in a multimodal analgesic protocol and ii. administering IV rather than oral acetaminophen.
- NSAIDs/COX-2 inhibitors administered in the perioperative period have consistently demonstrated i. decreased inflammatory markers, ii. reduced postoperative opioid consumption and iii. reduced pain scores compared to placebo. However, the majority of studies fail to show clinically relevant reduction in morphine consumption or pain scores.

ii. Gabapentinoids

During the past 10-15 years, gabapentin and pregabalin have gained considerable attention in the postoperative pain context, as a mean to reduce central sensitization induced by surgery evoked nociception and inflammation. However, since publication of a well conducted MA 3 years ago, it is now evident that neither pregabalin nor gabapentin is associated with clinically relevant decrease in in-hospital or long-term pain scores (3-6 months and 3-4 years after surgery). Only patients receiving pregabalin had a 15% reduction in opioid consumption first 24 hours after surgery, however, in this patient group an increased incidence of sedation was observed (RR1.44 [95% CI 1.07-1.94]; p=0.02)[23]. [N.B. It is possible that patients at high risk for developing severe acute postoperative pain following TJA (ex. chronic opioid consuming patients, preoperative neuropathic pain, severe preoperative chronic pain) will benefit from pregabalin].

iii. Peripheral nerve blocks (PNBs)

THR:

Nerve supply related to the incision: **Skin;** L2-L4 dermatomes. The lateral cutaneous femoral nerve does not consistently cover (too anterior or inferior to the incision)! **Deeper structures;** The incision through tensor fasciae latae (TFL) and medius/maximus muscles is innervated by the superior and inferior gluteal nerves.

Nerve supply of the hip joint: **Anterior**; art. branches from the i. femoral nerve, ii. obturator nerves. **Posterior;** art. branches from the i. nerve to quadratus femoris, ii. superior gluteal nerve and iii. sciatic nerves.

To block the nerves from the lumbosacral plexus supplying the area of incision for THA has proven difficult. This is best illustrated in a recent Cochrane review (i. only few sham blocks, ii. primarily old small studies without ERPs and iii. an overall quality of evidence rated low to very low), where 45 RCTs investigated the effects of PNBs on pain scores, morphine requirement, PONV and ambulation (lumbar plexus block, fascia iliaca compartment block, supra inguinal fascia iliaca block, femoral nerve block, femoral lateral cutaneous nerve block and obturator nerve block)[24]. PNBs only had a clinically relevant reduction in pain scores (3.2 cm on a 10 cm scale) at rest on arrival in the postoperative care unit (patients had GA). As for any other time point, only lumbar plexus block showed reduced (but not clinically meaningful) pain scores. No difference in morphine requirements, PONV or ambulation were documented. While lumbar plexus block might have some effect on pain scores following THA, motor

function is impaired with the risk of reduced safe mobilisation and in-hospital falls. Since the Cochrane review, case reports on new peripheral nerve blocks for THA have been published;

- PEricapsular Nerve Group block (PENG-block)
- Erector Spinae Block (ESP)
- Quadratus lumborum block (QL).

So, while we at present don't have a 'gold-standard' PNB for THA, future clinical studies of these new 'blocks on the block' can (hopefully soon) inform us if either of them can provide a meaningful clinical improvement of recovery within a multimodal ERP protocol.

TKR:

The medial parapatellar incision evokes pain from anterior sensory nerves:
i. infrapatellar branch of the saphenous nerve, ii. the medial retinacular nerve (the terminal branch of the medial vastus muscle nerve) and iii. anterior branch of the medial femoral cutaneous nerve – all 3 nerves originate from the femoral nerve.

The intra-articular excision evokes pain from structures innervated by posterior sensory nerves:

The popliteal nerve plexus is derived from i. tibial nerve and ii. posterior branch of the obturator nerve.

Unlike THA, there is amble evidence that PNBs for TKAs improves in-hospital recovery (pain, nausea, morphine requirements, ambulation) while possible long-term effects are not established. A recently published Network Meta-analysis of 170 RCTs on pain control after TKA included 16 techniques, of which 10 were PNBs in different combinations[25]! Unsurprisingly, blocking the femoral and sciatic nerves offered optimal balance of low pain scores, low opioid consumption and a large knee range of motion during the initial 72 hours. However, blocking these two nerves also results in complete motor block of the leg, increasing risk of late ambulation and in-hospital falls.

It follows, that the goal of a PNBs within an ERP protocol is to provide clinically relevant reduction in pain scores and morphine consumption to enable early mobilisation with fewest possible side-effects. Based on this, the adductor canal block (ACB) has been proposed as the 'gold-standard' for TKA. Ultrasound guided injection of LA lateral to the femoral artery between the ASIS and the base of the patella (anatomically this is in the femoral triangle, proximal to the adductor canal) blocks the anterior sensory nerves to the knee and hence the medial parapatellar incision. The block will inadvertently also block the motor branches to m. vastus medialis, but this only accounts for ca 8% of total quadricep muscle power - the ACB therefore enables safe ambulation compared with the femoral nerve block and provides same analgesic and morphine sparing qualities[26]. Characteristics of the ACB:

- 20-30 ml 0.25-0.375% bupivacaine is recommended
- Single shot is not inferior to continuous infusion
- Liposomal bupivacaine has not proven beneficial
- Adjuvants (clonidine, dexamethasone and dexmedetomidine) prolongs analgesic effect of ACB < 2 hours, so not recommended.

Blocking the popliteal plexus to account for the intra-articular excision component, can be done either by the surgeon (local infiltration of LA) or ultrasound guided (infiltration of LA between the posterior artery and capsule of knee (IPACK), or posterior obturator nerve). However, it is yet to be proven if blocking the posterior sensory nerves adds meaningful reduction in pain and morphine consumption when combined with an ACB.

The importance of a multidisciplinary team

A dedicated multidisciplinary team sharing the mutual perioperative goal of a 'risk and pain free' patient journey will improve quality of patient care with a possible 'downstream' effect on patients' postoperative recovery trajectory.
Working as a team, rather than in independent silos, creates transparency and facilitates the relevant feedback on the service provided to patients which is so necessary for continual improvement.

References

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. British journal of anaesthesia. 1997;78(5):606-17.
2. Zhu S, Qian W, Jiang C, Ye C, Chen X. Enhanced recovery after surgery for hip and knee arthroplasty: a systematic review and meta-analysis. Postgraduate medical journal. 2017.
3. Buvanendran A, Della Valle CJ, Kroin JS, Shah M, Moric M, Tuman KJ, et al. Acute postoperative pain is an independent predictor of chronic postsurgical pain following total knee arthroplasty at 6 months: a prospective cohort study. Regional anesthesia and pain medicine. 2019.
4. Richebé P, Capdevila X, Rivat C. Persistent Postsurgical PainPathophysiology and Preventative Pharmacologic Considerations. Anesthesiology. 2018;129(3):590-607.
5. Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. Br J Anaesth. 2018;121(4):804-12.
6. Kurien T, Arendt-Nielsen L, Petersen KK, Graven-Nielsen T, Scammell BE. Preoperative Neuropathic Pain-like Symptoms and Central Pain Mechanisms in Knee Osteoarthritis Predicts Poor Outcome 6 Months After Total Knee Replacement Surgery. The journal of pain : official journal of the American Pain Society. 2018.
7. Aasvang EK, Lunn TH, Hansen TB, Kristensen PW, Solgaard S, Kehlet H. Chronic pre-operative opioid use and acute pain after fast-track total knee arthroplasty. Acta anaesthesiologica Scandinavica. 2016;60(4):529-36.
8. Jorgensen CC, Petersen MA, Kehlet H, Lundbeck Foundation Centre for Fast-Track H, Knee Replacement Collaborative G. Preoperative prediction of potentially preventable morbidity after fast-track hip and knee arthroplasty: a detailed descriptive cohort study. BMJ open. 2016;6(1):e009813.
9. Memtsoudis SG, Rasul R, Suzuki S, Poeran J, Danninger T, Wu C, et al. Does the impact of the type of anesthesia on outcomes differ by patient age and comorbidity burden? Regional anesthesia and pain medicine. 2014;39(2):112-9.
10. McIsaac DI, Bryson GL, van Walraven C. Association of Frailty and 1-Year Postoperative Mortality Following Major Elective Noncardiac Surgery: A Population-Based Cohort Study. JAMA surgery. 2016;151(6):538-45.
11. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ open. 2018;8(2):e017689.
12. Hwang JS, Kim SJ, Bamne AB, Na YG, Kim TK. Do glycemic markers predict occurrence of complications after total knee arthroplasty in patients with diabetes? Clinical orthopaedics and related research. 2015;473(5):1726-31.
13. Munting KE, Klein AA. Optimisation of pre-operative anaemia in patients before elective major surgery - why, who, when and how? Anaesthesia. 2019;74 Suppl 1:49-57.
14. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ (Clinical research ed). 2000;321(7275):1493.
15. Johnson RL, Kopp SL, Burkle CM, Duncan CM, Jacob AK, Erwin PJ, et al. Neuraxial vs general anaesthesia for total hip and total knee arthroplasty: a systematic review of comparative-effectiveness research. Br J Anaesth. 2016;116(2):163-76.
16. Harsten A, Kehlet H, Ljung P, Toksvig-Larsen S. Total intravenous general anaesthesia vs. spinal anaesthesia for total hip arthroplasty: a randomised, controlled trial. Acta anaesthesiologica Scandinavica. 2015;59(3):298-309.
17. Harsten A, Kehlet H, Toksvig-Larsen S. Recovery after total intravenous general anaesthesia or spinal anaesthesia for total knee arthroplasty: A randomized trial. British Journal of Anaesthesia. 2013;111(3):391-9.
18. Hickson CJ, Metcalfe D, Elgohari S, Oswald T, Masters JP, Rymaszewska M, et al. Prophylactic antibiotics in elective hip and knee arthroplasty: an analysis of organisms reported to cause infections and National survey of clinical practice. Bone & joint research. 2015;4(11):181-9.
19. Dissanayake R, Du HN, Robertson IK, Ogden K, Wiltshire K, Mulford JS. Does Dexamethasone Reduce Hospital Readiness for Discharge, Pain, Nausea, and Early Patient Satisfaction in Hip and Knee Arthroplasty? A Randomized, Controlled Trial. The Journal of arthroplasty. 2018;33(11):3429-36.
20. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Bini SA, Clarke HD, et al. Tranexamic acid in total joint arthroplasty: the endorsed clinical practice guides of the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society. Regional anesthesia and pain medicine. 2019;44(1):7-11.
21. McEvoy MD, Scott MJ, Gordon DB, Grant SA, Thacker JKM, Wu CL, et al. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: part 1-from the preoperative period to PACU. Perioperative medicine (London, England). 2017;6:8.
22. Thybo KH, Hagi-Pedersen D, Dahl JB, Wetterslev J, Nersesjan M, Jakobsen JC, et al. Effect of Combination of Paracetamol (Acetaminophen) and Ibuprofen vs Either Alone on Patient-Controlled Morphine Consumption in the First 24 Hours After Total Hip Arthroplasty: The PANSAID Randomized Clinical Trial. Jama. 2019;321(6):562-71.
23. Hamilton TW, Strickland LH, Pandit HG. A Meta-Analysis on the Use of Gabapentinoids for the Treatment of Acute Postoperative Pain Following Total Knee Arthroplasty. The Journal of bone and joint surgery American volume. 2016;98(16):1340-50.
24. Guay J, Johnson RL, Kopp S. Nerve blocks or no nerve blocks for pain control after elective hip replacement (arthroplasty) surgery in adults. The Cochrane database of systematic reviews. 2017;10:Cd011608.
25. Terkawi AS, Mavridis D, Sessler DI, Nunemaker MS, Doais KS, Terkawi RS, et al. Pain Management Modalities after Total Knee Arthroplasty: A Network Meta-analysis of 170 Randomized Controlled Trials. Anesthesiology. 2017;126(5):923-37.
26. Grevstad U, Mathiesen O, Valentiner LS, Jaeger P, Hilsted KL, Dahl JB. Effect of adductor canal block versus femoral nerve block on quadriceps strength, mobilization, and pain after total knee arthroplasty: a randomized, blinded study. Regional anesthesia and pain medicine. 2015;40(1):3-10.

Anaesthesia for Scoliosis Surgery

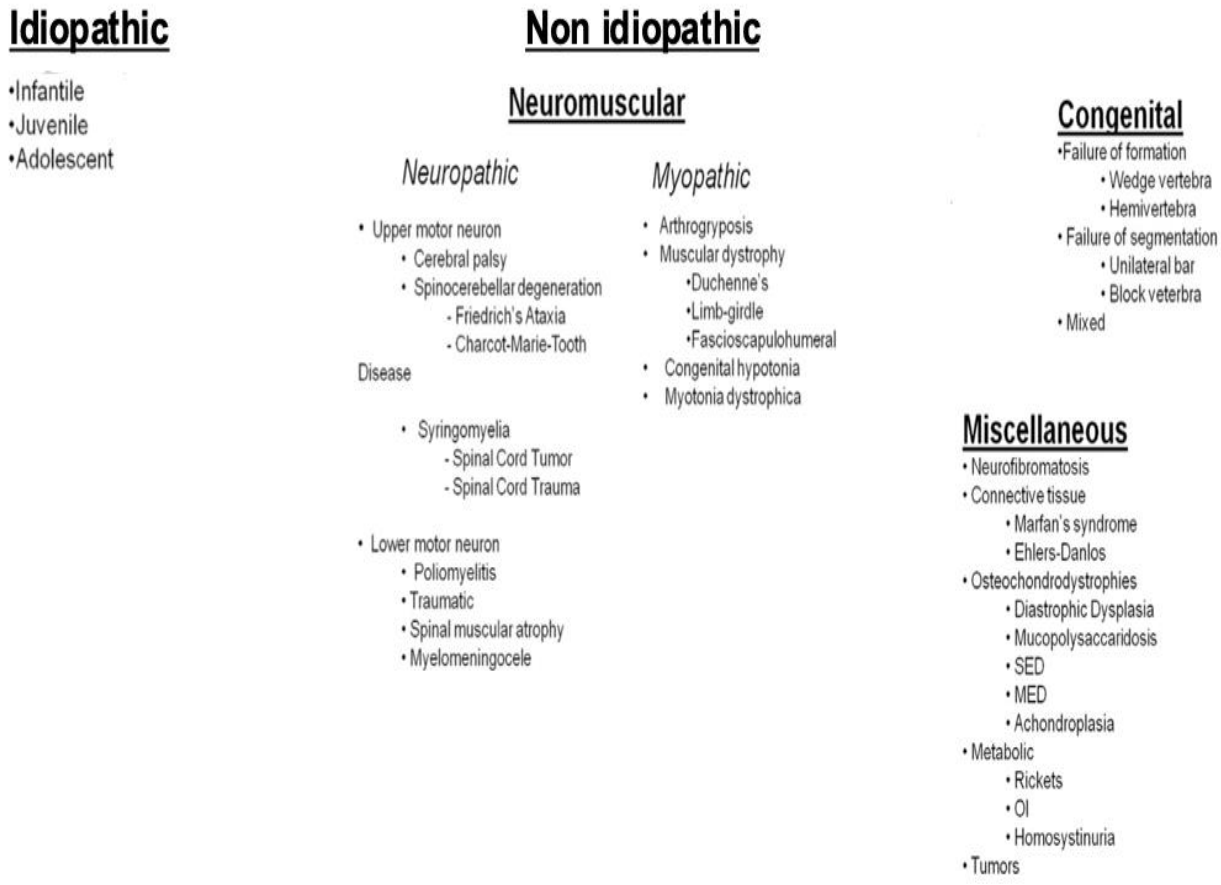
Dr Noshina Khan

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Scoliosis is condition of lateral curvature and rotation of the thoracolumbar vertebrae, resulting in rib cage architectural deformities, which eventually have an impact on cardio respiratory function. When left untreated, patients suffer chronic pain, worsening respiratory function, with consequential right ventricular impairment, as well as rapid decline in quality of life and increased morbidity and mortality. In effort to prevent curve progression preserve cardio respiratory function, surgical stabilization and fusion is offered prior to functional impairment (ideally).

Classification

A variety of classifications exist based on aetiology, onset or curve types. The most commonly usable classification is based on aetiological type and this itself might be divided into two main groups,



Adolescent Idiopathic scoliosis (AIS) (70%)

- Most common group, commonly presenting around 10-16 yrs of age
- Girls are more affected than boys, and 10 times more likely to present with curves >30^{o}, progressing to require surgery.
- These patients do not have any associated diseases, however the cardio respiratory functional impingement is progressive as the spinal curvature becomes more exaggerated.
- AIS patients commonly have rightward curves.
- A left facing convexity in a male patient should always alert one to the increased likelihood of the patient belonging to NIS group with increased association of cardiac, genitourinary and muscular congenital disorders; or the likelihood of a cyst or syrinx.

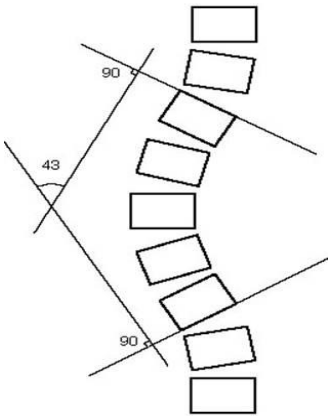
Non-Idiopathic scoliosis (NIS)

These patients present with scoliosis as an additional complication or *symptom of a more severe condition/syndrome*. They require special consideration given the high likelihood *of complex comorbidities* related to their underlying disease. Their functional reserve is limited by their comorbidities as well as the severity of the scoliosis. As a result, NIS patient require a comprehensive preoperative workup, ongoing care from other medical specialities and are also more likely to require ICU support post operatively.

Patients with neuromuscular disorders form the majority of this group.

Cobb Angle- what does anaesthetist really need to know?

The Cobb Angle was orthopaedic "Gold Standard" for the assessment of scoliosis. A larger Cobb angle relates to greater disease severity.



It is measured by first identifying the two most tilted vertebrae in a curve. Lines are drawn along the top of the superior tilted vertebra and the bottom of the inferior tilted vertebra. Two more lines are drawn perpendicular to the vertebral lines. The second set of line are to be extended until they intersect. they The resulting angle is measured, and the number is expressed in degrees. *A lateral curvature with an angle of >10^{o} is diagnosed as a scoliosis*. While this has become the standard to describe severity of this condition, it is a limited assessment:

- Scoliosis is 3 dimensional rotation and curvature; Cobb angles are measured in a 2D plane on an X-ray. Measurements don't always reflect curve severity.
- Measurements can differ depending on which vertebrae are chosen
- Even small deviations with the first set of lines may result in greater in accuracies when the angle is measures.
- Due to these inaccuracies, combination of measuring systems, as well as investigations such as CT and MRI are used, in conjunction with a functional assessment of the patient has been suggested to determine severity of disease impact.

Pre-Operative Evaluation

Because of the potential for significant pulmonary, cardiac, and neurologic comorbidities associated with advanced scoliosis, a detailed past medical history and physical examination for patients undergoing surgical correction is essential. Documentation of pre-existing neurological deficit paramount.

Baseline exercise tolerance and respiratory function should be noted and serves as a general predictor of *the reserve capacity to withstand surgery*, particularly in healthy AIS.
All patients require a baseline Hb (and a G&S at the very least.)
A chest X ray is usually available, and often the Cobb Angle may suggest the degree of cardiorespiratory dysfunction to expect.

Cobb Angles

- >40^{o} degrees are offered surgical stabilization. AIS will usually have no or very little no functional cardio respiratory limitation, or restrictive lung conditions
- >65^{o} healthy AIS patients begin to experience some restrictive pattern pulmonary disease (on PFTs), with minor functional limitation subjectively noted.
- >100^{o} may experience dyspnoea, functional limitation, and reduced capacity to cough and clear secretions
- >124^{o} severe functional impingement and limitation of activities experienced by patients. The severity of the curve results in severe alveolar hypoventilation, V/Q mismatching, and eventual respiratory failure, pulmonary hypertension, with consequential right ventricular decompensation.

Thus AIS with Cobb angles greater than 65^{o} should have lung function tests, and those who are symptomatic, or with Cobb angles >100^{o}, LFTs as well as ABG should be considered for adequate anaesthetic planning. Severe scoliosis and evidence of right ventricular hypertrophy or dysfunction, ought to have more thorough investigation like an echo over and above pulmonary function tests and a baseline ABG and ECG.

NIS have greater functional impediment than suggested by their Cobb Angle as a result of co-existing neuromuscular weakness and possible cardiorespiratory complications of their underlying illnesses. Assessment effort tolerance in this group can be challenging in presence if mental delay, or limited ambulation. In this light, LFTs not only assess the impact of reduced chest wall compliance reflected by restrictive lung disease patterns, but FEV_1 provides an indication of patient's capacity to cough and adequately clear secretions post operatively and thus determines the degree of ICU support required post surgically.

ABGs, electrolyte measurements as well as baseline renal functions are routinely required for NIS as opposed to AIS, whose investigations are symptom and disease progression-dependant.

Echocardiography is necessary in NIS group, due to a higher prevalence of cardiac abnormalities. (Duchenne's muscular dystrophy is associated with cardiomyopathy).

A retrospective review of paediatric patients who had pulmonary function testing prior to spinal fusion demonstrated that patients with preoperative:

- FEV_1<40% predicted,
- vital capacity <60%,
- inspiratory capacity <30 mL/kg, or
- total lung capacity <60% were more likely to require prolonged postoperative mechanical ventilation than those patients who did not have them.

Preoperative testing can thus facilitate better anticipated post-operative placement as well as planning and decisions regarding multi-disciplinary support.

Pre-operative Optimization

Surgical correction of scoliosis deformity is ***non-urgent surgery***. It is advised to ensure patients' pre-operative baseline is as optimal as possible with regards to:

1. **Nutritional status**- NIS require better caloric supplementation. Better outcomes regarding post-operative wound healing
2. **Pre-operative anaemia**- haematinics, erythropoietin
3. **Pulmonary function**
   Rx underlying RTI and rebook as appropriate
   Optimization of reversible airways obstruction
   Preoperative physiotherapy and incentive spirometry
   NCPAP mask and device fitted and arranged pre op for patients with OSAS. (neuromuscular NIS)
   Planning for correct post-operative placement based on anticipated degree of respiratory support
4. **Optimise cardiovascular function**
   Mx of RVF, cardiomyopathy

5. **Pain management**
   NIS and severe AIS may experience chronic/ neuropathic pain
   Consulting with pain team for pre-operative analgesic plan that may be extended beyond post-operative period
6. NIS require pre-emptive multi-disciplinary involvement and co-ordination to streamline care.
7. **Premedication**
   Some anaesthetists do prescribe short acting benzodiazepines like midazolam preoperatively. It is best to avoid longer acting hypnotics as they delay emergence and some impede IOMN signals. (I personally favour IV Dexmedetomidine with monitors applied in the induction room as I am better able to time pharmacokinetics with IONM measurements and wake up testing. Other routes of administration also possible if sedation is required pre IV)
   EMLA is a consideration if an IV is to be secured before induction of anaesthesia.

Monitors and Equipment

In addition to standard ASA anaesthetic equipment:

- 2x IV lines with claves- one of which should be large bore in event of fluid/ blood resuscitation required
- A-line and transducer in order to facilitate serial ABG measurements to optimize ventilation, Hb as well as electrolytes.
- Convection warming blanket(s) and warmer(s), temperature probe
- TCI/ TIVA pumps
- BIS monitor
- Cell saver
- Group and Screen available at local Blood bank. (or Blood available in theatre if blood bank facilities are not within reasonable reach of hospital premises.)
- Wilson Frame/Jackson table or similar for optimal prone positioning, as well as head rings, gel supports and padding.
- Calf compressors/ TED stockings
- Reinforced ETT/ DLT/Bronchial blockers as determined by surgical approach and preference

Intra-operative Considerations

Intra-operative positioning and anaesthetic techniques depend on surgical approach, the need for IONM, attempts to minimise blood loss, patient baseline and post-op placement.

Surgical Approach

A. <u>Posterior Spinal Fusion</u>

- Prone positioning- Placing the patient in the prone position challenging and calls for planned, coordinated teamwork. Risks of disrupting anaesthesia and dislodgement of IV lines, ETT, as well as patient (sometimes staff) injury need to be anticipated.
- Suitable Jackson table, or Wilson frame as well as head supports and sufficient padding required
  In addition to the universal complications of surgery in the prone position, there is the added risk of post-operative visual loss in spinal surgery. These topics best studied separately.
- Greater blood loss than an anterior release approach
- Requires re enforced well secured ETT
- Parenteral analgesia can be supplemented with intra thecal morphine or epidural catheter for bupivacaine infusion at the end of operation. (not popular). Wound infusion catheters are also an option.

B. <u>Anterior Release Approach (AR)</u>

- Patient lies in lateral position, and theatre table is angulated for thoraco-lumbar approach.
- The surgeon may require access to upper thoracic spine, thus will require deflation of the lung on the surgical side. DLT or bronchial blocker will be needed. Alternatively, the surgeon may retract the lung gently. All considerations and principles of OLV need to be adhered to in order to prevent post op pulmonary complications.

- Analgesia: multimodal, parenteral as well as well as local anaesthetic by means of a wound infiltration catheter, rib blocks, paravertebral block.
- AR surgery associated with less blood loss than PSF.

C. Combined PIF and AR surgery
Associated with massive bloodloss.it is possible to stage procedures, thereby allowing patients time to recover from the impact of each approach

D. Endoscopic Minimal Access Approach
This approach may be used for anterior release or, more recently, posterior fusion surgery. This minimally invasive approach is still novel to most, and currently still presents a steep surgical learning curve. The assumption is that the advantage is less blood loss, shorter hospital stay, earlier mobilization, as well as less pain due to less muscle dysfunction in early post-op phase; and consequentially lower analgesic requirement. Currently endoscopic surgery does take much longer than the standard approach. Despite faster mobilization and return to function in the first month, no difference in outcomes over open surgery has been proven in the long run to date.

Temperature control

Large areas of exposure, lengthy surgical time, alongside massive bleeding and fluid shifts and peripheral vasodilation leading to poor conservation of core heat as a result of anaesthesia, are all issues contributing to heat loss. *Hypothermia is always easier to prevent than manage*. I encourage pre-warming from induction room, elevation of ambient theatre temperature, and the use of forced air warmers, warm IV fluids, blood warmers and the use of adhesive plastic to keep the patient dry as per literature.
Failure to manage heat loss results in:

- Hypothermia induced coagulopathy hence increased blood loss,
- Increased myocardial demands, and worsened surgical stress factors
- Altered pharmacokinetics
- Poor wound healing
- Diminished TcMEP signals
- Delayed wake up

Please consider consulting the literature for more detail

Blood Conservation Strategies

Extensive soft tissue dissection, bone decortication, osteotomies, and instrumentation involved with surgical correction of AIS can lead to significant blood loss. Blood loss varies greatly, in PSF blood loss estimation average 400-1000mls as opposed to AR approach with an average of 300-500 mls. NIS patients, particularly those with connective tissue disorders and neuromuscular conditions have even greater blood losses (likely due to their abnormal dystrophin). Other factors thought to exacerbate bleeding include hypothermia-induced coagulopathy, poor patient positioning with venous engorgement of epidural plexus, as well as the number of vertebrae involved. Excessive perioperative blood loss places patients at risk for infection, hemodynamic instability, cardiopulmonary dysfunction, renal failure, and possible death. Also, allogenic blood transfusion presents additional risks for patients, including potential blood-borne infection, transfusion reaction, electrolyte imbalance, coagulopathy, and increased risk of SSI. Measures should be taken to reduce the risk of bleeding and deal with potential haemorrhage, and decrease the rates of allogenic transfusions:

Pre admission

- Ensure patient's pre-op Hb is optimal and supplement with iron or erythropoietin as appropriate. Trials suggest as a bare minimum HB should be at least 2 g/dl above chosen TTV (transfusion trigger value)
- Preoperative autologous donation (not feasible for my centre)

Day of surgery

- Confirm Blood Bank has a G&S as well as sufficient valid sample (in case products required).

Prevent intra-operative losses

- Ensure perfect prone *positioning* to prevent engorgement epidural veins
- Maintain *normothermia*
- *Acute normovolaemic haemodillution.*
- *Targeted BP control*, appropriate to surgical stage, without sacrificing perfusion of vital organs and *optimising flow to spinal cord*. **Deliberate hypotension SBP<80mmHg is not advised.** This technique has been associated increased risk of post op visual loss, paralysis and ischaemia to vital organs (lung heart, kidney). *Moderate patient appropriate lowering MAP during the surgical approach in order to reduce intra-operative blood loss must be balanced with maintaining a MAP necessary for spinal cord perfusion.*
  Carefully controlled relative hypotension (aim for MAP reduced by 25% of normal baseline in healthy patients) during surgical exposure reduces intraoperative blood loss, and facilitates better surgical field, without compromising tissue perfusion, which should remain the primary priority. During critical stages of procedure, i.e. instrumentation, a higher MAP is favoured in order to ensure spinal cord perfusion. SCPP= MAP- (CVP +any extra impedance to blood flow including surgical force upon pedicle screw insertion). Currently our surgical team favours a MAP of **at least** 70mmHg -75mmHg provided TcMEPs remain unchanged.
- *Tranexamic acid* is an effective, safe, and cheap method to reduce operative blood loss in paediatric spine surgery and possibly reduces the rate of allogenic transfusions. The optimal dose and regimen of administration is still contentious. Higher vs lower dose studies suggest higher doses result in marginally reduced rates of bleeding, though many remain concerned about possible side effects. The use of Tranexamic acid made no difference when MAPs were above targeted thresholds upon initial dissection.
- *Transfusion trigger values,* in heathy AIS with an un-alarming intraoperative course, a more restrictive TTV of 7-8g/dl is accepted as more liberal triggers of 10 g/dl offered no additional benefit in routine surgery.
- *Point of care coagulation testing*- TEG use reduces the need for blood products and therefore they increase safety for patients.
- Cell salvage systems (*Cell Saver*) used intraoperatively to collect blood from the surgical field, filter debris, and provide a source of autologous blood for re-transfusion. has been shown to reduce the need for allogenic transfusion in paediatric spine surgery in studies where the collecting bowel had a smaller volume (150ml opposed to 250ml) and the surgery was longer than 6 hours or EBL was >30% of EBV.
- *Surgical technique* The proper sequence of intraoperative steps associated with reduced blood loss includes:
    - Meticulous use of with cautery or diathermy, for soft tissue bleeding
    - Use of topical haemostatic agents,
    - Plan for and manage bone bleeding post decortication with application of bone.
    - Details on this are beyond my scope.

Additional reading

1. Theusinger, O. M., & Spahn, D. R. (2016). Perioperative blood conservation strategies for major spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 41–52. http://doi.org/10.1016/j.bpa.2015.11.007
2. Verma, K., Kohan, E., Ames, C. P., Cruz, D. L., Deviren, V., Berven, S., & Errico, T. J. (2015). A Comparison of Two Different Dosing Protocols for Tranexamic Acid in Posterior Spinal Fusion for Spinal Deformity: A Prospective, Randomized Trial. *International Journal of Spine Surgery*, *9*, 65. http://doi.org/10.14444/2065

Intra-Operative Neuro-monitoring

This is a vast topic, and while I have outlined the essential points to note, I do recommend reading at least one of the suggested articles. Become more familiar with IONM modalities, contra-indications and possible side effects, as well as best anaesthetic techniques utilised.

Additional reading

1. Wijesingha, S., Smith, C., Levin, D. N., Strantzas, S., & Steinberg, B. E. (2019). Intraoperative neuromonitoring in paediatric spinal surgery. *Orthopaedics and Trauma*, *31*(6), 165–171. http://doi.org/10.1016/j.bjae.2019.01.007 (short and neat)
2. Bithal, P. (2014). Anaesthetic considerations for evoked potentials monitoring. *Journal of Neuroanaesthesiology and Critical Care*, *1*(1), 2–12. http://doi.org/10.4103/2348-0548.124832 (detailed)
3. Spinal cord monitoring, UCT Department of Anaesthesia, Part I Refresher Course, 2017, Cape Town.

4. Van Der Walt, J. J. N., Thomas, J. M., & Figaji, A. A. (2013). Intraoperative neurophysiological monitoring for the anaesthetist: Part 1: A review of the theory and practice of intraoperative neurophysiological monitoring. *Southern African Journal of Anaesthesia and Analgesia*, *19*(3), 139–144. (overall view, conscience)

Correction of spinal deformity places the spinal cord and the nerve roots at risk for injury, which may result in loss of motor and/or sensory function. Intraoperative monitoring of corticospinal tract and/or dorsal column allows for early identification of potential neurological impairment and subsequent intervention to prevent this becoming a permanent injury.

Of the variety of IONM modalities available, using Transcranial Motor Evoked Potentials (TcMEP) and Somatosensory Evoked Potentials (SSEPs) is regarded as the standard of care for patients undergoing major spinal surgery. It also provides continuous feedback and to an extent, this replaces the *Stagnara wake up test*, which can be dangerous, time consuming and only provides information at a specific point in time (snapshot vs real time ccTV cam). SSEP+ TcMEP **and a neurophysiologist** is considered the best standard of care, especially with complex spine tumour resection.

For the purpose of corrective spinal surgery, the use of *TcMEPs alone* or in combination with multimodal monitoring; as opposed to SSEPs alone, was found to be *more sensitive to alert the surgical team* to possible breach of spinal cord integrity. Thus, for the purpose of simplicity and cost saving, it is still considered safe and effective to use TcMEP alone for scoliosis corrective surgery. TcMEP involve application of electrical transcranial stimulation of CTS tract and measuring the latencies and amplitudes of the responses in distal limb muscle group (cMAPs).

Compared with SSEPs, TcMEPs are more sensitive to reduced spinal cord blood flow secondary to vascular insult or hypotension. In addition, MEPs change earlier than the SSEP signals, which facilitates quicker diagnosis of impending spinal-cord injury. SSEPs are essentially averaged signals and provide less real time feedback, (not as delayed as a wake up test).

Where MEPs fail, however, is that they become less effective when used on immature neurological tracts, (unreliable in very young <6 years) and they are more sensitive than SSEPs to anaesthetic techniques. Surgical teams using only TcMEPs have a lower threshold for requesting intra operative wake up testing when signalling becomes aberrant despite surgical and physiological optimisation, hence it is my personal practice to ensure all patients are consented for this pre operatively.(“In case our normal tests fail”) Also, while some surgeons do not re-test neurological function after wound closure, and so patients are able to rouse slowly in high care, the orthopaedic team at our institution prefers a rapid post-operative emergence in order to test whether the patient is able to move distal limbs on command. (Not if patient is unable to obey commands, like the very young or NIS who have developmental delays.) Another failure with IOMN is the lack of a consensus and variation in protocols or what is considered alert criteria. Ultimately the alert criteria vary across institutions and surgical preference.

Conduct of Anaesthesia with IONM

The success of IOM procedures is partly governed by the level of coordination between the surgical, anaesthetic and neurophysiological teams and by understanding how physiological as well as pharmacological factors impact neurological signalling**.**

Most anaesthetic agents result in a dose related depression of SSEPs and even more so TcMEPs. The inhibitory effect of inhalation-based anaesthetics on the firing rates of anterior horn cells is well described, and it results in a reduction of TcMEPs recorded from peripheral muscles.
These effects may extend beyond the discontinuation of the agent, and so may interfere with establishment of TcMEP baseline readings done at prior to incision. This is less of a problem when SSEPs are used in conjunction with TcMEPs as SSEPs are more robust with low doses of volatile agents. Muscle relaxants abolish MEP signals via disruption of NMJ and are also avoided when monitoring is in use.

A Propofol-based total intravenous anaesthetic (TIVA/TCI) is generally favoured as this approach has the least effect on neuro-monitoring. Given the request for rapid emergence at the end of the case, and the cumulative effects of a lengthy Propofol infusion, it is imperative that one is cognisant of the decrement time of the TCI model used, and that the infusion is discontinued timeously. Much literature is available regarding the co-administration of Midazolam, Ketamine or Dexmedetomidine infusions as a Propofol-sparing technique, to decrease its total cumulative dose, with varying success. These

agents may delay post-operative wake up as well as affect TcMEP signalling if higher doses are used. It becomes a delicate balance between signal optimisation and adequate anaesthetic depth. Scoliosis corrective surgery is a painful procedure and a balanced multi-modal analgesic technique is always advised. This includes a combination of short and best choice of opiate i.e. Sufentanyl vs Remifentanil for intra operative use. I feel each of the two have their own merit and no studies suggest improved outcome based on either. Personally I favour Remifentanil due to its property of rapid titration, however I am aware of its role in OIH and attempt to counteract this. I also use long-acting opioids (morphine), as well as analgesic doses of Ketamine and IV Paracetamol. Some practitioners incorporate Lignocaine infusions (with or without $MgSO_4$), though this is not my practice due to the cumulative effects.

