

# Medical Viva

## Summaries

## Examination Report

The medical viva tests the ability of a candidate to identify and assess the severity and stability of a specified medical condition. It is not a pre-anaesthetic assessment.

Candidates are expected to take a focused history, elicit relevant physical signs and from these, determine the functional status of the system to which they are directed. They are expected to be able to interpret ECG's, CXR's, blood results, Pulmonary Function Tests and other investigations, which are relevant to the progress of the condition or its complications.

An understanding of the management of acute aspects of the medical condition is expected and candidates should also be able to discuss medical optimisation.

Criteria for assessment include

- professionalism in dealing with patients
- an appropriate history which explores risk factors, degree of severity, progression, response to therapy and long-term management (where appropriate) for a disease state
- physical examination that elicits key signs in an efficient, logical sequence
- an organised presentation of findings which interprets and integrates history, examination and investigations

Candidates should be mindful that they are interacting with patients. Difficulties may well arise in the course of the exam and candidates need to demonstrate some flexibility in their approach to the patient.

Candidates who score well

- demonstrate respect for the patient
- elicit a comprehensive history relevant to the system
- evaluate the functional impact of the condition
- perform a fluent and accurate physical examination
- integrate the information into a reliable and succinct summary
- prioritise and correctly interpret relevant investigations

For each viva:

- Identify condition & cause
- Elicit symptoms & signs – targeted history & examination
- Assess severity, stability & complications
- Current treatment – adequate or inadequate?
- Potential for medical optimisation?
- Presentation of findings
- Interpretation of relevant investigations
  - Pathology tests, ECG, respiratory function tests, echocardiograms, x-rays, CT/MRI scans etc.
- Discussion of the case
  - Functional status
  - Implications for anaesthesia & surgery
- Possible discussion of potential emergencies

You will be assessed on:

- History taking
- Physical examination
- Communication skills
- Clinical judgment
- Synthesis of findings
- Professionalism
- Organisation
- Efficiency
- Overall impression

## Cardiovascular

## Aortic Stenosis (Oxford p62, Stoelting p40)

- Obstruction to left ventricular systolic outflow across the aortic valve
- Causes
  - Age-related degeneration + calcification of aortic leaflets with subsequent stenosis (develops 60-80 years)
  - Presence of congenital bicuspid rather than tricuspid aortic valve (develops 30-50 years)
  - Rheumatic heart disease
  - Infective endocarditis

### Clinical Features

- History
  - Chest pain/angina, breathlessness/dyspnoea, syncope
  - Decreased exercise tolerance due to inability of heart to adequately ↑ SV to meet ↑ metabolic demands
  - Rheumatic fever
  - Risk factors similar to those of IHD (hypertension, ↑ chol)
- Examination
  - Pulse – plateau or anacrotic pulse or pulse may be late peaking + of small volume
  - Palpation – displaced hyperdynamic apex beat, thrill over aortic area
  - Auscultation
    - Narrowly split or reversed S2 because of delayed left ventricular ejection
    - Mid-systolic ejection murmur, maximal over aortic area + extending into carotids
    - Murmur loudest with patient sitting up + in full expiration
- Investigations
  - ECG – LVH + strain
  - CXR – normal until LV begins to fail, may see calcified aortic annulus or prominent ascending aorta from post-stenotic aortic dilation
  - Echocardiogram – identification of trileaflet versus bileaflet aortic valve, thickening + calcification of aortic valve, decreased mobility of aortic valve leaflets, left ventricular hypertrophy & left ventricular systolic or diastolic dysfunction; measurement of AVA + transvalvular pressure gradients
  - Cardiac catheterisation – may be necessary when severity cannot be determined by echo

### Severity

- Symptoms do not correlate well with stenosis severity – some patients with severe disease can be asymptomatic
- Symptoms & average time to death post onset:
  - Exertional **chest pain/angina** – 5 years
  - Exertional **syncope** – 3 years
  - Exertional **dyspnoea** – 2 years
- Signs indicating severe AS:
  - Thrill in aortic aorta
  - Left ventricular failure (very late sign)
  - Paradoxical splitting of S2
  - Late peaking murmur
  - Presence of S4
- Echocardiogram

Indicator	Mild	Moderate	Severe
<b>Aortic valve area (cm<sup>2</sup>)</b>	>1.5	1.0-1.5	<1.0
<b>Indexed AVA (cm<sup>2</sup>/m<sup>2</sup>)</b>			<0.6
<b>Mean gradient (mmHg)</b>	<25	25-40	>40
<b>Jet velocity (m/s)</b>	<3	3.0-4.0	>4.0

- Exercise stress testing – not suitable for symptomatic patients, may be used to evaluate asymptomatic patients, hypotension or failure to increase BP with exercise = poor prognostic finding

**Table 8. Stages of Valvular AS**

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
<b>A</b>	<b>At risk of AS</b>	<ul style="list-style-type: none"> <li>Bicuspid aortic valve (or other congenital valve anomaly)</li> <li>Aortic valve sclerosis</li> </ul>	<ul style="list-style-type: none"> <li>Aortic <math>V_{max} &lt; 2</math> m/s</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>B</b>	<b>Progressive AS</b>	<ul style="list-style-type: none"> <li>Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or</li> <li>Rheumatic valve changes with commissural fusion</li> </ul>	<ul style="list-style-type: none"> <li>Mild AS: Aortic <math>V_{max}</math> 2.0–2.9 m/s or mean <math>\Delta P &lt; 20</math> mm Hg</li> <li>Moderate AS: Aortic <math>V_{max}</math> 3.0–3.9 m/s or mean <math>\Delta P 20</math>–39 mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>Early LV diastolic dysfunction may be present</li> <li>Normal LVEF</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>C: Asymptomatic severe AS</b>					
<b>C1</b>	<b>Asymptomatic severe AS</b>	<ul style="list-style-type: none"> <li>Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</li> </ul>	<ul style="list-style-type: none"> <li>Aortic <math>V_{max} \geq 4</math> m/s or mean <math>\Delta P \geq 40</math> mm Hg</li> <li>AVA typically is <math>\leq 1.0 \text{ cm}^2</math> (or AVAI <math>\leq 0.6 \text{ cm}^2/\text{m}^2</math>)</li> <li>Very severe AS is an aortic <math>V_{max} \geq 5</math> m/s or mean <math>\Delta P \geq 60</math> mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>LV diastolic dysfunction</li> <li>Mild LV hypertrophy</li> <li>Normal LVEF</li> </ul>	<ul style="list-style-type: none"> <li>None: Exercise testing is reasonable to confirm symptom status</li> </ul>
<b>C2</b>	<b>Asymptomatic severe AS with LV dysfunction</b>	<ul style="list-style-type: none"> <li>Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</li> </ul>	<ul style="list-style-type: none"> <li>Aortic <math>V_{max} \geq 4</math> m/s or mean <math>\Delta P \geq 40</math> mm Hg</li> <li>AVA typically <math>\leq 1.0 \text{ cm}^2</math> (or AVAI <math>\leq 0.6 \text{ cm}^2/\text{m}^2</math>)</li> </ul>	LVEF $< 50\%$	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>D: Symptomatic severe AS</b>					
<b>D1</b>	<b>Symptomatic severe high-gradient AS</b>	<ul style="list-style-type: none"> <li>Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening</li> </ul>	<ul style="list-style-type: none"> <li>Aortic <math>V_{max} \geq 4</math> m/s or mean <math>\Delta P \geq 40</math> mm Hg</li> <li>AVA typically <math>\leq 1.0 \text{ cm}^2</math> (or AVAI <math>\leq 0.6 \text{ cm}^2/\text{m}^2</math>) but may be larger with mixed AS/AR</li> </ul>	<ul style="list-style-type: none"> <li>LV diastolic dysfunction</li> <li>LV hypertrophy</li> <li>Pulmonary hypertension may be present</li> </ul>	<ul style="list-style-type: none"> <li>Exertional dyspnea or decreased exercise tolerance</li> <li>Exertional angina</li> <li>Exertional syncope or presyncope</li> </ul>
<b>D2</b>	<b>Symptomatic severe low-flow/low-gradient AS with reduced LVEF</b>	<ul style="list-style-type: none"> <li>Severe leaflet calcification with severely reduced leaflet motion</li> </ul>	<ul style="list-style-type: none"> <li>AVA <math>\leq 1.0 \text{ cm}^2</math> with resting aortic <math>V_{max} &lt; 4</math> m/s or mean <math>\Delta P &lt; 40</math> mm Hg</li> <li>Dobutamine stress echocardiography shows AVA <math>\leq 1.0 \text{ cm}^2</math> with <math>V_{max} \geq 4</math> m/s at any flow rate</li> </ul>	<ul style="list-style-type: none"> <li>LV diastolic dysfunction</li> <li>LV hypertrophy</li> <li>LVEF <math>&lt; 50\%</math></li> </ul>	<ul style="list-style-type: none"> <li>HF</li> <li>Angina</li> <li>Syncope or presyncope</li> </ul>
<b>D3</b>	<b>Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS</b>	<ul style="list-style-type: none"> <li>Severe leaflet calcification with severely reduced leaflet motion</li> </ul>	<ul style="list-style-type: none"> <li>AVA <math>\leq 1.0 \text{ cm}^2</math> with aortic <math>V_{max} &lt; 4</math> m/s or mean <math>\Delta P &lt; 40</math> mm Hg</li> <li>Indexed AVA <math>\leq 0.6 \text{ cm}^2/\text{m}^2</math> and</li> <li>Stroke volume index <math>&lt; 35 \text{ mL}/\text{m}^2</math></li> <li>Measured when patient is normotensive (systolic BP <math>&lt; 140</math> mm Hg)</li> </ul>	<ul style="list-style-type: none"> <li>Increased LV relative wall thickness</li> <li>Small LV chamber with low stroke volume</li> <li>Restrictive diastolic filling</li> <li>LVEF <math>\geq 50\%</math></li> </ul>	<ul style="list-style-type: none"> <li>HF</li> <li>Angina</li> <li>Syncope or presyncope</li> </ul>

AR indicates aortic regurgitation; AS, aortic stenosis; AVA, aortic valve area; AVAI, aortic valve area indexed to body surface area; BP, blood pressure; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction;  $\Delta P$ , pressure gradient; and  $V_{max}$ , maximum aortic velocity.

### Left ventricular hypertrophy

#### Voltage criteria

##### Limb leads

- R wave in lead 1 plus S wave in lead III  $> 25$  mm
- R wave in lead aVL  $> 11$  mm
- R wave in lead aVF  $> 20$  mm
- S wave in lead aVR  $> 14$  mm

##### Precordial leads

- R wave in leads V4, V5, or V6  $> 26$  mm
- R wave in leads V5 or 6 plus S wave in lead V1  $> 35$  mm
- Largest R wave plus largest S wave in precordial leads  $> 45$  mm

#### Non-voltage criteria

- Delayed ventricular activation time  $\geq 0.05$  s in leads V5 or V6  $\geq 0.05$  s
- ST segment depression and T wave inversion in the left precordial leads

The specificity of these criteria is age and sex dependent

## Treatment

- No medical treatment will improve or halt progression
  - Avoidance of strenuous activity in severe AS
  - Sodium restriction if heart failure present
  - Gentle diuresis for volume overload as preload dependent
  - Control hypertension but avoid vasodilators
  - Maintain sinus rhythm
- Symptomatic patients require surgery because there is a 50% mortality rate at 2 years with medical therapy alone
  - Aortic valve replacement is a class I indication for patients with (1) severe AS, (2) asymptomatic severe AS with LVEF <50%, & (c) asymptomatic severe AS undergoing CABG or surgery on the aorta or other heart valves
  - Transcatheter aortic-valve replacement (TAVR) has been shown to reduce mortality by 20% in patients with severe AS & coexisting conditions that exclude them as candidates for surgical valvular replacement
  - Percutaneous aortic balloon valvuloplasty serves best as palliative therapy in severely symptomatic patients who are not surgical candidates & as a bridge to surgery in haemodynamically unstable adult patients

**Table 9. Summary of Recommendations for AS: Timing of Intervention**

Recommendations	COR	LOE
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity $\geq 5.0$ m/s) and low surgical risk	IIa	B
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity $\geq 4.0$ m/s (or mean pressure gradient $\geq 40$ mm Hg) with a valve area $\leq 1.0$ cm <sup>2</sup> at any dobutamine dose	IIa	B
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF $\geq 50\%$ if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	IIa	C
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C

**Table 10. Summary of Recommendations for AS: Choice of Surgical or Transcatheter Intervention**

Recommendations	COR	LOE
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk	I	A
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival $>12$ mo	I	B
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)	IIa	B
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B

## Anaesthesia

- Haemodynamic goals
  - Low normal HR (avoid tachycardia)**
  - Maintain sinus rhythm**
  - Increase LV preload (maintain a full ventricle)**
    - Optimize intravascular fluid volume to maintain venous return + LV filling
  - Increase SVR**
  - Maintain PVR**
- Patients with severe AS have a fixed CO & cannot compensate for falls in SVR which result in hypotension, myocardial ischaemia & a downward spiral of reduced contractility causing further falls in BP + coronary perfusion
- Management includes prevention of hypotension & any haemodynamic changes that will decrease CO
- Selected anaesthetic technique should maintain afterload & avoid tachycardia in order to maintain the balance between myocardial oxygen demand + supply in the presence of a hypertrophied ventricle + reduced coronary flow

- All anaesthetic drugs need to be titrated very carefully
- Induction
  - GA preferable to epidural/spinal anaesthesia (danger of hypotension due to afterload reduction)
  - Can be accomplished with an IV induction agent that does not decrease SVR
  - Performing operation using LA infiltration may be the safest method of all (surgery dependent)
- Maintenance
  - Accomplished with combination of nitrous oxide + volatile anaesthetic + opioids or by opioids alone
  - Decreases in SVR are undesirable
  - Aim to maintain BP at pre-induction levels
    - Treat hypotension with direct acting  $\alpha$ -agonists (metaraminol/phenylephrine) → improve systolic + diastolic LV function
  - Intravascular fluid volume should be maintained at normal levels
  - Arrhythmias must be treated promptly or haemodynamic collapse may occur
    - Bradycardia requires prompt treatment with glycopyrrolate/atropine/ephedrine
    - Persistent tachycardia can be treated with  $\beta$ -blockers such as esmolol
    - Supraventricular tachycardia should be promptly terminated with electrical cardioversion
    - Defibrillator should be available – patients have propensity to develop ventricular dysrhythmias
    - CPR is unlikely to be effective in patients with AS because it is difficult, if not impossible, to create an adequate SV across a stenotic aortic valve with cardiac compressions
  - Effective analgesia avoids catecholamine induced tachycardia + hypertension & risk of cardiac ischaemia
- Monitoring
  - Use of invasive monitoring determined by complexity of surgery & severity of AS
  - IAL should be routine except for very short procedures (commence before induction)
  - Consider TOE monitoring
- Postoperative
  - Low threshold for ICU/HDU admission
  - Meticulous attention to fluid balance & postoperative pain management
  - Infusions of vasoconstrictors may be required to maintain haemodynamic stability
  - Avoid NSAIDs – patients at risk of postoperative renal dysfunction

## Potential Questions

*What is the average rate of haemodynamic progression in patients diagnosed with aortic stenosis?*

- Increase in aortic jet velocity of 0.3 m/s per year
- Increase in mean trans-aortic pressure gradient of 7 mmHg per year
- Decrease in aortic valve area of 0.1 cm<sup>2</sup> per year

*What is aortic sclerosis?*

- Aortic sclerosis is defined as focal areas of valve calcification + leaflet thickening with an aortic velocity < 2.5 m/s
- Present in 25% of patients >65 years & progression to aortic stenosis occurs in ≈10% of patients within 5 years
- Associated with a 50% increased risk of MI + cardiovascular death

*What is the effect of dynamic manoeuvres on systolic cardiac murmurs?*

Manoeuvre	Hypertrophic Cardiomyopathy	MVP	Aortic Stenosis	Mitral Regurgitation
Valsalva strain phase (↓ preload)	Louder	Longer	Softer	Softer
Squatting or leg raise (↑ preload)	Softer	Shorter	Louder	Louder
Hand grip (↑ afterload)	Softer	Shorter	Softer	Louder

*What is Lee's Revised Cardiac Risk Index?*

- Tool to assess perioperative risk of major cardiac complications
- One point for each:
  1. High risk surgery (intraabdominal, intrathoracic, suprainguinal vascular)
  2. IHD
  3. CCF
  4. CVA/TIA
  5. Diabetes requiring insulin
  6. Renal impairment (serum Cr >180  $\mu$ mol/L)

Points → 0 = 0.4% risk, 1 = 1% risk, 2 = 7% risk, ≥3 = 11% risk

## Mitral Regurgitation (Oxford p68, Stoelting p37)

- Retrograde blood flow into the left atrium resulting from an incompetent mitral valve
- Causes:
  - Primary MR results from leaflet, chordal or papillary muscle abnormalities
    - Leaflet MR – complication of endocarditis, rheumatic fever or MVP
    - Chordal MR – follows chordae rupture after AMI or bacterial endocarditis
    - Papillary muscle MR – results from ischaemic posterior papillary muscle dysfunction
  - Secondary MR
    - Mitral valve usually normal
    - Severe LV dysfunction is caused either by CAD, related myocardial ischaemia or idiopathic myocardial disease
    - Abnormal & dilated LV causes papillary muscle displacement, which in turn results in leaflet tethering with associated annular dilatation that prevents coaptation
    - LVF leads to varying amounts of MR when the mitral annulus dilates
  - Other causes:
    - Trauma, congenital heart disease (endocardial cushion defect), LVH, cardiomyopathy, myxomatous degeneration, SLE, RA, ankylosing spondylitis & carcinoid syndrome
- Fraction of left ventricular SV that regurgitates into LA depends on:
  1. Size of mitral valve orifice
  2. Heart rate
  3. Pressure gradients across mitral valve

## Clinical Features

- History
  - Fatigue + weakness (due to ↓CO), dyspnoea (due to ↑LAP)
  - Acute MR presents as pulmonary oedema +/or cardiogenic shock (causes include papillary muscle rupture/dysfunction with MI, trauma/surgery or leaflet perforation/chordal rupture from IE)
- Examination
  - General – tachypnea
  - Pulse – normal or sharp upstroke due to rapid left ventricular decompensation; AF
  - Palpation – displaced + forceful apex beat, parasternal impulse
  - Auscultation
    - Soft S1, loud S3
    - Apical pan-systolic murmur with radiation to axilla
- Investigations
  - ECG – left atrial enlargement, LVH, AF
  - CXR – LA + LV enlargement, mitral annular calcification, cardiomegaly, pulmonary congestion
  - Echocardiography – dilated LA, hyperdynamic LV, quantification of severity + associated pulmonary hypertension
  - Cardiac catheterisation – to confirm severity or to rule out presence of CAD in patients being evaluated for surgical replacement

## Severity

- Signs indicating severe chronic MR – small volume pulse, enlarged left ventricle, soft S1 + loud S3, early diastolic rumble, signs of pulmonary hypertension, signs of LV failure
- Echocardiogram

Indicator	Mild	Moderate	Severe
Regurgitant volume (ml/beat)	<30	30-59	≥60
Regurgitant fraction (%)	<30	30-49	≥50
Regurgitant orifice area (cm <sup>2</sup> )	<0.2	0.2-0.39	≥0.4

- Other values to look at – indicate significant left ventricular dysfunction:
  - Ejection fraction <60%
  - End-systolic diameter >45mm

**Table 15. Stages of Primary MR**

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Hemodynamic Consequences	Symptoms
<b>A</b>	<b>At risk of MR</b>	<ul style="list-style-type: none"> <li>Mild mitral valve prolapse with normal coaptation</li> <li>Mild valve thickening and leaflet restriction</li> </ul>	<ul style="list-style-type: none"> <li>No MR jet or small central jet area &lt;20% LA on Doppler</li> <li>Small vena contracta &lt;0.3 cm</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>B</b>	<b>Progressive MR</b>	<ul style="list-style-type: none"> <li>Severe mitral valve prolapse with normal coaptation</li> <li>Rheumatic valve changes with leaflet restriction and loss of central coaptation</li> <li>Prior IE</li> </ul>	<ul style="list-style-type: none"> <li>Central jet MR 20%–40% LA or late systolic eccentric jet MR</li> <li>Vena contracta &lt;0.7 cm</li> <li>Regurgitant volume &lt;60 mL</li> <li>Regurgitant fraction &lt;50%</li> <li>ERO &lt;0.40 cm<sup>2</sup></li> <li>Angiographic grade 1–2+</li> </ul>	<ul style="list-style-type: none"> <li>Mild LA enlargement</li> <li>No LV enlargement</li> <li>Normal pulmonary pressure</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>C</b>	<b>Asymptomatic severe MR</b>	<ul style="list-style-type: none"> <li>Severe mitral valve prolapse with loss of coaptation or flail leaflet</li> <li>Rheumatic valve changes with leaflet restriction and loss of central coaptation</li> <li>Prior IE</li> <li>Thickening of leaflets with radiation heart disease</li> </ul>	<ul style="list-style-type: none"> <li>Central jet MR &gt;40% LA or holosystolic eccentric jet MR</li> <li>Vena contracta ≥0.7 cm</li> <li>Regurgitant volume ≥60 mL</li> <li>Regurgitant fraction ≥50%</li> <li>ERO ≥0.40 cm<sup>2</sup></li> <li>Angiographic grade 3–4+</li> </ul>	<ul style="list-style-type: none"> <li>Moderate or severe LA enlargement</li> <li>LV enlargement</li> <li>Pulmonary hypertension may be present at rest or with exercise</li> <li><b>C1:</b> LVEF &gt;60% and LVESD &lt;40 mm</li> <li><b>C2:</b> LVEF ≤60% and LVESD ≥40 mm</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>D</b>	<b>Symptomatic severe MR</b>	<ul style="list-style-type: none"> <li>Severe mitral valve prolapse with loss of coaptation or flail leaflet</li> <li>Rheumatic valve changes with leaflet restriction and loss of central coaptation</li> <li>Prior IE</li> <li>Thickening of leaflets with radiation heart disease</li> </ul>	<ul style="list-style-type: none"> <li>Central jet MR &gt;40% LA or holosystolic eccentric jet MR</li> <li>Vena contracta ≥0.7 cm</li> <li>Regurgitant volume ≥60 mL</li> <li>Regurgitant fraction ≥50%</li> <li>ERO ≥0.40 cm<sup>2</sup></li> <li>Angiographic grade 3–4+</li> </ul>	<ul style="list-style-type: none"> <li>Moderate or severe LA enlargement</li> <li>LV enlargement</li> <li>Pulmonary hypertension present</li> </ul>	<ul style="list-style-type: none"> <li>Decreased exercise tolerance</li> <li>Exertional dyspnea</li> </ul>

\*Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

ERO indicates effective regurgitant orifice; IE, infective endocarditis; LA, left atrium/atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; and MR, mitral regurgitation.

**Table 16. Stages of Secondary MR**

Grade	Definition	Valve Anatomy	Valve Hemodynamics*	Associated Cardiac Findings	Symptoms
<b>A</b>	<b>At risk of MR</b>	<ul style="list-style-type: none"> <li>Normal valve leaflets, chords, and annulus in a patient with coronary disease or cardiomyopathy</li> </ul>	<ul style="list-style-type: none"> <li>No MR jet or small central jet area &lt;20% LA on Doppler</li> <li>Small vena contracta &lt;0.30 cm</li> </ul>	<ul style="list-style-type: none"> <li>Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities</li> <li>Primary myocardial disease with LV dilation and systolic dysfunction</li> </ul>	<ul style="list-style-type: none"> <li>Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy</li> </ul>
<b>B</b>	<b>Progressive MR</b>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities with mild tethering of mitral leaflet</li> <li>Annular dilation with mild loss of central coaptation of the mitral leaflets</li> </ul>	<ul style="list-style-type: none"> <li>ERO &lt;0.20 cm<sup>2</sup>†</li> <li>Regurgitant volume &lt;30 mL</li> <li>Regurgitant fraction &lt;50%</li> </ul>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities with reduced LV systolic function</li> <li>LV dilation and systolic dysfunction due to primary myocardial disease</li> </ul>	<ul style="list-style-type: none"> <li>Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy</li> </ul>
<b>C</b>	<b>Asymptomatic severe MR</b>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet</li> <li>Annular dilation with severe loss of central coaptation of the mitral leaflets</li> </ul>	<ul style="list-style-type: none"> <li>ERO ≥0.20 cm<sup>2</sup>†</li> <li>Regurgitant volume ≥30 mL</li> <li>Regurgitant fraction ≥50%</li> </ul>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities with reduced LV systolic function</li> <li>LV dilation and systolic dysfunction due to primary myocardial disease</li> </ul>	<ul style="list-style-type: none"> <li>Symptoms due to coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy</li> </ul>
<b>D</b>	<b>Symptomatic severe MR</b>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities and/or LV dilation with severe tethering of mitral leaflet</li> <li>Annular dilation with severe loss of central coaptation of the mitral leaflets</li> </ul>	<ul style="list-style-type: none"> <li>ERO ≥0.20 cm<sup>2</sup>†</li> <li>Regurgitant volume ≥30 mL</li> <li>Regurgitant fraction ≥50%</li> </ul>	<ul style="list-style-type: none"> <li>Regional wall motion abnormalities with reduced LV systolic function</li> <li>LV dilation and systolic dysfunction due to primary myocardial disease</li> </ul>	<ul style="list-style-type: none"> <li>HF symptoms due to MR persist even after revascularization and optimization of medical therapy</li> <li>Decreased exercise tolerance</li> <li>Exertional dyspnea</li> </ul>

\*Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.

†The measurement of the proximal isovelocity surface area by 2D TTE in patients with secondary MR underestimates the true ERO due to the crescentic shape of the proximal convergence.

2D indicates 2-dimensional; ERO, effective regurgitant orifice; HF, heart failure; LA, left atrium; LV, left ventricular; MR, mitral regurgitation; and TTE, transthoracic echocardiogram.

## Treatment

- Medical therapy – directed toward treatment of source or its complications (eg. AF, IHD, IE, HTN, heart failure)
  - Acute severe MR – afterload reduction with SNP ( $\uparrow$  aortic flow,  $\downarrow$  LV size + restores MV competence); if hypotensive add inotropes or IABP
  - Chronic MR – antihypertensives (ACE inhibitors,  $\beta$  blockers)
- Surgery – only definitive treatment
  - Repair is preferred to replacement as it restores valve competence, maintains functional aspects of mitral valve apparatus & avoids prosthesis insertion
  - Class I indication in patients with (1) acute severe MR, (2) symptomatic patients with severe primary MR despite optimal medical therapy + LVEF  $>30\%$ , (3) asymptomatic patients with severe MR but with evidence of declining LV function (LVEF 30-60% &/or left ventricular end-systolic diameter  $>40\text{mm}$ )
  - Survival may be prolonged if surgery performed before EF is  $<60\%$  or before LV is unable to contract to an end-systolic dimension of 45 mm (normal  $<40\text{ mm}$ )
  - Patients with EF  $<30\%$  or a left ventricular end-systolic dimension  $>55\text{ mm}$  do not experience improvement with mitral valve surgery
  - Concomitant MV repair/replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications
  - Percutaneous mitral valve repair – MitraClip device approved for use in patients with significant symptomatic degenerative MR who have too high risk for surgery

**Table 17. Summary of Recommendations for Chronic Primary MR**

Recommendations	COR	LOE
MV surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF $>30\%$	I	B
MV surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30%-60% and/or LVESD $\geq 40\text{ mm}$ , stage C2)	I	B
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet	I	B
MV repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished	I	B
Concomitant MV repair or replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications	I	B
MV repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF $>60\%$ and LVESD $<40\text{ mm}$ ) in whom the likelihood of a successful and durable repair without residual MR is $>95\%$ with an expected mortality rate of $<1\%$ when performed at a Heart Valve Center of Excellence	IIa	B
MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure $>50\text{ mm Hg}$ )	IIa	B
Concomitant MV repair is reasonable in patients with chronic moderate primary MR (stage B) undergoing cardiac surgery for other indications	IIa	C
MV surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF $\leq 30\%$ (stage D)	IIb	C
MV repair may be considered in patients with rheumatic mitral valve disease when surgical treatment is indicated if a durable and successful repair is likely or if the reliability of long-term anticoagulation management is questionable	IIb	B
Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B
MVR should not be performed for treatment of isolated severe primary MR limited to less than one half of the posterior leaflet unless MV repair has been attempted and was unsuccessful	III: Harm	B

**Table 18. Summary of Recommendations for Chronic Severe Secondary MR**

Recommendations	COR	LOE
MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR	IIa	C
MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)	IIb	B
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	IIb	C

## Anaesthesia

- Haemodynamic goals
  - Maintain sinus rhythm
  - High normal HR  $\approx 80\text{bpm}$
  - Maintain preload
  - Maintain contractility
  - Decrease afterload (avoid increases in SVR)

- Induction
  - Avoid increases in SVR or decreases in HR
  - Decreases in SVR caused by neuraxial anaesthesia may be beneficial
  - Pancuronium may be a useful muscle relaxant due to a modest increase in HR
- Maintenance
  - Isoflurane, desflurane + sevoflurane are all acceptable choices because of their increase in HR, decrease in SVR & minimal negative inotropic effects
  - When myocardial function is severely compromised, opioid-based anaesthesia may be considered, although caution is advised because narcotics can produce significant bradycardia that is very deleterious in MR
- Preload can be difficult to estimate – for major non-cardiac surgery TOE may be useful to monitor magnitude of regurgitant flow
- Pulmonary hypertension is common in advanced disease → avoid factors that ↑ pulmonary artery pressure such as hypoxia, hypercarbia, high inspiratory pressures + acidosis

## Mitral Stenosis (Oxford p66, Stoelting p34)

- Narrowing of MV orifice that prevents proper opening during diastole & obstructs blood flow from LA to LV
- Primarily affects females
- Causes:
  - Rheumatic (most common)
  - Other – congenital parachute valve (all chordae insert into one papillary muscle - rare), RA, SLE, carcinoid syndrome, left atrial myxoma, following mitral valve repair

Symptoms develop with exercise at  $<2.5\text{cm}^2$  & at rest with  $<1.5\text{cm}^2$

### Clinical Features

- History
  - Symptoms – dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea ( $\uparrow\text{LAP}$ ), haemoptysis (ruptured bronchial veins), hoarseness (compression of L recurrent laryngeal nerve against pulmonary artery by dilated LA), ascites, oedema, fatigue (pulmonary HTN)
- Examination
  - General – tachypnea, ‘mitral facies’, peripheral cyanosis
  - Pulse – normal or reduced in volume, AF due to LA enlargement
  - JVP – normal, prominent a wave if pulmonary HTN, loss of a wave if AF
  - Palpation – tapping quality of apex beat, right ventricular heave, palpable P2 (pulmonary HTN)
  - Auscultation
    - Loud S1
    - Loud P2 (pulmonary HTN)
    - Opening snap
    - Low-pitched rumbling diastolic murmur (best heard with bell of stethoscope with patient in left lateral position)
- Investigations
  - ECG – LA enlargement (broad, biphasic P waves in lead V1), AF, RVH, right axis deviation
  - CXR – straightening of left cardiac border caused by enlarged LA, mitral calcification, prominence of pulmonary arteries (pulmonary HTN), pulmonary congestion + oedema (Kerley B lines)
  - Echocardiography – quantification of severity, estimate of pulmonary artery systolic pressure
  - Cardiac catheterisation – allows measurement of PAP & transmural pressure gradients

### Severity

- Signs indicating severe MS
  - Small pulse pressure, soft S1 (immobile valve cusps), early opening snap (due to  $\uparrow\text{LAP}$ ), long diastolic murmur (persists as long as there is a gradient), diastolic thrill at apex, signs of pulmonary HTN
- Echocardiogram

Indicator	Mild	Moderate	Severe
<b>Mitral valve area (<math>\text{cm}^2</math>)</b>	$>1.5$	1.0-1.5	$<1.0$
<b>Mean gradient (mmHg)</b>	$<5$	5-10	$>10$
<b>Pulmonary artery systolic pressure (mmHg)</b>	$<30$	30-50	$>50$

**Table 13. Stages of MS**

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
<b>A</b>	<b>At risk of MS</b>	• Mild valve doming during diastole	• Normal transmural flow velocity	• None	• None
<b>B</b>	<b>Progressive MS</b>	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA $>1.5 \text{ cm}^2$	• Increased transmural flow velocities • MVA $>1.5 \text{ cm}^2$ • Diastolic pressure half-time $<150 \text{ ms}$	• Mild-to-moderate LA enlargement • Normal pulmonary pressure at rest	• None
<b>C</b>	<b>Asymptomatic severe MS</b>	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA $\leq 1.5 \text{ cm}^2$ • (MVA $\leq 1.0 \text{ cm}^2$ with very severe MS)	• MVA $\leq 1.5 \text{ cm}^2$ • (MVA $\leq 1.0 \text{ cm}^2$ with very severe MS) • Diastolic pressure half-time $\geq 150 \text{ ms}$ • (Diastolic pressure half-time $\geq 220 \text{ ms}$ with very severe MS)	• Severe LA enlargement • Elevated PASP $>30 \text{ mm Hg}$	• None
<b>D</b>	<b>Symptomatic severe MS</b>	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA $\leq 1.5 \text{ cm}^2$	• MVA $\leq 1.5 \text{ cm}^2$ • (MVA $\leq 1.0 \text{ cm}^2$ with very severe MS) • Diastolic pressure half-time $\geq 150 \text{ ms}$ • (Diastolic pressure half-time $\geq 220 \text{ ms}$ with very severe MS)	• Severe LA enlargement • Elevated PASP $>30 \text{ mm Hg}$	• Decreased exercise tolerance • Exertional dyspnea

The transmural mean pressure gradient should be obtained to further determine the hemodynamic effect of the MS and is usually  $>5 \text{ mm Hg}$  to  $10 \text{ mm Hg}$  in severe MS; however, due to the variability of the mean pressure gradient with heart rate and forward flow, it has not been included in the criteria for severity.

LA indicates left atrial; LV, left ventricular; MS, mitral stenosis; MVA, mitral valve area; and PASP, pulmonary artery systolic pressure.

