Eastern Health
Guide for Pre-operative Assessment of Patients for Elective Surgery

2021

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General Disclaimer

We are not peri-operative experts

Patients will not always fall within guidelines. This document is by no means an exhaustive list and is designed to cover common comorbidities

When in doubt, always refer to the anaesthetist rostered on to the pre-admission clinic for additional guidance

Where possible, references from EH protocols and international guidelines have been listed

All comorbidities should be taken into consideration of the patient, the surgery and the urgency of the operation. Deviations from normal pre-operative evaluation and management may occur if there is not enough time for pre-operative optimisation.

Purpose of Pre-Admission Clinic (PAC)

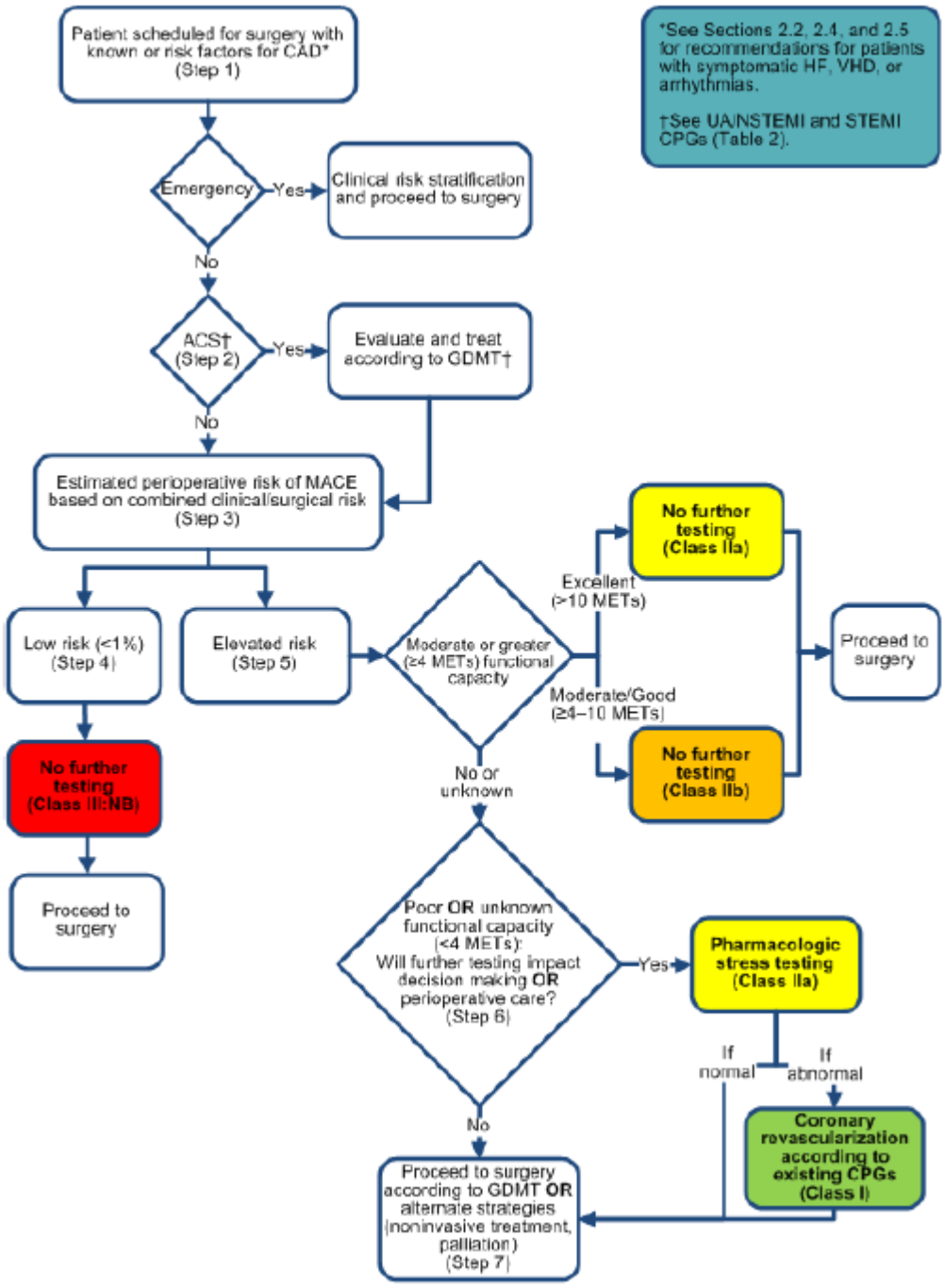
The general purpose of anaesthetic evaluation of a patient prior to surgery can be covered by the following points:

- Risk stratify patient
- Optimise readiness for surgery
- Opportunity to institute life-style changes
- Review anaesthetic history/medical history
- Review medications and modify as necessary
- Organise investigations and rationalise reasoning
- Plan anaesthetic – airway, analgesia, monitoring, disposition
- Obtain consent and discuss plan with patient

Cardiovascular

General Assessment of Patients with Cardiac Comorbidities for Surgery

Figure: AHA Guidelines 2014 on Stepwise Approach to Peri-operative Cardiac Assessment for CAD



Step 1: In patients scheduled for surgery with risk factors for or known CAD, determine the urgency of surgery. If an emergency, then determine the clinical risk factors that may

influence perioperative management and proceed to surgery with appropriate monitoring and management strategies based on the clinical assessment

Step 2: If the surgery is urgent or elective, determine if the patient has an ACS. If yes, then refer patient for cardiology evaluation and management

Step 3: If the patient has risk factors for stable CAD, then estimate the perioperative risk of MACE on the basis of the combined clinical/surgical risk. This estimate can use the American College of Surgeons NSQIP risk calculator (http://www.surgicalriskcalculator.com) or incorporate the RCRI with an estimation of surgical risk

Step 4: If the patient has a low risk of MACE (<1%), then no further testing is needed, and the patient may proceed to surgery

Step 5: If the patient is at elevated risk of MACE, then determine functional capacity with an objective measure or scale such as the DASI. If the patient has moderate, good, or excellent functional capacity (≥4 METs), then proceed to surgery without further evaluation

Step 6: If the patient has poor (<4 METs) or unknown functional capacity, then the clinician should consult with the patient and perioperative team to determine whether further testing will impact patient decision making or perioperative care. If yes, then pharmacological stress testing is appropriate

Step 7: If testing will not impact decision making or care, then proceed to surgery according to GDMT or consider alternative strategies, such as noninvasive treatment of the indication for surgery (e.g., radiation therapy for cancer) or palliation

Lee Revised Cardiac Risk Index (RCRI)

Estimates risk of cardiac complications after noncardiac surgery
Step 3 in AHA 2014 guidelines for estimating peri-operative risk of MACE

1 point for each factor

1. High risk surgery
   Intraperitoneal; intrathoracic; suprainguinal vascular
2. Ischaemic Heart Disease
   History of myocardial infarction (MI); history of positive exercise test; current chest pain considered due to myocardial ischemia; use of nitrate therapy or ECG with pathological Q waves
3. CCF
   Pulmonary oedema, bilateral rales or S3 gallop; paroxysmal nocturnal dyspnea; chest x-ray (CXR) showing pulmonary vascular redistribution
4. Cerebrovascular disease
   Prior transient ischemic attack (TIA) or stroke
5. Insulin treatment
6. Renal impairment Cr >176umol/L

Risk of major cardiac event

RCRI 0 = 0.4%, 1 = 0.9%, 2 = 6.6%, ≥ 3 = 11%
AHA 2014 defines elevated risk as >1% (means score of ≥ 2)

Update in 2019 to reflect literature and validation studies suggesting original RCRI had significantly underestimated the risk
These figures should be used when talking to patients about their peri-operative CVS risk but not used in AHA flowchart

Risk of major cardiac event
RCRI 0 = 3.9%, 1 = 6.0%, 2 = 10.1%, ≥ 3 = 15%

Metabolic Equivalents (METS)

One metabolic equivalent (MET) is defined as the amount of oxygen consumed while sitting at rest and is equal to 3.5 ml O2 per kg body weight x min
Used in further risk stratification after Step 5 AHA 2014
Subjective and can be unreliable depending on patient reporting

The figures in the following table are only estimates of METS and should be used as a guide. There will be variation based on level of intensity that the patient performs the activities at
Table: Metabolic Equivalents of Common Daily Activities

Activity	**METS**
Climbing a flight of stairs	4.7
Household Chores	
Gardening	3.5-4.4
Grocery shopping	2-7
Washing windows	4.9
Cooking	2.5
Mowing lawn	3-5
Wood cutting	5-7
Recreational Activities	
Aerobic dancing	3.9-6
Cycling 10km/hr	4.8
Car driving	2
Cricket	6.1
Fishing	2-3

Golf - carrying clubs	5.1
Golf - riding cart	2-3
Hiking	6
Walking 3km/hr	1.8
Jogging 9km/hr	8.8
Running 13km/hr	12.9
Soccer	10.3
Swimming 2km/hr (80 laps of 25m pool)	4.3
Tennis	4-7
Yoga	3.2

Dukes Activity Status Index (DASI)

Estimates functional capacity
Demonstrated in studies to have better correlation with CPET testing compared with estimating METS
More complicated to use at bedside, requires calculator

DASI score used to calculate predicted VO_2 peak
VO_2 peak (mL/kg/min) = 0.43 × DASI + 9.6
An adequate VO_2 peak for major surgery is ≥15mL/kg/min
This is equivalent to a DASI score of ⩾12.5

Table: Duke Activity Status Index

Is the patient able to:	**Yes**	**No**
Take care of self (e.g. eating, dressing, bathing, using the toilet)	+2.75	0
Walk indoors	+1.75	0
Walk 1–2 blocks on level ground	+2.75	0
Climb a flight of stairs or walk up a hill	+5.5	0
Run a short distance	+8.0	0
Do light work around the house (e.g. dusting, washing dishes)	+2.7	0

Do moderate work around the house (e.g. vacuuming, sweeping floors, carrying in groceries)	+3.5	0
Do heavy work around the house (e.g. scrubbing floors, lifting or moving heavy furniture)	+8.0	0
Do yardwork (e.g. raking leaves, weeding, pushing a power mower)	+4.5	0
Have sexual relations	+5.25	0
Participate in moderate recreational activities (e.g. golf, bowling, dancing, doubles tennis, throwing a baseball or football)	+6.0	0
Participate in strenuous sports (e.g. swimming, singles tennis, football, basketball, skiing)	+7.5	0

Pre-operative Trans-thoracic Echocardiogram (TTE)

When to perform TTE pre-operatively

No known disease
Dyspnoea of unknown origin
Patients unable to ascertain functional capacity and performing pharmacological stress testing
New murmur found on examination

Known cardiac comorbidities
LV dysfunction with no imaging in last year
Valvular disease of moderate or greater severity with no imaging in last year
If worsening symptoms or change in clinical status then repeat TTE warranted sooner

Ischaemic Heart Disease (IHD)

Important elements on history and examination

- Diagnosis, hospitals for management
- Dates of events/interventions - percutaneous intervention (PCI), cardio-pulmonary bypass (CABG)
- Medical therapy and compliance- statins, beta blockers/antihypertensives, anti-anginals, anti-platelets

- Residual symptoms/functional capacity; residual disease not stented; recurrent disease after interventions
- Cardiac failure symptoms and management
- Recent investigations - coronary angiograms, cardiac CTs, TTE
- Implanted devices

Elective non-cardiac surgery should be delayed for:
- 14 days after balloon angioplasty
- 30 days after bare metal stent (BMS) implantation
- 365 days after drug eluting stent (DES) implantation

Subject to discussion with treating cardiologist/EH cardiology team

Patients are often on dual anti-platelet therapy (DAPT) and these should only be ceased after the above time periods have elapsed
Aspirin should always be continued in the peri-operative period if possible
If sooner than the above, a balance of cardiac thrombosis and surgical bleeding risk should be considered. This should at least involve discussion with cardiology and anaesthesia teams. Post-operatively, high risk patients may need to be referred to HDU for monitoring

Common anti-platelet drugs
- Aspirin (Cartia, Aspro, Aspec)
- Clopidogrel (Plavix)
- Ticagrelor (Brilinta)
- Prasugrel (Effient)
- Dipyridamole (Persantine)
- Aspirin/clopidogrel (CoPlavix)
- Aspirin/dipyridamole (Asasantin)

Aortic Stenosis (AS)

Important elements on history and examination
- Cause of aortic stenosis - bicuspid, calcific, rheumatic
- Diagnosis, progression
- High risk symptoms - dyspnoea/CCF, syncope, angina
- Dates of interventions - transcatheter aortic valve implantation (TAVI), prosthetic valve replacement
- Ejection systolic murmur that radiates to carotid arteries, delayed/diminished carotid upstroke, single or paradoxically split S2
- Concurrent LV dysfunction, IHD

If high risk symptoms (CCF, syncope or angina) present in patients with moderate or greater severity AS, patient must be reviewed by a cardiologist prior to elective surgery

Grading of Severity
Table: Severity of Aortic Stenosis

Severity	**Mild**	**Moderate**	**Severe**

Mean Valve Gradient (mmHg)	<20	20-39	≥40
Valve Area (cm^2)	>1.5	1.1-1.5	≤1
Peak Velocity (m/sec)	<3	3-3.9	≥4
Dimensionless Index (LVOT:AS Vmax)	>0.5	0.25-0.5	<0.25

Discuss with anaesthetist in PAC if:

- Severe AS
- Moderate or severe AS with exercise tolerance < 4 METS
- Moderate or severe AS with LVEF < 40%

Aortic Regurgitation (AR)

Important elements on history and examination

- Cause of aortic regurgitation - bicuspid, calcific, rheumatic, aortic dilatation
- Diagnosis, progression
- Dates of interventions - prosthetic valve replacement
- High risk symptoms - dyspnoea, angina
- Diastolic murmur loudest in the 2nd intercostal space at the right sternal edge, soft A2, widened pulse pressure, collapsing (‘waterhammer’) pulse. Corrigan’s Sign - visible neck pulsation. De Musset’s Sign - head nodding. Quincke’s Sign - visible capillary pulsations in the nail beds
- Concurrent aortic dilatation, LV dysfunction

Grading of Severity

Table: Severity of Aortic Regurgitation

Severity	**Mild**	**Moderate**	**Severe**
Effective Regurgitant Orifice Area (mm^2)	<10	10-29	≥30
Regurgitant Volume (mL)	<30	30-59	≥60
Diastolic Flow Reversal in Descending Aorta	Absent/brief	Intermediate	Holodiastolic flow reversal

Most patients with aortic regurgitation do not need to be reviewed by anaesthetics before surgery as this condition is generally well tolerated with anaesthesia

Discuss with anaesthetist in PAC if there are any concerns re: patient’s functional capacity

Mitral Stenosis (MS)

Important elements on history and examination

- Rare in Australia
- Cause of mitral stenosis - rheumatic fever, calcific disease
- Diagnosis, progression
- Dates of interventions - prosthet
- ic valve replacement
- Low pitched diastolic murmur heard best at the apex, mitral facies - malar flush on cheeks, peripheral cyanosis, signs of right heart failure, loud S1 with opening snap
- Concurrent pulmonary hypertension, atrial fibrillation

Grading of Severity
Table: Severity of Mitral Stenosis

Severity	**Mild**	**Moderate**	**Severe**
Mean Valve Gradient (mmHg)	<5	5-10	>10
Valve Area (cm^2)	>1.5	1.0-1.5	<1.0
Pulmonary Artery Pressure (mmHg)	<30	30-50	>50

Discuss with anaesthetist in PAC if:

- Concurrent pulmonary hypertension
- Severe MS
- Moderate or severe MS with exercise tolerance < 4 METS

Mitral Regurgitation (MR)

Important elements on history and examination

- Cause of mitral regurgitation - valve prolapse, LV dysfunction and cardiomyopathy
- Diagnosis, progression
- Dates of interventions - prosthetic valve replacement
- Apical pansystolic murmur radiating to the axilla, soft S1, loud S3, displaced and forceful apex beat
- Concurrent LV dysfunction, atrial fibrillation

Grading of Severity
Table: Severity of Mitral Regurgitation

Severity	**Mild**	**Moderate**	**Severe**
Effective Regurgitant Orifice Area (mm^2)	<20	20-39	≥40

Regurgitant Volume (mL)	<30	30-59	≥60
Pulmonary vein flow	Systolic dominance	Systolic blunting	Systolic flow reversal

Like aortic regurgitation, this condition is generally well tolerated with anaesthesia. Refer patients to anaesthetic PAC if LVEF < 40% or METS < 4

Tricuspid Stenosis (TS)

Important elements on history and examination

- Rare in Australia
- Cause of tricuspid stenosis - rheumatic, endocarditis, carcinoid
- Diagnosis, progression
- Dates of interventions - prosthetic valve replacement
- Rarely diagnosed at bedside, difficult to hear murmur
- Concurrent mitral stenosis, tricuspid regurgitation

Grading of Severity
Table: Markers of Haemodynamically Significant Tricuspid Stenosis

Mean Valve Gradient (mmHg)	≥5
Valve Area (cm^2)	≤1
Inflow time-velocity integral (cm)	>60
Dilated inferior vena cava	Present

Refer all patients with haemodynamically significant tricuspid stenosis to anaesthetic PAC

Tricuspid Regurgitation (TR)

Important elements on history and examination

- Common, physiologically normal to have trace-mild TR
- Cause of tricuspid regurgitation - rheumatic, valve prolapse, RV dilation
- Diagnosis, progression
- Dates of interventions - prosthetic valve replacement
- Pansystolic murmur, maximal on inspiration, large v waves in JVP, right ventricular heave, hepatomegaly
- Concurrent pulmonary hypertension

Grading of Severity
Table: Severity of Tricuspid Regurgitation

Severity	**Mild**	**Moderate**	**Severe**

Effective Regurgitant Orifice Area (mm^2)	Not defined	Not defined	≥40
Regurgitant Volume (mL)	Not defined	Not defined	≥45
Hepatic vein flow	Systolic dominance	Systolic blunting	Systolic flow reversal

Patients do not need to be seen by anaesthetic PAC unless they have concurrent pulmonary hypertension or RV dysfunction

Pulmonic Stenosis (PS) and Pulmonic Regurgitation (PR)

These are very uncommon diseases in Australia, mostly as consequences of uncorrected congenital heart disease
You will not be expected to assess and manage patients with these conditions pre-operatively
Refer all patients to anaesthetic PAC

Pulmonary Arterial Hypertension (PAH)

Confers 14-29% morbidity in non-cardiac surgery, mortality up to 18%

WHO Classification of Pulmonary Hypertension
Primary
Group 1: pulmonary arterial hypertension
Idiopathic, genetic, drug/toxin, connective tissue diseases, HIV, persistent pulm hypertension of newborn (PPHN)
Secondary
Group 2: due to left heart disease
LVF, valvular disease
Group 3: due to lung disease and/or chronic hypoxia
COPD, OSA, interstitial lung disease/IPF, high altitude
Group 4: chronic thromboembolic pulmonary hypertension (CTEPH)
Group 5: pulmonary hypertension with unclear multifactorial mechanisms
5.1 Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

Table: Severity of Pulmonary Hypertension

Severity	Mild	Moderate	Severe
Mean Pulmonary Artery Pressure (mmHg)	20-40	41-55	>55

Note pulmonary pressures are calculated by measuring tricuspid regurgitant jet velocity and therefore are subject to inaccuracies

Important elements on history and examination

- Cause of PAH
- Obtain a detailed assessment of the patient's functional capacity as morbidity increases with decreasing functional capacity
- Very little interventions have been shown to decrease morbidity associated with pulmonary hypertension. The exception is phosphodiesterase inhibitors (Bosentan/sildenafil) prescribed in Group 1 PAH patients. These medications must be continued during the peri-operative period
- Concurrent RV failure or dysfunction is very concerning and surgeries beyond minor should be avoided where possible

Where possible, patients with moderate or greater severity of pulmonary hypertension should be referred to anaesthetic PAC to discuss peri-operative monitoring and CVS risk; post-operative discharge to HDU is likely
Prolonged fasting and hypovolaemia should be avoided, discuss this with the anaesthetist in PAC

Heart Failure/Cardiomyopathy

Prevalence of 0.5% of Australian population
Men almost twice as likely to have heart failure compared to women
Only definitive treatment is cardiac transplantation; medications can help reduce mortality

- ACEI/ARB 60% – CONSENSUS, SOLVD
- Beta blockers – MERIT-HF, CIBIS II
- Aldosterone antagonists – RALES
- Treatment of anaemia in CCF/renal failure also improves mortality
- Diuretics/digoxin NOT associated with improved mortality, only symptomatic control

Important elements on history and examination

- Cause of heart failure - ischaemic, valvular, drug, hypertensive
- Diagnosis - last known TTE/TOE
- Associated comorbidities - ischaemic heart disease, valvular lesions, pulmonary hypertension
- Last follow-up with cardiology, stability of heart function and symptoms, alterations to medications
- Compliance with medical therapy
- "Dry weight" and daily fluid restriction
- Evidence of active failure - hypoxia, dyspnoea, decreasing exercise tolerance, bilateral crepitations in chest, peripheral pitting oedema

- Ensure correspondence from cardiology and recent investigations available on CPF
- Consider preop NT pro BNP to look at control of cardiac failure.