Summary of Anaesthetic Factors affecting Intra-operative TcMEP

Pharmacological

Drug	Latency	Amplitude	Notes
Volatile agents	↑	↓	Isoflurane > sevoflurane or desflurane Effect at 0.3-0.5 MAC
Nitrous oxide	↑	↓	Potent effect on neuronal nicotinic acetylcholine receptors. Avoid
Propofol	↑ Dose-dependent	↑ Dose-dependent	Rapid metabolism allows titration during TIVA
Thiopentone	↑↑	↓↓	CMAP very sensitive to barbiturates
Etomidate	↓	↑	Use in combination with TIVA to enhance EP quality
Ketamine	↑	↑	Ketamine ↑ ICP Use in combination with TIVA to enhance EP quality
Midazolam	↑↑	↓↓	Prolonged marked suppression of MEPs
Dexmedetomidine	↑	↓	Used in combination with other agents to decrease dose of TIVA
Fentanyl	Preserved at high doses Fentanyl at 60 µg/kg preserved SSEP	Dose-dependent ↓ Fentanyl at 50 µg/kg BAEPs preserved	Preserved SSEPs and MEPs at high doses
Pethidine	Preserved EPs at high dose	SSEP amplitude	
Morphine	↑ Dose-dependent	↓	
Remifentanyl	Preserved	↓	Remifentanyl used in combination with isoflurane or TIVA. Rapid metabolism allows titration
Intrathecal opioids	SSEPs unaffected	Unaffected	
Muscle relaxants	MEPs abolished	MEPs abolished	Used to prevent patient movement during transcranial MEPs Used to ↓ EMG interference Keep T1 at 10-20% of baseline response Keep train of four at 2/4 twitches

Non-pharmacological

Parameter	Effect
Blood flow	**MAP <60 mm Hg is an important risk factor for spinal-cord injury during spinal deformity surgery. Autoregulation may not ensure adequate spinal-cord perfusion during the increased stress placed on the spinal cord with corrective surgery. In children > 6yrs, its preferable to maintain MAP about 70mmHg or more during instrumentation.**
Blood rheology	**Anaemia decreases oxygenation of spinal cord. Ultimately it's a balanve between rheology as well as oxygen carrying capacity. Minimum transfusion targets depend on patient co morbid illness. Healthy AIS most use 7 g/dl as a TT if uneventful intra op course. In presence of nerurological injury, current practice suggests maintaining HB above 8-9g/dl**
Blood glucose s-Sodium s-Potassium	**Keep within normal values to ensure adequate neuronal function**
Temperature	**Signal loss of amplitude, and increased latency occurs with hypothermia. Maintaining normothermai is as important for EP signal as patient outcome relating to its adverse effects on patient physiology and blood loss. Cold irrigation of neuronal structures alters EPs**
Intracranial pressure	**↓ Amplitude and ↑ latency with raised intracranial pressure. Late**
Ventilation	**Hypoxaemia alters EPs by means of global ischemia Severe hypocardia is associated CNS vasoconstriction, thereby reducing blood flow and consequently EPs**

Benzodiazepines
Small studies found no difference in EP signals when midazolam was co administered in small doses with propofol TCI. Given that midazolam may increase time to emergence at the end of a case and its impact on the possibility of a wake up test, it is not my personal practice to use this technique.

Ketamine
Ketamine will increase SSEP and TcMEP amplitudes, and it is useful when administered in low doses, as an analgesic, a co hypnotic and also to amplify signals which may decline after lengthy anaesthetics, as a result of excessive accumulation. The literature does mention ketamine-based anaesthetics, but this method makes anaesthetic depth as well as EEG reading difficult to interpret. In higher doses, it will impede emergence.

Anticonvulsants
Gabapentin and Pregabalin are used in spine surgery patients to treat neuropathic pain. These medications bind the α^2 subunit of calcium-gated ion channels and decrease sensory neuron excitability by inhibiting the release of neurotransmitters. These agents may be effective for postoperative analgesia, treatment of spastic pain, preoperative anxiolysis, and prevention of chronic pain. The use of these drugs is thought not to severely affect IONM if used pre operatively for analgesia.

Small trials involving Gabapentin indicate conflicting results. It is suggested that this drug may result in better pain scores and less opiate consumption within first 28 hours post operatively. Another study indicated that there was no difference in post-operative pain when Gabapentin was initiated preoperatively.

Due to the side effect profile of these drugs our institution does not encourage route administration, but rather to reserve prescription for opiate intolerant patients after thorough consultation with our pain team. It is thus reserved for select cases at their discretion.

α Adrenergic Agonists
α^2agonists have become increasingly popular as an adjunct in anaesthesia.
Aside from their analgesic, anxiolytic and sympatholytic benefits, rat studies indicate they may be facilitating better neurological recovery in the context of ischemia. These studies have not been extended to clinical trial. Not many definitive studies exist concerning the effect on IONM when used in combination with a balanced Propofol TIVA.

- **Clonidine**

While extensively used during the peri-operative period as an analgesic adjunct, only one small study observed its effect on IONM when administered during anaesthesia. A single IV bolus of 1-2 ug/kg at the start of the procedure was found to obliterate TcMEPs, not indirectly related to decrease in MAP. Thus it is not advised for use intra operatively.

- **Dexmedetomidine**

It is 8 times more selective than clonidine for α^2receptor. Sedation properties are mediated via agonism of α^2-adrenoceptors primarily in the locus coeruleus of the pons where it results in dose-dependent inhibition of norepinephrine release. It is postulated that this results in disinhibition of the ventrolateral preoptic nucleus which then releases inhibitory neurotransmitters. It is likely that effects in the pain pathway are mainly at the level of the spinal cord where stimulation of α^2 receptors in the substantia gelatinosa of the dorsal horn reduces the release of nociceptive neurotransmitters such as substance P. While we know its effects occur pre and post synaptically in the spinal cord, no definitive data is available regarding its effect on IONM. To date, a summary of the literature regarding its use in spinal cord corrective surgery suggests:

- It is both opiate and Propofol sparing in opiate/Propofol- TIVA
- Trials have compared intra operative Dexmedetomidine infusion followed by 24hour infusion post op, vs Ketamine or saline placebo in patients going for major spine surgery. The pain free interval was slightly in favour for Ketamine and both drugs resulted in decreased opiate consumption. Follow up studies using higher doses of Dexmedetomidine have indicated no benefit. More detailed larger studies wrt spine surgery required
- Small trials suggest it may prevent hyperalgesia related to Remifentanil use. Dexmedetomidine has been reported to depress NMDA receptor-mediated synaptic transmission in animal models

as well as reduce spinal NMDA receptor phosphorylation in the dorsal horn, which was found to be up-regulated after remifentanil infusion

- Experimental studies show Dexmedetomidine has neuroprotective effects in hypoxic–ischaemic and traumatic brain injury models in rats. This neuroprotection appears to be afforded by the action of the drug on α^{2A}-receptors and at imidazoline receptors. The clinical relevance of these findings is yet to be fully evaluated.
- It does facilitate a smoother emergence, hence is a popular choice of drug in Awake craniotomy procedures. This may be extrapolated to wake up testing in scoliosis surgery.
- Furthermore, there are a few reports questioning post-operative disorder sleep reported up to six months' post wake up testing being more prevalent with Remifentanil-Propofol anaesthetics opposed to Sufentanyl-Propofol. Studies with knee arthroplasty patients indicated Dexmedetomidine MAY decrease the incidence of sleep disturbance. While no randomised prospective trials have been published with regards to spine surgery, I wonder whether Dexmedetomidine counteracts the negative effect of Remifentanil in this regard. Currently my clinical practice suggests this however my sample size is miniscule and so scientifically unproven.
- Orthopaedic clinical trials question its use as a hypotensive agent to minimise intra operative bleeding- quite possibly only due to its effect on MAP and other drugs afford the same benefit.

Multiple small studies indicate conflicting outcomes regarding the effect of Dex on IONM. Each centre has their own Propofol, opiate and sometimes even inhalational anaesthetic protocol, and it becomes difficult to form comparisons without standardization, or when the trial includes a drug known to depress IONM. As a consequence, the varying trial results have led to a cautious approach when using this drug.

Post-Operative Care

Scoliosis correction involves prolonged surgery with significant blood loss and potentially difficult postoperative pain management. Most AIS patients are extubated immediately after surgery to enable early neurological assessment. Invasive monitoring is continued in a high dependency area. There is great emphasis on early physiotherapy, and downscaling of parental to oral non-opioid based analgesia to ensure rapid discharge and return to function. Children with neuromuscular disease or significantly reduced cardio-respiratory capacity require an intensive care environment for closer monitoring, ventilation support and to allow haemodynamic, temperature and metabolic abnormalities to be corrected.

Pain Management

Good postoperative analgesia is essential to allow frequent physiotherapy and early mobilization, and so reduce the risk of respiratory complications. Post-operative pain management requires a multimodal approach, combining simple analgesics, systemic opioids, as well as a variety of adjuncts, anticonvulsants, α_2 agonists and regional anaesthesia to reduce the burden of side effects related to opiate heavy analgesic plans.

Intra-thecal opiate and intra operative surgical epidural placement
Studies have indicated that small does of intra thecal morphine does not affect IONM if placed at commencement of surgery. Epidural placement under surgical vision or paravertebral blocks/catheter, post procedure, have been used, however is not without risks. While placement of epidural under direct vision was favoured previously, currently most prefer to avoid neuraxial techniques, since it impedes re testing of motor function on wake up and also masks symptoms of post-operative development of neurological impairment. Ross et al demonstrated lower pain scores when using wound infusion catheters specifically in AIS. Our current practice is subcutaneous infiltration with Bupivacaine but no indwelling catheter on the basis of surgical preference.
There is growing evidence to support the use of several non-opioid pharmacological analgesic classes including Gabapentinoids, IV paracetamol, and nonsteroidal anti-inflammatory drugs, after major orthopaedic surgery.

NSAIDS

Ketorolac has been shown to improve analgesia and reduce opioid consumption while reducing both opioid-related gastrointestinal side effects and LOS in general paediatric orthopaedic and paediatric spinal fusion patients. Although some have cautioned against the use of ketorolac in major orthopaedic surgery because of concerns about platelet dysfunction and impaired bone healing, there is growing evidence that ketorolac is safe.

Dexmedetomidine/Ketamine
The effects of DEX on pain scores were positive but not overwhelming as previously mentioned. Further study is necessary to determine the clinical usefulness and cost-effectiveness of using DEX routinely in this patient population. A definitive recommendation for the best pain control regiment cannot be made from the results of this study. I allow the operative Dex infusion to continue to completion in High Care at a lowered rate.
Ketamine is continued either as infusion (0.25mg/kg/hr) or via PCA.

IV Paracetamol
Currently our institution aims to encourage rapid down scale from parenteral opiates, Ketamine and Dexmedetomidine to a PCA and IV paracetamol the day after surgery(D1), followed by oral analgesia with rescue IM opiate for break through pain thereafter. The use of a Fentanyl patch, may be favoured where available, to reduce the further impedance to mobility caused by the PCA. This only pertains to healthy AIS with uncomplicated intra operative courses, and is ultimately dependant on patient pain scores. Prolonged use of opiates results in increased risk of post-op ileus and superior mesenteric artery (SMA) syndrome so mobilization should be encouraged as soon as feasible. At least one regular anti-emetic, such as Ondansetron, should be available. Laxatives may counteract constipation in longstanding opiate use.

Additional reading
Dunn, L. K., Durieux, M. E., & Nemergut, E. C. (2016). Non-opioid analgesics: Novel approaches to perioperative analgesia for major spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 79–89. http://doi.org/10.1016/j.bpa.2015.11.002

Early mobilization and physiotherapy

Given that the majority of AIS patients are otherwise healthy, high-functioning children preoperatively, returning them to their preoperative level of function or better in a timely fashion is critically important. In a survey conducted at Shriners hospital, spinal deformity surgeons published in 2007 revealed that, within the Shriners system, therapy for AIS patients was aimed at moving patients early, with the goal of sitting on POD1, standing on POD2, and walking on POD2 or 3. Tarrant et al's prospective study of AIS patients undergoing PSF found that, on average, these patients return to school full-time 10 weeks postoperatively, and over 50% returned to unrestrained physical activity by 24 weeks postop. Early drain removal on POD1 has been found to expedite mobilization and decrease patient discomfort.

Peri-operative Complications

Rapid assessment and treatment of acute postoperative complications including coagulopathy, myocardial injury, acute stroke, VTE, ileus, and/or acute kidney injury can circumvent major morbidity or mortality.

Post-operative blindness
- Anterior and posterior ischaemic optic neuritis
- Central retinal artery occlusion
- Cortical blindness
- Corneal injury

Additional reading
Kla, K. M., & Lee, L. A. (2016). Perioperative visual loss. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 69–77. http://doi.org/10.1016/j.bpa.2015.11.004

Pulmonary Complications can contribute to prolonged hospital stays, especially among patients with pre-existing pulmonary disease. Scoliosis is associated with progressive restrictive lung disease, and thoracic surgery impedes respiration due to postoperative pain, anaesthesia, and immobilization.

Pneumonia, respiratory failure requiring prolonged mechanical ventilation, bronchospasm, and atelectasis are the common complications seen following PSF; however, these pulmonary complications are much more common among neuromuscular NIS patients. Nonetheless, AIS patients with a history of poor exercise tolerance, a curve exceeding 80°- 100^{o}, or a history of severe reactive airway disease stand to benefit from a pre-operative pulmonary evaluation, as previously mentioned. As previously mentioned, pre-operative LFTs may provide an indication of the degree of post-operative respiratory support that may be required.
Postoperative fluid management requires careful attention. Some ongoing blood loss is likely, and paralytic ileus is possible. Decreased urine output may also result from syndrome of inappropriate antidiuretic hormone, so injudicious use of crystalloid may result in further ileus, nausea, pulmonary oedema. Furthermore, poor intra operative maintenance of renal blood flow may result in AKI. Each patient should have their volume status regularly assessed and ongoing losses should be replaced. A full blood count, coagulation studies and serum electrolytes measurement should be repeated after surgery.

Early **return to nutrition** is desirable.

Prevent surgical site infection by administering the correct prophylactic antibiotic (Kefzol) before surgical incision. This should be repeated 4 hourly intra operatively as well as 8 hourly for 24 hours post op.

Postoperative thromboprophylaxis
Although a well-known complication of adult spine surgery venous thromboembolism is an infrequently reported complication in paediatric scoliosis surgery. The only large series on this topic queried a large nationwide database (the National Inpatient Sample) on in-hospital VTE following spine fusion surgery in patients under the age of 18. The incidence of VTE was found to be approximately 21 events per 10,000 spine fusion surgeries. Risk factors included syndromic or congenital scoliosis, as well as increasing age and spine fusion surgery for fracture. However, this series likely underestimates the true incidence of VTE, as it only examined in-hospital events, and VTE may develop in the weeks and months following spine surgery. At this time, there are no formal recommendations regarding perioperative chemoprophylaxis for AIS children < 13yrs, especially since there is mobilization from the first day. Mechanical devices may be considered. Post pubescent AIS, or those with additional risk factors for VTE, mechanical prophylaxis recommended in first 24 hours and thereafter Clexane prophylactic dose may be considered.

Skin breakdown or pressure ulcers commonly affect the tongue, nose, chin knees and toes. Please refer to the suggested reading for more detail.

Peripheral nerve injury as result of poor positioning
Most commonly affected include brachial plexus, medial and ulnar nerve. New-onset neurologic deficits referable to the spine should prompt emergent imaging to rule out spinal cord or nerve root compression from a hematoma. New-onset neurologic deficits referable to the brain/brainstem should prompt emergent CT (or MRI) and CTA (or MRA) to look for large vessel occlusion.

Additional reading
Swann, M. C., Hoes, K. S., Aoun, S. G., & Mcdonagh, D. L. (2016). Postoperative complications of spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 103–120. http://doi.org/10.1016/j.bpa.2016.01.002

General nice reads for a summary on the whole topic
1. Wijesingha, S., & Smith, C. (2017). Anaesthetic considerations in spinal deformity surgery. *Orthopaedics and Trauma*, *31*(6), 422–424. http://doi.org/10.1016/j.mporth.2017.09.014
2. Kynes, J. M., Evans, F. M., Hodgetts, V., & Wilson, K. (2015). Surgical Correction of Scoliosis Anaesthetic Considerations. *World Anaesthesia Tutorial of the Week*, (July), 1–7.

References

1. D., A., H.K., M., & P.R., C. (2016). A comparative evaluation of Dexmedetomidine with midazolam as an adjuvant to propofol anaesthesia for spinal surgical procedures under motor evoked potential monitoring. *Anaesthesia, Pain and Intensive Care*. Retrieved from http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L612154604
2. Wahlquist, S., Wongworawat, M., Nelson, S., Teng, W. N., Tsou, M. Y., Chen, P. T., … Lethbridge, M. (2017). Clonidine administration during intraoperative monitoring for paediatric scoliosis surgery: Effects on central and peripheral motor responses. *Spine Deformity*, *6*(4), 422–424. http://doi.org/10.1016/j.jspd.2018.01.001
3. Swann, M. C., Hoes, K. S., Aoun, S. G., & Mcdonagh, D. L. (2016). Postoperative complications of spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 103–120. http://doi.org/10.1016/j.bpa.2016.01.002
4. Ajmi, T., Saeed, H., Faryan, K., & Akeel., A. (2017). Efficacy of Tranexamic Acid in Reducing Blood Loss and Blood Transfusion in Idiopathic Scoliosis; a Systematic Review and Meta-Analysis. *International Journal of Advanced Research*, *5*(2), 1024–1035. http://doi.org/10.21474/ijar01/3248
5. Kla, K. M., & Lee, L. A. (2016). Perioperative visual loss. *Best Practice and Research:* Ailon, T., Sure, D. R., Smith, J. S., & Shaffrey, C. I. (2016). Surgical considerations for major deformity correction spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 3–11. http://doi.org/10.1016/j.bpa.2015.11.005
6. *Clinical Anaesthesiology*, *30*(1), 69–77. http://doi.org/10.1016/j.bpa.2015.11.004
7. Ailon, T., Sure, D. R., Smith, J. S., & Shaffrey, C. I. (2016). Surgical considerations for major deformity correction spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 3–11. http://doi.org/10.1016/j.bpa.2015.11.005
8. Verma, K., Kohan, E., Ames, C. P., Cruz, D. L., Deviren, V., Berven, S., & Errico, T. J. (2015). A Comparison of Two Different Dosing Protocols for Tranexamic Acid in Posterior Spinal Fusion for Spinal Deformity: A Prospective, Randomized Trial. *International Journal of Spine Surgery*, *9*, 65. http://doi.org/10.14444/2065
9. Neira, V. M., Ghaffari, K., Bulusu, S., Moroz, P. J., Jarvis, J. G., Barrowman, N., & Splinter, W. (2016). Diagnostic accuracy of neuromonitoring for identification of new neurologic deficits in paediatric spinal fusion surgery. *Anaesthesia and Analgesia*, *123*(6), 1556–1566. http://doi.org/10.1213/ANE.0000000000001503
10. Ho, R., & Irwin, M. G. (2018). Anaesthesia for major spinal surgery. *Anaesthesia and Intensive Care Medicine*, *19*(4), 159–163. http://doi.org/10.1016/j.mpaic.2018.01.012
11. Sadhasivam, S., Boat, A., & Mahmoud, M. (2009). Comparison of patient-controlled analgesia with and without Dexmedetomidine following spine surgery in children. *Journal of Clinical Anaesthesia*, *21*(7), 493–501. http://doi.org/10.1016/j.jclinane.2008.12.017
12. Lerman, J. (2011). Perioperative management of the paediatric patient with coexisting neuromuscular disease. *British Journal of Anaesthesia*, *107*(SUPPL. 1), 79–89. http://doi.org/10.1093/bja/aer335
13. Choudhury, M. Z. B., Tsirikos, A. I., & Millner, P. A. (2017). Neuromuscular scoliosis: clinical presentation, types of deformity, assessment and principles of treatment. *Orthopaedics and Trauma*, *31*(6), 350–356. http://doi.org/10.1016/j.mporth.2017.09.005
14. Fletcher, N. D., Marks, M. C., Asghar, J. K., Hwang, S. W., Sponseller, P. D., & Newton, P. O. (2018). Development of Consensus Based Best Practice Guidelines for Perioperative Management of Blood Loss in Patients Undergoing Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis. *Spine Deformity*, *6*(4), 424–429. http://doi.org/10.1016/j.jspd.2018.01.001
15. Teles, A. R., Ocay, D. D., Bin Shebreen, A., Tice, A., Saran, N., Ouellet, J. A., & Ferland, C. E. (2018). Evidence of impaired pain modulation in adolescents with idiopathic scoliosis and chronic back pain. *Spine Journal*, *19*(4), 677–686. http://doi.org/10.1016/j.spinee.2018.10.009
16. Menga, E. N., Spessot, G. J., & Bendo, J. A. (2015). Anaesthesia and neuromonitoring. *Seminars in Spine Surgery*, *27*(4), 197–200. http://doi.org/10.1053/j.semss.2015.04.003
17. Yoshihara, H., Paulino, C., & Yoneoka, D. (2018). Predictors of Increased Hospital Stay in Adolescent Idiopathic Scoliosis Patients Undergoing Posterior Spinal Fusion: Analysis of National Database. *Spine Deformity*, *6*(3), 226–230. http://doi.org/10.1016/j.jspd.2017.09.053
18. De la Garza-Ramos, R., Samdani, A. F., Sponseller, P. D., Ain, M. C., Miller, N. R., Shaffrey, C. I., & Sciubba, D. M. (2016). Visual loss after corrective surgery for paediatric scoliosis: incidence and risk factors from a nationwide database. *Spine Journal*, *16*(4), 516–522. http://doi.org/10.1016/j.spinee.2015.12.031
19. Pieters, B. J., Anderson, J. T., Price, N., Anson, L. M., & Schwend, R. M. (2018). Low-Dose Versus High-Dose Postoperative Naloxone Infusion Combined With Patient-Controlled Analgesia for Adolescent Idiopathic Scoliosis Surgery: A Randomized Controlled Trial. *Spine Deformity*, *6*(4), 430–434. http://doi.org/10.1016/j.jspd.2018.01.005
20. Perez-Ferrer, A., Gredilla-Díaz, E., de Vicente-Sánchez, J., Navarro-Suay, R., & Gilsanz-Rodríguez, F. (2015). Characteristics and quality of intra-operative cell salvage in paediatric scoliosis surgery. *Revista Española de Anestesiología y Reanimación (English Edition)*, *63*(2), 78–83. http://doi.org/10.1016/j.redare.2015.10.003
21. El-Gohary, M. M., & Arafa, A. S. (2010). Dexmedetomidine as a hypotensive agent: Efficacy and hemodynamic response during spinal surgery for idiopathic scoliosis in adolescents. *Egyptian Journal of Anaesthesia*, *26*(4), 305–311. http://doi.org/10.1016/j.egja.2010.07.001
22. Adogwa, O., Elsamadicy, A. A., Sergesketter, A. R., Ongele, M., Vuong, V., Khalid, S., … Bagley, C. A. (2018). Interdisciplinary Care Model Independently Decreases Use of Critical Care Services After Corrective Surgery for Adult Degenerative Scoliosis. *World Neurosurgery*, *111*, e845–e849. http://doi.org/10.1016/j.wneu.2017.12.180
23. Haber, L. L., Womack, E. D., Sathyamoorthy, M., Moss, J. A., & Shrader, M. W. (2018). Who Needs a Pediatric Intensive Care Unit After Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis? *Spine Deformity*, *6*(2), 137–140. http://doi.org/10.1016/j.jspd.2017.08.006

24. Verma, K., Lonner, B., Dean, L., Vecchione, D., & Lafage, V. (2013). Reduction of mean arterial pressure at incision reduces operative blood loss in adolescent idiopathic scoliosis. *Spine Deformity*, *1*(2), 115–122. http://doi.org/10.1016/j.jspd.2013.01.001
25. Levin, D. N., Strantzas, S., & Steinberg, B. E. (2019). Intraoperative neuromonitoring in paediatric spinal surgery. *BJA Education*, *19*(5), 165–171. http://doi.org/10.1016/j.bjae.2019.01.007
26. da Rocha, V. M., de Barros, A. G. C., Naves, C. D., Gomes, N. L., Lobo, J. C., Villela Schettino, L. C., & da Silva, L. E. C. T. (2015). Use of tranexamic acid for controlling bleeding in thoracolumbar scoliosis surgery with posterior instrumentation. *Revista Brasileira de Ortopedia (English Edition)*, *50*(2), 226–231. http://doi.org/10.1016/j.rboe.2015.03.007
27. Wenk, M., Pöpping, D. M., Chapman, G., Grenda, H., & Ledowski, T. (2013). Long-term quality of sleep after remifentanil-based anaesthesia: A randomized controlled trial. *British Journal of Anaesthesia*, *110*(2), 250–257. http://doi.org/10.1093/bja/aes384
28. Sarwahi, V., Wendolowski, S., Galina, J. M., Lo, Y., & Amaral, T. D. (2017). The Learning Curve of Minimally Invasive Surgery in Adolescent Idiopathic Scoliosis. *The Spine Journal*, *17*(10), S234. http://doi.org/10.1016/j.spinee.2017.08.132
29. Thompson, M. E., Kohring, J. M., McFann, K., McNair, B., Hansen, J. K., & Miller, N. H. (2014). Predicting excessive hemorrhage in adolescent idiopathic scoliosis patients undergoing posterior spinal instrumentation and fusion. *Spine Journal*, *14*(8), 1392–1398. http://doi.org/10.1016/j.spinee.2013.08.022
30. Wijesingha, S., Smith, C., Levin, D. N., Strantzas, S., & Steinberg, B. E. (2019). Intraoperative neuromonitoring in paediatric spinal surgery. *Orthopaedics and Trauma*, Scott-Warren, V. L., & Sebastian, J. (2016). Dexmedetomidine: its use in intensive care medicine and anaesthesia. *BJA Education*, *16*(7), 242–246. http://doi.org/10.1093/bjaed/mkv047*31*(6), 165–171. http://doi.org/10.1016/j.bjae.2019.01.007
31. Liu, J. M., Fu, B. Q., Chen, W. Z., Chen, J. W., Huang, S. H., & Liu, Z. L. (2017). Cell Salvage Used in Scoliosis Surgery: Is It Really Effective? *World Neurosurgery*, *101*, 568–576. http://doi.org/10.1016/j.wneu.2017.02.057
32. Calderón, P., Deltenre, P., Stany, I., Kaleeta Maalu, J. P., Stevens, M., Lamoureux, J., … Dachy, B. (2018). Clonidine administration during intraoperative monitoring for pediatric scoliosis surgery: Effects on central and peripheral motor responses. *Neurophysiologie Clinique*, *48*(2), 93–102. http://doi.org/10.1016/j.neucli.2017.11.001
33. Dunn, L. K., Durieux, M. E., & Nemergut, E. C. (2016). Non-opioid analgesics: Novel approaches to perioperative analgesia for major spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 79–89. http://doi.org/10.1016/j.bpa.2015.11.002
34. Entwistle, M. A., & Patel, D. (2006). Scoliosis surgery in children. *Continuing Education in Anaesthesia, Critical Care and Pain*, *6*(1), 13–16. http://doi.org/10.1093/bjaceaccp/mki063
35. Theusinger, O. M., & Spahn, D. R. (2016). Perioperative blood conservation strategies for major spine surgery. *Best Practice and Research: Clinical Anaesthesiology*, *30*(1), 41–52. http://doi.org/10.1016/j.bpa.2015.11.007
36. Van Der Walt, J. J. N., Thomas, J. M., & Figaji, A. A. (2013). Intraoperative neurophysiological monitoring for the anaesthetist: Part 1: A review of the theory and practice of intraoperative neurophysiological monitoring. *Southern African Journal of Anaesthesia and Analgesia*, *19*(3), 139–144. Retrieved from http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L369208501%5Cnhttp://www.sajaa.co.za/index.php/sajaa/article/view/1066/1270%5Cnhttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=22201181&id=doi:&atitle=Intraoperative+neurophysiologi
37. Muhly, W. T., Sankar, W. N., Ryan, K., Norton, A., Maxwell, L. G., DiMaggio, T., … Flynn, J. M. (2016). Rapid Recovery Pathway After Spinal Fusion for Idiopathic Scoliosis. *Pediatrics*, *137*(4), e20151568–e20151568. http://doi.org/10.1542/peds.2015-1568
38. Bithal, P. (2014). Anaesthetic considerations for evoked potentials monitoring. *Journal of Neuroanaesthesiology and Critical Care*, *1*(1), 2–12. http://doi.org/10.4103/2348-0548.124832
39. Kynes, J. M., Evans, F. M., Hodgetts, V., & Wilson, K. (2015). Surgical Correction of Scoliosis Anaesthetic Considerations. *World Anaesthesia Tutorial of the Week*, (July), 1–7.
40. Ho, R., & Irwin, M. G. (2018). Anaesthesia for major spinal surgery. *Anaesthesia and Intensive Care Medicine*, *19*(4), 159–163. http://doi.org/10.1016/j.mpaic.2018.01.012

Update on the Management of Predicted Difficult Airways
Safe strategies for 2019 and beyond

Prof. Ross Hofmeyr

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Introduction

All patients presenting for any form of anaesthesia (including procedures under local and regional/neuraxial blocks) should undergo adequate assessment of the airway prior to case commencement. Although the literature has demonstrated that preoperative airway assessment is far from perfect in preventing unanticipated airway difficulty[1-3] – and all anaesthetists should be ready to rescue an unanticipated failed attempt at airway management swiftly and effectively[4-7] – we must also have safe, evidence-based and practical approaches to managing patients in whom preoperative assessment predicts difficulty.[8]

The priority in selection of a strategy is patient safety, followed by considerations such as patient comfort, practitioner preference, and convenience. Although it may be argued that performing a technique with which we are familiar and comfortable is likely to be best for the patient, this should not be used as an excuse for unsafe, outdated, or "one size fits all" approaches to the difficult airway.

The critical questions when a patient has been determined to have predictors of airway difficulty are:

1. Which of the routine approaches to airway management (facemask ventilation, intubation, supraglottic airway placement, or front of neck airway access) are likely to be difficult?
2. Is this patient likely to desaturate rapidly despite pre-oxygenation if/when they become apnoeic (i.e. a "physiologically difficult airway")?
3. Should this patient's airway be secured before induction of anaesthesia?

Options for Management of Predicted Difficult Airways

Patients who have predictors for airway difficulty which *do not* preclude airway rescue using facemask ventilation, supraglottic device or surgical airway can usually be anaesthetised after ideal preparation and preoxygenation, and the airway managed asleep. Ideally, assistance by anaesthesia colleagues and the surgeon should be immediately available in the theatre. A strategy which includes video laryngoscopy and an endotracheal tube introducer (or dual endoscopy) on the first attempt, with rescue devices prepared and apnoeic oxygenation in place is reasonable. For instance, this strategy may be employed for a morbidly obese, bearded patient with high Mallampati grade and bull neck, who nonetheless has good neck mobility and mouth opening.

Patients with predicted difficulty where rescue options are limited, significant anatomical abnormality is present, or whom are likely to desaturate rapidly, should always prompt strong consideration of intubation with preservation of spontaneous respiration. Historically, a common recommendation was gas induction followed by intubation, with administration of neuromuscular blockers only once the airway was secure. However, this has been associated with high rate of failure.[1] If airway management with preservation of spontaneous ventilation is desirable, it is most safely achieved by awake intubation.[9] For example, a patient with ankylosing spondylitis who has fixed neck flexion and somewhat limited mouth opening will be a challenging intubation, and supraglottic or front-of-neck rescue will be difficult or impossible. Although it may be feasible to maintain oxygenation with a facemask, if this also proves impossible the situation will be dire. To borrow a concept from Slinger, the "NPIC" principle applies (*Noli pontes ignii consumere – Don't burn your bridges*), and a strategy of awake tracheal intubation by flexible endoscopy would be the safest primary approach.

Patients with severe airway difficulty who are failed by optimal attempts at awake tracheal intubation can be considered for awake tracheostomy or extracorporeal oxygenation, but this must be planned and executed electively.

The patient with major anatomical or physiological predictors of difficulty who is unable to tolerate awake airway management is a conundrum and challenge. This includes patients without the ability to comprehend and consent (children, intellectual disabilities and psychiatric patients), those with reduced level of consciousness due to trauma, illness, intoxicants or hypoxia, and patients who are distraught or combative. In these settings, it may be necessary to induce anaesthesia with preservation of spontaneous ventilation, or alternatively provide the patient with enough analgesia/sedation to tolerate the procedure. A re-emerging concept is the use of ketamine, either to provide analgo-sedation to facilitate preoxygenation ("DSI" – delayed sequence induction/intubation),[10] or in combination with airway topicalization to allow intubation with spontaneous ventilation ("KOBI" – ketamine-only bathing intubation).[11]

Oxygenation Strategies During Predicted Difficult Airway Management

Regardless of the technique selected, it is essential to maintain oxygenation throughout airway management. As a minimum, optimal preoxygenation should be performed with a snug-fitting facemask with end-tidal gas monitoring to demonstrate $E_tO_2 \geq 80\%$ prior to commencement. In healthy patients with normal physiology, this will provide good oxygenation for 7-8 minutes. However, patients with increased oxygen consumption, reduced FRC or pulmonary pathology are likely to have a much shorter safe apnoeic period.

During airway manipulation/instrumentation with spontaneous respiration, nasal oxygenation strategies are highly effective in maintaining saturation. Ideally, this is achieved using a warmed, humidified, high-flow cannula system (THRIVE).[12] At adequately high flows (30 – 70 L/min), this also provides some continuous positive airway pressure, which helps maintain airway patency and aids flexible endoscopy.[13] Furthermore, it maintains preoxygenation and may provide apnoeic oxygenation in the event that the patient accidentally becomes apnoeic. In the absence of THRIVE, normal nasal cannulae set to the maximum attainable flow can be tolerated for short periods and may provide the same advantage.[14,15]

Where induction of anaesthesia is planned prior to intubation, high flow nasal oxygenation combined with manoeuvres to maintain upper airway patency will extend the safe apnoea time beyond the limits of preoxygenation.[15]

Indications for Awake Tracheal Intubation (ATI)

Awake tracheal intubation should be considered for all patients with predicted difficult airway management. While the application to a specific patient is always at the judgement of the anaesthetist, certain factors may be considered to require mandatory awake intubation, where as other predictors simply make it advisable.

Mandatory ATI:

- Severely limited or no mouth opening
- Mask ventilation likely to be impossible
- Penetrating airway trauma with undifferentiated injury
- Prior airway difficulty after which a practitioner has documented a requirement for ATI

Advisable ATI:

- Head and neck pathology, particularly causing anatomical abnormality
- Impending/progressive airway compromise
- Limitation in neck mobility, particularly fixed neck flexion
- Predictors of difficult airway rescue (SGA or FONA)
- Nasal intubation required in combination with difficult laryngoscopy
- History of previous learning of tracheal surgery or radiotherapy
- Mandatory intubation in a patient with known or anticipated subglottic tracheal stenosis

Safe Performance of Awake Tracheal Intubation

Awake tracheal intubation is underutilised in most hospitals, but has a high success rate and excellent safety profile, which does not "burn bridges." A full description of safe techniques for performing awake tracheal intubation is beyond the scope of these notes. It is ideally learnt (in conjunction with the practical skills required) in the format of a hands-on workshop followed by supervised practice in the operating theatre. In 2019, the Difficult Airway Society will be publishing evidence-based guidelines for ATI, formulated by international expert consensus in which we have participated.[9] A summary of the practical considerations are listed below.

ATI should be considered for all patients with predicted airway difficulty. Checklists and/or cognitive aids should be used for patient identification and preparation. Teamwork and excellent preparation are essential. Supplemental oxygen must be provided from commencement throughout performance. Experts agree that intubation in the sitting position with warmed, humidified, high-flow oxygen is preferable.

Effective topicalization is fundamental to safe and successful ATI. Lignocaine is the drug of choice, up to a maximum of 9 mg/kg. Topical vasoconstriction is recommended, with phenylephrine now preferred to cocaine. Local airway blocks have been associated with increased risk of local anaesthetic systemic toxicity, decreased patient satisfaction, and although they may be used by suitably skilled practitioner, still require topicalization to anaesthetise the entire airway. Evidence for the use of anti-sialagogues is lacking.

Analgesia which provides minimal sedation should be provided, preferably by a second practitioner. Sedation should never be used to overcome inadequate topicalization. Single-drug strategies are preferable. Dexmedetomidine or Remifentanil by controlled infusion have demonstrated the best profiles in the literature; Propofol and Midazolam should be avoided.

The literature suggests that awake video laryngoscopy/intubation has equivalent success and patient acceptability to flexible fibre-optic/endoscopic intubation. The technique should be selected based on the anatomical considerations and practitioner skill with the various techniques. There is no evidence to suggest superiority of disposable versus multi-use flexible scopes. ETT selection is important; Parker flex-tip and ILMA tubes are superior to standard or reinforced PVC tubes. There is no consensus on the superiority of oral or nasal intubation, although the author prefers the nasal approach due to improved geometry, stability, and inability of the patient to bite the endoscope or tube.

No more than two attempts by the initial practitioner and one by a more experienced colleague should be allowed. An algorithm (in press)[9] has been proposed to manage failed ATI. Induction of anaesthesia should not be performed until tube placement has been confirmed both visually and with capnography. Training for awake tracheal intubation should be available in all specialist anaesthesia departments, and should form part of registrar training.

Further resources

The reader may access written and video training materials on difficult airway management at the open access website www.OpenAirway.org. Material specific to airway endoscopy and awake tracheal intubation can be obtained at www.OpenAirway.org/courses/AEIOU, which includes access to the full course manual for a locally relevant South African workshop.