## Treatment

- Medical
  - Anticoagulation for prevention of systemic embolic events
  - Ventricular rate control with  $\beta$  blockers/non-dihydropyridine calcium channel blockers/digoxin & aggressive treatment of tachyarrhythmias
  - Treat congestive heart failure with diuretics + sodium restriction
- Surgery
  - Closed surgical valvotomy
  - Open surgical valvotomy
  - Mitral valve replacement
  - Percutaneous balloon mitral valvotomy

**Table 14. Summary of Recommendations for MS Intervention**

Recommendations	COR	LOE
PMBC is recommended for symptomatic patients with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage D) and favorable valve morphology in the absence of contraindications	I	A
Mitral valve surgery is indicated in severely symptomatic patients (NYHA class III/IV) with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage D) who are not high risk for surgery and who are not candidates for or failed previous PMBC	I	B
Concomitant mitral valve surgery is indicated for patients with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage C or D) undergoing other cardiac surgery	I	C
PMBC is reasonable for asymptomatic patients with very severe MS (MVA $\leq 1.0 \text{ cm}^2$ , stage C) and favorable valve morphology in the absence of contraindications	IIa	C
Mitral valve surgery is reasonable for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage D), provided there are other operative indications	IIa	C
PMBC may be considered for asymptomatic patients with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage C) and favorable valve morphology who have new onset of AF in the absence of contraindications	IIb	C
PMBC may be considered for symptomatic patients with MVA $> 1.5 \text{ cm}^2$ if there is evidence of hemodynamically significant MS during exercise	IIb	C
PMBC may be considered for severely symptomatic patients (NYHA class III/IV) with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stage D) who have suboptimal valve anatomy and are not candidates for surgery or at high risk for surgery	IIb	C
Concomitant mitral valve surgery may be considered for patients with moderate MS (MVA 1.6–2.0 $\text{cm}^2$ ) undergoing other cardiac surgery	IIb	C
Mitral valve surgery and excision of the left atrial appendage may be considered for patients with severe MS (MVA $\leq 1.5 \text{ cm}^2$ , stages C and D) who have had recurrent embolic events while receiving adequate anticoagulation	IIb	C

## Anaesthesia

- Haemodynamic goals (similar to AS given fixed CO state)
  - **Low normal HR (avoid tachycardia)**
  - **Maintain sinus rhythm**
  - **Maintain preload**
  - **Increase SVR**
  - **Maintain PVR**
- Preoperative medication
  - Used to decrease anxiety-induced tachycardia
  - Drugs used for HR control should be continued ( $\beta$ -blockers, digoxin, calcium channel blockers)
  - Treat diuretic-induced hypokalaemia
  - Discontinue anticoagulation for major surgery with anticipated significant blood loss
- Induction
  - Avoid drugs likely to ↑ HR (ketamine) or to precipitate hypotension from histamine release
- Maintenance
  - Minimise sustained changes in HR, myocardial contractility, SVR + PVR
  - Suggest narcotic anaesthetic or balanced anaesthetic with low concentrations of volatile
  - Nitrous oxide may cause pulmonary vasoconstriction, particularly if pulmonary hypertension is present
- Monitoring – consider IAL +/- TOE
- Postoperative
  - Risk of pulmonary oedema & right sided heart failure continues into postoperative period
  - Pain & hypoventilation can increase HR + PVR
  - May require continued mechanical ventilation, particularly after major thoracic/abdominal surgery

## Aortic Regurgitation (Oxford p 64, Stoelting p42)

- Retrograde blood flow into the left ventricle from the aorta as a result of an incompetent aortic valve
- Causes:
  - Leaflet abnormalities – IE, rheumatic fibrosis, trauma with valvular rupture, congenital bicuspid aortic valve, myxomatous degeneration, ankylosing spondylitis
  - Aortic root or ascending aorta abnormalities – annuloaortic ectasia, Ehlers-Danlos syndrome, Marfan's syndrome, systemic hypertension, aortic dissection

### Clinical Features

- History
  - Symptoms – many asymptomatic until late stages
    - Dyspnoea on exertion, fatigue, palpitations (hyperdynamic circulation), syncope, chest pain
- Examination
  - Pulse + BP – bounding pulses, wide pulse pressure, decreased DBP
  - Neck – prominent carotid pulsations
  - Palpation – displaced + hyperkinetic apex beat
  - Auscultation – decrescendo high-pitched early diastolic murmur along left sternal border, soft A2
  - Hill's sign – >20mmHg difference in popliteal + brachial BP
- Investigations
  - ECG – LVH
  - CXR – aortic dilation, enlarged LV, normal cardiac silhouette with pulmonary oedema (acute AR)
  - Echocardiography – quantification of severity
  - Cardiac catheterisation – indicated in selected patients to assess degree of left ventricular dysfunction + AR, when echocardiographic parameters are inconclusive & to determine if there is coexistent CAD

### Severity

- Signs indicating severe chronic AR – collapsing pulse, wide pulse pressure, long decrescendo diastolic murmur, left ventricular S3, soft A2, Austin Flint murmur, signs of LV failure
- Echocardiogram

Indicator	Mild	Moderate	Severe
Regurgitant volume (ml/beat)	<30	30-59	≥60
Regurgitant fraction (%)	<30	30-49	≥50
Regurgitant orifice area (cm <sup>2</sup> )	<0.1	0.1-0.29	≥0.3

**Table 11. Stages of Chronic AR**

Stage	Definition	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
<b>A</b>	<b>At risk of AR</b>	<ul style="list-style-type: none"> <li>Bicuspid aortic valve (or other congenital valve anomaly)</li> <li>Aortic valve sclerosis</li> <li>Diseases of the aortic sinuses or ascending aorta</li> <li>History of rheumatic fever or known rheumatic heart disease</li> <li>IE</li> </ul>	<ul style="list-style-type: none"> <li>AR severity: none or trace</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>B</b>	<b>Progressive AR</b>	<ul style="list-style-type: none"> <li>Mild-to-moderate calcification of a trileaflet valve bicuspid aortic valve (or other congenital valve anomaly)</li> <li>Dilated aortic sinuses</li> <li>Rheumatic valve changes</li> <li>Previous IE</li> </ul>	<ul style="list-style-type: none"> <li><b>Mild AR:</b> <ul style="list-style-type: none"> <li>Jet width &lt;25% of LVOT;</li> <li>Vena contracta &lt;0.3 cm;</li> <li>RVol &lt;30 mL/beat;</li> <li>RF &lt;30%;</li> <li>ERO &lt;0.10 cm<sup>2</sup>;</li> <li>Angiography grade 1+</li> </ul> </li> <li><b>Moderate AR:</b> <ul style="list-style-type: none"> <li>Jet width 25%–64% of LVOT;</li> <li>Vena contracta 0.3–0.6 cm;</li> <li>RVol 30–59 mL/beat;</li> <li>RF 30%–49%;</li> <li>ERO 0.10–0.29 cm<sup>2</sup>;</li> <li>Angiography grade 2+</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Normal LV systolic function</li> <li>Normal LV volume or mild LV dilation</li> </ul>	<ul style="list-style-type: none"> <li>None</li> </ul>
<b>C</b>	<b>Asymptomatic severe AR</b>	<ul style="list-style-type: none"> <li>Calcific aortic valve disease</li> <li>Bicuspid valve (or other congenital abnormality)</li> <li>Dilated aortic sinuses or ascending aorta</li> <li>Rheumatic valve changes</li> <li>IE with abnormal leaflet closure or perforation</li> </ul>	<ul style="list-style-type: none"> <li><b>Severe AR:</b> <ul style="list-style-type: none"> <li>Jet width ≥65% of LVOT;</li> <li>Vena contracta &gt;0.6 cm;</li> <li>Holodiastolic flow reversal in the proximal abdominal aorta</li> <li>RVol ≥60 mL/beat;</li> <li>RF ≥50%;</li> <li>ERO ≥0.3 cm<sup>2</sup>;</li> <li>Angiography grade 3+ to 4+;</li> <li>In addition, diagnosis of chronic severe AR requires evidence of LV dilation</li> </ul> </li> </ul>	<p><b>C1:</b> Normal LVEF (≥50%) and mild-to-moderate LV dilation (LVESD ≤50 mm)</p> <p><b>C2:</b> Abnormal LV systolic function with depressed LVEF (&lt;50%) or severe LV dilatation (LVESD &gt;50 mm or indexed LVESD &gt;25 mm/m<sup>2</sup>)</p>	<ul style="list-style-type: none"> <li>None; exercise testing is reasonable to confirm symptom status</li> </ul>
<b>D</b>	<b>Symptomatic severe AR</b>	<ul style="list-style-type: none"> <li>Calcific valve disease</li> <li>Bicuspid valve (or other congenital abnormality)</li> <li>Dilated aortic sinuses or ascending aorta</li> <li>Rheumatic valve changes</li> <li>Previous IE with abnormal leaflet closure or perforation</li> </ul>	<ul style="list-style-type: none"> <li><b>Severe AR:</b> <ul style="list-style-type: none"> <li>Doppler jet width ≥65% of LVOT;</li> <li>Vena contracta &gt;0.6 cm,</li> <li>Holodiastolic flow reversal in the proximal abdominal aorta,</li> <li>RVol ≥60 mL/beat;</li> <li>RF ≥50%;</li> <li>ERO ≥0.3 cm<sup>2</sup>;</li> <li>Angiography grade 3+ to 4+;</li> <li>In addition, diagnosis of chronic severe AR requires evidence of LV dilation</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Symptomatic severe AR may occur with normal systolic function (LVEF ≥50%), mild-to-moderate LV dysfunction (LVEF 40%–50%), or severe LV dysfunction (LVEF &lt;40%);</li> <li>Moderate-to-severe LV dilation is present.</li> </ul>	<ul style="list-style-type: none"> <li>Exertional dyspnea or angina or more severe HF symptoms</li> </ul>

AR indicates aortic regurgitation; ERO, effective regurgitant orifice; HF, heart failure; IE, infective endocarditis; LV, left ventricular; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVOT, left ventricular outflow tract; RF, regurgitant fraction; and RVol, regurgitant volume.

## Treatment

- Medical
  - Acute:
    - Afterload reduction – vasodilators (SNP)
    - Diuretics for pulmonary oedema
    - Avoid β blockers that can prolong diastole
    - Surgical referral for cardiogenic shock
  - Chronic:
    - Vasodilator therapy with ACE inhibitors or nifedipine
    - Diuretics + sodium restriction for heart failure
- Surgery – reserved for:
  - Patients with acute severe AR & cardiogenic shock
  - Patients with haemodynamically stable severe AR undergoing CABG or surgery on the aorta or other heart valves
  - Symptomatic patients with chronic severe AR
  - Evidence of systolic dysfunction with LVEF <50%
  - Asymptomatic patients with severe AR & LVEF >50% but with left ventricular dilation (echocardiographic end-systolic dimension >50 mm or >65 mm with low surgical risk)

**Table 12. Summary of Recommendations for AR Intervention**

Recommendations	COR	LOE
AVR is indicated for symptomatic patients with severe AR regardless of LV systolic function (stage D)	I	B
AVR is indicated for asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF <50%) (stage C2)	I	B
AVR is indicated for patients with severe AR (stage C or D) while undergoing cardiac surgery for other indications	I	C
AVR is reasonable for asymptomatic patients with severe AR with normal LV systolic function (LVEF ≥50%) but with severe LV dilation (LVESD >50 mm, stage C2)	IIa	B
AVR is reasonable in patients with moderate AR (stage B) who are undergoing other cardiac surgery	IIa	C
AVR may be considered for asymptomatic patients with severe AR and normal LV systolic function (LVEF ≥50%, stage C1) but with progressive severe LV dilation (LVEDD >65 mm) if surgical risk is low*	IIb	C

**Anaesthesia**

- Haemodynamic goals
  - **Maintain sinus rhythm**
  - **High normal HR ≈80bpm**
  - **Maintain preload**
  - **Maintain contractility**
  - **Decrease afterload (avoid increases in SVR)**
- Induction can be achieved with any IV induction agent with or without inhalational anaesthesia that does not decrease HR or increase SVR
  - Bradycardia increases amount of backward flow leading to LV volume overload
  - Abrupt increases in SVR can precipitate LVF, requiring treatment with a vasodilator for afterload reduction & an inotrope to increase contractility
- Spinal & epidural anaesthesia are well tolerated
- Maintenance is provided with nitrous oxide plus a volatile anaesthetic &/or opioid
- Intravascular fluid volume should be maintained at normal levels to provide for adequate cardiac preload
- Treat SVT/AF associated with hypotension promptly with synchronised DC cardioversion
- Persistent bradycardia can be treated with β-agonists
- Consider IAL monitoring

## Heart Failure (Oxford p54, Stoelting p120)

- Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood – as a result the heart fails to meet oxygen demand
  - May result from disorders of the pericardium, myocardium, endocardium, heart valves or great vessels, or from certain metabolic abnormalities, but most patients have symptoms due to impaired LV myocardial function
- 2% of Australian population have heart failure & prevalence rises with advancing age (>10% if >70 years)
- Cardinal manifestations are dyspnea + fatigue, which may limit exercise, & fluid retention, which may lead to pulmonary +/or splanchnic congestion +/or peripheral oedema
- Recently, the classification of heart failure has been divided into:
  - **Heart failure with reduced ejection fraction (HF-REF) / systolic heart failure**
    - Symptoms typical of heart failure
    - Clinical signs of heart failure
    - Reduced left ventricular systolic function (LVEF <50%)
  - **Heart failure with preserved ejection fraction (HF-P EF) / diastolic heart failure**
    - Symptoms typical of heart failure
    - Clinical signs of heart failure
    - Normal or only mildly reduced LVEF >50% & LV not dilated
    - Evidence of abnormal LV relaxation, filling, diastolic distensibility or diastolic stiffness supported by the presence of elevated BNP or NT-BNP levels in some circumstances &/or relevant structural heart disease (LVH/LA enlargement)
- In most patients, abnormalities of systolic + diastolic dysfunction coexist, irrespective of EF
  - Systolic HF – more common among middle-aged men because of its association with CAD
  - Diastolic HF – usually seen in elderly women because of its association with HTN, obesity + DM after menopause

Symptoms	Signs
Typical	More specific
Breathlessness	Elevated jugular venous pressure
Orthopnoea	Hepatojugular reflux
Paroxysmal nocturnal dyspnoea	Third heart sound (gallop rhythm)
Reduced exercise tolerance	Laterally displaced apical impulse
Fatigue, tiredness, increased time to recover after exercise	Cardiac murmur
Ankle swelling	
Less typical	Less specific
Nocturnal cough	Peripheral oedema (ankle, sacral, scrotal)
Wheezing	Pulmonary crepitations
Weight gain (>2 kg/week)	Reduced air entry and dullness to percussion at lung bases (pleural effusion)
Weight loss (in advanced heart failure)	Tachycardia
Bloated feeling	Irregular pulse
Loss of appetite	Tachypnoea (>16 breaths/min)
Confusion (especially in the elderly)	Hepatomegaly
Depression	Ascites
Palpitations	Tissue wasting (cachexia)
Syncope	

## Clinical Features

- History
  - LV failure – exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea
  - RV failure – ankle/sacral/abdominal swelling, anorexia, nausea
- Examination

	<b>LV failure</b>	<b>RV failure</b>
<i>General</i>	Tachypnoea (due to ↑ pulmonary pressures) Central cyanosis (due to pulmonary oedema) Cheyne-Stokes breathing Peripheral cyanosis (due to low CO) Hypotension Cardiac cachexia	Peripheral cyanosis (due to low CO)
<i>Pulse + JVP</i>	Sinus tachycardia due to ↑ sympathetic tone Low pulse pressure (low CO) Pulsus alternans (alternate strong + weak beats)	Low volume pulse (low CO) Raised JVP due to raised venous pressure
<i>Apex beat</i>	Displaced with dilation of LV Dyskinetic on anterior MI or dilated CMP Palpable gallop rhythm	Right ventricular heave
<i>Auscultation</i>	Left ventricular S3 Functional MR (2° valve ring dilatation)	Right ventricular S3 Pansystolic murmur of functional TR
<i>Lung</i>	Basal inspiration crackles (pulmonary congestion) Crackles + wheeze throughout lung fields (pulmonary oedema)	Pleural effusions
<i>Other</i>	Signs of RV failure	Tender hepatomegaly, pulsatile liver Pitting ankle + sacral oedema, ascites
<i>Causes</i>	Myocardial disease (IHD, CMP) Volume overload (AR, MR, PDA) Pressure overload (HTN, AS)	LV failure (severe chronic LVF causes raised pulmonary pressures resulting in 2° RVF) Volume overload (ASD, 1° TR) Pressure overload (PS, pulmonary HTN) Myocardial disease (RV MI, CMP)
<i>Precipitating causes</i>	Anaemia, thyrotoxicosis, AF	

- Investigations
  - Bloods – BNP (<100pg/ml = heart failure unlikely, 90% NPV; >500pg/ml = heart failure likely, 90% PPV), renal dysfunction, liver enzymes, Na, Mg, K
  - ECG – sinus tachycardia/bradycardia, AF, ventricular arrhythmias, myocardial ischaemia/infarction, Q waves, LVH, AV block, QRS duration >120ms + LBBB morphology
  - CXR – cardiomegaly, pulmonary congestion, pulmonary oedema
  - Echocardiography – most useful test in diagnosis

Measurement	Abnormality	Clinical implications
<b>Parameters related to systolic function</b>		
LV ejection fraction	Reduced (<50%)	LV global systolic dysfunction
LV fractional shortening	Reduced (<25%)	LV radial systolic dysfunction
LV regional function	Hypokinesis, akinesis, dyskinesis	Myocardial infarction/ischaemia Cardiomyopathy, myocarditis
LV end-diastolic size	Increased (diameter ≥60 mm, >32 mm/m <sup>2</sup> , volume >97 mL/m <sup>3</sup> )	Volume overload HF likely
LV end-systolic size	Increased (diameter >45 mm/>25 mm/m <sup>2</sup> , volume >43 mL/m <sup>3</sup> )	Volume overload HF likely
LV outflow tract velocity time integral	Reduced (<15 cm)	Reduced LV stroke volume
<b>Parameters related to diastolic function</b>		
LV diastolic dysfunction parameters	Abnormalities of the mitral inflow pattern, tissue velocities (e') or the E/e' ratio	Indicate LV diastolic dysfunction degree and suggest level of filling pressure
Left atrial volume index	Increased (volume >34 mL/m <sup>3</sup> )	Increased LV filling pressure (past or present) Mitral valve disease
LV mass index	Increased: >95 g/m <sup>2</sup> in women and >115 g/m <sup>2</sup> in men	Hypertension, aortic stenosis, hypertrophic cardiomyopathy
<b>Parameters related to valvular function</b>		
Valvular structure and function	Valvular stenosis or regurgitation (especially aortic stenosis and mitral regurgitation)	May be the cause of HF or a complicating factor or the result of HF (secondary mitral regurgitation) Assess dysfunction severity and haemodynamic consequences Consider surgery
<b>Other parameters</b>		
RV function (e.g.TAPSE)	Reduced (TAPSE <16 mm)	RV systolic dysfunction
Tricuspid regurgitation peak velocity	Increased (>3.4 m/s)	Increased RV systolic pressure
Systolic pulmonary artery pressure	Increased (>50 mmHg)	Pulmonary hypertension likely
Inferior vena cava	Dilated, with no respiratory collapse	Increased right atrial pressure RV dysfunction, volume overload Pulmonary hypertension possible
Pericardium	Effusion, haemopericardium, calcification	Consider tamponade, malignancy, systemic diseases, acute or chronic pericarditis, constrictive pericarditis

## Severity

- NYHA classification based on functional status – intended for patients who have structural heart disease & symptoms of heart failure

<b>Class I</b>	Ordinary physical activity does not cause symptoms
<b>Class II</b>	Symptoms occur with ordinary exertion
<b>Class III</b>	Symptoms occur with less than ordinary exertion
<b>Class IV</b>	Symptoms occur at rest

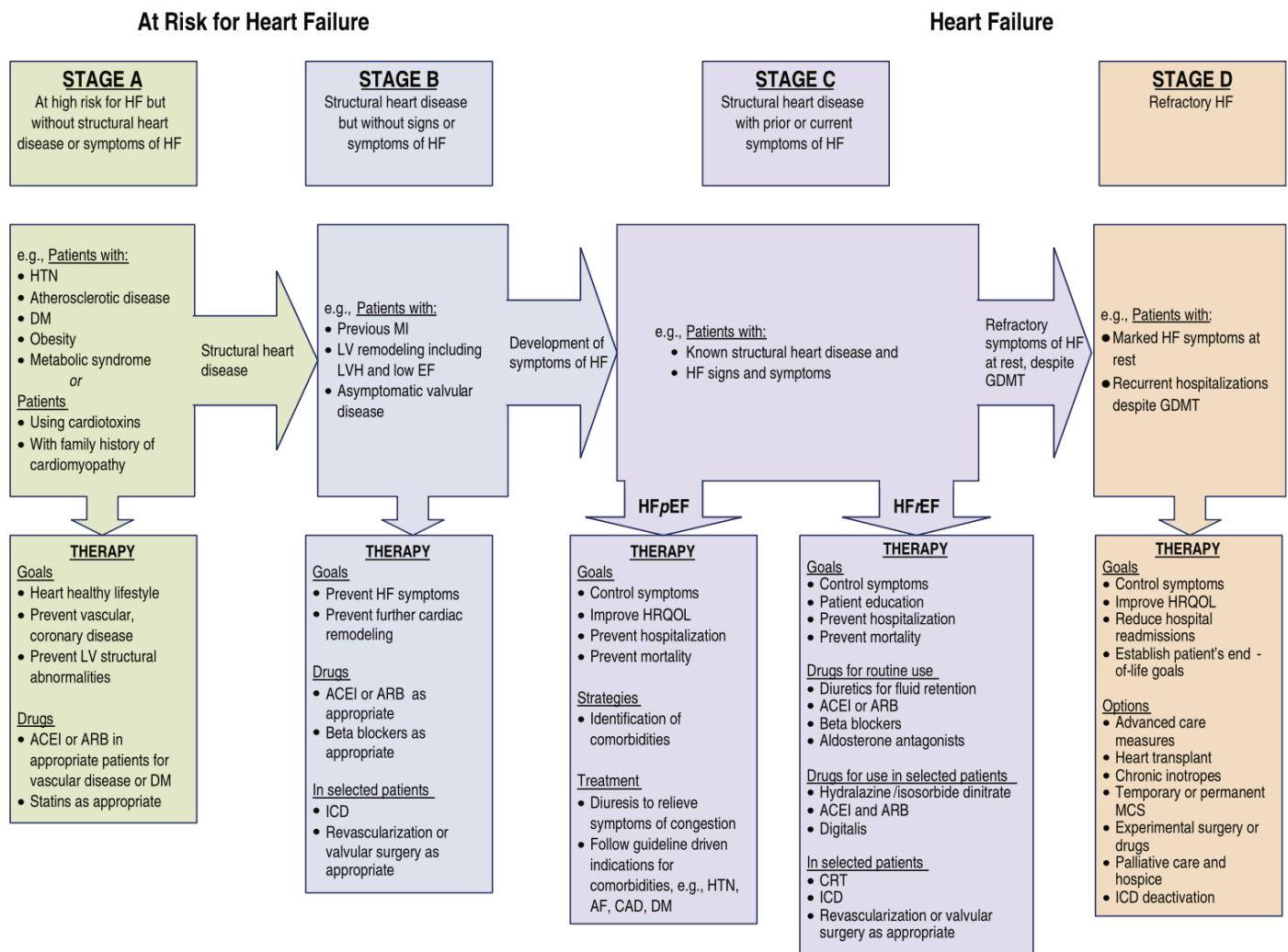
- ACC/AHA classification based on disease progression

<b>Stage A</b>	Patients at high risk of heart failure but without structural heart disease or symptoms of heart failure
<b>Stage B</b>	Patients with structural heart disease but without symptoms of heart failure
<b>Stage C</b>	Patients with structural heart disease with previous or current symptoms of heart failure
<b>Stage D</b>	Patients with refractory heart failure requiring specialized interventions

## Treatment

- Medical
  - ACE inhibitors, angiotensin II receptor blockers, β blockers, diuretics, digoxin, vasodilators, statins
- Surgical
  - Biventricular pacing/cardiac resynchronization therapy – recommended for patients with NYHA class III or IV disease with LVEF <35% & QRS duration 120-150 milliseconds
  - Implantation of a cardioverter-defibrillator (ICD) for prevention of sudden death – indications:
    - If CAD is cause – EF <30% or EF <40% if electrophysiologic study demonstrates inducible ventricular dysrhythmias
    - Other causes – after first episode of syncope or aborted VT/VF

- Recommended therapy by stage in the development of heart failure:



## Anaesthesia

- Consider (1) degree of heart failure, (2) cause & nature of cardiomyopathy, & (3) surgical procedure
- Perioperative cardiovascular risk is inversely proportional to maximal functional capacity
- Preoperative – cardiology consult, continuation of heart failure medications, ensure stable & no decompensation, treat precipitating factors, consider timing (emergency versus elective)
- Intraoperative – little evidence that any one anaesthetic technique is superior to another, ‘stable’ anaesthesia with as little myocardial depression or change in afterload as possible, IAL + CVL monitoring
- Postoperative – adequate analgesia, HDU/ICU

## **Ischaemic Heart Disease** (2014 ACC/AHA guidelines, Oxford p46, Stoelting p1)

- Condition in which there is an inadequate supply of blood & oxygen to a portion of the myocardium – typically occurs when there is an imbalance between myocardial oxygen supply & demand due to atherosclerotic coronary artery disease

### **Clinical Features**

- History
  - Determine if new onset, stable chronic CAD or ACS (STEMI/NSTEMI/UA)
  - Symptoms – at rest or with exertion?
    - Chest discomfort/pain – angina typically lasts 3-5 min but usually does not last >30 min
    - Associated fatigue, dyspnoea, weakness, lightheadedness, nausea, diaphoresis, altered mental status + syncope
  - Women + diabetics – may not present with classic symptoms, manifest more frequently with dyspnoea
  - Previous ACS (STEMI, NSTEMI, UA) & treatment received – presence of coronary stents/DAPT/CABG
- Examination
  - May be normal – perform cardiovascular examination
- Investigations
  - FBC – anaemia, electrolytes, fasting cholesterol panel, HbA1c for glycemic control
  - ECG – assess for prior cardiac injury
  - Exercise / pharmacological stress testing – risk stratification
  - Echocardiogram – assess LVEF
  - Coronary artery calcium score estimated from non-contrast CT – used to improve cardiovascular disease risk classification, CAC score  $\geq 300$  = high risk
  - Coronary angiography – assess coronary anatomy for revascularisation

### **Severity**

- Canadian Cardiovascular Society angina grading scale:

<b>Class I</b>	Angina only during strenuous or prolonged physical activity
<b>Class II</b>	Slight limitation, with angina only during vigorous physical activity
<b>Class III</b>	Moderate limitation, angina with everyday living activities
<b>Class IV</b>	Severe limitation, inability to perform any activity without angina or angina at rest

### **Treatment**

- Lifestyle modification – exercise, smoking cessation, weight loss, Mediterranean diet
- Medical
  - Treatment of hypertension, dyslipidemia (statins) & diabetes
  - Angina – nitrates (isosorbide mononitrate, GTN),  $\beta$  blockers (metoprolol, carvedilol), calcium channel blockers (amlodipine, verapamil)
  - Antiplatelet agents – aspirin or clopidogrel (combination does not  $\downarrow$  cardiovascular events in stable disease – CHARISMA trial)
  - Treatment of subsequent heart failure – ACE inhibitors for patients with chronic CAD + LVEF  $<40\%$
- Surgical
  - Percutaneous coronary intervention (PCI) – suitable in patients with suitable anatomy with refractory or lifestyle limiting angina who have failed optimal medical management; PCI has not been shown to reduce long-term rates of MI or death in patients with stable chronic CAD
  - Coronary artery bypass graft (CABG) surgery – class I indications for chronic CAD patient:
    - High grade ( $>50\%$ ) left main CAD
    - Left main CAD-equivalent anatomy including  $>70\%$  luminal stenosis in left anterior descending artery + left circumflex arteries
    - 3-vessel disease with LVEF  $<50\%$
    - Single- or 2-vessel CAD with a large area of viable myocardium at risk
    - Severe angina despite medical therapy if CABG can be performed with acceptable risk

### **Anaesthesia**

- 60 days or more should elapse after a myocardial infarction before NCS in the absence of coronary intervention – a recent MI (defined as having occurred within 6 months of NCS) is an independent risk factor for perioperative stroke & increased perioperative mortality

- Invasive cardiovascular monitoring (IAL, CVP, CO monitoring) should be used in addition to standard monitoring in high risk patients; ECG monitoring should be CM5 configuration or similar
- No evidence that any particular technique is superior
- Avoid tachycardia & hypo/hypertension to minimise myocardial ischaemia
- Good analgesia is important since uncontrolled pain is a potent cause of tachycardia – regional blocks can be very effective
- Central neuraxial blocks ameliorate the hypercoagulable state seen following anaesthesia & surgery
- Haemoglobin levels should be kept >90g/L
- Maintain normothermia
- Myocardial ischaemia may occur during emergence & extubation – hypertension & tachycardia should be anticipated & avoided – consider use of short-acting β blockers (esmolol)
- Consider postoperative HDU admission for close monitoring

## Potential Questions

*What are the risk factors for the development of ischaemic heart disease?*

- Male gender
- Increasing age
- Hypercholesterolemia (specifically a high ratio of low- to high-density lipoprotein)
- Hypertension
- Smoking
- Diabetes mellitus
- Obesity
- Sedentary lifestyle
- Genetic factors/family history

*How would you manage coronary stents perioperatively?*

Coronary stents:

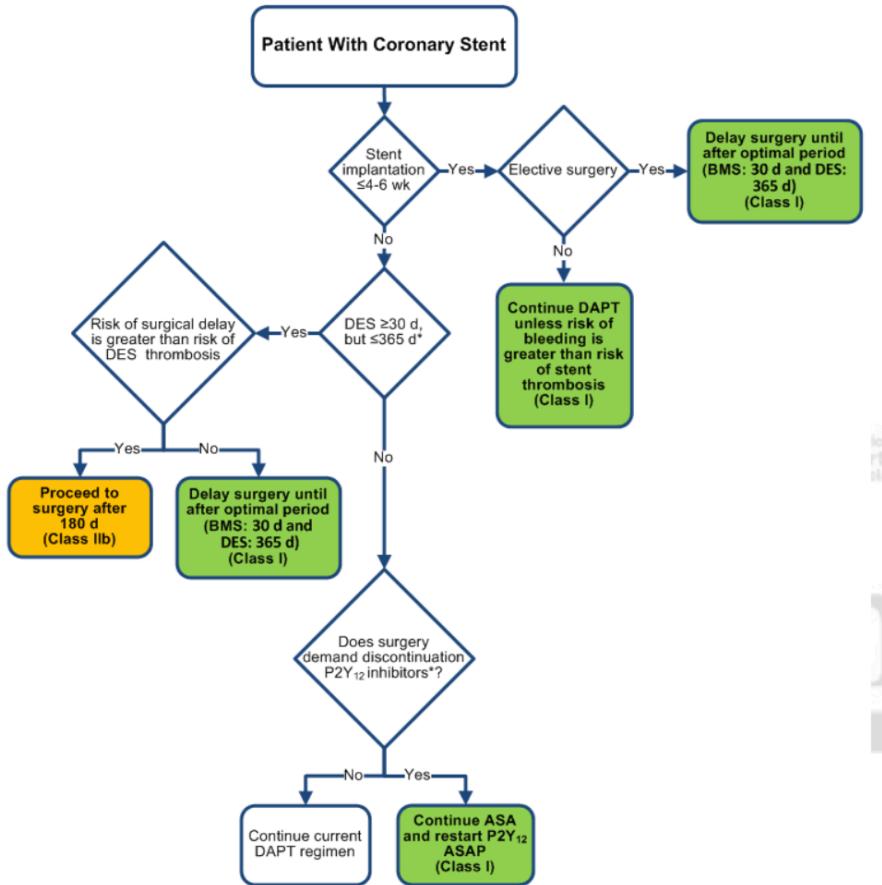
- Broadly divided into bare-metal stents (BMS) & drug-eluting stents (DES)
- May block after insertion because of thrombosis or re-stenosis
  - DAPT is required to prevent thrombosis until endothelialisation of the stent occurs
  - Stent restenosis occurs as a result of smooth muscle cell overgrowth
- BMS endothelialise quickly & reduce the risk of thrombosis but carry an increased risk of restenosis
- DES release an anti-proliferative drug to inhibit smooth muscle cell proliferation to reduce restenosis rates; unfortunately, this also slows stent endothelialisation which results in a greater risk of thrombosis without DAPT
- BMS carry a risk of restenosis of ≈14% per year (peaking at 4-9 months), whereas DES carry a restenosis risk of ≈4% over the first year
- Certain patient populations carry increased risk of stent thrombosis – patients with stents for bifurcating lesions, multiple or overlapping stents, stent length >25mm, recent MI, triple vessel disease, LVEF <30%, DM & renal insufficiency

Timing:

- Elective NCS should be delayed **30 days after BMS implantation**
- Elective NCS should optimally be delayed **365 days after DES implantation**
- Elective NCS **after DES implantation may be considered after 180 days** if the risk of further delay is greater than the expected risks of ischaemia and stent thrombosis
- Elective NCS **should not be performed within 30 days after BMS implantation or within 12 months after DES implantation** in patients in whom DAPT will need to be discontinued perioperatively

Dual antiplatelet therapy:

- In patients undergoing **urgent NCS during the first 4-6 weeks after BMS or DES implantation, DAPT should be continued** unless the relative risk of bleeding outweighs the benefit of the prevention of stent thrombosis
- In patients who have received coronary stents and must undergo surgical procedures that **mandate discontinuation of thienopyridine therapy**, it is **recommended that aspirin be continued if possible and the thienopyridine be restarted as soon as possible after surgery**
- Management of the perioperative antiplatelet therapy should be determined by a consensus of the surgeon, anaesthesiologist, cardiologist, and patient, who should weigh the relative risk of bleeding versus prevention of stent thrombosis



Colors correspond to the Classes of Recommendations in Table 1.

\*Assuming patient is currently on DAPT.

ASA indicates aspirin; ASAP, as soon as possible; BMS, bare-metal stent; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; and PCI, percutaneous coronary intervention.

### What is the definition of myocardial infarction?

#### Criteria for acute myocardial infarction

The term myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical setting consistent with myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for myocardial infarction:

- Detection of rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischaemia with at least one of the following:
  - Symptoms of ischaemia;
  - ECG changes indicative of new ischaemia [new ST-T changes or new left bundle branch block (LBBB)];
  - Development of pathological Q waves in the ECG;
  - Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Sudden, unexpected cardiac death, involving cardiac arrest, often with symptoms suggestive of myocardial ischaemia, and accompanied by presumably new ST elevation, or new LBBB, and/or evidence of fresh thrombus by coronary angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood.
- For percutaneous coronary interventions (PCI) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 3 × 99th percentile URL have been designated as defining PCI-related myocardial infarction. A subtype related to a documented stent thrombosis is recognized.
- For coronary artery bypass grafting (CABG) in patients with normal baseline troponin values, elevations of cardiac biomarkers above the 99th percentile URL are indicative of peri-procedural myocardial necrosis. By convention, increases of biomarkers greater than 5 × 99th percentile URL plus either new pathological Q waves or new LBBB, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium have been designated as defining CABG-related myocardial infarction.
- Pathological findings of an acute myocardial infarction.

#### Criteria for prior myocardial infarction

Any one of the following criteria meets the diagnosis for prior myocardial infarction:

- Development of new pathological Q waves with or without symptoms.
- Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause.
- Pathological findings of a healed or healing myocardial infarction.

What are the ECG manifestations of acute myocardial ischaemia (in absence of LVH & LBBB)?

**ST elevation**

New ST elevation at the J-point in two contiguous leads with the cut-off points:  $\geq 0.2\text{mV}$  in men or  $\geq 0.15\text{mV}$  in women in leads V2-V3 &/or  $\geq 0.1\text{mV}$  in other leads

**ST depression & T wave changes**

New horizontal or down-sloping ST depression  $\geq 0.05\text{mV}$  in two contiguous leads &/or T wave inversion  $\geq 0.1\text{mV}$  in two contiguous leads with prominent R-wave or R/S ratio  $>1$

What are the anatomical relationships of leads?

- Inferior wall – II, III, aVF
- Anterior wall – V1-V4
- Lateral wall – I, aVL, V5, V6
- V4R – most useful lead for right ventricular infarction

What is the clinical classification of different types of myocardial infarction?

<b>Type 1</b>	Spontaneous myocardial infarction related to ischaemia due to a primary coronary event such as plaque erosion &/or rupture, fissuring or dissection
<b>Type 2</b>	Myocardial infarction secondary to ischaemia due to either increased oxygen demand or decreased supply, eg. coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension or hypotension
<b>Type 3</b>	Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischaemia, accompanied by presumably new ST elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography &/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood
<b>Type 4a</b>	Myocardia infarction associated with PCI
<b>Type 4b</b>	Myocardial infarction associated with stent thrombosis as documented by angiography or at autopsy
<b>Type 5</b>	Myocardial infarction associated with CABG

What are the indications for thrombolytic therapy?

- ST elevation  $>1\text{mm}$  in two contiguous limb leads or  $>2\text{mm}$  in two contiguous chest leads
- Posterior myocardial infarction
- LBBB

ST segment depression or enzymatic changes are not indications for thrombolytic treatment.

What are the diagnostic criteria for LBBB?