Table: NYHA Functional Classification of Heart Failure

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath)
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea (shortness of breath)
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases

Generally if symptoms are stable and there have been no changes in medical therapy recently, patients are safe to proceed with surgery
Exceptions - these patients should be reviewed by an anaesthetist to discuss implications for peri-operative morbidity and management plan

- Severe right heart failure with pulmonary hypertension - see Pulmonary Arterial Hypertension (PAH)
- Hypertrophic Obstructive Cardiomyopathy (HOCM)
- LVEF <40% with moderate or severe aortic stenosis
- Concurrent untreated/residual coronary artery disease

Atrial Fibrillation

Atrial fibrillation is the most common perioperative arrhythmia with potentially increasing incidence as progressively older patients present for surgery
Supraventricular arrhythmia characterised by complete absence of coordinated atrial contractions

Important elements on history and examination

- Diagnosis, paroxysmal or permanent
- Management - rate control, elective DC reversions, implanted cardiac device
- Anticoagulation - warfarin, NOACS
- Associated comorbidities - ischaemic heart disease, HTN, valvular disease
- Previous strokes

Patients must have adequate rate control before proceeding with elective surgery. Refer to cardiology for further optimisation if HR >100
Preoperative medications for rate control should be continued until day of surgery
Decisions on continuation of anticoagulation are patient and procedure dependent; discuss with the surgeon involved and consider whether a spinal anaesthetic is a viable option. If yes, withhold anticoagulation for an appropriate duration (see Anticoagulants)

Patient with the Implanted Cardiac Device - Pacemakers and Defibrillators

Type of Pacemaker/details

- Indication for placement
- Date of insertion
- Life of battery
- Pacemaker make and model
- Location
- Number of leads
- Setting
- Combined Automatic Implantable Cardioverter Defibrillator (AICD)
- CRT

Pacing Modes

Table 1 The Generic Pacemaker Code (adapted from Bernstein and colleagues[4] with permission from John Wiley & Sons Ltd)

Position I: pacing chamber(s)	Position II: sensing chamber(s)	Position III: response(s) to sensing	Position IV: programmability
O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	I = Inhibited	R = Rate modulation
V = Ventricle	V = Ventricle	T = Triggered	
D = Dual (A+V)	D = Dual (A+V)	D = Dual (A+V)	

Pacemaker Check

- Organise if none within 1 year if major surgery
- % dependence
- Arrhythmias/underlying rhythm
- Response to magnet
- Battery life

The main concern with implanted cardiac devices is interference from surgical diathermy. Decisions on whether to use monopolar or bipolar diathermy can generally be made on the day of surgery. If there are specific concerns from the surgical consultant, discuss with the anaesthetist in PAC

Respiratory

Smoking

The health/disease/illness burden of tobacco in Australia and New Zealand is a major one with approximately 15,500 deaths attributable to tobacco in Australia each year and 5000 in New Zealand.
Smoking is the single greatest preventable cause of death and ill health, accounting for 8% of the total disease burden in Australia and costing the economy an estimated $31.5 billion in tangible costs.
Smoking cessation before surgery has been shown to improve surgical outcome. Although there is some controversy about optimal timing of smoking cessation there is agreement that longer quitting is best.
Benefit of perioperative period as “teachable moment” for health advocacy

Unsupported cessation is only successful 4-7%
Three point cessation strategy AAR (Ask, Advise, Refer)
Ask – ask about smoking status even if known, reinforces that tobacco use is a significant issue
Advise – explain specific perioperative risks that smoking poses
Refer – GP, pharmacists, Quitline

Benefits of cessation prior to surgery

1. Quitting for a day will lower carboxyhaemoglobin and nicotine levels and could be expected to improve tissue oxygen delivery
2. Quitting for as little as three weeks was shown to improve wound healing
3. Six to eight weeks quitting means sputum volumes are not increased compared to non-smokers and pulmonary function is improved
4. Immune function is significantly recovered by six months quitting

Pharmacological interventions:

- Nicotine substitution
- Bupropion
- Varenicicline

Chronic Obstructive Pulmonary Disease (COPD)

Estimated one in seven Australians over the age of 40 has COPD
COPD is an umbrella term for the lung diseases:

- Emphysema
- Chronic bronchitis
- Bronchiectasis
- Chronic Asthma

Unlike asthma, it is characterised by an obstructive ventilatory defect with **no** demonstrable reversibility with bronchodilators
Diagnosis of COPD is confirmed by the presence of persistent airflow limitation (post-bronchodilator $FEV_1/FVC < 0.7$; also known as FER)

Important elements on history and examination

- Diagnosis
- Compliance with bronchodilator therapy
- Medication regime, recent steroid use or steroid dependence
- Progression/deterioration of pulmonary function tests (PFTs); most recent PFT should be within 1 year of major surgery and available on CPF
- Current smoking status
- Recent exacerbations and hospitalisations; requirements for intubation
- Home oxygen use
- Exercise tolerance and functional status. If the patient isn't very active, ask about ADLs and household tasks as per DASI
- Examination - hyper-expansion of chest "barrel chest", peripheral clubbing in fingers, cyanosis and resting SpO2, wheeze on auscultation of chest

Global Initiative for Chronic Obstructive Lung Disease (GOLD)
Table: Severity of COPD as per GOLD

Class	FEV_1 % of predicted
1 Mild	≥ 80%
2 Moderate	50-79%
3 Severe	30-49%
4 Very severe	< 30%

Updated GOLD Score (2021)

Major surgery should be delayed until 6 weeks after most recent exacerbation to minimise risk of respiratory complications peri-operatively
Ideally patient should be fully weaned off steroids at this point as well
A spinal anaesthetic without sedation may be ideal for these patients if surgery is in lower half of body without entering the abdominal cavity
Bronchodilator therapy should be continued on day of surgery

Always counsel patients to cease smoking, preferably >4/52 prior to surgery even if temporary
If recent deterioration in exercise function/symptoms (e.g. increase in sputum production, fevers, new dyspnoea at rest) is detected on history, patient should be reviewed by a respiratory physician prior to elective surgery

Refer the following patients to anaesthetic PAC if having major surgery:

- Resting hypoxia (SpO2 <95%)
- On home oxygen therapy
- Steroid dependent
- FEV1 <50% predicted or <1L

- FVC <1.5L
- TLCO or KCO <40% predicted
- Thoracic surgery or major abdominal surgery with moderate or greater severity COPD, surgery duration expected >3 hours
- Concurrent pulmonary hypertension
- Exacerbation within last 6 weeks and patient for surgery that cannot be delayed due to medical reasons

Asthma

Asthma is characterised by a reversible obstructive ventilatory defect on PFTs (i.e. bronchodilator responsive)

Ensure patients have well controlled symptoms and are compliant with medical therapy
These patients do not need to be seen in anaesthetic PAC unless they experience frequent exacerbations of symptoms or are steroid dependent
Similar to COPD, asthma patients should have elective surgery delayed for 6/52 post any exacerbation and be ideally weaned off steroids by the time they have surgery
Any preventer inhaler therapy should be continued up to day of surgery

Interstitial Lung Disease (ILD)/Idiopathic Pulmonary Fibrosis (IPF)

Interstitial lung disease is group of diseases characterised by restrictive ventilatory defects and impaired oxygen transfer factor on PFTs

Important elements on history and examination
- Diagnosis, age of onset
- Cause/exposure
- Functional status and exercise tolerance
- Concurrent pulmonary hypertension; recent TTE in last year must be performed if METS < 4
- Recent exacerbations and hospitalisations
- PFTs performed within 1 year of major surgery
- Home oxygen therapy
- Examination - fine inspiratory crepitations on auscultation of chest, peripheral clubbing, cyanosis/hypoxia, signs of pulmonary hypertension

Refer the following patients to anaesthetic PAC if having major surgery:
- Home oxygen therapy
- Immunosuppressed
- Concurrent pulmonary hypertension
- Resting hypoxia (SpO2 <95%)
- Recent infective exacerbation <6/52 ago
- TLCO <60% predicted
- FVC <80% predicted and thoracic surgery
- FVC <1.5L and having intra-cavity surgery

- Expected surgical duration >2 hours

Obstructive Sleep Apnoea (OSA)

See Obesity

Cystic Fibrosis

Cystic fibrosis (CF) is a multisystem autosomal recessive disease and the most common lethal genetic disease in caucasians. The disease is caused by mutations in a single gene on the long arm of chromosome 7 which encodes a 1480 amino acid protein called CF transmembrane regulator (CFTR).

CFTR is a chloride channel, found at the apical border of epithelial cells lining most exocrine glands in the body. All CF-causing mutations cause abnormal chloride conductance through the CFTR channel. The imbalance of Na/Cl to maintain a normal, thin mucus layer that is easily removed by cilia that lines the lungs and other organs. In CF, the mucus is viscid as it contains significantly less water and is therefore less well cleared by cilia.

Clinical Manifestations of CF:

- Respiratory tract
    - Viscid mucus secretions, hypertrophy of goblet cells, decreased mucociliary clearance
    - Abnormal viscid nasal secretions
    - Frequent LRTI, chronic hypoxaemia, cor pulmonale
    - Sinusitis, nasal polyposis
    - Chronic colonization of airways with pathogens, including pseudomonas aeruginosa, staphylococcus aureus, haemophilus influenzae, Stenotrophomonas maltophilia, Burkholderia cepacia and Aspergillus
- Hepatobiliary
    - Obstruction of bile ducts
    - Focal biliary cirrhosis, portal hypertension, multinodular biliary cirrhosis
- Gastrointestinal
    - Abnormal viscid intestinal secretions
    - Meconium ileus, recurrent abdominal pain
- Pancreas
    - Obstructed pancreatitis ducts, fibrosis
    - Pancreatic exocrine insufficiency, CF-related diabetes
- Bone
    - Impaired Calcium, Vitamin D absorption
    - Increased catabolism
    - Osteoporosis
- Skin
    - Increased chloride levels
    - Abnormal “sweat test:, diminished thermoregulation
- Infertility

    - 98% of men with CF suffer from congenital bilateral absence of the vas deferens, which leads to primary infertility.

Anaesthetic Management

Patients with CF may present electively for surgical procedures such as nasal polypectomy, enteral feeding, vascular access device placement etc. Patients with severe disease are best managed in a tertiary centre with multi-disciplinary input.

Preoperative

- Medical optimisation - “tune up” under respiratory care
    - Medication review
    - Daily chest physiotherapy; sequential bedside peak flow measurement
    - Nebulized drugs
    - Multidisciplinary management with liaison with patient’s usual CF team where possible
- History
    - Volume and purulence of sputum
    - Functional ability; patients often know if they are at baseline or not
    - Respiratory and non-respiratory components
- Investigations
    - CXR
    - ABG - hypercapnia may indicate increased risk of postoperative respiratory problems
    - Spirometry
        - Obstructive pattern commonly (decreased FEV1)
        - Patients with decrease in FEV1 to <1L, especially if hypoxaemic, may indicate need for postoperative ventilation
    - TTE - may help to determine if patients has RVH, cor pulmonale

Conduct of anaesthesia

- Where possible, central neuraxial block or regional anaesthesia can avoid airway manipulation and optimize postoperative analgesia
- Airway Management
    - LMA considered for short non-abdominal/thoracic procedures to reduce negative effects of GA on respiratory mechanics
    - ETT allows controlled gas exchange, tracheal suctioning of secretions
    - AVOID nasal intubation given high incidence of nasal polyposis
    - Humidified gases, aim for low airway pressures
    - Full reversal of neuromuscular blockade
- Positioning
    - Careful positioning and padding given malnutrition
- Temperature
    - Temperature monitoring important
    - Maintain normothermia
- Postoperative analgesia
    - Early mobilisation and physiotherapy
    - Avoid high dose opioids and potential for respiratory depression

- Aim for early extubation to reduce postoperative respiratory tract infection

Anti-coagulation

This section covers some basic principles behind managing anti-coagulation for patients undergoing elective surgery
For more detailed guidance of cessation and restarting anti-coagulation, please go to Anticoagulants and Antiplatelets

When managing anticoagulants prei-operatively, the aim is to balance thrombotic risk with bleeding risk during procedure; minimise or no residual anticoagulant effect during procedure

Factors to consider:

- Surgical procedure; minor or major
- Elimination half life
- Renal function/creatinine clearance
- Type of anaesthesia
- Indication for anticoagulation

Bridging Clexane and Warfarin

Warfarin should be ceased 5 days prior to all major surgery
The decision to NOT use bridging low molecular weight heparin (i.e. clexane/enoxaparin) is based on studies demonstrating an increased risk of major bleeding in patients who received bridging clexane pre-operatively with no benefit to thrombotic risk
However, these studies were mostly represented by patients with CHA2DS2-VASC scores of 1-3 and therefore patients with higher scores are still candidates for bridging clexane
For suggested bridging clexane strategies, please see Bridging Clexane Strategies - Objectify

Patients who do NOT need bridging clexane:

- AF low risk - CHA2DS2-VASC score 1-3 and/or no TIA/CVA in last 6 months
- Aortic valve/low risk - sinus rhythm, normal LV function, no prior embolism
- VTE low risk - no major VTE within last 3 months

Patients who require bridging clexane:

- AF high risk - CHA2DS2-VASC 4-6 and/or TIA/CVA within last 6 months
- Aortic valve/high risk - AF and/or poor LV function and/or prior VTE
- Mitral valve - all MVR
- VTE high risk - major VTE within last 3 months and/or previous events while off anticoagulants and/or active malignancy and/or antiphospholipid syndrome
- Cardiomyopathy +/- mural thrombus

CHA_2DS_2-VASc

The CHA2DS2-VASc score is one of several risk stratification schema that can help determine the 1 year risk of a TE event in a non-anticoagulated patient with non-valvular AF

	CHA2DS2-VASC Clinical Characteristics	Points
C	Congestive Heart Failure	1
H	Hypertension	1
A2	Age ≥ 75	2
D	Diabetes	1
S2	PHx Stroke or TIA	2
V	Vascular Disease	1
A	Age 65-74	1
Sc	Sex/Gender - Female	1

CHA2DS2-VASC Score	Annual Risk of Stroke
0	0
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.2%

Obesity

The prevalence of obesity has increased across the globe.
Obesity is associated with several physiological changes which should be taken into account for the planning for anaesthesia and recovery in the patient.

The classification of obesity defined by BMI as per the World Health Organization is:

- Obesity: BMI of ≥30 kg/m2
- Morbid obesity: BMI of ≥40 kg/m2

Preoperative risks in obese patients

- Increasing BMI have been independently associated with pulmonary complications following surgeries e.g. bariatric surgery. It has also been independently associated with adverse outcomes including greater hospital length of stay, estimated blood loss, surgical site infections, renal failure, longer operative times and prolonged assisted ventilation.
- The Obesity Surgery Mortality Risk Score [OS-MRS] is useful for predicting mortality after obesity surgery.

Refer all patients who are severely obese to be reviewed by an anaesthetist prior to a major surgery.

Who should see the Anaesthetist at PAC:

All patients with the following:

- BMI ≥50 kg m^{-2}.

- Moderate or severe OSA.

- Significant medical conditions such as Ischaemic Heart Disease, Cardiac Failure, Renal Dysfunction

    - Exercise tolerance <4 METS (i.e. unable to climb 1 flight of stairs without stopping)

    - Previous anaesthesia or pain issues

    - Patient concerns

    - Surgical concerns

Comorbidities

The following conditions should be screened in all obese patients prior to having major elective surgery

1. Obstructive Sleep Apnoea (OSA)

- This is prevalent in severely obese patients

- Obese patients should be screened specifically for OSA using screening tool e.g. STOP-Bang (https://www.mdcalc.com/stop-bang-score-obstructive-sleep-apnea) or Berlin Questionnaires (https://sleepdiagnostics.com.au/berlinquestionnaire)

S	Snoring? Do you snore loudly (loud enough to be heard through closed doors, or your bed partner elbows you for snoring at night)?
T	Tired? Do you often feel tired, fatigued or sleepy during the daytime (such as falling asleep during driving)?
O	Observed? Has anyone observed you stop breathing or choking/gasping during your sleep?
P	Pressure? Do you have or are being treated for high blood pressure?
B	BMI >35kg/m2
A	Age > 50 years old?
N	Neck circumference Male: 17 inches or larger? Female: 16 inches or larger?
G	Gender = Male?