References

1. Cook TM, Woodall N, Harper J, Benger J. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 2: intensive care and emergency departments. *Br J Anaesth.* 2011;106(5):632-642.
2. Kristensen MS, Moller J. Airway management behaviour, experience and knowledge among Danish anaesthesiologists--room for improvement. *Acta anaesthesiologica Scandinavica.* 2001;45(9):1181-1185.
3. Norskov AK. Preoperative airway assessment - experience gained from a multicentre cluster randomised trial and the Danish Anaesthesia Database. *Dan Med J.* 2016;63(5).
4. Hagberg CA, Connis RT. Difficult Airway Society 2015 guidelines for the management of unanticipated difficult intubation in adults: not just another algorithm. *British Journal of Anaesthesia.* 2016;116(2):309.
5. Frerk C, Mitchell VS, McNarry AF, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth.* 2015.
6. Mushambi MC, Kinsella SM, Popat M, et al. Obstetric Anaesthetists' Association and Difficult Airway Society guidelines for the management of difficult and failed tracheal intubation in obstetrics. *Anaesthesia.* 2015;70(11):1286-1306.
7. Chrimes N. The Vortex: a universal 'high-acuity implementation tool' for emergency airway management. *Br J Anaesth.* 2016;117 Suppl 1:i20-i27.
8. Cook TM, Woodall N, Frerk C. A national survey of the impact of NAP4 on airway management practice in United Kingdom hospitals: closing the safety gap in anaesthesia, intensive care and the emergency department. *Br J Anaesth.* 2016;117(2):182-190.
9. Ahmad I, El-Boghdadly K, Bhagrath R, et al. Difficult airway society guidelines for awake tracheal intubation. *In press.* 2019.
10. Weingart SD, Trueger NS, Wong N, Scofi J, Singh N, Rudolph SS. Delayed sequence intubation: a prospective observational study. *Ann Emerg Med.* 2015;65(4):349-355.
11. Merelman A, Perlmutter M, Strayer R. Alternatives to Rapid Sequence Intubation: Contemporary Airway Management with Ketamine. *Western Journal of Emergency Medicine.* 2019;20(3):466-471.
12. Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. *Anaesthesia.* 2015;70(3):323-329.
13. Gustafsson IM, Lodenius Å, Tunelli J, Ullman J, Jonsson Fagerlund M. Apnoeic oxygenation in adults under general anaesthesia using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) – a physiological study. *BJA: British Journal of Anaesthesia.* 2017;118(4):610-617.
14. Bhagwan SD. Levitan's no desat with nasal cannula for infants with pyloric stenosis requiring intubation. *Paediatric anaesthesia.* 2013;23(3):297-298.
15. Weingart SD, Levitan RM. Preoxygenation and prevention of desaturation during emergency airway management. *Ann Emerg Med.* 2012;59(3):165-175 e161.

Perioperative Analgesia in Children
Recent Controversies and Discussion Points

Dr Karmen Kemp

Red Cross War Memorial Children's Hospital
University of Cape Town

A dedicated paediatric pain service is becoming a standard of care in paediatric hospitals and centers that treat a large number of kids. In smaller centers with staffing constraints, pain management can be improved by the standardisation of clinical routines and protocols. Pain assessment tools have been sufficiently validated in children and neonates[10] and must become part of routine observations. Hospitals must choose 2 or 3 assessment tools to cover the range of age groups treated and most suited to their patient population. The use of the same assessment tool by multiple disciplines and staff categories allows for comparison, continuity, effective education and improved compliance to protocol.

The ESPA Pain Management Ladder Initiative published in 2018 aimed to improve pain management by providing guidelines for analgesia for specific common surgical procedures. What makes this guideline different is that they consider countries and settings with different resources and skill levels and they divide guidelines into basic, intermediate and advanced options.[1]

Neonatal Pain

Pain pathways to perceive pain are developed by 25 weeks gestation and inhibitory pathways only mature halfway through infancy.[8] Inadequate neonatal analgesia increases the hormonal stress response, morbidity and mortality and affects pain perception in later life.

Paracetamol

Although oral and rectal paracetamol exhibits a ceiling effect of analgesia, intravenous paracetamol achieves higher central effect site concentration and results in higher analgesic potency. Paracetamol is less opioid sparing than non-steroidal anti-inflammatory drugs (NSAIDS), but forms an integral part of multimodal analgesia. It should be noted that intravenous paracetamol only reaches its peak analgesic effect after 1-2 hours.

Asthma & paracetamol

There has been controversy regarding a causal relationship between paracetamol use in infancy and early childhood and the development of asthma and atopy. Current studies are methodologically flawed and bias cannot be excluded. Further research is needed and current inclusion of paracetamol in all age groups is supported for its superior side effect profile.

Non-steroidal anti-inflammatory drugs (NSAIDS)

NSAIDS have an opioid sparing effect of 30-40%. When combined with paracetamol it provides better analgesia than either agent on it's own. It should not be used in infants younger than 6 months or in patients with dehydration, renal impairment, peptic ulcer disease or coagulation disorders.

Tonsillectomy

There is not sufficient evidence to prove an increased risk of bleeding following tonsillectomy with most NSAIDS with the exception of Ketorolac. Most practitioners agree that the opioid sparing benefit outweighs the risk of bleeding by far.

Asthma

Only 3-5% of asthmatic children have Aspirin-induced-asthma (AIA) and 0,3% have NSAID exacerbated respiratory disease (NERD). It is therefor unnecessary to omit NSAIDS in all children with asthma and a careful history should be used to exclude children at risk of AIA/NERD. NSAIDS should be used with caution in asthmatic children with severe eczema, multiple allergies and nasal polyps. Biomarkers for genetic variants of asthma sensitive to NSAIDS are being investigated and will enable us to identify patients at risk.

Bone healing

There is concern regarding delayed bone healing with the use of NSAIDS. There is currently no clear evidence that allows surgeons to advocate for or against the use of NSAIDS following orthopaedic procedures. NSAIDS may affect the early phase of bone healing but is dependent on type, timing and length of exposure. A retrospective review by Kay et al, of 221 children post fracture repair did not show an increased risk of bleeding or wound infection with the use of Ketorolac and there were no cases of delayed union or malunion. The short-term use of Ibuprofen, Diclofenac and Ketorolac outweighs the risk but should be avoided in spinal fusion procedures, limb lengthening procedures or cases with previous bone healing difficulty.

Regional anaesthesia

Dosing

All children should receive some form of local or regional anaesthesia unless contraindicated. The more widespread availability of ultrasound makes regional nerve blocks more reliable. A large safety study has confirmed safe dosing guidelines for racemic bupivacaine in children. Bupivacaine is gradually being replaced by Ropivacaine and Levobupivacaine. Although slightly higher doses of Ropivacaine have been reported to achieve lower toxic plasma concentrations, it is advised to use the same dosing guidelines for Bupivacaine, Ropivacaine and Levobupivacaine.

Acute Compartment Syndrome (ACS)

The concern that epidural anaesthesia, single shot nerve block or continuous peripheral catheter infusions mask the diagnosis of ACS, remains controversial. A joint meeting of the European Society of Regional Anaesthesia (ESRA) and the American Society of Regional Anaesthesia (ASRA)[3] concludes that there is no current evidence that regional anaesthesia increases the risks of delayed diagnosis of ACS. They found a lack of evidence to issue specific recommendations but suggest “best practice rules”[3] to reduce the risk of undiagnosed ACS. This entails:

- For single shot peripheral or neuraxial blocks; use 0,1-0,25% Bupivacaine, Ropivacaine or Levobupivacaine as they are less likely to mask ischeamic pain
- For continuous infusions, limit local anaesthetic concentrations to 0,1%
- For high risk areas such as tibial compartment and forearm surgery, limit concentration as well as volume to be infused
- Use additives with caution as they increase density and duration of block
- High risk patients should have appropriate follow up by acute pain service to allow early detection of warning signs
- If ACS is suspected, compartment pressure measurement should be assessed urgently

Other controversies regarding regional anaesthesia include regional anaesthesia under general anaesthesia or deep sedation, the use of air or saline as a loss of resistance technique and the use of a test dose. These are discussed in detail in the ESRA/ASRA report on Controversial Topics in Pediatric Regional Anesthesia in 2015.[3]

Opioids

Opioids still form an integral part of multimodal anaesthesia perioperatively despite multiple opioid sparing alternatives. Opioids should always be prescribed for postoperative breakthrough pain. Although morphine has an increased effect in neonates due to an immature blood brain barrier[9] and reduced protein binding it can still be safely used in reduced doses in unventilated neonates if they are monitored in a high care setting. Morphine exposure in the first 12 weeks of life rapidly matures opioid metabolism and may require higher dosing regimes.

Opioid metabolism – genetic variability

The current focus on opioid dependence in the general population as well as a renewed understanding of the genetic variability of opioid metabolism via CYP2D6 enzymes has led to a marked drop in opioid prescription for take home analgesia. The latest recommendations from several Drug and Health Boards[4] warn against the use of codeine in children younger than 12 years. Although several practitioners now prescribe alternative oral opioid formulations such as tramadol, oxycodone and hydrocodone, one should be cautioned that these formulations are also partially metabolised by CYP2D6 and could still pose a risk of respiratory depression in rapid metabolisers.

Acute Compartment syndrome and PCA

Concerns regarding PCA opioids[6] delaying the diagnosis of acute compartment syndrome have largely been refuted as long as patients are regularly observed for increased analgesic requirements and other signs of ACS.

Obstructive sleep apnoea (OSA)

It is well known that children with OSA have a greater risk for postoperative hypoxia and adverse respiratory events following adenotonsillectomy. It is also accepted that opioid analgesia exacerbates this risk. It is controversial whether this increased risk is due to an increased opioid sensitivity in children with recurrent hypoxic episodes. This hypothesis suggests either up-regulation of the mu-receptor or an increased number of mu-receptors. A recent study by Montana et al disputes increased sensitivity in OSA patients by comparing pupil size with Remifentanil infusion in patients with and without OSA.[5] No difference in pupil size was observed between groups and it is stated that Remifentanil miosis dose response curves parallel respiratory depression response curves. This finding is in stark contrast with Brown et al[7] that finds a direct correlation between the severity of hypoxaemia and the enhanced analgesic morphine sensitivity in children with OSA.

Regardless of the causation of increased adverse events, the recommendation still remains to halve the usual opioid dose in patients with OSA. It is not advised to completely omit opioids as OSA patients also have a higher incidence of hyperalgesia. Alternative analgesics such as Ketamine and alpha-2 agonists, although opioid sparing, don't provide the same level of analgesia on it's own.

In conclusion

Controversial concerns and invalidated research should not prevent us from providing adequate analgesia across all age groups and in different resource settings. Regular assessment, good practice guidelines and education will lower the risk in favour of benefit.

References

1. Vittinghoff et al. Postoperative pain management in children: Guidance from the pain committee of the European Society for Paediatric Anaesthesiology (ESPA Pain Management Ladder). Ped Anes 2018:28:493-506
2. Lönnqvist et al. Postoperative analgesia in infants and children. Br J Anaesth 2005:95:59-68
3. Suresh et al. The Eurpean Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint committee Practice Advisory on Contro versial Topics in Pediatric Regional Anesthesia. Regional Anesthesia and Pain Medicine 2015:40:5:526-532
4. Tobias et al. Codeine: Time to say “No”. Paediatrics October 2016:138:4
5. Montana et al. Opioid sensitivity in children with and without obstructive sleep apnea. Anesthesiology 2019:130
6. Kay et al. Complications of ketorolac use in children undergoing operative fracture care. J Pediatr Orthop 2010:30:7:655-658
7. Brown et al. Recurrent hypoxemia in children is associated with increased analgesic sensitivity to opiates. Anesthesiology 2006; 105:665–9
8. Wolf et al. Development of pain and stress responses. Procedings of the 4th European Congress of Paediatric Anaesthesia, Paris 1997
9. Haidon et al. Analgesia for Neonates. Continuing Education in Anaesthesia, Critical Care and Pain. Aug 2010:10:4:123-127
10. Witt et al. A Guide to Pain Assessment and Management in the Neonate. Curr Emerg Hosp Med Rep (2016) 4:1–10

Dr Gareth Kantor

Anaesthetist in Private Practice
Co-Founder: Best Care Always

Quality Improvement

How to fix the health care system – or at least a small part of it

Gareth Kantor

April 2019

Table of Contents

Overview – What's QI? Do we need it? Why? 3
KEY STEPS 4
Start: Choose a Problem. Or did the problem choose you? 4
QI Frameworks 5
The Psychology of Change 6
Stakeholder Mapping 6
Diffusion of Innovation 7
Introducing the Model for Improvement 7
What are you trying to accomplish? Set an aim 8
Process Mapping 8
Develop an Aim Statement 9
Measurement: How do you know a change is an improvement? 10
Measuring for QA vs QI vs Research 10
Plotting Data Over Time - Run Charts 11
Collecting Data 13
What Changes Can You Make - that Will Result in an Improvement? 14
The Driver Diagram - Identify Changes by Identifying what influences the Outcome 14
Cause & Effect Diagrams 15
PDSA Cycles 15
Final Thoughts 17
REFERENCES 17
YOUR PRE-WORKSHOP ASSIGNMENT 19
A QI Toolkit 20

Overview – What's QI? Do we need it? Why?

As a doctor you try to deliver the best care possible to your patients. You work hard to acquire knowledge, skills and clinical decision-making ability, and apply them diligently. You hold yourself to a high standard **individually** as do the leaders of our **discipline**, for example by setting you the difficult College examinations that I hope you will pass. ☺

Delivering the best care possible is made challenging by the **complex nature of health systems**[1]. Innumerable factors interact to influence results in a non-linear fashion.

That the SA public health system generates less than perfect patient outcomes is fairly obvious. Despite much greater per capita funding the private sector also experiences significant challenges to quality and safety. Recognition of the **quality and safety gap** - between what we know (e.g. from research) and what we do (i.e. the outcomes the system actually delivers) - became more apparent about 20 years ago [2,3] in countries with well-resourced health care, where **"improvement science"** then took off. Recent impact includes a 40% reduction in preventable infection and other hospital-acquired complications in the US[4], with similar successes seen in some SA hospitals.

> Modern QI originated in the work of W. Edwards Deming (1900-1993) an engineer and statistician who after World War II championed the work of an earlier pioneer, Walter Shewhart (1891-1967). This work established industrial quality control and made use of the "Shewhart [PDCA] Cycle" to maximise learning from changes to processes. Deming developed these methods further in Japan in the 1950s and 60s and is credited with helping drive the "Japanese economic miracle" which transformed the country from the devastation of war to the 2nd largest economy in the world in a few short years.

Professional exposure to "quality problems" - i.e. **waste, delays, errors, ineffectiveness, preventable harm, inequity, disrespect for patients and professionals** – may infect you with a need to act. You have resisted this feeling up to now, because the idea of improving care seems daunting. This is as true for "junior" doctors who feel they lack the experience or authority to make change as it is for professionals up the teaching hospital hierarchy including those in the private sector.

Trainees on the front lines of patient care are in fact well placed to "see" system problems. You are most directly affected by these problems, more receptive to new ideas, and most invested in the future. With a trained eye, the right tools, and permission/encouragement to act, you can generate and successfully implement ideas to improve care.

QI is a systematic approach to making changes that lead to **better patient outcomes, stronger system performance and enhanced professional development**. QI methodology is effective because it is designed for complex systems, is evidence-based[5,6] and there is an expanding literature describing how to do it and what works.

The best way to learn Quality Improvement is to do QI – tackle a problem. In this set of notes I imagine that you have developed the urge to improve some aspect of care in your hospital and describe a proven approach for doing so. This approach to QI is the **Model for Improvement**, a simple yet effective tool for achieving positive change. MFI can be used to improve an aspect of care in any clinical area.

QI is different from research, particularly in how data is used, though it uses the **scientific method**. It is also different from "audit" which is one form of Quality Assurance (QA).

Doing QI can be **fun and worthwhile**, especially if it gets results; one project can lead to another and make a significant impact on patient care and improve your sense of professional purpose.

Sustaining improvement is hard. Embedding these methods in a **system of management**[7,8], is key to establishing high performance health care. A certain amount of **redesign** of funding and care delivery, may be necessary. These are important topics for another day.

The following notes are based on the **TIPS QI Guide**[9] which was developed by trainees in the UK NHS and is aimed at encouraging professionals who have not done quality improvement work before to take on a QI project.

KEY STEPS

- Identify your problem
- Build will
- Set an aim and define a measure(s)
- Develop ideas for interventions
- PDSA

Start: Choose a Problem. Or did the problem choose you?

A good place to start is with a **problem based on your own interests, values or previous experience** (positive or negative) which you are therefore motivated to tackle.
e.g. Caring for an oncology patient and learning what made the biggest difference to this person in their last days of life could inspire you to improve end of life care for others.
e.g. Making a drug error in theatre resulting in serious harm may be motivate you to find ways to prevent similar events in the future.

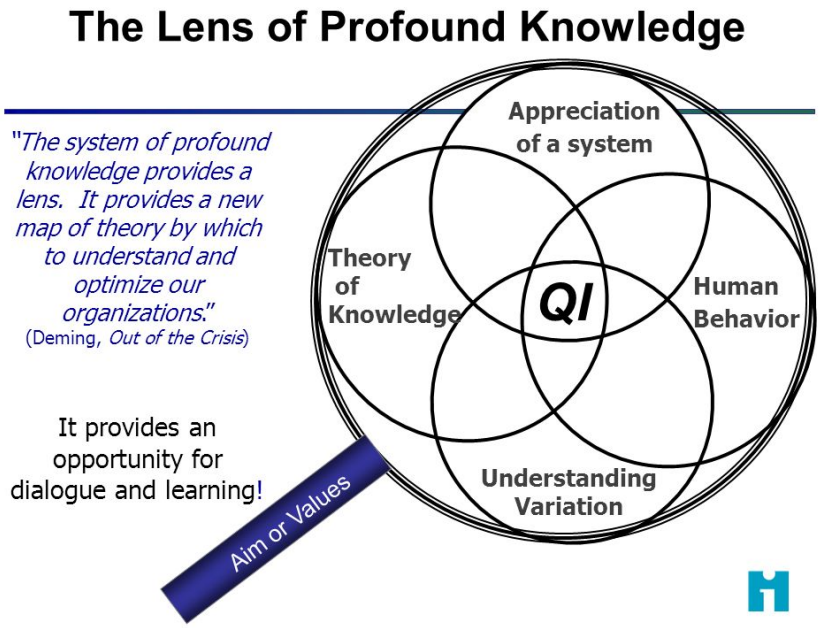
"Annoyances" encountered daily in clinical life are opportunities for improvement. Though these things may seem small, they create waste, especially of time, with important knock-on effects, for example: delay in antibiotic administration for sepsis, hurried patient evaluation, cumulative delay in the rest of the theatre list.
e.g. time spent searching for equipment in the storage room may prompt a project to reorganise it and significantly reduce these delays.

New research findings and guidelines are published frequently and are also a good source of QI project. Select one recommendation from one piece of guidance and try to increase the proportion of patients receiving that aspect of care.
e.g. Ensuring routine pregnancy testing before surgery in women of child-bearing age[10]
e.g. A recent guideline for the prevention of postoperative infection in cardiac surgery recommends oral hygiene, starting at home 2 days before scheduled cardiac surgery, continuing on the morning of surgery and ending on the morning after surgery[11]*.*

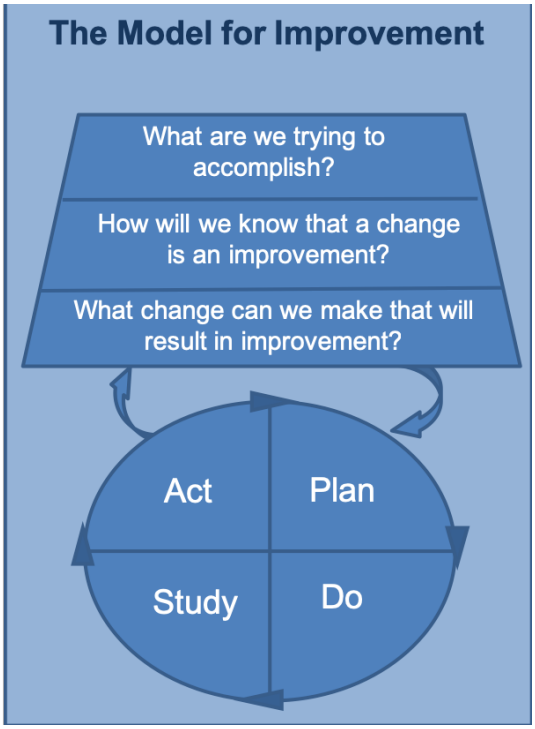
Limit the scope – the number of individual aspects of care you plan to improve – **and scale** – the number of patients or different clinical areas you plan the improvement in. Learn what works, then scale up. Co-operation with small changes to practice is more likely than with large ones. Many improvement ideas can be tried in rapid succession. Plant a seed and work on the conditions for growth over time rather than placing an adult tree in potentially inhospitable foreign soil.

QI Frameworks

WE Deming's ideas about improvement are summarised in his "system of profound knowledge."



The Model for Improvement (MFI), developed by Tom Nolan and associates, is a simple yet effective way to cut through complexity and achieve results.



Psychology of Change

Improvement is only part technical process change; it is heavily dependent on **behaviour and culture change**. Processes, guidelines and pathways designed without acknowledging human behaviour and psycho-social factors are likely to disappoint. Improvement requires working with others - doctors, nurses, pharmacists, ward clerks, managers, even patients - to achieve goals. You have to persuade them that a problem exists, is important, and that something can be done about it.
e.g. Chances of success are better if the theatre or ICU unit manager is supportive and asks other nurses to use your new process, the ward clerk knows exactly how the changes work, your consultant's suggestions were included, the pharmacist's too, and a surgeon likes your idea and shares it with her colleagues.

If people feel like something is being done "to them" (or to the way they work) their instinctive response is to dig in and defend the status quo:

- "Why are you bothered about this? It works fine already."
- "This isn't really my problem, you do something about it."
- "We've tried many times to improve this already and it's never worked."

To generate "buy-in" people should feel included in the improvement process. The following QI tools assist in navigating this part of the improvement journey but ultimately you should be guided by how things are perceived "on the ground" and adapt accordingly.

Stakeholder Mapping

"Stakeholder" refers to anyone who could be affected or have an interest in what you are trying to do. All stakeholders have a level of interest and influence in your project. This tool helps you decide **who you might need to get "on side"** and just **how engaged you need them to be**.

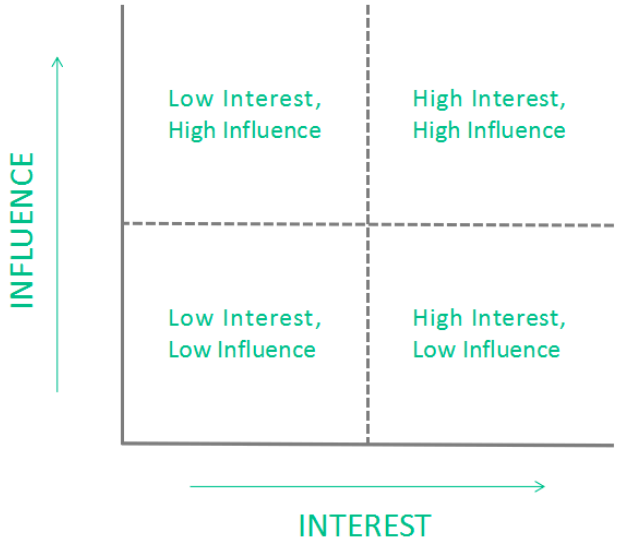


Figure 3.1 Stakeholder Map Template

High interest, low influence – "keep informed". Many people potentially affected by changes to practice do not have much influence but can provide useful feedback and suggest ideas of their own. They can be willing participants in the changes you are making and may be willing to help in other ways such as collecting data. The term "low influence" refers not just to formal authority, but social influence too.

e.g. A well-liked Enrolled Nurse with a particularly strong personality can potentially have high social influence, despite having relatively low formal influence.

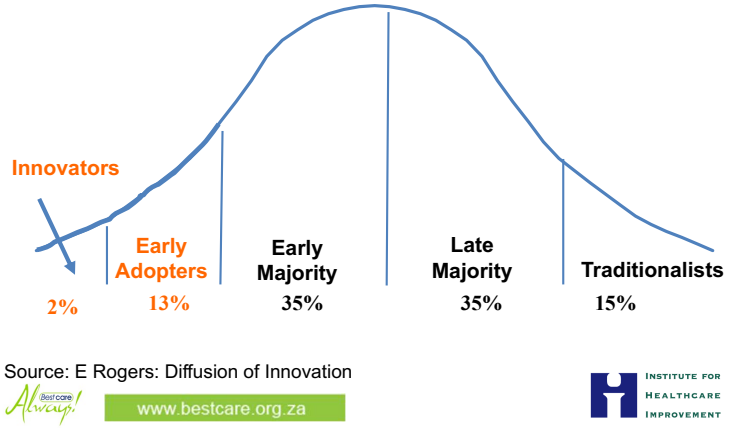
Low interest, high influence – "keep satisfied". People in senior or managerial positions are pressured from ground up and top down. They will often be too busy to take an active, regular role in your project. However they could place an insurmountable barrier in the way if changes are being made to the way their departments work without being aware of them. They are crucial to have on-side, and you will need to find a way to do this by articulating how what you are doing is relevant to them. These are people who you need a "yes" from, but they don't need to necessarily know all the details.

High interest, high influence – "work with closely". These people have authority and can actively champion your work. They are directly affected by what you are doing, or perhaps have a personal interest. They can suggest how to overcome barriers you face and can be good for bouncing ideas off of. You will need at least one of these people on your team, typically a senior consultant or clinical director.

Low interest, low influence – "monitor". Some people will be affected only slightly by what you are doing and are not particularly interested either. Ensure there is no resistance to your changes brewing, which could spill over to others.

Diffusion of Innovation

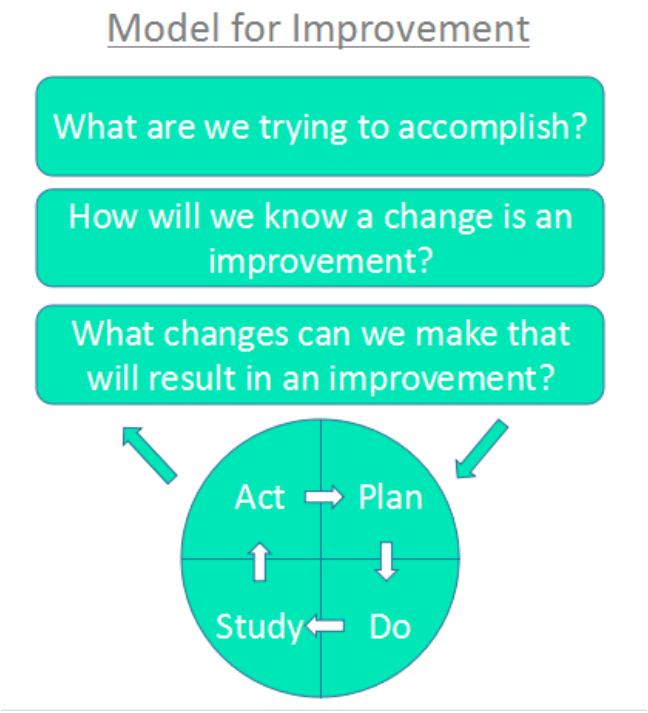
Stakeholders vary from those who warm immediately to your changes to traditionalists who are never convinced, and everything in between. Over time, if successful, more and more people appreciate the benefits your changes (innovations) have brought.



Colleagues open to your new ideas from the start are innovators or early adopters. When faced with opposition to what you are doing from a **laggard**, don't feel you have to win them over. You'll spend huge amounts of time and effort with little progress. Accept their criticism and focus your energy on those who are more willing to work with your changes.

Introducing the Model for Improvement

The Model for Improvement (MFI) is a deceptively simple yet effective model for making change. Its purpose is to provide a framework for testing and learning, not just blindly implementing an idea. Follow it stepwise, ensuring you can answer each question in turn, then use PDSA cycles.



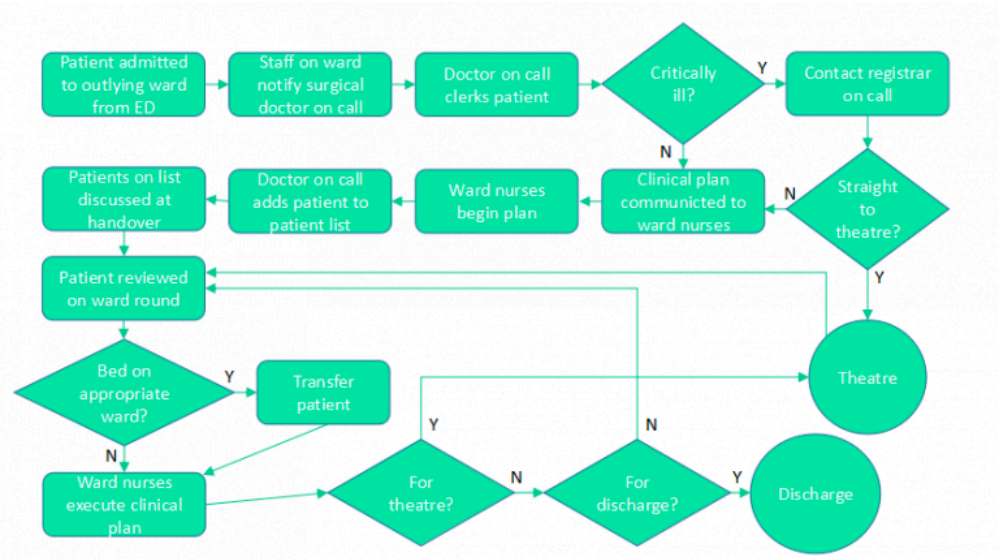
The Model for Improvement

What are you trying to accomplish? Set an aim

Before making changes you need to know your purpose, your aim, informed by a solid understanding of the nature of the problem you are trying to solve. It's time to make a process map.

Process Mapping

Clinical processes can be understood as a sequence of steps performed by various professionals. As individuals we understand our own role but often do not completely understand the entire process in detail. A process map is a flowchart depiction of a process and is **a tool for achieving shared understanding**. Everyone involved should agree what the steps are. The map can be surprisingly complex and reveal many steps that do not "add value" from the perspective of the "customer". The map should be sufficiently detailed - too broad and you may miss smaller parts of the process that are in fact the problem areas (e.g. the printer seems to always have no paper).



A process map for surgical admissions

> Until **Artificial Intelligence** completely takes over, clinical processes will be run by people. Building support for a QI project therefore requires explanation of how the problem is relevant to others. Spend time thinking through the problem and noting how it affects you, your patients, surgeons, nurses, other theatre team members, nurses in recovery, the ward, managers, the lab, the whole hospital, etc. Use these points to get people to support your project.
> *e.g. A manager might be more interested in an idea that could free up beds, a nurse more concerned about improvement of patient satisfaction, and hopefully everyone cares about an idea that can improve patient safety.*

Develop an Aim Statement

To answer the question "what are we trying to accomplish?", express the purpose of the project in an **aim statement** which communicates clearly what you are trying to do. This helps get everyone on side, co-operating with changes to practice, collecting data, etc.

A good aim statement says **what**, by **how much** and by **when**. It also keeps the project manageable - small enough to succeed (e.g. one ward, rather than a whole hospital) but still a **stretch** i.e. the current system cannot deliver the outcome you wish to achieve. Successful QI projects often pick a narrow focus but drill down into the topic to find what works and doesn't, rather than trying to tackle many different things superficially.

An aim sets a target. Baseline data and experience elsewhere can inform what we think is possible. Going forward you may find your initial target is met easily or is far too ambitious. In these circumstances it's OK (unlike in research), to **revise your aim**.

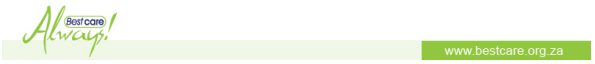
Defining the Aim

To reduce …… (VAP, CLA-BSI, SSI, CA-UTI)

By ……. amount

By implementing the whole ……bundle
to every patient every time

By September 2012 (in 18 months)



Aim statement template from the Best Care Always campaign

Good aim statements	**Lousy aim statements**
To reduce the average pain score of patients on admission to the orthopaedic ward from ED by 2 points (score out of 10), in 4 months	To deliver a teaching session on breaking bad news to all registrars in 3 months [not measurable over time]
60% of asthmatic patients aged above 35yrs with COPD symptoms to have spirometry performed at GP practice by 31st October 2018	We aim to ensure patients get daily bloods [not specific, no target, no time frame,]
95% of patients on long-term NSAIDs to be prescribed a concurrent PPI in 4 months.	By 2017 we will have reduced the number of falls [not specific, no target]
To reduce the number of falls in patients aged over 65yrs on ward B2 by 50% by 5th December 2018	It is a priority of the hospital to reduce the number of cardiac arrests by employing 10 more nurses [not specific, no target, not realistic, no time frame]
70% of cases of death not referred to the coroner, for the family to receive the medical certificate of cause of death within 24hrs, in 2 months	

Measurement: How do you know a change is an improvement?

The only reliable way to know if a change brings about improvement is to collect data. Data is not always quantitative i.e. conversation, reflection, "impressions" and other qualitative feedback are useful - but numbers are usually needed to decide if you are meeting a QI aim.

Measuring for QA vs QI vs Research

	Research	Judgement	Improvement
Goal	New knowledge (not its applicability)	Comparison Reward / punishment Spur for change	Process understanding Evaluating a change
Hypothesis	Fixed	None	Multiple and flexible
Measures	Many	Very few	Few
Time period	Long, past	Long, past	Short, current
Sample	Large	Large	Small
Confounders	Measure or control	Describe and try to measure	Consider but rarely measured
Risks in improvement settings	Ignores time based variation Over-engineers data collection	Ignores time based variation Over-reaction to natural variation	Incorrectly perceived as 'inferior statistics'

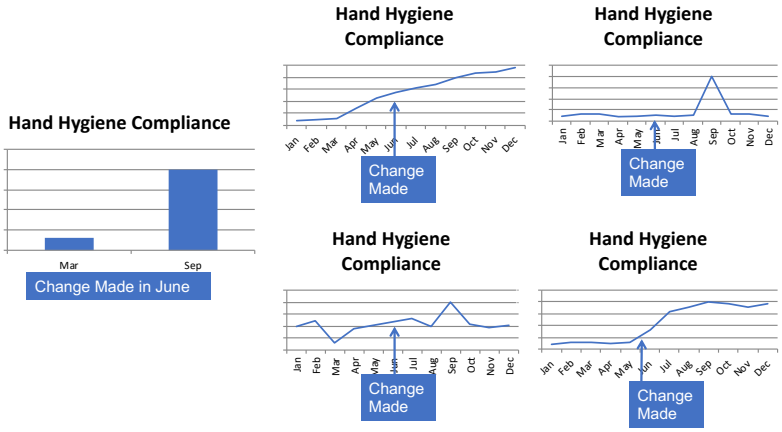
Source: Solberg – Three Faces of Performance Improvement

The difference between measurement for "judgment" (i.e. audit, QA), improvement and research. Research defines what is possible, measurement for judgment (e.g. audit, QA) tells us how we are currently performing, and QI is the process of moving from how we perform now towards what is possible (and beyond).

Plotting Data Over Time - Run Charts

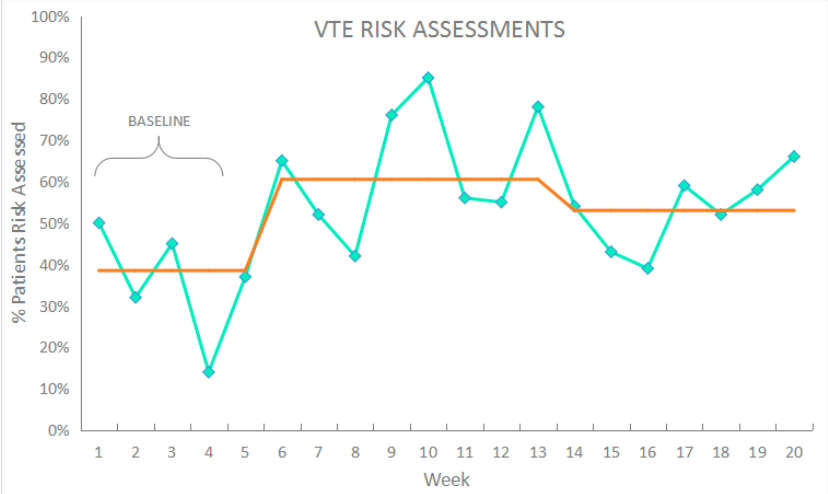
- In QI projects, **data collection is continuous and ongoing**, regardless of whatever else is happening in the project, together with continuous testing and learning through PDSA.
- Multiple data points are used to plot **data over time** in a type of line graph known as a **run chart**. A run chart is a form of **time series.** It is a run chart is a line graph with time on the x-axis, and the measure of interest on the y-axis.
- It is important to have some **baseline data**; to improve you need to know where you are starting from. Ideally 12 data points, although this is not always possible.
- **Plot the median** of the data points. The median is less skewed by unusual data points. Add each new data point on the end of the chart as you go.
- Individual data points do not represent the true current performance of your measure, but the **median line** does. Day-by-day or week-by-week fluctuations in the data points are the normal ebb and flow of any system. This is called **"normal variation"**.

What is the real story?



In a typical audit cycle, and in some research designs, data is collected only twice. We can miss underlying trends, and confuse normal variation for effects of the intervention. Data over time captures performance over many more time points, and therefore many more conditions, providing a more representative picture and better learning about process.