Diagnostic criteria for LBBB:

- QRS duration  $\geq 0.12\text{ seconds}$
- Broad monophasic R wave in leads I, V5 + V6
- Absence of Q waves in leads V5 + V6

Associated features:

- Displacement of ST segment & T wave in an opposite direction to the dominant deflection of the QRS complex (appropriate discordance)
- Poor R wave progression in the chest leads
- RS complex, rather than monophasic complex, in leads V5 + V6
- Left axis deviation – common but not invariable finding

## Cardiomyopathies (Oxford p72)

- Diseases of the myocardium associated with cardiac dysfunction
- Classification according to anatomy & physiology:
  1. **Dilated cardiomyopathy** (includes peripartum cardiomyopathy) – defined by the presence of left ventricular dilatation & left ventricular systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease sufficient to cause global systolic impairment
  2. **Hypertrophic cardiomyopathy** – defined by the presence of increased ventricular wall thickness or mass in the absence of loading conditions (hypertension, valve disease) sufficient to cause the observed abnormality
  3. **Restrictive cardiomyopathy** – defined as ventricular physiology in the presence of normal or reduced diastolic volumes (of one or both ventricles), normal or reduced systolic volumes & normal ventricular wall thickness
  4. **Arrhythmogenic right ventricular cardiomyopathy** – defined by the presence of right ventricular dysfunction, with or without left ventricular disease, in the presence of histological evidence for the disease &/or electrocardiographic abnormalities
  5. **Unclassified cardiomyopathy** – includes – left ventricular non-compaction, Takotsubu & cirrhotic cardiomyopathy

### **Dilated Cardiomyopathy**

- Causes – idiopathic + familial, alcohol, post-viral, peripartum, drugs (doxorubicin), Duchenne's muscular dystrophy, haemochromatosis
- Manifests as cardiac failure with an enlarged poorly contractile heart; SV is initially preserved by dilatation + increased LV end-diastolic volume
- Functional mitral + tricuspid incompetence occurs commonly due to dilatation of valve annulus, exacerbating heart failure

### **Clinical Features**

- History
  - Usually presents as heart failure (left before right)– exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea
  - Functional mitral + tricuspid regurgitation
  - Arrhythmias + embolic phenomena
  - Treatment
  - Family history
- Examination
  - Signs of heart failure & MR + TR
- Investigations
  - Bloods - renal dysfunction, liver function, electrolytes
  - ECG – ST + T wave abnormalities, LBBB, premature beats, AF, LVH
  - CXR – cardiomegaly, pulmonary congestion, pulmonary oedema
  - Echocardiogram – typically reveals four chamber dilation (especially LV), global hypokinesis + valvular regurgitation

### **Treatment**

- Medical
  - Fluid restriction, low sodium diet
  - Heart failure medications – diuretics, ACE inhibitors, vasodilators
  - Amiodarone for arrhythmias (has least myocardial depressant effect)
  - Anticoagulation (embolisation risk)
- Surgical
  - Biventricular pacing
  - Defibrillator (ICD)
  - Heart transplantation

### **Anaesthesia**

- Maintain sinus rhythm
- Adequate volume loading
- Normal SVR
- Avoid myocardial depression – inotropic support is frequently required with dobutamine or PDE inhibitors
- Invasive cardiovascular monitoring – IAL, CVL, CO monitor, TOE

## Hypertrophic Obstructive Cardiomyopathy (HOCM)

- Unknown aetiology – possibly inherited as an autosomal dominant condition in >50% of cases (sarcomeric heavy chain or troponin gene mutation)
- Causes dynamic obstruction of left ventricular outflow during systole
  - Main feature is asymmetric hypertrophy of interventricular septum, which obstructs outflow tract when it contracts
  - Ventricular systole associated with movement of anterior mitral valve leaflet towards the septum (systolic anterior motion) & outflow tract is further obstructed (may cause MR in some patients)
  - Results in pressure overload of left ventricle
  - Diastolic dysfunction evidence on echocardiogram

### Clinical Features

- History
  - Present with symptoms similar to AS – angina, dyspnoea, syncope, palpitations
  - Family history of sudden death (secondary to VF or a sudden increase in outflow obstruction)
- Examination
  - Pulse – sharp, rising + jerky
  - JVP – prominent a wave due to forceful atrial contraction
  - Palpation – double or triple apical impulse due to presystolic expansion of ventricle caused by atrial contraction
  - Auscultation – late systolic murmur at lower left sternal edge + apex (due to the obstruction), pansystolic murmur at apex (due to MR); outflow murmur increased by valsalva maneuver/standing + decreased by squatting
- Investigations
  - ECG – LVH
  - Echocardiogram – essential to estimate degree of functional obstruction, asymmetric LVH & systolic anterior motion of mitral valve
- Definitive diagnosis made by endomyocardial biopsy + DNA analysis – but only in patients who cannot be diagnosed by other means
- Severity
  - Syncope or presyncope suggest high risk of sudden death
  - Signs of heart failure or MR

### Treatment

- Medical
  - $\beta$  blockers lessen myocardial oxygen requirement + blunt SNS activity
  - Calcium channel blockers (verapamil)
  - Amiodarone – effective to prevent paroxysms of AF
- Surgical
  - Myectomy – relieved outflow tract obstruction by excising part of the septal myocardium involved in the dynamic obstruction
  - Alcohol septal ablation
  - ICD implantation

### Anaesthesia

- Maintain a 'large ventricle' since dynamic obstruction is reduced
- Invasive haemodynamic monitoring
- Goals
  - Low normal HR
  - Maintain sinus rhythm
  - Adequate volume loading – avoid hypovolemia
  - High normal SVR
  - Low ventricular contractility (inotropes contraindicated as LVOT exacerbated by increased myocardial contractility)
- Metaraminol (direct acting  $\alpha$  agonist) may be used in an emergency

## **Restrictive Cardiomyopathy**

- Rare condition
- Commonest cause is myocardial infiltration by amyloid
- Other causes – idiopathic, eosinophilic endomyocardial disease, endomyocardial fibrosis, haemochromatosis + granulomas (sarcoid)
- Characterised by stiff ventricles that impair ventricular filling
- Right heart failure often prominent
- Echocardiography shows diastolic dysfunction
- Will see signs of heart failure with minimal cardiomegaly or systolic dysfunction

## **Clinical Features**

- History
  - Cardiorespiratory symptoms often present at late stage, symptoms similar to heart failure
    - Paroxysmal nocturnal dyspnoea, orthopnoea, exercise intolerance, fatigue
    - Angina – primarily in amyloidosis
- Examination (similar to constrictive pericarditis)
  - Pulse + BP – pulsus paradoxus, low BP, AF with infiltrative disease
  - JVP - raised, prominent x + y descents
  - Palpation – usually palpable (impalpable in constrictive pericarditis)
  - Auscultation – distant heart sounds, early S3
  - Signs of right heart failure – peripheral oedema, hepatomegaly, splenomegaly
- Investigations
  - ECG – conduction abnormalities, low voltage
  - CXR – signs of pulmonary congestion with minimal cardiomegaly
  - Echocardiogram – diastolic dysfunction, atrial enlargement, increased LV wall thickness

## **Treatment**

- Medical – similar to diastolic heart failure – diuretics, digoxin, anticoagulation for AF
- Surgical
  - ICD may be necessary for ventricular dysrhythmias in cardiac sarcoidosis
  - Cardiac transplant is NOT an option for sarcoidosis as infiltration will recur

## **Anaesthesia**

- Hazardous
- Avoid peripheral vasodilatation, myocardial depression & reduced venous return – may cause catastrophic cardiovascular decompensation + precipitate cardiac arrest
- Spontaneous respiration is preferable to avoid PPV compromising venous return
- Ketamine is useful for induction because it increases myocardial contractility + peripheral resistance
- Goals
  - Maintain sinus rhythm
  - Adequate volume loading
  - High normal SVR
  - Avoid myocardial depression

## Atrial Fibrillation (Oxford p86, Stoelting p80)

- Defined as a supraventricular tachyarrhythmia characterised by uncoordinated atrial activation with consequent deterioration of atrial mechanical function
- Two key features:
  1. *Rapid atrial depolarization* – reduces effective atrial contractile function, which increases stasis within atrium, thrombosis & risk of systemic thromboembolism
  2. *Irregular ventricular response* – varies widely from slow (30-40bpm) to very rapid (200bpm)
- Most common sustained arrhythmia
- Associated with specific cardiovascular conditions:
  - Valvular heart disease (classically mitral stenosis + regurgitation)
  - Coronary artery disease
  - Systemic hypertension
  - Some congenital heart diseases (ASD)
- Factors associated with increased risk of AF
  - Increasing age
  - Myocardial infarction, mitral or tricuspid disease, hypertension, myocarditis, hypertrophic cardiomyopathy, heart failure
  - Acute exacerbations of asthma/COPD
  - Electrolyte imbalances – ↓K, ↓Mg, ↓ or ↑Ca
  - Acute infection – pneumonia, sepsis
  - Phaeochromocytoma, hyperthyroidism
  - Alcohol use
  - Surgery – cardiothoracic
- Classification

<b>Paroxysmal AF</b>	AF that terminates spontaneously or with intervention within 7 days of onset Episodes may recur with variable frequency
<b>Persistent AF</b>	Continuous AF that is sustained > 7 days
<b>Longstanding persistent AF</b>	Continuous AF > 12 months duration
<b>Permanent AF</b>	Joint decision by patient & clinician to cease further attempts to restore &/or maintain sinus rhythm
<b>Non-valvular AF</b>	AF in absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair

## Clinical Features

- History
  - Symptoms – palpitations, dyspnoea, dizziness, presyncope, syncope, chest pain, fatigue, heart failure
  - Determine if paroxysmal or persistent
  - Current treatment
  - Thromboembolic risk assessment – ask about previous TIA/CVA, hypertension, CCF, diabetes
- Examination
  - Irregular pulse
  - Irregular jugular venous pulsations
  - Associated heart failure
  - Associated myocardial abnormalities – hypertrophic cardiomyopathy
  - Associated valvular disease – MS, MR, MVP
- Investigations
  - INR – warfarin therapy
  - ECG – irregular rhythm, loss of P waves, variable ventricular rate
  - TFT – exclude thyrotoxicosis as precipitant
  - CXR
  - TTE – structural defects, ↑LA size + mass = positive predictors of AF
  - TOE – before cardioversion to detect LA thrombus
  - Stress test (exercise or pharmacological) – useful if coronary ischaemia suspected
  - Holter monitor – useful to determine ventricular rate & diagnosis

## Severity

- Canadian Cardiovascular Society Severity of Atrial Fibrillation (CCSSAF) scale:

<b>Step 1 - Symptoms</b>
Identify the presence of the following symptoms:
- Palpitation
- Dyspnoea
- Dizziness, presyncope or syncope
- Chest pain
- Weakness or fatigue
<b>Step 2 - Association</b>
Is AF, when present, associated with the above-listed symptoms?
<b>Step 3 - Functionality</b>
Determine if the symptoms associated with AF (or the treatment of AF) affects the patient's functionality (subjective QOL)

<b>Class 0</b>	Asymptomatic with respect to AF
<b>Class 1</b>	Symptoms attributable to AF have <i>minimal</i> effect on patient's QOL - Minimal &/or infrequent symptoms - Single episode of AF without syncope or heart failure
<b>Class 2</b>	Symptoms attributable to AF have a <i>minor</i> effect on patient's general QOL - Mild awareness of symptoms in patients with persistent/permanent AF - Rare episodes (eg. less than a few per year) in patients with paroxysmal or intermittent AF
<b>Class 3</b>	Symptoms attributable to AF have a <i>moderate</i> effect on patient's general QOL - Moderate awareness of symptoms on most days in patients with persistent/permanent AF - More common episodes (eg. more than every few months) or more severe symptoms, or both, in patients with paroxysmal or intermittent AF
<b>Class 4</b>	Symptoms attributable to AF have a <i>severe</i> effect on patient's general QOL - Very unpleasant symptoms in patients with persistent/paroxysmal AF - Frequent & highly symptomatic episodes in patients with paroxysmal or intermittent AF - Syncope thought to be due to AF - Congestive heart failure secondary to AF

- CHADS<sub>2</sub> score or CHA<sub>2</sub>DS<sub>2</sub>-VASc score recommended for assessment of stroke risk:

<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc Acronym</b>	<b>Score</b>
<i>Congestive heart failure</i>	1
<i>Hypertension</i>	1
<i>Age &gt;75 years</i>	2
<i>Diabetes mellitus</i>	1
<i>Stroke/TIA</i>	2
<i>Vascular disease</i>	1
<i>Age 65-74 years</i>	1
<i>Sex – Female</i>	1
<b>Maximum score</b>	<b>9</b>
<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc Score</b>	<b>Adjusted Stroke Rate (% per year)</b>
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	15.20

<b>CHADS<sub>2</sub> Acronym</b>	<b>Score</b>
<i>Congestive heart failure</i>	1
<i>Hypertension</i>	1
<i>Age &gt;75 years</i>	1
<i>Diabetes mellitus</i>	1
<i>Stroke/TIA</i>	2
<b>Maximum score</b>	<b>6</b>
<b>CHADS<sub>2</sub> Score</b>	<b>Adjusted Stroke Rate (% per year)</b>
0	1.9
1	2.8
2	4.0
3	5.9
4	8.5
5	12.5
6	18.2

## Treatment

- New-onset AF
  - Unstable (hypotension, pulmonary oedema or angina) → synchronised cardioversion (shock 100-200J)
  - Stable → rate control, cardioversion +/- heparin (debated)

- Acute rate control (aim <100bpm) →  $\beta$  blockers (**metoprolol, esmolol**), calcium channel blockers (**verapamil, diltiazem**), **amiodarone, digoxin + magnesium**
  - $\beta$  blockers should not be used if left ventricular function is depressed or unknown
  - Digoxin is better in patients with preexisting heart failure because it does not have negative inotropic effects
  - Calcium channel blockers induce more hypotension than other agents
- Acutely, pharmacologic cardioversion (flecainide) is less commonly used than electrical cardioversion
- Thromboembolism risk with cardioversion if duration of AF >48 hours or unknown; two approaches to mitigate this risk:
  - Anticoagulate continuously for 3 weeks before & a minimum of 4 weeks after cardioversion
  - Start anticoagulation & perform TOE to determine if thrombus present in left atrial appendage
- Chronic
  - Ventricular rate control (aim <80bpm)
    - $\beta$  blockers (**metoprolol, bisoprolol**), calcium channel blockers (**verapamil, diltiazem**), **digoxin**
  - Rhythm control strategies
    - **Flecainide** – avoid in heart failure or CAD because of negative inotropic + proarrhythmic effects
    - **Sotalol** – risk of inducing excessive QT prolongation & torsades des pointes
    - **Amiodarone** – potential toxicity so reserved for patients resistant to other agents
    - **Catheter or surgical ablation**
  - As per the AFFIRM and RACE trials, either rate control or rhythm control strategies show no difference in composite cardiovascular end points of death, CHF, bleeding, drug side effects or thromboembolism → both approaches have similar outcomes as long as appropriate anticoagulation is maintained based on individual stroke risk
  - Anticoagulation to reduce stroke risk
    - Recommended for patients with AF who have mechanical heart valves & non-valvular AF with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score ≥ 2
    - Options – **warfarin** (vitamin K antagonist), **dabigatran** (direct thrombin inhibitor; not for mechanical valves) or **rivaroxaban + apixaban** (factor Xa inhibitors)
      - Warfarin ↓ annual stroke risk by 64% compared to placebo & by 37% compared to antiplatelet therapy
    - Major risk is bleeding – risk factors include ↑ age, heart failure, anaemia & EtOH/NSAID use

## Anaesthesia

- Perioperative anticoagulation management
  - Bridging therapy (UFH/LMWH) recommended for all patients with AF & a mechanical heart valve
  - For patients with AF & no mechanical heart valve, decisions regarding bridging therapy should balance the risks of stroke & bleeding

Cease warfarin 5 days prior to surgery		
Risk Stratum	CHADS <sub>2</sub> Score & Other Considerations	Perioperative LMWH (Clexane)
High risk	CHADS <sub>2</sub> score 5 & 6 Recent (within 3 months) stroke or TIA Rheumatic valvular heart disease	5 doses of 1mg/kg Start on operation day -3 Twice daily dosing Last dose in morning on operation day -1
Medium risk	CHADS <sub>2</sub> score 3 & 4	3 doses of 0.5mg/kg Start on operation day -3 Last dose in morning of operation day -1
Low risk	CHADS <sub>2</sub> score 0 & 2 No prior stroke or TIA	No LMWH
Recommence warfarin on night of surgery		
Continue LMWH until INR in target range		

- Recognise reduced ventricular filling & cardiac output due to loss of atrial kick
- Monitor electrolytes
- Most common postoperative tachydysrhythmia – especially in elderly patients undergoing cardiothoracic surgery

## Potential Questions

How are anti-arrhythmics classified?

### Class 1

- Inhibit fast Na channels during depolarization (phase 0) of cardiac action potentials with resultant decreases in depolarization rate & conduction velocity
  - Ia – Na channel blockade prolongs refractory period of cardiac muscle – *quinidine, procainamide*
  - Ib – Na channel blockade shortens refractory period of cardiac muscle – *lignocaine*
  - Ic – Na channel blockade has no effect on refractory period of cardiac muscle – *flecainide, propafenone*

### Class 2

- Decrease the rate of spontaneous phase 4 depolarisation resulting in decreased ANS activity – β blockade – *esmolol, metoprolol*

### Class 3

- Inhibit K channels resulting in prolongation of cardiac depolarisation, AP duration & effective refractory period – K channel blockade – *amiodarone, sotalol*

### Class 4

- Inhibit inward slow Ca currents that may continue to the development of VT – Ca channel blockade – *verapamil, diltiazem*

## Cardiac Implantable Electronic Devices (Oxford p94)

### Indications

<i>Permanent Pacemaker</i>	<i>Implantable Cardiac Defibrillators (ICDs)</i>
<ul style="list-style-type: none"> <li>Symptomatic SA node dysfunction</li> <li>Symptomatic AV node dysfunction</li> <li>Post-MI heart block</li> <li>Sick sinus syndrome</li> <li>Long QT syndrome</li> <li>Biventricular pacing for resynchronisation in heart failure</li> </ul>	<ul style="list-style-type: none"> <li>Prior cardiac arrest (VF/VT)</li> <li>NYHA class II or III non-ischemic dilated cardiomyopathy, EF &lt;30%</li> <li>Prior MI (&gt;40days), EF &lt;30%</li> <li>Structural heart disease or inherited arrhythmia syndromes (long QT, Brugada)</li> <li>Syncope of unknown origin</li> </ul>

### Pacemaker Code – PSRPM

Position 1	Position 2	Position 3	Position 4	Position 5
<b>Pacing</b>	<b>Sensing</b>	<b>Response</b>	<b>Programmability</b> <i>(specifies absence or presence of rate modulation)</i>	<b>Multisite Pacing</b> <i>(is there biventricular pacing?)</i>
O = none A = atrium V = ventricle D = dual (A+V)	O = none A = atrium V = ventricle D = dual (A+V)	O = none I = inhibited T = triggered D = dual (T+I)	O = none R = rate modulation	O = none A = atrium V = ventricle D = dual (A+V)

### ICD Code – SATP

Position 1	Position 2	Position 3	Position 4
<b>Shock Chamber(s)</b> <i>(defibrillation)</i>	<b>Antitachycardia Pacing Chamber(s)</b>	<b>Tachycardia Detection</b>	<b>Antibradycardia Pacing Chamber(s)</b> <i>(pacemaker)</i>
O = none A = atrium V = ventricle D = dual (A+V)	O = none A = atrium V = ventricle D = dual (A+V)	E = electrogram H = haemodynamic	O = none A = atrium V = ventricle D = dual (A+V)

### Assessing Severity

- Functional status & underlying cardiovascular disease

### Anaesthesia

Preoperatively:

- Determine if device is present & its functionality (eg. PPM or ICD)
- Notify cardiology department about planned procedure, potential sources of electromagnetic interference, admission date & anticipated post-procedural arrangements
- Request a device check
- Decide if reprogramming (programmer or magnet) is necessary
  - PPM needs to be reprogrammed to an asynchronous mode without rate responsiveness if patient pacemaker-dependent & distance from device to source of EMI is <15 cm
  - ICD will require suspension of antitachycardia function if there will be EMI associated with the procedure
- Confirm availability of cardiac technician for surgery date

Intraoperatively:

- Ensure availability of a backup source of pacing & defibrillation (pads on if high-risk)
- Assess pacemaker function with 5-lead ECG (disable filter artefact) & peripheral pulse monitoring
- Manage EMI – minimise diathermy use (short, irregular bursts + lowest energy level), consider bipolar diathermy or harmonic scalpel, avoid diathermy path being across pacemaker system
- Manage pacemaker dysfunction due to EMI
- Emergency management of pacemaker failure or dysrhythmia

Postoperatively:

- Return altered programming to previous settings as soon as possible – keep patient in monitored environment with backup source of pacing & defibrillation until settings restored
- Formal pacemaker testing if dysfunction occurred

## Long-QT Syndrome

QTc : Men  $\geq 450$ msec; Women  $\geq 470$ msec; caused by malfunctioning ion channels impairing ventricular repolarisation.  
(Women more likely as longer QT)

Predisposes to polymorphic VT – Torsades de Pointes

Strongest association if QTc  $> 500$ msec → tachycardia reduces the time for repolarisation & increases risk of TdP

Types:

- i. **Acquired** (most common), causes: Drugs (amiodarone, quinidine, erythromycin, droperidol, haloperidol, procainamide, flecainide, methaone); Electrolytes ( $\downarrow K \downarrow Mg$ ); Starvation; Intracranial injury; HOCM
- ii. **Congenital** - (+8 other genotypes)
  - a. Jervell- Lange- Neilsen syndrome – autosomal recessive + congenital deafness
  - b. Romano-Ward syndrome – autosomal dominant

### Key points in history

History of syncopal events - usually associated with ↑ sympathetic stimulation

Episodes of VT/VF + treatments

Family history of sudden death or inherited disorders

Medications:

- potential causative agents
- Beta Blockers (reduce mortality from 50 → 5% over 10yrs) often incorporated with PPM

Having pacemaker with higher backup rate can prevent the bradycardia that precedes TdP + abort the dysrhythmia

If undifferentiated, ask about other causes of sudden death – CAD, myocardial disease, valvular disease, aortic disease (dissection) + other electrophysiologic diseases

### Key bedside signs

May be few signs

AICD – signifies previous episode of VT/VF

### Differential diagnosis

Sudden cardiac death causes as above (Coronary; Myocardial; Valvular; Aortic; Electrophysiologic)

Other electrophysiologic abnormalities associated with sudden death:

- Sick sinus syndrome
- Brugada syndrome – autosomal dominant Na channel mutation, common in Asian men – ECG shows persistent ST elevation V1-V3 with RBBB

### Medical management and optimization

#### Pre-op optimisation:

- All should be on Beta Blockers with HR  $< 130$ bpm during exercise or no change with Valsalva
- Electrolytes – K, Mg, Ca should be normal range, Check pre-op ECG for QTc
- Check AICD + have backup defib pads on patient
- Premed for calm patient

#### Intra-op

- Monitoring – 5lead ECG, IAL
- Aim to avoid excessive sympathetic activity – laryngoscopy, intubation, extubation
- Avoid drugs which prolong QT
- Have management plan ready for arrhythmia – pacing, defib, drugs (Mg)

#### Post-op

- Continue β blocker, good analgesia, continuous ECG monitoring

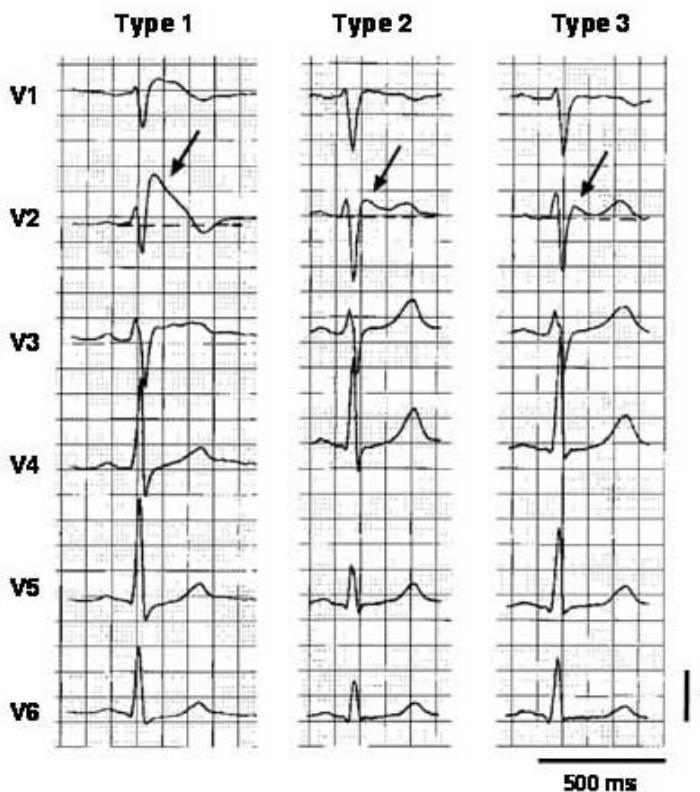
### **Anaes Drugs**

- Volatiles – Prolong QT
- Propofol – No effect
- Thiopentone – Prolong QT
- Midazolam – No effect
- Sux – Prolong QT
- NDMRs – No effect
- Atropine + Glyco – Prolong QT
- Droperidol – Prolong QT

## Brugada Syndrome (aka Idiopathic Ventricular Fibrillation)

- Familial disorder characterized by spontaneous idiopathic ventricular fibrillation
- Prevalence  $\approx$  1:10,000 to 5:10,000 in general Western population; higher frequency in eastern countries
- One of the most frequent causes of sudden death in patients with a structurally normal heart
- Autosomal dominant genetic inheritance
- Pathophysiology
  - Caused by mutations in gene encoding the  $\alpha$ -subunit of voltage-gated sodium channel type V (SCN5A)
  - A reentrant mechanism has been evoked
  - Loss of the dome of the AP occurs because of an ion imbalance during phase 1 of the AP
  - Increasing the K current increases ST-segment elevation, whereas interventions increasing Ca current diminish ST-segment elevation & vice versa
- Diagnosis
  - Based on typical electrocardiographic pattern of ST-segment elevation in leads V1 to V3 & incomplete or complete RBBB
  - Three ECG patterns have been described:

Characteristic	Type 1	Type 2	Type 3
J wave amplitude	$\geq 2$ mm	$\geq 2$ mm	$\geq 2$ mm
T wave	Negative	Positive or biphasic	Positive
ST-T configuration	Coved-type	Saddleback	Saddleback
ST segment, terminal portion	Gradually descending	Elevated by $\geq 1$ mm	Elevated by $< 1$ mm



*Three types of ST-segment elevation in Brugada syndrome, as shown in the precordial leads on ECG in the same patient at different times.*

- ⇒ Left panel shows a type 1 ECG pattern with pronounced elevation of the J point (arrow), a coved-type ST segment, and an inverted T wave in V1 and V2
- ⇒ Middle panel illustrates a type 2 pattern with a saddleback ST-segment elevated by  $> 1$  mm
- ⇒ Right panel shows a type 3 pattern in which the ST segment is elevated  $< 1$  mm

- Genetic studies can confirm diagnosis, but a negative result does not exclude it
- Clinical aspects
  - Syncope & cardiac arrest, typically occurring in 3<sup>rd</sup> + 4<sup>th</sup> decade of life, usually at rest or during sleep; however, all ages can be symptomatic
  - Classification of patients is not clearly established, but history of syncope & spontaneous ECG modifications seems to bear a bad prognosis
  - Intracardiac defibrillators have been used successfully
- Precautions before anaesthesia
  - Obtain full family & personal history
  - Evaluate cardiac status (clinical, ECG)
  - Evaluate perioperative electrolyte levels (Na, Ca, K)
- Anaesthetic considerations
  - Successful anesthetic management of patients with Brugada syndrome has been described for general & regional anesthesia
  - Resuscitation devices must be present at all times (internal or external defibrillator)

- Perioperative cardiac monitoring is imperative
  - In high-risk patients (syncope & spontaneous ECG modifications), benefit of preoperative ICD implantation must be considered
- Pharmacological implications
  - Perioperative fluid regimen must carefully consider the absolute necessity of electrolyte equilibrium
  - Calcium blockers should be avoided
  - Amiodarone has been used successfully in some patients
- Other conditions to be considered
  - Arrhythmogenic Right Ventricular Dysplasia
    - Most often inherited disease of the myocardium resulting in cardiomyopathy & risk of sudden death in otherwise healthy young adults

## **Pulmonary Hypertension** (Stoelting p114)

- Defined by WHO as an increase in mean pulmonary arterial pressure > 25 mmHg at rest as assessed by right heart catheterisation

### **Clinical Features**

- History
  - Symptoms – dyspnoea, angina (RV ischaemia), syncope (low CO with failing RV), oedema
  - Functional status
  - Treatment, specific drugs (anticoagulation, infusions)
  - Investigations to date
- Examination
  - General signs – tachypnea, peripheral cyanosis, cold extremities, hoarseness (due to pulmonary artery compression of left recurrent laryngeal nerve)
  - Pulse – small volume due to low CO
  - JVP – elevated with prominent a wave
  - Chest
    - Right ventricular heave
    - Auscultation
      - Systolic ejection click (due to dilatation of pulmonary artery)
      - Loud P2 (due to forceful valve closure because of high pulmonary artery pressures)
      - Right ventricular 4<sup>th</sup> HS (reflects diastolic filling of hypertrophied + non-compliant RV)
      - Pulmonary ejection murmur (due to pulmonary artery dilatation causing turbulent flow)
      - Pansystolic murmur of TR
      - Diastolic murmur of PR (if dilatation of pulmonary valve occurs)
  - Peripheral oedema
  - Hepatomegaly, ascites
- Investigations for cause & severity
  - CXR – prominent pulmonary vessels, cardiomegaly, parenchymal lung disease
  - ECG – right axis deviation, RV strain or hypertrophy, RBBB
  - ABG – hypoxemia
  - RFTs – low DLCO, obstructive or restrictive pattern
  - CT chest or V/Q scan – abnormal perfusion
  - 6MWT – reduced total distance (normal >400m) predicts worse prognosis, monitors treatment response
  - Echocardiography – systolic pulmonary artery pressure (estimated from velocity of TR & right atrial pressure using Bernoulli equation – SPAP =  $4v^2 + RAP$ ), right atrial enlargement, reduced tricuspid annular phase systolic excursion (TAPSE), pericardial effusion
  - Right heart catheterisation – gold standard for diagnosis

### **Differential Diagnosis – Classification**

- Pulmonary arterial hypertension – idiopathic PAH, heritable, drug induced, associated with connective tissue diseases/portal hypertension/HIV
- Pulmonary hypertension due to left heart disease – left ventricular systolic/diastolic dysfunction, valvular (mitral + aortic) disease
- Pulmonary hypertension due to lung diseases &/or hypoxia – COPD, interstitial lung disease, OSA
- Chronic thromboembolic pulmonary hypertension
- Pulmonary hypertension with unclear multifactorial mechanisms – haematological disorders, sarcoidosis, metabolic disorders, tumour obstruction, chronic renal failure

### **Severity**

- Functional classification based on symptomatology – important predictor of survival:
  - Class I + II – 6 years
  - Class III – 2.5 years
  - Class IV – 6 months

<i>Class I</i>	Patients with PH but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnoea or fatigue, chest pain or near syncope.
<i>Class II</i>	Patients with PH resulting in a slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnoea or fatigue, chest pain or near syncope.
<i>Class III</i>	Patients with PH resulting in marked limitation of physical activity. Less than ordinary activity causes undue dyspnoea or fatigue, chest pain or near syncope.
<i>Class IV</i>	Patients with PH with an inability to carry out physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnoea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

**Table 3** Variables used in clinical practice to determine response to therapy and prognosis in patients with PAH

Variables	Good response to therapy and better prognosis
WHO functional class	Class I or II
Echocardiography/CMR	Normal/near normal RV size and function
Hemodynamics	Normalization of RV function (RAP<8 mmHg and CI>2.5–3.0 L/min/m <sup>2</sup> )
6 min walking distance	>380–440 m; may not be aggressive enough in young individuals
Cardiopulmonary exercise testing	Peak VO <sub>2</sub> >15 mL/min/kg and EqCO <sub>2</sub> <45 L/min/L/min
B-type natriuretic peptide level	Normal

- Mean pulmonary artery pressure
  - Mild 25-40mmHg
  - Moderate 40-55mmHg
  - Severe >55mmHg

## Treatment

### Medical

- Oxygen therapy (aim SpO<sub>2</sub>>90%)
- Diuretics – used to minimise intravascular fluid overload in patients with right ventricular failure
- Digoxin – improves cardiac function
- Warfarin – used to minimise small vessel thrombosis
- Pulmonary vasodilators – reduce pulmonary artery pressure & improve 6MWT distances + pulmonary hemodynamics
  - Epoprostenol (synthetic prostacyclin)
  - Iloprost (prostacyclin analogue)
  - Bosentan (endothelin receptor antagonist)
  - Sildenafil (PDE5 inhibitor)
  - Nifedipine (calcium channel blocker) – limited to small minority of patients who demonstrate a significant vasodilator response at cardiac catheterisation

### Surgical

- Transplantation (lung or heart-lung) – reserved for patients deteriorating on pulmonary vascular directed therapy
- Balloon atrial septostomy – considered if refractory to medical management
- Pulmonary thromboendarterectomy – cure for pulmonary hypertension associated with chronic thromboembolic disease

## Anaesthesia

- Preoperative medications – maintain all pulmonary vasodilators & oxygen, chronic anticoagulation should be replaced with heparin
- Avoid sedative premedication as hypercarbia + respiratory acidosis increase PVR
- Induction – use opioids to block cardiorespiratory response to intubation
- Maintenance – opioids maintained at surgical analgesic level, volatile agents can be used, maintain adequate muscle relaxation
- Monitors – IAL, CVL, TOE
- Postoperative – ICU admission, adequate analgesia

## Potential Questions

### What is the perioperative morbidity & mortality?

- Perioperative morbidity appears to be in the range of 14-42% & includes respiratory failure, heart failure, dysrhythmias, sepsis, renal insufficiency, hepatic dysfunction + myocardial ischaemia/infarction
- Postoperative mortality rates vary between 1-8%

### What are some predictors of a worse outcome for non-cardiac surgery?

- ECG with right axis deviation
- Right ventricular hypertrophy
- Cardiac index < 2.5 L/min/m<sup>2</sup>
- Right ventricular myocardial performance index > 0.75
- Right atrial pressure > 8 mmHg
- Right ventricular systolic blood pressure : systolic blood pressure ratio > 0.66
- 6 minute walk test < 380 m
- Cardiopulmonary exercise testing with peak oxygen consumption < 15ml/min/kg
- Elevated BNP or troponin levels

### What are your specific intraoperative goals?

- Avoid increased pulmonary vascular resistance (avoid N<sub>2</sub>O, hypoxaemia, hypercarbia, acidosis, hypothermia, sympathetic tone, pain)
- Avoid high airway pressures, PEEP, alpha agonists
- Avoid decreased right ventricular preload
- Maintain right ventricular contractility (early inotropic support)
- Maintain left ventricular afterload (care with neuraxial)
- Specific haemodynamic goals:

- Systolic BP  $\geq$  90mmHg +/or 40mmHg above systolic pulmonary artery pressure
- MAP  $\geq$  65mmHg +/or 20mmHg above mean pulmonary artery pressure
- Mean pulmonary artery pressure < 35mmHg or 25mmHg lower than MAP
- PVR/SVR ratio < 0.5 or aim for preoperative PVR/SVR ratio
- Right atrial pressure the lowest that maintains MAP  $\geq$  65mmHg
- Cardiac index  $\geq$  2.2 L/min/m<sup>2</sup>

*What are the management options for an intraoperative pulmonary hypertensive crisis?*

<i>General principles</i>
<ul style="list-style-type: none"> <li>• Ensure good oxygenation</li> <li>• Avoid hypoxic pulmonary vasoconstriction</li> <li>• Avoid hypercarbia, acidosis and hypothermia</li> <li>• Avoid high airway pressures</li> <li>• Optimise right ventricular preload</li> <li>• Reduce right ventricular afterload</li> <li>• Maintain coronary blood flow</li> <li>• Maintain sinus rhythm</li> </ul>
<i>Maintain arterial blood pressure and cardiac output</i>
<ul style="list-style-type: none"> <li>• Vasopressors – noradrenaline, vasopressin</li> <li>• Inotropes – adrenaline, dobutamine</li> <li>• Inodilators – milrinone, enoximone</li> </ul>
<i>Intravenous vasodilators (caution if low systolic blood pressure)</i>
<ul style="list-style-type: none"> <li>• Milrinone</li> <li>• Prostacyclin</li> <li>• Iloprost</li> <li>• Sildenafil</li> </ul>
<i>Selective pulmonary vasodilation</i>
<ul style="list-style-type: none"> <li>• Iloprost (nebulised)</li> <li>• Prostacyclin (nebulised)</li> <li>• Nitric oxide</li> </ul>

*What are the diagnostic criteria for RBBB?*

Diagnostic criteria for RBBB:

- QRS duration  $\geq$  0.12 seconds
- A secondary R wave in V1 or V2
- Wide slurred S wave in leads I, V5 + V6

Associated feature:

- ST segment depression & T wave inversion in right precordial leads

## **Peripheral Vascular Disease** (Stoelting p169)

- Often elderly with severe co-existing medical problems & limited functional reserve
- Manifestation of generalised atherosclerosis, including cerebral & coronary circulations

### **Clinical Features**

- History
  - Claudication
    - Painful, aching numbness in muscle groups induced by exercise
    - Distance to induce leg pain, collaterals develop in chronic disease + reduce symptoms
  - Assess risk factors – smoking, DM, dyslipidemia, hypertension, chronic renal disease
  - Functional capacity + impact on daily life
  - Medication history and compliance
  - Previous surgical history – often require multiple revascularization procedures
  - Consider AHA/ACC cardiovascular risk & role of  $\beta$  blockers
- Examination
  - Peripheral pulses in limbs
  - Look for any lower limb skin changes, hair loss, temperature difference in limbs, ulcers
  - BP in both arms looking for subclavian disease
  - Auscultate heart + carotid arteries for murmurs/bruits
  - Palpate abdomen for AAA
  - *Buerger's test* – passive leg elevation (goes pale) followed by leg flushing in a dependent position (suggests arterial disease)
  - ABI <0.50 with symptoms – invasive therapies need to be considered
- Investigations
  - ECG – cardiac disease
  - CXR – usually heavy smoking history
  - Echocardiogram – if signs of heart failure or valvular disease
  - CT angiogram of lower limbs
- Differential diagnosis
  - Causes of claudication – most commonly atherosclerosis, could also be – acute arterial diseases (dissection, embolism), occluded aneurysms, radiation, vasospasm

<i>ABI</i>		
Normal		1-1.2
Mild PAD		0.81-0.99
Mod		0.5-0.8
Severe		<0.5

### **Treatment**

- Medical
  - Smoking cessation, exercise
  - Anti-hypertensives, statins, diabetes control
  - Antiplatelet agents – aspirin or clopidogrel
- Surgical
  - Lower limb revascularisation – stenting vs open repair/bypass, vein vs polytetrafluoroethylene
  - Thrombolysis/fasciotomies

### **Anaesthesia**

Goals of anaesthesia for lower limb revascularisation procedures:

- Haemodynamically stable – avoid tachycardia, hypo/hypertension
- Maintain CO + oxygen delivery to tissues
- Avoid significant anaemia + optimize oxygen carrying capacity
- Attenuate stress response to surgery
- Maintain renal function + body temperature
- Provide good postoperative analgesia

Conflicts – GA vs Regional – regional theoretical advantage in reducing stress response to surgery + hypercoagulable state; may also improve lower limb flow from vasodilation; however, often long procedures on patients with anticoagulant therapy; no effect on long-term outcome

## Atrial Septal Defect (ASD) (Oxford p78, Stoelting p49)

- Accounts for 1/3 of congenital heart disease in adults
- Affects females more than males (2-3:1)
- Anatomically can form from:
  - Ostium secundum (70%) – defect in septum not involving AV valves
  - Ostium primum (20%) – large opening in interatrial septum involving AV valves

### Clinical Features

- Mostly asymptomatic in early years if small & remain undetected
- Large ASD can result in:
  - Dyspnoea on exertion
  - Right heart failure
  - Supraventricular dysrhythmias
  - Recurrent pulmonary infection
  - Paradoxical embolism
- Examination
  - Palpation – normal or enlarged RV
  - Auscultation – fixed split S2, tricuspid flow murmur + pulmonary systolic ejection murmur
  - Ostium primum can be associated with MR + TR
- Investigations
  - ECG – right axis deviation, incomplete RBBB, AF
  - CXR – dilated pulmonary arteries
  - Echocardiogram – location of ASD

### Severity

- When ASD >2cm, left atrial blood will start to shunt to right atrium, resulting in more pulmonary blood flow & pulmonary hypertension if untreated
- When pulmonary blood flow is >1.5 times of systemic blood flow, the ASD should be closed surgically to prevent irreversible pulmonary hypertension

### Anaesthesia

- Increase in SVR can increase L → R shunt
- High FiO<sub>2</sub> use will decrease PVR & increase pulmonary blood flow + left-to-right shunt
- Meticulous with air bubbles – chance of paradoxical air embolism
- Transient SVT & AV conduction defects common during early postoperative period

## **Ventricular Septal Defect (VSD)** (Oxford p78, Stoelting p51)

- Most common congenital cardiac abnormality in infants & children; in the adult population, VSDs are the most common congenital heart defect excluding a bicuspid aortic valve
- Large number close spontaneously by the time a child reaches 2 years of age
- 70% located at intraventricular septum, 20% at muscular portion of septum, 5% below aortic valve causing AR & 5% near junction of mitral + tricuspid valve