Scoring criteria:

- Low risk of OSA: yes to 0-2 questions
- Moderate risk: yes to 3-4 questions
- High risk: yes to 5-8 questions

Observed apnoeas most significant predictor for mod-sev OSA
Score ≥3 sensitivity for moderate OSA (93%), severe OSA (99%)
Score 4-5, chance of having moderate/severe OSA approaches 50%; usually used as cut off for delay surgery and investigate
False negative rate of 16+%
Increase sensitivity if elevated bicarb ≥28 on UEC

- If the patient has known OSA, the severity of disease and adequacy of treatment should be evaluated.
    - OSA is associated with increased sensitivity to respiratory depressant effects of sedatives and opioids
    - There is a tendency to obstruct the airway when sedated or during bag mask ventilation
    - There might be an increased difficulty with laryngoscopy

- Patients should also be screened for associated medical conditions e.g. obesity hypoventilation syndrome, coronary artery disease, pulmonary hypertension and insulin resistance.

2. Obesity hypoventilation syndrome (OHS)

- Most patients with OHS have OSA, ~ ⅔ have pulmonary hypertension
- The presence of awake alveolar hypoventilation in an obese individual which cannot be attributed to other conditions associated with alveolar hypoventilation
- There is no validated method for screening. If you have a strong clinical suspicion for this, perform an arterial blood gas/serum electrolyte test(s) to screen for carbon dioxide retention and hypoxaemia
- An echocardiogram is useful to assess global cardiac and right heart function and the presence of pulmonary hypertension
- Patients with OHS are sensitive to sedatives and opioids, supplemental oxygen may increase hypercapnia. These patients may also be more likely to have difficulty weaning from mechanical ventilation including during emergence from anaesthesia.

3. Hypertension and cardiovascular disease

- Strongly associated with raised BMI
- Preoperative management of poorly controlled hypertension (SBP >170 mmHg; DBP >110 mmHg) is important for nonurgent surgery
- Obesity increases risks for cardiovascular diseases including coronary heart disease, cerebrovascular disease, heart failure and atrial fibrillation
- As recommended by the American Heart Association (AHA) on cardiovascular evaluation and management of severely obese patients undergoing surgery, severely obese patients with at least one risk factor for coronary heart disease (smoking, diabetes, HTN, hyperlipidaemia) or poor exercise tolerance should have a chest radiograph and 12-lead ECG prior to surgery
- Further investigations may be organized based on the results of these tests.

4. Diabetes Mellitus (DM) and Metabolic Syndrome

- Type 2 DM is strongly associated with obesity
- Elevated preoperative glycated haemoglobin (HbA1C) levels are associated with an increased risk of preoperative morbidity
- Metabolic syndrome is associated with a higher risk of morbidity after surgery
- Registry studies from the American College of Surgeons National Surgical Quality IMprovement Program (NSQIP) database have found that patients with modified metabolic syndrome (i.e. obesity, hypertension and diabetes) were at higher risk of complications and prolonged length of stay after some surgeries and mortality after various non-cardiac procedures and liver surgery.

Preoperative preparation

- Patients with OSA or OHS using Continuous Positive Airway Pressure (CPAP) should be instructed to adhere to their treatment regimen. Benefits of adhering to the therapy include improved cardiac parameters and improved ventilatory drive in patients with OHS.
- Patients should be advised to bring their CPAP machine with them into hospital,
- Patients with previous weight loss surgery, particularly gastric banding, should be assessed for signs or symptoms of dysphagia that may indicate an increased risk of aspiration
- Obese patients may be poor candidates for day surgery if the procedure requires general anaesthesia and opioid administration. In such settings, we would advise patients to be admitted for at least overnight observation in a monitored setting

ICU/HDU Referrals:

HDU/ICU referrals should ideally come from PAC. Criteria for ICU admission are:

Absolute

- Body mass index (BMI) >60 kg/m^2
- Severe obstructive sleep apnoea (those stabilised on CPAP are no longer considered severe) and/or Obesity Hypoventilation Syndrome
- Requirement of continuous cardiac monitoring for cardiac abnormalities or other significant medical comorbidities
- Complex revision bariatric surgery- expected long procedure/ revisional bypass surgery
    - *Relative*
- Difficult to manage diabetes

Endocrine

Diabetes

The goal or pre-operative assessment of patients with diabetes is to ascertain the degree of control of diabetes
Pre-operative hyperglycaemia, independent of diabetic status increases the risk of peri-operative morbidity and mortality
Important elements on history and examination

- Type of diabetes, age of diagnosis
- Hypoglycaemic regimen, diet, OHGs, insulin
- Adequacy of BSL control, HbA1C
- Symptoms of hyperglycaemia (DKA, polyuria, thirst, weight loss) and hypoglycaemia (dizziness, LOC, seizure, sweat)
- Comorbidities – IHD, CVA, PVD, HTN, neuropathy (postural hypo, dizziness, erectile dysfx), eyes, renal, autonomic dysfunction

Optimal HbA1c is <7 for elective surgery and patients with Hba1c values above this are at significantly increased risk of mortality and morbidity. Patients with elevated Hba1c should be referred back to endocrinology for optimisation of their diabetes before proceeding.

With regard to medication management preoperatively, see relevant section. If there are doubts, contact pharmacy for further advice

Patients should have an admission BSL taken, and if on SGLT 2 inhibitors, should have a ketone taken at the same time

Thyroid Disease

Thyroid disease is common and the prevalence is higher in women and with increasing age.

The general approach to these patients is to ensure they are euthyroid prior to having major elective surgery. This can be achieved by clinical history/exam and thyroid function tests.

Patients who need thyroid medications altered should be referred to endocrinology

Hypothyroidism

- Hypometabolism results in decreased cardiac output mediated by reduction in heart rate and contractility
- Hypoventilation can occur due to respiratory muscle weakness and reduced pulmonary responses to hypoxia and hypercapnia
- Decreased gut motility results in constipation and ileus
- Metabolic abnormalities include hyponatraemia, increased serum creatinine, reduced clearance of some drugs (e.g. antiepileptics, anticoagulants, hypnotics, opioids)
- Decreased red blood cell mass and normochromic, normocytic anaemia

Potential Complications from Hypothyroidism

- If surgery is urgent, do not delay but be aware that minor perioperative complications might occur e.g. peri and postoperative ileus, hypotension, hyponatraemia and CNS dysfunction; also increased sensitivity to opioids
- Myxedema coma is a rare postoperative complication. Hallmarks are decreased mental status and hypothermia, but hypotension, bradycardia, hyponatraemia, hypoglycaemia and hypoventilation.

Hyperthyroidism

Potential Complications from Hyperthyroidism

- Atrial fibrillation occurs in about 8% of patients and more common in older patients.
- Subclinical hyperthyroidism is associated with increased rates of atrial ectopy and 3x increased risk of AF
- Dyspnoea may occur for variety of reasons including increased oxygen consumption and CO2 production, respiratory weakness and decreased lung volume
- Weight loss due to increased calorigenesis and gut motility and associated hyperdefecation and malabsorption. Patient may be malnourished
- Thyroid storm

Systemic effects of hyperthyroidism should be treated following referral to endocrinology.
Treatments include:

- Propanolol: inhibits conversion of T4 to T3 peripherally. Also reduces heart rate and cardiac output as well as hypermetabolism from hyperthyroidism. Target heart rate should be <100bpm.
- Radioactive iodine: typically only used to prepare a patient for surgery in a short timeframe. Dose is 3 drops tds.
- Carbimazole/methimazole: inhibits thyroid peroxidase and inhibits thyroid iodine uptake, decreasing production of T4 and T3
- Propylthiouracil : inhibits thyroid peroxidase centrally and decreases peripheral conversion of T4 -> T3. Rare side effects include agranulocytosis, hepatotoxicity, cholestatic jaundice. Notably, PTU crosses the placenta less and is the preferred treatment in pregnancy-related thyrotoxicosis

Airway Considerations

Potential mass effect from goitre
Patients should be asked about/examined for:

- Lying flat
- Tracheal deviation
- Stridor
- Dysphagia
- Voice changes
- Neck movement limitation
- Pemberton’s sign.

They may need CT to look for a retrosternal extension of the goitre, which has anaesthetic and surgical implications, as well as respiratory function tests to look for the extent to which tracheal compression is affecting respiratory mechanics.
Nasendoscopy to examine cord function may also be useful.
Refer to ENT if this is the case; major surgery should be delayed if presence of airway compression from a goitre is evident

Pheochromocytoma

Pheochromocytomas are a rare catecholamine-secreting tumour which may arise anywhere in the sympathetic chain but typically originate in the adrenal gland (medullary chromaffin cells)
It is unusual for patients to have a phaeochromocytoma and not have them surgically removed. Refer all patients to PAC for anaesthetic review

Phaeochromocytomas described as a disease of 10s:

- 10% are bilateral : 90 % unilateral
- 10% extra-adrenal: 90 % adrenal
- 10% are malignant/metastatic : 90% are benign
- 10% are dopamine secreting; 90 % are noradrenaline secreting
- 10 % are familial; 90 % are spontaneous

Associated Syndromes
Multiple Endocrine Neoplasia (MEN)

- 2a: triad of phaeochromocytoma/adrenal medullary hyperplasia, medullary thyroid cancer, hyperparathyroidism
- 2b: pheochromocytoma, medullary thyroid carcinoma, mucosal neuromas, ganglioneuromas of the GIT, marfanoid habitus

Neurofibromatosis

- 1% incidence of pheochromocytoma

Von-Hippel Lindau

- 14% incidence of pheochromocytoma, also associated with cerebellar haemangioblastoma and retinal angiomas

Systemic Implications
Cardiovascular:

- Hypertension , often refractory and paroxysmal - the commonest sign; headache is the commonest symptom
- Chronically increased SVR
- LV hypertrophy in response to chronic hypertension
- Palpitations; also increased risk of arrhythmias and myocardial ischemia
- High output cardiac failure

Respiratory:

- Neurogenic pulmonary oedema

Neurological:

- Headache
- Increased risk of CVA secondary to hypertension
- Increased ICP

- Hypertensive encephalopathy
- Nausea and vomiting (dopamine secreting tumours)
- anxiety/ sense of doom (adrenaline secreting tumours)

Endocrine:

- increased risk of diabetes due to impaired insulin release

Preoperatively:
Investigations:

- 24 hour urinary free catecholamines, metanephrines, VMA
- Imaging to determine tumour location (MRI/CT/MIBG)
- ECG: LVH, arrhythmias, ischemic changes
- Echocardiography: evaluate structural changes, look for evidence of cardiac failure
- FBE: increased HCt
- UEC: end-organ dysfunction from chronic hypertension -> renal impairment
- Screen for hyperglycemia
- Consider PTH levels, calcitonin levels, and CMP to look for multiple endocrine neoplasia

Preop control of blood pressure as per the Roizen criteria is recommended.
Roizen Criteria:

- Blood pressure <160/90 for at least 24 hours pre-op
- No orthostatic hypotension with BP < 80 /45
- No ST/T wave changes for 1 week pre-op
- < 5 PVCs/min

Preoperative Medication Management:
The goals are to control blood pressure, heart rate, arrhythmias, and normalise circulating volume. Typically, alpha-blockade is first established then beta blockade is begun (in order to prevent unopposed alpha activity). Commonly this process requires 2-3 weeks.

Alpha blockade:
Phenoxybenzamine: 10 mg bd as a starting dose; increasing depending on response (may be as high as 200 mg daily). Dose is sufficient when patient develops postural hypotension/nasal stuffiness.

- Non selective, irreversible
- Also blocks a2 receptors -> tachycardia
- Long half-life - 24 hours.
- Note: not always available

Prazosin

Addisons disease

Addison's disease is characterised by reduced or absence of glucocorticoid secretion. There may also be associated mineralocorticoid deficiency
Patients do not need to be referred to anaesthetic PAC; however a discussion should be had with endocrinology to formulate a plan for peri-operative steroid supplementation

Primary hypoadrenalism:

- 80 % are due to autoimmune destruction of the adrenal cortex
- Other causes- tuberculosis, carcinoma, adrenalectomy, hypoperfusion -> adrenal ischemia

Secondary hypoadrenalism:

- Prolonged corticosteroids
- Hypopituitarism

Relative hypoaldosteronism

- May be seen in critically unwell patients

Diagnosis of Addisons is often difficult, as symptoms are non-specific, and diagnosis may be delayed until patients present with florid Addisonian crisis and profound refractory hypotension. There is also an increased risk of Addisonian crisis or acute adrenal crisis in the perioperative period. This risk appears to be greater with general anaesthesia but has been reported even after regional or sedation techniques have been used.

Symptoms of Addisons include fatigue, anorexia, postural hypotension, weight loss, nausea and vomiting, and pigmentation changes. Addisons is also associated with hypoglycemia, hyponatremia and hyperkalemia.

In patients who have been on long term high doses of steroids, in particular, there is a significant risk of adrenal axis suppression and secondary hypoadrenalism. In these patients, consider endocrine referral and steroid supplementation, especially if the steroid dose is > 15 mg of prednisolone or equivalent per day.

Steroid supplementation should be considered if there is refractory hypotension in the perioperative period, and patients with suspected adrenal crisis should be referred to endocrinology and the intensive care unit.

Acromegaly

Acromegaly is a chronic, progressive multisystem disorder caused by excess secretion of growth hormone, most typically from a functioning pituitary macroadenoma. It typically manifests as local mass effect and as systemic excess of GH and is often significantly advanced at the time of diagnosis. Even following surgical resection, the pre-existing consequences of acromegaly put these patients at a higher risk perioperatively.
Refer all patients with acromegaly to the anaesthetic PAC for assessment prior to elective major surgery

Systemic effects and anaesthetic considerations have been listed below.
Airway:

- Hypertrophy of the upper airway including macrognathia, macroglossia, and excess soft tissue deposition in the larynx and pharynx -> glottic and subglottic stenosis
- Recurrent laryngeal nerve palsy may occur
- Increased risk of difficult airway; preoperative nasendoscopy may be helpful. Awake fiberoptic or video assisted intubation should be considered.

Respiratory

- Increased risk of OSA, which is associated with airway difficulty, cardiac disease, pulmonary hypertension and postoperative cardiorespiratory failure

- May have kyphoscoliosis and proximal myopathy leading to restrictive lung disease
- Preoperative TTE should be considered if there is concern re pulmonary hypertension and right heart disease as a consequence of OSA
- Patients with OSA should be asked to bring in their CPAP if possible.
- Depending on the nature of the surgery HDU referral +/- admission should be considered

Cardiovascular

- Refractory hypertension
- Eccentric LVH
- Increased risk of IHD, arrhythmias including heart block, cardiomyopathy and biventricular dysfunction
- Patients should have preoperative ECGs
- Preoperative TTE should be considered

Endocrine

- Increased risk of diabetes
- Random and fasting BSLs, as well as HbA1C, may be of use
- 30% of patients with acromegaly also have goitre which may cause tracheal compression

Peripheral

- Proximal myopathy and peripheral neuropathy may occur from nerve compression by hypertrophy
- Carpal tunnel syndrome may occur from hypertrophy ->inadequate ulnar collateral flow if radial arterial line inserted

Carcinoid Tumor

Carcinoid tumours are a neuroendocrine tumour which secrete hormones and amines. They may arise from a number of different anatomical locations including the lungs and gastrointestinal tract
Patients who have carcinoid syndrome diagnosed will often have the tumour excised.
Referral to anaesthetic PAC only needs to occur if the patient has symptoms

In 10% of patients, carcinoid syndrome occurs, which is characterised by the secretion of vasoactive substances leading to systemic effects.
Symptoms described are flushing, sweating, autonomic instability, particularly palpitations, and right-sided valvular disease, particularly tricuspid stenosis and pulmonary stenosis.

- Left heart disease not seen unless there is bronchial carcinoid or known right-to-left shunt
- Carcinoid-related heart disease occurs in up to 60% of carcinoid syndrome and significantly increases mortality and morbidity.

Patients may also experience bronchospasm , particularly in response to exercise.
GIT symptoms including diarrhea and nausea are also common.

Carcinoid crisis is a severe form of carcinoid syndrome and typically presents in response to the physiological changes seen in the perioperative period. It is characterised by profound autonomic instability, bronchospasm, and flushing.

In the preoperative period typically the diagnosis of carcinoid syndrome is already established and the patient is being referred for curative surgery. If the diagnosis is suspected, take urinary 5HIAA levels and serum chromograffin A levels, and refer to endocrinology. Localisation can be done through somatostatin receptor scintigraphy.

Treatment of carcinoid disease is essentially surgical, although octreotide can be used to mitigate symptoms. Surgical treatment may involve: primary resection, debulking of metastases, and management of acute complications like bowel obstruction.

If elective primary resection is arranged, in PAC the issues to address are:

- Examine for systemic complications of carcinoid syndrome
- Evaluate cardiac function: ECG, TTE
- Correction of electrolyte disturbances and treatment of diarrhea
- Arrange for early admission for octreotide infusion (50 mcg/hr) for 12- 24 hours, and endocrine review.
- Pre-treatment with serotonin receptor antagonists (cyproheptadine, ketanserin)

Intraoperatively patients may have profound hypo or hypertension. Intraoperatively, octreotide infusion should be continued.
Hypotension should be treated with octreotide boluses (25-50 mcg intravenously) vasopressin or phenylephrine.

- Indirect acting vasoactive agents should also be avoided as patients may have exaggerated response
- Beta-agonism may increase the release of vasoactive substances and therefore autonomic instability

Hypertension can be treated with either alpha or beta receptor blockade, as well as 5HT-3 receptor antagonists and glucagon.

Drugs which result in the release of histamine should be avoided (morphine, atracurium) as patients with carcinoid may have extremely exaggerated hypotension in response to these.

Bronchospasm may also occur, and is usually responsive to steroids.

Control of pulmonary pressures and optimisation of pulmonary vascular resistance may be necessary if there is right heart disease and pulmonary hypertension. The intraoperative release of vasoactive substances may also lead to significant rises in PVR and pulmonary arterial pressures.

Patients may need to be admitted to ICU for haemodynamic monitoring in the postoperative period.

Chronic Liver Disease

Prior to surgery, the etiology, duration and severity of patients with hepatic dysfunction should be determined. Risk stratification should be performed and medical optimization conducted as appropriate.

Generally patients with CLD who are stable and do not have any further interventions for medical optimisation prior to surgery do not need to be referred to anaesthetic PAC. However, HDU level monitoring for post-op may be required. This can be discussed with the anaesthetist in PAC if there are concerns
RISK SCORES for predicting postoperative mortality in patients with cirrhosis

Child-Pugh Classification

- Used to assess risk of non-shunt operations
- Correlated with perioperative mortality and morbidity
- Also correlates with survival in patients not undergoing surgery
- Also associated with likelihood of developing complications of cirrhosis e.g. variceal haemorrhage

Category	**+1**	**+2**	**+3**
Bilirubin (umol/L)	<34	34-51	>51
Albumin (g/L)	>35	28-35	<28
INR	<1.7	1.7-2.2	>2.2
Ascites	Absent	Slight	Moderate
Encephalopathy	No	Gr1-2	Gr3-4

Score and pre-operative morbidity/mortality

- Class A 5-6 survival 100% 1yr, 85% 2yr
- Class B 7-9 survival 81% 1yr, 57% 2yr
- Class C 10-15 survival 45% 1yr, 35% 2yr

Model for End-stage Liver Disease (MELD-Na) score

- Was adopted for use in prioritizing patients awaiting liver transplantation and has increasing role in predicting outcomes in patients with liver disease in the non-transplantation setting
- In Jan 2016, was updated to include serum sodium as factor in the calculation of the MELD score (MELD-Na Score)
    - Hyponatraemia is an independent prognostic factor
- Continuous scale (with higher values representing more severe liver disease) based on a formula that assigns weights to the patient's serum bilirubin, creatinine and INR.
- Based on 4 parameters
    - Bilirubin levels
    - Creatinine

    - INR
    - Na
- Scores 10-15 = increased perioperative risk; should be on waitlist for liver transplant
- Scores >15 indicates patient should NOT undergo elective surgery

Systemic Implications

Liver disease can affect other organ systems and therefore have implications for preoperative management.