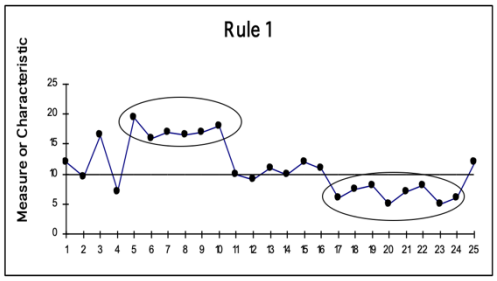
To identify changes from normal variation, statistically-based, visual rules allow for these inferences. The 4 **run-chart rules** or patterns are known as **"shift"**, **"trend"**, **"run"**, and **"astronomical value"**. They have less than roughly a 5% likelihood of occurring by chance.



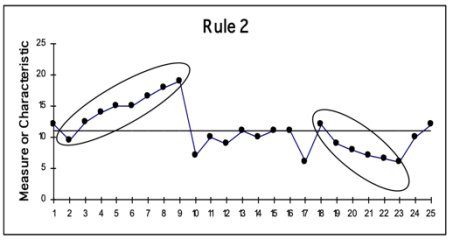
Example of a Run Chart. In this project, one data point was collected each week for just over 4 months. Baseline data was collected in the first 4 weeks, before any changes to practice were made. The orange line represents the median. Two shifts[1] occurred (week 7 and week 14).

[1] A "shift" is where 6 consecutive points are either all above or all below the existing median. If there is no significant change 50% of points will be above the median line and 50% below. Once you see 6 consecutive points either all above or all below the existing median, you "shift" the median line. Take the median of these 6 points and starting from the first of these points, plot the median line as your recalculated value forwards in time. In the chart the median shifted up at week 6; weeks 6 – 11 were all consecutive points above the previous median. It shifted down at week 14, as points 14 – 19 were all consecutively below where the median was. This is the "proof" that an improvement has been made. If your aim is to increase the percentage of patients on the surgical ward to get VTE risk assessments within the first 24 hours of admission to 90% in 4 months – then you are looking to shift the median above 90%, not just achieve a single data point there.

Rule 1: SHIFT
A shift in the process is **six** or more consecutive points either all above or all below the median line. Values that fall on the median line do not count towards or break a shift – skip values on the median and continue counting.



Rule 2: TREND
A trend is **five** or more consecutive points all going up or all going down. If two successive points have the same value, only the first counts towards the trend – like values do not count towards or break a trend. Ignore the second point and continue counting with the next point on the chart.

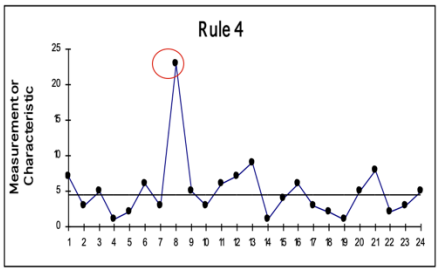


Rule 3: RUNS
A run is a series of points either above or below the median line (points on the median line are ignored). The number of runs can be easily calculated by counting the number of times the data line crosses the median line and adding one to that total. A non-random effect – a significant change in the observations – is signalled by having too few or too many runs in relation to the number of 'useful' points on the graph (i.e. ignoring the points sitting on the median). A special table is used to determine the upper and lower limits on this value.

Number of useful observations	Too few runs	Too many runs
15	4	12
16	5	12
17	5	13
18	6	13
19	6	14
20	6	15
21	7	15
22	7	16
23	8	16
24	8	17
25	9	17
26	9	18
27	9	19

Number of useful observations	Too few runs	Too many runs
28	10	19
29	10	20
30	11	20
31	11	21
32	11	22
33	11	22
34	12	23
35	13	23
36	13	24
37	13	25
38	14	25
39	14	26
40	15	26

Rule 4: ASTRONOMICAL VALUES
An astronomical value is one that appears highly unusual in a 'blatantly obvious' fashion – not just taking the highest or lowest point on the chart. Not a precise definition, but one that can generally be agreed with colleagues.



IHI's QI Essentials toolkit is an excellent resource covering run charts and other QI tools[12]. Robert Lloyd from IHI has a series of videos that nicely explain their use.

Collecting Data

Collecting data for research tends to be a lot of work; collecting data for improvement is less laborious and more feasible.

A reasonable time frame for data collection is **weekly**. Define a time period between data points and collect at these set points. **One data point per week** is usually a good target, and gives you nearly 20 data points (which is ideal) over a 4 month period. With only monthly data, there may be insufficient points for a meaningful run chart analysis within the project time frame. It may be appropriate to have one point per "event", regardless of the actual number of days between them – such as theatre list 1, theatre list 2 etc.

Collecting this much data may seem daunting, but each data set can be small. How much data do you need? In research we go for as large a sample as possible to statistically power the study. In QI the detection of a significant change using run charts comes from the shift and trend rules of the position of points in comparison to the median, not the sample size of individual points.

Collect just enough data to tell you what you need to know. In practice **sampling** a handful of patients is enough; 8 randomly-selected patient notes every Friday is better than 40 patient notes once a month. The former provide 4-5 data points for your run chart, the latter only 1.

Electronic systems for can be good sources for QI data - large volumes of baseline data that are time-stamped. In our setting, manual collection may be the default. Enlist team-mates to help when you are unavailable, such as when you are on leave. You may be able to make minor adaptations to

existing forms/documents. Nationally or institutionally mandated data e.g. WHO checklist completion rates, can be used; speak to senior staff to see what already exists.

To actually make run charts all you need is the data on paper or in a spreadsheet format.

What Changes Can You Make - that Will Result in an Improvement?

You know what you are trying to accomplish through defining an **aim**; by using **data over time** you will establish whether that aim is reached. The next question is what changes to make to bring about the improvement you are seeking.

A common pitfall is to apply a single idea for an intervention. A silver bullet rarely exists. Better to rapidly test many different changes on a small scale to figure out what works best. Your change idea could have a high chance of success but you should explore more as there are usually good ones not yet thought of.

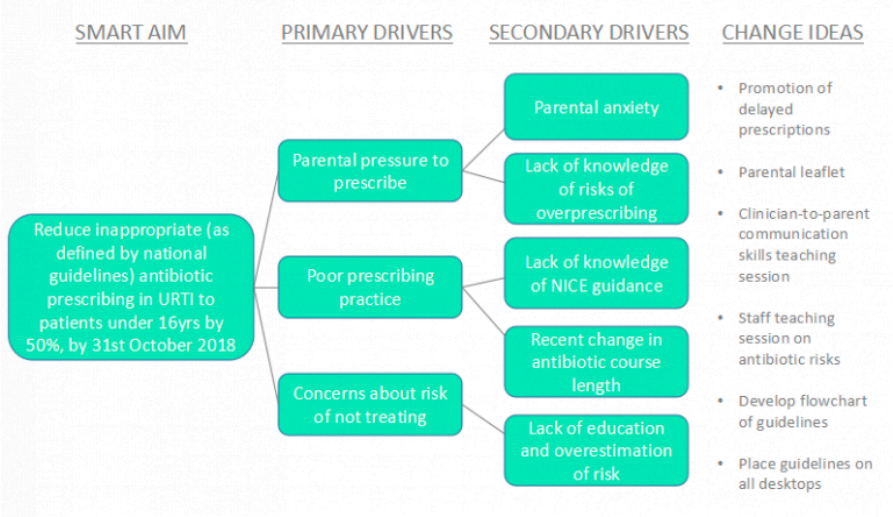
e.g. A project aimed at reducing postoperative pain revolved around delivering an educational intervention ("teaching session"). The stated aim was "teach 90% of registrars how to perform a TAP block in 3 months". A restated aim to "reduce the average pain score on arrival in the ward of major abdominal surgery patients by 2 points in 3 months" could produce a better formed QI project. A teaching session on how to perform TAP blocks could be one of several ideas used to meet the aim. The aim is focused directly on the patient rather than the staff, and there is scope to try other ideas alongside the teaching session.

The Driver Diagram - Identify Changes by Identifying what influences the Outcome

A driver diagram is a useful tool for exploring changes/interventions in complex systems in which many factors influence a clinical practice. A driver diagram helps you build a theory or roadmap for achieving your intended aim including different change ideas that may be crucial for success.

To construct a driver diagram place your aim at the left hand side. Branch the factors that influence the aim to the right. Primary Drivers are the main influences. Secondary Drivers are the specifics and themselves influence the primary drivers. Secondary drivers help you to think of ideas for improving practice ("change ideas") for some of them. The aim itself and the primary drivers are usually too large to directly impact, but secondary drivers can be addressed more easily.

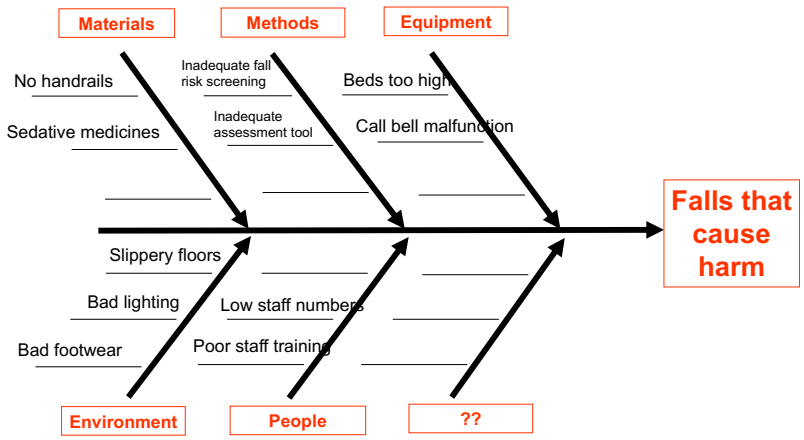
Like a project aim, driver diagrams often require revision as a project proceeds due to deeper knowledge of the problem; it is common to have multiple updated versions.



Driver Diagram Example. There were multiple ideas for improvement tried (the "change ideas"), and these came from breaking down the things that influence the aim (outcome) to the level of the secondary drivers.

Cause & Effect Diagrams

A Cause and Effect Diagram (also called a fishbone diagram or Ishikawa diagram) provides an organised pictorial display of possible causes of problems. The primary branch represents the effect (the quality characteristic that is intended to be improved and controlled) and is labelled on the right side of the diagram. Each major branch of the diagram corresponds to a major cause (or class of causes) that directly relates to the effect. Minor branches correspond to more detailed causal factors. Illustrating the relationship between cause and effect helps you identify factors needed to ensure success of an improvement effort.



Example of a Cause & Effect Diagram

PDSA Cycles

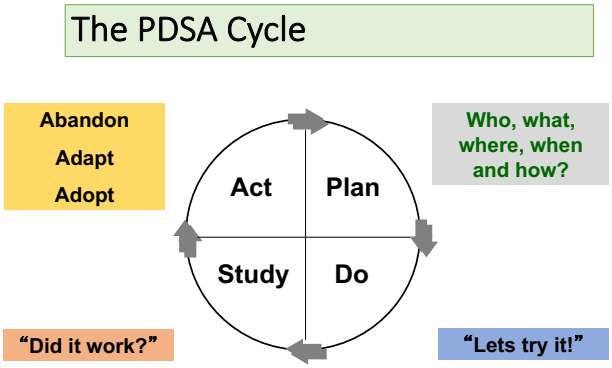
The framework for testing ideas is the Plan-Do-Study-Act (PDSA) cycle.
Download a template here -

Plan. What change are we going to test? When are we going to do it? Who will be responsible? How will it be done? What do we expect will happen?

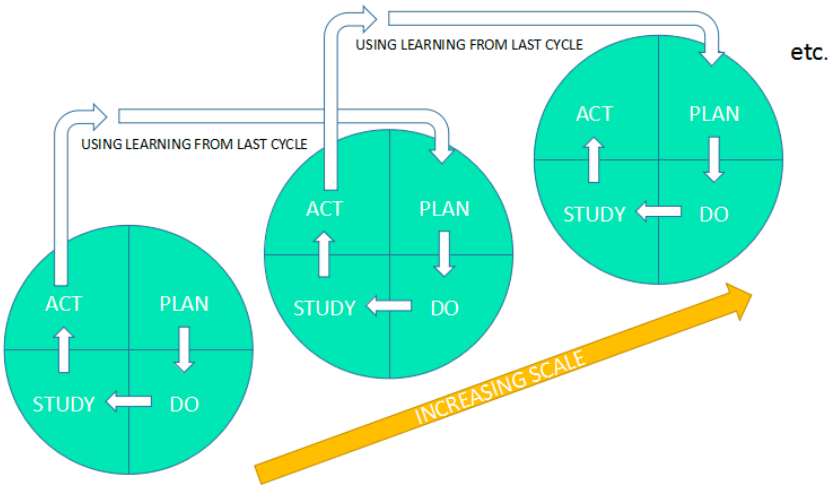
Do. Go out and try it. Note any deviations from the Plan.

Study. The most important step, often missed! What happened? Was it as expected? If not, why? What have we learned about what we tried?

Act. How will what we learned in 'Study' inform our next cycle? Should we **adopt** the change on a larger scale? Was it so ineffective that we should **abandon** this particular change? Can we **adapt** the change to be more effective next time?



- Some new ideas will work well, others won't. Your ideas may not improve anything at first but the **learning from each test** is a successful step on the journey to improvement.
- Tests should be done continuously but on a small scale initially. Try the first PDSA cycle on just **a single patient, or a single list or a single ward** round. This allows rapid testing, with minimal resources. If unsuccessful, there is little consequence.
- Staff are more likely to support small scale changes, rather than a large and permanent change to the way they work. Multiple small cycles provide many opportunities for feedback and input from colleagues, leading to further "buy-in".
- The completion of one cycle leads to the next. Eventually they "ramp up". Scale can be increased if/when a change is working well. When you get to "Act", you can adopt the change on a larger scale or adapt what you've done while scaling. e.g. 10 patients this cycle from 3 in the previous. Multiple "ramps" are possible, one for each new change idea tested.
- The overall goal is improving the measure from your aim on the run chart. It is also to gain knowledge about the changes that have the largest positive influence. These changes have potential to be spread elsewhere, widening the impact of your work.



Ramping Up PDSA Cycles. e.g. Cycle #1: start with one patient and get feedback, tweak the intervention; cycle #2: use it on an entire list of 6 patients, tweak more; cycle #3: get more feedback, try with other surgeons. No limit to the number of cycles, as long learning is taking place.

Final Thoughts

Improvement may not happen in the time scale available to your QI project. But you are likely to learn something useful that will inform the next attempt to improve; others can avoid wasting time learning exactly the same thing.

Academic opportunities in QI include publication in journals devoted to QI such as BMJ Open Quality or BMJ Quality & Safety. Consider submitting an abstract to the ISQUA International Conference (which is in Cape Town this year) or the IHI/BMJ International Forum on Quality (Johannesburg 2020). Record everything you do, including "negative" results, so that establishing and communicating what you have learned is easy.

If you find this material interesting there may be opportunities to explore further - using the LifeQI platform. The W Cape Dept of Health has a quality assurance department and staff. The Best Care Always web site (www.bestcare.org.za) describes a national campaign, which is ongoing in some organisations, and has local and international resource links.

Political and economic pressures mean tougher years ahead for the SA health system. QI methods can be used by clinicians to address everyday problems in the clinical workplace. Adopted more widely there is potential to achieve system level priorities - better patient outcomes and experience, population health, lower cost, and enhancement of professional life[13, 14].

REFERENCES

1. Lipsitz LA. Understanding health care as a complex system: the foundation for unintended consequences. *JAMA*. 2012;308(3):243-244. doi:10.1001/jama.2012.7551.
2. Kohn LT, Corrigan JM, Donaldson MS. *To Err Is Human*.; 2000. doi:10.17226/9728.
3. *Crossing the Quality Chasm*. National Academies Press; 2001. doi:10.17226/10027.
4. AHRQ. *AHRQ National Scorecard on Hospital-Acquired Conditions: Updated Baseline Rates and Preliminary Results 2014-2017*.; 2019. https://www.ahrq.gov/professionals/quality-patient-safety/pfp/2014-final.html. Accessed April 5, 2019.

5. Ogrinc G, Mooney SE, Estrada C, et al. The SQUIRE (Standards for QUality Improvement Reporting Excellence) guidelines for quality improvement reporting: explanation and elaboration. *Qual Saf Health Care*. 2008;17 Suppl 1(January 2009):i13-32. doi:10.1136/qshc.2008.029058.
6. McQuillan RF, Wong BM. The SQUIRE Guidelines: A Scholarly Approach to Quality Improvement. *J Grad Med Educ*. 2016;8(5):771-772. doi:10.4300/jgme-d-16-00558.1.
7. Institute for Healthcare Improvement: Executing for System-Level Results: Part 1. http://www.ihi.org/resources/Pages/ImprovementStories/ExecutingforSystemLevelResultsPart1.aspx. Accessed April 4, 2019.
8. Toussaint JS. Hospitals Can ' t Improve Without Better Management Systems. 2015.
9. TIPS QI. https://tipsqi.co.uk/. Accessed April 3, 2019.
10. Routine preoperative tests for elective surgery. *BJU Int.* 2018;121(1):12-16. doi:10.1111/bju.14079.
11. Pedersen P, Haakonsen S, Madsen I. *Clinical Guideline: Systematic Perioperative Oral Hygiene in Reduction of Postoperative Infections after Elective Thoracic Surgery in Adults.*; 2015.
12. Institute for Healthcare Improvement. IHI's QI Essentials Toolkit. http://www.ihi.org/resources/Pages/Tools/Quality-Improvement-Essentials-Toolkit.aspx.
13. Barry, Wehmiller. IHI Framework for Improving Joy in Work. *Work Am Med Assoc Baylor Scott White Heal Bellin Heal Syst*. 2017.
14. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood)*. 2008;27(3):759-769. doi:10.1377/hlthaff.27.3.759.

YOUR PRE-WORKSHOP ASSIGNMENT

What is the problem?
Before the workshop, think about a problem you see every day in your hospital - in theatre, ICU or preop clinic. Choose something of personal interest, or a recurring problem, or perhaps some aspect of a new guideline or evidence-based practice. It can be something small. This list may spark an idea.

- Pregnancy test not done before surgery
- Don't know everyone's name in theatre
- My laryngoscope has a dull light / absent size 3 blade / is not clean
- No Ambu bag in my theatre
- Wrong (prophylactic) antibiotic - or wrong timing
- Syringe swap (medication error) - specific example
- Ultrasound [/other] machine is missing
- Patients are late coming down from the ward, tonsillectomy list, first case of the day
- I don't know where my preop (postop) patients are
- Preop Hb [l/other lab tests] were not done
- Machine check not done
- This theatre was not properly cleaned
- Theatre temp is too high/low
- This theatre is too noisy
- Communication problems
- Waste of water/electricity/etc
- No hand hygiene solution in the dispensers
- No pain score measurement after abdominal surgery
- You are a junior registrar doing a minor afternoon list (abscesses) – you feel there is a problem with inappropriate cases, for this list e.g. multiple abscesses, septic patients, multiple comorbidities, or patients have eaten…
- Preop Hb not done (or done, inappropriately)
- VTE prophylaxis not administered

Who is affected?
Describe at least 3 stakeholders, how the problem affects them and why they might care

List at least 3 causes of the problem
Use a cause and effect diagram

List at least 3 changes you think would lead to improvement
Use a driver diagram

How will you know they will be an improvement?
Make an aim statement

A QI Toolkit

Category	Tool	Typical Use of Tool
Strategic Planning	Driver Diagram	Visualizes a team's theory of the key drivers or contributors to achieving a project aim. A roadmap for achieving the overall project aim.
	Project Planning Form	Enables a team to systematically plan the different components that results in a full picture view of the project, strengthening monitoring and evaluation.
Viewing Systems and Processes	Flow Chart/Process Map	Visual display of connected steps in a process that enables analysis for improvement, and standardization of a process.
	Failure Modes and Effects Analysis (FMEA)	Systematic and proactive analysis of where harm may occur in a process, and devising improvements to prevent these harms.
Organizing Information	Cause and Effect Diagram/ Fishbone Diagram	Organizes and displays multifactorial root causes contributing to an effect or outcome, thereby enabling identification of change ideas for improvement.
Documenting Tests of Change	PDSA Worksheet	Documenting plans, actions, and quantitative and qualitative learnings from tests of change.
Understanding Variation	Run Charts and Control Charts	Study variation in data over time; analyzes the impact of change ideas on performance; differentiates between common and special cause variation.
	Pareto Chart	Identifies the vital few contributors to a problem where targeting improvement would lead to the greatest impact.
	Histogram	Displays variation in continuous data that aids data analysis.
Understanding Relationships	Scatter Diagram	Helps determine any cause-and-effect relationship between two variables.

Adapted from The Improvement Handbook, August 2007 Edition and the IHI's QI Essential Toolkit
http://www.ihi.org/communities/blogs/choose-the-right-qi-tool-for-health-care-or-daily-life

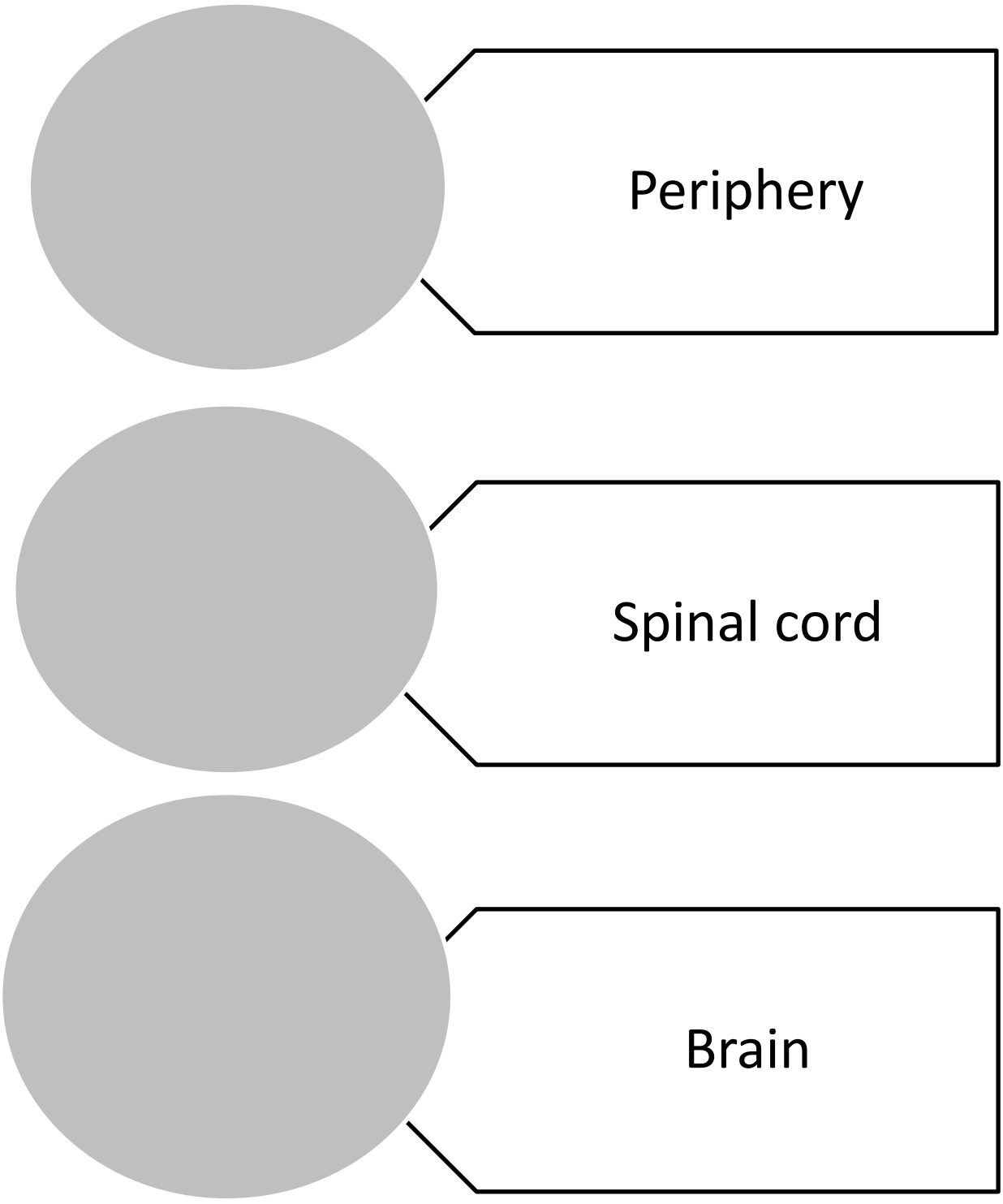
Pain workshop

Drs Janieke van Nugteren, Rowan Duys, Tory Madden, Prof Romy Parker

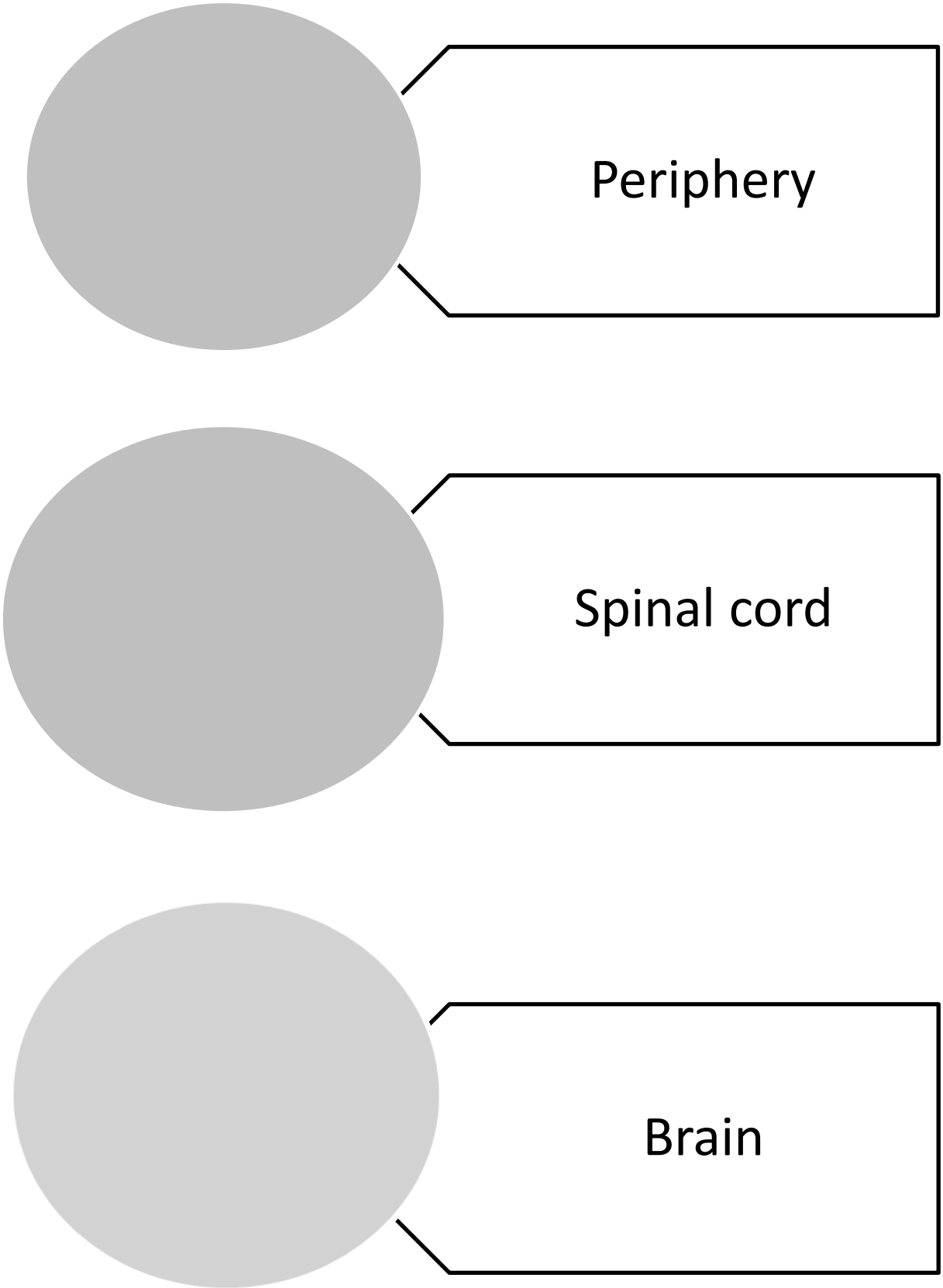
Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Recommended reading:
A Feizerfan, G Sheh, Transition from acute to chronic pain, *Continuing Education in Anaesthesia Critical Care & Pain*, Volume 15, Issue 2, April 2015, Pages 98–102.

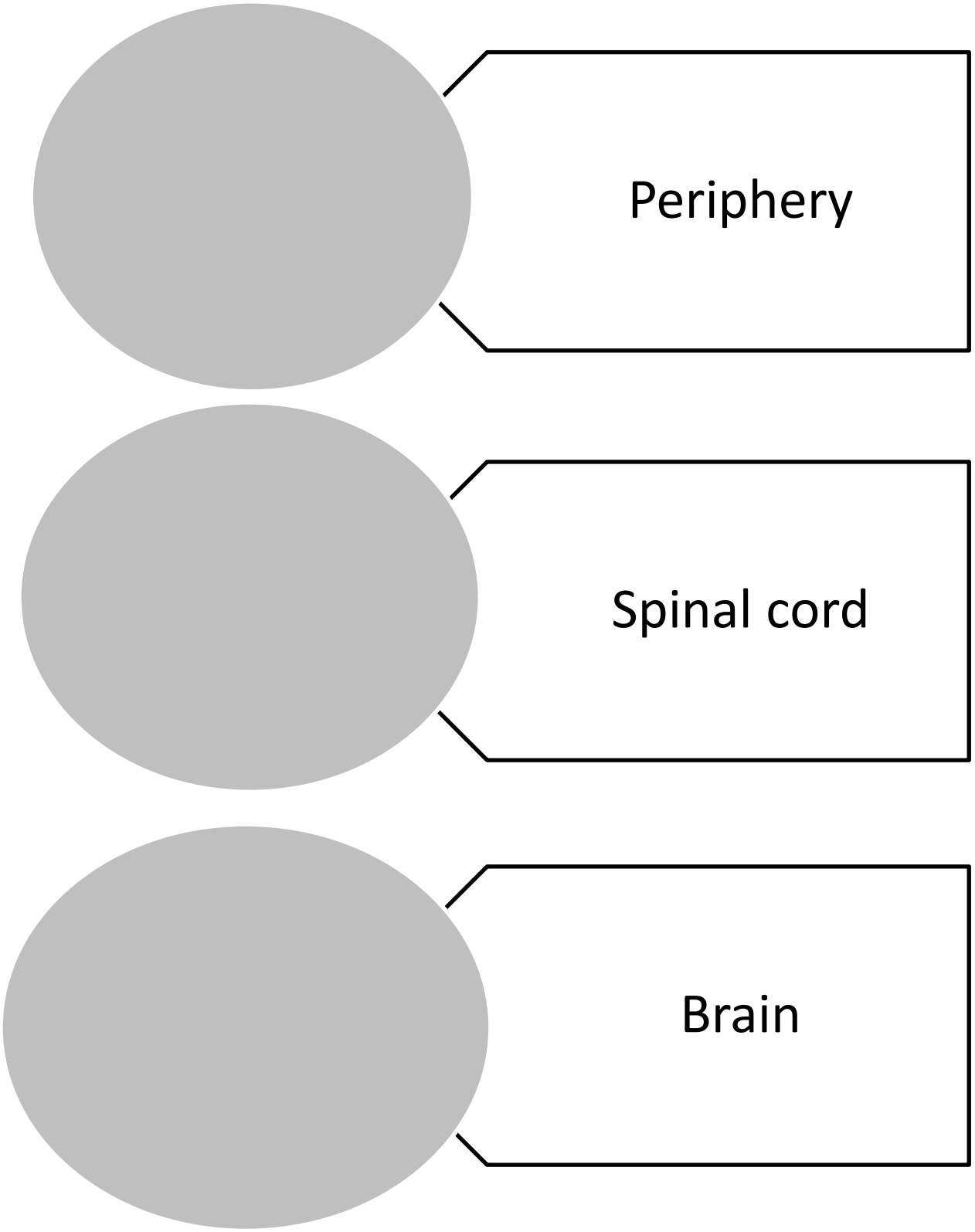
Case 1



Case 2



Case 3



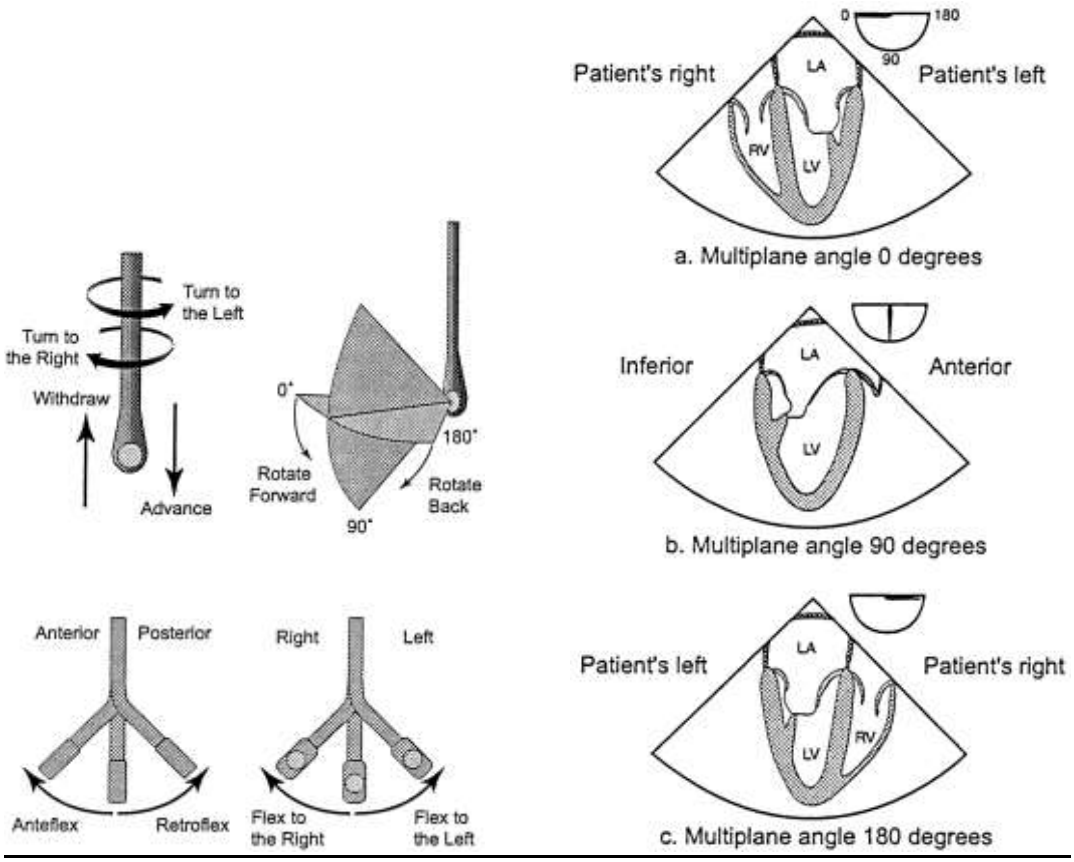
Notes page

Paper 3 Topics

Contributors: Dr Ettienne Coetzee
Dr Alma de Vaal
Dr Nicole Fernandes
Dr Adriaan Myburgh
Dr Mariesa Nock
Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Transoesophageal echocardiography image interpretation

Dr Adriaan Myburgh



Getting started: Connect ECG leads. Enter patient details.

Gain: Amplification of echoes- Adjust so the chambers are black but the mitral valve leaflets are bright.

TGC (Time Gain Compensation) Gain adjusted by the depth (time) of echo.

Depth: Distance from transducer scanned: Set at 10-12 cm.

Colour flow Doppler
Adjust until noise (speckles) appears on screen and then reduce until it just disappears. (set between 50- 60 cm/s.)

Doppler

Doppler echocardiography calculates blood-flow velocities in cardiac chambers and in the great vessels. Blood-flow velocities can be converted to pressure gradients (in mmHg) according to the simplified Bernoulli Equation.

Pulsed or continuous Doppler:

Doppler is displayed as a plot of velocity (y-axis) versus time (x-axis).
Analyze for shape, intensity, acceleration, deceleration, pressure half time, peak velocity, and velocity time integral.
Measuring the peak velocity of the profile can be used to calculate peak pressure gradient.
Tracing the border of the profile can provide mean pressure gradient and velocity time integral.
Use pulsed Doppler for low velocities and continuous Doppler for high velocities.

Peak pressure gradient:

The peak velocity of flow imparted to a mass of blood is dependent on the pressure gradient applied:
$PG=4x\ V^2$ (Modified Bernoulli equation)
If flow is not parallel to Doppler interrogation then $PG= 4x\ V^2 \cos \theta$ (within 20 °).
Beam should be aligned to less than 20 degrees with axis of flow. Parallel flow is most accurate since cosine 0=1.
A 20 degree angle gives a 6% error in velocity measurement since cosine 20 = 0.94

Pressure half time:

The time taken for the passive equilibration of pressures between two chambers is dependent on the size of the opening between them, i.e. the rate of pressure decay is a measure of the size of the opening. Use for AI or MS assessment. Larger orifice= larger blood volume exchange = faster pressure gradient drop.
Smaller orifice = smaller blood volume exchange = slower pressure gradient drop.