### **Clinical Features**

- Examination
  - Acyanotic
  - Palpation – hyperkinetic displaced apex, thrill at left sternal edge
  - Auscultation
    - Pan-systolic murmur, maximal at lower left sternal edge, louder on expiration
    - S3 + S4 possible
- Investigations
  - ECG
    - No signs if small VSD
    - Left atrial enlargement if large VSD
    - Right axis deviation, right atrial enlargement + RVH if pulmonary hypertension

### **Severity**

- Pulmonary hypertension & R → L shunt (shunt reversal) occurs in large defect with time

### **Anaesthesia**

- As per ASD, large increase in SVR or decrease in pulmonary resistance will increase L → R shunt – hence, volatiles with IPPV are great (decrease SVR + increase PVR)
- No need for IE prophylaxis

## Post-Cardiac Transplant (Oxford p74, Stoelting p27)

- Indicated in any patient with end-stage heart failure despite maximal medical & device therapy (good candidates have single organ dysfunction)
- Dilated cardiomyopathy & coronary artery disease make up 90% of recipients
- Survival – 90% at 1 year, 70% at 5 years, 50% at 10 years

## Clinical Features

- History
  - Indication for & time since transplant surgery
  - Assess functional status of transplanted heart – exercise tolerance, symptoms of heart failure
  - Ask about surveillance programme & results – endomyocardial biopsy for rejection, echocardiogram for graft function, angiography for coronary disease
  - Clarify CMV status
  - Ask about episodes of proven or suspected graft rejection (acute or chronic)
    - Ask about donor coronary artery disease (diffuse obliterative coronary arteriopathy)
      - Present in 50% after 5 years
      - Symptoms related to onset of LV dysfunction or arrhythmia; do not present with angina because heart is denervated
      - Reflects a chronic rejection process in vascular endothelium
      - Principal limitation to long-term survival – leads to myocardial ischaemia, LV dysfunction, arrhythmias + sudden death
  - Ask about current & past immunosuppressive therapy (cyclosporine, azathioprine, prednisolone) – check doses, compliance & side effects
  - Ask about increased incidence of cancer (especially lymphoproliferative + cutaneous)
  - Ask about presence of implanted cardiac devices (10% develop bradyarrhythmias requiring PPM)
- Examination
  - May be relatively few signs if successful transplant
  - Relative tachycardia from vagal denervation – loss of HR variability to valsalva
  - Median sternotomy scar
  - Right IJ scar from recurrent endomyocardial biopsy
  - Signs of heart failure
  - Cushingoid appearance from steroid use
- Investigations
  - Bloods – FBC for bone marrow suppression, electrolytes, renal function, liver function
  - ECG – 2 P waves (represents SA node of recipient + donor), RBBB (may be due to increased right heart pressure or abnormal heart position after surgery), low voltage may indicate myocardial oedema, look for myocardial ischaemia
  - CXR – cardiomegaly
  - Echocardiogram & angiogram results
  - Biopsy reports & rejection status

## Treatment

- Immunosuppressive triple therapy – calcineurin inhibitor (cyclosporine, tacrolimus), purine synthesis inhibitor (azathioprine, mycophenolate mofetil) & T cell dependent immunity suppression (prednisolone)
  - Important side effects – hypertension, nephrotoxicity, bone marrow suppression, hepatotoxicity, opportunistic infections, diabetes + osteoporosis

## Anaesthesia

- Preoperative – liaise with transplant team, continue ongoing immunosuppression, give stress doses of corticosteroids, check all investigations, cardiac device check, note high resting HR (90-100bpm)
- Intraoperative – monitoring depends on surgery, meticulous aseptic technique, avoid cannulation of right internal jugular (used as access site for endomyocardial biopsies), general or regional can be performed, maintain coronary perfusion pressure, consider antibiotic prophylaxis, aim for normovolemia because of CO dependence on preload, treat hypotension with direct-acting sympathomimetics, vagolytic effect of atropine + glycopyrrolate are lost – direct acting chronotropic agents such as ephedrine + isoprenaline should be available, changes in HR no longer indicate depth of anaesthesia, tachycardia in response to stress/pain is blunted, careful positioning + handling of patient due to steroid-induced osteoporosis or skin fragility, medication must be based on degree of liver + renal function
- Postoperative – continue immunosuppressant medication, normal regimens for postoperative analgesia, consider monitoring in HDU/ICU

# Respiratory

## Chronic Obstructive Pulmonary Disease (COPD) (Oxford p114, Stoelting p188)

- Characterised by progressive development of airflow limitation that is not fully reversible
- Usually a combination of *chronic bronchitis* & *emphysema*
  - *Chronic bronchitis* – defined clinically as the daily production of sputum for 3 months a year for at least 2 consecutive years
    - ‘Blue bloater’ – overweight, peripheral oedema, low alveolar ventilation, CO<sub>2</sub> retention, marked cor pulmonale development
  - *Emphysema* – defined histologically by dilatation & destruction of the airways distal to the terminal bronchioles
    - ‘Pink puffer’ – thin, tachypnoeic, breathless at rest, normal to decreased CO<sub>2</sub>, decreased diffusing capacity
- Risk factors – smoking, respiratory infection, occupational exposure (dust, coal, textiles), genetic factors ( $\alpha_1$  antitrypsin deficiency)

### Clinical Features

- History
  - Symptoms – productive cough, wheeze, dyspnoea, impaired exercise tolerance, ankle oedema, weight loss
  - Sputum production
  - Frequency of exacerbations, corticosteroid use, hospital + ICU admissions
  - Oxygen therapy
  - Smoking cessation, medical therapies, pulmonary rehabilitation, chest physiotherapy
  - Other diseases associated with smoking
- Examination
  - Pursed lip breathing (emphysema), accessory muscle use, loose cough + sputum, cyanosis (late chronic bronchitis)
  - Chest
    - Hyperinflated, reduced chest expansion
    - Increased resonance on percussion
    - Decreased breath sounds with end-expiratory wheeze or early inspiratory crackles
    - Prolonged expiratory phase
  - Signs of right ventricular failure + cachexia (advanced disease)
- Investigations
  - Bloods – polycythaemia 2° persistent hypoxemia, leukocytosis during acute exacerbation
  - ABG – hypoxemia + hypercapnia in advanced cases
  - CXR – hyperinflation (tall narrow heart, >6 anterior ribs, low flat diaphragm), bullae + decreased vascular markings, thickened bronchial markings, enlarged right side of heart, pneumonia, PTX
  - RFTs
    - Decreased FEV1/FVC ratio
    - Decreased FEF<sub>25-75%</sub> (forced expiratory flow at 25% to 75% of FVC)
    - Increased RV 2° slowing of expiratory airflow + gas trapping behind prematurely closed airways
    - Normal to increased FRC + TLC
    - Advantage of ↑RV + FRC is an enlarged airway diameter + ↑ elastic recoil for exhalation, but the cost is greater WOB at higher lung volumes
    - Decreased DLCO (emphysema)
  - ECG
    - Right heart strain (ST depression/TWI in right precordial leads V1-3 + inferior leads II, III, aVF)
    - RVH (right axis deviation, large R wave in V1, deep S wave in V6)
    - P pulmonale (right atrial enlargement) – large P wave in lead V1
  - Echocardiogram – assess cardiac function
- Severity assessment
  - **GOLD criteria** – spirometric classification, limited by fact that it does not take into account systemic manifestations

Stage of COPD	FEV1%	FEV1/FVC%	Symptoms
<b>0 – At risk</b>	≥80	>70	None
<b>1 – Mild</b>	≥80	<70	Variable
<b>2 – Moderate</b>	50-79	<70	Mild to moderate
<b>3 – Severe</b>	30-49	<70	Limit exertion
<b>4 – Very Severe</b>	<30	<70	Limit daily activities

- **BODE index** – BMI, degree of obstruction (measured by FEV1), dyspnoea (measured by modified MMRC dyspnea questionnaire in a 6MWT) & exercise capacity → better than FEV1 alone at predicting risk of death in patients with COPD

## Treatment

- Smoking cessation
- Bronchodilators –  $\beta_2$  agonists, anticholinergics, methylxanthines
- Inhaled & systemic glucocorticoids
- Mucolytics
- Intermittent broad spectrum antibiotics
- Vaccinations – pneumococcal + influenza
- Long term oxygen therapy for >15 hrs/day – improves 3 year survival by 50% (aim to achieve PaO<sub>2</sub> 60-80mmHg)
- Surgery
  - Bullectomy
  - Lung volume reduction surgery – palliative treatment, most beneficial in patients with both predominantly upper-lobe emphysema + low baseline exercise capacity, improves exercise capacity but does not confer a survival advantage over medical therapy
  - Lung transplantation – considered in end-stage disease with FEV<sub>1</sub> <25% predicted
  - Endobronchial valves (under trial – allow air to escape from a pulmonary lobe + not enter it) – improves lung function/symptoms/exercise tolerance but more frequent exacerbations

## Anaesthesia

- Comprehensive preoperative evaluation & optimization
- Regional anaesthesia preferred over GA + IPPV (associated with adverse outcomes)
- General anaesthesia
  - Risk of haemodynamic compromise on induction + initiation of IPPV – consider IAL, avoid ETT if possible
  - Preoxygenation with CPAP – reduces atelectasis
  - Monitor for air trapping + development of intrinsic PEEP – capnography trace that does not reach plateau, expiratory flow does not reach zero
  - Reduce harmful effects of air trapping – allow more time for exhalation (reduce I:E ratio), apply PEEP, treat bronchospasm
  - Extubation – ensure full reversal of neuromuscular blockade, good oxygenation & PaCO<sub>2</sub> value close to the normal preoperative value
- Ensure effective analgesia – epidural if appropriate to surgical procedure
- Avoid hypoventilation due to residual anaesthesia or opioids – may lead to hypercarbia + hypoxia
- Consider postoperative HDU/ICU admission, saline/bronchodilator nebulization, suctioning, physiotherapy & early mobilization

## Potential Questions

*What is the scoring system for the modified Medical Research Council (MMRC) dyspnoea questionnaire?*

Score 0 = patient not troubled with breathlessness except with strenuous exercise

Score 1 = shortness of breath when hurrying or walking up a slight hill

Score 2 = patient walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on level ground

Score 3 = patient has to stop for breath after walking  $\approx$ 100m or after a few minutes on level ground (severe dyspnoea)

Score 4 = patient is too breathless to leave house or breathless when dressing/undressing (very severe dyspnoea)

*What are the criteria for oxygen therapy?*

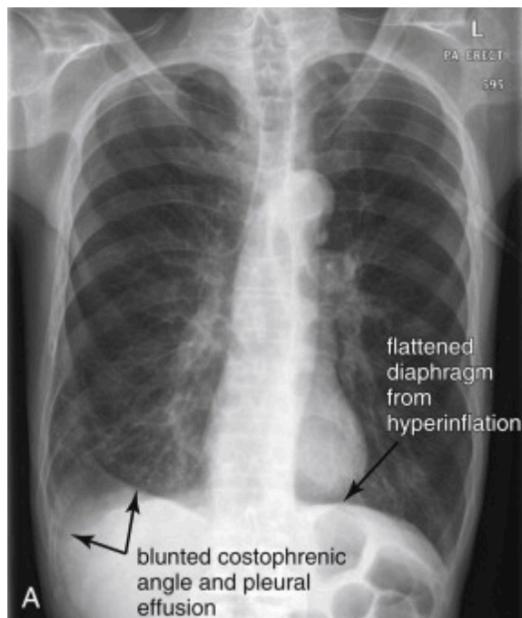
- Clinically stable patients with PaO<sub>2</sub>  $\leq$ 55mmHg (corresponds to SpO<sub>2</sub>  $\leq$ 88%)
- Patients with PaO<sub>2</sub> 55-59mmHg (corresponds to SpO<sub>2</sub> 89%) AND signs of tissue hypoxia such as pulmonary hypertension, cor pulmonale, erythrocytosis, oedema from right heart failure or impaired mental status

*What are the major risk factors associated with postoperative pulmonary complications?*

- Patient related:
  - Age > 60 years
  - ASA > 2
  - Congestive heart failure
  - Preexisting pulmonary disease (COPD)
  - Smoking
- Procedure related:
  - Emergency
  - Abdominal/thoracic/head+neck/neurosurgery/vascular/aortic aneurysm
  - Prolonged duration >3 hours
  - General anaesthesia
- Test predictors:
  - Albumin level <35mg/L

What are some risk-reduction strategies to decrease the incidence of postoperative pulmonary complications?

- Preoperative:
  - Encourage smoking cessation (regardless of the interval before surgery)
  - Treat evidence of expiratory airflow obstruction
  - Treat respiratory infection with antibiotics
  - Initiate patient education regarding lung volume expansion maneuvers
- Intraoperative:
  - Use minimally invasive surgery (endoscopic) techniques when possible
  - Consider regional anaesthesia
  - Avoid surgical procedures likely to last longer than 3 hours
- Postoperative:
  - Institute lung volume expansion maneuvers (voluntary deep breathing, incentive spirometry, CPAP)
  - Maximise analgesia (neuraxial opioids, intercostal nerve blocks, PCA)



#### Diagnostic criteria for right ventricular hypertrophy

(Provided the QRS duration is less than 0.12 s)

- Right axis deviation of +110° or more
- Dominant R wave in lead V1
- R wave in lead V1 ≥ 7 mm

#### Supporting criteria

- ST segment depression and T wave inversion in leads V1 to V4
- Deep S waves in leads V5, V6, I, and aVL

## **Bronchiectasis** (Oxford p116, Stoelting p195)

- Chronic suppurative disease of the airways that can cause expiratory airflow obstruction
- Characterised by abnormal + permanent dilatation of bronchi → increased susceptibility to recurrent or persistent bacterial infection due to impaired mucociliary activity + mucus pooling in dilated airways
- Causes:
  - Congenital – cystic fibrosis, 1° ciliary dyskinesia, panhypogammaglobinemia, congenital structural defects
  - Acquired – lung infections (pneumonia, lung abscess, TB, fungal, viral), localised airway obstruction (FB, neoplasm), inflammation (allergic bronchopulmonary aspergillosis, inflammatory pneumonitis)
- 13% mortality rate

### **Clinical Features**

- History
  - Cough + sputum production – baseline & with exacerbations
  - Onset of respiratory problems, childhood infections, colonizing organisms, frequency of exacerbations
  - Recent precipitating causes of admissions - ?infection ?hemoptysis
  - Treatment – physiotherapy, postural drainage, antibiotics, bronchodilators, surgery
  - Infertility with cilia dysmotility syndromes
- Examination
  - Fever, cachexia, sinusitis
  - Clubbing + cyanosis
  - Sputum – voluminous, purulent, foul-smelling, sometimes bloodstained
  - Chest – coarse pan-inspiratory or late inspiratory crackles over affected lobe
  - Signs of right heart failure
  - Kartagener syndrome (subgroup of 1° ciliary dyskinesia) = triad of bronchiectasis, sinusitis + situs inversus
- Investigations
  - FBC – anaemia may reflect chronic infection or blood loss, leukocytosis may mark infection severity, eosinophilia may suggest ABPA
  - Sputum cultures – guide antimicrobial therapy
  - CXR – hyperinflation, collapse (segmental/lobar), crowded lung markings, small cystic spaces at lung bases
  - HRCT chest – dilatation of airway lumen, non-tapering bronchi (tramlines), ballooned cysts at end of bronchus, varicose constrictions along airways
  - RFT – obstructive pattern followed by mixed pattern (obstructive + restrictive) develops as disease progresses
    - Severe disease – ↓ FEV1/FVC correlates with bronchial wall thickening on HRCT
    - Less sensitive indicator of disease severity than CT scanning
  - Bronchoscopy – helpful to evaluate hemoptysis, rule out obstructive lesions + remove mucus plugs

### **Treatment**

- Smoking cessation & maintenance of proper nutrition + hydration
- Chest physiotherapy & postural drainage
- Pharmacotherapy includes antibiotics to prevent + treat recurrent infection, anti-inflammatory agents, mucolytic agents & inhaled bronchodilators
- Pneumococcal vaccination + annual influenza vaccination
- Surgery – generally reserved for patients with localised disease that is poorly controlled by antibiotics
  - Massive hemoptysis (>200ml over a 24 hour period) may require surgical resection of involved lung or bronchial artery embolization
  - Cystic fibrosis – lung transplantation when FEV1 <30% predicted

### **Anaesthesia**

- Preoperative
  - Respiratory physician consultation – essential
  - Patient should be as fit as possible before elective surgery – postpone elective surgery if more respiratory symptoms than usual
  - Send sputum sample for culture (*Pseudomonas* most common organism cultured)
  - Antibiotics & physiotherapy for 3-10 days prior to surgery may be needed
  - Maximise bronchodilation by converting to nebulized bronchodilators
  - Increase prednisolone dose by 5-10 mg/day if on long-term steroids
- Intraoperative
  - Choose regional above general anaesthesia where possible
  - Intubation required for GA to facilitate removal of secretions
  - Consider DLT if unilateral bronchiectasis – lung isolation to prevent contamination of non-infected lung
  - Avoid instrumentation of nasal passage – high incidence of chronic sinusitis

- Short-acting anaesthetic & analgesic agents
- Extubate & recover in sitting position
- Postoperative
  - Regular physiotherapy
  - Monitor SpO<sub>2</sub> – supplemental oxygen therapy as required
  - Continue appropriate IV antibiotics for at least 3 days postoperatively
  - Maintain adequate nutrition

## Asthma (Oxford p110, Stoelting p182)

- Characterised by chronic airway inflammation, reversible expiratory airflow obstruction in response to various stimuli & bronchial hyperreactivity
- Episodic disease with acute exacerbations interspersed with symptom-free periods
- Exacerbating factors – allergens, drugs (NSAIDs,  $\beta$ blockers), infections, exercise, emotional stress

### Clinical Features

- History
  - Current symptoms – wheeze, cough (productive/nonproductive), dyspnoea, chest discomfort/tightness
  - Pattern of symptoms
    - Course over day, week or year
    - Typically recurrent or seasonal & worse at night or early morning
  - Age at onset, family history, precipitating or aggravating factors
  - Current medications, need for reliever & compliance
  - Previous exacerbations requiring oral steroids, admission to hospital or intubation in ICU
  - Smoking history
  - Functional capacity – limitation of activities?
- Examination
  - Wheezing
  - Tachypnea
  - Dry or productive cough
  - Tachycardia
  - Prolonged expiration
  - Prolonged forced expiratory time (decreased peak flow, decreased FEV1)
  - Use of accessory muscles of respiration
  - Hyperinflated chest ( $\uparrow$  anteroposterior diameter with high shoulders &  $\downarrow$  liver dullness on percussion)
  - Inspiratory & expiratory wheezes
  - Signs of severe asthma:
    - Appearance of exhaustion + fear
    - Inability to speak because of breathlessness
    - Drowsiness due to hypercapnia (preterminal)
    - Cyanosis
    - Tachycardia (pulse  $>130$  correlates with significant hypoxemia)
    - Pulsus paradoxus (more than 20mmHg)
    - Reduced breath sounds or 'silent' chest
- Investigations
  - ABG – guides severity classification
    - Mild asthma – normal PaO<sub>2</sub> + PaCO<sub>2</sub>
    - $\downarrow$  CO<sub>2</sub> + respiratory alkalosis = most common finding
    - Acute asthma attack –  $\uparrow$  RR + hyperventilation reflect neural reflexes in lung, not arterial hypoxemia
    - Increasing severity of expiratory airflow obstruction  $\rightarrow$  associated V/Q mismatch results in hypoxemia &  $\uparrow$  PaCO<sub>2</sub> with FEV1  $<25\%$  + respiratory muscle fatigue
  - PEF – not a substitute for spirometry when diagnosing asthma – limitations include – effort-dependent, considerable variation between instruments & wide range of normal values; useful for treatment response
  - RFT – obstructive pattern with bronchodilator responsiveness
    - Significant bronchodilator response = an increase in FEV1 of at least 200 mL & by at least 12%
  - CXR – hyperinflation, signs of infection
  - ECG – tachycardia, nonspecific ST-T wave changes during asthma attack, right heart strain
- Severity
  - According to the 2014 Australian Asthma Handbook, asthma severity in adults is defined by the type & amount of treatment needed to achieve good asthma control; an assessment of asthma severity at the time of diagnosis is no longer recommended & severity can only be assessed after treatment has started

Good control	Partial control	Poor control
All of: <ul style="list-style-type: none"><li>• Daytime symptoms <math>\leq 2</math> days per week</li><li>• Need for reliever <math>\leq 2</math> days per week</li><li>• No limitations of activities</li><li>• No symptoms during night or on waking</li></ul>	One or two of: <ul style="list-style-type: none"><li>• Daytime symptoms <math>&gt;2</math> days per week</li><li>• Need for reliever <math>&gt;2</math> days per week</li><li>• Any limitation of activities</li><li>• Any symptoms during night or on waking</li></ul>	Three or more of: <ul style="list-style-type: none"><li>• Daytime symptoms <math>&gt;2</math> days per week</li><li>• Need for reliever <math>&gt;2</math> days per week</li><li>• Any limitations of activities</li><li>• Any symptoms during night or on waking</li></ul>

- Classification based on severity of expiratory airflow obstruction

Severity	FEV1 (% predicted)	FEF <sub>25-75%</sub> (% predicted)	PaO <sub>2</sub> (mmHg)	PaCO <sub>2</sub> (mmHg)
<b>Mild (asymptomatic)</b>	65-80	60-75	>60	<40
<b>Moderate</b>	50-64	45-59	>60	<45
<b>Marked</b>	35-49	30-44	<60	>50
<b>Severe (<i>status asthmaticus</i>)</b>	<35	<30	<60	>50

### Treatment

- Controller treatments
  - Inhaled + systemic corticosteroids – fluticasone, budesonide, prednisone
  - Theophylline
  - Anti-leukotrienes – montelukast
- Relievers
  - $\beta$  agonists – salbutamol, salmeterol
  - Anticholinergics – ipratropium

### Anaesthesia

- Preoperative
  - Evaluation requires assessment of disease severity, effectiveness of current management & need for additional therapy before surgery
  - Patients should be free of wheezing & have a PEF or FEV1 >80% predicted or at the level of the patient's personal best before surgery
- Intraoperative
  - Aim to suppress airway reflexes & avoid bronchoconstriction – use propofol, ketamine, sevoflurane + lignocaine
  - Avoid histamine-releasing drugs
  - LMA less likely to precipitate bronchospasm than ETT
  - Avoid general anaesthesia where possible & use regional techniques
  - Ventilator settings → long I:E ratio, TV 8-10 ml/kg, slow rate 6-8 bpm, avoid PEEP
  - Extubate deep where appropriate – consider LMA exchange

## Restrictive Lung Disease (Oxford p120, Stoelting p197)

- Conditions where lung expansion is restricted
- Characterised by decreases in all lung volumes, decreased lung compliance & preservation of expiratory flow rates
- Classification:

<i>Acute intrinsic (pulmonary oedema)</i>	<i>Chronic intrinsic (interstitial lung disease)</i>	<i>Chronic extrinsic (extrapulmonary - diseases of chest wall, pleura + mediastinum)</i>
<ul style="list-style-type: none"><li>• ARDS</li><li>• Aspiration</li><li>• Neurogenic problems</li><li>• Opioid overdose</li><li>• High altitude</li><li>• Reexpansion of collapsed lung</li><li>• Upper airway obstruction (negative pressure)</li><li>• Congestive heart failure</li></ul>	<ul style="list-style-type: none"><li>• Sarcoidosis</li><li>• Hypersensitivity pneumonitis</li><li>• Eosinophilic granuloma</li><li>• Alveolar proteinosis</li><li>• Lymphangioleiomyomatosis</li><li>• Drug-induced pulmonary fibrosis</li></ul>	<ul style="list-style-type: none"><li>• Deformities of costovertebral skeletal structures – kyphoscoliosis, ankylosing spondylitis</li><li>• Sternum deformities</li><li>• Flail chest</li><li>• Pleural effusion</li><li>• Pneumothorax</li><li>• Mediastinal mass</li><li>• Pneumomediastinum</li><li>• Neuromuscular disorders (spinal cord transection, GBS, muscular dystrophies)</li></ul>

## Clinical Features

- History
  - Occupation, travel, habits, exposure
  - Duration of illness – helps distinguish between acute/chronic causes
  - Family history
  - Medication/radiation history – eg. gold, amiodarone, methotrexate
  - Symptoms of intrinsic causes – dyspnoea, dry cough, haemoptysis, pleuritic chest pain, wheezing
  - Symptoms of extrinsic causes – spinal deformity, muscle weakness, dyspnoea on exertion, impaired secretion control
- Examination
  - Chest wall deformity, dyspnoea, cachexia, obesity, clubbing, cyanosis
  - Auscultation – velcro-like crackles for interstitial lung disease
  - Cor pulmonale – right ventricular heave, loud P2
- Investigations
  - FBC – polycythaemia = chronic hypoxemia, leucocytosis = acute hypersensitivity pneumonitis
  - ABG – hypoxemia from V/Q mismatching (both dead space + shunt are increased)
  - CXR – according to underlying condition
  - CT – honeycomb, ground glass
  - RFTs – decrease in all lung volumes – reduced TL/FRC/RV, decreased lung compliance, increased FEV1/FVC ratio >80%, preservation of expiratory flow rates
  - DLCO – decreased in all intrinsic disease, normal excludes intrinsic causes, severity of reduction does not correlate with disease severity

## Anaesthesia

- Already reduced FRC worsens with supine position, GA + controlled ventilation
- Low FRC = faster volatile effects
- Reduce peak pressure if possible – but this is hard with reduced lung compliance – use pressure controlled ventilation with low tidal volumes + higher ventilator rate (similar to ARDS)
- Spontaneous ventilation, sitting up position + AFOI may be necessary for extrinsic compression (eg. mediastinal tumours)

Date: 30/01/01

Physician: SHARMA

Room: ACF MED

Age: 68

Height(in): 67  
(cm): 171Weight(lb): 147  
(kg): 67.0

Gender: Male

**Spirometry**

		Ref	Pre	Pre	Post	Post	Post
			Meas	% Ref	Meas	% Ref	% Chg
FVC	Liters	3.98	2.78	70			
FEV1	Liters	2.73	2.19	80			
FEV1/FVC %		70	79				
FEF25-75% L/sec		2.60	2.04	78			
FEF50% L/sec		3.67	2.98	81			
PEF L/sec		7.62	8.13	107			
FEF/FIF50		<4000	0.48				

**Lung Volumes**

VC	Liters	3.98	2.88	72
TLC	Liters	5.82	4.37	75
RV	Liters	2.30	1.49	65
RV/TLC %		40	34	
FRC PL	Liters	3.50	2.72	78
FRC DlL	Liters	3.50		
ERV	Liters	1.320	1.23	9003

**Diffusion**

DLCO	mL/mmHg/min	25.3	7.2	28
DL Adj	mL/mmHg/min	25.3	7.2	28
DLCO/VA	mL/mHg/min/L	4.17	1.72	41

Diag.: PULMONARY FIBROSIS

Meds.: Prednisone 20 mg

**Respiratory Mechanics**

Raw	cmH2O/L/sec	1.29	1.78	138
PI max	cmH2O	106		
PE max	cmH2O	198		

Smoker? No

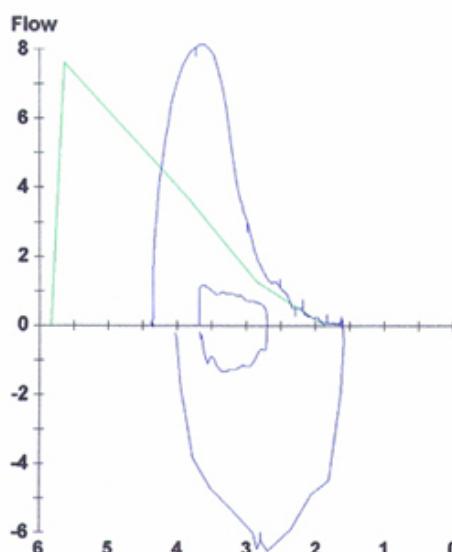
Pack Years:

Stopped? yrs. ago

Reason for test: ASSESSMENT

**Blood Gases**

FIO <sub>2</sub> %	pH	PCO <sub>2</sub> mmHg	PO <sub>2</sub> mmHg	HCO <sub>3</sub> meq/L	BE	Hb g/l	%HbO <sub>2</sub> %	%HbCO %	P(A-a)O <sub>2</sub> mmHg
Lvl 1									



Low DLCO

Low lung volumes overall

Relatively good expiratory effort

## Pneumothorax (PTX) (Stoelting p201+203)

- Presence of gas in pleural space caused by disruption of parietal (external penetrating injury) or visceral (tear or rupture in lung parenchyma) pleura
- Classification
  - *Primary spontaneous PTX*
    - Caused by subpleural bullae rupture – affects tall young males with no underlying lung disease
  - *Secondary PTX*
    - Associated with underlying respiratory disease that damages lung architecture – emphysema, asthma, lung abscess, pneumonia, end-stage fibrosis, Marfan's
  - *Traumatic PTX*
    - Follows blunt or penetrating chest trauma – rib fractures, penetrating chest wall injury or during pleural/pericardial aspiration
  - *Tension PTX*
    - Medical emergency – occurs when air accumulates in pleural cavity faster than it can be removed
      - increased intrathoracic pressure causes mediastinal shift, compression of functioning lung, inhibition of venous return & shock due to reduced cardiac output
    - May complicate primary spontaneous or secondary PTX but is most common during mechanical ventilation at high pressures & following traumatic PTX

## Clinical Features

- History
  - Dyspnoea, chest pain
  - 1<sup>st</sup> or recurrent presentation
  - Respiratory disease, trauma or recent procedure
  - Treatment
- Examination
  - Low SpO<sub>2</sub>, tachycardia
  - Reduced chest expansion on affected side
  - Hyperresonance on percussion if large
  - Reduced or absent breath sounds
  - Subcutaneous emphysema
  - Tension PTX
    - ↓SpO<sub>2</sub>, tachypnea, respiratory distress, hypotension
    - Distended neck veins (not in presence of hypovolemia)
    - Tracheal deviation (away from affected side)
    - Reduce chest movement
    - Absent breath sounds
- Investigations
  - CXR
- Severity
  - Small <30%
  - Moderate >30%
  - Complete
  - Tension

## Treatment

	<i>Small</i>	<i>Moderate</i>	<i>Complete</i>
<i>Primary spontaneous</i>	Observe	Aspirate	Chest drain
<i>Secondary</i>	Chest drain	Chest drain	Chest drain
<i>Traumatic</i>	Chest drain	Chest drain	Chest drain

- Chest drains removed when CXR confirms lung expansion & there has been no air leakage through the drain for >24 hours
- Tension PTX requires immediate decompression with a 14G cannula placed in 2<sup>nd</sup> intercostal space in MCL on affected side, followed by insertion of large chest drain in 5<sup>th</sup> intercostal space (anterior axillary line) + connection to an underwater seal drain

## Pneumonia (Stoelting p476)

- Defined as inflammation of the lung that is characterised by exudation into alveoli
- Classification
  - Community-acquired
  - Hospital-acquired
  - Occurring in a damaged lung
  - Occurring in an immunocompromised patient
- Typical bacteria
  - Community – Streptococcus pneumoniae (most common), Haemophilus influenza, Mycoplasma
  - Hospital – Staphylococcus aureus, Pseudomonas, Klebsiella
  - Aspiration – Klebsiella
  - Atypical – Legionella, Chlamydia, Mycoplasma pneumoniae

## Clinical Features

- History
  - Symptoms – fever, rigors, cough, pleuritic chest pain, dyspnoea, tachycardia, confusion
- Examination
  - Tachycardia, tachypnea, fever, hypotension
  - Chest
    - Reduced expansion on affected side
    - Increased vocal fremitus on affected side
    - Dull percussion
    - Bronchial breath sounds
    - Inspiratory crackles
    - Increased vocal resonance
    - Pleural rub
- Investigations
  - FBC, ELFT, CRP, blood cultures (rule out bacteremia)
  - Blood antibody titers for Mycoplasma
  - ABG – hypoxemia in severe cases, reflects intrapulmonary shunting of blood resulting from perfusion of alveoli filled with inflammatory exudates
  - Sputum MCS – guides antibiotic treatment, send for acid-fast bacilli if suspect TB & PCR for Chlamydia
  - CXR – lobar opacification suggests typical, diffuse infiltrates suggest atypical, pleural effusion
  - Urine Legionella antigen test
- Severity
  - CURB-65 score – estimates mortality of community-acquired pneumonia to help determine inpatient versus outpatient treatment
    - Confusion
    - Urea > 7mmol/L
    - Respiratory rate ≥ 30
    - SBP < 90mmHg
    - Age > 65 yearsCURB-65 score > 1 = requires inpatient treatment
  - Other
    - Old age & coexisting organ dysfunction have a negative impact
    - Temperature ≤ 35°C or ≥ 40°C
    - Respiratory rate ≥ 30
    - Altered mental status
    - SBP < 90 mmHg
    - Heart rate ≥ 125
    - Laboratory findings & other results indicative of a poor prognosis
      - Hypoxia (PO<sub>2</sub> < 60mmHg or SpO<sub>2</sub> < 90%)
      - Effusion
      - Anaemia
      - Renal BUN > 64mg/dL
      - Glucose > 250mg/dL
      - Acidosis pH < 7.35
      - Na < 130 mmol/L
- Pneumonia Severity Index (PSI) – estimates mortality for patients with community-acquired pneumonia
- Complications – pleural effusion, lung abscess, bacteremia, respiratory failure

## Treatment

- Antibiotic therapy – follow local patterns of antibiotic resistance

- Supplemental oxygen
- Intravenous fluids for rehydration

### **Anaesthesia**

- Delay if acute pneumonia present (ideally)
- Fluid management can be challenging
  - Often dehydrated with renal insufficiency
  - Overhydration may worsen gas exchange + morbidity
- Choose regional or general anaesthesia (if appropriate)
- General anaesthesia
  - Protective ventilation strategy – TV 6-8 ml/kg ideal body mass + mean airway pressures < 30cmH<sub>2</sub>O
  - Actively remove secretions via ETT

## **Obstructive Sleep Apnoea (OSA)** (Oxford p122+638, Stoelting p320)

- Most common medical disorder of sleep
- Defined as cessation of breathing for longer than 10 seconds
  - OSA is a repetitive obstruction of the upper airway during sleep that causes arterial hypoxemia & often leads to a reduced quality of sleep
  - Referred to as OSA syndrome when it is accompanied by excessive daytime sleepiness
- Hypopnoea = a reduction in size or number of breaths compared with normal ventilation
- Apnoea = occurs when pharyngeal airways collapse

### **Clinical Features**

- History
  - Symptoms – snoring, daytime fatigue or sleepiness, observed apneas
  - Complications – psychosocial problems, cognitive dysfunction, depression, impaired glucose tolerance, dyslipidemia, hypertension, heart failure, pulmonary hypertension
  - Treatment – CPAP, surgery
- Examination
  - ↑BMI, large neck circumference, large tongue, large tonsils, retrognathia, low-hanging soft palate
- Investigations
  - FBC – polycythaemia
  - Pulse oximetry
  - ABG – baseline, check CO<sub>2</sub>
  - ECG
    - Right heart strain (repolarization abnormality due to RVH or dilatation – ST depression/T wave inversion in right precordial leads V1-3 + inferior leads II, III, aVF)
    - RVH (right axis deviation, large R wave in V1, deep S wave in V6)
    - Right atrial enlargement – large P wave in lead V1
  - Echocardiography – if abnormal ECG
  - Polysomnography (overnight sleep study) – gold standard for diagnosis & determines severity based on **apnoea-hypopnoea index (AHI)** + oxygen desaturation index (ODI)
    - *AHI = number of apnoea or hypopnoea periods lasting 10 seconds or longer per hour of sleep*
    - |                 |       |
|-----------------|-------|
| <b>Normal</b>   | 0-5   |
| <b>Mild</b>     | 5-15  |
| <b>Moderate</b> | 15-30 |
| <b>Severe</b>   | >30   |
    - *ODI = number of times per hour of sleep that arterial oxygen saturation drops by 4% or more from baseline*

### **Treatment**

- Sustained weight loss, decreased alcohol intake & smoking cessation
- CPAP nasal mask (set between 5-20cmH<sub>2</sub>O) – alleviates symptoms, use for 3 months can reverse OSA-induced cardiovascular dysfunction & improves existing comorbidities
- Nocturnal oxygen
- Surgery – uvulopalatopharyngoplasty

### **Anaesthesia**

- Preop – avoid sedative drugs, bring CPAP machine, pre-book HDU bed if severe
- Intraop – avoid long-acting opioids, regional better than GA if possible, anticipate difficult BMV + intubation
- Postop – extubate awake + sitting, nurse upright, continuous pulse oximetry for 24 hours postop, HDU admission, aim to maintain patient's preoperative oxygen saturation, titrate oxygen to minimum required as oxygen can increase apnoea duration + cause CO<sub>2</sub> retention in some patients by delaying the arousing effect of hypoxaemia

### **Potential Questions**

*What are the causes & risk factors for OSA?*

Causes:

- Increased BMI
- Adenotonsillar hypertrophy
- Craniofacial abnormalities
- Congenital conditions & anatomic abnormalities – such as cerebral palsy, Down syndrome, hemifacial microsomia + Pierre Robin syndrome
- Acromegaly

*OSA – associated with increased risk of postoperative O<sub>2</sub> desaturation, respiratory failure, AF, cardiac events, ICU transfers & longer hospital stay*

### Risk factors:

- Age older than 50 years
- Male gender
- Diabetes mellitus type 2
- Alcohol or sedative use
- Smoking
- Nasal congestion
- Macroglossia
- Tonsil + adenoid hypertrophy
- Retrognathia
- Menopause

### What is STOP-BANG?

STOP-BANG Questionnaire - used to screen patients for OSA	
1. Snoring: do you snore loudly (loud enough to be heard through closed doors)?	No
Yes	No
2. Tired: do you often feel tired, fatigued or sleepy during daytime?	No
Yes	No
3. Observed: has anyone observed you stop breathing during your sleep?	No
Yes	No
4. Blood pressure: do you have or are you being treated for high blood pressure?	No
Yes	No
5. BMI: BMI more than 35?	No
Yes	No
6. Age: age over 50 years old?	No
Yes	No
7. Neck circumference: neck circumference >40cm?	No
Yes	No
8. Gender: male?	No
Yes	No

High risk of OSA = yes to ≥3 questions  
Low risk of OSA = yes to <3 questions  
A score of ≥3 has shown a high sensitivity for detecting OSA - 93% for moderate & 100% for severe OSA

### What does polysomnography include?

Full polysomnography includes monitoring of chest movement, airflow dynamics, HR + BP, arterial oxygen saturation & EEG, all during sleep.