Hepatic Encephalopathy

- Contributed by metabolic factors e.g. hypoxia, hypovolaemia, alkalaemia, hypoglycaemia, hypokalaemia and hyponatraemia. These can be modified by anaesthetic management. Sedatives e.g. benzodiazepines can exacerbate hepatic encephalopathy.
- Increased risk for pulmonary aspiration

Haematological abnormalities

- Patients with liver dysfunction may have abnormal coagulation including prolongations of the PT, INR and activated partial thromboplastin time (aPTT), mild thrombocytopenia and elevated D-dimer.
- Fresh Frozen Plasma is NOT routinely administered to correct INR.
- Where available, viscoelastic tests (e.g. thromboelastography (TEG)) may be useful in guiding preoperative correction of haemostatic abnormalities
- If closed cavity surgery (e.g. craniotomy) is planned, perioperative haemostatic management should be individualized and may require more aggressive correction of INR.

Electrolyte abnormalities

- Hyponatraemia should be corrected slowly to avoid central pontine myelinolysis
- In general, it has been suggested that serum Na shouldn't be corrected in these patients unless serum Na drops below 120mEq/L
- Hypokalaemia and metabolic alkalosis may trigger or exacerbate hepatic encephalopathy. Therefore, hypokalaemia should be corrected preoperatively and ventilation should be maintained to achieve normal end tidal CO2.

Cardiovascular disease

- Patients with liver cirrhosis often have a hyperdynamic circulation with low systemic vascular resistance (SVR) and high cardiac output (CO)
- Cirrhotic cardiomyopathy describes a normal to increased cardiac output and contractility at rest but blunted response to stress that may lead to heart failure
- Cautious management of perioperative IV fluids to avoid volume overload
- Some forms of liver disease e.g. Nonalcoholic steatohepatitis (NASH) or Nonalcoholic fatty liver disease (NAFLD) and hepatitis C may be associated with an increased incidence of coronary artery disease and cardiac morbidity and mortality.
- Patients with portal hypertension may develop portopulmonary hypertension (PPHTN). Therefore, cirrhotic patients undergoing major surgery should be screened preoperatively with resting echocardiography
    - Patients with severe PPHTN (Mean PAP >50 mmHg) are at risk of right heart failure, perioperative morbidity and mortality.

Pulmonary complications

- Patients with ascites may have Ventilation/Perfusion mismatch, pleural effusion and decreased lung capacity
- Those with massive ascites may not tolerate lying supine for induction of anaesthesia or during procedures performed under monitored anaesthesia care or regional anaesthesia

Hepatopulmonary syndrome (HPS)

- Defect in arterial oxygenation caused by intrapulmonary vascular dilators in presence of CLD; no formal criteria
    - A-a gradient ≥15-20mmHg, resting PaO2 <70mmHg
    - TTE with bubble test (bubbles pass through dilated pulmonary vasculature)
- Severity based on PaO2; mild >80, mod 60-80, severe 50-60, very severe <50
- Worsens survival of cirrhotic patients independent of Child Pugh and MELD scores but a lot of contradictory evidence in literature
- Only proven treatment is liver transplant

Portal Hypertension

- Leads to formation of varices, circulatory, functional and biochemical abnormalities and ascites
- During abdominal surgery, fluids administration should eg to decrease pressure in portal system to reduce bleeding

Hepatorenal Syndrome (HRS)

- Historically any patient with AKI and CLD with no other evidence of intrinsic renal disease and classified by timeframe of deterioration in kidney function
- HRS now diagnosed as Cr incr >26.5umol/L or 1.5 fold incr and:
    - Failure to respond to volume exp with albumin
    - No recent nephrotoxins, no shock
    - No structural kidney diease (no proteinuria/haematuria, normal renal US)
- Treatment supportive in view of bridging to transplant – albumin vol expansion and splanchnic vasoconstrictors (terlipressin)
    - Terlipression higher affinity for vasopressin 1 in splanchnic than vasopressin 2 in kidneys
    - TIPS in pts not responding to pharm Mx

Specific Anaesthetic Considerations

Effects of liver disease on anaesthetic drug administration:

- Liver disease can alter pharmacokinetics of anaesthetic agents by changing drug metabolism, protein binding and volume of distribution. There may also be a reduction in efficiency of drug removal due to reduced hepatic blood flow secondary to portocaval shunting.
- Modifications (e.g. dose reduction, titration to effect) should be considered for patients who have advanced chronic liver disease especially when accompanied by portal hypertension
- Metabolism of drugs with high liver extraction ratios e.g. lidocaine is affected by reduced hepatic blood flow
- Metabolism of drugs with low extraction ratios e.g. midazolam is affected more by protein binding and hepatocellular dysfunction

Sedative hypnotics

- Patients with liver disease are more sensitive to the pharmacodynamic effects of induction agents. Clinical recovery times may be prolonged after discontinuation of propofol infusions.

Neuromuscular blocking agents

- Liver disease may affect onset, metabolism and duration of action
- Should be titrated to effect and administration guided by monitoring with a peripheral nerve stimulator
- Suxamethonium is metabolized by plasma cholinesterase, an enzyme reduced in patients with advanced liver disease (prolonged duration of action).
- Pancuronium metabolised in the liver; little dependence on liver for clearance
- Vecuronium 25% hepatic metabolism; depends on liver (and renal) clearance (20% unchanged)
- Rocuronium 20% hepatic metabolism; HIGH hepatic clearance 60% unchanged
- Atracurium and cisatracurium undergo organ-independent elimination and hence their half-life and duration of action are not affected by liver disease.

Analgesia

- Opioids have reduced metabolism
    - Dosing intervals should be increased to avoid drug accumulation
- Multimodal opioid sparing approach for postoperative pain control would include paracetamol (3g/day considered safe in general)
- Avoid NSAIDs due to renal toxicity and bleeding risk

Chronic Renal Impairment

Dialysis-dependent patients frequently require surgery for various reasons related to end stage renal disease such as vascular access procedures, renal transplantation, parathyroidectomy, etc

Renal failure patients do not need to be referred for anaesthetic PAC if they are on stable medical therapy. However, a peri-operative plan for dialysis and fluid management should be documented in EMR in discussion with the renal team
Bear in mind that patients with CKD may be predisposed to other medical comorbidities like IHD, CVAs and PVD

For patients undergoing elective surgery who are on maintenance haemodialysis, a haemodialysis treatment should be performed when practical, on the day before/day of the procedure. For those on peritoneal dialysis, their treatments are generally performed until just prior to the procedure.

General considerations

- Type of dialysis -- haemodialysis, peritoneal dialysis
- Frequency of dialysis
- Date and time of most recent dialysis
- Type and location of dialysis access
- Daily fluid intake and any fluid restrictions
- Daily urine output
- Target weight (“Dry weight”)
    - Usually determined by outpatient renal physician as documented on dialysis chart
    - Patients may not have achieved this after their last dialysis session

Investigations

- Serum Urea and Creatinine concentrations
- Serum electrolyte concentrations
    - Hyperkalaemia is a potential indication for preoperative dialysis. All patients with an elevated serum K concentration should have a 12-lead ECG.
        - ECG changes result from alterations in the transcellular potassium gradient rather than the absolute serum potassium value.
        - For elective surgery, induction of anaesthesia in a patient with a serum K level <5.5 mmol/L is generally acceptable
        - For emergency surgery in a patient with K ≥5.5, management depends on ECG/surgical factors. The anaesthetist may have to initiate medical management if haemodialysis preoperatively is not possible.
    - Decisions regarding treatment of electrolyte imbalance will depend upon the urgency of surgery, likely influence of surgery on further electrolyte imbalance e.g. tissue damage, anticipated blood loss and fluid shifts, chronicity of the electrolyte(s) imbalance

Fluid management

- The goal of dialysis prior to surgery is to reach the estimated target weight.
- Clinically significant pulmonary oedema is another potential indication for preoperative dialysis
- Optimal volume status prior to surgery depends on the anticipated fluid losses during surgery
    - If too much fluid is removed with preoperative dialysis, risk of intraoperative hypotension due to anaesthesia-induced systemic vasodilatation is increased. This may result in significant complications e.g. thrombosis of the arteriovenous access site
    - Conversely, if euvolaemia is not achieved and the patient received a large fluid load during surgery, pulmonary oedema may occur in the immediate postoperative period, necessitating dialysis and possibly noninvasive positive pressure ventilation or mechanical ventilation.

Heparinization

- Perioperative coagulopathy may be avoided by performing heparin-free dialysis on the day of surgery or by waiting for coagulation status to normalize after hemodialysis with heparin (typically 4h post heparin)

Associated Comorbidities

- Dialysis dependent patients often have multisystem comorbidities
- Cardiovascular
    - Coronary artery disease (accelerated)
    - Hypertension
    - Pulmonary hypertension
    - Atrial fibrillation
    - Heart failure
- Venous thrombosis which may make insertion of central venous access challenging
- Haematological disorders
    - Anaemia (generally do not transfuse stable ESKD patients with Hb>7g/dL in the absence of specific indication)
    - Coagulation abnormalities
    - Uraemia induced platelet dysfunction (may need IV desmopressin 0.3mcg/kg)
- Cerebrovascular disease
- Peripheral vascular disease especially if patients have diabetes
- Gastrointestinal disorders
    - Gastroparesis (increased risk of pulmonary aspiration)
    - Oesophageal/gastric disorders

Neurology

It is necessary to consider the perioperative care of patients with neurologic diseases, understand the pathophysiologic mechanism of these disorders, prevent adverse intraoperative events and evaluate new neurological changes that may occur perioperatively. In addition, anaesthetists need to consider the impact of the condition on anaesthetic management so as to minimize adverse perioperative event.

All patients with symptomatic carotid stenosis or stroke within the preceding 3 months should be referred to vascular surgery and neurology for evaluation prior to elective surgery

Cerebrovascular Disease

Patients with cerebrovascular disease are at risk for perioperative stroke and those with asymptomatic carotid stenosis are also at risk for major adverse cardiac events (MACE)

Perioperative stroke is defined as stroke occurring within 30 days after surgery.
The overall incidence of clinically evident stroke after noncardiac, non neurologic surgery is reported to be 0.1-0.8%. The incidence of unrecognized stroke may however be as high as 7% in patients 65 years and older.

Risk factors

Patient factors

- Old age
- Cardiovascular disease
- Prior stroke/TIA
    - Time course of increased risk of perioperative stroke after prior stroke is uncertain but may be increased for at least 3 months. The risk is highest in the first few months after TIA/ischaemic stroke and declines over time.
    - For urgent/emergency surgery, the risk of stroke should be part of the preoperative shared decision making.
    - As workup, cardiac investigation for structural abnormalities and ECG should be performed to look for arrhythmias. Carotid ultrasound should also be considered as carotid stenosis may indicate a need for surgical carotid endarterectomy before proceeding with non urgent surgery.
- Renal disease
    - Pre-existing renal failure, dependence on dialysis have been associated with an increased risk of perioperative stroke
- Diabetes
- COPD
- Female gender
- Carotid stenosis
- Tobacco use

Surgical factors

- Cardiac surgery
- Neurosurgery
- Carotid endarterectomy

- Major vascular surgery
- Major intraabdominal surgery
- Pulmonary resection
- Transplant surgery
- Arthroplasty
- Shoulder surgery in the beach chair position
- Head and neck surgery

Perioperative strokes are predominantly ischaemic rather than haemorrhagic. These can be embolic, thrombotic or haemodynamic (hypoperfusion of watershed areas)

Strategies for Stroke Risk Reduction

- Delaying elective surgery after ischaemic stroke if possible (at least 3 months after stroke, if possible up to 9 months)
- Use cardioselective beta blockers when possible
- Maintaining blood pressure within 20% of baseline
- Appropriate management of anticoagulation in patients with AF/conditions that predisposes them to thromboembolism
- Statin therapy (weak evidence supporting the starting of statins preoperatively to reduce risk of perioperative stroke)

Seizure Disorders

Patients on stable medical therapy for epilepsy do not need to be referred to anaesthetic PAC
Patients with poor seizure control prior to surgery are at a higher risk of a perioperative seizure; these patients should be reviewed by neurology to optimise their medication regime prior to elective surgery

- If patient is expected to be unable to take medication orally post-op, a referral to neurology pre-operatively should be made to form a plan for post-operative IV anti-epileptic therapy

Important elements on history and exam

- Associated comorbidities
    - Congenital syndromes often have multisystem involvement
- Seizure type and frequency
    - How well is epilepsy controlled? This will predict the risk of postoperative seizure occurrence
    - Timing of last seizure and most recent neurology review
    - Triggers
- Antiepileptic medication
    - Current drug therapy, dosage regimes
    - Times of most recent dose
    - Recent changes in medication regime

Patients with preexisting seizure disorders generally need to have antiseizure medications continued perioperatively either parenterally or with small sips of water

- It is essential to avoid disrupting antiepileptic medication preoperatively.
- Patients should be advised to take their regular medications on the morning of surgery and regular dosing re-established as soon as possible postoperatively.

Anaesthetic sedative/hypnotic agents have proconvulsant and anticonvulsant effects that vary with dose and physiologic situation. Overt seizures caused by general anaesthetic drugs are rare

- The incidence of GA-related seizures is unknown.
- N2O provokes seizures in animal models but has not been replicated in humans.
- Pethidine is the opioid with strongest association with myoclonus and tonic-clonic seizure activity. However, fentanyl, alfentanil, sufentanil and morphine have been reported to cause generalized seizure in patients after low-moderate dose, particularly after intrathecal use.
- Ketamine and tramadol have both been associated with an decrease in seizure threshold
- Benzodiazepines in clinical practice possess potent anticonvulsant properties

Seizures under general anaesthesia are relatively rare but may occur in patients with poorly controlled epilepsy. They are difficult to diagnose, especially if NMBAs have been used

- Suggestive signs: rising end tidal CO2, Tachycardia, Hypertension, increased muscle tone, pupillary dilation, increased O2 consumption

Parkinson Disease

- Cardinal features include tremor, rigidity, bradykinesia and impaired postural reflexes, autonomic dysfunction (e.g. orthostatic hypotension), abnormal sweating, sialorrhea and the inability to regulate temperature.
- Patients with Parkinson Disease are susceptible to postoperative delirium/cognitive impairment
- The major perioperative issues in these patients are assessments of swallowing and pulmonary function
    - Patients are at risk of postoperative aspiration and should be taught voluntary airway protection technique
    - Dysphagia is common due to bradykinesia/rigidity of pharyngeal musculature which may be exacerbated by missed medication doses in the perioperative period. Residual dysphagia from endotracheal intubation may also occur.
    - Patients are also at risk of postoperative pulmonary complications, due to rigidity, bradykinesia, kyphosis, pharyngeal dysfunction and sialorrhea that further compound the restrictive dysfunction
- There must be appropriate use of antiparkinsonian medications and maintenance of volume status.
    - Antiparkinsonian drugs should NOT be withheld preoperatively as abrupt withdrawal may lead to flares of parkinson symptoms. Motor and bulbar symptoms may complicate anaesthetic management and rarely, neuroleptic malignant syndrome or related withdrawal syndromes.
    - They should be restarted as soon as possible after surgery (for patients with postoperative dysphagia, orally disintegrating carbidopa-levodopa is a potential treatment. Levodopa can be crushed and given via NGT).

    - If oral intake is not possible the use of apomorphine should be considered
    - ONE exception is that antiparkinsonian drugs are often withheld on the morning of surgery for deep brain stimulators in order to improve surgeon ability to locate the substantia nigra
- Preoperative investigations may include
    - Pulmonary function tests
    - Arterial blood gas
- Postoperative management
    - Reinstitution of antiparkinsonian medications as soon as possible
    - Incentive spirometry
    - Postural drainage
    - Avoid phenothiazines which are centrally acting dopamine antagonists, and may provoke a parkinsonian crisis.
    - Patients with parkinsons are also at risk of respiratory complications, particularly aspiration if bulbar dysfunction is present, but also may have associated autonomic dysfunction

Deep Brain Stimulators

Increasingly, patients with Parkinsons disease are being offered deep brain stimulators, and presenting for unrelated surgery at a later stage. If your patient has a deep brain stimulator in situ, the main issue is electromagnetic interference and the effect of diathermy or other electrosurgical equipment.

- Identify the type of device which has been implanted
- Date of insertion
- Device settings including current control modes (patients may be able to control their own device using an external controller)
- Location of pulse generator and batteries

Contact the neurologist or deep brain stimulator specialist involved in the patients' care. Typically the neurostimulator is disabled for surgery and turned back on again following completion of the operation. It should subsequently be checked by a deep brain stimulator specialist or technician. Patients may have symptoms of Parkinson's occurring following disabling of the deep brain stimulator but will usually still respond to levodopa therapy.
Diathermy:

- Use bipolar diathermy if possible
- If monopolar diathermy is essential, use low-voltage mode at the lowest possible setting
- The neurostimulator and leads are typically subclavicular and run posterolaterally along the neck. The diathermy pad should be placed as far away from here as is feasible.

Defibrillators

- Safety with external defibrillators is not established in patients with DBS
- Defibrillation may damage neurostimulators
- Position defibrillation pads as far away from the stimulator and generator as possible and perpendicular
- Use the lowest energy output possible
- Device must be checked following defibrillation once patient is stable

The other issue that may arise is that the device may have non rechargeable batteries and emergency replacement of the battery through surgical access may be necessary. This should be done at a hospital with neurosurgical facilities where possible.

Multiple Sclerosis

Signs and symptoms of Multiple Sclerosis (MS) may worsen in the postoperative period due to stress associated with the surgery, perioperative fever or infection.

MS is an autoimmune disease of inflammation, demyelination and axonal damage to the CNS. The disease progression may be subacute with relapses and remissions or chronic and progressive.

Clinically, there are 3 main types:

- Relapsing-remitting: episodic symptoms with remissions
- Primary progressive: no remissions, progressive neurologic deterioration
- Secondary progressive: chronically progressive with remissions

Treatment consists of:

- During acute attacks, mainly corticosteroids
- immunosuppressants/immunomodulators to prevent progression e.g. Glatiramer acetate, Interferon-B
- Symptomatic: carbamezepine, gabapentin, baclofen/dantrolene (spasticity), anticholinergics (bladder and bowel disturbances)

Patients should have a thorough baseline neurological history and examination during their pre-operative evaluation. Patients may also have limited physiologic reserve (neurologic and respiratory), and are less tolerant of stressors e.g. postoperative residual muscle relaxant.