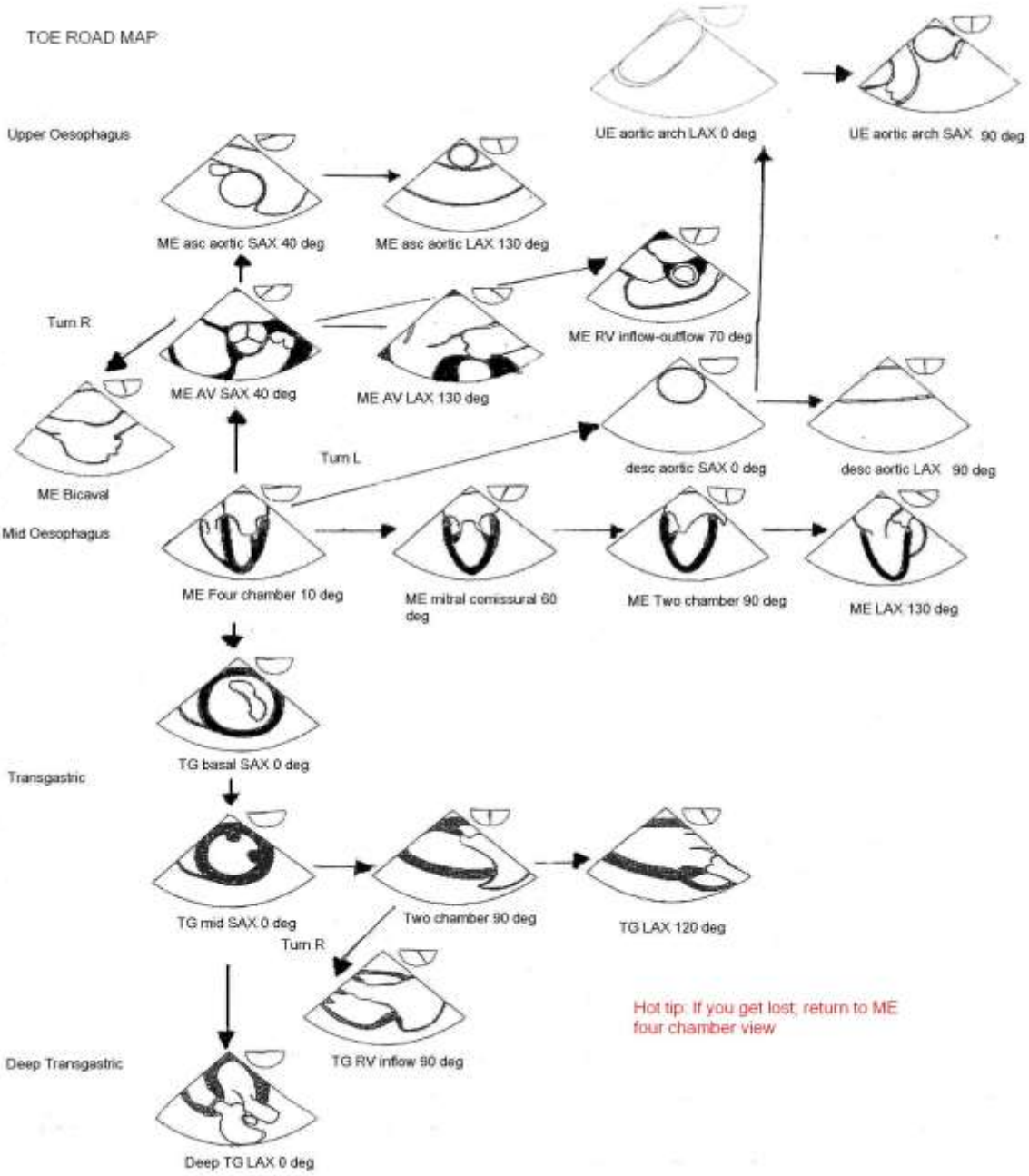
Velocity time integral: (VTI)

Tracing the border of the velocity profile allows integration of all velocities.
VTI= area under the curve= velocity x time= (cm/sec) (sec)= cm (actually cm/beat)
The VTI of the LVOT multiplied by the area of the LVOT will give the stroke volume.
CO= SV x HR
$SV= VTI \times \pi r^2 = VTI \times 0.785\ d^2$

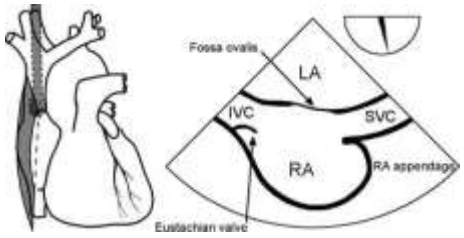
Continuity Equation:

In a system with no leaks or regurgitation, flow is equal at all parts but velocity is not.
$(Area_1)(VTI_1) = (Area_2)(VTI_2)$
The continuity equation can be rearranged as desired to find an unknown area.
$(Area_1) = (Area_2)(VTI_2)/(VTI_1)$

Standard views



LEFT ATRIUM & INTERATRIAL SEPTUM



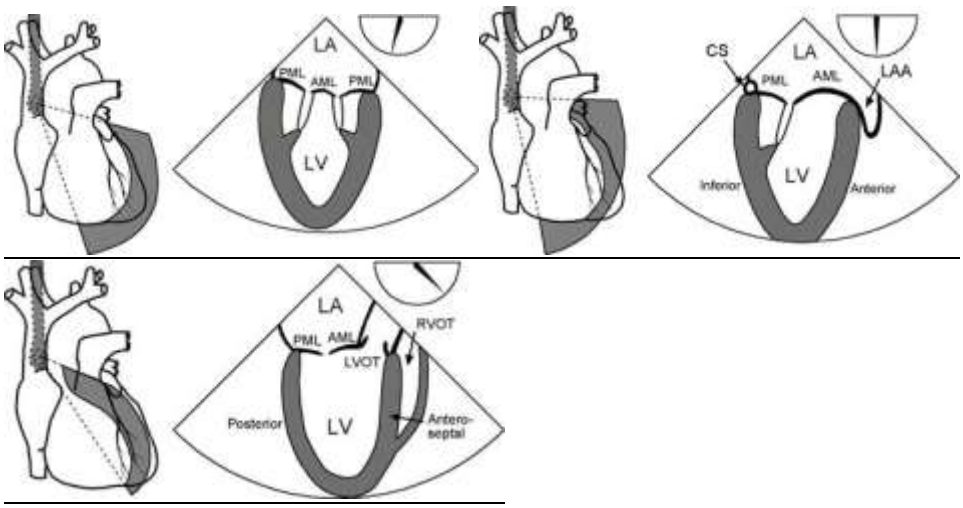
Left atrium:

Size 19-40 mm
Structure. Look for: Thrombi, and in LAA, ASD, tumours
Function: Pulmonary venous flow (PW doppler) SDA waves = (reservoir, conduit, contractile function of atria)
Spontaneous echo (smoke) seen in MS
The pulmonary venous inflow velocity is examined by placing the PWD sample volume in a pulmonary vein 0.5 to 1.0 cm proximal to the LA. The LUPV is usually the easiest to identify and the most parallel to the Doppler beam. CFD imaging is useful in locating pulmonary venous flow and aligning the Doppler beam parallel to its direction, decreasing the scale (Nyquist limit) to 20–30 cm/s to detect the lower velocity venous flow.

Interatrial septum
The IAS consists of the thin fossa ovalis centrally and thicker limbus regions anteriorly and posteriorly. The IAS is examined with CFD to detect interatrial shunts.
Decreasing the Nyquist limit of the CFD is useful for detecting low velocity blood flow through an atrial septal defect or patent foramen ovale. Ten milliliters of agitated saline or blood can be injected into the RA as positive airway pressure is released to detect interatrial shunt, looking for the appearance of contrast in the LA in fewer than five cardiac cycles.

The mid esophageal bicaval view generally provides the best view of the IAS as well as the body and appendage of the RA and the vena cavae.

MITRAL VALVE



The longer of the two leaflets is the anterior leaflet.

Structure: Leaflets, MVA, HOCM, Systolic anterior motion (SAM)
ME Ao Long axis 120 degrees: A2 P2, turn R: A3 P3, turn L : A1 P1
ME commissural view60 degrees: P1 A2 P3 (P1 closest to LAA)
Function: Colour, Regurgitation, look for restrictive movement, billowing, prolapse, flail, cleft
Doppler: Colour/ CW or PW

Trans mitral Doppler for MS and LV Diastolic function:
Place sample volume at the level of leaflet tips in diastole.
E (early) and A (Atrial) Wave ratio (E/A ratio)
TDI on MV annulus E' A'
E/E' ratio
To calculate SV the sample volume should be placed at the level of the mitral annulus

Mitral stenosis:

Look for LA size, “smoke”, doming, thrombus, calcification, and hockey stick deformity.

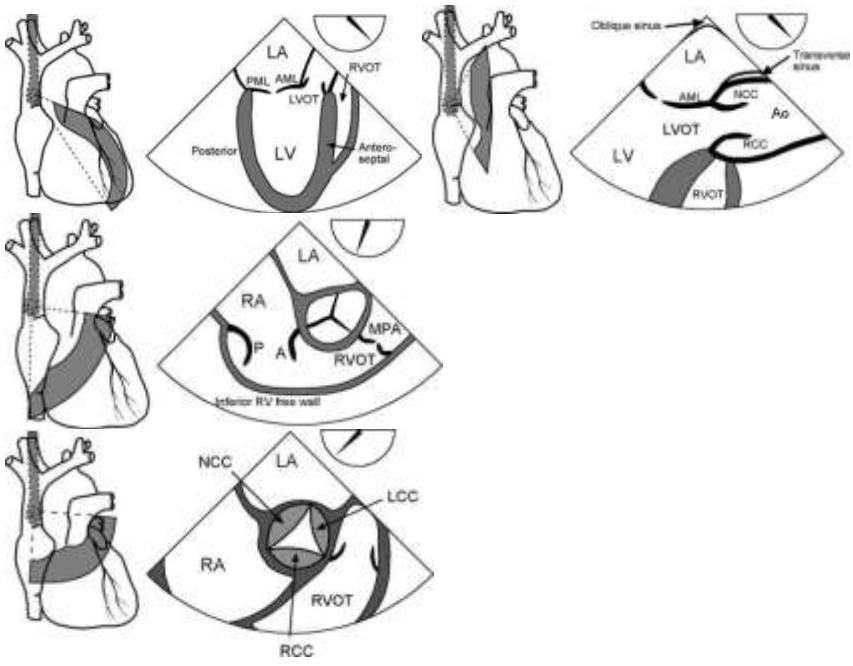
	Normal	Mild	Moderate	Severe
MVA (cm^2)(direct)	4-6	1.5-2.5	1-1.5	<1
MVA ($220/P_{1/2}T$)	4-6	1.5-2.5	1-1.5	<1
MVA (Continuity=$0.785xD^2_{LVOT}$ x VTI_{LVOT}/VTI_{MV}	4-6	1.5-2.5	1-1.5	<1
Mean Pressure Gradient = $4xV^2$ (mmHg)	<3	≤5	5-10	>10
$P_{1/2}T$ (ms)	<89	90-149	150-219	>220

Mitral Regurgitation

For repair look for: Mobility, leaflet thickening, calcification, and annular size.

	Mild	Moderate	Severe
Jet Area/LA area	<20	20-40%	>40%
$RF=SV_{MV}-SV_{AV}/SV_{MV}$	20-30 % = vol<30 ml	30-50% = vol 30-59 ml	>50%= vol .60 ml
Vena contracta Jet Area	≤3mm < 4 cm^2	3-7mm 4-10 cm^2	≥7mm >10 cm^2
Pulmonary Venous Flow:	Normal SDA	Blunting of S wave	Reversal of S wave

AORTIC VALVE AND LVOT



Aortic valve:

(Structure: bicuspid, tricuspid, Cusps, calcification, AVA, Abscess & Function: Colour flow Doppler)

The AV is located close to the center of the heart.
The aortic root includes the AV annulus, cusps, sinus of Valsalva, coronary artery ostia, sino- tubular junction, and proximal ascending aorta.

The LVOT is the outflow portion of the LV just inferior to the AV.

Intra aortic air usually enters the right coronary artery. The right coronary cusp lies anterior (lowermost in display). The non coronary cusp lies adjacent to the intra atrial septum.

The mid esophageal AV long axis view is the best cross-section for assessing the size of the aortic root by measuring the diameters of the AV annulus, sinuses of Valsalva, sino- tubular junction, and proximal ascending aorta.
The diameter of the AV annulus is measured during systole at the points of attachment of the aortic valve cusps to the annulus and is normally between 1.8 and 2.5 cm.

LV outflow Doppler: Use CW Doppler in Transgastric (120) and Deep Transgastric long axis outflow (PW Doppler for LVOT)
Blood flow velocity in the LVOT is measured by positioning the PWD sample volume in the center of the LVOT just proximal to the AV. Flow velocity through the AV is measured by directing the CWD beam through the LVOT and across the valve cusps. Normal LVOT and AV flow velocities are less than 1.5 m/s.
CFD imaging of the LVOT and AV is useful for directing the Doppler beam through the area of maximum flow when making these velocity measurements.

Aortic Stenosis:

Measure annulus diameter, ST junction diameter

	Normal	Mild	Moderate	Severe
AVA cm^2 (planimetry) or continuity= $0.785 \times d^2_{LVOT} \times VTI_{LVOT}/VTI_{AV}$	>2.5	1.5- 2 >0.85 cm^2/m^2	1 – 1.5 0.6- $0.85cm^2/m^2$	<1 $0.6cm^2/m^2$
Mean Pressure gradient mm Hg (P_{max}) Peak velocity		<20 <3m/s	20-40	>40 4m/s
Velocity ratio		> 0.5	0.25-0.5	< 0.25

Aortic Regurgitation

	Mild	Moderate	Severe
Jet area/LVOT Area			>60 %
Jet width /LVOT diameter (M-mode)	<25%		>65%
Regurgitant fraction (RF)= $SV_{AV} - SV_{MV} / SV_{AV}$	<30%	30 -50%	>50%
Pressure ½ time ms	>500	200-500	<200
Regurgitation in descending Ao			Holo-diastolic reversal

ASCENDING AORTA AND AORTIC ROOT:

Look for aneurysms, atheroma, dissection, Coronary arteries

Normal diameter Ao root= 21-34 mm (28mm)

Aortic Atheroma

Grade 1: Normal

Grade 2: intimal thickening

Grade 3: less than 5 mm

Grade 4: more than 5 mm

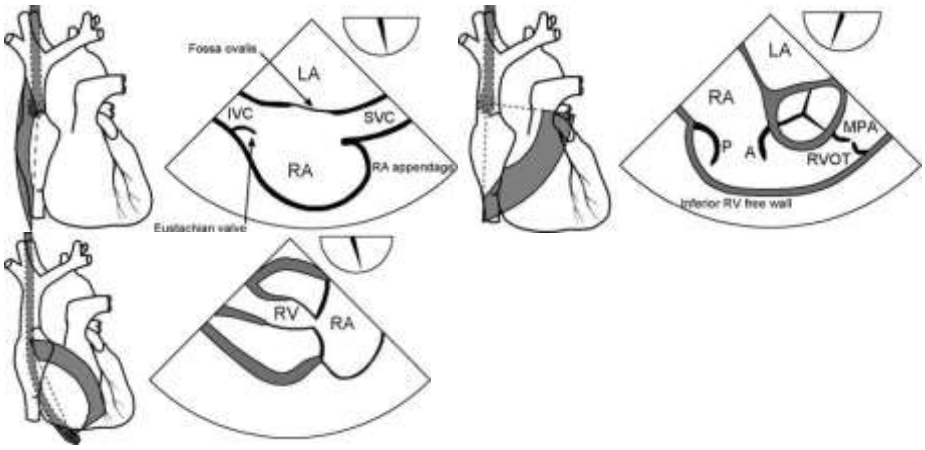
Grade 5: mobile of any size

DESCENDING AORTA:

Look for: Atheroma, dissections, IABP position, fluid in L pleural space.

Most of the thoracic aorta is adjacent to the esophagus.
However, because the air filled trachea is interposed between the esophagus and the distal ascending aorta and proximal aortic arch, these regions cannot be seen.

RIGHT ATRIUM, RIGHT VENTRICLE, TRICUSPID VALVE, & PULMONARY ARTERY AND VALVE



Right Atrium

Structure: Crista terminalis (below SVC), Eustachian valve (above IVC), central venous lines and PPM leads, ASD, PFO, Coronary sinus (with Thebesian valve). PW Doppler in IVC/Liver vein: SDA waveform

Right Ventricle:

Structure: Size compared to LV: RV=1/3 LV =2/3 (LV makes out apex of heart)

Function: FAC (normal > 35 %); TAPSE normal >15 mm

Septum, Chordae, VSD

The RV consists of the free wall, the septal wall, and the RV outflow tract (RVOT), which enclose an asymmetrical, crescent shaped cavity.
The free wall of the RV is thinner than that of the LV, normally less than 5 mm at end diastole.
The shape of the RV cavity in short axis provides information regarding RV function. The septal wall of the RV is normally convex toward the crescent shaped RV cavity. RV pressure or volume overload can cause flattening or leftward deviation of the septal wall, producing an elliptical or circular short-axis shape of the RV cavity.

Tricuspid valve:

Structure: Vegetations, Thrombi, mobility

Function: TR

Doppler: CW for maximum tricuspid regurgitant velocity (TR_{max}) PG= 4x V^2, (PAP= TR + CVP)

The TV is composed of three leaflets (anterior, posterior, and septal), chordae tendinae, papillary muscles, annulus, and RV walls. It is examined with the same cross-sections used to examine the RV. In the mid esophageal four-chamber view, the TV is seen with the septal leaflet to the right of the display and the anterior leaflet to the left

The transgastric views provides the best images of the tricuspid chordae tendinae because they are perpendicular to the ultrasound beam

Tricuspid regurgitation

	Mild	Moderate	Severe
Vena contracta		<7mm	≥7 mm
Hepatic vein flow pattern	S dominant	S blunting	S reversal

Pulmonic valve and pulmonary artery:

The pulmonary artery lies at a right angle to the Ao.

Look for: Structure, Pulmonary emboli/ masses.

Function: Pulmonary gradient, VTI and PA diameter = CO

The PV is a tri-leaflet, semilunar valve. The leaflets are thinner and farther from the esophagus, and therefore more difficult to image with TOE.
The mid esophageal AV short axis view provides a view of the PV.
The mid esophageal RV inflow-outflow view displays the PV in long- axis and is useful for detecting pulmonic regurgitation by CFD. The main PA is seen in the upper esophageal aortic arch short axis view.

LEFT VENTRICLE AND SYSTOLIC FUNCTION

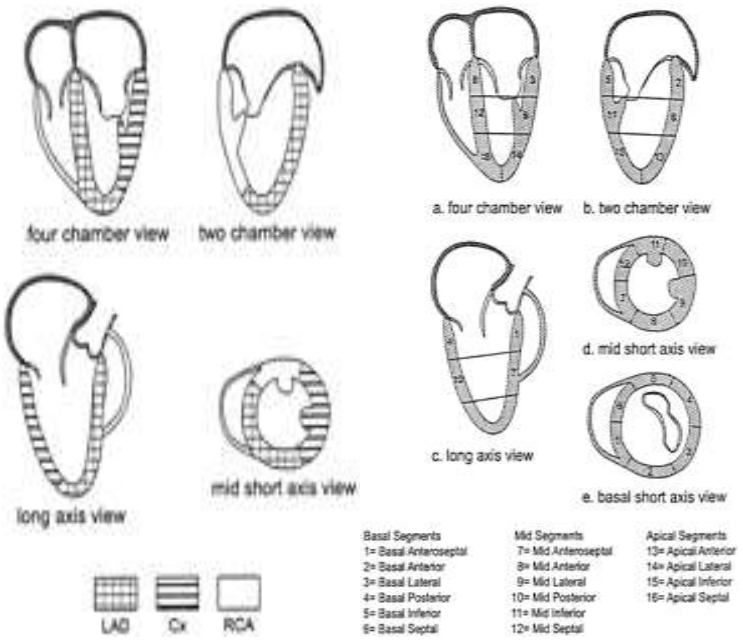
Structure: Septum, Hypertrophy, VSD, Thrombi, Aneurysms, Papillary muscles, Pericardial effusions

Normal LV short axis diameter is less than 5.5 cm, and LV wall thickness is less than 1.2 cm. End diastolic and end systolic areas of the LV chamber may be measured in this cross-section for calculation of fractional area change as an index of LV systolic function. M-mode is very useful.

Function: Kinesia, EF

Qualitative grading scale for wall motion

Normal (> 30% thickening)
Mildly hypokinetic (10-30% thickening)
Severley hypokinetic (<10 % thickening)
Akinetic
Dyskinetic (moves paradoxically and thins during systole)



Diastolic dysfunction:

Trans-mitral PW Doppler: look at E (early) and A (atrial) filling of the LV.

Impaired relaxation has the E/A ratio typically reduced to <1. Most disease processes associated with diastolic dysfunction initially produce this pattern, with a normal LA pressure.

As the disease progresses LA pressure tends to rise, producing changes, which tend to minimize the effects of impaired relaxation and produce a normal-looking pattern to pseudo-normalization.

Further disease progression is associated with a reduction in chamber compliance and restrictive filling develops with an E/A ratio typically >2.

PITFALLS AND ARTEFACTS

Reverberation artefact: A second image of the descending thoracic aorta can be seen below the true aorta.

Normal structures:

- Atrial Membranes
- Ridge between Pulmonary vein and LAA (Warfarin ridge)
- Crista terminalis in SVC RA junction
- Eustachian valve at IVC RA junction
- Chiari network in the RA
- Moderator band in the RV
- Thebesian Valve at opening of the coronary sinus, making the passage of a retrograde cardioplegia cannula into the coronary sinus difficult.
- Transverse sinus: the transverse sinus is a pericardial reflection between the ascending aorta and LA and PA. If it contains pericardial fluid, it will appear as an echo free space in the shape of a crescent or triangle. It may be mistaken for the left main coronary artery
- Enlarged coronary sinus

HAEMODYNAMIC CALCULATIONS

Pressure in originating chamber = pressure in receiving chamber + pressure gradient (through regurgitant valve)

Bernouilli equation = $4 (V)^2$, V in m/s

Continuity equation: Q1=Q2 → stroke volume 1 = SV2 → CSA 1 x VTI 1 = CSA 2 x VTI 2

CSA (cross sectional area = πr^2 or $\pi d^2/4 = 0{,}785\ d^2$)

Ultrasound image interpretation

Dr Ettienne Coetzee

A 26-year-old male patient has suffered penetrating chest and abdominal trauma. His abdomen is tender and the surgical team wants to proceed to laparotomy as soon as possible. The emergency team has started intravenous fluid resuscitation and has provided a venturi face mask. He has the following vital data:

- Blood pressure (Systolic/diastolic): 86/40 mmHg
- Pulse rate: 145 bpm
- Peripheral pulse oximeter: 85%

You are called to assess the patient for theatre. He appears shocked. He has reduced breath sounds bilaterally with no chest radiograph available yet. He has no head trauma but appears confused. You perform ultrasound evaluation of his chest with ultrasound images as below.

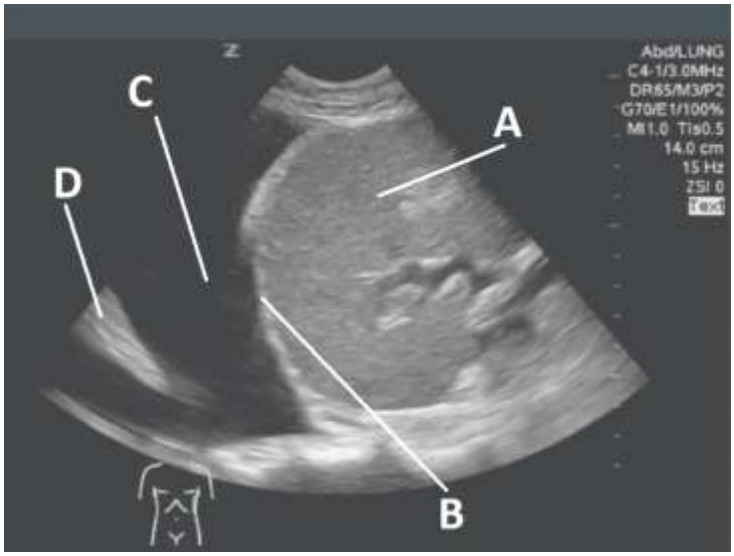


Figure 1 – Left-sided chest U/S

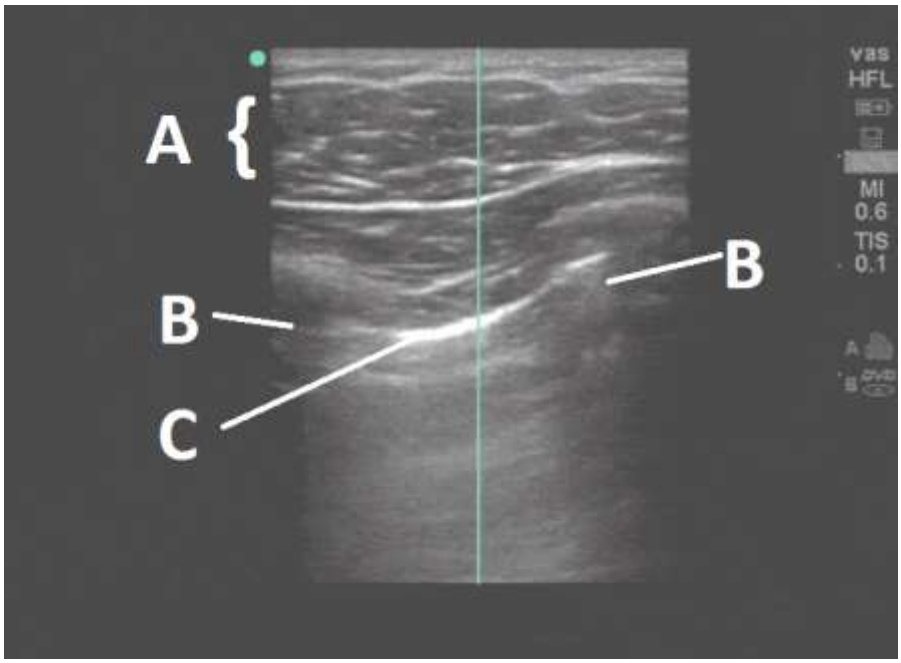
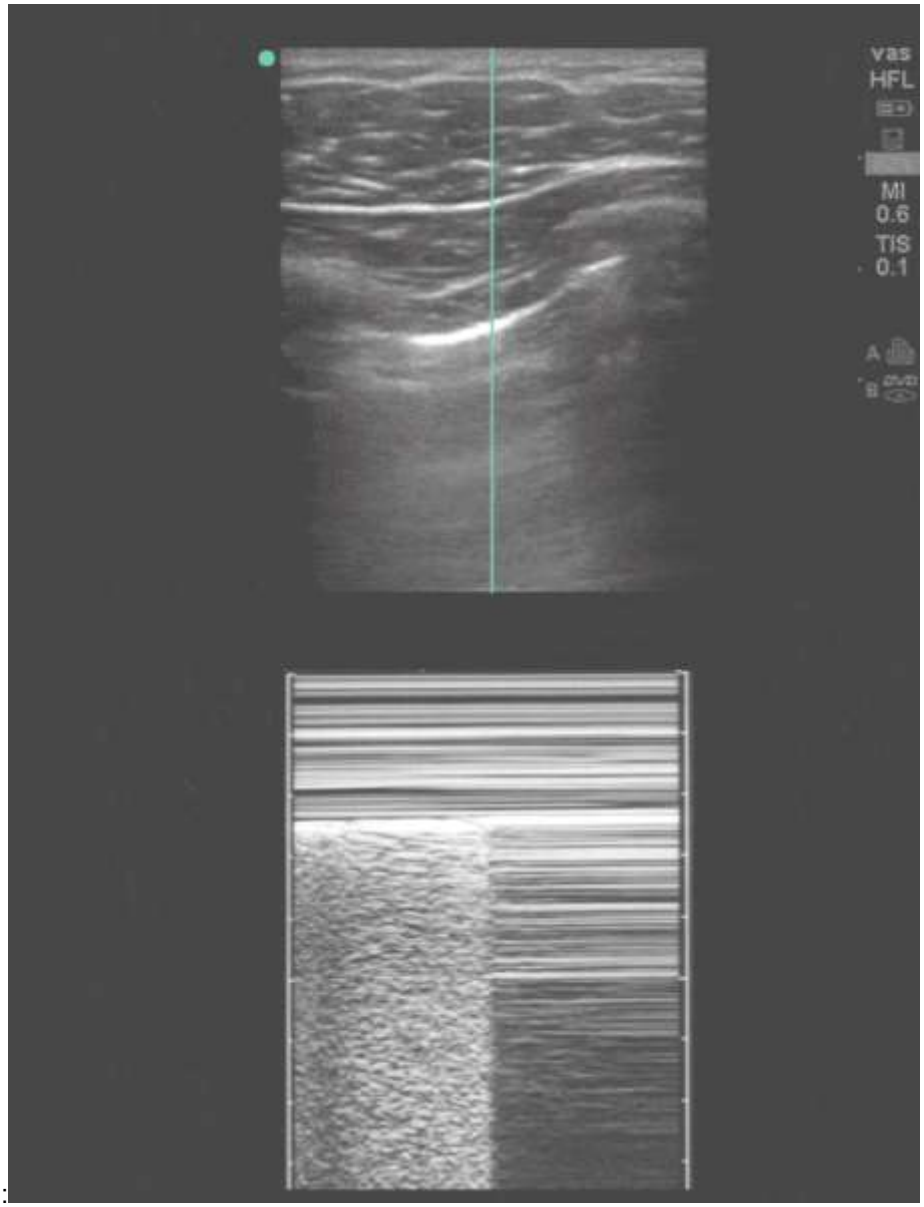


Figure 2 – Right-sided chest U/S

Questions

1. Provide the correct labels for the figures above.
2. What pathology can be seen in figure 1?

3. When you apply M-Mode to the image in *figure 2*, you find the following:



:

Figure 3 - M-Mode

a. What is the diagnosis?
b. What is the significance of the specific M-Mode finding from above?

4. What would be your management prior to going to theatre?
5. You perform a focused cardiac ultrasound while transferring this patient. What specific signs will you look for?

Answers and explanation

Anatomical annotations: Figure 1:

A – Spleen (left sided)
B – Diaphragm
C – Pleural effusion (likely haemothorax)
D – Compressed inferior pole of the lung

The Point Of Care U/S (POCUS) findings from above are commonly performed in the emergency department. *Figure 1* indicates lung ultrasound of the left chest. To achieve this view the cardiac ultrasound probe is used and placed on the lateral chest wall, with the orientation marker pointed towards the patient's head and the ultrasound beam in line with the axial axis of the patient. The probe can be placed at the lower costal margin and moved superiorly until the diaphragm can be **visualised, this being the important landmark. The goal is to evaluate the chest for pneumothorax or** effusions, especially of significance in the above case study.
Figure 1 illustrates a significant pleural effusion, likely a haemothorax in this scenario. The tell-tale signs are the large hypoechoic mass (C) with the compressed inferior lung (D). With such large effusions, the diaphragm is also very clearly visible, as opposed to the absence of effusions resulting in well aerated lungs providing acoustic shadowing of the diaphragm and often obscuring a clear, uninterrupted view.
Figure 2 is an ultrasound performed on the anterior chest wall. It can be performed at multiple levels. The goal is to visualise two opposing ribs (B), with their intercostal space and to specifically find the pleural interface. Normal pleura should move during respiration and gives a characteristic "walking-ants" pattern on 2D U/S. When M-Mode is used, the characteristic "seashore" image can be seen, resulting from the sliding of parietal- and visceral pleura (*figure 3*). The pleural interface causes a bright echogenic artefact (C) since it creates an air- fluid interface.

Anatomical notations: Figure 2:

A – Subcutaneous tissue
B – Ribs
C – Pleura
The M-Mode *(figure 3)* illustrates classic "seashore" and "barcode" alternation. The "seashore" is seen (as mentioned from before) during normal pleural sliding. The so-called "barcode" pattern indicates the absence of pleural sliding and is highly indicative of a pneumothorax. When both patterns are visible, the lung-point has been identified. This is the point where the tip of the lower border of normal lung slides over the pneumothorax and can be used to evaluate expansion or extent of the pneumothorax.

Clinical management appropriate to this case, prior to theatre, should include:

Ongoing intravenous fluid resuscitation after sufficient large-bore cannulae have been placed. Prior to controlling the haemorrhage, a hypotensive haemostatic fluid strategy should be aimed for, unless neuroprotection outweighs the risk for permissive hypotension. Early use of appropriate blood products, guided by bed-side investigations (such as haemoglobin analysis and thromboelastography). With penetrating thoraco-abdominal injuries, the patient should be evaluated for risk of massive transfusion with initiation of such protocols where applicable. One such risk score is the ABC risk score, which can predict the potential for massive transfusion. This patient scores positive on all four indices (penetrating nature of injury, systolic pressure < 90 mmHg, heart rate > 120 bpm and positive ultrasound findings). The use of tranaxemic acid can be considered.
General measures should also include:

- Ongoing secondary survey to evaluate for occult injuries
- maintaining normothermia
- judicious use of analgesics

Both pleural cavities will also require the insertion of intercostal drains, since both likely contribute to the poor oxygenation. Improving the pulmonary perfusion will likely also improve cardiac output and therefore may aid in restoring haemodynamic stability. This coupled with the potential of transforming into a tension pneumothorax during positive pressure ventilation will therefore make placement of both drains mandatory.

Cardiac ultrasound:

Specific signs that could aid in the resuscitation:
Excluding pericardial effusion. Cardiac tamponade is usually a clinical diagnosis, but significant pericardial effusions can cause haemodynamic instability by impeding ventricular filling. Most cardiac views of the standard focused assessment (FATE) will provide information about cardiac effusions with the subcostal view being most appropriate.

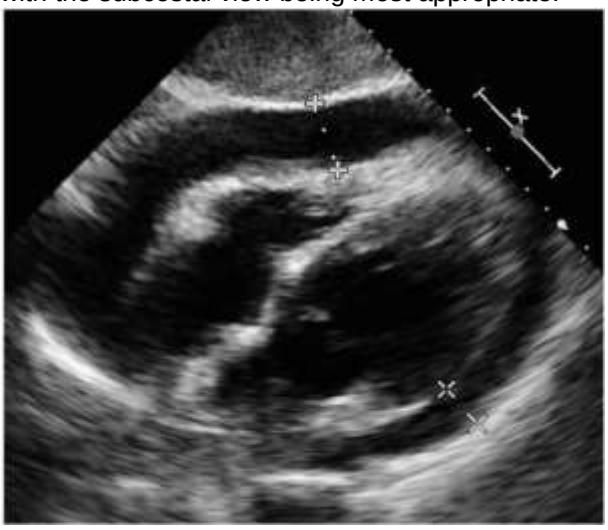
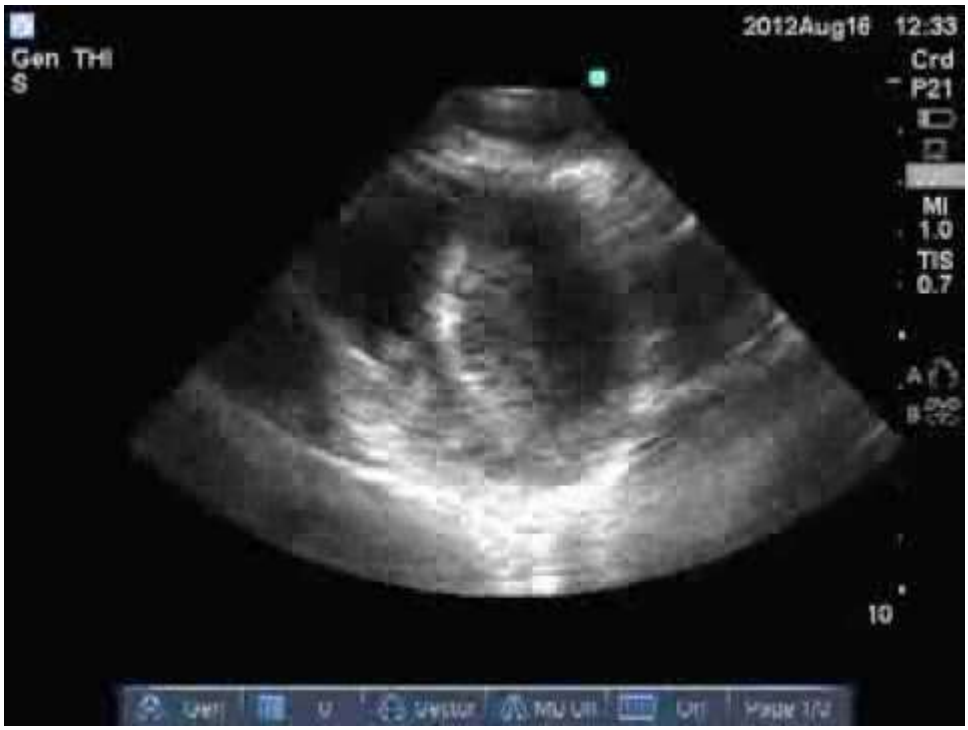


Figure 4 - Pericardial tamponade

Assessing haemodynamic parameters. The ventricular filling characteristics can provide information about adequacy of intravascular volume resuscitation. Low left ventricular end-diastolic volume can indicate insufficient IV fluid therapy and can aid the decision to increase resuscitation efforts. The parasternal short-axis view of the left ventricle is most useful at interrogating the LVEDV.



The presence of ventricular wall motion abnormalities could also indicate injury to the myocardium or coronary artery circulation.