### What is the difference between OSA & OHS?

- Obesity hypoventilation syndrome (OHS) is the long-term consequence of OSA
- It is characterised by nocturnal episodes of central apnoea (apnoea without respiratory efforts) reflecting progressive desensitization of the respiratory centre to nocturnal hypercarbia
- At its extreme, OHS culminates in pickwickian syndrome, which is characterised by obesity, daytime hypersomnolence, arterial hypoxemia, polycythaemia, hypercarbia, respiratory acidosis, pulmonary hypertension & right ventricular failure

## Cystic Fibrosis (Oxford p, Stoelting p196)

- Autosomal recessive genetic disorder with variable expression
- Cause is a mutation in a single gene on chromosome 7 that encodes the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) ( $\Delta F508$  mutation = most common)
  - Mutation results in defective chloride ion transport in epithelial cells in lungs, pancreas, liver, GIT & reproductive organs
  - Decreased Cl transport accompanied by decreased Na + water transport → results in dehydrated, viscous secretions that are associated with luminal obstruction as well as destruction & scarring of various exocrine glands
- Median survival 37 years; lung disease responsible for most of mortality, followed by liver cirrhosis

### **Clinical Features**

- History
  - Symptoms – chronic cough (purulent sputum) + dyspnoea, nasal congestion with loss of smell, greasy + smelly faeces, frequent respiratory infections, failure to gain weight despite eating appropriate amounts, bloating + constipation,
  - Severity – current exercise tolerance, recent hospitalisation, chest infections (colonisation with *Pseudomonas aeruginosa*), requirement of IVABs, oxygen or BiPAP at home
  - Non-pulmonary manifestations – diabetes, pancreatic insufficiency (taking enzyme supplements?), liver disease (chronic liver questions), infertility
- Examination
  - General – thin, malnourished
  - Respiratory – digital clubbing, nasal polyps, increased anteroposterior chest diameter, crackles, expiratory wheeze
  - GIT – abdominal distension, jaundice, hepatomegaly
- Investigations
  - FBC, U+E, coagulation study, LFTs, BGL
  - ABG – hypoxemia, hypercapnia
  - ECG – right axis deviation, RBBB
  - Echocardiography – evidence of cor pulmonale – right ventricular hypertrophy +/or dilatation, increased tricuspid regurgitant velocity, flattening + paradoxical movement of interventricular septum, dilated main pulmonary artery, hypokinesis of RV wall, right ventricular systolic dysfunction
  - CXR -
  - RFTs – obstructive pattern usually seen with a decrease in FEV1 & FVC/FEV1
    - FEV1 < 1L may indicate need for postoperative ventilation
- Diagnosis
  - Based upon the presence of –
    - One or more characteristic clinical features,
    - A history of CF in a sibling, or
    - A positive newborn screening test
  - plus
    - Laboratory evidence of an abnormality in the CFTR gene or protein (refers to either elevated chloride levels in a 'sweat test' or genetic testing)
- Severity
  - People with CF-related diabetes have worse lung function, more impaired nutrition, more frequent hospitalisation & higher mortality than CF patients without diabetes

Site	Pathology	Clinical Manifestation
<i>Lower respiratory tract</i>	Viscid mucous secretions, goblet cell hypertrophy, ↓ mucociliary clearance	Frequent LRTI, chronic hypoxemia, cor pulmonale
<i>Upper respiratory tract</i>	Abnormal viscid nasal secretions	Sinusitis, nasal polyposis
<i>Hepatobiliary system</i>	Obstruction of bile ductules	Focal biliary cirrhosis, portal hypertension, multinodular biliary cirrhosis
<i>Gastrointestinal tract</i>	Abnormally viscid intestinal secretions at level of terminal ileum in neonate	Meconium ileus, recurrent abdominal pain (distal intestinal obstruction syndrome)
<i>Pancreas</i>	Obstructed pancreatic ducts, fibrosis	Pancreatic exocrine insufficiency, CF-related diabetes
<i>Reproductive system</i>	Congenital absence of vas deferens, viscid cervical secretions	Infertility
<i>Bone</i>	Impaired calcium + vitamin D absorption, increased catabolism	Osteoporosis
<i>Skin</i>	Increased chloride levels	Abnormal 'sweat test', diminished thermoregulation

## **Treatment**

- Pancreatic enzymes, vitamin + mineral supplements, glycemic control
- Physical therapy – percussion with postural drainage
- Bronchodilators for airway obstruction + bronchial hyperreactivity
- Mucolytics – nebulized dornase alpha + inhaled hypertonic saline
- Anti-inflammatories – oral corticosteroids, ibuprofen + azithromycin (macrolide prophylaxis slows rate of decline in FEV1 due to its antimicrobial + anti-inflammatory actions)
- Inhalation therapy with gentamicin or tobramycin for chronic suppression & eradication of *Pseudomonas* (not well supported by literature)
- Oral or systemic antibiotics guided by sputum culture for acute/subacute exacerbations
- Oxygen therapy
- Gene therapy with nebulized plasmid DNA – aims to produce normal CFTR in the airways
- Surgery – lung transplantation, liver transplantation

## **Anaesthesia**

- Optimise before surgery (liaise with patient's usual multidisciplinary team) – includes medication review, more intense daily physiotherapy, nebulised drugs & treatment of active infections
- Regional preferred, where possible – avoids airway manipulation & optimises postoperative analgesia
- LMA with spontaneous ventilation may minimise detrimental effects of GA on respiratory mechanics
- ETT facilitates tracheal suctioning of secretions intraoperatively & allows improved control of gas exchange – but remember to keep airway pressures as low as possible
- Humidified & warmed gases to avoid drying of mucous
- Avoid nasal intubation due to high incidence of nasal polyposis
- Maintenance with volatiles will aid bronchodilation
- Short acting drugs to facilitate rapid emergence
- Careful positioning & padding due to cachexia
- Postoperative – HDU/ICU admission in advanced disease, early extubation, chest physiotherapy, early mobilisation

## Lung Cancer (Oxford p366+382, Stoelting p504, Slinger)

Leading cause of cancer death, 5 Types: (1) Adenocarcinoma (32%), (2) Squamous cell (29%), (3) Small cell (18%), (4) Large cell (9%), (V) Bronchoalveolar (3%)

### **Key points in history**

Ask about symptoms – haemoptysis, dyspnoea, cough, chest pain, wt loss, fatigue, lethargy

Risk factors – smoking history, occupational exposure, chronic lung scarring (TB, fibrosis)

Diagnosis achieved by FNA?, Bronchoscopy?

Imaging + investigations thus far – staging requires tissue diagnosis; CT imaging for local effects + sizing, PET for metastatic disease

### **4 M's**

**Mass effect** – obstructive pneumonia, lung abscess, SVC syndrome, Pancoast syndrome, recurrent laryngeal or phrenic nerve compression, mediastinal compression

**Metabolic effects** – Eaton-lambert syndrome, hypercalcaemia, hyponatraemia, Cushing's syndrome

**Metastasis** – brain, bone, liver, adrenal

**Medications** – chemotherapy – bleomycin (pul toxic); doxorubicin (cardiac toxicity); renal toxicity (cisplatin)

### **Key bedside signs**

Cigarette staining, weight loss, finger clubbing, hoarse voice from recurrent laryngeal nerve compression

Pancoast syndrome – neoplasm of superior lung with involvement of brachial plexus (arm/hand wasting + pain), cervical sympathetic nerves (Horner's Syndrome), compression of blood vessels + oedema

Chest signs will vary – fixed inspiratory wheeze over large bronchus, pneumonia, effusions, abscess

### **Key investigations**

Imaging – CXR – often normal, CT looking for size lymphadenopathy, PET

Biopsy/washings + diagnosis

RFTs – PPO FEV1, PPO DLCO

Cardiopulmonary testing – VO2 Max

### **Medical management & measure of optimal treatment**

Pre-op optimization of resp function

- Smoking cessation
- Dilation of airways if reversible component
- Loosening + removal of secretions
- Psychological – information, motivation, nutrition

Generally if FEV1 >2L patient could tolerate a pneumonectomy; if FEV1 >1.5L could tolerate lobectomy

Pre-op assessment of respiratory function – 3 legged stool

1. Respiratory mechanics – PPO FEV1 >40% - minimal risk; <30% high mortality risk
2. Cardiopulmonary testing – VO2 max >15mls/kg/min acceptable = 600m on 6MWT = ~4METs. VO2max <10mls/kg/min absolute contraindication
3. Lung parenchymal function – PPO DLCO >40% good outcome; <30% non-survival

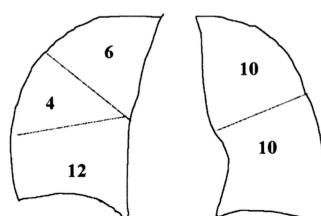
\*\* Can use V/Q scanning to assess distribution + tissue function in borderline cases

### The“3-legged” Stool of Pre-thoracotomy

#### Respiratory Assessment

<u>Respiratory Mechanics</u>	<u>Cardio-Pulmon. Reserve</u>	<u>Lung Parench. Function</u>
FEV 1* (ppo > 40%)	VO2 max.* (>15ml/kg/min)	DLCO* (ppo > 40%)
MVV, RV/TLC, FVC	Stair climb>2flight, PaO2 > 60 6 min walk, PaCO2 <45 Exercise SpO2<4%	

(\* most valid test)

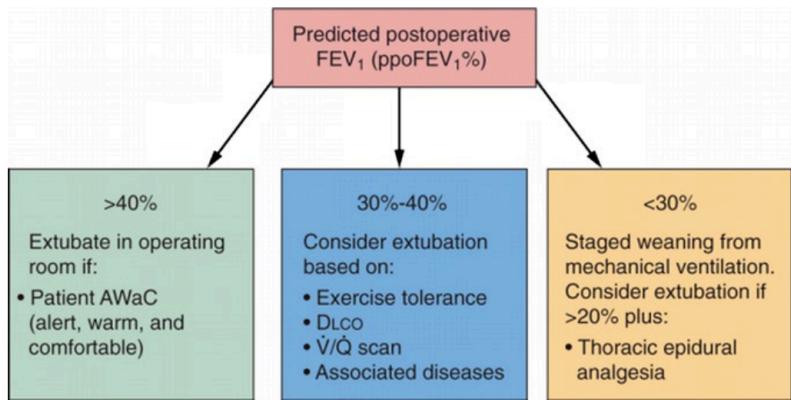


PPO FEV1 = preoperative FEV1 x (1- % functional lung tissue removed/100)

Intraoperative considerations during pneumonectomy:

- Lung isolation techniques
- Analgesic plan
- Restrictive fluid management (<20ml/kg in 1<sup>st</sup> 24 hours)
- Special considerations in thoracic patients – air trapping, bronchospasm, mass effect
- Closure, repositioning + tube exchange

- Post-thoracotomy anaesthetic management



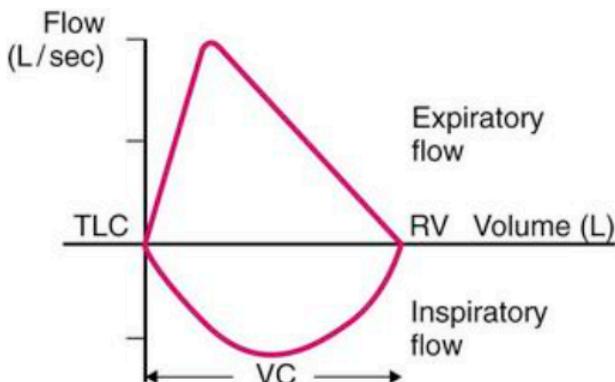
#### Early post-op complications

- Mediastinal shift/cardiac herniation
- SVT/AF
- Pulmonary oedema
- Haemorrhage
- Vocal cord dysfunction
- Chylothorax
- Bronchopleural fistula

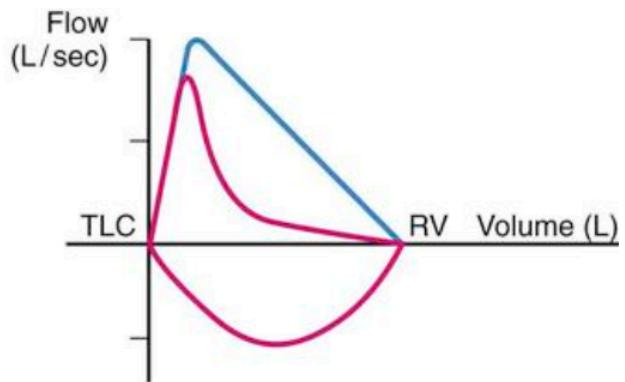
#### Lung cancer type & anaesthetic considerations:

Type	Considerations
Squamous cell	Central lesions (predominantly) Mass effects: obstruction, cavitation Hypercalcemia Hypertrophic pulmonary osteoarthropathy.
Adenocarcinoma	Peripheral lesions Metastases (distant) Growth hormone, corticotropin
Small cell	Central lesions (predominantly) Few surgically treatable Paraneoplastic syndromes Lambert-Eaton syndrome Fast growth rate Early metastases
Carcinoid	Proximal, intra-bronchial
Benign (predominantly)	No association with smoking 5-year survival >90%
Mesothelioma	Carcinoid syndrome (rarely) Intraoperative hemorrhage Direct extension to diaphragm, pericardium, etc.

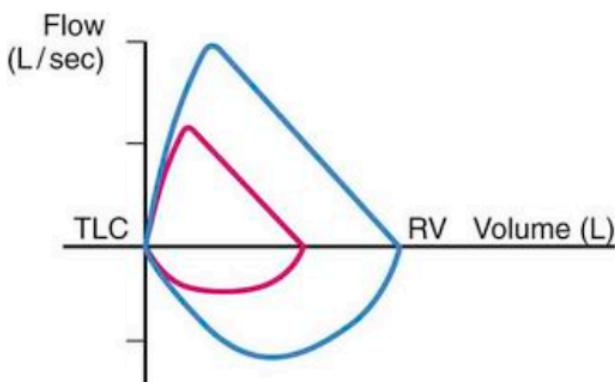
### Flow-volume loops



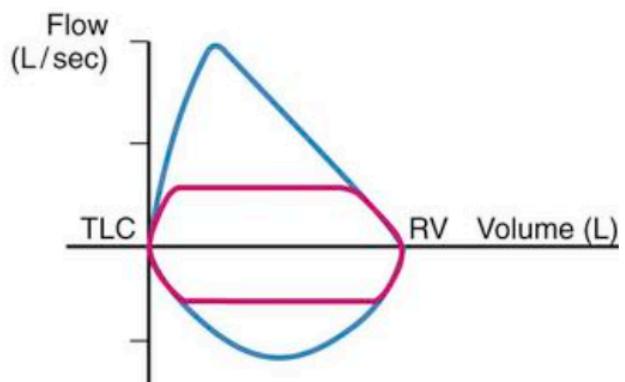
A. Normal



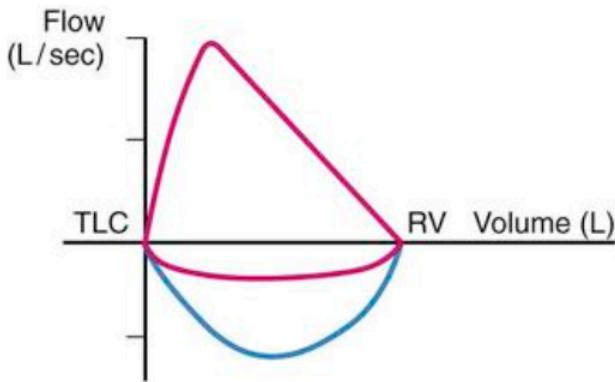
B. Emphysema



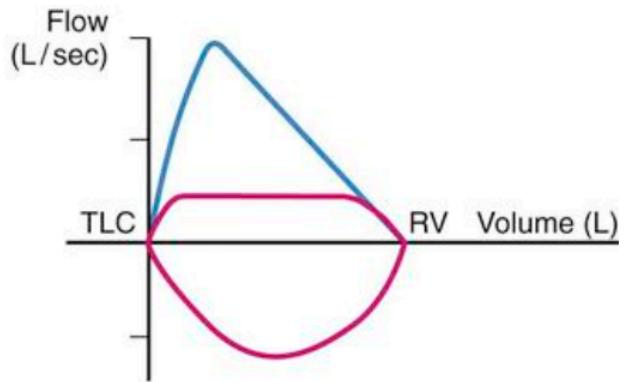
C. Unilateral main-stem bronchial obstruction



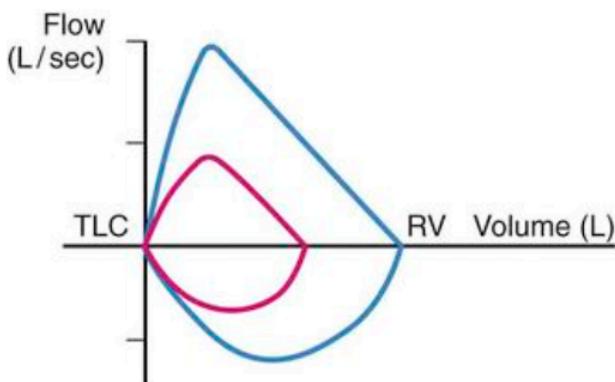
D. Fixed UAO



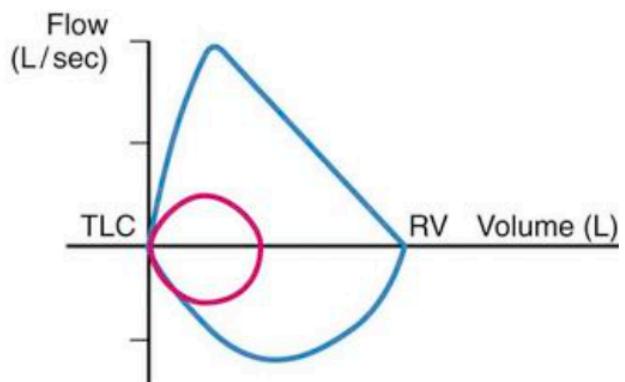
E. Variable extrathoracic UAO



F. Variable intrathoracic UAO



G. Restrictive parenchymal lung disease



H. Neuromuscular weakness

## Post-Lung Transplantation (Oxford p125, Stoelting p214)

### Clinical Features

- History
  - What was indication/original lung disease?
    - COPD – FEV1 <25%, PaCO<sub>2</sub> >55mmHg
    - CF, Bronchiectasis – FEV1 <30%, PaCO<sub>2</sub> >50mmHg (usually double lung transplant)
    - Idiopathic Pulmonary Fibrosis – progressive symptoms, DLCO <60%
    - Primary Pulmonary Hypertension – NYHA class III or IV or mPAP >55mmHg
    - Eisenmenger's Syndrome – severe symptoms (although 2 year prognosis not improved)
  - Ask about transplant – how long ago, how many lungs transplanted, was the heart also transplanted
  - Complications – acute rejection episodes, stenosis of bronchial anastomosis, colonization
  - Current medications & immunosuppressive therapy (doses, agents, side effects)
  - Current exercise tolerance & level of dyspnoea?
- Examination
  - Cushingoid appearance, thoracotomy scars, breathlessness + accessory muscle use
  - Sputum production + cough
  - Auscultation – normally clear but listen for signs of infection + bronchiolitis obliterans (end-inspiratory pops/squeaks)
    - Bronchiolitis obliterans – chronic rejection, a fibroproliferative process that targets the small airways & leads to submucosal fibrosis + luminal obliteration; uncommon during first 6 months but incidence exceeds 60% in patients who survive at least 5 years; insidious onset characterised by dyspnoea, cough, ↓FEV1 + colonisation of airways with *Pseudomonas aeruginosa*
- Investigations
  - RFTs – look for obstructive/restrictive disease patterns, loss of parenchymal function (↓DLCO)
    - Chronic rejection – ↓FEV1, ↓VC, ↓TLC, ↑A-a gradient
  - ABG – PaO<sub>2</sub>, PaCO<sub>2</sub>
  - CXR/CT chest
  - ECG – watch for heart/lung transplant
  - Echocardiogram – left + right sided heart function, estimation of RVSP
  - Heart catheterization – CAD, valvular function, pulmonary HTN
  - Biopsy results/recent bronchoscopy

### Treatment

- Maintenance immunosuppression with triple therapy:
  - Calcineurin inhibitors, block IL-2 gene transcription (cyclosporine, tacrolimus)
    - Side effects – hypertension, nephrotoxicity, hyperkalemia, hepatotoxicity, diabetes, neurotoxicity (seizures), anaemia, leucopenia, thrombocytopenia
  - Antimetabolites, purine synthesis inhibitors (azathioprine, mycophenolate mofetil)
    - Side effects – anaemia, leucopenia, thrombocytopenia, hyperglycemia, nephrotoxicity, hepatotoxicity
  - Corticosteroids, T-cell dependent immunity suppression + inhibition of IL-2 production (prednisone, methylprednisolone)
    - Side effects – susceptibility to infections, decreased wound healing, suppression of hypothalamic-pituitary-adrenal axis, hyperglycemia, fat redistribution (buffalo hump, moon-facies, fat loss from extremities), decreased skeletal muscle mass, osteoporosis, peptic ulceration, psychosis

### Anaesthesia

- Preoperative – focus on:
  - Function of transplanted lung
  - Possibility of rejection or infection of transplanted lung
  - Effects of immunosuppressive therapy on other organ systems -
  - Disease of the native lung
  - Planned surgical procedure & its effects on the lungs
- Intraoperative
  - Patients loose cough reflex below level of tracheal anastomosis & do not effectively clear secretions unless awake
  - Regional anaesthesia recommended – diminished cough reflex, risk of pulmonary infection, potential for bronchoconstriction
  - Place ETT just distal to vocal cords in order to avoid damage to anastomosis site
  - IPPV may be complicated by differences in lung compliance between native & transplanted lung
  - If need DLT – place endobronchial lumen in native lung bronchus to avoid damage to anastomosis site
- Postoperative
  - Aim for rapid recovery of respiratory function & early extubation

**Table 1** Side effects and toxicity of the commonly used immunosuppressive agents

Agent	Side effect/toxicity
Cyclosporine A	Hypertension Neurotoxicity (tremor, paresthesias, headache, confusion, seizures) Nephrotoxicity Hepatotoxicity Hyperkalemia/hypomagnesemia Gastric atony, nausea, vomiting Gingival hyperplasia, hypertrichosis
Glucocorticoids	Hypertension/fluid retention Psychosis, mood changes Glucose intolerance Adrenal suppression Electrolyte abnormalities Peptic ulcerations, pancreatitis Osteoporosis, myopathy, aseptic necrosis Poor wound healing, cataracts
Azathioprine	Hepatotoxicity, pancreatitis Nausea, vomiting Myelosuppression Arthralgias, rash, stomatitis
Tacrolimus (FK 506)	Hypertension, dyspnea, palpitations Headache, tremor, paresthesias, seizures, focal neurological deficits Nephrotoxicity, hyperkalemia Glucose intolerance, nausea, vomiting Thrombocytopenia
Antilymphocyte globulin	Leukopenia/thrombocytopenia Systemic symptoms
Muromonab-CD3 (OKT3)	Noncardiogenic pulmonary edema Encephalopathy/aseptic meningitis Systemic symptoms
Mycophenolate mofetil (MMF)	Hypertension Hyperkalemia/hypophosphatemia Anemia Arrhythmias (tachycardia) Muscle weakness

[\*\*Pulmonary Fibrosis\*\*](#)

[\*\*Fibrosing Alveolitis\*\*](#)

[\*\*Phrenic Nerve Palsy\*\*](#)

[\*\*Tuberculosis\*\*](#)

[\*\*Kartagener's Syndrome\*\*](#)

## Gastrointestinal/Renal

## **Acute Liver Failure** (Oxford p141, Stoelting p281)

- Syndrome defined by the occurrence of encephalopathy, coagulopathy & jaundice in an individual with previously normal liver function or well-compensated liver disease
- Subclassified according to King's Classification (based on a time scale + has prognostic implications)
  - **Hyperacute** – if encephalopathy develops within 7 days after the onset of jaundice; 36% survival rate
  - **Acute** – if encephalopathy develops within 8-28 days after the onset of jaundice; 26% survival rate
  - **Subacute** – if encephalopathy develops within 5-26 weeks after the onset of jaundice; 14% survival rate
- Causes
  - Common – paracetamol overdose, idiosyncratic drug reaction, acute viral hepatitis, alcoholic hepatitis + acute fatty liver of pregnancy
  - Less common – Wilson's disease, Reye's syndrome

### **Clinical Features**

- History
  - Range of symptoms – from nausea, vomiting + abdominal discomfort to confusion, agitation + coma
  - Ask about previous state of health, history of cirrhosis (to differentiate from decompensated chronic liver disease), FHx of liver failure & risk factors for viral hepatitis (IVDU, travel, sexual history, tattoos)
  - Thorough drug history
- Examination
  - Formal assessment of encephalopathy score (1 = slow mental function, 2 = inappropriate behavior, 3 = permanent somnolence, 4 = coma)
  - Look for jaundice, coagulopathy, hypoglycemia, hypotension, septic shock + renal failure
    - Note blood pressure (hypotension with low SVR + high CO) + urine output (oliguric renal failure)
  - Abdomen – evaluate liver + spleen size, presence of ascites
  - Signs of chronic liver disease
- Investigations
  - FBC (high WCC in inflammation, platelets, anaemia in bleeding)
  - Coagulation studies
  - Biochemistry screen – renal impairment, elevated ALT + AST
  - Blood glucose
  - ABG + lactate
  - Ammonia ( $>114\mu\text{mol/L}$  → development of severe cerebral oedema)
  - Paracetamol level
  - Immunological, microbiological + toxicology screen

### **Treatment**

- HDU/ICU admission
- Invasive monitoring – CVL, IAL
- Fluid resuscitation, inotropic support (noradrenaline)
- Prophylactic antimicrobials with broad-spectrum coverage of gram positive + negative activity & anti-fungal (eg. piptaz with fluconazole)
- Early enteral feeding
- Intubation if grade 3 or 4 encephalopathy
- Renal replacement therapy
- Mannitol for  $\uparrow$ ICP & seizure control
- N-acetyl cysteine for paracetamol overdose
- Consideration of liver transplantation – patient selection based on KCH prognostic criteria

**Table 2 King's College Hospital prognostic criteria** (originally devised as prognostic criteria to predict patient survival without liver transplantation but now used as selection criteria for potential liver transplant recipients)

Paracetamol hepatotoxicity	Non-paracetamol hepatotoxicity
Arterial pH $<7.30$ (7.25 if given N-acetyl cysteine) or All three of the following: <ul style="list-style-type: none"><li>• Prothrombin time <math>&gt;100</math> s</li><li>• Creatinine <math>&gt;300 \mu\text{mol litre}^{-1}</math></li><li>• Grade III encephalopathy</li></ul>	Prothrombin time $>100$ s or Any three of the following: <ul style="list-style-type: none"><li>• Unfavourable aetiology (seronegative or drug-associated fulminant hepatic failure)</li><li>• Jaundice <math>&gt;7</math> days before encephalopathy</li><li>• Age <math>&lt;10</math> or <math>&gt;40</math> yr</li><li>• Prothrombin time <math>&gt;50</math> s</li><li>• Serum bilirubin <math>&gt;300 \mu\text{mol litre}^{-1}</math></li></ul>

## Chronic Liver Disease/Cirrhosis (Oxford p142, Stoelting p279)

- Two main types of chronic liver disease – chronic hepatitis & cirrhosis
- Important causes:
  - Chronic hepatitis – HCV, HBV, autoimmune, drug induced, Wilson's disease,  $\alpha 1$ -antitrypsin deficiency
  - Cirrhosis – alcohol, HCV, HBV, drugs, non-alcoholic steatohepatitis, primary sclerosing cholangitis, primary biliary cirrhosis, haemochromatosis, Wilson's disease, chronic constrictive pericarditis,  $\alpha 1$ -antitrypsin deficiency, idiopathic

### Clinical Features

- History
  - May be asymptomatic or have symptoms – fatigue, pruritis, bleeding, abdominal pain, nausea, anorexia, myalgia, jaundice, dark urine, pale stools, fever, weight loss
  - Exposure to alcohol + drugs & risk factors for exposure to hepatitis B or C
  - Family history
  - Treatment
- Examination
  - Hands – leuconychia, clubbing, palmar erythema, bruising, asterixis
  - Face – jaundice, scratch marks, spider naevi, fetor hepaticus
  - Chest – gynaecomastia, loss of body hair, spider naevi, bruising, pectoral muscle wasting
  - Abdomen – hepatosplenomegaly, ascites, signs of portal hypertension (splenomegaly, collateral veins / haematemesis from oesophageal or gastric varices, ascites), testicular atrophy
  - Legs – oedema, muscle wasting, bruising
  - Fever – occurs in up to 1/3 of patients with advanced cirrhosis or if there is infected ascites
- Presence of  $\geq 2$  of the following signs suggests cirrhosis – spider naevi, palmar erythema, splenomegaly or ascites, abnormal collateral veins on abdomen, ascites
- Investigations
  - Bilirubin
  - FBC – anaemia, thrombocytopenia
  - Coagulation studies – coagulopathy
  - Hepatic function – albumin, prothrombin time/INR, glucose
  - Liver injury – ALT, AST, ALP, GGT, LDH
  - Alpha-fetoprotein – elevated in hepatocellular carcinoma
  - Autoantibodies, metabolic (Fe, copper,  $\alpha 1$ -antitrypsin, TFTs) & viral markers
  - Abdominal ultrasound/CT – portal hypertension, ascites, liver size + masses
  - Ascitic fluid evaluation – cell count, culture, protein
  - Liver biopsy

### Severity

- **Modified Child-Pugh classification**
  - Reasonably reliable predictor of survival in many liver diseases & predicts the likelihood of major complications of cirrhosis, such as bleeding from varices + spontaneous bacterial peritonitis

Sign of Hepatic Dysfunction	1 point	2 points	3 points
<b>Encephalopathy grade</b>	None	1-2	3-4
<b>Ascites</b>	Absent	Mild	Moderate to severe
<b>Bilirubin</b>	<35 $\mu\text{mol/L}$	36-60 $\mu\text{mol/L}$	>60 $\mu\text{mol/L}$
<b>Albumin (g/L)</b>	>35 g/L	28-35 g/L	<28 g/L
<b>INR or prothrombin time</b>	<1.7 or 1-4 secs	1.7-2.3 or 4-6 secs	>2.3 or >6 secs

Points	Class	1 year survival	2 year survival	Perioperative mortality
$\leq 6$	A	100%	85%	<5% (10% for intraabdominal surgery)
7-9	B	81%	57%	5-50% (30% intraabdominal surgery)
$\geq 10$	C	45%	35%	>50% (80% for intraabdominal surgery)

- **Model for End-Stage Liver Disease (MELD) score**
  - Predicts prognosis of patients with liver disease + portal hypertension & currently used to establish priority listing for liver transplantation
  - Calculated from three non-invasive variables:
    1. Serum creatinine concentration
    2. Serum bilirubin level
    3. INR
  - MELD score =  $3.8 [\log \text{bilirubin}] + 11.2 [\log \text{INR}] + 9.6 [\log \text{creatinine}] = 6.4$

- **Paediatric End-stage Liver Disease (PELD) system**
  - Used for children <12 years
  - Based on:
    1. Serum bilirubin level
    2. INR
    3. Serum albumin
    4. Age
    5. Nutritional status
- Complications
  - Ascites & spontaneous bacterial peritonitis
  - Portal hypertension (portal pressure >10mmHg) & variceal bleeding
  - Hyperdynamic circulation (high CO, low SVR)
  - Hepatic encephalopathy
    - Grade 0 = normal mental state
    - Grade 1 = mental changes – lack of awareness, anxiety, euphoria, reduced attention span, impaired ability to add + subtract
    - Grade 2 = lethargy, disorientation (for time), personality changes, inappropriate behaviour
    - Grade 3 = stupor, but responsive to stimuli; gross disorientation, confusion
    - Grade 4 = coma
  - Hepatorenal syndrome
  - Hepatopulmonary syndrome – defined by a high plasma creatinine + low urine sodium excretion, which does not respond to volume loading, in the absence of intrinsic renal disease
  - Portopulmonary hypertension
  - Anaemia
  - Coagulopathy
  - Hepatocellular carcinoma & cholangiocarcinoma

## Treatment

- Treatment of acute complications
  - Portal hypertension – propranolol
  - Variceal bleeding – haemostatic resuscitation, urgent endoscopy with injection/banding of varices
  - Ascites – sodium + fluid restriction, spironolactone, frusemide, albumin, abdominal paracentesis
  - Spontaneous bacterial peritonitis – cefotaxime, norfloxacin, trimethoprim/sulfamethoxazole
  - Encephalopathy – remove precipitants, minimise absorption of dietary nitrogenous substances with lactulose
  - Hepatorenal syndrome – ocreotide, dopamine
- Long-term management
  - Treat underlying cause
  - Avoid hepatotoxic drugs & alcohol
  - Monitor for complications
  - Consider liver transplantation

## Anaesthesia

- Preoperative
  - Comprehensive history, examination + investigations to identify disease severity + complications
  - Ascertain diagnosis of HCV or HBV – infectious risk to staff
  - Coagulation profile before surgery – correct abnormalities
  - Check for anaemia, hypoglycemia & electrolyte abnormalities
  - Avoid sedative premedication if encephalopathic but give ranitidine for aspiration risk
- Intraoperative
  - Aspiration risk due to increased gastric volumes & delayed gastric emptying – ETT with RSI + cricoid
  - Consider invasive monitoring (IAL, CVL) – cardiomyopathy with alcoholic liver disease
  - Contraindicated – TOE probe placement, nasogastric tubes & oesophageal temperature probes
  - Account for changes to pharmacokinetics (due to impaired hepatic synthetic function, increased Vd, decreased plasma protein binding of medications + decreased drug clearance) & avoid hepatotoxic agents
  - Maintain adequate hepatic blood flow – diseased liver susceptible to damage from relative hypoperfusion or hypoxaemia because hepatic blood supply is dependent on hepatic arterial blood flow in the presence of portal hypertension
  - Avoid renal hypoperfusion – can worsen hepatorenal syndrome
  - Monitor neuromuscular function due to decreased metabolism (rocuronium) & chance of increased suxamethonium effect due to decreased plasma cholinesterase – cisatracurium + atracurium preferred
  - Neuraxial techniques contraindicated with coagulopathy
- Postoperative
  - Consider HDU/ICU admission – common causes of mortality in perioperative period → sepsis, renal impairment, bleeding & worsening of hepatic failure with encephalopathy

## Haemochromatosis

- Autosomal recessive disorder that disrupts the body's regulation of iron & is characterised by increased accumulation of iron in various organs (liver, kidney, pancreas, heart, adrenals, pituitary, joints, testes)
- Results in macronodular cirrhosis, diabetes from pancreatic fibrosis & cardiac iron deposition, often with heart failure, conduction abnormalities + coronary atherosclerosis
- Mutation in HFE gene on chromosome 6 – C282Y or H63D are two most important mutations
- Incidence 1:250, 1 in 10 people are carriers

### **Clinical Features**

- History
  - Ask about age at onset
    - Most asymptomatic at diagnosis & symptoms are insidious + extent of organ involvement varies
    - Although present from birth, tissue injury does not begin until age 30-40 years
    - Men – more likely to experience clinical disease + manifestations begin earlier in life
  - Ask about cirrhosis, hepatocellular carcinoma, diabetes, arthritis + bronze skin pigmentation
  - Ask about dilated cardiomyopathy, heart failure + arrhythmias/conduction disturbances
  - Ask about hypothyroidism + pituitary failure
  - Treatment – frequency of venesections
- Examination
  - Bronze skin pigmentation
  - Arthritic joint abnormalities – most commonly affecting the metacarpophalangeal joints, proximal interphalangeal joints, knees, feet, wrists, back + neck
  - Hepatomegaly
  - Polyneuropathy
  - Additional signs of chronic liver disease, hypothyroidism, diabetes + cardiovascular disease
- Investigations
  - Elevated transferrin saturation – values >45% indicate further testing (best screening test)
  - Elevated serum transferrin level
  - Elevated serum ferritin – good evidence of iron overload (>300mcg/L in men + >200mcg/L in women) but remember it is also an acute-phase reactant
  - Elevated serum iron
  - Elevated AST, ALT + ALP
  - Hyperglycemia
  - HFE mutation analysis
  - Liver biopsy – iron deposition in hepatocytes, bile ducts + supporting tissues (gold standard for diagnosis)
  - ECG – conduction abnormalities, echocardiogram – cardiomyopathy

### **Treatment**

- Should begin before any organs are damaged to prevent associated conditions
- Weekly phlebotomy
  - Best initiated as soon as the diagnosis is made – returns life expectancy to normal if no cirrhosis/diabetes
  - Goal = serum ferritin level <50mcg/L + transferrin saturation <30%
  - Erythroid growth factors may be used to maintain adequate Hb during aggressive phlebotomy
  - Therapeutic phlebotomy may mitigate or prevent some manifestations such as fatigue, elevated liver enzymes, hepatomegaly, abdominal pain, arthralgias + hyperpigmentation; other complications do not respond to phlebotomy
- Iron chelation therapy with deferoxamine (SC/IV) or deferasirox (PO) – not commonly used – may be used in patients with haemochromatosis associated with significant anaemia unresponsive to erythroid growth factors or severe end-organ involvement
- Multiple organ (liver, heart, pancreas) transplantation may be required