Patients with MS who have weakness are at increased risk of hyperkalaemia with administration of succinylcholine and have an unpredictable response to the effects of nondepolarizing NMBAs.

Temperature should be monitored closely and hyperthermia avoided during the postoperative period to minimize risk of temporary MS relapse.

GA and epidural anaesthesia with low concentrations of LA are considered safe. Spinal anaesthesia has been implicated in postoperative exacerbation.

Arnold Chiari Malformation

Arnold Chiari malformations are anatomical abnormalities of the cerebellum, brainstem and craniocervical junction with the end result being cerebellar shift into the spinal canal

Significant issues:

- Increased ICP secondary to hydrocephalus
- C1/2 instability : increased risk of cervical cord injury
- Increased risk of latex allergy
- Brainstem dysfunction: stridor, apneas, bulbar palsies
- Autonomic instability : arrhythmias, bradycardia, labile blood pressures
- Seizures

If a general anaesthetic is performed, the key issues are to avoid increases in ICP which may subsequently cause brainstem herniation, and to try and provide rapid emergence for postoperative neurological examination, as Arnold-Chiari malformation is associated with increased risk of brainstem dysfunction with respiratory compromise. Excessive extension of the neck should be avoided as there may also be anatomic abnormalities of the upper cervical spine.

These patients should be considered as latex-allergic.

If neuraxial anaesthesia is planned the key issue is the increased risk of tonsillar or cerebellar herniation from increased ICP compared to pressure within the spinal canal. MRI of brain and spine should be considered to look for the level of the malformation and any associated abnormalities, and neurological consult should be considered. Principles of neuraxial anaesthesia in this population: use smallest needle possible, minimise number of tries (most senior operator).

Patients with known Arnold-Chiari malformation, particularly if symptomatic, should be discussed with anaesthesia. HDU admission should be considered if GA is performed because of the risk of respiratory complications post-operatively.

Myasthenia Gravis (MG)

MG is an autoimmune disorder characterized by fatigable weakness of skeletal muscles. This is due to an antibody-mediated immunologic attack directed at acetylcholine receptors (or receptor-associated proteins) in the postsynaptic membrane of the neuromuscular junction.

The main anaesthetic concern for such patients are their unpredictable sensitivity to nondepolarizing Neuromuscular blocking agents (NMBAs) whilst being resistant to succinylcholine. They are also at risk of post-operative myasthenic crisis, and in patients with severe myasthenia gravis they are at risk of prolonged post operative ventilation.

Patients with MG who are seen at a pre-admission clinic should have their preoperative preparation for elective surgery coordinated with their neurologist.

Elective surgery should be conducted during a stable phase of the disease so as to minimize the postoperative risks of myasthenic crisis. The surgery should be scheduled as early in the day as possible.

Important elements on history and examination

- Bulbar symptoms (may predispose to aspiration)
    - Dysphagia
    - Dysarthria
    - Nasal or low-intensity speech
- Respiratory symptoms
    - Shortness of breath
    - Patients will need preoperative pulmonary evaluation (PFT) if patients require a GA. This will help to establish a baseline for extubation and a postoperative care plan/destination.
- Previous exacerbations or myasthenic crisis requiring endotracheal intubation
- Associated diseases
    - Thyroiditis
    - Rheumatoid arthritis
    - Systemic Lupus Erythematosus
- Myasthenia Gravis Therapy

Risk Factors for postoperative ventilation requirement (Leventhal Criteria)

- Vital Capacity <2-2.9L
- Duration of MG (>6 years)
- Pyridostigmine dose >750mg/day
- History of chronic pulmonary disease
- Preoperative bulbar symptoms
- History of myasthenic crisis
- Intraoperative blood loss >1L
- Serum antiacetylcholine receptor antibody >100nmol/mL
- More pronounced decremental response (18-20%) on low frequency repetitive nerve stimulation

Specific Medication considerations

- Anticholinesterase agents
    - Consider continuing anticholinesterase agents (i.e. pyridostigmine or neostigmine) up to and including morning of surgery, with the acceptance that they might affect response to NMBAs .
    - In addition, the response to NMBA reversal agents may be unpredictable or insufficient.
    - If the anticholinesterase agents are discontinued, there is a risk of development of respiratory and bulbar weakness.
    - If IV dosing of pyridostigmine is required intraoperatively, the dose is approximately 1/30th the oral dose (1mg IV = 30mg PO)
- Glucocorticoids
    - Beware the risk of hypothalamic pituitary axis suppression and adrenal insufficiency in the perioperative period
- Plasmapheresis

    - Preoperative plasma exchange is associated with a decreased risk of post operative respiratory crisis
    - In high risk patients, discuss with neurology for consideration of early admission for preoperative plasma exchange

Anaesthesia Management Summary

- Where possible, local/regional anaesthesia considered
    - If neuraxial anaesthesia performed, avoid mid-thoracic/higher levels as may lead to paralysis of accessory muscles of breathing.
    - Be cautious if performing brachial plexus blocks e.g. supraclavicular/interscalene blocks as may paralyze diaphragm on side of block which may not be tolerated by patients with respiratory compromise
- AVOID use of neuromuscular blocking agents (NMBAs) wherever possible
    - Total intravenous anaesthesia (TIVA) with infusions of propofol and remifentanil may help avoid use of NMBAs
    - Other IV agents to blunt response to laryngoscopy and intubation would include IV lidocaine (IV 1- 1.5mg/kg) and esmolol (10-50mg)
    - If NMBAs are necessary, suggest rocuronium/vecuronium with reversal using sugammadex. Nondepolarizing NMBAs should be administered in incremental, small doses of 0.1-0.2 times the ED95, titrated to effect. If administered, the degree of neuromuscular blockade should be monitored using a quantitative train-of-four nerve stimulator.
    - Patients may be resistant to succinylcholine due to decreased number of ACh receptors. The ED95 of succinylcholine in these patients is about 2.6 times that of normals (0.8 vs 0.3mg/kg). Since succinylcholine is metabolised by plasma cholinesterase, treatment with anticholinesterase medication may prolong the effect of succinylcholine.
    - Myasthenic patients are also at higher risk of developing phase II neuromuscular block especially with repeated succinylcholine doses.
- Use ultra-short/short-acting sedatives, hypnotics and anaesthetic agents to minimize depression on emergence from anaesthesia
- Medication interactions
    - Antibiotics - may affect neuromuscular transmission e.g. aminoglycosides and macrolides can cause weakness
    - Local anaesthetics - may potentiate the effects of NMBAs
    - Others that may exacerbate weakness
        - Beta blockers, Calcium channel blockers, antiepileptics, phenothiazines, diuretics, procainamide, magnesium, opioids
- Postoperative analgesia
    - Multimodal to minimize opioid side effects

Eaton Lambert syndrome

Eaton Lambert syndrome is also known as myasthenic syndrome, but is instead caused by IgG antibodies to presynaptic calcium channels resulting in decreased ACh release. It is an autoimmune condition associated with malignancy in 50-60% of patients, and is most commonly associated with small cell lung cancer.

Typically it affects proximal muscle groups, especially the lower limbs, and is also associated with bulbar dysfunction, autonomic dysfunction and hyporeflexia. Strength generally increases with activity, but fatiguability is present in almost 30 % of patients. In order to differentiate between Eaton-Lambert syndrome and myasthenia gravis, tensilon testing can be used (no response in Eaton-Lambert, improvement in MG).

Anaesthetic concerns are essentially similar to those of myasthenia gravis, particularly with regard to risk of respiratory failure and the need for postoperative ventilation if general anaesthesia is used. Similarly, regional techniques are preferred, with the exception of interscalene or supraclavicular block , which may worsen respiratory function.

However, unlike myasthenia gravis, post-operative weakness is not reversed by anticholinesterase treatment.

Additionally, autonomic dysfunction is present in up to 30% of patients with Eaton-Lambert.

Patients also exhibit increased sensitivity to both depolarising and non depolarising muscle relaxants, unlike myasthenia gravis, where there is a resistance to suxamethonium.

Chronic Spinal Cord Injury

Chronic spinal cord injury generally occurs weeks to years following acute spinal cord injury, from changes in sympathetic output leading to hypertonia, exaggerated reflexes, and spasticity.

All patients with chronic spinal cord injury should be discussed with the anaesthetist and checked for preexisting advanced care plan

Considerations for anaesthesia include:
Airway:

- Potential difficult airway
- Limited mobility of neck, especially if previous surgery
- May have tracheostomy if high spinal cord injury. Typically tract is well formed by the time the changes of chronic spinal cord injury occur.

Respiratory:

- Loss of accessory muscles of ventilation including intercostals, and diaphragmatic muscles, depending on the height of the lesion
- May have better ventilation upright cf supine depending on lesion height; may need abdominal binders etc to improve ventilation
- Weak cough even with lower lesions, if abdominal muscles involved; difficulty with expelling lung secretions
- Decreased VC, FRC; depending on height lesion
- Marked bradycardia may occur in response to suctioning
- If the lesion is high, may be tracheostomy dependent

CVS

- Increased risk of bradyarrhythmias
- Increased risk of cardiovascular disease
- Decreased blood volume- prone to postural hypotension

- Increased risk of thromboembolic complications

Endocrine

- Increased risk of diabetes
- Delayed gastric emptying and increased risk of aspiration
- Loss of muscle
- Poikilothermia- cannot generate heat below the level of the injury or compensate for heat loss

Autonomic Hyperreflexia

Autonomic hyperreflexia or dysreflexia is a phenomenon seen following high spinal cord injuries (above T6), occurring in roughly 50% of patients with chronic spinal cord injury. It is most commonly seen in complete and higher lesions, and is unlikely if the lesion is below T10. It can occur in the acute phase but can develop up to a year following the injury.

Essentially stimuli can cause significant dysfunction depending on where it is in relation to the level of injury due to altered balance between the sympathetic and the parasympathetic nervous systems. Common stimuli include pain, urinary retention or bowel distension, and surgical stimulus.

Below injury:

- Massive autonomic discharge below injury level
- Profound vasoconstriction -> increased ICP, retinal hemorrhage, seizures, myocardial injury or infarct, acute pulmonary oedema

Above injury:

- SNS surge
- Compensatory vasodilation above level of injury , but no vasodilatory response below level of injury
- Typically results in a reflex bradycardia;
- May also have flushing, blurred vision, nausea, and sweating

If seen in PAC, the key issues to note are the level and completeness of the lesion, as well as whether there is a known history of autonomic hyperreflexia. If previous anaesthetic records are available they should be consulted.

Autonomic hyperreflexia can be prevented either by the use of spinal anaesthesia (more reliable than epidural anaesthesia) or the use of a deep general anaesthetic. Triggers (catheter insertion, surgical stimulus) should be avoided until anaesthesia is satisfactory.

Spinal anaesthesia prevents autonomic hyperreflexia but may be technically challenging to perform, and very difficult to assess.

The key sign of hyperreflexia is typically hypertension although AV block and bradycardia may occur. Management of hyperreflexia includes withdrawal of the stimulus, analgesia, deepening of anaesthesia, and quick-acting, titratable vasodilator therapy (eg GTN 5-200 mcg, hydralazine 10-20 mg prn, phentolamine 5 mg IV prn).

Rheumatology

Several rheumatic diseases are associated with increased risks of coronary artery disease, arrhythmias, heart failure or cardiac death.

Airway management may be difficult in patients with cervical spine or temporomandibular joint disease. Airway manipulation in patients with severe cervical subluxation can result in spinal cord injury or death. In addition, positioning for the surgery may be difficult if patients have limited range of motion of their joints.

General Principles

Assess disease activity and optimize medications

- Liaise with rheumatologist if any concerns regarding disease activity

Assess cardiovascular risk
Reduce thrombosis risk in patients with antiphospholipid syndrome
Be aware of immunosuppressive medications and implications on perioperative wound infections , prosthetic joint infection etc.

- Glucocorticoids:
    - Risk of surgical site infections
    - Risk of haemodynamic instability due to HPA suppression and adrenal insufficiency
    - Prolonged use may impair wound healing, increase risk of GI haemorrhage/ulcer
- Nonbiologic DMARDs: may increase risk of infection by affecting immune response but stopping them prior to surgery may lead to flare up of disease activity
- Biologic DMARDs: often withhold this and plan elective surgery at the end of the dosing cycle.

Rheumatoid Arthritis

Specific considerations

- Increased risk of atlantoaxial subluxation and neurologic damage. Risk factors associated with C1-C2 instability include glucocorticoid use, seropositivity, nodular disease and erosive peripheral joint disease.
    - Lateral cervical radiographs with flexion and extension views of the cervical spine may detect significant subluxation and should be obtained prior to surgery in patients with neck pain or neurologic symptoms or those without symptoms if at high risk
- Cricoarytenoid joint disease may result in difficult intubation. The physical symptoms include dyspnoea, hoarseness, dysphagia, odynophagia, sensation of fullness in the throat, pain with speech and radiation of pain to the ears.
- Anaemia
    - Mild hypochromic anaemia may correlate to general disease activity
- Neutropenia
    - Occurs in patients with Felty syndrome

    - If neutrophil counts are extremely low and lead to recurrent infection, granulocyte-colony stimulating factor (G-CSF) can be administered.

Ankylosing Spondylitis

Specific considerations related to spinal and costovertebral ankylosis

- Multi-system disease with extra-articular features:
    - Increased risk of aortic regurgitation and cardiovascular disease, conduction defects, cardiomegaly, cardiomyopathy, pericardial effusion
    - Increased risk of restrictive lung disease related to reduced chest wall & spine mobility, also parenchymal fibrosis
    - Neuro: spondylolisthesis (cord compression), uveitis
    - Haematology: anaemia of chronic disease
- Potential difficult airway
    - Endotracheal intubation may be difficult. Patients may require awake fibreoptic intubation
- Patients may have significant kyphotic deformities and surgical positioning would be a challenge. Pressure care is important.
- Regional anaesthesia may be a challenge/impossible given extensive ligamentous calcification and heterotopic ossification. Also difficult due to axial spine fusion, epidural space obliteration and underlying radiculopathies/neuropathic pain.
    - Higher risk epidural haematoma
    - Paramedian approach may be better
- Medications implications: steroids, immunomodulators, marrow suppression, platelet dysfunction, renal impairment, ? need for steroid coverage, increased risk of infection

Scleroderma

Autoimmune disorder with systemic implications (systemic sclerosis) characterised by skin induration from tissue fibrosis, chronic inflammatory infiltration, fibroproliferative vasculopathy, and immune alterations.

Specific anaesthesia considerations

- Patients are at risk of myocardial ischaemia and non-epicardial coronary artery disease due to fibrosis.
- Cardiovascular
    - Patients with scleroderma are at increased risk of pulmonary hypertension, heart failure, conduction block and arrhythmias.
- GI
    - Patients may also suffer from oesophageal disease and gastric motility dysfunction which increases their risk of aspiration.
- Respiratory
    - Pulmonary fibrosis, restrictive lung disease, pulmonary HTN, cor pulmonale
    - Preoperative pulmonary function tests and arterial blood gases may be indicated, depending on the complexity of the planned surgery
    - Potential for hypoxaemia (fibrosis), acute lung injury/barotrauma (restrictive lung disease)

- Renal disease may also cause hypertension or renal crisis
    - Associated with renal artery stenosis
    - Steroid use should be avoided
- Skin
    - Raynaud's, vasoconstriction may be a contraindication to radial arterial line placement
    - Difficult vascular access/positioning/monitoring due to dermal thickening.
    - At risk of nerve entrapment
- Potential difficult airway
    - Decreased mouth opening (microstomia) and limited neck extension may make intubation difficult.
    - Nasal/oral telangiectasia may increase risk of bleeding
- Increased risk of peripheral nerve damage, flexion contractures
- Arterial lines may precipitate Raynaud's crisis
- Patients may also have a prolonged response to local anaesthetic agents used for peripheral nerve blocks, care with neuraxial
- Eye dryness. Meticulous eye protection under anaesthesia.

Scleroderma may also be associated with CREST Syndrome which is characterised by calcinosis, Raynaud's phenomena, oesophageal dysmotility, systemic sclerosis, and teleangiectasia .

Investigations which should be ordered in PAC:

- Cardiovascular
    - ECG
    - TTE
- Respiratory
    - CT chest
    - RFTs
    - TTE
    - PFTs (typically are performed every six months). Typically restrictive defect and reduced DLCO)
- Renal
  UEC, CMP
- GIT:
  LFTs: derangement from immunosuppression, organ involvement, hypoalbuminemia
- Haematological:
  FBE: anaemia of chronic disease, platelet dysfunction; VIt K malabsorption-> increased INR

The prognosis in scleroderma, especially if multi organ dysfunction is present, is poor. No therapy is effective in stopping the underlying pathology.

- Raynauds
    - prazosin/ACE-I/CCB
        - Patients with scleroderma are at increased risk of pulmonary hypertension, heart failure, conduction block and arrhythmias.
- Sclerosis

    - Immunosuppression: azathioprine, mycophenolate, methotrexate, cyclophosphamide,
- Pulmonary HTN :
    - Sildenafil, oxygen therapy, inhaled prostacyclins
- GIT
    - PPIs
    - octreotide
- Renal
    - ACE-I

Sarcoidosis

Sarcoidosis is a multisystem disorder characterised by the formation of granulomas. The cause is unclear. The peak incidence is at 20-40 years and it is more common in women than in men.

Systemic implications and Anaesthetic considerations

- Cardiovascular
    - Cardiac granulomas occur in 25% of patients
    - Cardiomyopathy from muscular granuloma; most commonly in LV free wall or in the interventricular septum
    - Conduction abnormalities from granuloma in the conducting system -> arrhythmias and increased risk of syncope and sudden death
    - Fibrosis of pulmonary vasculature -> pulmonary hypertension
    - Patients with known sarcoidosis should have a baseline ECG performed, and TTE considered to look for structural abnormalities as well as right heart failure and pulmonary hypertension.
- Respiratory
    - Pulmonary infiltration and granuloma -> restrictive lung disease. Baseline RFTs should be performed.
    - Laryngeal sarcoidosis can occur -> obstructive lung disease , and potentially difficult airway. Sizing down of ETT should be considered if patients have vocal changes. RFTs should be considered.
    - Pulmonary hypertension: preoperative TTE should be considered.
- Neurologic
    - CNS granulomas occur in up to 25%
    - Cranial nerve palsies, seizures, cognitive dysfunction, and ataxia can occur
- Renal
    - Hypercalcemia and renal calculi can cause renal failure
    - Granulomatous nephritis can occur but is rare
    - Baseline UEC/CMP should be done to look for calcium levels and baseline renal function
- Haematological
    - Splenomegaly and hepatomegaly are common. Consider FBE to look for platelet dysfunction and LFTs to look for abnormalities.
- Pregnancy: typically pregnancy leads to a remission of sarcoidosis but relapses post-partum are common

Typically patients with sarcoidosis are only commenced on treatment when organ function is compromised. Treatment includes corticosteroids, immunosuppressants, non-steroidals and calcium chelators.