Data interpretation

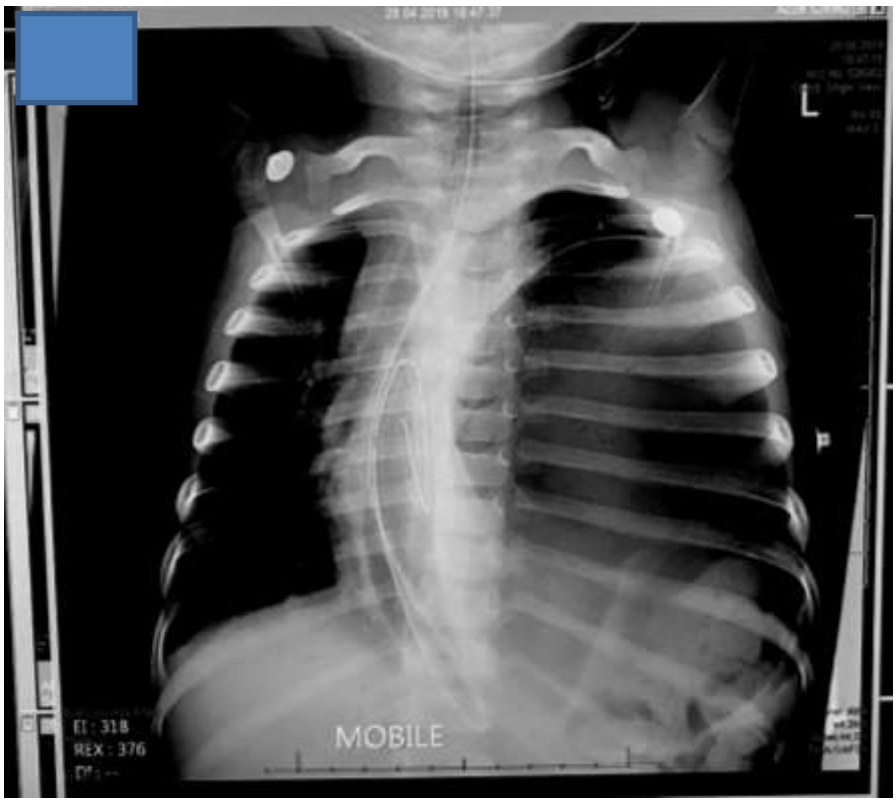
Dr Alma de Vaal

A previously well 2 year old boy presents to the emergency room with acute respiratory distress. He is shocked with a low blood pressure and delayed capillary refill time. There is a history of vomiting and abdominal pain.

His vitals are as follows:

Heart rate 154 bpm
Blood pressure 65/43
SaO2 79%
Respiratory rate 47/min
Capillary refill time > 4 seconds

He receives an intravenous fluid bolus and an X-ray is ordered.



Questions

1) Describe the radiographic abnormalities and provide a differential diagnosis: (3)

2) A nasogastric tube cannot be advanced into the stomach. What is the likely reason for this? How do you confirm the diagnosis (2)?

The arterial blood gas has the following values:

pH	7.14	
pCO_2	6.04 kPa	45,3mmHg
pO_2	7.05 kPa	52,88mmHg
BE	-12.6 mmol/L	
HCO_3^-	13.6 mmol/L	
Lactate	9.6 mmol/L	
Na	138 mmol/L	
K	5.8 mmol/L	
Cl	110 mmol/L	
Ca^{2+}	1.26 mmol/L	
Glucose	3.8 mmol/L	
SaO_2	79%	
p50	5.32 kPA	
Haemoglobin	9.3 g/dl	

3) Suggest an appropriate management strategy of the patient based on the arterial blood gas. (5)

4) What intra-operative problems may be encountered?

Answers

1) The chest x-ray of a 2 y old child shows a space-occupying mass or lesion in the left hemi-thorax: this has made the mediastinum shift towards the right. The trachea and the heart are shifted to the right with little or no lung tissue visible on the left. The nasogastric tube is curled up into the esophagus. A differential diagnosis would be:

a) Cystic lesion in the chest
b) Hydatid cyst
c) Diaphragmatic hernia with bowel in the chest cavity

2) The nasogastric tube cannot be advanced because bowel and stomach have herniated through the diaphragmatic defect into the left hemithorax. The diagnosis is one of incarcerated diaphragmatic hernia. They could give some contrast and confirm an obstruction, or they could do a CT scan to confirm the herniation of bowel into the chest cavity. However, he is acutely ill and the decision for surgery needs to be made urgently.

3) The arterial blood gas shows the following: a primary metabolic acidosis and a respiratory acidosis. There is hyperchloraemia, hyperlactatemia, hyperkalemia and a large base deficit. He is also hypoxaemic.

A: Intubate to improve oxygenation and protect the airway from aspiration
B: Lung protective ventilation: ventilate carefully as most of his tidal volume would go to his right lung. (small volumes and high rates with peep)
C: Fluid bolus, with a crystalloid. 10ml/kg and avoid normal saline that will worsen his hyperchloraemic acidosis. A colloid can also be considered
D: Shift his potassium and give him calcium gluconate / calcium carbonate
E: A central line for possible inotrope requirement

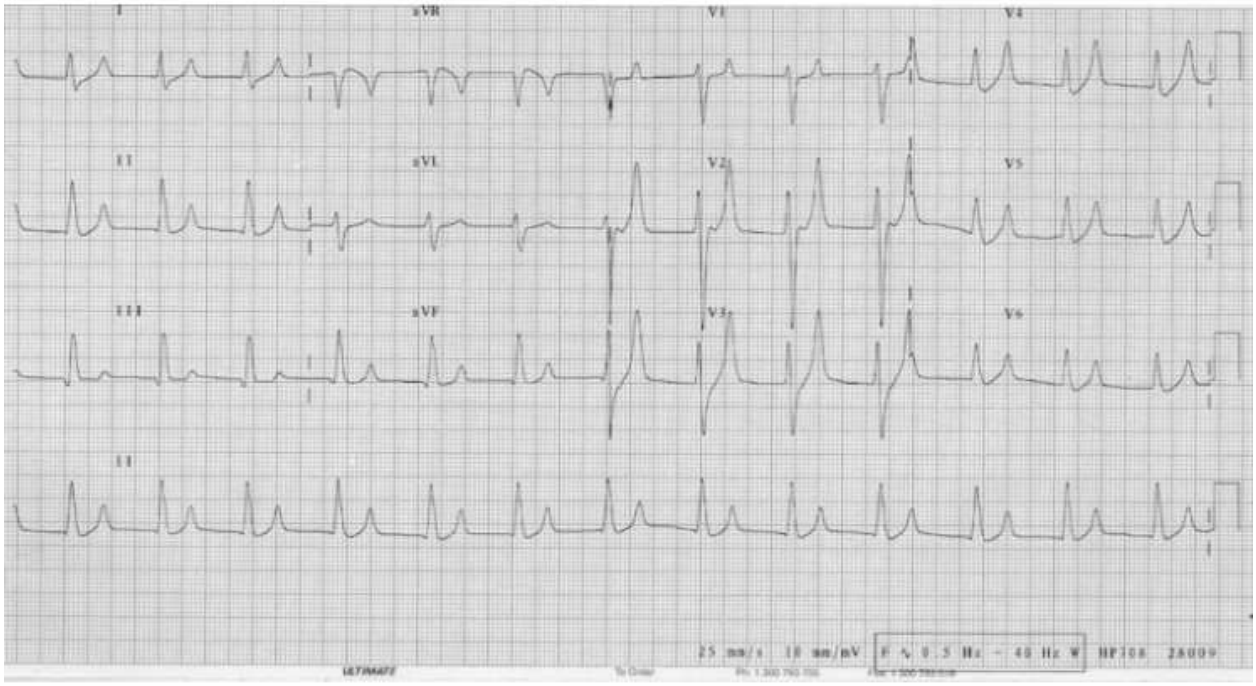
4) Patient to be taken to theatre: Theatre should be prepared as for any other emergency case with all appropriate equipment available and checked.

a) Reperfusion injury when incarcerated bowel is released (ensure fluid bolus given or fluid available as well as inotropes that might be needed)
b) bleeding (ensure a cross-match is done)
c) possible re-expansion pulmonary oedema with hypoxaemia and shunt (V/Q mismatch
d) hyperkalemia and worsening of acidosis

ECG interpretation

Dr Mariesa Nock

A 72 year old woman sustains a fall in her home and is unable to get up again. She is found by family members 2 days after the fall. She complains of hip pain and her leg appears shortened and rotated. She is brought to the emergency department. She is seen by an Orthopaedic surgeon wants to bring her to theatre for a Dynamic Hip Screw for a neck of femur fracture.
Other medical history: Known with Type 2 Diabetes, Hypertension and osteoarthritis.
Medication: Enalapril, Spironolactone ,Metoprolol, Celecoxib
On arrival she is confused with a Glasgow Coma Scale of 13/15. Initial observations: BP 80/60mmHg, Heart rate 78/min Oxygen saturation 90% on facemask oxygen. She is tachypnoeic and has audible midtone crepitations at both lung bases. A urine catheter is inserted and there is minimal drainage of urine. No blood results are available yet.
An ECG is done which shows the following:



Questions:

1. List the abnormalities visible on this ECG (2)
2. What is the most likely electrolyte disturbance that would explain the above ECG(1)
3. Describe the management options of this medical emergency (resulting in the above ECG changes). (7)

Answers

1. Tall tented T-waves, Loss of P-waves, (2)
2. Hyperkalaemia (1)
3. Management:

- **Stabilise the myocardium**:
  - **Calcium Chloride: Dose:** Calcium Chloride 10% 5-10mL.3 x more potent than Calcium gluconate.Complication: severe thrombophlebitis.
  - **Calcium Gluconate: Dose:** Calcium gluconate 10% 5-10mL. Less potent, less irritating to veins
- **Drive Potassium into the Cell:**
  - **Insulin & Glucose**
    Dose: IV fast acting insulin (actrapid) 10-20 units and glucose/dextrose 50g 25-50ml
    Insulin drives potassium into cells and administering glucose prevents hypoglycaemia.
    Begins to work in 20-30mins reduces potassium by 1mmol/L and ECG changes within the first hour
  - **Sodium Bicarbonate**
    Dose: 50- 200mmol of 8.4% Sodium Bicarbonate
    Bicarbonate is only effective at driving potassium intracellularly if the patient is acidotic
    Begins working in 30-60 minutes and continues to work for several hours.
  - **Salbutamol**
    Dose: 10-20mg via nebulizer
    Beta 2 agonist therapy lower K via either IV or nebulizer route.
    Salbutamol can lower potassium level 1mmol/L in about 30 minutes, and maintain it for up to 2 hours.
    Very effective in renal patients that are fluid overloaded
- **Eliminate Potassium From the Body:**
  - **Kayexelate**
    Dose: 15-45g orally or rectally, mixed with sorbitol or lactulose
    Sodium polystyrene sulfonate is a large insoluble molecule that binds potassium in the large intestine, where it is excreted in faeces
    Effects take 2-3 hours
  - **Furosemide**
    Dose: 20-80mg depending on hydration status
    Potassium wasting diuretic. Helps to urinary excrete potassium in conjunction with hydration or fluid overloaded patients
  - **Dialysis**
    Is the gold standard for removing potassium from the body. Provides immediate and reliable removal.
    Can lower potassium by 1mmol/L in first hour and another 1mmol/L over the next 2 hours.

Source: https://litfl.com/hyperkalaemia-management/

Paper Three Questions

Dr Nicole Fernandes

Question 1

The following results are from a patient in your ICU:

Blood gases on 40% O_2 face mask:

	Arterial	Mixed venous
PO_2 (kPa) (mmHg)	12.2 (92.7)	3.8 (28.8)
SO_2 (%)	96.3	52.1
PCO_2 (kPa)	6.1 (46.3)	7.2 (54.7)
TCO_2 (mmol/L)	35.1	39.1
pH	7.47	7.44
BE (mmol/L)	9.5	12.1
Hb (g/dl)	13.6	13.6

Haemodynamic parameters:

	Systemic arterial	Pulmonary arterial
BP systolic (mmHg)	119	37
Diastolic (mmHg)	81	25
Mean (mmHg)	94	30
PAWP (mmHg)	16	
CVP (mmHg)	12	
Heart rate (BPM)	124	
Cardiac output (l/min)	3.3	

Questions

Using the above results, calculate the following. Please show all calculations and also units.

a) CaO_2 (Arterial oxygen content). (3)
b) CvO_2 (Venous oxygen content). (3)
c) CcO_2 (End capillary oxygen content) (3)
d) Shunt fraction. (4)
e) VO_2 (Oxygen consumption per minute) (3)
f) DO_2 (Oxygen delivery per minute) (2)
g) SVR (Systemic vascular resistance) (2)

Answers

a) CaO_2 = (Hb x 1.36) * (SaO_2/100) + (PaO2 * 0.0031)

CaO_2 ml/dl
Hb g/dl
PaO_2 mmHg – if using PaO2 in kPa, conversion factor becomes 1.36 (Huffner's constant- varies in texts from 1.34 – 1.39; represents the amount of oxygen bound to haemoglobin)

CaO_2 = (13.6 * 1.36) * (96.3/100) + (92.7 * 0.0031)
= (18.496) * (0.963) + (0.28737)
= 18.1 ml/dl

CvO_2 = (Hb * 1.36) * (SvO_2/100) + (PvO_2 * 0.0031)

b) Units and parameters as described in part (a).

CvO_2 = (13.6 * 1.36) * (52.1/100) + (28.8 * 0.0031)
= (18.496) * (0.521) + (0.08928)
= 9.7 ml/dl

c) Pulmonary end capillary oxygen tension is assumed to equilibrate with alveolar oxygen tension. Therefore the alveolar gas equation is used to calculate PAO_2 and this value replaces the PcO_2. The end capillary oxygen saturation is assumed to be 100% in the absence of anatomical shunts.

Therefore:

CcO_2 = (Hb * 1.36) * (ScO_2/100) + (PAO_2 *0.0031)

Units and parameters as described in Part (a).

By the Alveolar Gas Equation:

$PAO_2 = FiO_2 (P_B - P_{H2O})$ - ($PaCO_2$ / R)

Where
PAO_2 is measured in mmHg
P_B is barometric pressure in mmHg – 760 at sea level
P_{H2O} is water vapour pressure in mmHg – 47
$PaCO_2$ is measured in mmHg
R is the Respiratory Quotient, a constant which is usually 0.8 assuming a normal diet

PAO_2 = 0.4 (760 – 47) - (46.3/0.8)
= 285.2 – 57.875
= 227.3 mmHg

CcO_2 = (Hb * 1.36) * (ScO_2/100) + (PAO_2 *0.0031)
= (13.6 * 1.36) * (100/100) + (227.3 * 0.0031)
= 18.496 + 0.7
= 19.2 ml/dl

d) $Q_S/Q_T = \frac{(CcO_2 - CaO_2)}{(CcO_2 - CvO_2)} * 100$

Where:

Q_S/Q_T is the shunt fraction as a percentage
CaO_2 is the arterial oxygen content, as calculated in PART (a), in ml/dl
CvO_2 is the venous oxygen content, as calculated in PART (b), in ml.dl
CcO_2 is the end capillary oxygen content, as calculated in PART (c), in ml/dl

Therefore:

$Q_S/Q_T = \frac{(CcO_2 - CaO_2)}{(CcO_2 - CvO_2)} * 100$

= (19.2 – 18.1) / (19.2 – 9.7) *100
= (1.1/9.5) *100
= 11.6 %

e) $VO_2 = CO * [(CaO_2 - CvO_2) *10]$

Where

VO_2 is the oxygen consumption per minute in ml/min
CO is the cardiac output in l/min
CaO_2 is the arterial oxygen content, as calculated in PART A, in ml/dl
CvO_2 is the venous oxygen content, as calculated in PART B, in ml/dl

The arterial-venous oxygen content difference MUST be multiplied by 10 in order to convert the units of ml/dl to ml/L. This allows VO_2 to be expressed in the appropriate units of ml/min.

Therefore:

$VO_2 = CO * [(CaO_2 - CvO_2) *10]$
= 3.3 * [(18.1 – 9.7) * 10]
= 3.3 * (8.4 * 10)
= 3.3 * 84
= 277.2 ml/min

f) $DO_2 = CO * (CaO_2 * 10)$

Where

DO_2 is the oxygen delivery per minute in ml/min
CO is the cardiac output in l/min
CaO_2 is the arterial oxygen content, as calculated in PART A, in ml/dl
The arterial oxygen content MUST be multiplied by 10 in order to convert the units of ml/dl to ml/L. This allows DO_2 to be expressed in the appropriate units of ml/min.

g) SVR = (MAP – CVP) /CO * 80

Where:

SVR is systemic vascular resistance in dyne.sec.cm^{-5}. SVR may also be expressed in Woods units – in this case one would omit the multiplication by the conversion factor of 80.
MAP is the mean arterial pressure in mmHg
CVP is the central venous pressure in mmHg
CO is the cardiac output in l/min

Therefore:

SVR = (MAP – CVP) /CO * 80
= (94-12)/3.3 * 80
= 24.8 * 80
= 1987.9 dyne.sec.cm^{-5}

Question 2

A 36-year old, 74kg man is in ICU following pituitary fossa surgery. He has remained intubated following surgery because of a reduced GCS. There are no focal signs. He is currently only on enoxaparin for thromboprophylaxis. Day five ICU results are as follows:

Blood:

Na	116 mmol/l
K	4.9 mmol/l
Cl	84 mmol/l
Total CO_2	18 mmol/l
Creatinine	110 umol/l
Urea	12 mmol/l
Glucose	8 mmol/l

Urine:

Na	105 mmol/l
Creatinine	2.5 mmol/l

Questions

a) List two possible reasons for the hyponatraemia (2)

b) How is the fractional excretion of sodium (FeNa) calculated? (1)

c) The calculated FeNa is 4%. What is the most likely diagnosis? Justify your answer. (2)

Answers

a) Intracranial surgery, particularly in the pituitary fossa, commonly leads to disturbances of sodium balance. The two most likely causes for hyponatraemia in this case are:

Syndrome of Inappropriate ADH Secretion
Cerebral Salt Wasting syndrome

b) The FeNa is the percentage of sodium filtered by the kidney which is excreted in the urine.

It is calculated in two parts:

Determine how much sodium is excreted in the urine (after reabsorption has taken place)

- Calculated by multiplying the urine sodium concentration by the urinary flow rate
- This is the NUMERATOR of the FeNa equation

Find the ratio of that excreted to the total amount of sodium that was filtered by the kidney

- Calculated by multiplying the plasma sodium concentration by the glomerular filtration rate (using creatinine filtration)
- This is the DENOMINATOR of the FeNa equation

The above gives us the following equation:

$$[(\underline{Sodium}_{urinary} \times Flow\ rate_{urinary}) \div ((\underline{Sodium}_{plasma}) \times ((\underline{Creatinine}_{urinary} \times Flow\ rate_{urinary}) \div (\underline{Creatinine}_{plasma})] \times 100$$

One can then cancel out the flow rates, simplifying to the standard equation:

$$FeNa = 100 \times [(Sodium_{Urine} \times Creatinine_{Plasma}) / (Sodium_{Plasma} \times Creatinine_{Urine})$$

c) The purpose of calculating FeNa is to determine the cause of acute renal failure. A high FeNa value suggests an intrinsic renal issue or salt wasting, rather than prerenal disease. In this case CSW is more likely than SIADH. The table below describes the likely causes of both low and high FeNa. Absolute values of urine Na excretion aid in the diagnosis – urine Na > 20mEq/L suggests an intrinsic renal issue.

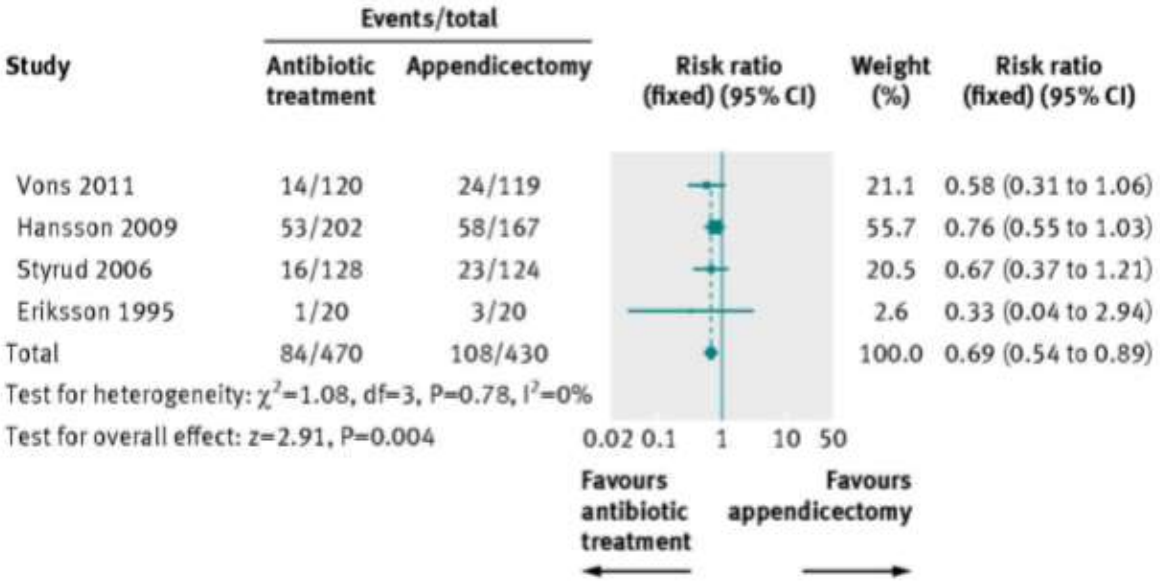
Value	Diagnosis	Description
< 1 %	Prerenal disease	Indicates that the kidney is still able to reabsorb and conserve sodium. Pathology is likely extrinsic to the urinary system eg. Response to decreased renal perfusion
> 3 %	Acute tubular necrosis/ intrinsic renal disease/ salt wasting	Indicates salt wasting either due to acute tubular necrosis or other forms of intrinsic renal disease.
1-3%	Obstruction	Obstructive renal disease may initially cause a low FeNa, but as the obstruction leads to renal injury the FeNa will increase.

Special circumstances

- In paediatrics values are unreliable due to the immature tubules inability to fully reabsorb sodium
- Diuretic therapy resulting in sodium excretion makes the test difficult to interpret – must be used in conjunction with other clinical data

Question 3

Researchers undertook a meta-analysis of randomised controlled trials to establish the safety and efficacy of antibiotic treatment compared with appendectomy as primary treatment for uncomplicated appendicitis. The primary outcome measure was the presence of several pre-set (fixed) complications. The results of the meta-analysis for complications are presented in the forest plot below.



Questions

a) Identify the study that contributed most to the meta-analysis. (1)

b) What determines the contribution size of included trials to the meta-analysis? (1)

c) Identify the trials that showed a significant difference between treatment groups regarding the risk for predetermined complications. Explain your answer briefly. (2)

d) Regarding heterogeneity
   i) Describe and motivate the statistical heterogeneity between the sample estimates of the population relative risk. (2)
   ii) Explain the implication of this finding. (1)

e) How do you interpret the finding of the meta-analysis regarding the total overall population relative risk at the mentioned 95% confidence interval? (2)

Answers

a) Hansson 2009.

The weighting of the studies in a forest plot is represented by the size of the box on the chart – the bigger the square, the more weight the study has. In this instance the weight is also represented as a percentage alongside the forest plot, but this information may not always be provided.

b) The number of participants in the trial.
This is purely based on trial size. The quality of the study is not taken into account at all. This is a potential flaw of meta-analyses – a poorly conducted study will carry a significant weight and influence the outcome if its numbers are sufficiently large.

c) None of the individual trials showed a significant difference.
The forest plot represents the Risk Ratio and 95% confidence intervals for each of the studies. A risk ratio of 1 means there is no difference between the groups. The line down the middle of the Forest plot is known as the line of no significance (in this case a RR of 1). Any line which crosses the line of no significance renders the study insignificant. One can also look to the numerical representation of the 95% confidence interval. If this range of numbers includes 1 (or in some cases 0, if ratios are not represented) then the study is insignificant.

d) The I^2 is 0%. This means the included studies show no heterogeneity and are highly comparable.
Heterogeneity on a Forest Plot is represented by the I^2 value. This describes the consistency of the included studies – a low I^2 indicates that the included studies are similar and comparable and that the findings of the meta-analysis are less likely to be due to chance. An I^2 less than 50% is considered to be favourable. Higher I^2 values mean that the studies are very dissimilar and their findings may therefore not be comparable.

e) The overall finding of the meta-analysis is that antibiotic treatment is significantly favoured. The overall RR is 0.69, and the 95% CI does not cross 1, indicating significance.
This finding illustrates the fact that despite the individual studies showing no significance, the larger pooled numbers may reveal a significant result. The small included studies may have alerted one to the signal that a difference is present, but only on pooling results and analysing larger numbers of study participants a significant result is found. The very low heterogeneity increases the likelihood that the finding is truly significant.

Single Best Answer (SBA) Practice Questions

Contributors:

Drs D. Batty, K. Bergh, K. Bester, K. Bhagwan, M. Casey, A. de Vaal, R. Gray, R. Haylett, H. Meyer, M. Nejthardt, M. Nock, C. Simons

Dept of Anaesthesia & Perioperative Medicine
University of Cape Town

Question 1

The bundle of actions most likely to result in ***suboptimal*** postoperative epidural analgesia for a Whipple's procedure is

a.
- Level of insertion: T8/9
- Method to identify epidural space: loss of resistance to saline
- Catheter length in epidural space: 5 cm
- Use of multiport epidural catheter

b.
- Level of insertion: T8/9
- Method to identify epidural space: loss of resistance to air
- Catheter length in epidural space: 3 cm
- Use of uniport epidural catheter

c.
- Level of insertion: T8/9
- Method to identify epidural space: loss of resistance to air
- Catheter length in epidural space: 6 cm
- Use of multiport epidural catheter

d.
- Level of insertion: T8/9
- Method to identify epidural space: loss of resistance to saline
- Catheter length in epidural space: 4 cm
- Use of uniport epidural catheter

Question 2

Which of the following are most likely to reduce intraoperative blood loss during a liver resection for a metastatic lesion?

a. Maintain CVP > 5 cm H_20 plus tranexamic acid
b. Maintain CVP < 5 cm H_20 plus tranexamic acid
c. Maintain CVP > 5 cm H_20 plus cell salvage
d. Maintain CVP < 5 cm H_20 plus cell salvage

Question 3

The obstetrician on call asks you to anaesthetise a patient who urgently requires a caesarean section for fetal distress. Once you have assessed the patient, you decided that spinal anaesthesia is safe and appropriate. Before injecting the Bupivacaine intrathecally, you make sure that you observe CSF backflow. Unfortunately, it turns out that your spinal block is inadequate for the procedure.
The least likely reason for a failed elective obstetric spinal anaesthetic, administered after observing CSF backflow, is

a. The dura mater acted as a flap valve across the opening of the pencil point needle
b. The arachnoid mater acted as a flap valve across the opening of the pencil point needle
c. The opening of the pencil point needle 'straddles' the dura
d. The backflow observed, was not CSF

Question 4

A 74-year-old man with COPD is undergoing a left pneumonectomy for adenocarcinoma of the lung. While on one lung ventilation, his SpO_2 falls to 84% on an FiO_2 of 100% with no increase in airway pressures or change in tidal volume. Bronchoscopy confirms a correctly placed double lumen tube. Five cmH_2O of PEEP is applied. Which one of the following options is most likely to result in a significant improvement in SpO_2?

a. Applying CPAP to the non-dependent lung
b. Asking the surgeon to clamp the left pulmonary artery
c. Increasing PEEP to the dependent lung
d. Instituting manual two lung ventilation

Question 5

In addition to covering the surgical site and administering 100% oxygen, which positioning manoeuvre is appropriate in a patient with a suspected venous air embolism during posterior fossa craniectomy?

a. Left lateral decubitus head down
b. Supine head down
c. Right lateral decubitus head down
d. No change in position

Question 6

The safest way of securing the airway of a neonate with a Gross C/Vogt IIIb tracheo-oesophageal fistula, after suctioning the upper oesophageal pouch and performing an inhalational induction is

a. Lignocaine spray to the cords → bronchoscopic examination → intubation (ETT tip below the fistula) → muscle relaxant.
b. Muscle relaxant → bronchoscopic examination → intubation (ETT tip below the fistula)
c. Lignocaine spray to the cords → intubation (ETT tip below the fistula) → muscle relaxant.
d. Lignocaine spray to the cords → bronchoscopic examination → intubation (ETT tip below the fistula)

Question 7

The best way to manage hypotension in a brain-dead organ donor is to administer 250ml of colloid and commence an infusion of

a. Adrenaline
b. Noradrenaline
c. Phenylephrine
d. Vasopressin

Question 8

During invasive blood pressure monitoring using the radial artery, one can expect to see a wide pulse pressure

a. In an 85-year-old patient
b. In someone with aortic stenosis
c. If there is an air bubble in the line
d. In a patient with polycythaemia

Question 9

A 20-year-old patient suffered a burn injury to 50% of his body surface area. Which statement with regards to the hypermetabolic syndrome of burns is true?

a. The hypermetabolic syndrome should abate by 4-6 weeks post injury.
b. Fatty infiltration of the liver could result from excessive lipolysis.
c. Hypermetabolic syndrome of burns is characterised by a resting tachycardia without a change in core temperature.
d. Initiation of enteral feeds should be delayed due to associated gastroparesis.

Question 10

A parturient who suffers from systemic lupus erythematosus is in active labour and requests an epidural. Which statement is true?

a. If her electrolytes and urea were checked in the last 24 hours, there is no need for further special investigations.
b. Her risk for deep venous thrombosis is similar to other parturients' risk.
c. The most significant neurological risk for this patient is that of having a stroke.
d. Maternal antibodies can cause neonatal tachycardia

Question 11

What statement is true with regards to neurological complications following regional analgesia:

a. Spinals pose a higher risk than epidurals because the needle is inserted intrathecally.
b. The risk of paraplegia or death from neuraxial techniques is about 1:25 000.
c. Neuropathies associated with peripheral nerve blocks are usually permanent, but mild.
d. Diabetic patients have a higher risk of complications than the general population.

Question 12

A 60-year old patient with chronic obstructive airways disease and a mild upper respiratory tract infection presents for radiofrequency ablation for atrial fibrillation in the catheterisation laboratory. Which of the following anaesthetic techniques will be associated with the best outcome:

a. General anaesthesia with a shallow ventilatory pattern.
b. Deep isoflurane anaesthesia with continuously monitored deep muscle relaxation.
c. Local anaesthesia with light fentanyl and midazolam sedation.
d. Ketamine anaesthesia with a native airway.

Question 13

"Good clinical practice" principles ensure that

a. The identities and data of subjects are accessible to all.
b. Studies are designed well enough that no monitoring of projects is needed.
c. The welfare of trial subjects is prioritised.
d. Data is in keeping with current knowledge.

Question 14

Who should give consent for electroconvulsive therapy (ECT)?

a. No consent is needed for a patient admitted under the Mental Health Care Act.
b. If a patient is an assisted mental health care user, their applicant can give consent.
c. The Minister of Health must give consent for an involuntary health care user.
d. A voluntary health care user's applicant can give consent.

Question 15

Why should the analysis of an adverse clinical incident be structured?

a. A structured process will limit the extent of the investigation.
b. A structured process will clearly indicate which individual was at fault.
c. A structured process will ensure that no report needs to be formulated.
d. A structured process will encourage staff who are interviewed to feel less threatened.

Question 16

A 60-year-old male is booked for a laparoscopic inguinal hernia repair. His lung function shows the following results:

	Pre-bronchodilator	Post bronchodilator	Predicted (mean)
FEV_1	1.6 L	1.65 L	3.54 L
FVC	4.0 L	4.1 L	5.0 L

What is the most likely diagnosis and management pre-operatively?

a. Severe asthma patient with reversibility; this patient should be cancelled and optimized.
b. Gold Stage II COPD with reversibility; patient should be cancelled and treated with a course of steroids.
c. Gold Stage III COPD with no significant reversibility; patient should be done with caution.
d. Severe restrictive lung disease; this patient should be done under regional anaesthesia to avoid intubation and ventilation.

Question 17

A 16 year old boy is undergoing resection following neo-adjuvant chemotherapy for an osteosarcoma of his distal femur. His full blood count is as follows:
Haemoglobin: 9.5g/dl
White cell count: 3.0 $x10^9$/L
Platelets: 154$X10^9$/L

What blood conservation techniques would be most appropriate in this case?

a. Perioperative allogenic blood transfusion
b. Cell salvage with cross-matched blood available
c. Tourniquet on the lower limb, tranexamic acid and cross-matched blood available
d. Patient should be cancelled and his anaemia optimized with iron and erythropoetin
e. Pre-deposited autologous blood donation

Question 18

A 4-year-old boy presents for a muscle biopsy for suspected muscular dystrophy following a fall off in motor-milestones and a positive Gower's sign. Which one of the following statements is true?

a. He carries a significant risk of malignant hyperthermia and all the necessary precautions should be taken.
b. Post-operative respiratory insufficiency should be anticipated
c. Propofol may affect the biopsy result and should be avoided
d. An uneventful previous volatile anaesthetic is not an indication of proven safety of volatiles for this child

Question 19

Cerebral palsy is a spectrum of movement or posture disorders resulting from an injury or insult to the fetal or infant developing brain. Patients may be on a variety of medications to control movements, muscle tone and seizures. Baclofen is a $GABA_B$ agonist which can be given orally or intrathecally to reduce spasticity. Patients on oral baclofen who are unable to tolerate oral intake post-operatively may go into acute withdrawal. Which of the following statements regarding the withdrawal state is true?

a. Withdrawal may result in painful spasms and seizures for which parenteral benzodiazepines such as intravenous midazolam or rectal diazepam are the best management.
b. Withdrawal may result in muscle weakness and respiratory failure, this should be monitored for closely with respiratory support (non-invasive or full ventilation) available as indicated.
c. Psychosis and hypertension may result from Baclofen withdrawal and may be avoided by prophylactic haloperidol administration.
d. Severe gastrointestinal side effects may result with intractable vomiting and diarrhea which should be managed supportively with fluid replacement and symptomatic treatment with parenteral antiemetics.

Question 20

A 15-year-old child with 4-hour history of a supracondylar fracture and pulseless forearm refuses consent for surgery on the grounds of severe anxiety about death under anaesthesia. His father insists that surgery go ahead without the child's consent. Which of the following is true?

a. The treating physician may proceed with the parent's consent as the parent's will supersedes the child's.
b. According to The Children's Act (2005) surgery cannot be performed on a child over the age of 12 years against their wishes, an emergency application to the High Court or Children's Court must be made to obtain consent before proceeding.
c. The superintendent of the hospital may consent to the surgery proceeding on the child.
d. A mental health practitioner should assess the child's capacity to consent and if this is found to be lacking surgery can proceed with the parent's consent.

Question 21

A 12-month-old girl has swallowed a button battery, chest X-ray shows it positioned at mid-oesophageal level. She had 125ml of formula milk four hours ago. Which of the following is true?

a. She requires oesophagoscopy and removal of the coin, but this should be delayed until 6 hours after ingestion of the formula to ensure adequate fasting.
b. Oesophagoscopy and removal of the coin should proceed without delay even though the child is not fasted.
c. Oesophagoscopy and removal of the coin may proceed without delay as the child is adequately fasted according to the updated fasting guidelines.
d. Guidelines for button battery ingestion advise against immediate removal and recommend a trial of passage.

Question 22

High frequency oscillatory ventilation (HFOV) uses tidal volume (V_T) less than dead space volumes with strict control of intrathoracic pressure variations. Which of the following statements is true?

a. HFOV is a good mode for neonatal lungs due to their high susceptibility to barotrauma.
b. HFOV is contra-indicated in neonatal lungs due to the high susceptibility to atelectrauma.
c. HFOV is a good mode for neonatal lungs unless an air leak is present.
d. HFOV cannot be used in neonates as it requires an endotracheal tube of at least 4.0mm internal diameter.

Question 23

Utilising the Beer-Lambert Law, cerebral oximetry allows for continuous non-invasive monitoring of cerebral oxygenation by the application of a set of light sources and detectors to the scalp, usually over the frontal lobe. Which of the following describes a limitation of this technology?

a. Patients must be paralysed as the electromyographic output of muscle contraction will interfere with the reading.
b. Hypothermia reduces accuracy of the measurement.
c. It only measures regional oxygenation so large areas of the brain remain unmonitored.
d. Utility in neonates is limited by an inability to measure oxygen saturation of fetal haemoglobin (HbF).

Question 24

In general, participation in research must be voluntary and predicated on informed choices. Voluntariness and informed choices are evidenced by the informed consent process which must take place before the research commences and be affirmed during the course of the study, as part of the commitment to an ongoing consent process. In some circumstances, research may not require prior consent. Which of the following describes a situation where consent is not required?

a. Observational research of people in a public space without the reasonable expectation of privacy and where no intervention is performed by the researcher.
b. An audit of a common practice (e.g. cannula insertion) with no intervention performed by the researcher.
c. Measuring practitioner satisfaction with a new intervention.
d. An audit of practice as a follow-up to an intervention staged on the basis of an original for which consent was acquired.

Question 25

With reference to critical incident reporting in clinical practice, which of the following statements is true?

a. Critical incident reporting is a mandatory professional obligation for all practitioners registered with the HPCSA.
b. Critical incident reporting should not identify the name and rank of the person whose action or inaction contributes to the incident.
c. When a critical incident is voluntarily reported there should be no sanction placed on the reporter.
d. Critical incident reporting should include no harm-incidents and near miss incidents as well as adverse events.