### **Anaesthesia**

- Preoperative – check that ferritin is at low end of normal – if not, postpone surgery (if possible) until this is achieved, treat coagulopathy & check for conduction abnormalities + cardiomyopathy
- Intraoperative – avoid myocardial depressants, titrate hepatic metabolized drugs to effect in patients with liver dysfunction, avoid hepatotoxic agents, avoid regional anaesthesia in presence of coagulopathy
- Postoperative – consider HDU/ICU

## Wilson's Disease

- Inherited disease (autosomal recessive) of copper metabolism dysfunction characterised by cirrhosis & central nervous system findings
- Caused by mutation in ATPase copper transporting beta-polypeptide gene
  - Defect in copper metabolism leads to decreased incorporation of copper into ceruloplasmin + reduction in biliary copper excretion
  - Results in deposition of copper into:
    - Liver – resulting in fatty intracellular accumulations progressing to deposition of collagen, fibrosis + nodular cirrhosis followed by development of portal hypertension + oesophageal/gastric varices
    - Brain – particularly basal ganglia, putamen, globus, pallidus + caudate, resulting in inflammation, gliosis + eventually loss of neurons
    - Kidney – resulting in Fanconi syndrome, aminoaciduria, glycosuria, phosphaturia + nephrolithiasis
    - Cardiac – copper deposition in heart, may develop cardiomyopathy, rhythm abnormalities + increased autonomic tone
    - Other systemic involvement – haemolytic anaemia, osteoporosis + spontaneous fractures, rhabdomyolysis + hypoparathyroidism
- Incidence 1:30,000

## Clinical Features

- History
  - Symptoms typically begin between 6-20 years of age
  - Ask about multisystem involvement – liver, neurology, kidney, cardiomyopathy, anaemia, fractures
  - Treatment received & compliance
  - Evaluate for penicillamine side effects (myasthenia-like syndrome)
- Examination
  - Eyes – *Kayser-Fleischer rings* (pathognomonic) – appear as brownish deposit at periphery of cornea
  - Skin – pigmentation + bluish discolouration at base of fingernails (azure lunulae)
  - Look for signs of acute liver failure/chronic liver disease
  - Neurological – mask-like facies, pseudobulbar involvement, drooling, dysphagia, dysarthria, intention tremor, loss of fine motor control, dystonia, incoordination + gait disturbance
  - Assess for rhythm disturbance + signs of heart failure (cardiomyopathy)
- Investigations
  - FBC, LFTs, coagulation studies, albumin level, renal function
  - Low serum uric acid + phosphorus
  - Low serum copper <65mcg/L
  - Low serum ceruloplasmin level <200mg/L
    - However, Wilson's disease is not a failure to produce ceruloplasmin – it is a failure of copper transport followed by coupling to ceruloplasmin
  - Elevated 24-hour urinary copper excretion
  - ECG + echocardiogram for arrhythmias + cardiomyopathy
  - Liver biopsy – increased hepatic copper content



## Treatment

- Chelating agents – penicillamine, trientine – lead to improvement of neurologic symptoms + prevention of cirrhosis
  - Penicillamine side effects – leucopenia, thrombocytopenia, aplastic anaemia, nephrotic syndrome + myasthenia-like syndrome
- Zinc – inhibits intestinal copper absorption
- Ammonium tetrathiomolybdate for neurologic symptoms
- Fulminant hepatic necrosis occurs in 25% + requires urgent liver transplantation (lifesaving)

## Anaesthesia

- Preoperative
  - Clinical evaluation of liver function & neurologic + cardiac status
  - Correct coagulopathy prior to surgery
  - Ensure uninterrupted penicillamine therapy in perioperative period
- Intraoperative
  - Consider degree of liver dysfunction when selecting anaesthetic agents
  - Caution with neuromuscular blocking agents in presence of myasthenia-like syndrome – may have difficulty reversing muscle relaxants
- Postoperative
  - Consider HDU/ICU – respiratory complications are common

## Hepatitis C

Key points in history + examination:

- Predominantly parenterally transmitted – particularly common in IVDU
- Majority of patients usually incidentally found & asymptomatic – fatigue most common symptom
- ~80% of infected patients develop chronic hepatitis over a 20 year period & 20-30% of patients with chronic hepatitis C develop cirrhosis
- Once cirrhosis develops – signs + symptoms of end-stage liver disease
- After 25yrs of infection ~4% develop hepatocellular carcinoma

Key investigations:

- Diagnosis based on positive HCV antibodies
- Quantitative HCV-PCR is useful in monitoring disease response
- Liver biopsy necessary to stage disease + estimate extent of fibrosis

Medical management + optimisation:

- Current therapy of pegylated interferon + oral ribavirin for 12 months – sustained response rates of 40%
- Ensure vaccinated against hepatitis A + B
- ESLD – transplant candidates – most commonest reason for liver transplant today

## Hepatitis B

Key points in history + examination:

- May be transmitted parenterally, sexually or via neonatal maternal transmission
- Most infected individuals seroconvert + develop immunity
- A small proportion develop chronic hepatitis B + ultimately cirrhosis & then have a high risk of developing hepatocellular carcinoma

Key investigations:

- Serology
  - HBsAg – marker of ongoing infection (diagnostic)
  - HBeAg – active viral replication
  - AntiHBs + antiHBc – previous infection
  - AntiHBs alone – vaccine induced immunity
  - HBV DNA – continued infectious state
- Liver biopsy important in staging patients with chronic hepatitis B

Medical management + optimisation:

- Antiviral therapy aimed at normalising ALT levels + stopping viral replication
- Treatment is with subcutaneous interferon or lamivudine or adefovir – have ~30% response rate
- Liver transplant can be considered but HBV recurs in transplanted liver + may be very aggressive

## **Chronic Kidney Disease (CKD)** (Oxford p128, Stoelting p341)

- Refers to a spectrum of disease in which a proven reduction in GFR has been present for more than 3 months
  - Defined as when GFR is <60ml/min for ≥3 months
- Causes:
  - Diabetic nephropathy
  - Hypertension
  - Glomerulonephritis (IgA nephropathy, SLE)
  - Polycystic kidney disease
  - Tubular interstitial nephritis (drug hypersensitivity, analgesic nephropathy)
  - Obstructive nephropathies (nephrolithiasis, prostatic disease)
  - Vascular diseases (renal artery stenosis, embolic disease, hypertensive nephrosclerosis)
  - Autoimmune diseases (SLE, amyloidosis)

### **Clinical Features**

- History
  - Determine cause, nature & course of CKD
  - Ask about uraemic symptoms to assess severity &/or adequacy of dialysis
    - Anorexia, nausea, vomiting, metallic taste, hiccups, pruritus, easy bruising, oedema
  - Find out if patient receives renal replacement therapy:
    - Modality- haemodialysis or peritoneal dialysis?
    - What access is it provided via – arteriovenous fistula, long-term haemodialysis catheter or Tenckhoff peritoneal dialysis catheter?
    - Last provided + next due?
    - 'Dry weight' (patient's normal weight following RRT), current weight
    - Fluid restrictions
    - Urine output (if any) produced per day
  - Orthopnoea + PND suggest fluid overload
  - High rate of cardiovascular disease – pericarditis, hypertension, heart failure, IHD
  - Medication history + potential nephrotoxins
  - Renal transplant – surgery/immunosuppression + side effects/rejection or on wait-list
- Examination
  - Mental state, pallor, bruising, scratch marks
  - Assess volume status
    - Dry mucous membranes, postural hypotension, tachycardia + ↑CRT suggest hypovolaemia
    - Oedema, weight gain, hypertension + ↑JVP suggest fluid overload
  - Arterio-venous fistulae, tenckhoff catheter, scars (dialysis, operations)
  - Hypertension, pericardial rub (uraemia), heart failure, peripheral oedema, volume overload
  - Lungs – chest crepitations + pleural effusions (pulmonary oedema)
  - Abdomen – hepatic congestion, enlarged kidneys + renal artery bruits
  - Peripheral myopathy (proximal), retinopathy, neuropathy (diabetes)
- Investigations
  - GFR – estimate disease severity
  - Serum urea + electrolytes
  - FBC – anaemia, infection
  - Coagulation studies – derangements may be present with chronic disease, uraemia + following recent RRT
  - Urinalysis – protein, infection
  - Renal ultrasound
  - Renal biopsy
  - ECG – cardiovascular disease common, hyperkalemia – flattened P waves, broad + bizarre QRS complexes + tall peaked T waves

### **Severity**

- Classified into five stages:

<i>Stage 1</i>	GFR ≥90 ml/min/1.73m <sup>2</sup>	Kidney damage with normal function
<i>Stage 2</i>	GFR 60-89 ml/min/1.73m <sup>2</sup>	Kidney damage with mildly reduced function
<i>Stage 3</i>	GFR 30-59 ml/min/1.73m <sup>2</sup>	Moderately reduced function
<i>Stage 4</i>	GFR 15-29 ml/min/1.73m <sup>2</sup>	Severely reduced function
<i>Stage 5</i>	<15 ml/min/1.73m <sup>2</sup>	Very severe disease or dependent on renal replacement therapies (end-stage renal disease)

### **Treatment**

- Provide adequate nutrition + calories & restrict dietary sodium, potassium + phosphate

- Smoking cessation
- Control hypertension – ACE inhibitors, ARBs, non-dihydropyridine calcium channel blockers
- Lipid management with statin
- Restrict fluid if significant oedema present
- Diuretics for fluid overload
- Correct electrolyte abnormalities
- Control of renal osteodystrophy with calcium supplementation + vitamin D
- Resistance training to preserve lean body mass + muscle function
- Correct anaemia + give EPO
- Phosphate binders for hyperphosphatemia
- Avoid radiocontrast agents
- Initiate dialysis – urgent indications = uraemic pericarditis, neuropathy, neuromuscular abnormalities, congestive heart failure, hyperkalemia + seizures
- Kidney transplantation in selected patients
- General management plan:

Stage	GFR	Consequences	Actions to Consider
3	30-59	Hypertension, 2° hyperparathyroidism	<ul style="list-style-type: none"> <li>• 6 monthly eGFR initially</li> <li>• 12 monthly eGFR if stable</li> <li>• Annual Hb, K, Ca, P</li> <li>• Treat hypertension</li> <li>• Immunise against hepatitis B</li> </ul>
4	15-29	<i>Plus</i> anemia, hyperphosphatemia	<ul style="list-style-type: none"> <li>• 3 monthly eGFR initially</li> <li>• 6 monthly eGFR if stable</li> <li>• 6 monthly Hb, K, Ca, P &amp; PTH</li> <li>• Start phosphate-restricted diet and phosphate binders</li> <li>• Correct vitamin D deficiency</li> <li>• Start vitamin D analogue</li> <li>• Plan renal replacement therapy, including vascular access</li> </ul>
5	<15	<i>Plus</i> sodium + water retention, anorexia, vomiting, reduced higher mental function	Plan elective start of dialysis or preemptive renal transplant
5	<5	<i>Plus</i> pulmonary edema, coma, fits, metabolic acidosis, hyperkalemia, death	Start dialysis or provide palliative care

## Anaesthesia

- Preoperative
  - Trend in serum creatinine + urea
  - Blood volume status (body weight, orthostatic hypotension, tachycardia)
  - Glucose management (if diabetic)
  - Blood pressure should be well controlled before elective surgery
  - Serum K ≤ 5.5 mmol/L on day of surgery
  - Coagulopathy – consider need for desmopressin
  - Patients on dialysis should undergo treatment 24hrs prior to theatre
  - Discuss renal transplant patients with local transplant surgeons + nephrologists
- Intraoperative
  - Drug selection important
  - Fluid balance monitoring
  - Induction hypotension likely given antihypertensive drugs + recent dialysis
  - Monitoring + access difficulties
  - Positioning – if poor nutritional status
- Postoperative
  - Caution with opioids + avoid NSAIDs
  - Restart regular medications ASAP

Induction agents	
Propofol	No interaction, safe to use in renal failure
Thiopentone	Reduction in dose of 30–50% is advised
Benzodiazepines	Reduction in dose of 30–50% is advised
Muscle relaxants	
Suxamethonium	Caution due to precipitant hyperkalaemia. If it is used there will be no alteration in action.
Atracurium and Cisatracurium	Acceptable to use due to ester hydrolysis and hoffmann elimination.
Rocuronium	Accumulation can occur due to renal excretion, leading to a prolonged NMB.
Analgesics	
NSAIDs	Simple analgesics, following the WHO analgesic ladder
	Should be avoided in renal failure
Opiates	
Morphine	Active metabolite morphine-6-glucoronide, potent respiratory depressant and analgesic. Renal excreted, therefore will accumulate in renal failure.
Pethidine	Active metabolite norpethidine, is renally excreted, accumulation may precipitate seizures
Alfentanil	Safe to use. Inactive metabolites
Fentanyl	Safe to use. Inactive metabolite, which is renally excreted.
Remifentanil	Plasma and tissue esterase activity is not affected by renal failure. Therefore, they are safe to use in renal failure.
Inhalation agents	
	Safe to use in renal failure. Concern has been raised regarding the use of sevoflurane, due to the decreased excretion of fluoride ions, which may accumulate and worsen renal failure. Further, its metabolite Compound A production has been shown to be nephrotoxic in rats, but no clinical effect is seen in humans

## Potential Questions

*What are the manifestations and mechanisms in CKD?*

<b>Manifestation</b>	<b>Mechanism</b>
Accumulation of nitrogenous waste products	Decrease in GFR
Acidosis	Decreased ammonia synthesis Impaired bicarbonate absorption Decreased net acid excretion
Sodium retention	Excessive renin production Oliguria
Sodium wasting	Solute diuresis Tubular damage
Urinary concentrating defect	Solute diuresis Tubular damage
Hyperkalemia	Decrease in GFR Metabolic acidosis Excessive potassium intake Hyporeninemic hypoaldosteronism
Renal osteodystrophy	Impaired renal production of 1,25-dihydroxycholecalciferol Hypophosphatemia Hypocalcaemia Secondary hyperparathyroidism
Growth retardation	Inadequate caloric intake Renal osteodystrophy Metabolic acidosis Anaemia GH resistance
Anaemia	Decreased EPO production Iron/folate/vitamin B12 deficiency Decreased erythrocyte survival
Bleeding tendency	Defective platelet function
Infection	Defective granulocyte function Impaired cellular immune functions Indwelling dialysis catheters
Neurologic symptoms (fatigue, poor concentration, headache, drowsiness, memory loss, seizures, peripheral neuropathy)	Uraemic factors(s) Aluminium toxicity Hypertension
Gastrointestinal symptoms (feeding intolerance, abdominal pain)	Gastroesophageal reflux Decreased gastrointestinal motility
Hypertension	Volume overload Excessive renin production
Hyperlipidemia	Decreased plasma lipoprotein lipase activity
Pericarditis, cardiomyopathy	Uraemic factor(s) Hypertension Fluid overload
Glucose intolerance	Tissue insulin resistance

*What findings are suggestive of inadequate haemodialysis?*

<b>Clinical</b>	<b>Chemical</b>
<ul style="list-style-type: none"> <li>• Anorexia, nausea, vomiting</li> <li>• Poor nutritional status</li> <li>• Depressed sensorium</li> <li>• Pericarditis</li> <li>• Ascites</li> <li>• Minimal weight gain or weight loss between treatments</li> <li>• Fluid retention &amp; systemic hypertension</li> </ul>	<ul style="list-style-type: none"> <li>• Decrease in blood urea nitrogen concentration during haemodialysis &lt;65%</li> <li>• Albumin concentration &lt;4g/dL (sign of malnutrition)</li> <li>• Predialysis blood urea nitrogen concentration &lt;50mg/dL (sign of malnutrition)</li> <li>• Predialysis serum creatinine concentration &lt;5mg/dL (sign of malnutrition)</li> <li>• Persistent anaemia (HCT &lt;30%) despite EPO therapy</li> </ul>

*What are the indications for renal replacement therapy?*

Clinical indications for urgent RRT – ‘aeiou’:

- A – acidosis
- E – electrolyte abnormalities (usually hyperkalemia)
- I – intoxication (with harmful drugs or agents that can be artificially cleared with RRT – eg. sodium valprolate, ethylene glycol)
- O – oedema/fluid overload
- U – uraemic consequences (eg. pericarditis, encephalopathy)

**Table 2** Indications for continuous renal replacement therapy

Classical:

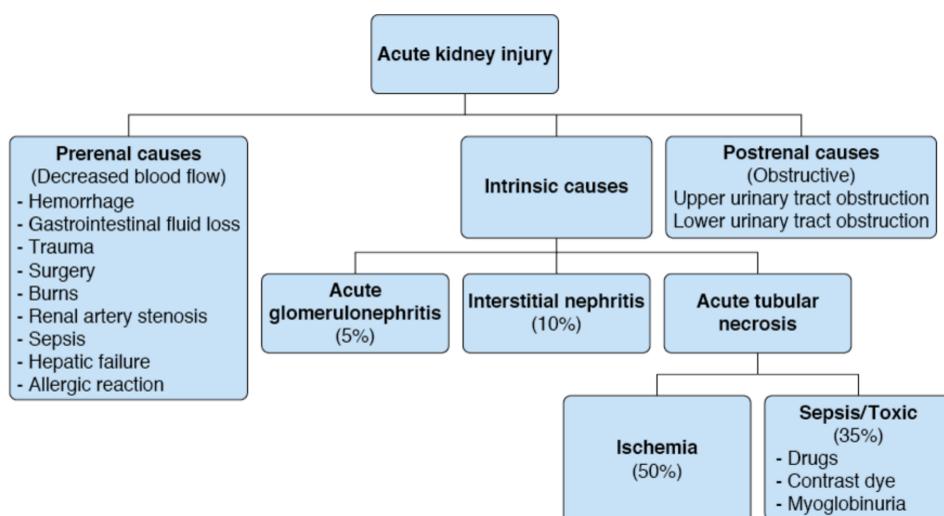
- Volume overload
- Metabolic acidosis ( $\text{pH} < 7.1$ )
- Hyperkalaemia ( $>6.5 \text{ mmol litre}^{-1}$ )
- Symptomatic uraemia (Pericarditis, encephalopathy, bleeding dyscrasias)
- Dialysable intoxications (e.g. lithium, ethylene glycol, methanol, aspirin, theophylline, vancomycin, procainamide)
- Hyperthermia (cooling)

Alternative:

- Endotoxic shock
- Hypothermia (rewarming)
- SIRS (pancreatitis, ARDS)
- Nutritional support
- Hepatic failure
- Deliberate hypothermia
- Severe dysnatraemia ( $<115 \text{ mmol litre}^{-1}$ ,  $>165 \text{ mmol litre}^{-1}$ )
- Traumatic rhabdomyolysis
- Plasmapheresis (Guillain–Barre syndrome, myasthenia gravis, thrombotic thrombocytopenic purpura)

Define acute kidney injury (AKI). What are the causes?

- AKI is defined as a syndrome of abrupt decline in renal excretory & homeostatic function



What are the RIFLE criteria?

- Highly sensitive interim staging system for AKI based on data that a small change in serum Cr influences outcome
  - Risk of renal dysfunction
  - Injury to the kidney
  - Failure of kidney function
  - Loss of kidney function
  - End-stage kidney disease
- Includes 3 grades of increasing severity of renal dysfunction & two clinical outcomes ('loss' & 'ESRD')
- Only one criterion (creatinine or urine output) has to be fulfilled to qualify for a stage
- Patients who receive RRT are considered to have met the criteria for stage 3 (failure) irrespective of the stage they are in at the time of RRT

<b>R</b>	Risk of renal dysfunction (stage 1) <i>1.5 fold ↑ in serum Cr or UO &lt;0.5ml/kg/hr for 6 hours</i>
<b>I</b>	Injury to the kidney (stage 2) <i>2.0 fold ↑ in serum Cr or UO &lt;0.5ml/kg/hr for 12 hours</i>
<b>F</b>	Failure of kidney function <i>3.0 fold ↑ in serum Cr or UO &lt;0.3ml/kg/hr for 24 hours</i>
<b>L</b>	Loss of kidney function for >4 weeks
<b>E</b>	ESRD – complete loss of renal function for >3months

- Most recent = Kidney Disease Improving Global Outcomes (KDIGO) staging criteria – no proven superiority in predicting the course of AKI over the original RIFLE criteria

<b>AKI stage</b>	<b>Serum creatinine</b>	<b>Urine output (ml/kg/hour)</b>
1	1.5–1.9 × baseline or >>0.3 mg/dl (>26.55 µmol/litre) increase	<0.5 for 6–12 hours
2	2.0–2.9 × baseline	<0.5 for ≥12 hours
3	3 × baseline or ≥4.0 mg dl (≥353.6 µmol/litre) increase or initiation of renal replacement therapy or in patients <18 years decrease in eGFR to <35 ml/minute/1.73 m <sup>2</sup>	<0.3 for ≥24 hours or anuria for ≥12 hours

*What is contrast-induced AKI (CI-AKI)?*

CI-AKI is defined as an increase in serum creatinine of more than 44 µmol/L or 25% above baseline at 48 hours following the contrast load. Factors increasing the risk of CI-AKI include preexisting hypovolemia & the use of high doses of iodinated, hyper-osmolar contrast media.

## Haemodialysis

### Clinical Features

- History
  - Indications of dialysis in acute renal failure:
    - Severe fluid overload
    - Refractory hypertension
    - Uncontrollable hyperkalemia
    - Nausea, vomiting, poor appetite, gastritis with hemorrhage
    - Lethargy, malaise, somnolence, stupor, coma, delirium, asterixis, tremor, seizures
    - Pericarditis (risk of hemorrhage or tamponade)
    - Bleeding diathesis (epistaxis, GI bleeding etc)
    - Severe metabolic acidosis
    - Blood urea nitrogen (BUN) >70-100 mg/dl
  - Indications of dialysis in chronic renal failure:
    - Pericarditis
    - Fluid overload or pulmonary oedema refractory to diuretics
    - Accelerated hypertension poorly responsive to antihypertensives
    - Progressive uremic encephalopathy or neuropathy such as confusion, asterixis, myoclonus, wrist or foot drop, seizures
    - Bleeding diathesis attributable to uremia
- Examination (as per CKD)
  - Mental state, pallor, bruising, scratch marks
  - Assess volume status
    - Dry mucous membranes, postural hypotension, tachycardia + ↑CRT suggest hypovolaemia
    - Oedema, weight gain, hypertension + ↑JVP suggest fluid overload
  - Arterio-venous fistulae, tenckhoff catheter, scars (dialysis, operations)
  - Hypertension, pericardial rub (uraemia), heart failure, peripheral oedema, volume overload
  - Lungs – chest crepitations + pleural effusions (pulmonary oedema)
  - Abdomen – hepatic congestion, enlarged kidneys + renal artery bruits
  - Peripheral myopathy (proximal), retinopathy, neuropathy (diabetes)
- Investigations
  - Serum urea + electrolytes (potassium, calcium, phosphate, magnesium)
  - FBC – anaemia
  - Coagulation studies
  - Blood sugar level

### Optimisation

- Anaemia – nutrition, supplements, EPO
- Normalise electrolytes + urea before surgery
- Blood pressure control
- Maximal medications for heart failure
- Nutritional status – dietitian review, water soluble vitamins removed by dialysis
- Know patient's 'dry weight' – if current weight is higher – risk of perioperative pulmonary oedema

### Anaesthesia

- Logistics of dialysis – as close to operation date as possible but a period of 6 hours should elapse before anaesthesia after dialysis to allow fluid compartment equilibration + clearance of residual heparin
- Uraemia may impair coagulation via platelet dysfunction
  - 0.3 microg/kg DDAVP
  - Cryoprecipitate
- Vascular access
  - Stay away from fistula except in emergency
  - Beware of identification band on fistula + compression of fistula during positioning
  - Avoid subclavian vein access, association with subclavian vein stenosis – preventing AV formation in that arm
- Drugs
  - Sevoflurane okay in ESRD
  - Low normal level of plasma cholinesterase – may prolong suxamethonium action
  - Atracurium/cisatracurium better than rocuronium/vecuronium but sugammadex may make rocuronium use okay

## Liver Transplant

## Kidney Transplant

# Endocrine

## Acromegaly (Oxford p162, Stoelting p404)

- Results from excessive GH secretion in adults, typically due to an anterior pituitary adenoma
- GH
  - Stimulates liver & other tissues to produce somatomedins which in turn promote growth
  - Protein anabolic hormone exerting its effects at ribosomal level
  - Diabetogenic – exerts an anti-insulin effect in muscle + increases hepatic glucose release
- Gigantism is the result of GH hypersecretion occurring before puberty & fusion of the epiphyses → results in massive skeletal & soft-tissue growth; however, acromegaly occurs when the growth plates have fused → only soft tissue & flat bone enlargement are possible

### Clinical Features

- Manifestations reflect parasellar extension of anterior pituitary adenoma & peripheral effects produced by excess GH
- History
  - Ask about current symptoms – headache, visual disturbances, rhinorrhea, voice changes, changes in appearance
  - Ask about comorbidities – duration, severity & functional capacity
  - Respiratory – sleep apnoea (60%), use of CPAP, previous difficult intubation
  - Cardiac – hypertension, coronary artery disease, cardiomyopathy, arrhythmias
  - Endocrine – diabetes (25%), hypopituitarism
  - GIT – colonic polyps & malignancy
  - Treatment to date & complications – medical, radiotherapy, surgical?
- Examination
  - General inspection
    - Body habitus/BMI
    - Greasy & thickened skin
  - Upper limb
    - Wide spade-like hands with osteoarthritic changes
    - Median nerve entrapment due to soft tissue overgrowth in carpal tunnel area
    - Proximal myopathy
    - Skin tags & acanthosis nigricans in axillae
  - Face & Eyes
    - Coarse facial features with large fleshy nose
    - Large supraorbital ridge causing frontal bossing
    - Thickened lips, enlarged tongue
    - Splayed & separated teeth with malocclusion
    - Mandibular enlargement with prognathism (jaw protrusion)
    - Visual field defect – classically bitemporal hemianopia due to compression of optic chiasm
    - Fundi – optic atrophy (due to nerve compression) & papilloedema (due to raised ICP)
  - Neck
    - Diffusely enlarged or multinodular thyroid
    - Listen for voice hoarseness
  - Chest
    - Coarse body hair, gynaecomastia
    - Heart – signs of arrhythmias, cardiomegaly & congestive cardiac failure due to IHD, hypertension or cardiomyopathy
  - Back
    - Kyphosis
  - Abdomen
    - Hepatic, splenic & renal enlargement
    - Testicular atrophy
  - Lower limbs
    - Osteoarthritis (hips & knees)
    - Pseudogout
    - Foot drop (due to common peroneal nerve entrapment)
- Investigations
  - Bloods
    - BSL (25% diabetic)
    - IGF-1 levels (increased in acromegaly)
    - GH levels
      - Measurement of single random GH level is not useful for diagnosis & does not correlate with severity

- Diagnosis confirmed by demonstrating failure of GH suppression to <0.4µg/L within 1-2 hours of an oral glucose load (75g)
    - Prolactin levels
      - Elevated in 25% of patients
    - Thyroid function, gonadotropins & sex steroids may be attenuated because of tumour mass effects
  - ECG – look for LVH
  - CXR
  - Echocardiography – look for systolic/diastolic dysfunction
  - MRI brain
- Is disease active or not?
    - Signs of active disease:
      - Large numbers of skin tags
      - Excessive sweating
      - Presence of glycosuria
      - Increasing visual field loss
      - Enlarging goiter
      - Hypertension
      - Headache

## Treatment

- Goal of treatment is to control GH + IGF-1 hypersecretion, ablate or arrest tumour growth, ameliorate comorbidities & restore pituitary function
- Trans-sphenoidal surgical resection is initial treatment of choice for most patients
  - Soft tissue swelling improves immediately after tumour resection
  - GH levels return to normal within 1 hour & IGF-1 levels normalise within 4 days
  - 10% of patients → acromegaly may recur several years after surgery
  - Hypopituitarism develops in up to 15% of patients postoperatively
  - Sub-frontal craniotomy performed when tumour extends above sella turcica
- Somatostatin analogues
  - Used as adjuvant treatment for preoperative shrinkage of large invasive macroadenomas + reduction of GH hypersecretion & to achieve biochemical control in those who decline surgery or when surgery fails
  - Exert their therapeutic effects through SSTR2 & SSTR5 receptors, both of which are expressed by GH-secreting tumours
  - **Octreotide acetate** = synthetic octreotide analogue
    - Suppresses integrated GH levels & normalizes IGF-1 levels in 75% of patients
  - Long-acting somatostatin depot formulations (**Octreotide** or **Lanreotide**) are preferred medical treatment
  - Side effects: nausea, abdominal discomfort, fat malabsorption, diarrhea, asymptomatic bradycardia & hypothyroxinemia
- GH receptor antagonists
  - **Pegvisomant** (administered by daily SC injection) antagonizes endogenous GH action by blocking peripheral GH binding to its receptor → suppresses serum IGF-1 levels & effects of excess endogenous GH
    - Note that GH levels remain elevated as it has no anti-tumour actions
- Dopamine agonists
  - **Bromocriptine** & **Cabergoline** – used as combined therapy with somatostatin analogues
- Irradiation or repeat surgery may be required for patients who cannot tolerate or do not respond to adjunctive medical therapy
  - Main disadvantages of radiotherapy include high rate of late hypopituitarism & slow rate of biochemical response
- Other
  - Management of systemic sequelae, including cardiovascular disease, diabetes & arthritis
  - Mandibular surgical repair may be indicated

## Anaesthesia

- Potentially difficult airway/difficult mask ventilation:
  - Distorted facial anatomy may interfere with face mask placement
  - Enlarged tongue + epiglottis predispose to upper airway obstruction & interfere with visualization of vocal cords by direct laryngoscopy
  - Distance between lips & vocal cords increased due to mandible overgrowth
  - Glottic narrowing (due to vocal cord enlargement) & subglottic narrowing may necessitate the use of an ETT with a smaller internal diameter than would be predicted based on the patient's age + size
  - Nasal turbinate enlargement may preclude the passage of nasopharyngeal or nasotracheal airways

- Preoperative history of dyspnea on exertion or hoarseness suggests involvement of larynx by acromegaly  
→ indirect laryngoscopy may be indicated to quantitate extent of vocal cord dysfunction
  - Prepare for AFOI if difficult intubation anticipated
- Monitoring:
  - IAL – inadequate collateral circulation (ulnar artery may be compromised in up to 50% of acromegalic patients & catheterization of radial artery could result in hand ischaemia) → USS Doppler before cannulation
  - Blood glucose concentrations – useful if associated diabetes or glucose intolerance
  - Peripheral nerve stimulation – used to guide dosing of non-depolarising muscle relaxants, particularly if skeletal muscle weakness is present
- Hormone supplementation: patients with preoperative hypopituitarism should receive hydrocortisone &/or thyroxine; consider preoperative endocrinology consult
- Heart failure: minimise further depression of cardiac function & optimise fluid therapy
- OSA: minimize opioid use, postoperative CPAP
- May need HDU/ICU bed
- Complications of pituitary surgery:
  - Major – CSF leak, meningitis, ischaemic stroke, vascular injury, intracranial haemorrhage, new cranial nerve palsy, visual loss & disorders of water imbalance (diabetes insipidus, SIADH)
  - Minor – sinus disease, septal perforation, epistaxis, wound infections & haematomas

## Potential Questions

*What are the causes of acromegaly?*

Excess GH secretion:

- Pituitary – somatotrope adenoma, mixed GH cell + prolactin cell adenoma
- Extrapituitary – pancreatic, ovarian or lung tumours, lymphoma

Excess GH-releasing hormone secretion:

- Central – hypothalamic hamartoma, choristoma, ganglioneuroma
- Peripheral – bronchial carcinoid, pancreatic islet cell tumour, small cell lung cancer, adrenal adenoma, medullary thyroid carcinoma, phaeochromocytoma

*What hormones are secreted by the pituitary gland?*

### ***Anterior Pituitary***

ACTH (adrenocorticotropic hormone)	Stimulates cortisol release from adrenal cortex
GH (growth hormone)	Anabolic effect on bone + muscle
TSH (thyroid stimulating hormone)	Impairs glucose utilisation + promotes lipolysis
FSH (follicle stimulating hormone)	Stimulates iodine binding by thyroid gland + thyroxine release
LH (luteinizing hormone)	Stimulates oestrogen production + egg maturation at female ovaries
Prolactin	Stimulates sperm production at male testes
MSH (melanocyte stimulating hormone)	Stimulates ovulation + progesterone production at female ovaries
Beta-endorphins	Stimulates testosterone production at male testes
<b><i>Posterior Pituitary</i></b>	Stimulates milk production
Oxytocin	Increases skin pigmentation
ADH (anti-diuretic hormone)	Inhibit pain sensation
	Stimulates uterine contractions
	Stimulates contractions of mammary milk ducts
	Promotes renal retention of water

## Diabetes & Complications (Oxford p156, Stoelting p376)

- Group of metabolic disorders characterised by hyperglycemia due to an absolute or a relative deficiency of insulin
- Long-term, poorly controlled blood sugar leads to multiorgan disease & failure, particularly the eyes, kidneys, nerves, heart & blood vessels
  - Risk factors for complications include long duration of diabetes, poor glycemic control, obesity, hypertension, hyperlipidemia, smoking & sedentary lifestyle
- Aetiological classification:

<b>Type 1A</b>
• Autoimmune destruction of pancreatic $\beta$ cells
<b>Adult Onset Type 1</b>
• Islet cell antibodies
<b>Type 2 (90%)</b>
• Insulin deficiency & resistance
• Combination of hereditary (high concordance rate in identical twins) & environmental (obesity, sedentary lifestyle, high carbohydrate food content) factors
<b>Due to other factors</b>
• Endocrine abnormalities – acromegaly, Cushing's syndrome, glucagonoma, phaeochromocytoma,
• Drugs – glucocorticoids, OCP, diuretics, phenytoin
• Insulin receptor unavailability +/- circulating antibodies
• Pancreatic disease – chronic pancreatitis, pancreatectomy, haemochromatosis, cystic fibrosis
• Genetic syndromes – maturity onset diabetes of the young (MODY), familial hyperlipidemia, lipotrophy, myotonic dystrophy, Down syndrome
<b>Gestational</b>
• Diabetes diagnosed during pregnancy that is due to pregnancy-related insulin resistance

## Clinical Features

- History
  - Age at diagnosis
  - Insulin required at start?
  - Problem that led to diagnosis?
    - Polyuria, thirst, weight loss, recurrent skin infections, screening assessment
  - Previous & current drug treatment
  - Diabetic diet?
  - Mode of blood sugar testing & usual levels
  - Problems with hypoglycaemia?
    - Sweating, confusion, malaise or unconsciousness
  - Ketoacidosis & hospital admissions
  - Complications – eyes, nerves, blood vessels, kidneys
  - Regular testing/consultation for complications?
- Examination
  - General inspection
    - Evidence of dehydration, obesity or recent weight loss
    - Abnormal endocrine facies (acromegaly or Cushing's)
    - Pigmentation (eg. haemochromatosis – bronze diabetes)
  - Lower limbs
    - Inspect skin for necrobiosis, hair loss, infection, pigmented scars, atrophy, ulceration, injection sites
    - Look for muscle wasting & Charcot's joints at ankles
    - Palpate temperature of feet & peripheral pulses
    - Assess for peripheral neuropathy
  - Arms
    - Look for injection sites & skin lesions
    - Palpate pulse & take BP lying + standing (autonomic neuropathy)
  - Eyes – visual acuity, fundoscopy, CN III palsies
  - Mouth – candida
  - Chest – targeted cardiorespiratory exam
  - Abdomen – palpate for hepatomegaly
- Investigations
  - Urine analysis for glucose, protein & infection
  - Bloods – FBC, renal function
  - ECG
  - Echocardiogram & stress testing

- Diagnostic criteria:
  - HbA1C 6.5%
  - OR
  - Fasting plasma glucose 7 mmol/L (fasting = no caloric intake for 8 hrs)
  - OR
  - 2-hour plasma glucose 11.1 mmol/L during an oral glucose tolerance test
  - OR
  - A random plasma glucose 11.1 mmol/L in a patient with classic symptoms of hyperglycemia or hyperglycaemic crisis
- Pre-diabetic patients = blood tests do not meet criteria for diabetes but are still higher than normal

### Treatment

- Changing lifestyle – diet & exercise
- Anti-diabetic agents:

<b>Insulin analogues</b>	Short, intermediate or long acting Given to mimic physiological pattern of insulin secretion in normal people so it covers both basal rate & postprandial response
<b>Glucagon-like peptide 1 receptor agonists</b>	Eg. <i>exenatide</i> Limit postprandial glucose rises & decrease glucagon secretion
<b>Dipeptidyl peptidase 4 inhibitors</b>	Eg. <i>sitagliptan</i> Prevent inactivation of glucagon-like peptide 1 & prolong effect of endogenously secreted incretin (intestine derived peptide)
<b>Thiazolidinediones</b>	Eg. <i>pioglitazone</i> Insulin sensitiser that acts by increasing efficiency of glucose transporters
<b>Biguanides</b>	Eg. <i>metformin</i> Improve insulin sensitivity, particularly in skeletal muscles Also decrease hepatic gluconeogenesis & decreases glycogenolysis
<b>Sulphonylureas</b>	Eg. <i>glibenclamide</i> Stimulates insulin release & improves peripheral sensitivity to insulin
<b>Meglitinides</b>	Eg. <i>glinides</i> Stimulate rapid insulin production
<b>Alpha glucosidase inhibitors</b>	Eg. <i>acarbose</i> Delays absorption of glucose in small intestine to decrease postprandial glucose surges
<b>Synthetic amylin analogues</b>	Eg. <i>pramlintide</i> Decreases glucagon secretion, delays gastric emptying & induces feeling of satiety

- Surgery
  - Bariatric surgery indicated for patients with type 2 & BMI 35
  - Pancreas transplant
  - Allogenic islet transplantation

### Why diabetes challenges anaesthesia & surgery

- Multiple associated comorbidities & multi-systems affected
- Obesity
- Cardiovascular risk factors & increased possibility of developing silent myocardial ischaemia
- Stiff joint syndrome may cause difficult airways
- Autonomic neuropathy may result in gastroparesis increasing aspiration risk
- Nephropathy may limit the use of intraoperative & postoperative NSAIDs
- Glycemic control needs to be maintained perioperatively
- More prone to wound infections
- Poor preoperative glycemic control associated with increased postoperative complications, including increased need for blood products & longer critical care + hospital stay

## Potential Questions

*What are the complications of diabetes?*

<b>Microvascular</b>
Eye disease <ul style="list-style-type: none"><li>• Retinopathy (non-proliferative/proliferative)</li><li>• Macular oedema</li></ul>
Neuropathy <ul style="list-style-type: none"><li>• Sensory &amp; motor (mono &amp; polyneuropathy)</li><li>• Autonomic – 50% type 1, 20% type 2</li></ul>
Nephropathy <ul style="list-style-type: none"><li>• Albuminuria &amp; declining renal function</li></ul>
<b>Macrovascular</b>
Coronary artery disease
Peripheral arterial disease
Cerebrovascular disease
<b>Other</b>
Gastrointestinal – gastroparesis, diarrhea
Genitourinary – uropathy, sexual dysfunction
Dermatologic
Infectious
Cataracts
Glaucoma
Cheiroarthropathy (thickened skin & reduced joint mobility)
Periodontal disease
Hearing loss

Other comorbid conditions associated with diabetes (relationship to hyperglycemia uncertain) – depression, OSA, fatty liver disease, hip fracture, osteoporosis (type 1), cognitive impairment/dementia, low testosterone in men

*What is the diagnostic triad for DKA?*

1. Ketonæmia  $\geq 3.0\text{mmol/L}$  or significant ketonuria
2. Blood glucose  $> 11\text{mmol/L}$  or known diabetes mellitus
3. Bicarbonate  $< 15\text{mmol/L}$ , venous pH  $< 7.3$ , or both

*What type of breathing is characteristic of DKA?*

Kussmaul's breathing ('air hunger') due to the acidosis.