Amyloidosis

Amyloidosis is a multisystem disorder characterised by extracellular fibril deposition. Primary amyloidosis is a spontaneous plasma cell disorder where immunoglobulin light chains accumulate. Secondary amyloidosis is linked to other conditions, which include multiple myeloma, and autoimmune conditions like rheumatoid arthritis.

Systemic implications and Anaesthetic considerations

- Cardiovascular
    - Restrictive cardiomyopathy
    - Diastolic dysfunction
    - Conducting abnormalities -> arrhythmias, including complete heart block, syncope, and sudden death
    - Accelerated coronary artery disease
    - Baseline ECG should be obtained. Preoperative TTE should be considered for elective surgery. 5-lead ECG should be considered.
- Respiratory
    - Interstitial lung disease and restrictive pattern on RFTs
    - Pulmonary hypertension from infiltrative cardiomyopathy and pulmonary vasculature infiltration: preoperative TTE should be considered.
- Airway:
    - Macroglossia -> increased risk of difficult airway
    - laryngo/tracheo/bronchial deposition of amyloid -> airway narrowing, obstructive lung disease which is not reversed by bronchodilators.
- Neurologic
    - Autonomic neuropathy - risk of aspiration
    - Mixed sensory and motor neuropathy
- GI
    - Dysphagia
    - Delayed gastric motility due to autonomic neuropathy
- Renal
    - Nephrotic syndrome and renal failure.
    - Baseline UEC to examine renal function
- Haematological
    - Factor X deficiency, coagulation factor deficiency and platelet dysfunction

Marfan’s Syndrome

Autosomal dominant connective tissue disorder with multisystem effects, and a range of clinical severity. There is no curative treatment. Marfan’s is associated with an increased risk of perioperative mortality and morbidity.

Systemic implications and Anaesthetic considerations

- Cardiovascular
    - Aortic dilatation and dissection (typically ascending aorta)
    - LV dilation and dysfunction
    - Mitral valve prolapse and mitral regurgitation
    - Cardiac conduction abnormalities and increased risk of sudden cardiac death
    - Spontaneous coronary artery dissection has also been reported
    - Should be on beta blockers; may also be on ACE-I. Preoperatively, check TTE for cardiac function but also for aortic root diameter. Consider cardiology referral if patient is not already seeing a cardiologist.
    - Intraoperatively, prevent changes in wall tension of aorta- avoid hypertension, hypotension, sudden changes in myocardial contractility, tachycardia. Avoid use of beta-agonists.
    - Sympatholysis for painful stimuli (eg laryngoscopy) is important
    - In pregnancy, parturients are at risk of aortic dissection from the cardiovascular changes of pregnancy. They should be linked in with cardiology early. Monthly TTEs to monitor root diameter, and planning re mode of delivery and monitoring is advised. Caesarean delivery is indicated if there is aortic dissection, root diameter of > 4.5 cm, severe aortic regurgitation, or heart failure. In labour, early epidural anaesthesia and invasive monitoring is recommended to prevent wall stress from contraction-related sympathetic stimulation. Ergometrine should be avoided following delivery.
- Respiratory
    - High incidence of spontaneous pneumothorax
    - May develop restrictive lung disease from kyphoscoliosis or chest wall abnormalities (associated with pectus carinatum and excavatum)
    - May develop emphysema over time due to decreased lung elasticity
    - Consider lung protective strategies
- Airway:
    - May be associated with difficult airway
    - High, arched palate with crowded mouth
    - C1/2 ligamentous instability
    - TMJ dislocation
- Neurological
    - Ductal and dural ectasia - higher risk of failed block, dural puncture, and PDPH
    - Structural changes in ligamentum flavum may make it more difficult to perform neuraxial blockade
    - Widening of the dural sac can lead to lower limb neurology, and even cauda equina
- Skeletal
    - Tall stature
    - Joint laxity -> increased risk of dislocation
- Eyes
    - Retinal detachment and lens dislocation may occur.

Ehler Danlos syndrome

Ehler Danlos is a connective tissue disorder characterised by joint hypermobility and tissue fragility. There are six subtypes classified by extent of disease and system affected, but all can result in multisystem disease.

Systemic effects and anaesthetic implications

- Airway:
    - C-spine instability
    - Tissue friability -> increased risk of upper airway bleeding
- Cardiovascular
    - Autonomic dysfunction
    - Aortic dilation and increased risk of dissection
    - Mitral valve prolapse and regurgitation
    - Conduction abnormalities
    - Increased risk of spontaneous vascular arterial aneurysm and rupture
    - Increased risk of vascular friability and bleeding tendency; bleeding often responds to desmopressin
- Respiratory
    - Increased risk of spontaneous pneumothorax
- Peripheral
    - Joint hypermobility -> recurrent dislocation, skin laxity
    - Increased risk of peripheral nerve injury and pressure injury as well as joint dislocation
    - Chronic pain secondary to recurrent dislocations
- Neurological
    - Increased risk of Tarlov cysts and tethered cord
    - Increased risk of spinal and epidural haematoma
    - Neuraxial is relatively contraindicated as a result
- Obstetric
    - Increased risk of uterine rupture and atony
    - Increased risk of preterm labour
    - If patient has vascular subtype, increased risk of aortic dissection. Pregnancy is not recommended in this cohort, but patients who do fall pregnant should be offered early termination, or LUSCS at 32 weeks.

Haematology

Porphyria

- Group of diseases which cause defects in haem metabolism leading to excessive secretion of porphyrins and porphyrin precursors. Of the porphyries the most significant is acute intermittent porphyria, where there is accumulation of porphobilinogen and ALA, which is neurotoxic.
- Rare: incidence 1-2/100, 000 with variable expression (80% of those with gene mutations will not manifest symptoms); most common in women aged 20-40 years
- May present with abdominal, neuropsychiatric, peripheral neuropathy, and autonomic dysfunction. Patients may also have the characteristic ‘port-wine’ urine.
- Acute porphyric crisis can be triggered by multiple causes encountered in the perioperative setting (drugs, stress, infection, starvation, dehydration, hormonal changes eg. menstruation and pregnancy)

Goals of management in porphyria are to prevent triggering an acute porphyric crisis. In particular, limit fasting time, ensure adequate hydration, and avoid drugs which may trigger. Drugs which may trigger exist on a spectrum of drugs which are safe, probably safe, possibly safe, probably not safe, and definitively porphyrogenic. For up-to-date information refer to https://porphyriafoundation.org/drugdatabase/.

	avoid	controversial	safe
sedatives/induction agents	Barbiturates etomidate	diazepam Ketamine althesin	Midazolam Propofol
volatiles	enflurane	Sevoflurane Halothane Isoflurane desflurane	nitrous
Muscle relaxants		Atracurium Pancuronium Rocuronium mivacurium	Suxamethonium Vecuronium

Local anaesthetics	Ropivicaine mepivicaine	Lignocaine cocaine	Bupivicaine prilocaine
antiemetics	Cimetidine metoclopramide	Ondansetron ranitidine	Promethazine Droperidol
analgesics	pentazocine	Diclofenac ketorolac	Opiates Aspirin Paracetamol
Cardiovascular drugs	Hydralazine Nifedipine Ephedrine phenoxybenzamine	Diltiazem Verapamil Sodium nitroprusside	Atropine Glycopyrrolate Neostigmine Beta agonists Beta blockers Adrenaline Magnesium
other	Phenytoin Sulfur drugs Aminophylline OCP ergometrine	Steroids	

If a crisis occurs, the goal is to decrease haem synthesis and reduce the production of porphyrin precursors:

General:

- Withdraw the precipitant
- Rehydrate aggressively and correct electrolyte disturbances, especially magnesium
- Analgesia
- Seek ICU and haematology advice

Specific Treatment

- Administration of glucose (400 g/day) intended to inhibit haem synthesis

- In severe attacks, Hematin 4 mg/kg/d for 4 days
- In moderate attacks, haem arginate 3 mg/kg IV d for 4 days
- Somatostatin may be of benefit
- Plasmapheresis may be of benefit

Management of complications:
- Autonomic dysfunction: consider the use of beta blockers to control tachycardia and hypertension; it may also decrease ALA synthetase activity
- Seizures: diazepam, clonazepam, propofol, magnesium, and gabapentin are safe.
- Respiratory failure and bulbar paresis: if intubation is necessary consider RSI
- Peripheral neuropathy: document extent

Pregnancy:
- No definitive evidence favours either neuraxial or general anaesthesia
- Epidurals have been safely used in labour
- Ergometrine is contraindicated but oxytocin has been safely used

Von Willebrand Disease

Haemorrhagic disease associated with reduced, abnormal, or absent von Willebrand factor
May be inherited (autosomal dominant) or more rarely, acquired
Variable in severity
Patients may report a history of easy bruising, frequent epistaxis, prolonged bleeding, and in females, menorrhagia.

Classification:
Type 1:
- Most common form of VWD
- Is a quantitative deficiency which typically results in mild clinical symptoms only
- Patients have typically 20-50% of normal VWF levels

Type 2:
- Qualitative deficiency with 5 subtypes
- May be autosomal dominant or recessive depending on subtype
- Clinical presentation and lab findings can be variable depending on subtype;
- Thrombocytopenia is not uncommon, especially in the 2 B subtype
- 2A and 2M subtype may respond to DDAVP, but thrombocytopenia may occur in the 2B subtype
- Bleeding is variable but may be severe

Type 3 :
- Complete absence of VWF
- Autosomal recessive inheritance
- Most severe form of VWD; typically results in severe bleeding comparable to haemophilia
- Does not respond to treatment with DDAVP

Testing for Von Willebrand disease is typically undertaken by haematology.
Tests include:
- Ristocetin cofactor activity: evaluates qualitative defect

- vWF antigen level: indicates deficiency in production as well as qualitative defect
- Factor VIII level: typically is decreased in VWD; in Type 3 levels are typically <10% and in 2N are < 5%; type 1 and 2 typically only have mild to moderate decrease in factor VIII level
- Integrated tests of bleeding (eg bleeding time, TEG, ROTEM) may be helpful if bleeding occurs but is unable to determine whether there is a qualitative or quantitative defect
- Desmopressin challenge may be undertaken by haematology to evaluate response to desmopressin.

Treatment depends on subtype of VWD and expected severity of bleeding in the perioperative context.

Desmopressin:
- Should be administered 30 minutes before procedure at a dose of .3 mcg/kg up to a maximum of 20 mcg
- Up to 3 daily doses may be considered but tachyphylaxis can occur.
- Should not be used in type 2B or type 3 VWD
- Expected duration of action is 6-10 hours
- May cause vasopressin-like effects leading to water retention

Tranexamic acid
- 25 mg/kg/dose (max 1.5 g /dose) orally tds for 5-7 days
- 10 mg/kg dose as a stat dose
- Often used in mucosal bleeding (epistaxis, gum bleeding)

Biostate/ VWF/FVIII plasma concentrate
- Contains 50 IU/ml of FVIII and 100 IU/ml of VWF
- Used in type 2 and Type 3 VWD and may be used in type 1 vWD if bleeding severe or if there is no response to DDAVP
- Dosing should be based on type of bleeding and severity

Type of bleeding	Dose of Biostate®
Oral mucosa/epistaxis/menorrhagia	25 Factor VIII units/kg (=50 von Willebrand Factor units/kg)
GI/GU bleed	40 Factor VIII units/kg (=80 von Willebrand Factor units/kg)
Joint/Muscle	40 Factor VIII units/kg (=80 von Willebrand Factor units/kg)
CNS bleed	60 Factor VIII units/kg (=120 von Willebrand Factor units/kg)
Trauma or surgery	60 Factor VIII units/kg (=120 von Willebrand Factor units/kg)

Blood products should be considered especially if bleeding is severe
- FFP
- Cryoprecipitate (contains factors VIII, XIII, vWF , and fibrinogen) at significantly higher concentrations than FFP
- Platelets

Anaesthetic Considerations:

- Determine the risk of bleeding and the consequences of bleeding
- Assess type and severity of bleeding
- Refer to haematology
- Send factor VIII levels 48 hours prior to surgery
- Obstetric: aim > 50 %
- Minor surgery: > 30 %
- Major surgery: > 50%
- Repeat factor VIII assay following treatment with factor VIII

Recommended Dosages of Factor VIII for Patients with Severely Reduced (<10%) Factor Levels

Type of Procedure	Dose (IU/kg)	Infusion Frequency	Target Levels
Major surgery	50	Daily	Trough factor VIII level >50% until healing complete (~5-10 days)
Minor surgery	40	Daily or every other day	Trough factor VIII level >30% normal level until healing complete (~2-4 days)
Dental extraction	30	Single dose	Factor VIII level >50% normal for 12 hours
Spontaneous bleeding episode	25	Daily	Factor VIII level >30% normal until bleeding stops (~2-4 days)
Delivery & puerperium	40	Daily before delivery & in the postpartum period	Factor VIII level >50% of normal level for 3-4 days

- If the patient has a DDAVP response give desmopressin .3 mcg/kg to a maximum of 20 mcg
- Consider tranexamic acid for 3-5 days

Obstetrics:

- Obtain baseline VIII, vWF, ristocetin cofactor tests early in pregnancy and repeat at 34 weeks. May need to be repeated if there is antepartum haemorrhage.
- Find out the patient's subtype and VIII level
- If a responder, administer desmopressin at onset of labour
- If a non-responder, consider cryoprecipitate
- VIII level targets in labour/Caesarean section are >50%; following delivery monitor levels and treat if levels are <25% or if there is clinically significant bleeding
- Epidural is considered safe if FVIII level and VWF level >50%

G6PD deficiency

Genetic condition resulting in failure to generate NADPH through glycolysis
X-linked trait which is more common in areas where malaria is endemic
May cause haemolytic anaemia in response to particular triggers including infection, surgical stress, hypothermia and metabolic abnormalities including hyperglycemia
Haemolysis can also occur during reperfusion following intraoperative ischaemia
Methaemoglobinemia may also occur, so drugs which result in methemoglobinemia should not be used
Drugs with oxidant effects should be avoided
Analgesia may prevent stress-induced haemolysis
Patients do not typically need referral to haematology unless haemolytic anaemia occurs

Drugs which should be avoided include:

- Prilocaine
- Lignocaine
- Metoclopramide
- Gentamicin
- Diazepam
- Gentamicin
- Penicillins
- Sulfonamides
- Aspirin
- Antimalarials
- Chloramphenicol
- Vitamin K
- Isoniazid
- Methylene blue
- Toluidine blue

Sickle Cell Disease

Sickle cell disease is a congenital haemoglobinopathy caused by the production of haemoglobin S, leading to a propensity to instability and sickling in the deoxygenated state. It is most common among Africans and south-west Asia. Heterozygous carriers typically only have 30-40% of HbS, typically do not sickle except under extreme conditions and are generally healthy. Homozygous carriers produce nearly all HbS, which leads to chronic haemolytic anaemia, recurrent intermittent attacks of sickling leading to vasoocclusive crises, end-organ damage, and early death. Sickling may be precipitated by cold, venous stasis, dehydration, physiological stress, and infection.

Investigations:

- Peripheral smear
- Haemolytic screen (may be normal in preop settin)
- Reticulocyte count
- Haemoglobin electrophoresis (diagnostic)
- Sickledex test (quick, detects levels of HbS >10% but is unable to differentiate between sickle cell trait and disease

Patients should also be screened for consequences of sickle cell disease by organ system.

Cardiac:

- Cardiomegaly
- CCF
- Pulmonary artery hypertension secondary to recurrent pulmonary infarction
- ECG, TTE should be considered

Respiratory

- Acute chest syndrome
- Recurrent pulmonary infarctions -> respiratory failure
- Pulmonary hypertension

- Consider TTE if there is concern re pulmonary HTN
- RFTs if major surgery is being performed
- DLCO may be reduced in the setting of recurrent pulmonary infarcts
- Chest physiotherapy if time allows

Head/Neck/airway:

- Upper airway hypertrophy
- Marrow hyperplasia leading to frontal bossing and maxillary overgrowth

Renal

- Renal impairment is common
- Patients should have baseline UEC performed

GIT

- Functional asplenism from autoinfarction of the spleen - immune incompetence
- Acute splenic sequestration may lead to splenectomy
- Liver function is typically preserved but gallstones are common- may have obstructive LFTs

Neuro:

- Increased risk of TIAs, thrombotic strokes, hemorrhagic strokes

Haematological:

- Risk of sickling -> vasoocclusive crisis
- Myelosuppression and immune incompetence
- Bone marrow failure and aplastic crisis may occur
- Risk of antibody formation if patients have had multiple previous transfusions

Considerations for the anaesthetist
The key issue is prevention of sickling during the perioperative period.
If seen preoperatively for an elective procedure:

- Referral to haematology
- Folic acid supplementation
- Hydroxyurea preoperatively reduces risk of vasocclusive crisis and transfusion need
- Early admission for preoperative hydration
- Check HbS level and consider preoperative transfusion to drop level <30 % or Hb concentration to > 100 - but haematology should be involved in this decision as there is also the risk of transfusion-related complications

No particular anaesthetic technique is known to be safer in patients with HbS. Both regional anaesthesia and general anaesthesia have been used safely.
Patients with sickle cell anaemia are typically not suitable for day surgery.

Goals of Anaesthesia:

- Prevent hypoxia
- Prevent hypotension
- Prevent acidosis
- Prevent hypothermia
- Prevent dehydration
- Prevent anaemia; aim Hb >100 g/L
- Avoid the use of tourniquets and minimise venous stasis; if a tourniquet must be used the limb should be carefully exsanguinated beforehand

- Avoid the use of adrenaline as this may precipitate sympathetic stimulation and sickling
- Cell salvage is not recommended but has been used in case reports

Sickling during the perioperative period- try to remove trigger if possible. Consult haematology and consider early transfusion/red cell transfusion exchange. Plasma exchange has been used in a number of case reports where there has been multiorgan failure from sickle cell crisis.

Thalassemia

Thalassemia is an autosomal recessive haemoglobinopathy which can affect either the alpha or beta chain of haemoglobin, leading to multiple organ system dysfunction in the long term.

Alpha Thalassemia affects the alpha subunit and typically results in only mild anaemia or no symptoms at all, as there is still the production of haemoglobin by functional alleles. Alpha-thalassemia alleles are common in southeast Asia and roughly 10% of the population are carriers with one dysfunctional allele. Where two dysfunctional alleles exist, it is referred to as alpha-thalassemia trait and there is only mild anaemia. If three non-functional alleles exist patients develop HbH disease and may have moderate to severe anaemia with hepatosplenomegaly but this is very rare . Four non-functional alleles is generally not compatible with fetal survival except with in utero transfusion and subsequent bone marrow transplantation. It is also very rare.

In general patients with alpha-thalassemia probably do not need to be referred to haematology or anaesthetics unless they are having major surgery or there is a co-existing issue (eg Jehovah's witness).