Question 26

Eight months after a traumatic spinal cord injury, a patient requires surgery to treat a urethral stricture. Regarding autonomic dysreflexia, the following statements are true EXCEPT:

a. A blood pressure of 120/80mmHg is inconsistent with the diagnosis of autonomic dysreflexia
b. Injuries below T6 and incomplete lesions are less likely to lead to autonomic dysreflexia than those above T6 and complete lesions
c. Signs include flushed, sweaty skin above the level of the spinal cord lesion and cool, pale skin below the level of the lesion
d. Both tachycardia and bradycardia may be present during an episode of autonomic dysreflexia

Question 27

Regarding the use of phenylephrine following neuraxial blockade in obstetric anaesthesia, the following statements are true EXCEPT:

a. Continuous infusion produces fewer episodes of hypotension than intermittent boluses
b. There is less umbilical artery acidaemia than with ephedrine usage
c. There is less bradycardia compared to ephedrine usage
d. It has not been shown to exhibit tachyphylaxis

Question 28

Intra-aortic balloon pump (IABP) increases the oxygen delivery to the myocardium and decreases the myocardial oxygen demand, thereby improving its function. Which of the following physiological effects are NOT seen with a well-functioning IABP?

a. Increased aortic diastolic pressure
b. Decreased left ventricular end-diastolic pressure
c. Decreased renal blood flow
d. Increased coronary blood flow

Question 29

Regarding a patient with acromegaly presenting for trans-sphenoidal resection of the pituitary gland tumour, which of the following statements is likely to be true?

a. Male patients with acromegaly are as likely to suffer from OSA (obstructive sleep apnoea) as female patients
b. The patient will likely have distal myopathy
c. The patient will likely have raised ACTH (adrenocorticoptrophic hormone) levels
d. The patient will likely have raised IGF-1 (insulin-like growth factor-1) levels

Question 30

Regarding anaesthesia for LASER ablation of vocal cord nodules in ENT surgery:

a. The airway of choice is a cuffed LASER-resistant endotracheal tube, the cuff filled with saline and methylene blue
b. The ideal gas mixture is oxygen with nitrous oxide, as oxygen supports combustion
c. Reduce oxygen concentration to ≤40 percent before use of any ignition source during procedures inside the airway
d. Allow at least 30 seconds for the both the fraction of inspired oxygen (FiO_2) and the fraction of expired oxygen (FeO_2) to be reduced to a safe level, before the surgeon activates the ignition source

Question 31

A 75 year old woman is being treated with broad spectrum antibiotics for ventilator associated pneumonia. She develops abdominal distension and diarrhoea; the likely diagnosis is Clostridium difficile. Her white cell count is $20x10^9$; she remains haemodynamically stable and does not require inotropes. The most appropriate first line therapy is:

a. Metronidazole 500mg TDS po
b. Metronidazole 500mg TDS IV
c. Vancomycin 125mg QID po
d. Vancomycin 500mg QID po *and* Metronidazole 500mg TDS IV

Question 32

An 80 year old woman presents with a 2 month history of severe, continuous burning pain in her right eye. She has also had a skin rash over the affected site which began a week after the onset of the pain. She has previously been treated with intermittent courses of prednisone for the management of her poorly controlled COAD. The likely diagnosis is:

a. Trigeminal neuralgia
b. Post-herpetic neuralgia
c. Giant cell arteritis
d. Polymyalgia rheumatica

Question 33

Anaesthesia for electroconvulsive therapy (ECT) is frequently provided in remote locations which has a bearing on its conduct and the efficacy of the treatment. Which of the following statements is most correct?

a. The presence of an anaesthetic machine is mandatory
b. Pipeline oxygen must be available
c. Suxamethonium is used primarily to prevent musculoskeletal injury
d. Propofol should be avoided as it prevents the induction of an adequate seizure

Question 34

A 2 year old, 14 kg child with an unrepaired Tetralogy of Fallot is booked for an elective umbilical hernia repair. Her oxygen saturations are 80% and she is on propanolol. Which is the most appropriate anaesthetic management goal?

a. Administer a high FiO_2
b. Decrease PVR
c. Avoid catecholamine surges
d. Decrease afterload

Question 35

2 year old, 14 kg child with an unrepaired tetralogy of fallot is booked for an elective umbilical hernia repair. During surgery you notice a sudden decrease in $ETCO_2$ and rapid desaturation. The most appropriate immediate management includes administration of:

a. Sodium bicarbonate, and adrenaline
b. Fentanyl, and phenylephrine bolus
c. Phenylephrine bolus, and lighten depth of anaesthesia
d. Magnesium, and esmolol bolus

Question 36

A 1 year old, 8 kg child is booked for a thoracotomy and ligation of a pulmonary ductus arteriosus (PDA). Her oxygen saturations are normal and she has no features of pulmonary hypertension. During anaesthesia left to right shunt through the PDA will decrease with which intervention?

a. Increased minute ventilation
b. Increased FiO_2
c. Increased anaesthetic MAC
d. Phenylephrine bolus

Question 37

Gastroschisis is associated with the following congenital condition:

a. Congenital heart disease
b. Beckwith-Wiedeman syndrome
c. Trisomy 21
d. Intestinal atresia

Question 38

You are asked to provide sedation for a 35 year old ASA 2 patient for ERCP. Which is the most appropriate statement?

a. Propofol is adequate as a sole agent
b. Supplemental oxygen may be administered to prevent hypoventilation
c. Use of continuous waveform capnography to monitor adequacy of ventilation is recommended
d. Bolus doses of midazolam can be used for analgesia throughout.

Question 39

Ketamine is widely used in subanaesthetic doses as a perioperative adjunct in acute pain. Regarding postoperative ketamine infusion for postoperative analgesia, which of the following statements is most accurate:

a. Poorly controlled cardiovascular disease, pregnancy, psychosis and moderate hepatic disease are all absolute contraindications;
b. The published evidence demonstrates a clear short-term, opioid sparing effect regardless of whether it is given as a bolus, infusion, or via PCA;
c. The primary issue preventing widespread adoption of ketamine infusions outside operative or intensive care unit settings is the potential for adverse psychomimetic effects which have been established as dose dependent for analgesic doses;
d. The recommended dosing range is a bolus of up to 0.5mg/kg and an infusion rate of up to 1mg/kg/hr

Question 40

Which of the following is not an absolute contraindication to liver transplant?

a. Severe cardiac or pulmonary disease
b. Uncontrolled sepsis including biliary sepsis
c. Ongoing alcohol or substance abuse
d. HIV infection

Question 41

An 18 year old man from the Democratic Republic of Congo is booked to come to theatre for an explorative laparotomy for an acute abdomen. You decide to assess him in the ward. He is unable to speak English and there is no interpreter available. According to the notes he has a 3 day history of severe abdominal pain. On examination he is mildly jaundiced and appears pale. You are unable to palpate his liver but you detect splenic enlargement and he has a very tender abdomen. His ward Hb is 6g/dl. You find a packet with medication on his bedside cupboard which contains hydroxyurea and folic acid.
The single investigation that has the best ability to confirm and define your suspected diagnoses is:

a. Haemoglobin electrophoresis
b. Liver function test
c. Sickledex test
d. A full blood count with blood smear

Question 42

A 14 year old mentally impaired girl is brought to theatre for a termination of pregnancy for which her mother has signed consent on her behalf. She is accompanied by her mother, who requests that a sterilisation is done at the same time, since the child does not have capacity to ever care for a child. The best way to proceed is:

a. To complete the termination of pregnancy but not the sterilisation and to obtain an Independent Medical Practitioner's assessment on whether sterilisation is in the best interest of the child.
b. To complete the termination of pregnancy and proceed with the sterilisation since the child lacks decisional capacity and it is in the child's best interest to be sterilised.
c. To obtain an assessment of the 14 year old child's mental capacity prior to proceeding with either the termination of pregnancy or sterilisation.
d. To proceed with the termination of pregnancy and inform the mom that legally the youngest age for sterilisation is 18 years

Question 43

Regarding the airway assessment of a 45 year old patient with acromegaly, which of the following statements is the most correct?

a. A score of Mallampati score of 1 indicates that vocal cord visualisation and intubation should be uncomplicated
b. Mask ventilation is usually without difficulty
c. If hoarseness if present, consider intubating with a smaller diameter endotracheal tube
d. All acromegalic patients will require awake fiberoptic intubation

Question 44

You are assessing a 45 year old male patient with acromegaly preoperatively. Which of the following statements is the most accurate regarding the predicted cardiovascular complications?

a. The left ventricle will have preserved diastolic function
b. The left ventricle will have preserved systolic function under stress
c. An echo of the left ventricle will always show concentric hypertrophy
d. The myocardium is hypertrophied which contributes to resulting coronary artery insufficiency

Question 45

You are anaesthetising a patient on the bariatric list. He has scored a 6 on the STOP BANG questionnaire. When planning the management of the airway, which of the following is NOT important?

a. Proper positioning of the patient in the "ramped" position prior to intubation
b. Preoxygenation in the flat supine position with CPAP to prolong time to desaturation on intubation
c. Be prepared for a difficult airway as it is 8 times more likely in patients with moderate to severe OSA
d. Avoid premedication with benzodiazepines to be given in the ward

Question 46

Which of the following is the LEAST correct regarding OSA in children?

a. OSA decreases the ventilatory response to carbon dioxide
b. OSA can be associated with learning difficulties at school
c. OSA is associated with a smaller risk of airway obstruction during induction of anaesthesia
d. OSA is associated with a greater incidence of postop respiratory complications

Question 47

Which of the following is correct regarding children undergoing middle ear surgery?

a. Are at an incereasd risk of postoperative nausea and vomiting
b. Should not undergo TIVA due to the risk of propofol infusion syndrome
c. May receive nitrous oxide throughout the procedure
d. Must always be paralysed and intubated for airway protection

Question 48

When using inhaled Nitric Oxide on a patient with ARDS, which of the following will improve oxygenation the most?

a. Decreasing alveolar dead space
b. Improving ventilation/perfusion matching
c. Decrease in pulmonary artery pressure improving RV performance
d. Decrease in the capillary leak of the alveoli

Question 49

Which of the following is the most common side effect seen when using inhaled Nitric Oxide in ICU?

a. Systemic hypotension
b. Methaemoglobinaemia
c. Pulmonary oedema
d. Pulmonary toxicity

Question 50

You are doing a bariatric surgery list and your patient scores 6 on the STOP BANG questionnaire. To diminish the risk of postoperative apnoeic episodes, which of the following will you avoid as part of your intraoperative analgesic technique?

a. A single bolus dose of tramadol
b. An intraoperative continuous infusion of remifentanil
c. Intravenous paracetamol
d. Intravenous infusion of lignocaine

Single Best Answer (SBA) Practice
Answers & Explanations

Question 1

The bundle of actions most likely to result in *suboptimal* postoperative epidural analgesia for a Whipple's procedure is

a.
- **Level of insertion: T8/9**
- **Method to identify epidural space: loss of resistance to saline**
- **Catheter length in epidural space: 5 cm**
- **Use of multiport epidural catheter**

b.
- **Level of insertion: T8/9**
- **Method to identify epidural space: loss of resistance to air**
- **Catheter length in epidural space: 3 cm**
- **Use of uniport epidural catheter**

c.
- **Level of insertion: T8/9**
- **Method to identify epidural space: loss of resistance to air**
- **Catheter length in epidural space: 6 cm**
- **Use of multiport epidural catheter**

d.
- **Level of insertion: T8/9**
- **Method to identify epidural space: loss of resistance to saline**
- **Catheter length in epidural space: 4 cm**
- **Use of uniport epidural catheter**

Answer
b
Explanation
Answer B contains 3 actions that have been well described to contribute to an unsatisfactory epidural block.

Level of insertion: T8/9
This is an appropriate level for the insertion of an epidural catheter for a Whipple procedure

Method to identify epidural space is a loss of resistance to air
Identifying the epidural space by a loss of resistance to air method is thought to increase the incidence of inadequate anesthesia. Dalens et al described two pediatric cases in which epidural bubbles were the cause of incomplete analgesia during epidural anesthesia. Using epidurography, Boezaart correlated a painful, unblocked segment in a parturient with an air-filled bubble in the T12-L1 region. A randomized study, comparing air versus saline to identify the epidural space in parturients, found a higher incidence of inadequate analgesia in the air group (36% versus 19%)

Catheter length in epidural space: 3 cm
Beilin et al used multi-orifice catheters and threaded them to 3cm, 5cm, or 7cm into the epidural space. Beilin subsequently found that the 5cm insertion was associated with the lowest incidence of inadequate blocks.

Uniport epidural catheter
There is some evidence that multi-orifice catheters are associated with a significantly lower incidence of unsatisfactory epidural blocks.

Reference: Portnoy D et al. Mechanisms and management of an incomplete epidural block for cesarean section. Anesthesiology Clin N Am 21 (2003) 39–57

Question 2

Which of the following are most likely to reduce intraoperative blood loss during a liver resection for a metastatic lesion?

a. **Maintain CVP > 5 cm H_20 plus tranexamic acid**
b. **Maintain CVP < 5 cm H_20 plus tranexamic acid**
c. **Maintain CVP > 5 cm H_20 plus cell salvage**
d. **Maintain CVP < 5 cm H_20 plus cell salvage**

Answer
b

Explanation:
Blood loss of >10 litre has been reported after liver resection, and large transfusions are a risk factor for major postoperative complications and liver failure. Patients with cirrhosis, steatosis, and after chemotherapy are at especially increased risk of coagulopathy and bleeding. Modern, multi-modal perioperative techniques have reduced mean blood loss to 300 – 900 ml. The use of intra-operative cell salvage in surgery for malignancy remains controversial.

During parenchymal resection hepatic inflow occlusion, the main source of bleeding is backflow from the valveless hepatic veins. The control of central and thus hepatic venous pressure is crucial to reduce the blood loss. It has been well documented that a CVP of > 5 cm H_2O significantly increases bleeding. However, the risks of maintaining a low CVP include cardiovascular instability and air embolism, but the theoretical risk of increasing postoperative renal dysfunction does not appear to be clinically important. Some patients require a CVP of > 5 cm H_2O for cardiovascular stability, and in these patients an individually tailored compromise needs to be achieved. Most patients will become hypotensive after induction, especially if an epidural is used, which can initially be treated with head down tilt and infusions of vasoconstrictors Pre-resection fluid transfusion should be restricted although small colloid boluses may be appropriate if urine output falls or in the presence of refractory hypotension. High CVP can be treated with diuretics or nitrate infusion. After the resection phase, circulating blood volume can be restored as the risk of bleeding, while still present, is much reduced. Blood requirements have been shown to be reduced by tranexamic acid in liver transplant and liver resection surgery.

Reference: Continuing Education in Anaesthesia, Critical Care & Pain | Volume 9 Number 1 2009

Question 3

The obstetrician on call asks you to anaesthetise a patient who urgently requires a cesarean section for fetal distress. Once you have assessed the patient, you decided that spinal anaesthesia is safe and appropriate. Before injecting the Bupivacaine intrathecally, you make sure that you observe CSF backflow. Unfortunately, it turns out that your spinal block is inadequate for the procedure.
The least likely reason for a failed elective obstetric spinal anaesthetic, administered after observing CSF backflow, is

a. **The dura mater acted as a flap valve across the opening of the pencil point needle**
b. **The arachnoid mater acted as a flap valve across the opening of the pencil point needle**
c. **The opening of the pencil point needle 'straddles' the dura**
d. **The backflow observed, was not CSF**

Answer
d

Explanation
The appearance of clear fluid at the needle hub is usually the final confirmation that the subarachnoid space has been entered. Rarely, however, the clear fluid is not CSF, but local anaesthetic injected as a 'top-up' for an epidural. This patient has not received an epidural where local anaesthetic could have been deposited. The other 3 options are all valid explanations for the observation of CSF backflow with a subsequent failed block.

Explanation: Option A & B
The dura mater AND arachnoid mater acted as a flap valve across the opening of the pencil point needle

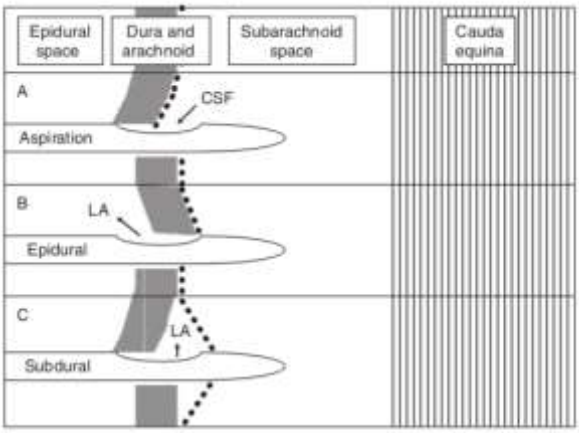


Fig 3 To show how the dura or arachnoid mater may act as a 'flap' valve across the opening of a pencil point needle. During aspiration (A) the dura/arachnoid are pulled back allowing CSF to enter the needle. During injection the dura (B) or arachnoid (C) is pushed forward and the local anaesthetic enters the epidural or subdural space.

Explanation: Option C
The opening of the pencil point needle 'straddle' the dura

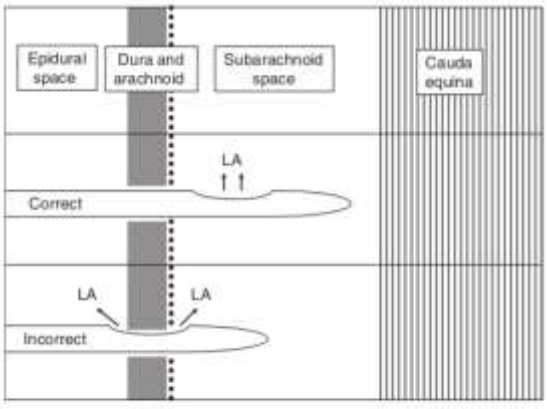


Fig 2 Possible positions of the tip of a pencil-point needle. If it is correctly placed (upper picture) all of the local anaesthetic solution will reach the subarachnoid space, but if the opening 'straddles' the dura (lower picture) some solution will be deposited in the epidural space.

Reference: Fettes PDW et al. Failed spinal anaesthesia: mechanisms, management, and prevention. British Journal of Anaesthesia 102 (6): 739–48 (2009)

Question 4

A 74-year-old man with COPD is undergoing a left pneumonectomy for adenocarcinoma of the lung. While on one lung ventilation, his SpO_2 falls to 84% on an FiO_2 of 100% with no increase in airway pressures or change in tidal volume. Bronchoscopy confirms a correctly placed double lumen tube. Five cmH_2O of PEEP is applied. Which one of the following options is most likely to result in a significant improvement in SpO_2?

a. **Applying CPAP to the non-dependent lung**
b. **Asking the surgeon to clamp the left pulmonary artery**
c. **Increasing PEEP to the dependent lung**
d. **Instituting manual two lung ventilation**

Answer
b

Explanation
With a correctly positioned double lumen tube and no change in airway pressure or tidal volume, the most likely cause of the hypoxaemia is a shunt. All the manoeuvres described may help, but clamping the pulmonary artery will have the most significant effect on SpO_2. Inflating the non-dependent lung can be done but may be difficult at certain stages of the procedure.

Reference: Final FRCA SBA Examples, June 2017

Question 5

In addition to covering the surgical site and administering 100% oxygen, which positioning manoeuvre is appropriate in a patient with a suspected venous air embolism during posterior fossa craniectomy?

a. **Left lateral decubitus head down**
b. **Supine head down**
c. **Right lateral decubitus head down**
d. **No change in position**

Answer
a

Explanation
A patient with **venous** air embolisation should be immediately placed into the left lateral decubitus position (Durant's manoeuvre), Trendelenburg position, or left lateral decubitus head down position. These positions place the right ventricular outflow tract inferior to the right ventricular cavity, causing the air to migrate superiorly into a position within the right ventricle from which air is less likely to embolise. The potential benefit of appropriate positioning was suggested by an animal experiment in which 40 percent of animals in the left lateral decubitus position survived the venous injection of a lethal amount of air (the experiment did not assess the left lateral decubitus head down or Trendelenburg position).

Reference: UpToDate: Air embolism

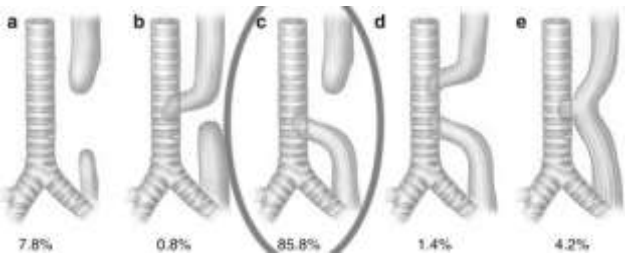
Question 6

The safest way of securing the airway of a neonate with a Gross C/Vogt IIIb tracheo-oesophageal fistula, after suctioning the upper oesophageal pouch and performing an inhalational induction is

a. **Lignocaine spray to the cords → bronchoscopic examination → intubation (ETT tip below the fistula) → muscle relaxant.**
b. **Muscle relaxant → bronchoscopic examination → intubation (ETT tip below the fistula)**

c. **Lignocaine spray to the cords → intubation (ETT tip below the fistula) → muscle relaxant.**
d. **Lignocaine spray to the cords → bronchoscopic examination → intubation (ETT tip below the fistula)**

Answer
a



Explanation
The upper pouch is aspirated and removed. Inhalational induction is performed maintaining spontaneous ventilation. Vigorous ventilation with a bag and mask should be avoided as this may cause gastric inflation. The airway is then sprayed with topical lignocaine and a bronchoscopic examination performed to confirm the diagnosis and position of the TOF, after bronchoscopy the neonate is intubated and the endotracheal tube is placed with the tip below the fistula if possible. Occlusion of the TOF with the endotracheal tube is not always feasible (TOF at the carina or more distally), and it may be necessary to perform endo-bronchial intubation and one lung ventilation until the TOF is ligated. The use of bronchial blockers or a Fogarty catheter to block the TOF has also been described. Once the tracheal tube has been correctly positioned hopefully with the fistula occluded, the baby may be given a muscle relaxant and ventilated.

Reference: Wilson G. Common Surgical Emergencies in Neonates and Infants. ARC 2011

Question 7

The best way to manage hypotension in a brain-dead organ donor is to administer 250ml of colloid and commence an infusion of

a. **Adrenaline**
b. **Noradrenaline**
c. **Phenylephrine**
d. **Vasopressin**

Answer
d

Explanation
Maintaining haemodynamic stability in brain-dead organ donors can pose a major challenge. During cerebral herniation, hypertension occurs, but this is usually self-limiting.

Hypotension will occur in most donors secondary to relative hypovolaemia exacerbated by reduced systemic vascular resistance. Crystalloid or colloid infusions should be titrated to achieve euvolaemia. Hydroxyethyl starch appears to be safe, with respect to renal graft function, and might limit the accumulation of extravascular lung water.

Early restoration of vascular tone aids haemodynamic stability and helps reduce the risk of excessive fluid administration. Vasopressin is considered as the first-line agent where hypotension is resistant to fluid therapy. It restores vascular tone, treats diabetes insipidus, minimizes catecholamine requirements, and is less likely than noradrenaline to cause metabolic acidosis or pulmonary

hypertension.

Reference: Continuing Education in Anaesthesia, Critical Care & Pain j Volume 12 Number 5 2012

Question 8

During invasive blood pressure monitoring using the radial artery, one can expect to see a wide pulse pressure

a. In an 85-year-old patient
b. In someone with aortic stenosis
c. If there is an air bubble in the line
d. In a patient with polycythaemia

Answer
a

Explanation
a) Loss of elasticity in the blood vessels causes the reflectance wave to arrive early, augmenting systolic blood pressure.
b) Pulse pressure will narrow
c) Trace will be dampened
d) Anaemia, not polycythaemia, will cause a hyperdynamic circulation

Question 9

A 20-year-old patient suffered a burn injury to 50% of his body surface area. Which statement with regards to the hypermetabolic syndrome of burns is true?

a. The hypermetabolic syndrome should abate by 4-6 weeks post injury.
b. Fatty infiltration of the liver could result from excessive lipolysis.
c. Hypermetabolic syndrome of burns is characterised by a resting tachycardia without a change in core temperature.
d. Initiation of enteral feeds should be delayed due to associated gastroparesis.

Answer
b

Explanation
a. It has been described up to 3 years after initial injury.
b. True, lipolysis is a major component of the hypermetabolic syndrome.
c. The baseline core temperature increases.
d. Nasojejunal tubes are used to bypass the stomach. Early enteral feeding is an essential to maintain gut integrity and supply sufficient nutrition in a catabolic state.

Question 10

A parturient who suffers from systemic lupus erythematosus is in active labour and requests an epidural. Which statement is true?

a. If her electrolytes and urea were checked in the last 24 hours, there is no need for further special investigations.
b. Her risk for deep venous thrombosis is similar to other parturients' risk.
c. The most significant neurological risk for this patient is that of having a stroke.
d. Maternal antibodies can cause neonatal tachycardia.

Answer
c

Explanation
a. Platelets may be low, and she is at higher risk of preeclampsia and HELLP syndrome.
b. Risk of DVT is 5-8 times higher than that for other parturients.
c. Correct – risk of stroke is increased by 6.5 times.
d. Congenital heart block is associated with maternal anti-SSA (Ro) and anti-SSB (La) antibodies.

Iozza I, Cianci S, Di Natale A, Garofalo G, Giacobbe AM, Giorgio E, De Oronzo MA, Politi S. Update on systemic lupus erythematosus pregnancy. *Journal of Prenatal Medicine 2010;4(4):67-73.*

Question 11

What statement is true with regards to neurological complications following regional analgesia:

a. Spinals pose a higher risk than epidurals because the needle is inserted intrathecally.
b. The risk of paraplegia or death from neuraxial techniques is about 1:25 000.
c. Neuropathies associated with peripheral nerve blocks are usually permanent, but mild.
d. Diabetic patients have a higher risk of complications than the general population.

Answer
d

Explanation
a. Epidurals pose higher risk.
b. Risk is 1:50 000 to 1:140 000.
c. Neuropathies are usually transient.
d. True.

Tierney S, Perlas A. Informed consent for regional anesthesia. *Curr Opin Anesthesiol 2018;31:614-621.*

Question 12

A 60-year old patient with chronic obstructive airways disease and a mild upper respiratory tract infection presents for radiofrequency ablation for atrial fibrillation in the catheterisation laboratory. Which of the following anaesthetic techniques will be associated with the best outcome:

a. General anaesthesia with a shallow ventilatory pattern.
b. Deep isoflurane anaesthesia with continuously monitored deep muscle relaxation.
c. Local anaesthesia with light fentanyl and midazolam sedation.
d. Ketamine anaesthesia with a native airway.

Answer
a

Explanation
a. Better long term outcomes have been associated with GA – probably due to improved catheter immobility. Catheter immobility is also promoted by shallow breathing patterns.
b. When ablating around the right upper pulmonary vein for AF, the phrenic nerve may need to be paced to ensure that the nerve isn't affected, hence muscle relaxants would have to be reversed if given.
c. Coughing and movement will decrease success rates.
d. The likelihood of movement is too high with dissociative anaesthesia. Secretions may cause problems.

Ashley EMC. Anaesthesia for electrophysiology procedures in the cardiac catheter laboratory. *Continuing Education in Anaesthesia, Critical Care & Pain 2012;12(5):230-236.*

Question 13

"Good clinical practice" principles ensure that

- **a. The identities and data of subjects are accessible to all.**
- **b. Studies are designed well enough that no monitoring of projects is needed.**
- **c. The welfare of trial subjects is prioritised.**
- **d. Data is in keeping with current knowledge.**

Answer
c

Explanation
a. Data and confidentiality should be protected.
b. Monitoring is part of GCP.
c. Correct
d. Data should be credible and accurate, but may replace or disagree with current knowledge.

Question 14

Who should give consent for electroconvulsive therapy (ECT)?

- **a. No consent is needed for a patient admitted under the Mental Health Care Act.**
- **b. If a patient is an assisted mental health care user, their applicant can give consent.**
- **c. The Minister of Health must give consent for an involuntary health care user.**
- **d. A voluntary health care user's applicant can give consent.**

Answer
b

Explanation
a. Consent is always needed. Patients can be admitted under the MHCA as voluntary, assisted or involuntary.
b. The applicant is often a family member, and is the person who applied for the admission of a patient incapable of making an informed decision. The patient should still be informed, and should ideally also give consent.
c. If such a patient refuses consent, and the team can justify treatment, the medical superintendent or head of the health establishment can be consulted, as well as the mental health review board.
d. A voluntary health care user should give consent themselves as long as they maintain the capacity to give consent. Refusal of treatment should lead to the use of other treatment modalities.

Segal J, Thom R. Consent procedures and electroconvulsive therapy in South Africa: impact of the Mental Health Care Act. *S Afr Psychiatry Rev 2006;9:206-215.*

Question 15

Why should the analysis of an adverse clinical incident be structured?

- **a. A structured process will limit the extent of the investigation.**
- **b. A structured process will clearly indicate which individual was at fault.**
- **c. A structured process will ensure that no report needs to be formulated.**
- **d. A structured process will encourage staff who are interviewed to feel less threatened.**

Answer
d

Explanation
a. Structure ensures a comprehensive investigation is done.
b. The purpose is not to blame individuals.
c. Structured processes make it easier to compile a report.
d. Correct.

Taylor-Adams S, Vincent C. Systems analysis of clinical incidents: the London protocol. *Clinical Risk 2004;10:211-220.*

Question 16

A 60-year-old male is booked for a laparoscopic inguinal hernia repair. His lung function shows the following results:

	Pre-bronchodilator	Post bronchodilator	Predicted (mean)
FEV_1	**1.6 L**	**1.65 L**	**3.54 L**
FVC	**4.0 L**	**4.1 L**	**5.0 L**

What is the most likely diagnosis and management pre-operatively?

a. Severe asthma patient with reversibility; this patient should be cancelled and optimized.
b. Gold Stage II COPD with reversibility; patient should be cancelled and treated with a course of steroids.
c. Gold Stage III COPD with no significant reversibility; patient should be done with caution.
d. Severe restrictive lung disease; this patient should be done under regional anaesthesia to avoid intubation and ventilation.

Answer:

c) FEV1/FVC <70% confirms obstructive lung disease. $FEV_{1\ (best\ value)}/FEV_1$ predicted (for gender, age and length) will determine the reversibility. Reversibility is defined as an improvement of 12% and 200ml in FEV_1 after bronchodilator administration. In this example FEV_1/FVC = 40% FEV_1/FEV_1 predicted = 46%
The change in FEV_1 after bronchodilation was only 50ml and the change in FVC was 100ml, this is not considered to be reversible

Patients with $FEV_1/FVC < 0.70$:

GOLD I: Mild $FEV_1 \geq 80\%$ predicted
GOLD II: Moderate $50\% \leq FEV_1 < 80\%$ predicted
GOLD III: Severe $30\% \leq FEV_1 < 50\%$ predicted
GOLD IV: Very severe $FEV_1 < 30\%$ predicted

Explanation:
a) It's unlikely that for a 60 year old patient to be a true asthmatic coming for an inguinal hernia repair and there is no reversibility as per definition.
b) This patient has obstructive lung disease FEV_1/FVC <70% and the FEV_1/FEV_1 Predicted is 46% which is not stage II. The steroids given to COPD patients in the past is not routinely given anymore.
d) With restrictive lung disease the FEV_1/FVC is normal and the total lung capacity is reduced. This is clearly not restrictive lung disease.

Question 17

A 16 year old boy is undergoing resection following neo-adjuvant chemotherapy for an osteosarcoma of his distal femur. His full blood count is as follows:
Haemoglobin: 9.5g/dl
White cell count: 3.0 x10^9/L
Platelets: 154X10^9/L

What blood conservation techniques would be most appropriate in this case?

a) Perioperative allogenic blood transfusion
b) Cell salvage with cross-matched blood available
c) Tourniquet on the lower limb, tranexamic acid and cross-matched blood available
d) Patient should be cancelled and his anaemia optimized with iron and erythropoetin
e) Pre-deposited autologous blood donation

Answer:
c) With regards to blood conservation techniques, c is the most appropriate answer. A tourniquet should be considered especially in lower limb surgery to prevent ongoing bleeding during surgery with time measured accurately to prevent muscle and nerve damage. Other surgical means include diathermy and topical vasoconstrictors. (adrenaline-soaked swabs and fibrin glue). Tranexamic acid: Antifibrinolytics are increasingly used during surgery to decrease blood loss by helping to prevent the breakdown of fibrin and promoting the maintenance of blood clots. Many trials have demonstrated its effectiveness.
Cross match is indicated when major blood loss is expected.

Explanation:
Patients at high risk of intra-operative blood loss should routinely undergo pre-operative risk assessment. It's not appropriate to address the anaemia the day before surgery as there are many consequences to blood transfusions and complications of elective procedures done on patients with low haemoglobin. Anaemia should be identified and further investigated preoperatively. Low levels should be optimized with iron and EPO where necessary. In a cancer patient it may be due to impaired red cell production or increased breakdown of red blood cells. In cancer patients, it might not be possible to delay surgery. These patients receive chemotherapy prior to surgery to increase survival, since they already all have micro-metastases on diagnoses. The window period between chemo and surgery is rather small and patients are often anaemic.

a) Giving this patient blood prior to surgery is simply not a blood conservation technique. This would also be the least desirable technique of managing anaemia. It's expensive and has side effects and complications.
b) Cell salvage in an option but controversial in cancer surgery and needs to be discussed with surgeon and oncologist. Sophisticated filters and washing techniques may be used if the tumor is not breached.
e) Perioperative autologous blood donation is a technique that is not used often anymore, it is very expensive and only done where other techniques have failed. This patient's starting haemoglobin is too low for this technique. (Hb of at least 11g/dL recommended)

Reference
Walsh, T. S., & Prowse, C. (2007). BCSH guidelines for policies on alternatives to allogeneic blood transfusion. 1. Predeposit autologous blood donation and transfusion, August 2006. *Transfus Med, 17*(5), 353; discussion 366. doi:10.1111/j.1365-3148.2007.00751.x

Question 18

A 4-year-old boy presents for a muscle biopsy for suspected muscular dystrophy following a fall off in motor-milestones and a positive Gower's sign. Which one of the following statements is true?

- **a. He carries a significant risk of malignant hyperthermia and all the necessary precautions should be taken.**
- **b. Post-operative respiratory insufficiency should be anticipated**
- **c. Propofol may affect the biopsy result and should be avoided**
- **d. An uneventful previous volatile anaesthetic is not an indication of proven safety of volatiles for this child**

Answer
d

Explanation

a. Muscular dystrophies are associated with Anaesthesia Induced Rhabdomyolysis (AIR) not Malignant hyperthermia. Conditions with a definite increased risk of MH are: the presence of a known MH causative mutation of RYR1, central core disease, minicore or multicore myopathy, core rod myopathy, King–Denborough syndrome, Native American myopathy (Lumbee tribe), uniform type I fibers myopathy (CNDMU1) and a minority of exertional rhabdomyolysis cases. Conditions with a weak association (risk probably not increased) carnitine palmitoyl deficiency II, hypokalemic periodic paralysis, Brody's disease
b. The respiratory and cardiovascular effects of these disorders tend to occur later in the disease when symptoms are well-established. The respiratory insufficiency is caused by weakness of the respiratory muscles as well as scoliosis which results from weakness of the paraspinal muscles. For short cases such as a muscle biopsy in a young patient who has only recently started exhibiting symptoms respiratory insufficiency is unlikely to be a problem.
c. Propofol may affect the muscle biopsy taken for mitochondrial myopathy but will have no affect on one for muscular dystrophy. It is important to check what the muscle biopsy will be examined for as each biopsy specimen is treated differently in the laboratory. If mitochondrial myopathy is being considered as a diagnosis propofol should be avoided altogether.
d. AIR, like MH is an idiosyncratic reaction, not occurring with every exposure to triggering agents (volatiles and suxamethonium), so an incident-free exposure to volatiles does not indicate that these are safe. Triggering agents should be completely avoided where a muscular dystrophy is suspected.

For a great review on the subject read:
Barbara W. Brandom, Francis Veyckemans, Neuromuscular diseases in children: a practical approach. *Pediatric Anesthesia* 2013; 23:765-9

Question 19

Cerebral palsy is a spectrum of movement or posture disorders resulting from an injury or insult to the fetal or infant developing brain. Patients may be on a variety of medications to control movements, muscle tone and seizures. Baclofen is a $GABA_B$ agonist which can be given orally or intrathecally to reduce spasticity. Patients on oral baclofen who are unable to tolerate oral intake post-operatively may go into acute withdrawal. Which of the following statements regarding the withdrawal state is true?

- **a. Withdrawal may result in painful spasms and seizures for which parenteral benzodiazepines such as intravenous midazolam or rectal diazepam are the best management.**
- **b. Withdrawal may result in muscle weakness and respiratory failure, this should be monitored for closely with respiratory support (non-invasive or full ventilation) available as indicated.**
- **c. Psychosis and hypertension may result from Baclofen withdrawal and may be avoided by prophylactic haloperidol administration.**

d. Severe gastrointestinal side effects may result with intractable vomiting and diarrhea which should be managed supportively with fluid replacement and symptomatic treatment with parenteral antiemetics.