Acidosis occurs because fat metabolism is increased to compensate for the lack of availability of glucose; excess acetyl-coenzyme A is produced, which is converted in the liver to ketone bodies, and two of these are organic acids.

## Parathyroid Disease (Oxford p168, Stoelting p400)

### **Hyperparathyroidism**

- Endocrine disorder caused by excessive secretion of PTH from parathyroid glands
- Classification
  - Primary
    - Autonomous PTH production – usually an adenoma causing ↑PTH, ↑calcium & ↓phosphate
    - Associated with familial MEN type 1
    - ↑PTH, ↑Ca
  - Secondary
    - Results from compensatory parathyroid hypertrophy due to chronic low calcium or vitamin D states
    - Complicates CKD
    - ↑PTH, normal or ↓Ca
  - Tertiary
    - Parathyroid hyperplasia progresses to autonomous secretion, behaving like an adenoma
    - ↑PTH, ↑Ca

### **Clinical Features**

#### *Stones, Bones, Abdominal Groans & Psychological Moans*

- Renal stones (back pain), polydipsia, polyuria
- Osteopenia, pseudogout, collapsed vertebral bodies with spinal deformity, pathological fractures
- Constipation, peptic ulcer, pancreatitis, nausea, vomiting
- Depression, dementia, confusion, somnolence
- Skeletal muscle weakness
- Anaemia
- Hypertension, prolonged PR interval, shortened QT interval
- Dehydration

#### Relevant investigations:

- Calcium >4.5 mmol/L is life threatening
- Expect hypophosphatemia, hypomagnesemia, high PTH, hyperchloraemia, increased ALP (from bone resoprtion) & hypercaluria
- ECG – prolonged PR interval, short QT interval
- Xray hands to look for periosteal erosions

### **Treatment**

- Primary – hypercalcemia treatment followed by subtotal or total parathyroidectomy

#### Management of hypercalcemic crisis:

- Severe hypercalcemia >4.5 mmol/L can be rapidly + transiently lowered with phosphate (500ml of 0.1M neutral solution over 6-8 hours)
- Rehydration with normal saline (4-6L often required)
- Pamidronate (60mg in 500ml over 4 hours) is 1<sup>st</sup> line treatment, rapid + long-lasting effect
- Calcitonin (4U/kg IV) causes a rapid but temporary decease in skeletal release of Ca + phosphate
- 2<sup>nd</sup> line treatment – forced diuresis with frusemide (40mg IV Q4H) once euvoalaemic
- Hydrocortisone (200-400mg IV daily) in patients with malignancy
- Haemodialysis reserved for patients with renal failure

- Secondary – control underlying disease

### **Anaesthesia**

- No specific drugs or techniques
- Proceed only if intravascular volume restored, ECG normal, total serum calcium < 3mmol/L & no cardiovascular/renal involvement
- Careful monitoring of neuromuscular blockade if non-depolarising muscle relaxants used (↑Ca causes skeletal muscle weakness + antagonises NDMR effects)

## Hypoparathyroidism

- Present when secretion of PTH is absent or deficient or peripheral tissues are resistant to the effects of the hormone
- Causes:
  - Decreased or absent PTH
    - Accidental removal of parathyroid glands during thyroidectomy
    - Parathyroidectomy to treat hyperplasia
  - Resistance of peripheral tissues to effects of PTH
    - Pseudohypoparathyroidism (congenital)
    - Hypomagnesemia
    - Chronic renal failure

## Clinical Features

Depend on rapidity of onset of hypocalcemia

- Look for scars on neck
- Acute
  - Perioral paresthesias, restlessness, seizures
  - Refractory heart failure
  - Neuromuscular irritability
    - Inspiratory stridor/laryngospasm
    - Tetany, hyperrlexia
    - Chvostek sign – tapping gently on facial nerve under ear causes brisk twitches on same side of face
    - Troussseau sign – tourniquet on arm causes contraction of hand
- Chronic
  - Fatigue, skeletal muscle cramps
  - Prolonged QT interval
  - Lethargy, cerebration deficits, personality changes
  - Cataracts, calcification of subcutaneous tissues + basal ganglia, skull thickening

## Treatment

- Acute hypocalcemia – 10% calcium chloride IV infusion until signs of neuromuscular irritability disappear
- Long term – calcium & vitamin D

## Anaesthesia

- Prevent further decreases in serum calcium concentration – avoid iatrogenic hyperventilation, avoid rapid administration of blood transfusions

## Potential Questions

*What are the causes of hypercalcemia?*

1. Hyperparathyroidism
2. Thyrotoxicosis
3. Adrenal insufficiency
4. Malignancy
5. Sarcoidosis
6. Immobilisation
7. Drugs – frusemide, thiazide diuretics, exogenous Ca or vitamin D, tamoxifen, β agonists

*What are the causes of hypocalcemia?*

1. Overhydration with calcium-free IV fluids
2. Massive blood transfusion
3. Hypoparathyroidism
4. After parathyroid surgery
5. Hypomagnesaemia
6. Metabolic alkalosis
7. Chronic renal failure
8. Vitamin D deficiency
9. Osteomalacia
10. Sepsis or other critical illness
11. Burns
12. Anticonvulsant therapy

## Thyroid Disease (Oxford p164+580, Stoelting p386)

### **Hyperthyroidism**

- Causes – three most common:
  1. Grave's disease (autoimmune disease where circulating IgG antibodies stimulate TSH receptors)
  2. Multinodular goitre
  3. Toxic adenoma

### **Clinical Features**

- History – weight loss, heat intolerance, sweating, palpitations, diarrhea, tremor, irritability, anxiety, fatigue
- Examination
  - Fine tremor, palmar erythema, moist + warm peripheries, tachycardia, AF
  - Proximal myopathy, brisk reflexes
  - Eyes – exophthalmos (protrusion of eyeball from orbit), lid lag, chemosis
  - Neck exam
  - CVS – high output CCF, systolic flow murmurs, cardiomegaly
  - Legs – pretibial myxedema
  - Airway – tracheal deviation/compression
- Investigations
  - ↑ T<sub>4</sub> ↑ T<sub>3</sub>
  - ↓ TSH <0.03 (normal 0.5-5.0 mU/L)
  - Thyroid autoantibodies
  - CT neck for airway evaluation
  - Eye exam

### **Treatment**

- Medications
  - Thionamides (4-8 weeks for full effect)
    - Carbimazole – inhibits thyroid peroxidase & conversion of iodide to iodine
    - Propylthiouracil – inhibits tyrosine iodination & extra-thyroidal conversion of T<sub>4</sub> to T<sub>3</sub>
  - Propranolol – attenuates symptoms & inhibits extra-thyroidal conversion of T<sub>4</sub> to T<sub>3</sub>
  - Iodine – excessive iodine inhibits iodide binding, reduces hormone synthesis & reduces effect of TSH; beneficial preoperative side effect is reduction in thyroid gland vascularity
  - Radioactive iodine – ablates thyroid in severe/recurrent disease
- Surgery – prompt control but T<sub>4</sub> half-life is 6-8 days
- Thyroid storm (life-threatening exacerbation of hyperthyroid state with evidence of decompensation in one or more organ systems) – management requires prompt recognition, treatment of precipitating factors, effective β-blockade, initiation of a thionamide, glucocorticoids (hydrocortisone) & subsequent treatment with iodine

### Hypothyroidism

- Causes
  - Chronic autoimmune (Hashimoto's) thyroiditis
  - Iatrogenic – thyroidectomy, external neck irradiation, radioiodine therapy, lithium, amiodarone
  - Rarer – dietary iodine deficiency, sarcoidosis

### **Clinical Features**

- History – fatigue, lethargy, weight gain, slow speech, cold intolerance, decreased sweating, constipation
- Examination
  - Mental sluggishness, hypothyroid speech (slow, nasal + deep pitch), deafness
  - Hands – cyanosis, swelling, dry + cold skin, bradycardia, small volume pulse from decreased CO, carpal tunnel
  - Face – yellow skin, alopecia, loss of eyebrows, swelling, periorbital oedema
  - Chest – pericardial effusion, pleural effusion
  - Peripheries – proximal myopathy, non-pitting oedema, peripheral neuropathy, slow reflexes
  - Peripheral neuropathy, slow reflexes
- Investigations
  - Subclinical hypothyroidism – TSH 5-10 mU/L with normal T<sub>3</sub> + T<sub>4</sub>
  - Hypothyroidism – TSH >20 mU/L with reduced T<sub>3</sub> + T<sub>4</sub>
  - Autoantibodies

### **Neck exam:**

- Note any hoarse voice (recurrent laryngeal n palsy) & inspect for scars, swelling & prominent veins
- Ask patient to swallow & look for thyroid enlargement
- Palpate from behind, feeling for masses – note size, shape, consistency, mobility & tenderness
  - Attempt to palpate lower border - ? retrosternal extension – percuss
- Feel for cervical lymphadenopathy & palpate each carotid pulse
- Check tracheal position
- Auscultate gland for bruits
- Pemberton's sign – ask patient to lift arms over head, look for facial flushing, distended neck veins, inspiratory stridor – a test for thoracic inlet obstruction due to retrosternal goiter/other mass

**Treatment**

- Thyroid hormone replacement – thyroxine PO with goal of ameliorating symptoms + normalising TSH levels in 2 weeks
- Surgical management of any associated symptomatic goiter causing pain or compression of local structures
- Myxoedematous coma (decompensated form of hypothyroidism characterised by coma, hypoventilation, bradycardia, hypotension + severe dilutional hyponatremia) – intravenous T4 (levothyroxine 400mcg bolus) + T3 (levothyronine 50mcg slow bolus) replacement, glucocorticoid administration until adrenal insufficiency excluded (hydrocortisone 100mg IV QID), supportive measures & treatment of precipitant triggers

## Cushing's Syndrome (Oxford p174, Stoelting p396)

- Cushing's syndrome is caused by excessive levels of glucocorticoids
- Divided into two forms:
  - ACTH-dependent – inappropriately high plasma ACTH concentrations stimulate adrenal cortex to produce excessive cortisol
    - Cushing's disease (70%) – secondary to pituitary ACTH production (usually microadenoma)
    - Ectopic ACTH syndrome (15%) – associated with oat cell lung carcinoma
  - ACTH-independent – caused by excessive production of cortisol by abnormal adrenocortical tissue that is not regulated by secretion of CRH + ACTH
    - Benign or malignant adrenocortical tumours
    - Exogenous cortisol administration

### Clinical Features

- History
  - Exogenous steroid intake & indication for use
  - Most common symptom = relatively sudden onset weight gain (central) with associated moon face
  - Hypertension, OSA, GORD
  - Diabetes – impaired glucose tolerance
  - Skeletal muscle wasting + weakness (difficulty climbing stairs)
  - Osteoporosis + fractures
  - Immunusuppression – predisposition to infection
- Examination
  - Moon-like facies with plethora + telangiectasia
  - Central obesity, buffalo hump (due to fat deposition over interscapular area)
  - Thin skin, bruising, excessive pigmentation
  - Proximal muscle wasting
  - Purple abdominal striae
  - Hypertension
- Investigations
  - Bloods
    - ↑Na, ↑HCO<sub>3</sub>, ↑glucose
    - ↓K, ↓Cl, ↓Ca
  - ABCG – metabolic alkalosis
  - ECG – LVH (hypertension), high voltage QRS + inverted T waves (revert after curative surgery)
- Diagnosis
  - Screening tests:
    - *24 hour urinary free cortisol* – elevated cortisol confirms a pathological cause (normal 450-700 nmol/L)
    - *Short dexamethasone suppression test*
      - Dexamethasone 1mg given orally at midnight
      - Normal individuals show suppression of morning serum cortisol
  - Establishing the cause:
    - *High dose dexamethasone suppression test*
      - Eight doses of dexamethasone 2mg given orally over 48 hours
      - Suppression of serum cortisol in pituitary dependent Cushing's disease but not in ectopic ACTH secretion or adrenal Cushing's
    - *Serum ACTH concentration*
      - High – Cushing's disease
      - Low – adrenal tumour, exogenous cortisol administration
      - Very high – ectopic ACTH syndrome
    - *Imaging to locate tumour* – MRI of pituitary fossa, CT/MRI of adrenal glands

### Clinical features of Cushing's disease

Affected body system/organ	Clinical features
Musculoskeletal	Proximal myopathy, osteoporosis
Skin	Easy bruising, fragile skin, hirsutism, acne, abdominal striae
Metabolic	Hypokalaemia, hypernatraemia, alkaloasis
Cardiovascular	Hypertension, ECG abnormalities, impaired left ventricular function
Endocrine	Impaired glucose tolerance, diabetes
Appearance	Redistribution of body fat: Moon face, 'buffalo hump', truncal obesity
Other	Sleep apnoea, gastrointestinal reflux, renal stones

### Treatment

- Transsphenoidal microadenectomy for Cushing's disease (pituitary adenoma); some patients not cured by transsphenoidal surgery require pituitary irradiation + bilateral total adrenalectomy
- Adrenal gland removal for adrenal adenoma or carcinoma
- Metyrapone or ketoconazole (both adrenal enzyme inhibitors) if surgery not an option

### Anaesthesia

- Poorly controlled hypertension & ECG abnormalities

- Obesity & OSA – rapid desaturation due to ↓FRC
- Potentially difficult airway
- GORD with aspiration risk – need for preoperative acid suppression therapy & RSI
- Electrolyte abnormalities & impaired glucose tolerance
- Muscle relaxants – decrease initial dose due to skeletal muscle weakness, hypokalemia may increase sensitivity to non-depolarising agents
- Careful positioning – susceptibility to pressure sores & fractures because of fragile skin & osteoporosis
- Supplemental steroids may be required preoperatively if iatrogenic Cushing's syndrome

### Potential Questions

*What are the physiological effects of excess cortisol secretion?*

- Systemic hypertension
- Hyperglycemia
- Skeletal muscle weakness
- Osteoporosis
- Obesity
- Menstrual disturbances
- Poor wound healing
- Susceptibility to infection

*What is the difference between glucocorticoids & mineralocorticoids?*

Both classes of steroids synthesized by adrenal cortex.

Glucocorticoids – eg. cortisol – affect the metabolism of carbohydrates, fats + proteins & are important in mediating the response to fasting + stress.

- » Liver – protein catabolism, gluconeogenesis
- » Cardiovascular system – maintenance of responsiveness to catecholamines
- » Kidney – weak mineralocorticoid activity
- » Immune – anti-inflammatory, immunosuppression, slowed healing

Mineralocorticoids – eg. aldosterone – are essential for electrolyte & fluid balance.

- » Kidney – Na reabsorption, K + H excretion

*What are the complications after pituitary surgery?*

- Risk of potential airway difficulty due to nasal packing
- Avoid postoperative positive pressure ventilation (eg. CPAP) – risk of tension pneumocephalus, venous air embolism + introduction of bacteria into subarachnoid space
- Need for glucocorticoid & thyroxine replacement therapy
- Panhypopituitarism
- Pituitary apoplexy – acute onset of hypopituitarism because of bleeding into the tumour or infarction – can lead to blindness, cranial nerve palsies + ↑ICP
- Persistent CSF rhinorrhea
- Meningitis
- Diabetes insipidus (from manipulation of pituitary stalk)
- Hypothalamus injury (direct or hypoperfusion) – may manifest as DI, body temperature dysregulation, progressive obesity, loss of memory functions + disruption of circadian sleep rhythms
- SIADH (usually develops few days after surgery)
- Stroke

## Steroids

### **Perioperative Steroid Replacement Therapy**

Patients taking >10mg/day of prednisone on a long-term basis are at risk of perioperative cardiovascular collapse due to inadequate endogenous glucocorticoid production in response to the surgical 'stress'. Although this complication is extremely rare, it must be prevented with perioperative steroid supplementation.

<b>Minor surgery</b> eg. hernia
Usual oral steroid dose preoperatively OR hydrocortisone 25mg IV at induction
<b>Moderate surgery</b> eg. hysterectomy
Usual oral steroid dose preoperatively PLUS hydrocortisone 25mg IV at induction followed by 100mg over 24 hours for 1 day
<b>Major surgery</b> eg. cardiac
Usual oral steroid dose preoperatively PLUS hydrocortisone 25mg IV at induction followed by 100mg over 24 hours for 2-3 days

If <10mg/day – no additional steroid cover required

Patients formerly taking regular steroids:

- < 3 months since stopped – treat as though still on steroids
- > 3 months since stopped – no preoperative steroids necessary

### **Equivalents**

Prednisone	10mg
Prednisolone	10mg
Hydrocortisone	40mg
Methylprednisolone	8mg
Dexamethasone	1.5mg

### **Side Effects (corticosteroids)**

1. Increased susceptibility to bacterial & fungal infections
2. Decreased wound healing
3. Suppression of hypothalamic-pituitary-adrenal (HPA) axis
  - o Cortisol release in response to stress is blunted or does not occur
  - o Adrenal response may be depressed for >1year after corticosteroid-induced HPA suppression
  - o Replacement therapy needed in patients who have recently been treated with corticosteroids
4. Metabolic
  - o Anti-insulin & carbohydrate sparing effect leading to hyperglycemia
    - » Inhibits use of glucose in peripheral tissues & promotes hepatic gluconeogenesis
    - » Dose requirements for oral hypoglycemic agents & insulin may increase
  - o Increased lipolysis & redistribution of fat with a characteristic centripetal distribution
    - » Increased fat deposition in back of neck (buffalo hump), subclavicular area + face (moon facies) & loss of fat from extremities
  - o Protein catabolic effect
    - » Mobilises amino acids from peripheral tissues
    - » Leads to decreased skeletal muscle mass, osteoporosis, skin thinning & a negative nitrogen balance
5. Osteoporosis
  - o Due to diminished collagen synthesis by osteoblasts & increased collagen breakdown by collagenase
6. Peptic ulceration
  - o May decrease the normal protective barrier provided by gastric mucus
7. CNS dysfunction
  - o Increased incidence of neuroses & psychoses
  - o Behavioural changes include manic depression & suicidal tendencies
8. Inhibition of normal growth (growth suppression in children)

Nervous/Musculoskeletal  
Skin/Connective Tissue  
Other

## Neuromuscular Disorders

- Consist of a heterogeneous group of diseases that affect skeletal muscle via abnormalities at multiple sites
- Classified into hereditary conditions or acquired syndromes:

<i>Hereditary</i>	<i>Acquired</i>
<p>Peripheral neuropathies:</p> <ul style="list-style-type: none"><li>• Charcot-Marie-Tooth</li><li>• Fredrich's ataxia</li></ul> <p>Dystrophicas:</p> <ul style="list-style-type: none"><li>• Duchenne's muscular dystrophy</li><li>• Becker's muscular dystrophy</li></ul> <p>Myotonias – group of hereditary degenerative diseases of skeletal muscle characterised by persistent contracture (myotonia) after voluntary muscle contraction:</p> <ul style="list-style-type: none"><li>• Myotonic dystrophy</li><li>• Myotonia congenita</li><li>• Hyper/hypokalemic periodic paralysis</li><li>• Acid-maltase deficiency (Pompe's disease)</li></ul> <p>Metabolic/mitochondrial disorders</p>	<ul style="list-style-type: none"><li>• Motor neuron disease</li><li>• Multiple sclerosis</li><li>• Guillain-Barre syndrome</li><li>• Peripheral neuropathy – diabetes mellitus</li><li>• Myasthenia gravis</li><li>• Eaton Lambert syndrome</li><li>• Inflammatory myopathies</li><li>• Critical illness polyneuropathy &amp; myopathy</li></ul>

## Myotonic Dystrophy (aka Dystrophica Myotonica) (Oxford p266, Stoelting p446)

- Most common & most serious myotonia affecting adults
  - "Myotonia" = failure of muscle to relax following contraction
- Autosomal dominant inheritance
- Incidence 2.4-5.5 cases per 100,000

### **Pathophysiology**

Related to abnormal sodium +/- chloride channels, which results in the muscle being in an abnormal hyperexcitable state. This results in repetitive action potentials & sustained muscle contraction, manifesting in the inability to relax muscle groups. Inability to relax is due to abnormal calcium metabolism leaving unsequestered calcium intracellularly & available for contraction.

### **Clinical Features**

- Multisystem disease with progressive involvement of skeletal, cardiac & smooth muscle
- Presents in early adulthood (20s-30s) & death from pneumonia/heart failure by 60s

<i>General</i>
Frontal baldness
Expressionless facies 2° facial weakness
Ptosis, cataracts
Muscle wasting & weakness affecting sternocleidomastoid + proximal limb muscles
Inability to relax hand grip (myotonia)
Behavioural & cognitive problems
<i>Bulbar</i>
Dysphagia, dysarthria, recurrent aspiration
<i>Respiratory</i>
Muscle weakness
Poor clearance of secretions + ineffective cough
Restrictive lung defect
Central respiratory drive depression – long standing hypoventilation with diminished ventilatory response to hypoxia + hypercapnia
Central & obstructive sleep apnoea
Cor pulmonale
<i>Cardiovascular</i>
Cardiomyopathy
Dysrhythmias + conduction defects (atrio-ventricular block)
Mitral valve prolapse (20%)
<i>Gastrointestinal</i>
Oesophageal dysmotility, delayed gastric emptying
Intestinal pseudo-obstruction
Cholelithiasis
<i>Endocrine</i>
Diabetes
Hypothyroidism
Gonadal atrophy
Adrenal insufficiency
<i>Behavioural &amp; cognitive problems</i>

- History:
  - Onset of symptoms & how diagnosis was made (muscle biopsy)?
  - Organ systems involved?
    - MSK – muscle weakness, bulbar dysfunction (slurred speech, poor swallow + chew)
    - RESP – aspiration episodes, coughing during meals, previously treated pneumonias, sleep apnoea (STOP-BANG)
    - CVS – palpitations, arrhythmias, cardiomyopathy, dyspnoea on exertion, pacemakers
    - GIT – difficulty swallowing, dietary restrictions, reflux
  - Treatment to date
- Examination
  - Respiratory & cardiovascular signs
  - Triad of frontal baldness, mental retardation & cataracts
- Investigations
  - Electromyographic findings are diagnostic – prolonged discharges of repetitive muscle action potentials

- ECG + echocardiography for cardiac reserve
- CXR for lung fields
- RFTs + ABG for respiratory reserve
- U&Es & glucose to exclude endocrine dysfunction
- During pregnancy – exacerbation of symptoms common; uterine atony & retained placenta complicate vaginal delivery

### Treatment

- No specific treatment – aim to manage symptoms & minimise disability
- Drugs used to reduce myotonia:
  - Sodium channel blockers – melexitine, carbamazepine, phenytoin, procainamide, quinine
    - MOA = depress Na influx into skeletal muscle cells & delay return of membrane excitability
    - May worsen cardiac conduction abnormalities
  - Tricyclic antidepressants – imipramine
  - Benzodiazepines
  - Calcium antagonists
  - Taurine
  - Prednisone
- General + regional anaesthesia & NMJ blockers are not able to prevent or relieve muscle contraction

### Anaesthesia

- Avoid factors that may precipitate myotonia
  - Drugs – suxamethonium, neostigmine
  - Hypothermia, shivering
  - Mechanical or electrical stimulation – eg. surgical manipulation, electrocautery
- Increased sensitivity to sedatives & analgesic agents
- Depolarising muscle relaxants (suxamethonium)
  - Not recommended → can lead to difficult or impossible intubation 2° exaggerated contracture, master spasm & laryngospasm
  - May also result in an exaggerated hyperkalemia response in advanced cases because of dystrophic muscle changes
- Non-depolarising muscle relaxants
  - Response is normal, some reports of increased sensitivity
  - Pick agent with a short recovery index eg. atracurium
  - Use of a nerve stimulator may provoke muscle contraction leading to misdiagnosis of tetany
- Anticholinesterase drugs (neostigmine)
  - Avoid if possible → may precipitate contractures due to increased sensitivity to acetylcholine
- Aspiration risk 2° dysphagia & altered gastric motility
  - Premedicate with sodium citrate, ranitidine +/- metoclopramide
  - Secure airway with ETT
  - RSI with cricoid pressure warranted
- Access to pacemaker equipment because of conduction defects
- Temperature monitoring & control
- Glycemic monitoring
- Troublesome spasm may be helped by infiltration of local anaesthetic directly into the affected muscle; quinine 600mg IV & phenytoin 3-5mg/kg IV slowly have been effective in some cases
- Postoperative critical care monitoring
- Rhabdomyolysis
  - Myotonias may spontaneously induce rhabdomyolysis due to sustained muscle contraction

## **Muscular Dystrophy** (Oxford p268, Stoelting p444)

- Group of inherited muscle diseases characterised by painless degeneration & atrophy of skeletal muscles
- Caused by an absence or deficiency of dystrophin, a muscle protein essential for normal muscle structure & function
  - Dystrophin gene mutation results in loss of intracellular mechanical stabilization of actin to muscle cell plasma membrane; also has a role in calcium regulation
- Characterised by:
  - Progressive, symmetrical skeletal muscle weakness & wasting but no evidence of skeletal muscle denervation
  - Intact sensation & reflexes
  - Increased permeability of skeletal muscle membranes
- Spectrum of severity depends on genetic mutation & degree of muscle involvement
- Classification based on pattern of inheritance:
  - Sex-linked:
    - Duchenne's (no dystrophin)
    - Becker's (partially absent dystrophin)
  - Autosomal dominant:
    - Facioscapulohumeral dystrophy
    - Nemaline rod muscular dystrophy
    - Oculopharyngeal dystrophy
  - Autosomal recessive:
    - Limb girdle dystrophy
- Most common form = Duchenne's muscular dystrophy

Weakness in a male patient could be:  
- muscular dystrophy  
- myasthenia  
- myotonic dystrophy  
- cerebral palsy  
- motor neurone disease

### ***Duchenne's Muscular Dystrophy***

- Sex-linked recessive inheritance
- Affects 1 in 3,500 live male births

### **Clinical Features**

- Apparent by age 2-5 years, wheelchair-bound by 8-10 years, & death by 25 years (2° congestive heart failure +/or pneumonia)
- Initial symptoms include a waddling gait, frequent falling & difficulty climbing stairs – all reflect involvement of the proximal skeletal muscle groups of the pelvic girdle
- Pseudohypertrophy of calf muscles (affected muscles become larger 2° fatty infiltration)
- Predisposed to long bone fractures 2° skeletal muscle atrophy
- Degeneration of cardiac muscle:
  - Conduction defects
  - Characteristic ECG – tall R waves in V1, deep Q waves in limb leads, short PR interval & sinus tachycardia
  - Dilated cardiomyopathy (50% have this by 15 years)
  - Mitral regurgitation 2° papillary muscle dysfunction or decreased myocardial contractility
- Severe respiratory muscle weakness & weak cough lead to loss of pulmonary reserve & accumulation of secretions → predisposition to recurrent pneumonia
- Kyphoscoliosis contributes to further restrictive lung disease
- Sleep apnoea & development of pulmonary hypertension
- Possible vascular smooth muscle dysfunction → increased bleeding during surgery
- Intellectual impairment often present
- History
  - Symptom onset, progression & functional limitations
  - Cardiorespiratory problems
  - Speech/swallow problems
  - Oesophageal reflux?
  - Affected family members?
  - Any recent anaesthetics?
- Examination
  - Progressive, symmetrical muscle weakness & wasting
  - Severe proximal muscle weakness
  - Normal sensation, intact reflexes
  - Kyphoscoliosis
  - Cardiorespiratory examination – look for cardiomyopathy, mitral valve prolapse, pneumonia
- Investigations
  - Serum creatinine kinase

- Used to track disease progression – elevated early due to increased skeletal muscle membrane permeability & skeletal muscle necrosis, reduced to below normal as muscles atrophy
- ECG, CXR, ABG, RFTs
- Echocardiography

### Treatment

- Glucocorticoids (prednisone) – slow decline in muscle strength & function; continued when non-ambulatory
- Cardiac mx – heart failure medications eg. ACE inhibitors,  $\beta$  blockers
- Gastrointestinal mx – diet control & supplementation, drugs for gastric reflux & constipation
- Orthopaedic mx – tendon surgery for tendoachilles contractures, posterior spinal fusion for scoliosis

### Anaesthesia

- Aspiration risk 2° hypomotility of GIT & weak laryngeal reflexes
- Suxamethonium – contraindicated as it can provoke rhabdomyolysis, hyperkalemia &/or cardiac arrest 2° $\uparrow$ K or VF
- Non-depolarising muscle relaxants – avoid or use sparingly as a delay in onset/offset is usually seen, potentially leading to a prolonged block
- Case reports of a malignant hyperthermia-like picture with prolonged use of volatile agents
  - Not substantiated by prospective studies
  - Thought to be a separate disease eg. anaesthesia-related rhabdomyolysis, not a true MH
  - Exercise extreme caution, TIVA advised for GA if unable to use regional anaesthesia
- High risk of postoperative pulmonary complications

## **Motor Neuron Disease** (Oxford p265)

- Progressive condition of unknown aetiology
- Characterised by degeneration of motor neurons in the *motor cortex, brainstem nuclei & anterior horn cells of the spinal cord*
- Can affect...
  - Upper motor neurons predominantly – primary lateral sclerosis
  - Lower motor neurons predominantly – progressive spinal atrophy
  - Combination – amyotrophic lateral sclerosis (classic form)
- Prevalence 6/100,000
- Peak age 50-70 years
- Men > women
- 90% die within 5 years of diagnosis → aspiration pneumonia is commonest cause of death

### **Clinical Features**

- Variable presentation
  - LMN variant – muscle weakness, atrophy & fasciculations of small hand muscles
  - UMN variant – spastic weakness of limbs
- Brisk reflexes in all forms with no sensory loss
- Bulbar & respiratory muscle dysfunction
- No effect on ocular muscles
- No bladder disturbance
- History
  - Diet & swallow function, solids/fluid diet
  - Frequency of chest infections – indication of aspiration
- Examination
  - Patients with advanced disease will often have long term tracheostomy for airway protection
  - General skeletal muscle atrophy
  - Autonomic dysfunction
    - Orthostatic hypotension
    - Resting tachycardia
    - Syncope
  - Upper motor neuron signs
    - Muscle weakness in all muscle groups with little muscle wasting
    - Spasticity – increased tone with associated clonus
    - Increased reflexes
    - Extensor (Babinski) plantar response (upgoing toe)
  - Lower motor neuron signs
    - Weakness more obvious distally than proximally
    - Prominent muscle wasting
    - Reduced tone
    - Reduced reflexes
    - Normal or absent plantar response
    - Fasciculations
  - Bulbar dysfunction
- Severity
  - Rapid progression
  - Respiratory & bulbar muscle involvement
  - Dependence of ADLs

Bulbar muscles control speech, swallowing & chewing

### **Treatment**

- Muscle relaxants (eg. baclofen, benzodiazepines) to reduce spasticity
- Botulin toxin to treat jaw spasms or drool
- Excessive saliva – treated with glycopyrrolate or amitriptyline
- Combinations of dextromorphan + quinidine have been used to reduce pseudobulbar effect
- Riluzole (glutamate antagonist) – prolongs time to ventilation + tracheostomy by 3 months but does not relieve symptoms
- Analgesia

### **Anaesthesia**

- Aspiration risk

- Hyperkalemic response to suxamethonium
- Use non-depolarising muscle relaxants in reduced doses with continuous monitoring due to increased sensitivity
- Respiratory complications common, with the risk of postoperative ventilation & subsequent weaning difficulties, infection & atelectasis
- Prepare for autonomic dysfunction
  - Hypotension can occur with postural changes, airway pressure, blood loss & dehydration
  - Hypertension can occur with intubation, stress & pain

## **Guillain-Barre Syndrome** (Oxford p264, Stoelting p269)

- Most common cause of acute flaccid paralysis
- Affects all ages but bimodal tendency towards young adults & elderly
- Autoimmune inflammatory polyneuropathy of motor, sensory, autonomic & cranial nerves
- Occurs as an immune response following a viral or bacterial gastrointestinal or respiratory infection
  - Antigen mimics Schwann cell epitope & affected axons undergo lymphocytic infiltration + demyelination
  - Commonest pathogen = *Campylobacter jejuni*
- Evolves over the course of 3-4 weeks, with complete recovery eventually occurring in <90% of patients; 10% die & 10% permanently disabled

### **Clinical Features**

- Progressive motor weakness, usually ascending from legs (proximal more than distal)
- Areflexia
- Facial palsy & bulbar weakness
- Ophthalmoplegia
- Sensory symptoms (paresthesias often precede weakness + paralysis)
- Severe pain (girdle area)
- Respiratory muscle weakness leading to respiratory failure
  - Decreased forced exhalation & impaired cough
  - Rapid shallow breathing 2° inspiratory muscle weakness
  - Mechanical ventilation indicated when VC <15ml/kg or PEF <250L/min
  - Tracheostomy may be necessary
- Autonomic dysfunction
  - Under or over activity of both sympathetic & parasympathetic systems
  - Arrhythmias, wide fluctuations in BP + pulse, urinary retention, ileus & excessive sweating
- History
  - Focused neurological history – symptoms, severity, onset (typically 7-10 days after infective illness), duration
  - Dyspnoea, fatigue, respiratory distress?
  - Treatment received
- Examination
  - Appearance? Respiratory distress?
  - Complete neurological exam – cranial nerves, motor, sensory, autonomic, reflexes
    - Generalised muscle weakness, ascending from lower to upper limbs
    - Wasting is rare
    - Reflexes reduced or absent
    - Sensory loss minimal
  - Respiratory weakness – assess FEV1, FVC + PEF
  - Other – HR + rhythm, BP
- Investigations
  - Nerve conduction studies/EMG
  - CSF analysis – typically increased protein & <10 mononuclear cells/mm<sup>2</sup>
  - RFTs
- Diagnosis based on clinical features, CSF fluid examination & neurophysiological studies

### **Criteria for diagnosis of Guillain–Barré syndrome**

<b>Essential criteria</b>	<b>Supporting criteria</b>
Progressive weakness of limbs due to neuropathy	Clinical features including motor weakness, mild sensory signs, cranial nerve involvement, autonomic involvement
Areflexia	Cerebrospinal fluid shows raised protein (>0.55 g/dl) after the first week with <10 white cells/ml
Duration of progression of weakness <4 weeks	Neurophysiological tests suggest either demyelination or axonal loss

- Differential diagnosis:
  - Peripheral neuropathy (critical illness, diabetic neuropathy)
  - NMJ disorder (myasthenia gravis)
  - Muscle disorder (periodic paralysis, infections)
  - CNS disorder (stroke, encephalitis)

### Treatment

- Primarily supportive & directed at intensive respiratory care + treatment of autonomic dysfunction
- Plasmapheresis & IV immunoglobulin hasten recovery + alleviate harmful immune system effects
- Corticosteroids & immunosuppressive therapy generally not effective
- Conventional analgesic drugs & those that specifically target neuropathic pain

### Anaesthesia

- Avoid suxamethonium – can precipitate hyperkalemic arrest
- Non-depolarising muscle relaxants – sensitivity may vary from extreme sensitivity to resistance depending on disease phase
- Autonomic dysfunction
  - Exaggerated HR & BP responses
    - Need invasive monitoring (IAL), large bore IV access, hydration maintenance & direct-acting vasopressors + antihypertensives readily available
  - Hypovolemia, positional changes & PPV → severe hypotension
  - Intubation & surgical stimulation → severe hypertension
  - Atropine can cause paradoxical bradycardia
- Avoid peripheral nerve blockade → multi-hit hypothesis of nerve injury
- Anticipate postoperative mechanical ventilation

### Possible Questions

*What are the clinical indications for intubation & ventilation?*

1. Vital capacity < 15ml/kg or peak expiratory flow < 250L/min
2. Maximal inspiratory pressure (MIP) < 30cmH<sub>2</sub>O
3. Maximal expiratory pressure (MEP) < 40cmH<sub>2</sub>O
4. Decrease of > 30% in vital capacity, MIP or MEP

*How is plasmapheresis & IV immunoglobulin administered? Side effects & contraindications?*

Typically one or the other is commenced when the patient becomes non-ambulatory or develops respiratory decompensation.