Patients with beta thalassemia, however, should be referred to haematology and to anaesthetics as there are not only haematological, but multi-system effects.

Beta thalassemia results in three different phenotypes: minor, intermediate, and major. The issue is that there is a lack of beta-globin chain production and a surplus of alpha-globin chains, which results in ineffective haematopoiesis, anaemia, and systemic damage from iron overload.

Cardiac:
- Acutely: myocarditis, pericarditis
- Biventricular dilated cardiomyopathy and congestive heart failure; initially high output CCF; may also develop restrictive cardiomyopathy and valvulopathies
- Repolarisation abnormalities , AT prolongation and increased risk of malignant arrhythmia and sudden death

Respiratory:
- Restrictive lung disease from lung fibrosis; may also develop obstructive lung dysfunction
- Reduced diffusion capacity
- Interstitial oedema

- Pulmonary hypertension in up to 50% with intermedia and 75% of those with major

Renal:

- Renal tubular dysfunction,
- Nephrotoxicity from iron chelation

Endocrine:

- Anterior pituitary dysfunction - growth retardation, hypogonadism
- Diabetes is common especially in adolescence and early adulthood
- Primary hypothyroidism and hypoparathyroidism

Bone:

- Craniofacial deformities which may result in difficult airway (19% risk of difficult airway if maxillary hypertrophy exists)
- Typically tend to have high, arched palates which may result in poor LMA fit
- May also have tonsillar enlargement from lymphoid hyperplasia -> difficult BMV and intubation

Liver:

- Haemochromatosis
- Hepatitis, hepatic fibrosis

Neurological:

- Spinal cord dysfunction and cauda equina from compensatory extramedullary hyperplasia
- Increased incidence of cognitive defects
- Increased risk of bone fractures

Haematological:

- Iron overload
- Anaemia + a degree of chronic intravascular haemolysis
- Hypercoagulable state with increased risk of thrombotic complications:venous thrombus is more common in intermedia; arterial thrombus is more common in major
- Hypersplenism which may result in need for splenectomy
- Transfusion dependence in major, which increases risk of antibody formation

For elective surgery, patients with beta-thalassemia should be referred to anaesthetics and to haematology for optimisation. Baseline investigations (FBE, UEC, LFTs, iron level, ECG) should be ordered, and depending on the type of surgery and the clinical concern regarding systemic manifestations of beta thalassemia, other investigations should be considered, in particular TTE, RFTs, Holter monitor, and ABG.

If there is concern regarding cardiac failure or cardiac manifestations of beta thalassemia referral to cardiology is recommended.

Patients with beta thalassemia intermedia and major are usually transfusion-dependent to a degree, and have a degree of iron overload leading to treatment with chelation therapy. Desferrioxamine and transfusion should be discussed with haematology.

Optimal haemoglobin target is not known but aiming for a haemoglobin of 100 g/l is considered safe. The use of blood conservation strategies is recommended. Cell salvage has also been safely used in this context.

In rare cases, people may have sickle cell trait and thalassemia trait. These patients should be discussed in depth with haematology.

Haemophilia

Haemophilia A is a deficiency in FVIII, which is X-linked and affects 1 in 5000 males, resulting in serious coagulopathy and spontaneous haemorrhage. Haemophilia B is a Factor IX deficiency, and also X-linked but 10 times rarer than haemophilia A. The two conditions have similar bleeding tendencies. Women are generally asymptomatic carriers, but can still be at increased risk of perioperative bleeding.

Severity is based on factor levels, and is clinically correlated. Coagulation studies may be normal, aside from prolonged APTT, and patients should have factor levels performed.

Mild: 5-25% factor level activity, typically asymptomatic but may have increase bleeding in major surgery
Moderate: 1-5% factor level activity; generally asymptomatic, but may note increased bleeding in normal life, as well as with minor surgery, but this is generally not life threatening
Severe: <1% factor level activity; spontaneous hemorrhage including haemarthrosis and muscle haematomas

Anaesthetic implications:

- Take a detailed history of type of haemophilia and its severity
- Ask about previous response to DDAVP, use of recombinant factors, previous transfusions and known antibodies/ blood reactions
- Discuss with haematology re perioperative planning; liaise with blood bank to ensure that factor concentrates are available; discuss risk/benefit for regional or neuraxial techniques. Note that the minimum safe factor levels or platelet count in this population is not known.
- Typically patients with haemophilia need 80-100% correction of factor VIII level before proceeding with surgery and this should be confirmed prior to surgery. Postoperatively factor levels should be maintained for up to 6 weeks following major surgery and 1-2 weeks for other procedures.
- Inhibitor levels should be checked as high-risk patients may need to receive either recombinant VII or FEIBA
- Increased risk of bleeding; should be considered in the context of surgical bleeding risk as well
- Increased risk of antibody formation if repeated transfusions have occurred in the past ; also increased risk of blood-borne diseases
- Joint deformities, contractures may increase risk of pressure injury
- Chronic pain from recurrent haemarthroses may make pain management complex
- Care should be taken with vascular access, invasive monitoring, BP cuffs, and tourniquets. Care should also be taken to prevent mucosal trauma (laryngoscopy, ETT, NGT, temp probe insertion)
- Intraoperatively, avoid hypothermia, acidosis, hypocalcemia
- Avoid DVT chemoprophylaxis and NSAIDs where possible

Considerations in pregnancy:

Typically women are haemophilia carriers only, but if the fetus is male, they should be managed by a multidisciplinary team in the antenatal period. Genetic testing of the foetus can be done at 10 weeks or at 18-20 weeks. The safest mode of delivery is not known, but the decision should be made based on the haemophilia status of the child and the parturient's own factor levels.

- Normal vaginal delivery is fine if labour is not prolonged
- Avoid instrumental delivery if possible (high risk of intracranial haemorrhage in haemophiliac neonates)
- Elective Caesar may be safest if the neonate is suspected to have haemophilia
- Neuraxial analgesia can be performed if factor VIII levels > .5 IU/ml

Treatment:

- DDAVP: .3 mcg/kg commenced 30 minutes prior to procedure
- Daily doses up to tds;
- May develop tachyphylaxis after 2 days
- Not useful in severe haemophilia A or in haemophilia B
- Not approved for use in children or in pregnant women
- Antifibrinolytics
- Tranexamic acid 250 mg - 1 g tds
- Recombinant factor VIII
- Recombinant factor IX

Type of bleed	Haemophilia A	Haemophilia B	Comment
	Recombinant FVIII(8)	Recombinant FIX(9)	
Joint	40 units/kg Day 1 20 units/kg or usual home prophylaxis dose Day 2 & 4	50 units/kg Day 1 25 units/kg or usual home prophylaxis dose Day 2 & 5	Factor replacement may be modified when intravenous access is difficult, particularly in toddlers. E.g. 40 units/kg Day 1 & Day 2. Intravenous cannula may be left insitu with patient returning for Day 2 dose. (As an outpatient, intravenous cannula should not be left insitu for > 24 hours.)
Muscle (minor)	30 units/kg	50 units/kg	
Muscle (major)	50 units/kg	75 units/kg	Calf and forearm bleeds may lead to compartment syndrome and be limb threatening. Arrange haematology and surgical review. Involvement of ileopsoas muscle may be associated with significant blood loss and mandates haematology review.
Oral Mucosa & Dental	30 units/kg	50 units/kg	Antifibrinolytic therapy is critical.
Epistaxis (active)	30 units/kg	50 units/kg	Apply local measures (pressure). Antifibrinolytic therapy effective in preventing recurrence.
Gastrointestinal	50 units/kg	75 units/kg	Haematology and gastroenterology review required. Lesion is usually found. Antifibrinolytic therapy may be helpful.
Genitourinary	50 units/kg	75 units/kg	Evaluate for all causes however lesion not usually found. Antifibrinolytic therapy contraindicated in haematuria.
CNS/head	75 units/kg	125 units/kg	Always treat with factor replacement prior to CNS imaging. Haematology & Neurosurgical review.
Trauma or surgery	50 - 75 units/kg	75 - 125 units/kg	Consultation with haematologist essential.

Chronic Pain and Opioid Tolerance

Please refer to Acute Pain Service

- Oral morphine equivalence doses (OMED) greater than 60mg/day
  With any of
- Signs or history of aberrant opioid or benzodiazepines use (including those on opioid substitution therapy)
- Chronic pain
- Co-existing anxiety and depression
- Significant medical comorbidities such as BMI > 50, OSA.

General Principles

- **Always** check Safecript to confirm opioid doses and dispensing history.
- Slow-release opioids are not indicated for the management of chronic non-cancer pain- hospital admissions are opportunities to address this.
- Majority of morbidity and mortality is due to combinations of opioids with other sedating drugs- in particular benzodiazepines, but also take care with gabapentinoids.
- Don't abruptly cease opioids or the patient may experience withdrawal.
    - Don't skip opioids when fasting.
- In most cases, continue current opioid use up to surgery if the patient is stable and the OMED is less than 60mg/day. If there are multiple opioids or abeberent use, refer to the APS who may recommend a dose reduction strategy or opioid rotation.

Expect tolerance if OMEDs >60mg/day

- Higher than normal doses may be needed in conjunction with adjuncts and multimodal analgesia.

Disposition – higher acuity area; sensitivity to further opioids and resp depression
Long-term opioid use is a dose-dependent risk factor for sleep-disordered breathing, which requires appropriate perioperative assessment, monitoring and management.

Strongly consider regional technique if suitable.

Opioid Conversion/Rotation

- Rotating opioids to either buprenorphine or methadone prior to surgery has been associated with a reduction in total OMEDs, tolerance and opioid induced hyperalgesia. This should be done in consultation with the APS and/or a pain specialist.
- Opioid calculator can be found on http://www.opioidcalculator.com.au/ or download the ANZCA FPM Opioid Calculator app from your usual App Store.
- When rotating doses it is usual practice to reduce the total OMED by approximately 25% to allow for incomplete cross-tolerance.

In order to calculate an oral Morphine Equivalent Daily Dose (oMEDD), multiply the current daily opioid dose by the conversion factor in column 3.

For example, oMEDD of oxycodone 40mg/day = 40 x 1.5 = 60mg/day

CURRENT OPIOID		CONVERSION FACTOR	PROPRIETARY NAMES
ORAL (SWALLOWED) PREPARATIONS *Note: Modified release formulations are marked MR*			
Morphine	mg/day	1	Anamorph, Kapanol (MR), MS Contin (MR), MS Mono (MR), Ordine, Sevredol
Oxycodone	mg/day	1.5	Endone, OxyContin (MR), OxyNorm, Targin (MR)
Hydromorphone	mg/day	5	Dilaudid, Jurnista (MR)
Codeine	mg/day	0.13	Aspalgin, Codalgin, Panadeine, Panadeine Forte, Mersyndol, Nurofen Plus, others
Dextropropoxyphene	mg/day	0.1	Di-Gesic, Doloxene
Tramadol	mg/day	0.2	Durotram-XR (MR) , Tramal, Tramadol SR (MR), Zydol, Zydol SR (MR), others
Tapentadol	mg/day	0.3	Palexia-SR (MR), Palexia-IR
SUBLINGUAL PREPARATIONS			
Buprenorphine	mg/day	40	Suboxone, Subutex, Temgesic
RECTAL PREPARATION *Note: Absorption from rectal administration is highly variable*			
Oxycodone	mg/day	1.5	Proladone
TRANSDERMAL PREPARATIONS			
Buprenorphine	mcg/hr	2	Norspan
Fentanyl	mcg/hr	3	Denpax, Durogesic, Dutran, Fenpatch, Fentanyl Sandoz
PARENTERAL PREPARATIONS			
Morphine	mg/day	3	DBL morphine sulphate injection, DBL morphine tartrate injection
Oxycodone	mg/day	3	OxyNorm FI
Hydromorphone	mg/day	15	Dilaudid FI, Dilaudid-HP FI
Codeine	mg/day	0.25	Codeine phosphate injection USP
Pethidine	mg/day	0.4	Pethidine injection BP
Fentanyl	mcg/day	0.2	DBL fentanyl injection, Sublimaze
Sufentanil	mcg/day	2	
Faculty of Pain Medicine, ANZCA – June 2021			

Fentanyl Patches

Use is inappropriate for acute pain due to it's pharmacokinetics.
Even the smallest fentanyl patch of 12 mcg/hr = 36mg/day OMED.
Patches should be left on patient during surgery but care should be taken as heat can increase absorption of active drug (e.g. forced air warmers)

Opioid Replacement Therapy

Methadone

Is a long-acting opioid used for pain management and opioid substitution therapy.

- Physeptone tablets (treatment of pain)
- Methadone syrup (mainly used for opioid substitution therapy but can be used in palliative care for cancer pain)

Pharmacology

- Racemic mixture of 2 enantiomers - R and S-methadone
- R-methadone - full mu opioid receptor agonist
- S-methadone - NMDA antagonist (major) and serotonin and norepinephrine reuptake inhibition (minor)
- Higher affinity to mu receptors than morphine, similar to fentanyl
- Metabolised by multiple hepatic cytochromes (3A4, SD6, 1A2, 1B2) - drug interactions
- Main metabolite is inactive and therefore safe in renal failure; 2 minor metabolites metahdol and normethadol that behave like methadone
- Half-life 8-59 hours
- Can cause prolonged QT
- Biphasic elimination- alpha phase is 8-12 hours which corresponds with analgesic effect (reason dividing dose in acute pain can provide benefit) and beta phase is 30-60 hours which is the agonist effect that avoids withdrawal in addiction.

Long receptor occupancy so less available receptor and cross tolerance - high risk of adverse effects

Patients who are on methadone therapy should have their methadone as normal on the day of surgery.
Ratio of conversion of oral to IV methadone is usually 1mg oral:0.5mg IV methadone.
Conversion to other opioids is not straightforward (or linear) as the dose can be impacted by drug-drug interactions and should be discussed with the APS, pain specialist or addiction medicine.

Intra-operative analgesia should be based around providing adequate analgesia and preventing withdrawal, accounting for tolerance and hyperalgesia. Any opioid can be used for breakthrough analgesia such as oxycodone or tapentadol. If oral absorption is an issue post-operatively, conversion to parenteral methadone (or other opioid) should be done in consultation with a specialist.

Buprenorphine

Suboxone- Buprenorphine & naloxone sublingual, bypass hepatic first pass metabolism

- Naloxone included to reduce misuse potential.
- Suboxone tends to be used for opioid substitution therapy.

Patients on Suboxone therapy should have their daily dose on day of surgery

Buprenorphine pharmacology

- Partial agonist with high affinity for mu opioid receptor ceiling effect on respiratory depression
- Full analgesic effect clinically but in test tube ceiling effect on mu opioid receptor
- Partial antagonist at kappa opioid receptor decr euphoria
- Literature suggests that 8-12mg buprenorphine occupies ~50% receptors; prevents withdrawal and leaves ~50% receptors for analgesia with higher than normal dose of opioids
- Half life 28 hours
- In clinical practice, buprenorphine should be treated as a full agonist. At higher doses consider the patient opioid tolerant.

Subutex is a buprenorphine only furmulaton sublingual tablet (0.4mg, 2mg and 8mg) used for pain management in those at risk of aberrant opioid misuse.

Norspan patch is a transdermal buprenorphine patch used for pain management.

Depot buprenorphine (Sublocade (100 or 300mg monthly), Buvidal (weekly or monthly)) has recently been listed in the PBS for use in opioid substitution therapy. Suggest treating like any opioid tolerant patient.

Patients on buprenorphine for opioid dependence or substitution should be referred to the APS.

Elderly patients

Aging is associated with a progressive loss of functional reserve in all organ systems.

Preoperative anaesthetic evaluation requires an assessment of the presence and stability of medical conditions, treatments, functional reserve, cognitive ability and risk factors for postoperative cognitive dysfunction.

Cardiovascular System

- Labile intraoperative blood pressure due to vascular stiffening and autonomic changes function, consider withholding 1-2 days taking into account blood pressure control
- Intraoperative hypotension can be exacerbated by
    - Vasodilatory effects of anaesthetic agents
    - Laparoscopic insufflation of abdomen
    - Sympatholysis post neuraxial block
    - Impaired beta receptor responsiveness limits ability to increase cardiac output by increasing heart rate, hence patients are more reliant on vascular tone and preload
    - Impaired baroreflex responsivity
- Left ventricular hypertrophy
    - Impaired diastolic filling and dysfunction is present in about 50% of patients older than 65 years of age.
    - They are vulnerable to significant hypotension during atrial arrhythmias due to dependence on atrial kick for filling during diastole
    - Diastolic dysfunction also increases the risk of development of pulmonary oedema during fluid administration
- Other cvs pathology
    - Ischaemic heart disease
    - Calcific aortic stenosis
    - Fibrosis of cardiac conduction system with increased incidence of atrial fibrillation or cardiac conduction abnormalities and hypertension

Respiratory system

- Chest wall stiffening and decreased elasticity of lung parenchyma
- Increased compliance and closing capacity means small airway closure infringing on FRC-> poor oxygen reserve
- Increased ventilation/perfusion mismatch
- Reduced forced expiratory volume, vital capacity and maximal rate of oxygen consumption
- Increased dead space
- Increased alveolar-arterial gradient
- Diminished ventilatory response to hypercapnia and hypoxaemia
- Decreased respiratory muscle strength and impaired cough mechanism
- Impaired pharyngeal function
- Undiagnosed chronic obstructive pulmonary disease (COPD) or OSA

- Exaggerated respiratory depressant effects of opioids, benzodiazepines, volatile inhalation agents and hence increased risk of hypoxaemia, hypercapnia and respiratory failure

Hepatic system
- Decreased hepatic blood flow, mass and function hence slower metabolism of anaesthetic agents
- Decreased albumin levels hence larger free-drug concentrations of highly protein bound drugs e.g. propofol
- Decreased albumin levels are also independently associated with increased risk of mortality and morbidity

Renal system
- Decreased glomerular filtration rate, creatinine clearance, renal functional reserve
- Patients often have comorbidities e.g. diabetes, hypertension and vascular disease that impact renal function
- Implications on anaesthesia
    - Increased plasma concentration of renally excreted IV agents
    - Decreased ability to handle salt/water load
    - Increased susceptibility to nephrotoxic effects of medications/IV contrast

Haematological system
- Anaemia due to Fe deficiency, chronic disease/inflammation, malnutrition, bone marrow malfunction

Pharmacokinetic changes
- Decreased total body water (10-15%), muscle mass and hence lower central compartment volume
    - Need to lower induction dose of anaesthetic agent e.g. propofol
- Increased body fat (20-40%) leads to larger volume of distribution for lipid soluble agents and large adipose reservoir that prolonged clinical drug effect
- Elimination half-life longer and clearance decreased due to renal/hepatic dysfunction

Assessment for frailty
- Frailty is defined as aging-related syndrome of physiologic decline and reduced tolerance to medical and surgical interventions
- Frail elderly patients often have an increased burden of symptoms, medical complexity and decreased physiologic reserve that exceeds advanced age alone
- Frailty predicts postoperative morbidity(e.g. delirium/cognitive impairment) and mortality. It also predicts a longer hospital length of stay and long term functional decline
- Identifying frailty can help with discussions regarding surgical techniques, postoperative recovery strategies and likely outcomes. It can also allow optimization of the medical condition, improvement of physiologic reserve with a prehabilitation program which may include exercise training, nutritional supplementation and liaising with a geriatrician for postoperative care and discharge planning.
- There are several multidimensional tools to assess preoperative frailty

    - An example is the Frailty index (proportion of deficits present out of the total number of age-related health variables considered)
    - The Edmonton Frailty Score: series of questions which examine cognitive and physical disability as well as functional limitations

Other preoperative assessments

- Baseline cognitive function
- Medication history to allow reconciliation of medications

Anaesthetic considerations

- Elderly patients are more sensitive to anaesthetic agents and may require a dose reduction
- All opioids are more potent in older patients which have the potential to cause respiratory depression. The increased brain sensitivity and decreased clearance of opioids mean that these patients are at higher risk of hypoventilation or apnoea.
- Benzodiazepines should be avoided if possible
- Patients with Alzheimer disease/other types of dementia may be taking cholinesterase inhibitors (e.g. donepezil, galantamine) which may lead to decreased plasma cholinesterase, hence prolonging the duration of succinylcholine
    - Cholinesterase inhibitors may also interfere with the action of anticholinesterase agents e.g. neostigmine and may cause unpredictable responses to these agents
- Cautious fluid management intraoperatively
    - Avoid dehydration, prevent inadequate tissue perfusion
- Avoidance of hypothermia
    - Perioperative hypothermia is more pronounced and prolonged in older adults
- Multimodal postoperative analgesia
    - Opioids may precipitate or worsen delirium. Inadequate pain relief also associated with greater likelihood of delirium

Specific Medications and Management [Referenced from Perioperative Medication Management Guideline (3553)]

Cardiovascular

ACE Inhibitors/ARB

- Withholding medication
- Continue UNLESS Major surgery/fluid shift or blood loss expected
- Restarting medication
    - Restart D2 post-operatively (or within 48 hours), if BP and eGFR return to baseline

Additional comments

- There can be an individualized decision to continue/discontinue ACEI based on the indications for the medication, patient's blood pressure control, type of surgery and anaesthesia planned.Mostly, they are withheld on the morning of surgery. However, if the indication is for heart failure or poorly controlled hypertension, they should be continued to avoid further exacerbation of these conditions.
- Continuing ACEI till day of surgery can increase risk of perioperative hypotension but reduces risk of postoperative hypertension which increases risk of adverse cardiac events
- Resume these agents as soon as possible postoperatively, failure to restart ARBs within 48 hours after surgery has been associated with increased 30-day mortality.