Correct answer & explanation:
a
Baclofen, a $GABA_B$ receptor agonist, decreases spasticity by inhibiting the release of the excitatory neurotransmitters aspartate and glutamate in the dorsal horn of the spinal cord (Rex lamina II and III). It can be given orally or intrathecally via a subcutaneously implanted continuous infusion device attached to a subarachnoid catheter inserted at T12–L1. Intrathecally, it is effective in smaller doses and is associated with fewer of the systemic side-effects which include muscle weakness, respiratory depression, incontinence, and drowsiness. The devices can last for 6–7 year and need refilling every 3–6 months depending on their size. These devices can be easily overlooked, and their presence should be actively sought by the attending anaesthetist.
Patients who cannot tolerate oral baclofen in the immediate postoperative period may develop acute withdrawal symptoms which include anxiety, disorientation, painful acute muscle spasms, status dystonicus, seizures, bradycardia, and hypotension. These complications can be attenuated by the administration of rectal diazepam or an i.v. midazolam infusion titrated to effect. Where this has been deemed necessary patients should be monitored in a high dependency environment for signs of sedation, hypotonia, and respiratory depression.
Recommended reading:
DP Prosser, N Sharma, Cerebral palsy and anaesthesia, Continuing Education in Anaesthesia Critical Care & Pain BJA Education, 2010 10(3): 72–76

Question 20

A 15-year-old child with 4-hour history of a supracondylar fracture and pulseless forearm refuses consent for surgery on the grounds of severe anxiety about death under anaesthesia. His father insists that surgery go ahead without the child's consent. Which of the following is true?

a. The treating physician may proceed with the parent's consent as the parent's will supersedes the child's.
b. According to The Children's Act (2005) surgery cannot be performed on a child over the age of 12 years against their wishes, an emergency application to the High Court or Children's Court must be made to obtain consent before proceeding.
c. The superintendent of the hospital may consent to the surgery proceeding on the child.
d. A mental health practitioner should assess the child's capacity to consent and if this is found to be lacking surgery can proceed with the parent's consent.

Answer:
c

Explanations:
"A child may consent to the performance of a surgical operation on him or her, or on his or her child, if the child is over the age of 12 years and is of sufficient maturity and has the mental capacity to understand the benefits, risks, social, and other implications of the surgical operation, and is duly assisted by his or her parent or guardian." Children's Act 2005
"The child's best interests are paramount in every matter concerning a child." Constitution of The Republic of South Africa

a. The parent's will does not supersede the child's. Child consent is required over 12 years of age with parental assent. Proceeding in this case would be against the expressed will of the patient and should not be done without invoking a higher authority.
b. There is insufficient time in this case to wait for even an emergency application to the court. This surgery should be performed 6 hours or less from the time of arterial compromise.
c. "The superintendent of a hospital, or the person in charge of the hospital in the absence of the superintendent, may consent to the medical treatment of, or surgical operation on, a child, if the treatment or operation is necessary to preserve the child's life, and is so urgent that it cannot be deferred." Children's Act (2005)
d. The HPCSA's interpretation of the Children's Act requires that the practitioner taking consent for the procedure assess the capacity of the child to consent. It is impractical to insist on a

mental health assessment in an emergency case. Surgery cannot proceed with the parent's consent if this is different from the child's (see explanation 1.)

For further reading:
Christina Lundgren. Consent…who gives it for anaesthesia for children? *South Afr J Anaesth Analg* 2013;19(6):280-281

Question 21

A 12-month-old girl has swallowed a button battery, chest X-ray shows it positioned at mid-oesophageal level. She had 125ml of formula milk four hours ago. Which of the following is true?

a. **She requires oesophagoscopy and removal of the coin, but this should be delayed until 6 hours after ingestion of the formula to ensure adequate fasting.**
b. **Oesophagoscopy and removal of the coin should proceed without delay even though the child is not fasted.**
c. **Oesophagoscopy and removal of the coin may proceed without delay as the child is adequately fasted according to the updated fasting guidelines.**
d. **Guidelines for button battery ingestion advise against immediate removal and recommend a trial of passage.**

Correct answer
b

Explanation
Button battery ingestions result in significant morbidity and mortality in children—before, during, and even after removal. The injuries created by a button battery lodged in the oesophagus develop rapidly and can be severe. The current of the button battery, conducted through saliva and the tissue drives a highly alkaline caustic injury, leading to liquefactive tissue necrosis.[Hoagland et al] The amount of tissue damage is directly related to the length of time the battery is in contact with the tissue so immediate removal is a priority.

a. Any delay should be avoided, the case should continue despite the recent intake of formula.
b. Fasting guidelines for children have been altered to allow for clear fluids to be given up to an hour pre-opeatively. The guideline for breast milk remains at four hours and for all other liquids and solids 6 hours fasting time is still recommended. The new guidelines on clear fluids follow the publication of substantial evidence from large trials in which a liberalized fasting regimen was applied and to date the new recommendations have been endorsed by SASA, SPANZA, APA, ESPA, CSA amongst other international anaesthetic associations.
c. Trial of passage is not recommended in this age group irrespective of the size of the battery. It MAY be considered in patients over 12 years of age in batteries confirmed to be <12mm diameter.

Recommended reading:
**Ing RJ, Hoagland M, Mayes L, Twite M. The anesthetic management of button battery ingestion in children. *Can J Anaesth*. 2018; 65:309–318.
**Consensus statement on clear fluids fasting for elective pediatric general anesthesia. *South Afr J Anaesth Analg* 2019;25(1)S1-S5

Other information in the answer comes from:
Hoagland M et al. Anesthetic Implications of the New Guidelines for Button Battery Ingestion in Children. *Anesthesia & Analgesia*. 2019 *in print*

Question 22

High frequency oscillatory ventilation (HFOV) uses tidal volume (V_T) less than dead space volumes with strict control of intrathoracic pressure variations. Which of the following statements is true?

a. **HFOV is a good mode for neonatal lungs due to their high susceptibility to barotrauma.**
b. **HFOV is contra-indicated in neonatal lungs due to the high susceptibility to atelectrauma.**
c. **HFOV is a good mode for neonatal lungs unless an air leak is present.**
d. **HFOV cannot be used in neonates as it requires an endotracheal tube of at least 4.0mm internal diameter.**

Answer
a - HFOV is primarily used in neonates because it is a great mode for preventing or reducing barotrauma.

Explanation
b. HFOV will reduce atelectrauma by ventilating in the "safe zone", maintaining the intrathoracic pressure within a constant and very narrow window preventing over distension (causing barotrauma) and premature collapse (causing atelatrauma).
c. HFOV can be used when air leak is present (such as caused by barotrauma from conventional ventilation).
d. HFOV can be performed through any of the commercially available ETT sizes.

Recommended reading:
Duval ELIM, Markhorst DG and van Vught AJ. High frequency oscillatory ventilation in children: an overview. *Respiratory Medicine CME* 2009(2): 155–161

Question 23

Utilising the Beer-Lambert Law, cerebral oximetry allows for continuous non-invasive monitoring of cerebral oxygenation by the application of a set of light sources and detectors to the scalp, usually over the frontal lobe. Which of the following describes a limitation of this technology?

a. **Patients must be paralysed as the electromyographic output of muscle contraction will interfere with the reading.**
b. **Hypothermia reduces accuracy of the measurement.**
c. **It only measures regional oxygenation so large areas of the brain remain unmonitored.**
d. **Utility in neonates is limited by an inability to measure oxygen saturation of fetal haemoglobin (HbF).**

Correct answer & explanation:
c
a. Cerebral activity monitors (a modality employed in many depth of anaesthesia monitors) may experience interference from electromyographic signals but cerebral oximetry is measuring passage and absorption of light through tissue not electrical activity.
b. While hypothermia causing vasoconstriction may reduce the ability of peripheral pulse oximeters to function this is not true of cerebral oximeters as hypothermia does not cause cerebral vasoconstriction. Hypothermia will reduce cerebral metabolism and, all else being equal, will result in a rise in cerebral oxygenation.
c. The light will pass through a small area of the brain directly underneath the probe and all measurements will reflect the oxygenation of this area only. Placing sensors bilaterally will reduce the effect of this artifact as simultaneous changes to both readings are ore likely to reflect an effect on the whole brain.
d. The absorbances of red and near-IR light by HbF is essentially the same as HbA and thus SpO2 measurement is as reliable in newborns as in adults. Cerebral oximetry is a very useful monitor in neonates having surgery as cerebral perfusion in this population is driven by flow

(cardiac output) more than pressure so the traditional practice of monitoring blood pressure does not correlate accurately with cerebral perfusion.

Recommended reading:
Tosh W and Patteril M, Cerebral Oximetry, *BJA Education*, 2016 (12): 417-21

Question 24

In general, participation in research must be voluntary and predicated on informed choices. Voluntariness and informed choices are evidenced by the informed consent process which must take place before the research commences and be affirmed during the course of the study, as part of the commitment to an ongoing consent process. In some circumstances, research may not require prior consent. Which of the following describes a situation where consent is not required?

a. **Observational research of people in a public space without the reasonable expectation of privacy and where no intervention is performed by the researcher.**
b. **An audit of a common practice (e.g. cannula insertion) with no intervention performed by the researcher.**
c. **Measuring practitioner satisfaction with a new intervention.**
d. **An audit of practice as a follow-up to an intervention staged on the basis of an original for which consent was acquired.**

Answer
a

Explanation
"Research involving observation of people in public spaces and natural environments usually need not undergo formal ethics review, provided that
• the researcher does not interact directly with individuals or groups
• the researcher does not stage any intervention
• the individuals or groups do not have a reasonable expectation of privacy
• dissemination of research findings does not identify individuals or groups"
Ethics in Health Research Principles, Processes and Structures, Department of Health, Republic of South Africa, 2015

Question 25

With reference to critical incident reporting in clinical practice, which of the following statements is true?

a. **Critical incident reporting is a mandatory professional obligation for all practitioners registered with the HPCSA.**
b. **Critical incident reporting should not identify the name and rank of the person whose action or inaction contributes to the incident.**
c. **When a critical incident is voluntarily reported there should be no sanction placed on the reporter.**
d. **Critical incident reporting should include no harm-incidents and near miss incidents as well as adverse events.**

Answer & explanation
d
Critical incident reporting has become more widely accepted as an effective way to improve anaesthetic safety and has continued to highlight the importance of human errors and system failures. The qualitative information gathered can be used to develop strategies to prevent and manage existing problems, as well as to plan further initiatives for patient safety.
The "National Procedural Manual for Patient Safety Incident Reporting and Learning" gives the following definitions:

- Incident: An incident can be a near miss, no harm incident or harmful incident (adverse event).
- Near miss: an incident which did not reach the patient.
- No harm incident: an event which reached a patient, but no discernible harm resulted.

- Harmful incident (adverse event): results in harm to a patient that is related to medical management, in contrast to disease complications or underlying disease. Medical management includes all aspects of care from interaction with health care provider to discharge of a patient from medical treatment or health care facility.

The National Health Act no 61 of 2003 Section 47, subsection 1 stipulates that all health establishments must comply with the quality requirements and standards prescribed by the Minister after consultation with the National Health Council. To this end the National Core Standards (NCS) have been established and are applied to every health establishment in the country. Domain 2 of the NCS relates to patient safety, clinical governance and clinical care. In relation to adverse events it states the requirement that:
"Adverse events or patient safety incidents are promptly identified and managed to minimise patient harm and suffering."
"Adverse events are routinely analysed and managed to prevent recurrence and learn from mistakes."

1. Not reporting a critical incident is not on its own directly punishable by the HPCSA although it does reflect a deviation from expected ethical standards of practice.
2. The name and rank of the person should be included in the report to the supervisor but the name may be anonymized for reporting beyond this level. The rank of the person may be relevant in establishing the conditions which contributed to the event and so should not be left out.
3. While a no-blame culture is integral to critical event reporting there is no legal precedent for a guarantee of no consequences for those involved in the incident. For example if analysis of the event concludes that the reporter requires further training this may be mandatory.
4. No-harm and near-miss events all need to be reported through the critical incident reporting system as they may reveal latent errors in the system the correction of which may prevent future critical incidents.

Recommended reading:
Choy CY. Critical incident monitoring in anaesthesia. *Current Opinion in Anaesthesiology* 2008, 21(2):183–186

Other information in the answer comes from:

- National Policy for Patient Safety Incident Reporting and Learning in the Public Health Sector of South Africa *July 2016*
- National Core Standards for Health Establishments in South Africa, National Department of Health, Abridged version, 2011

Question 26

Eight months after a traumatic spinal cord injury, a patient requires surgery to treat a urethral stricture. Regarding autonomic dysreflexia, the following statements are true EXCEPT:

a. A blood pressure of 120/80mmHg is inconsistent with the diagnosis of autonomic dysreflexia
b. Injuries below T6 and incomplete lesions are less likely to lead to autonomic dysreflexia than those above T6 and complete lesions
c. Signs include flushed, sweaty skin above the level of the spinal cord lesion and cool, pale skin below the level of the lesion
d. Both tachycardia and bradycardia may be present during an episode of autonomic dysreflexia

Answer
a. A blood pressure of 120/80mmHg is inconsistent with the diagnosis of autonomic dysreflexia

Explanation
b. True. Autonomic dysreflexia may occur following spinal cord injuries below T6 and those that are incomplete but the symptoms are milder
c. True

d. True. Reflex bradycardia due to vagal stimulation is common but tachycardia is may also be seen.

During episodes of autonomic dysreflexia, blood pressure may rise to as high as 300/220mmHg. In less severe episodes, blood pressure will still rise but since resting blood pressure is usually lower after spinal cord injury, a blood pressure of 120/80mmHg is still consistent with a diagnosis of autonomic dysreflexia.

Question 27

Regarding the use of phenylephrine following neuraxial blockade in obstetric anaesthesia, the following statements are true EXCEPT:

a. Continuous infusion produces fewer episodes of hypotension than intermittent boluses
b. There is less umbilical artery acidaemia than with ephedrine usage
c. There is less bradycardia compared to ephedrine usage
d. It has not been shown to exhibit tachyphylaxis

Answer
c. There is less bradycardia compared to ephedrine usage

Explanation
a. Smoothest blood pressure control achieved as an infusionLess acidosis on umbilical sampling;
b. Conflicting evidence as to whether it produces less actual fetal acidosis
d. Tachyphylaxis has been reported

Question 28

Intra-aortic balloon pump (IABP) increases the oxygen delivery to the myocardium and decreases the myocardial oxygen demand, thereby improving its function. Which of the following physiological effects are NOT seen with a well-functioning IABP?

a. Increased aortic diastolic pressure
b. Decreased left ventricular end-diastolic pressure
c. Decreased renal blood flow
d. Increased coronary blood flow

Answer
c. Decreased renal blood flow

A well-functioning IABP will increase aortic diastolic pressure, decrease LVEDP and increase coronary blood flow. However, if positioned incorrectly (too low) in the descending aorta, it may partially occlude renal artery perfusion during inflation.

Question 29

Regarding a patient with acromegaly presenting for trans-sphenoidal resection of the pituitary gland tumour, which of the following statements is likely to be true?

a. Male patients with acromegaly are as likely to suffer from OSA (obstructive sleep apnoea) as female patients
b. The patient will likely have distal myopathy
c. The patient will likely have raised ACTH (adrenocorticoptrophic hormone) levels
d. The patient will likely have raised IGF-1 (insulin-like growth factor-1) levels

Answer
d. The patient will likely have raised IGF-1 (insulin-like growth factor-1) levels

Explanation
a. OSA is more common in males than females
b. The patient is more likely to have proximal myopathy
c. Local destruction of the anterior pituitary gland by a GH-secreting tumour results in reduced production of other pituitary hormones, like ACTH

Growth hormone stimulates the production of IGF-1 peripherally which acts by inducing cell proliferation and reducing apoptosis which ultimately leads to the characteristic features of the condition.

Question 30

Regarding anaesthesia for LASER ablation of vocal cord nodules in ENT surgery:

a. The airway of choice is a cuffed LASER-resistant endotracheal tube, the cuff filled with saline and methylene blue
b. The ideal gas mixture is oxygen with nitrous oxide, as oxygen supports combustion
c. Reduce oxygen concentration to ≤40 percent before use of any ignition source during procedures inside the airway
d. Allow at least 30 seconds for the both the fraction of inspired oxygen (FiO_2) and the fraction of expired oxygen (FeO_2) to be reduced to a safe level, before the surgeon activates the ignition source

Answer
a. The airway of choice is a cuffed LASER-resistant endotracheal tube, the cuff filled with saline and methylene blue

Explanation
b. Nitrous oxide **supports** combustion
c. Reduce oxygen concentration **to ≤30** percent before use of any ignition source during procedures inside the airway
d. Allow **minimum of 90 seconds with high flow rate/3-5 minutes under normal conditions** for the both the fraction of inspired oxygen (FiO_2) and the fraction of expired oxygen (FeO_2) to be reduced to a safe level, before the surgeon activates the ignition source

References:
UpToDate: Fire safety in the operating room
Author: Charles E Cowles, Jr, MD, MBA
Section Editor: Joyce A Wahr, MD, FAHA
Deputy Editor: Nancy A Nussmeier, MD, FAHA

Question 31

A 75 year old woman is being treated with broad spectrum antibiotics for ventilator associated pneumonia. She develops abdominal distension and diarrhoea; the likely diagnosis is Clostridium difficile. Her white cell count is $20x10^9$; she remains haemodynamically stable and does not require inotropes. The most appropriate first line therapy is:

a. Metronidazole 500mg TDS po
b. Metronidazole 500mg TDS IV
c. Vancomycin 125mg QID po
d. Vancomycin 500mg QID po *and* Metronidazole 500mg TDS IV

Answer
c. Vancomycin 125mg QID po

Explanation

a. Previous preferred antibiotic; correct route of administration

b. Previous preferred antibiotic; incorrect route of administration

d. New guidelines: management of fulminant c. difficile with septic shock

References:
McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Disease. 2018

Question 32

An 80 year old woman presents with a 2 month history of severe, continuous burning pain in her right eye. She has also had a skin rash over the affected site which began a week after the onset of the pain. She has previously been treated with intermittent courses of prednisone for the management of her poorly controlled COAD. The likely diagnosis is:

a. Trigeminal neuralgia
b. Post-herpetic neuralgia
c. Giant cell arteritis
d. Polymyalgia rheumatica

Answer
b. Post-herpetic neuralgia

Explanation
a. Trigeminal neuralgia – very similar demographic, usually affecting teeth, gums, lips, jaw, cheek

c. Giant cell arteritis – very similar demographic, associated with PMR, usually improved with steroids

d. Polymyalgia rheumatic – very similar demographic, eye pain very atypical, usually arthralgia

Question 33

Anaesthesia for electroconvulsive therapy (ECT) is frequently provided in remote locations which has a bearing on its conduct and the efficacy of the treatment. Which of the following statements is most correct?

a. The presence of an anaesthetic machine is mandatory
b. Pipeline oxygen must be available
c. Suxamethonium is used primarily to prevent musculoskeletal injury
d. Propofol should be avoided as it prevents the induction of an adequate seizure

Answer
c. Suxamethonium is used primarily to prevent musculoskeletal injury

Explanation
a. Machine not mandatory – can be administered with open circuit

b. Cylinder gases may be used

d. Propofol MAY diminish the induction of an adequate seizure but has other advantages (safety profile etc) that make it attractive to remote site anaesthesia

Question 34

A 2 year old, 14 kg child with an unrepaired Tetralogy of Fallot is booked for an elective umbilical hernia repair. Her oxygen saturations are 80% and she is on propanolol. Which is the most appropriate anaesthetic management goal?

a. **Administer a high FiO_2**
b. **Decrease PVR**
c. **Avoid catecholamine surges**
d. **Decrease afterload**

Answer
c. Avoid catecholamine surges which may cause acute infundibular spasm
The principles of intraoperative management to minimise right to left shunt in tetralogy of fallot include; maintain SVR, adequate preload, avoid tachycardia, and avoid triggers which increase dynamic right ventricular outflow obstruction.

Explanation
a) Whilst a high FiO2 is appropriate management during a hypercyanotic spell, it is not usually necessary during maintenance of anaesthesia. PAO_2 is usually normal.
b) PVR is typically normal in tetralogy of fallot. The resistance to flow occurs proximally within the RVOT.
d)Decreasing afterload (SVR) will promote right to left shunt and worsen the cyanosis

Ref: https://www.youtube.com/watch?v=YeGsTffRuJY

Question 35

A 2 year old, 14 kg child with an unrepaired Tetralogy of Fallot is booked for an elective umbilical hernia repair. During surgery you notice a sudden decrease in $ETCO_2$ and rapid desaturation. The most appropriate immediate management includes administration of:

a. **Sodium bicarbonate, and adrenaline**
b. **Fentanyl, and phenylephrine bolus**
c. **Phenylephrine bolus, and lighten depth of anaesthesia**
d. **Magnesium, and esmolol bolus**

Answer
b) This scenario is describing a hypercyanotic spell.
Fentanyl may be appropriate if there is concern the spell has been precipitated by a painful stimulus, and phenylephrine will increase the SVR, thereby decreasing the right to left shunt

Explanation:
a) Sodium bicarbonate may be appropriate to treat acidosis and may have a direct effect on relaxation of the infundibulum, but adrenaline will increase contractility and spasm therefore worsening the dynamic RVOT obstruction
c) Phenylephrine will increase the SVR, thereby decreasing the right to left shunt, but lightening the depth of anaesthesia may trigger hypercyanotic spells when the patient is stimulated. It is likely more appropriate to increase the depth of anaesthesia to reduce sympathetic tone.
d) Magnesium is likely to decrease the SVR, thereby increasing the right to left shunt and increasing the cyanosis and is not indicated. Esmolol is a very effective treatment for hypercyanotic spells. The rapid onset beta-blockade has a significant effect on sympathetic tone resulting in relaxation of the dynamic RVOT obstruction. It can be a life-saving intervention during a severe hypercyanotic spell.

Question 36

A 1 year old, 8 kg child is booked for a thoracotomy and ligation of a pulmonary ductus arteriosus (PDA). Her oxygen saturations are normal and she has no features of pulmonary

hypertension. During anaesthesia left to right shunt through the PDA will decrease with which intervention?

- **a. Increased minute ventilation**
- **b. Increased FiO_2**
- **c. Increased anaesthetic MAC**
- **d. Phenylephrine bolus**

Answer
c) Increasing the anaesthetic MAC will decrease the SVR.
In this acyanotic congenital cardiac lesion with increased pulmonary blood flow secondary to left to right shunt, the shunt flow will be increased with an increase in SVR and/or decrease in PVR, and decreased with a decrease in SVR and/or increase in PVR.

Explanation
a) Increasing the minute ventilation may cause a respiratory alkalosis which will decrease the PVR
b) Increasing the FiO_2 will cause pulmonary vasodilation and decrease the PVR
d) Phenylephrine will increase the SVR

Sommer RJ et al. Pathophysiology of Congenital Heart Disease in the Adult, Part I: Shunt Lesions. *Circulation*. 2008;117:1090-1099

Question 37

Gastroschisis is associated with the following congenital condition:

- **a. Congenital heart disease**
- **b. Beckwith-Wiedeman syndrome**
- **c. Trisomy 21**
- **d. Intestinal atresia**

Answer
d)Intestinal atresia

Explanation
a, b & c) These are all associated with omphalocoele (exomphalos)

Question 38

You are asked to provide sedation for a 35 year old ASA 2 patient for ERCP. Which is the most appropriate statement?

- **a. Propofol is adequate as a sole agent**
- **b. Supplemental oxygen may be administered to prevent hypoventilation**
- **c. Use of continuous waveform capnography to monitor adequacy of ventilation is recommended**
- **d. Bolus doses of midazolam can be used for analgesia throughout.**

Answer
c. Continuous waveform capnography is recommended to monitor adequacy of ventilation for all sedations. This will be doubly useful in a patient in a prone position for a procedure which may have a prolonged duration.

Explanations
a. Propofol will not be adequate as a sole agent. It will be useful to add other agents such as analgesics, both for the purpose of analgesia and to lessen the dose of propofol required.
b. Oxygen does not prevent hypoventilation
d. Midazolam does not provide analgesia

Question 39

Ketamine is widely used in subanaesthetic doses as a perioperative adjunct in acute pain. Regarding postoperative ketamine infusion for postoperative analgesia, which of the following statements is most accurate:

a. **Poorly controlled cardiovascular disease, pregnancy, psychosis and moderate hepatic disease are all absolute contraindications;**
b. **The published evidence demonstrates a clear short-term, opioid sparing effect regardless of whether it is given as a bolus, infusion, or via PCA;**
c. **The primary issue preventing widespread adoption of ketamine infusions outside operative or intensive care unit settings is the potential for adverse psychomimetic effects which have been established as dose dependent for analgesic doses;**
d. **The recommended dosing range is a bolus of up to 0.5mg/kg and an infusion rate of up to 1mg/kg/hr**

Answer
b.The published evidence demonstrates a clear short-term, opioid sparing effect regardless of whether it is given as a bolus, infusion, or via PCA.

Explanation
a. Poorly controlled cardiovascular disease, pregnancy, psychosis and moderate hepatic disease are all absolute contraindications to ketamine being used in this way. **(These are all relative contraindications)**
c. The primary issue preventing widespread adoption of ketamine infusions outside operative or intensive care unit settings is the potential for adverse psychomimetic which have been established as dose dependent for subanaesthetic doses. **(No dose dependency established at subanaesthetic doses for psychomimetic side effects)**
d. The recommended dosing range is a bolus up to 0.5 mg/kg and an infusion rate of up to 1mg/kg /hr**. (bolus up to 0.35mg/kg and infusion rate up to 1mg /kg/hr)**

Question 40

Which of the following is not an absolute contraindication to liver transplant?

a. **Severe cardiac or pulmonary disease**
b. **Uncontrolled sepsis including biliary sepsis**
c. **Ongoing alcohol or substance abuse**
d. **HIV infection**

Answer & Explanation
d. HIV infection – only AIDS is an absolute contraindication

Question 41

An 18 year old man from the Democratic Republic of Congo is booked to come to theatre for an explorative laparotomy for an acute abdomen. You decide to assess him in the ward. He is unable to speak English and there is no interpreter available. According to the notes he has a 3 day history of severe abdominal pain. On examination he is mildly jaundiced and appears pale. You are unable to palpate his liver but you detect splenic enlargement and he has a very tender abdomen. His ward Hb is 6g/dl. You find a packet with medication on his bedside cupboard which contains hydroxyurea and folic acid.
The single investigation that has the best ability to confirm and define your suspected diagnoses is:

a. **Haemoglobin electrophoresis**
b. **Liver function test**
c. **Sickledex test**
d. **A full blood count with blood smear**

Answer

a

Explanation
The suspected diagnosis is Sickle Cell Disease. Sickle cell diseases are inherited in an autosomal co-dominant way, with the homozygous expression of the abnormal gene (HbSS) producing sickle cell disease. These patients have no normal adult haemoglobin (HbA) and only have HbS, HbA2 and HbF, with approximately 95% haemoglobin as HbS. Patients who are heterozygous for HbS (sickle cell trait) are carriers but are asymptomatic and have a normal life expectancy.
The gold standard for diagnosis of sickle cell disease is by haemoglobin electrophoresis.
The simpler Sickledex test confirms the presence of HbS, however electrophoresis is required to distinguish the phenotype.
The Sickledex test uses sodium metabisulphite as a reducing agent that causes HbS to precipitate in a hyperosmolar phosphate buffer solution to produce a cloudy suspension. The Sickledex test is not reliable in the neonatal period as there are low levels of HbS and high levels of HbF that has normal solubility, and may result in a false negative result. It becomes reliable after 6 months of age when the HbF levels have dropped.
Haemoglobin electrophoresis is the only method of distinguishing phenotype.
Source: http://www.frca.co.uk/Documents/153%20Sickle%20cell%20disease%20in%20children.pdf

Question 42

A 14 year old mentally impaired girl is brought to theatre for a termination of pregnancy for which her mother has signed consent on her behalf. She is accompanied by her mother, who requests that a sterilisation is done at the same time, since the child does not have capacity to ever care for a child. The best way to proceed is:

a. To complete the termination of pregnancy but not the sterilisation and to obtain an Independent Medical Practitioner's assessment on whether sterilisation is in the best interest of the child.
b. To complete the termination of pregnancy and proceed with the sterilisation since the child lacks decisional capacity and it is in the child's best interest to be sterilised.
c. To obtain an assessment of the 14 year old child's mental capacity prior to proceeding with either the termination of pregnancy or sterilisation.
d. To proceed with the termination of pregnancy and inform the mom that legally the youngest age for sterilisation is 18 years

Answer: c

Explanation:

a. Not the best answer since the child's mental capacity should also be assessed prior to proceeding with Termination of Pregnancy. A child of 12 years or older may consent to surgical treatment with the assent of a parent or guardian (Section 129 of The Children's act 2005)
b. For children who lacks capacity the best interest principle prevails, but her mental capacity has not yet been established.
c.
d. Neither procedure should be carried out without determining mental capacity and ability to consent. For termination of pregnancy no lower age limit exists. No consent other than that of the pregnant woman (female of any age) shall be required for the termination of a pregnancy (Section 5 of The Choice on Termination of Pregnancy Act 92 of 1996). For sterilisation the lower age limit is 18 years (Sterilisation act of 1998 and the Sterilisation amendment act 3 of 2005) Minors may only be sterilised if their life would be jeopardised or their health seriously impaired by a failure to do so. in such cases, a sterilisation can be carried out if the parents/guardian have consented and an independent medical practitioner, after consulting

with the child concerned, makes a written statement that the sterilisation would be in the best interests of the child.

Source: https://www.medicalprotection.org/docs/default-source/pdfs/booklet-pdfs/sa-booklets/consent-to-medical-treatment-in-south-africa---an-mps-guide.pdf?sfvrsn=47b64eac_4

Question 43

Regarding the airway assessment of a 45 year old patient with acromegaly, which of the following statements is the most correct?

a. **A score of Mallampati score of 1 indicates that vocal cord visualisation and intubation should be uncomplicated**
b. **Mask ventilation is usually without difficulty**
c. **If hoarseness if present, consider intubating with a smaller diameter endotracheal tube**
d. **All acromegalic patients will require awake fiberoptic intubation**

Answer
c. If hoarseness if present, consider intubating with a smaller diameter endotracheal tube

Explanation
a. Despite having a MP score of 1 or 2 these patients often have difficult airways due to jaw hypertrophy and a larger tongue, soft palate and epiglottis. Consider a longer laryngoscope blade and have difficult airway equipment available.
b. Mask ventilation is often difficult. Facial bone and facial soft tissue hypertrophy may require a larger mask size. The larger tongue, soft palate and epiglottis may obstruct the airway soon after induction.
d. Although many acromegalic patients may require an awake fiberoptic intubation, some will be manageable with a longer laryngoscope blade, a larger mask, an oropharyngeal airway and a spare set of hands.

Question 44

You are assessing a 45 year old male patient with acromegaly preoperatively. Which of the following statements is the most accurate regarding the predicted cardiovascular complications?

a. **The left ventricle will have preserved diastolic function**
b. **The left ventricle will have preserved systolic function under stress**
c. **An echo of the left ventricle will always show concentric hypertrophy**
d. **The myocardium is hypertrophied which contributes to resulting coronary artery insufficiency**

Answer
d.The myocardium hypertrophies in acromegalic patients. This will contribute to coronary artery insufficiency along with the diastolic dysfunction that will be present (increased demand with decreased supply)

Explanation
a.LV hypertrophy results in diastolic dysfunction
b.Systolic function of the LV is preserved at rest, but under stress the EF will fall
c.The LV hypertrophy is normally eccentric, not concentric

Question 45

You are anaesthetising a patient on the bariatric list. He has scored a 6 on the STOP BANG questionnaire. When planning the management of the airway, which of the following is NOT important?

a. **Proper positioning of the patient in the "ramped" position prior to intubation**
b. **Preoxygenation in the flat supine position with CPAP to prolong time to desaturation on intubation**
c. **Be prepared for a difficult airway as it is 8 times more likely in patients with moderate to severe OSA**
d. **Avoid premedication with benzodiazepines to be given in the ward**

Answer

b. Preoxygenation with CPAP is important to prolong time to desaturation, BUT should NEVER be undertaken in the FLAT supine position. This position impairs lung volumes (including FRC) in the obese patient. Obese patients should be preoxygenated in a more seated attitude when possible to improve respiratory mechanics. This will prolong the time to desaturation.

Explanation

a. The ramped position is important in all patients to facilitate laryngoscopy. It is even more important in obese patients
c. A difficult airway is 8 times more likely in these patients. This is due to greater difficulty with mask ventilation, the greater likelihood of posterior collapse of the tongue etc on induction of anaesthesia (these patients are more sensitive to all sedative medication including propofol, volatile anaesthesia and neuromuscular blockers) and increased difficulty with laryngoscopy due to excess tissue in the airway.
d. As mentioned above patients with moderate – severe OSA exhibit increased sensitivity to sedatives and should never receive any sedatives including benzodiazepines in an unmonitored setting. Premedication is therefore usually avoided in these patients. Patient counselling and education is preferred to decrease anxiety.

Question 46

Which of the following is the LEAST correct regarding OSA in children?

a. **OSA decreases the ventilatory response to carbon dioxide**
b. **OSA can be associated with learning difficulties at school**
c. **OSA is associated with a smaller risk of airway obstruction during induction of anaesthesia**
d. **OSA is associated with a greater incidence of postop respiratory complications**

Answer

c. OSA is associated with an INCREASED risk of airway obstruction during the induction of anaesthesia. Patients with OSA exhibit an increased sensitivity in response to sedatives (including propofol and volatile anaesthesia).

Explanation

a. True, even more so when opiates are used
b. True
d. True, especially complications such as episodes of desaturation, bronchospasm and even respiratory failure.

Question 47

Which of the following is correct regarding children undergoing middle ear surgery?

a. Are at an incereasd risk of postoperative nausea and vomiting
b. Should not undergo TIVA due to the risk of propofol infusion syndrome
c. May receive nitrous oxide throughout the procedure
d. Must always be paralysed and intubated for airway protection

Answer
a. Middle ear surgery is a risk factor for postop nausea and vomiting

Explanation
b. Although children are at greater risk of propofol infusion syndrome, most middle ear surgery does not continue for long enough to put the child at risk. If surgery continues for many hours and a dose of greater than 4mg/kg/hr is required then care should be taken to screen for the onset of propofol infusion syndrome.
c. Nitrous oxide may diffuse into the middle ear space and this may create problems for the surgeon
d. Paralysis is unnecessary for middle ear surgery and some may deem it harmful as it may eliminate the chance of picking up awareness if a TCI is being used. Many anaesthetists successfully use LMA's for middle ear surgery providing there are no contraindications and the fit of the LMA is perfect even when the head is turned.

Question 48

When using inhaled Nitric Oxide on a patient with ARDS, which of the following will improve oxygenation the most?

a. Decreasing alveolar dead space
b. Improving ventilation/perfusion matching
c. Decrease in pulmonary artery pressure improving RV performance
d. Decrease in the capillary leak of the alveoli

Answer
b. As inhaled nitric oxide only works in the portion of the lung it can reach, it will selectively improve perfusion in ventilated portions of the lung. This in turn improves oxygenation.

Explanation
a. inhaled nitric oxide only marginally decreases alveolar dead space
c. Nitric oxide will decrease pulmonary artery pressures but this is not the mechanism by which it will improve oxygenation
d. Nitric oxide will not decrease the capillary leak of the alveoli

Question 49

Which of the following is the most common side effect seen when using inhaled Nitric Oxide in ICU?

a. Systemic hypotension
b. Methaemaglobinaemia
c. Pulmonary oedema
d. Pulmonary toxicity

Answer
d. Pulmonary toxicity is due to the reaction of nitric oxide with oxygen, resulting in the formation of nitrogen dioxide which is toxic the pulmonary tissue. Nitrous acid and peroxynitrite may also be formed.

Explanation

a. nitric oxide is inactivated by circulating haemoglobin and therefore it's half life is 2-6 seconds and hypotension is not seen

b. Nitric oxide use may result in the formation of methaemaglobin but this is clinically only important in patients with glucose 6 phosphate deficiency

c. Pulmonary oedema is a RARE side effect and may occur in patients with severe LV dysfunction – nitric oxide will improve the RV function, this in turn increases the LV preload which may result in pulmonary oedema in the face of severe LV dysfunction

Question 50

You are doing a bariatric surgery list and your patient scores 6 on the STOP BANG questionnaire. To diminish the risk of postoperative apnoeic episodes, which of the following will you avoid as part of your intraoperative analgesic technique?

a. A single bolus dose of tramadol
b. An intraoperative continuous infusion of remifentanil
c. Intravenous paracetamol
d. Intravenous infusion of lignocaine

Answer

a. Tramadol does have agonist activity on the mu opioid receptors and can therefore suppress the ventilatory response to carbon dioxide. This response will be exaggerated in patients with OSA and the use of opioids such as Tramadol will increase the incidence of postop apnoeas and desaturations. Tramadol also inhibits serotonin and noradrenalin reuptake which enhances the inhibitory effects of pain transmission in the spinal cord. In the scenario of moderate to severe OSA opioid free analgesic strategies are recommended such as Paracetamol, NSAIDs, intravenous Lignocaine infusions, Ketamine use, and alpha 2 agonists such as Dexmedetomidine.

Explanation

b. Remifentanil is an opioid analgesic but it is short acting (metabolised by plasma and tissue esterases). Remifentanil has a context sensitive half life of 3-4 min and is therefore safe to use in OSA patients.

c. and d. Paracetemol and intravenous Lignocaine are not associated with a suppressed ventilatory response to carbon dioxide. They are both safe to use intraoperatively.