Beta Blockers

- CONTINUE

Additional Comments

- BB reduce ischaemia by decreasing myocardial oxygen demand
- They may also help prevent/control arrhythmias
- Acute withdrawal of a BB pre/postoperatively can lead to substantial morbidity and mortality especially if they are used to manage angina

Alpha 2 agonists e.g. Clonidine, Moxonidine

- CONTINUE
- For patients already taking clonidine, abrupt withdrawal can precipitate rebound hypertension

Additional Comments

- In POISE-2 RCT -- patients undergoing noncardiac surgery. It showed that preoperative initiation of low-dose clonidine resulted in increased harm (NO change in mortality of myocardial infarction but INCREASE in clinically significant hypotension and nonfatal cardiac arrest)
    - Substudy of the trial also found NO benefit of perioperatively administered clonidine in reducing risk of AKI

Calcium Channel Blockers e.g. Amlodipine, Diltiazem

- CONTINUE

Additional Comments

- Limited data regarding risks and benefits of calcium channel blockers in the perioperative setting.
- Concerns raised about possible association between CCB and an increased risk of bleeding. Despite little data regarding CCB during perioperative period, these agents are relatively safe and have a theoretic benefit

Diuretics

- Withholding Recommendation
    - Withhold morning of major surgery only
    - Consider withholding for 1-2 days (avoid excess dehydration, risk of worsening heart failure or kidney impairment)

    - Further consideration if used for poorly controlled heart failure/severe renal failure where risk may outweigh benefit of withholding
- Restarting Recommendation
    - Restart post-operatively

Additional Comments

- 2 major physiological effects are hypokalaemia (could increase risk of perioperative arrhythmia) and hypovolaemia
- NO consensus on whether diuretics should be discontinued prior to elective surgery
- Advice is for patients who are taking diuretics for hypertension to withhold medication on the morning of surgery. Diuretics may theoretically increase risk of intraoperative hypotension.
- For patients receiving diuretic therapy to treat heart failure, diuretic continuation is based on assessment of volume status. In patients with heart failure in whom fluid balance has been more difficult to control, consider continuing the diuretic without interruption.

Digoxin

- CONTINUE. Obtaining a drug level preoperatively is not usually required

Additional Comments

- Digoxin is used to prevent hospitalization and readmission in patients with reduced left ventricular function and to control ventricular response in atrial fibrillation.

Statins

- CONTINUE

Additional Comments

- May prevent vascular events in the perioperative period

Anticoagulants and Antiplatelets

Antiplatelets

Aspirin

- Consult local unit regarding withholding of medications

Aspirin & Dipyridamole

- Withhold for 7 days and consider swapping to aspirin

Clopidogrel

- Withhold for 7 days

Prasugrel

- Withhold for 10 days

Ticagrelor

- Withhold for 10 days

Restarting Recommendation for ALL Antiplatelet therapy

- Low Bleeding Risk Procedure: ASAP after procedure e.g. night of procedure
- High Bleeding Risk Procedure: 24-48 hours following the procedure

Comments

- Low dose aspirin is usually continued (consult local unit policy)
- Cessation of antiplatelet therapy should only be made after consideration of the patient's risk of thrombosis and relative risk of surgical bleeding
- Check before stopping if patient has recent IHD, DES or CVA
- For DAPT (e.g. aspirin & clopidogrel), if it has been >12 months, withhold the second agent and continue aspirin. If patient is on a single agent other than aspirin and it has been >12 months, withhold the other agent and commence aspirin during the pre-op period.
- For patients taking dual antiplatelet therapy (DAPT) after PCI who need to undergo major noncardiac surgery, continuation of DAPT may increase risk of major bleeding, while discontinuation of 1 or both agents may increase risk of thrombotic event.
- Perioperative thrombotic cardiac events related to DAPT discontinuation include Myocardial infarction (MI), death, stent thrombosis and need for urgent repeat revascularization. Stent thrombosis is a proximate cause of death or MI. Premature cessation of DAPT is the strongest predictor of stent thrombosis, especially discontinuation of both agents. Stent thrombosis can lead to high rates of MI (50-70%) and death (10-40%). Prothrombotic and proinflammatory effects of surgery may predispose the coronary circulation to thrombosis, both at site of prior stent placement and at other sites of atherosclerotic lesions. Perioperative prothrombotic state may be mediated by increased platelet aggregation and decreased fibrinolysis.
- The risks of noncardiac surgery before 6 months are increased after both BMS and DES
- The risk of MI and cardiac death is highest within the first month after stent placement and no clear difference in risk between BMS and DES.
- It is best that the final decision to continue/discontinue antiplatelet therapy in the perioperative period should be made only after an informed discussion among the surgeon, managing cardiologist and patient has taken place.

Anticoagulants

- Warfarin
    - Withhold for 5 days and check INR
    - Restarting: see Objectify Policy 4453
- Dabigatran, Rivaroxaban, Apixaban
    - Withholding guidelines
        - Rivaroxaban and Apixaban: withhold for 72 hours
        - Dabigatran: Withhold for 5 days
        - Consider withholding for a further 24 hours if moderate renal impairment is present (< eGFR 50L/min)
    - Restarting
        - Low bleeding risk procedure: start/resume 24 hours after surgery and when surgeon considers safe for patient to be anticoagulated

        - High bleeding risk procedure: start/resume 48-72 hours after surgery and when the surgeon considers it safe for the patient to be anticoagulated. Consider alternative VTE prophylaxis in the interim

Other comments:

- Consider activated charcoal for patients with moderate or severe bleeding who present within 2 hours of last dose of Rivaroxaban/Apixaban

Bridging Clexane Strategies - Objectify

Strategy 1 – high risk for thrombosis, major procedure

- Withhold warfarin for 5 days prior to procedure (Day -5)
- Enoxaparin 1.5 mg/kg daily on days 2 and 3 before procedure (Day -2 and -3)
- Enoxaparin 1 mg/kg daily one day prior to procedure (Day -1)
- Day of procedure – nil pre-op enoxaparin
- * Post-procedure - if no haemostasis problems/risks: re-commence enoxaparin 40 mg daily at 6-12 hours OR heparin infusion at 12-18 hours, post skin closure
- Re-commence warfarin as soon as practical post procedure (expect 7-10 days before therapeutic INR)
- Days 3-4 post-procedure increase enoxaparin to 1 mg/kg bd OR 1.5 mg/kg daily
- Continue enoxaparin until INR >2 on two consecutive days

Strategy 2 – consider for urgent procedures such as fractured neck of femur or short procedures where secure haemostasis is required (e.g. Interventional radiology or endoscopy)

- Do not withhold warfarin
- Check INR pre-procedure
- If INR 1.5-2 administer prothrombin complex (Prothrombinex® 20 units/kg stat)
- INR >2 administer prothrombin complex 30 units/kg stat
- INR >3 administer prothrombin complex 40 units/kg stat
- Post-procedure continue warfarin if possible
- If not possible to continue warfarin - check INR Day 1 post-procedure. If INR <2 then give anticoagulation as per * Post-procedure options in Strategy 1

Strategy 3 – low (standard) risk for thrombosis

- Cease warfarin 4-5 days pre-op
- No pre-op bridging anticoagulation
- Give standard post-operative thromboprophylaxis as per guidelines
- Recommence warfarin as soon as possible post-procedure
- Continue thromboprophylaxis until INR>2

Endocrine Medications

Glucocorticoids

- CONTINUE
- If on long term steroids at doses of >15 mg or equivalent of prednisolone there is a risk of HPA axis suppression, which puts patients at risk of intraooprative adrenal crisis/Addisonian crisis. Steroid stress dosing should be considered in moderate to major risk surgery, and if there is refractory hypotension, steroid supplementation should be considered.

Metformin

- Withholding Recommendations
    - If undergoing major surgery, withhold on day of surgery
    - If minor surgery, NO need to to withhold
- Recommencing Recommendations
    - Recommence when tolerating oral diet and ensure normal renal function

Additional Comments

Many OHGAs have a prolonged duration of action and may cause hypoglycaemia up to 48 hours after they have been discontinued if the patient is unable to resume eating.

SGLT2 Inhibitors e.g. Empagliflozin, Dapagliflozin, Canagliflozin

- Withholding Recommendations
    - Withhold for 72 hours otherwise patients may be at risk of ketoacidosis
    - Euglycaemic diabetic ketoacidosis may be under-recognized in the postoperative period, given its atypical presentation and closer monitoring of ketones is required.
    - If patient is on a combination SGLT2/Metformin tablet e.g Jardiamet, Xigduo, Segluromet, consider withholding the SGLT2 component but continuing the metformin
    - Check ketones on admission. Safe to proceed if ketones <1.0
- Recommencing Recommendations
    - Recommence when resume/tolerate oral diet

GLP-1 Analogues (e.g. Dulaglutide, Exenatide, Liraglutide)

- CONTINUE

Insulin

- Detailed guidelines available on Objectify Policy 1969
- Safest is to use glucose insulin infusion during perioperative period

Additional Comments

- Maintain infusion with glucose support for 24hours and until patient resumes adequate oral intake
- Patients with Type I DM should be first on surgical morning list and will always need insulin even when fasting

- Temporary insulin may be required if patient is unwell/septic

Oral Contraceptive PIll (ORT)

- Continue
- High VTE Risk (consider withholding 4 weeks pre-surgery)
- Restart postoperatively, use alternate birth control methods for one week in addition

Post-menopausal hormone therapy (HRT)

- Continue
- High VTE Risk.
    - If indication is osteoporosis e.g. Raloxidene, then consider withholding 3 days before surgery. Patients on SERMs are at higher risk of VTE and appropriate prophylaxis should always be given in perioperative period
    - If indication is breast cancer prevention then consult treating oncologist

Thyroid Drugs

- Continue

Bisphosphonates for osteoporosis

- Withhold morning of surgery and restart post-operatively

Sildenafil

- Withhold 24h pre-operatively and restart post-op
- Do not withhold if indication is pulmonary HTN

Neurological Agents

Anti-epileptics

- Continue

Anti-Parkinsonian

- Continue
- Abrupt withdrawal may lead to flares of symptoms

Anti-retroviral

- Continue
- Viral resistance more likely to occur when doses are missed intermittently over extended period of time

Gout treatment

- Continue Colchicine and Allopurinol as surgery is known to precipitate acute gouty arthropathy

Naltrexone

- Withhold for 72 hours (limited evidence on duration to withhold and when to restart)
- Restart when patient no longer needs opioids
- Always maximize use of non-opioid pain management options e.g. blocks

Immunomodulators

Non-biological DMARDs (e.g. Methotrexate)

- Continue the current dose. Consult rheumatologist if they are being managed.

Comments: Systemic review shows MTX continuation perioperatively is safe, associated with reduced risk of flares and does not result in increased incidence of infection/poor wound healing. There is less data re hydroxychloroquine, sulfasalazine and Leflunomide.

Biological DMARDs (e.g. Monoclonal antibodies)

- Liaise with treating specialist
- Infliximab (Remicade): Withhold 6-8 weeks
- Etanercept (Enbrel): Withhold for 1 week
- Adalimumab (Humira): Withhold for 2 weeks
- Rituximab: Prolonged B-lymphocyte depletion can develop lasting up until 1 year post-Rx. Check B cell count and discuss with prescribing doctor re timing of elective surgery

Comments: Increased risk of post-operative infections in the biological DMARDs. Withhold pre-op and post-op (until wound healing has progressed to allow for suture/staple removal i.e. 1-2 weeks). Discuss with specialist re risk of cessation vs continuance

Corticosteroids (e.g. prednisolone)

- Continue

Comments: Consider providing additional glucocorticoid coverage in patients taking high dose of glucocorticoids pre-op (e.g. prednisolone >10mg/day for 3 weeks or more)

Discussion should be made with surgeon and prescribing doctor e.g. rheumatologist, gastroenterologist, to clarify individual's risk.

Analgesics

Opioid Replacement Therapy (Methadone, Buprenorphine +/- Naloxone)

- Continue and ensure regular dose is taken on day of surgery

- Early referral to APS recommended
- Opioid requirements for these patients may be high and unpredictable due to opioid tolerance. Multimodal analgesia and regional analgesic modalities should be employed where possible.

Opioids

- Continue and ensure regular dose on day of surgery
- High dose (OMED>50mg) discuss with anaesthetist and consider referral to APS

Intra-thecal morphine pumps

- Continue (notify anaesthetics)

NSAIDs

- Withhold for 3 days (Ibuprofen can be withheld for 24 hours)
- Restart postoperatively
- Where IV NSAIDs (e.g. IV parecoxib) given intraoperatively, consider waiting 12-24 hours before restarting PO NSAID
- Weigh up risks of procedural bleeding and pain control. Platelet function normalizes after 3 days usually.

Paracetamol/Neuropathic pain agents e.g. TCA/gabapentinoids/anti-epileptics

- Continue

Cortisone injections

- Continue

Other Medications

Psychiatric

TCAs/SSRIs/SNRIs/Mood Stabilizers (e.g. Lithium, Sodium Valproate)

- Continue
- Monitor serum levels perioperatively.
- Lithium: low threshold to check thyroid function pre-surgery; avoid NSAIDS as may lead to lithium toxicity.

Antipsychotics

- Continue and consult patient's psychiatrist if any concerns
- Check ECG for QT prolongation.
- May potentiate sedative and hypotensive effects of anaesthetics and opioid analgesics perioperatively

Benzodiazepines

- Continue
- Allow patients to take on day if needed and inform nursing staff

Psychostimulants

- Withhold morning dose and resume when patient stable

MOA-I irreversible (e.g. Phenelzine)

- Withhold for 14 days, discuss with psychiatrist
- Restart post-op

MOAI-I reversible (e.g. Moclobemide)

- Withhold for 1 day and restart post-op

Gastrointestinal Agents

H2 blockers and PPIs

- Continue
- If still symptomatic, consider increased dose 2-3 days pre-op

Pulmonary Agents

Inhaled Steroids, anticholinergics and beta agonists

- Continue

- Encourage smoking cessation ideally 6/52 preoperatively
- Encourage compliance and encourage patient to bring ventolin and self medicate as desired

Complementary Medications

Herbal Medications

- Continue Calcium, Folate, Mg, Vit A, D and Zinc (short term)
- All others withhold for 14 days and restart Post-op
    - There are theoretical reasons that these agents may increase perioperative morbidity. Purity and nature of some herbal medications is unclear.

Antenatal clinic referrals

Background: Early review in antenatal clinic should be organised for women who:
- Are at high risk of obstetric complications
- May be at increased risk of failure or complications with regional anesthesia
- May be at increased risk of complications with general anaesthesia
- Have had previous complications with either regional or general anaesthesia
- Have significant medical comorbidities
- Jehovah's witnesses to outline wishes in the event of requiring blood transfusion

This allows the anaesthetist to assess the woman, establish a plan for labour and delivery, and educate the patient.

Medical comorbidities:
- Neurological disorders: multiple sclerosis, myasthenia gravis, spinal cord injury, myopathies
- Cardiac disease: known structural heart disease, HOCM, or other conditions where haemodynamic changes may be dangerous for the patient
- Respiratory disease: severe asthma or COPD, cystic fibrosis
- Coagulopathy disorders : haemophilia, Von Willebrand disease, inherited coagulopathies; platelet deficiency or dysfunction
- Medical conditions requiring therapeutic anticoagulation
- Autoimmune disease with systemic implications : eg. SLE, ankylosing spondylitis, RA
- Porphyria
- Sickle cell disease
- Morbid obesity
- IVDU or opioid dependence
- Chronic renal failure
- Previous organ transplantation
- ASA >3
- Jehovah's witness

Antenatal comorbidities:
- Abnormal placentation (previa, accreta, or percreta)
- > 3 previous caesarean sections, or expected complex/difficult LUSCs
- Twin gestation
- Poorly controlled gestational diabetes or pre-eclampsia
- Gestational thrombocytopenia

Difficulties with anaesthesia:
General Anaesthesia:
- Difficult airway, either known or anticipated
- Anaphylaxis to an anaesthetic agent
- Suxamethonium apnea or family history thereof
- Malignant hyperthermia or family history thereof

Regional Anaesthesia
- Congenital abnormalities (eg kyphoscoliosis, myelomeningocoele, spina bifida)
- Previous spinal surgery (eg Harrington rods, discectomy, laminectomy)

- Previous failed spinal
- Severe needle phobia