IV Immunoglobulin:

- 0.4mg/kg daily for 5 days
- Side effects – nausea, fever, headache, transient rise in liver enzymes, encephalopathy, meningism, malaise, skin reactions, hypercoagulability, deterioration in renal function due to renal tubular necrosis, anaphylaxis
- Contraindications – IgA deficiency (increased incidence of anaphylaxis), previous anaphylaxis to immunoglobulin therapy, caution in renal impairment & congestive cardiac failure

Plasmapheresis:

- Typically, up to 5 exchanges are performed substituting 250ml/kg of plasma with 4% HAS
- Side effects – hypotension, hypocalcemia, coagulation abnormalities & septicemia
- Contraindications – haemodynamic instability, uncontrolled sepsis, severe haemostatic problems

*What is the morbidity & mortality?*

- 10% suffer long-term neurological sequelae & physical dependence; adverse outcome associated with *Campylobacter* species infection, old age, need for ventilatory support, anti-GM1 antibody, neurone specific enolase + S100 proteins in CSF, absent or reduced compound muscle action potential & inexcitable nerves + upper limb paralysis
- Symptom recurrence in 2-5% of cases
- ≈ 10% mortality; causes of death include cardiac arrest 2° autonomic dysfunction, respiratory infections, sepsis, pulmonary embolism, ARDS & respiratory failure

## Peripheral Neuropathy

- Can be sensory, motor, autonomic or mixed AND mononeuropathy or polyneuropathy
- Causes (DAAM IT BICH):
  - Drugs/toxins – isoniazid, vincristine, phenytoin, nitrofurantoin, cisplatin, heavy metals, amiodarone
  - Alcohol abuse + Amyloid
  - Metabolic – diabetes mellitus, chronic kidney disease
  - Immune mediated – Guillain-Barre syndrome
  - Tumour – lung carcinoma, leukaemia, lymphoma
  - B12, B1, B5, B6 vitamin deficiency
  - Idiopathic
  - Connective tissue disease or vasculitis – SLE, polyarteritis nodosa
  - Hereditary
- Causes of a predominant motor neuropathy:
  - Guillain-Barre syndrome
  - Hereditary motor & sensory neuropathy
  - Diabetes mellitus
  - Lead poisoning
  - Acute intermittent porphyria
- Causes of a predominant sensory neuropathy:
  - Uraemia
  - Vitamin B12 deficiency
  - Infectious (HIV)
- Causes of a painful peripheral neuropathy:
  - Diabetes mellitus
  - Alcohol
  - Vitamin B1 or B12 deficiency
  - Carcinoma
  - Porphyria
  - Arsenic or thallium poisoning

<i>Signs of UMN lesion</i>	<i>Signs of LMN lesion</i>
<ul style="list-style-type: none"> <li>• Weakness present in all muscle groups           <ul style="list-style-type: none"> <li>○ Lower limb – weakness may be more marked in flexor + abductor muscles</li> <li>○ Upper limb – weakness may be more marked in abductors + extensors</li> </ul> </li> <li>• Little muscle wasting</li> <li>• Spasticity – increased tone, associated clonus</li> <li>• Increased reflexes but absent superficial reflexes (eg. abdominal)</li> <li>• Extensor (Babinski) plantar response (upgoing toe)</li> </ul>	<ul style="list-style-type: none"> <li>• Weakness – may be more obvious distally than proximally &amp; flexor + extensor muscles are equally involved</li> <li>• Muscle wasting</li> <li>• Reduced tone</li> <li>• Decreased reflexes with normal or absent plantar response</li> <li>• Fasciculations</li> </ul>

## **Upper limb neuropathy**

- Brachial plexus (C5-T1)
  - Upper trunk – *Erb-Duchenne* (C5/C6) lesion
    - Loss of shoulder movement + elbow flexion – waiter's tip
    - Sensory loss over lateral aspect of arm, forearm + thumb
  - Lower trunk – *Klumpke* (C8/T1) lesion
    - Claw hand with paralysis of ALL intrinsic hand muscles
    - Sensory loss in ulnar side of hand and forearm
    - Horner's syndrome
- Radial nerve (C5-C8)
  - Wrist + finger tip drop
  - Tricep loss
  - Sensory loss over the anatomical snuff box
- Median nerve (C6-T1)
  - Sensory loss over palmar aspect of thumb index middle + lateral half of ring finger
- Ulnar nerve (C8-T1)
  - Wasting of intrinsic hand muscles (except LOAF)
  - Weak finger abduction + adduction
  - Ulnar claw
  - Sensory loss over little + medial half of ring finger

**Upper limb reflexes:**  
Biceps C5,C6  
Triceps C7,C8  
Supinator C5,C6

**Lower limb reflexes:**  
Knee L3,L4  
Ankle S1,S2  
Plantar S1

### **Lower limb neuropathy**

- Femoral nerve (L2,L3,L4) lesion
  - Weakness of knee extension
  - Preserved adductor strength
  - Loss of knee jerk
  - Sensory loss of inner aspect of thigh + leg
- Sciatic nerve (L4,L5,S1,S2)
  - Weakness of knee flexion (hamstrings)
  - Loss of power to all muscles below knee (causing a foot drop)
  - Knee jerk intact
  - Loss of ankle jerk + plantar response
  - Sensory loss posterior thigh + below knee
- Common peroneal nerve (L4,L5,S1)
  - Foot drop + loss of foot eversion only
  - Sensory loss over dorsum of foot

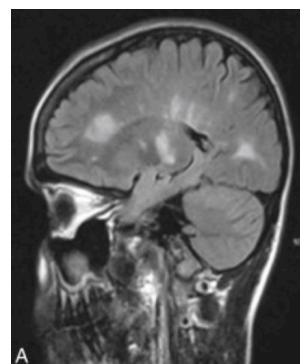
## Cranial Nerve Pathology

## Multiple Sclerosis (MS) (Stoelting p248)

- Most frequently occurring demyelinating neuromuscular disorder
- Autoimmune disease affecting CNS in genetically susceptible persons
- Aetiology remains unknown but multifactorial for:
  - Autoimmunity – autoreactive T & B cells
  - Environmental factors – Epstein-Barr virus, human herpes virus 6, low UV exposure, smoking
  - Genetics – high rate of concordance among twins & increased risk in individuals with a 1° relative with the disease
- Pathologically, characterised by diverse combinations of inflammation, demyelination & axonal damage in brain & spinal cord → plaques cause demyelination around axons, resulting in weakness, spasticity & sensory dysfunction; peripheral nerves are not affected

### Clinical Features

- Symptoms typically develop over a few days, remain stable for a few weeks, & then improve
- Clinical manifestations reflect sites of demyelination in CNS
  - Optic nerve inflammation (optic neuritis) → visual disturbance characterised by diminished visual acuity & defective pupillary reaction to light
  - Cerebellum → gait disturbances
  - Spinal cord → limb paresthesias, weakness, urinary incontinence, impotence
  - Ascending spastic paresis of skeletal muscles
  - Intramedullary cervical cord disease → electrical sensation that runs down the back into the legs in response to neck flexion (Lhermitte's sign)
- Course may be subacute, with relapses followed by remissions, or the course may be chronic & progressive
- Relapses are defined as a subacute onset of neurologic dysfunction that lasts for at least 24 hours
- Three main subtypes:
  - Relapsing-remitting (RRMS) 80% – episodic symptoms with remission
  - Primary progressive (PPMS) 20% – progressive neurologic deterioration without remissions
  - Secondary progressive (SPMS) – chronically progressive with remissions
- History:
  - Relapses, remissions
  - Triggers – infection, temperature, stress, trauma
  - Typical complaints & symptoms during exacerbation
    - Weakness, visual disturbances, numbness/tingling, gait ataxia, bladder dysfunction
  - Ability to cough & clear secretions
  - Medication list
    - Steroids – adrenal suppression
    - Mitoxantrone – cardiotoxic
    - Baclofen – potentiates neuromuscular blockade
    - Cyclophosphamide – pancytopenia, pulmonary fibrosis, myocarditis
  - Elicit steroid use & potential for adrenal suppression
- Examination:
  - Complete neurological exam
    - Look for limb ataxia
    - Check motor strength + sensation in all limbs
    - Check extraocular movements – nystagmus + internuclear ophthalmoplegia are common
    - Look for increased tone, increased reflexes + Babinski sign
    - Look for a tremor that increases in amplitude when the patient reaches toward a target
  - Autonomic neuropathy
- Investigations:
  - T2-weighted MRI shows multifocal lesions in CNS
  - Echocardiography if on mitoxantrone
- Diagnosis:
  - May be probable or definite on the basis of clinical features alone or clinical features in combination with oligoclonal immunoglobulin abnormalities in CSF, prolonged latency of evoked potentials reflecting slowed nerve conduction from demyelination & signal changes in white matter on cranial MRI
  - Based on revised McDonald criteria:



Clinical Presentation	Additional Data Needed for MS Diagnosis
≥2 attacks <sup>a</sup> ; objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack <sup>b</sup>	None <sup>c</sup>
≥2 attacks <sup>a</sup> ; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by: ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) <sup>d</sup> ; or Await a further clinical attack <sup>a</sup> implicating a different CNS site
1 attack <sup>a</sup> ; objective clinical evidence of ≥2 lesions	Dissemination in time, demonstrated by: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack <sup>a</sup>
1 attack <sup>a</sup> ; objective clinical evidence of 1 lesion (clinically isolated syndrome)	Dissemination in space and time, demonstrated by: For DIS: ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) <sup>d</sup> ; or Await a second clinical attack <sup>a</sup> implicating a different CNS site; and For DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or Await a second clinical attack <sup>a</sup>
Insidious neurological progression suggestive of MS (PPMS)	1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria <sup>d</sup> : 1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions 2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)

## Treatment

- No curative treatment – instead directed at symptom control & slowing disease progression
- *Corticosteroids*
  - Principal treatment for acute relapses
    - High-dose IV *methylprednisolone* for 5 days followed by 10 day *prednisone* taper
  - Immunomodulatory & anti-inflammatory effects that restore BBB, decrease oedema & improve axonal conduction
  - Do not alter long-term course of disease
- *Interferon β*
  - Treatment of choice for relapsing-remitting MS
  - Common side effect = transient influenza-like symptoms for 24-48 hours
- *Glatiramer acetate*
  - Mixture of random synthetic polypeptides that mimic myelin basic protein
  - Alternative to interferon β & most useful in patients who become resistant to interferon β
- *Azathioprine*
  - Purine analogue that depresses both cell-mediated & humoral immunity
  - Considered when patients show no response to interferon β or glatiramer therapy
- *Methotrexate*
  - Inhibits both cell-mediated & humoral immunity due to its anti-inflammatory effect
  - Beneficial in patients with secondary progressive MS
- *Mitoxantrone*
  - Immunosuppressive drug that inhibits lymphocyte proliferation
  - Limited to patients with rapidly progressive MS because of severe cardiac toxicity
- Symptomatic
  - Paroxysmal pain with *carbamazepine, phenytoin, gabapentin*
  - Spasticity with *baclofen, diazepam, dantrolene*
  - Depression with *antidepressants*
  - Bladder & bowel disturbance with *anticholinergics*

## Anaesthesia

- Postoperative exacerbation possible regardless of anaesthetic technique or drugs used
- Spinal anaesthesia implicated in postoperative exacerbations whereas exacerbations after epidural anaesthesia or peripheral nerve blockade have not been described → LAs may exacerbate symptoms due to increased sensitivity of demyelinated axons to LA toxicity
- Decreased relapse rate during pregnancy but increased in first 3 months postpartum
- Exercise caution when using suxamethonium if patient is debilitated – hyperkalemia

- Potential for prolonged response to non-depolarising muscle relaxant due to coexisting skeletal muscle weakness & decreased skeletal muscle mass
- Temperature maintenance is important – symptoms can deteriorate with increases in temperature
- Consider perioperative corticosteroid supplementation if long-term steroids
- Periodic neurological evaluation during postoperative period to detect exacerbations

Demyelination affecting	Clinical signs and symptoms	Anaesthetic implications
Brain	Depression, fatigue, painful seizures, pain syndromes, sensory deficits	Interaction with antidepressants, anticonvulsants agents used for treatment of pain
Corticospinal tracts	Upper motor neuron type of paralysis with spasticity, hyperactive deep reflexes, upgoing Babinski	Upregulation of acetylcholine receptors, altered response to muscle relaxants: N-M monitoring
Brain-stem, optic tracts, cranial nerves	Visual-impairment, nystagmus, diplopia, trigeminal neuralgia, dysarthria, dysphagia, depressed pharyngeal, laryngeal reflexes	Interaction with pain medications used for trigeminal neuralgia, Risk of aspiration— Use of Sellick's manoeuvre, H <sub>2</sub> blockers, proton-pump inhibitors, anti-emetics
Brain-stem and spinal cord	Autonomic dysfunction with cardiac dysrhythmia, Impaired control of ventilation, reduced response to raised pCO <sub>2</sub> , diaphragmatic paralysis, ventilatory problems due to reduced respiratory muscle strength, limb-weakness, paresthesias, sensory deficits, Pain-medications/Drugs for spasticity	Cardiac dysfunction Hypotension with Inhalational agents, regional techniques with poor response to fluid loading and pressor agents. Hypoventilation, hypoxaemia, apnoea, resp. failure post-operative O <sub>2</sub> /mechanical ventilation indicated. Cardiovascular, respiratory monitoring essential. Resistance/sensitivity to N-M blockers, N-M monitoring essential
Others	Even 0.5° rise in body temperature can cause exacerbation	Core and surface temperature monitoring

## Myasthenia gravis (Oxford p256, Stoelting p448)

- Chronic autoimmune disorder
- Caused by a decrease in functional postsynaptic acetylcholine receptors at NMJ resulting from their destruction/inactivation by circulating antibodies; origin of antibodies unknown, but a relationship to the thymus gland is suggested by the association of myasthenia gravis with thymus gland abnormalities
- Incidence 1 in 10,000 & prevalence 1 in 7,500
- Mostly affects women 20-30 years of age; men are often older than 60 years at presentation
  - Before age 40 – 2F:1M, 40% thymus enlargement
  - After age 40 – 1F:1M, 20% thymoma

### Clinical Features

- Clinical course often marked by periods of exacerbations & remissions
- Characterised by skeletal muscle weakness that *improves with rest*
  - Muscle weakness may be normal in well-rested patients but weakness occurs promptly with exercise
- Most commonly affects *ocular muscles*, but can affect any skeletal muscle (including respiratory muscles)
  - Ptosis & diplopia resulting from extraocular muscle weakness are most common initial complaints
  - Weakness of pharyngeal & laryngeal muscles results in *dysphagia, dysarthria & difficulty handling saliva* → high risk of pulmonary aspiration
  - Arm, leg or trunk weakness can occur in any combination & is usually asymmetrical
  - Muscle atrophy does not occur
- Myocarditis can result in atrial fibrillation, heart block or cardiomyopathy
- Classification & severity (Osserman-Genkins) based on skeletal muscle involvement & response to therapy

Type I	Ocular signs & symptoms only (10%) If disease confined to ocular muscles >3 years unlikely to experience any progression
Type IIA	Generalised mild muscle weakness responding well to therapy (slowly progressive) Respiratory muscles not involved
Type IIB	Generalised moderate muscle weakness responding less well to therapy (more rapidly progressive) Respiratory muscles may be involved
Type III	Acute fulminating presentation within 6 months &/or respiratory dysfunction Associated with high mortality rate
Type IV	Myasthenic crisis requiring artificial ventilation Results from progression of type I or II

- Associated with other autoimmune diseases, including – hypo/hyperthyroidism, rheumatoid arthritis, scleroderma, SLE & pernicious anaemia
- History – aimed at Leventhal criteria
  - Disease duration
  - Coexisting chronic respiratory disease
  - Treatment – pyridostigmine dose & other therapies
  - Bulbar dysfunction
- Examination
  - Look for thymectomy scar over sternum
  - Assess for diplopia & drooping eyelids
  - Muscle power decreases with use, little wasting, sensation intact & normal reflexes
  - Test for muscle fatigue
    - Oculomotor muscles – ask patient to sustain an upward gaze by looking up at the ceiling for 1 minute & watch for progressive ptosis
    - Orbicularis oculi – ask patient to close their eyes; if positive, within 30 seconds the lid margin will begin to separate, showing the sclera (peek sign)
    - Levator muscles of mouth – prolonged smiling looks more like a grimace (transverse smile sign)
    - Proximal limb girdle muscles – ask patient to hold their arms above the head; you can repeatedly press the abducted arms down until they weaken
  - Test bulbar function – ask to swallow glass of water
- Investigations
  - RFTs – VC <15ml/kg or <2.9L predicts need for postoperative mechanical ventilation

### Treatment

- Anticholinesterase drugs (1<sup>st</sup> line therapy)
  - Enhance neuromuscular transmission – effective because they inhibit the enzyme responsible for hydrolysis of acetylcholine & thus increase the amount of neurotransmitter available at the NMJ
  - Pyridostigmine commonly used
    - Dose tailored to response
    - Onset of effect 30 minutes, peak effect 2 hours, duration of effect 3-6 hours
    - High doses may induce more muscle weakness (cholinergic crisis)
- Thymectomy (median sternotomy or mediastinoscopy through a cervical incision)
  - Intended to induce remission or at least allow reduced dosages of immunosuppressive medications
- Immunosuppression
  - Indicated when skeletal muscle weakness is not controlled by anticholinesterase drugs
  - Either corticosteroids, azathioprine, cyclosporine or mycophenolate
- Short-term immunotherapy
  - Plasmapheresis
    - Removes antibodies from circulation & produces short-term clinical improvement in patients with myasthenia gravis who are experiencing myasthenic crises or are being prepared for thymectomy
    - Risk of infection, hypotension & pulmonary embolism with repeated treatment
  - Immunoglobulin
    - Same indications as for plasmapheresis – myasthenic crises or preparation for thymectomy
    - Temporary effect with no effect on circulating concentrations of antibodies

## Anesthesia

### Preoperative

- Possible associated autoimmune disease (myocarditis, thyroiditis) should be ruled out
- Elective surgery should be deferred in periods of relapse & ideally performed in periods of remission
  - Infection, electrolyte abnormalities, pregnancy, emotional stress & surgery can trigger exacerbations
- Aspiration risk
  - Laryngeal/pharyngeal involvement predisposes to inability to clear secretions & pulmonary aspiration
- Muscular groups affected, strength & course of exacerbations/remissions should be assessed by thorough history & examination
- Many patients require postoperative ventilation
  - Factors known to correlate with the need for mechanical ventilation postoperatively (Leventhal criteria):
    - Major body cavity surgery
    - Disease duration > 6 years
    - Coexisting chronic respiratory disease
    - Pyridostigmine dose > 750mg per day
    - Preoperative vital capacity < 15ml/kg
    - Type III & IV myasthenia gravis
    - Any degree of bulbar palsy
  - Poor bulbar function & a consistently reduced FVC are reliable indicators of the need for prolonged mechanical ventilation following surgery
- Continue anticholinesterase therapy up to the time of induction
- Corticosteroids are continued preoperatively & additional hydrocortisone is given on the day of surgery
- Premedication should be minimal

### Intraoperative

- Use regional anaesthesia if possible & avoid ester local anaesthetics (prolonged half-life as metabolized by cholinesterase)
- Abnormal neuromuscular response to both depolarizing & non-depolarising muscle relaxants (avoid if possible) → decision to use paralytics should be made on a case-by-case basis
  - Relatively resistant to effects of suxamethonium (but may see longer duration of action if patient taking cholinesterase inhibitors)
    - 95% effective dose is ≈ 2.6 times higher than normal – so still use normal dose
    - Mechanism for resistance unknown – but decreased number of ACh receptors at postsynaptic NMJ may play a role
  - Increased sensitivity to non-depolarising muscle relaxants
    - Due to reduced number of functional ACh receptors → balance between active & non-functional receptors modulates sensitivity
    - Initial dose should be decreased by one-half & response monitored using a peripheral nerve stimulator
    - Monitoring orbicularis oculi will overestimate neuromuscular blockade if ocular involvement
    - Ideally, avoid use of non-depolarising muscle relaxants

- Tracheal intubation can often be accomplished without muscle relaxants because of intrinsic muscle weakness & relaxant effect of volatiles anaesthetics on skeletal muscles
- Drugs used to treat myasthenia gravis can influence the response to muscle relaxants independent of the disease process – for example:
  - Anticholinesterase drugs inhibit not only true cholinesterase but also impair plasma pseudocholinesterase activity, which introduces the possibility of a prolonged response to suxamethonium
  - Corticosteroid therapy does not alter the dose requirements of suxamethonium but has been reported to produce resistance to the neuromuscular blocking effects of steroid muscle relaxants such as vecuronium
- Reversal of neuromuscular blockade
  - Should be achievable with standard doses of neostigmine if preoperative symptom control has been good
  - Avoidance of reversal is preferred since further doses of anticholinesterase may introduce the risk of overdose (cholinergic crisis)
  - Do not use more than equivalent dose of oral pyridostigmine → 1mg IV neostigmine = 30mg PO pyridostigmine
- Opioids – limit use as respiratory effects can linger into postoperative period
- Medications to avoid in patients with myasthenia gravis

<i>Do not use</i>	<i>Use with caution</i>
Beta-blockers Chloroquine, quinine, quinidine, procainamide IV magnesium Phenytoin Dantrolene (except if MH) Antibiotics – aminoglycosides, quinolones, macrolides Botulinum toxin	Non-depolarising muscle relaxants Benzodiazepines Phenothiazines, lithium, carbamazepine Oral magnesium Local anaesthetics in large amounts

#### *Postoperative*

- Extubation criteria
  - Comparison of strength & respiratory parameters to preoperative values (RFT, ABG)
  - Vital capacity > 25ml/kg, negative inspiratory force > -30cmH<sub>2</sub>O
  - Most stage III & IV patients will need postoperative ventilatory support
- Coordinate with neurologist for resumption of anticholinesterase treatment
  - NGT insertion if bulbar dysfunction & early return to oral therapy needed
  - Steroids, plasmapheresis &/or IV globulin may be necessary if unable to extubate & enteral malabsorption
- Postoperative weakness – differential includes:
  - Residual neuromuscular block
  - Cholinergic crisis
  - Myasthenic crisis
- HDU/ICU

## **Eaton Lambert Syndrome (Myasthenic Syndrome)** (Oxford p258, Stoelting p451)

- Acquired autoimmune disease
- Characterised by the presence of IgG antibodies to voltage-sensitive calcium channels that causes a deficiency of these channels at the motor nerve terminal which restricts calcium entry when the terminal is depolarized

### **Clinical Features**

- Proximal limb weakness (legs more than arms)
- Exercise improves with strength
- Muscle pain common
- Reflexes absent or reduced
- Look for evidence of coexisting small cell lung cancer

### **Treatment**

- Anticholinesterase drugs effective in myasthenia gravis do *not* produce an improvement in patients with myasthenic syndrome
- 3,4-diaminopyridine ↑ ACh release at NMJ & improves muscle strength
- Immunoglobulin ↑ muscle strength temporarily (6-8 weeks)

### **Anaesthesia**

- Sensitive to both depolarizing & non-depolarising muscle relaxants
- Antagonism of neuromuscular blockade with anticholinesterase drugs may be inadequate

### **Comparison of myasthenia gravis & myasthenic syndrome**

<b>Characteristic</b>	<b><i>Myasthenia Gravis</i></b>	<b><i>Myasthenic Syndrome</i></b>
<i>Manifestations</i>	Extraocular, bulbar + facial weakness Exercise causes fatigue Muscle pain uncommon Reflexes normal	Proximal limb weakness (legs > arms) Exercise improves muscle strength Muscle pain common Reflexes absent or decreased
<i>Gender</i>	Females > males	Males > females
<i>Co-existing pathologies</i>	Thymoma	Small cell lung cancer
<i>Response to muscle relaxants</i>	Resistance to suxamethonium Sensitive to non-depolarising muscle relaxants Good response to anticholinesterases	Sensitive to suxamethonium + non-depolarising muscle relaxants Poor response to anticholinesterases

## Parkinson's Disease (Oxford p246, Stoelting p245)

- Idiopathic & progressive neurodegenerative disorder characterised clinically by rigidity, resting tremor, postural instability & bradykinesia (slowness of movement)
- Common disease of middle to old age – prevalence 1% in people > 65 years
- Unknown cause – involves extrapyramidal system & increasing age is single most important risk factor
  - Dopaminergic neurons in substantia nigra are lost & intracellular Lewy bodies found in remaining neurons
  - Results in decreased dopaminergic activity + dominant cholinergic activity
  - Clinical signs evident when ≈80% of dopaminergic activity is lost
- Most common cause of parkinsonism (syndrome characterised by rigidity, tremor & bradykinesia)
  - Causes of parkinsonism:
    - Degenerative – parkinson's disease (85%), multi-system degeneration, familial parkinsonism
    - Drugs – reserpine, prochloroperazine
    - Structural lesions – normal pressure hydrocephalus, tumour, trauma
    - Toxic – MPTP, carbon monoxide, cyanide, manganese
    - Metabolic – hypoparathyroidism
    - Infective – encephalitis lethargica, AIDS
    - Vascular – multi-infarct disease

### Clinical Features

- History
  - Timing of onset of symptoms (usually > 65 yrs)
  - Progression since diagnosis
  - Functional limitation at present
  - Complications:
    - Dysphagia, aspiration
    - GORD, reduced GIT motility
    - Postural hypotension
    - Depression, dementia
  - Medication regimen & response to medications (doses & frequency reflect disease severity)
- Examination
  - Inspection – lack of facial expression ('mask-like facies'), flexed posture, few spontaneous movements
  - Gait & abnormal movements:
    - Shuffling gait (small steps + patient hardly raises feet from ground)
    - Difficulty in initiating walking but once it begins, patient hurries (festination) & has difficulty stopping
    - Lack of normal arm swing
    - Bradykinesia
      - Difficulty getting out of chair
      - Finger tapping test (ask patient to tap their fingers in turn onto a surface repeatedly, quickly with both hands at once) – will be slow + clumsy
      - Twiddling (rotating hands around each other in front of body) – will be slow + clumsy
  - Face
    - Mask-like facies, absent blinking, dribbling saliva
    - Glabellar tap (tap middle of patient's forehead with your middle finger) – positive sign when patient continues to blink as long as you tap
    - Monotonous, soft, faint speech
  - Arms
    - Resting tremor (often asymmetrical, 'pill-rolling'), finger-nose testing (tremor may decrease)
    - Tone (test at both wrists) – cogwheel or lead-pipe rigidity
    - Micrographia (small writing)
  - Respiratory exam if risk of aspiration or evidence of infection
- Investigations – as appropriate from examination
- Clinical diagnosis with no specific test – 4 cardinal signs used for diagnosis → **TRAP**
  - Tremor – resting
  - Rigidity – cogwheel type
  - Akinesia/bradykinesia – slowness of movement
  - Postural instability – failure of postural 'righting' reflexes leading to poor balance & falls

Motor and sensory	Resting tremor* Lead pipe/plastic rigidity* Slowness of movement Blank staring facial expression Soft monotonous voice Festinant gait Loss of arm swing on walking Restless legs syndrome
Cardiovascular	Orthostatic hypotension*
Respiratory	Restrictive ventilatory defect* Aspiration* Sleep apnoea (if prominent autonomic disturbance)* Respiratory dyskinesia (levodopa)*
Gastrointestinal	Sialorrhoea and drooling* Constipation Nausea (anti-Parkinson drugs)* Neurological dysphagia*
Genito-urinary	Bladder disturbance Sexual dysfunction
Neuropsychiatric	Depression Dementia Anxiety Sleep disturbance
Musculoskeletal	Muscle aches and cramps Flexion deformity of the neck*
Dermatological	Disordered sweating and oily skin Pressure sores

## Treatment

- Designed to increase concentration of dopamine in basal ganglia or decrease neuronal effects of acetylcholine
- Pharmacological:
  - **Levodopa** (dopamine precursor) & **Carbidopa** (peripheral dopa decarboxylase inhibitor) combination
    - Standard medical treatment – allows a reduction in levodopa dose & reduces peripheral dopaminergic side-effects (tachycardia, dysrhythmias, nausea, vomiting)
  - Dopamine agonists
    - Mimic action of dopamine at dopamine receptor
    - **Ropinirole, Pramipexole** – monotherapy in early disease or adjunct to combination therapy
    - **Apomorphine** – only parenteral agent, give by subcutaneous infusion perioperatively if NBM
  - MAO-B inhibitor – **Selegiline**
    - Inhibits dopamine catabolism in CNS & ? neuroprotective
    - Monotherapy in early disease or adjunct to combination therapy
  - Peripheral catechol-O-methyl transferase (COMT) inhibitors – **Entacapone**
    - Adjunct to combination therapy – smooths out end of dose 'off' periods
  - Antiviral agent – **Amantadine**
    - Monotherapy in early disease
    - Unclear MOA – reported to modulate dopamine + glutamate in CNS
- Surgical (reserved for patients with disabling & medically refractory disease):
  - **Implanted deep brain stimulating device** for tremor control
  - **Pallidotomy** – significant but short-lived improvement in levodopa-induced dyskinesias

## Anaesthesia

- Continue medical therapy up to start of anaesthesia & consider NGT insertion for intraoperative administration
  - Distressing symptoms develop as little as 3 hours after a missed dose
  - Acute withdrawal may precipitate neuroleptic malignant syndrome
- Consider apomorphine infusion (dose depends on challenge response)
- Beware of drug interactions – dopamine antagonists, pethidine, tramadol, SSRI/TCAs, antipsychotics, clonidine
- Premedication – glycopyrrrolate for sialorrhoea, fluiding loading
- Induction – autonomic neuropathy, hypovolemia, airway risk, aspiration risk
- Maintain normothermia to avoid shivering
- Regional – advantageous as patient remains conscious, can resume medications immediately postop & less PONV; disadvantageous as technically difficult, tremor is not abolished & poor cooperation if dementia
- General – advantageous as can insert NGT for medications & patient is still/no tremor; disadvantageous as may worsen an already compromised cough/respiratory function, PONV makes enteral medication difficult, opioids may exacerbate rigidity & drug interactions
- Postoperative
  - May not be able to operate PCA device or communicate pain scores
  - PONV – treat with domperidone (10mg PO Q4H), ondansetron (4mg IV) or cyclizine (50mg IV)
  - Aim for good PD control – involve neurologist, commence medications ASAP
  - Physiotherapy – respiratory + musculoskeletal
  - Complications – thromboembolism, pressure area damage, sputum retention, aspiration, delirium

## Rheumatoid Arthritis (Oxford p192, Stoelting p454)

- Most common chronic inflammatory arthritis, ≈ 1% of adults
- Affects women > men
- Peak incidence 7<sup>th</sup> decade of life

DDx of symmetrical deforming polyarthropathy:

- Rheumatoid arthritis
- Psoriatic arthritis
- Chronic gout
- Generalised osteoarthritis

### Clinical Features

- History
  - How was the diagnosis made & what were the presenting features?
  - Current activity of disease, duration of morning stiffness?
  - What joints are involved?
  - Non-articular features:
    - Lungs – dyspnoea – diffuse interstitial fibrosis or effusion, pain from pleuritis
    - Eyes – dry eyes from scleritis or Sjogren's syndrome
    - Nervous system – peripheral neuropathy, cord compression
    - Blood – anaemia of chronic disease
    - Heart – chest pain from pericarditis
  - Treatment to date & associated complications
- Examination
  - General inspection – Cushingoid appearance, weight
  - Peripheries
    - Hands – symmetrical small joint synovitis (PIP + MCP joints, DIP usually spared), ulnar deviation, volar subluxation of MCP joints, Z deformity of thumb with swan neck, Boutonniere deformity of fingers, wasting of small muscles of the hand
    - Elbows – nodules, flexion contractures
  - Face – dry eyes, scleritis, episcleritis, dry mouth, limited MO, TMJ crepitus, cricoarytenoid arthritis (acutely presents with hoarseness, painful swallowing + dyspnoea)
  - Neck – cervical spine tenderness/muscle spasm/↓ rotational movement (atlanto-axial instability affects 25%)
  - Heart – pericardial rub (pericarditis), diastolic murmur (AR)
  - Lung – effusion, fibrosis, infection, nodules
  - Abdomen – hepatomegaly, splenomegaly
- Investigations
  - Cervical spine x-rays (lateral flexion + extension views) indicated if pain radiating to occiput, paraesthesia to shoulders/arms with head movement or painless sensory loss in hands
    - Distance between posterior aspect of C1 arch & anterior aspect of odontoid peg should be no more than 3mm in adults (5mm in children) → atlanto-axial subluxation is indicated by separation of anterior margin of odontoid peg from posterior margin of anterior arch of C1 by > 3mm
      - 4 types – anterior (80%), posterior (<5%), vertical (10-20%), lateral/rotatory (5-10%)
  - Bloods – Hb, platelets, WCC, ESR, CRP, RF, ACPA (anti-cyclic citrullinated peptide antibodies)
  - CXR
  - ECG
  - Echocardiogram – pericardial effusion, AR
- American College of Rheumatology/European League Against Rheumatism 2010 Diagnostic Criteria – a score of 6 or more is required for a diagnosis of RA

Clinical criteria	Score
<b>A Joint involvement</b>	
1 large joint	0
2–10 large joints	1
1–3 small joints	2
4–10 small joints	3
> 10 small joints	5
<b>B Serology</b>	
Negative RF and ACPA	0
Low positive RhF or low positive ACPA	2
High positive RhF or high positive ACPA	3
<b>C Acute-phase reactants</b>	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
<b>D Duration of symptoms</b>	
< 6 weeks	0
≥ 6 weeks	1

## Treatment

- Non-pharmacologic – education, physiotherapy, occupational therapy
- Pharmacologic
  - NSAIDs
  - Corticosteroids – primarily used to overcome acute flares while patient becomes established on DMARDs
  - Disease modifying anti-rheumatic drugs (DMARDs)
    - Methotrexate (1<sup>st</sup> line)
    - Hydroxychloroquine
    - Cyclosporine
    - Leflunomide
    - Anakinra
    - Sulfasalazine
    - Azathioprine
    - Gold salts
  - Anti-TNF  $\alpha$  agents
    - Infliximab
    - Etanercept
- Surgical correction of deformities – shoulder, hip, knee

**Table 3** Disease modifying therapies for rheumatoid arthritis.

Drug	Mechanism of action	Specific potential toxicities
Methotrexate	Antimetabolite, folate poison	Interstitial lung disease Liver toxicity Ocular toxicity
Hydroxychloroquine	Blocks toll-like receptor on dendritic cells	Hypertension Nephrotoxicity Liver toxicity. Extensive hepato-enteric re-circulation
Cyclosporin	Calcineurin inhibitor, prevents IL-2 action	Pneumonia
Leflunomide	Anti-proliferative, inhibits pyrimidine synthesis	Stevens-Johnson syndrome
Anakinra	IL-1 receptor antagonist, reduces IL-1 signalling	Proportion of population are slow acetylators, and prone to toxicity Pancreatitis Glomerulonephritis
Sulfasalazine	Immunomodulation	
Azathioprine	Anti-proliferative, inhibits purine synthesis	
Gold salts	Unknown immunomodulation	

## Anaesthesia

- Increased cardiovascular risk in those with:
  - Seropositive disease (RF, ACPA)
  - Symptoms of heart failure
  - Poorly controlled disease
  - ‘Rheumatoid cachexia’
- Likely pre-existing anaemia – increased requirement for blood transfusion
- Very fragile skin – extreme care required when handling & positioning
- Deformities & fixation of joints can make positioning (especially pronation) difficult
- Patients are often in considerable pain – care required during examination & anaesthetic preparations
- Poor peripheral venous access & arterial + central venous access are often difficult
- Glucocorticoid supplementation is required if on long-term steroid therapy
- Risk of higher than expected spinal block
- Risk of post-extubation oedema due to cricoarytenitis
- Postoperative ventilation may be required for those with severe myopathy who are at risk of respiratory failure
- Possibility of perioperative neurological damage

## Possible Questions

What are the extra-articular features of rheumatoid arthritis?

**Table 1** Extra-articular manifestations of rheumatoid arthritis relevant to anaesthesia

System/organ	Key points relevant to anaesthesia
Cardiovascular	Pericardial effusions, pericarditis and cardiac tamponade
	Myocarditis, amyloidosis, and granulomatous disease
	Endocarditis and left ventricular failure
	Peripheral vasculitis and Raynaud's phenomenon
	Increased atherosclerosis and coronary heart disease
	Restrictive defect (fibrosing alveolitis)
Respiratory	Rheumatoid nodules
	Reduced chest wall compliance (costochondral disease)
	Pleural effusions
Haematological	Normocytic normochromic anaemia
	Iron deficiency anaemia (peptic ulceration and bleeding)
	Bone marrow depression from drug treatment
Hepatic and renal	Chronic renal failure from drug treatment (approx 25%)
	Hepatomegaly, splenomegaly
	Increased serum fibrinogen and alpha-1 acid glycoprotein
Neurological and ocular	Decreased serum albumin
	Peripheral neuropathy
	Autonomic dysfunction
	Kerato-conjunctivitis

### Spondyloarthropathies

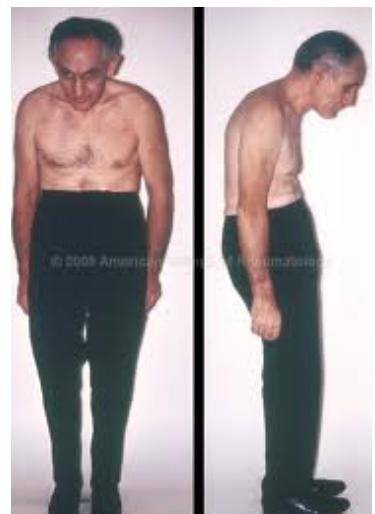
- Group of non-rheumatic arthropathies, including:
  - Ankylosing spondylitis
  - Reactive arthritis (Reiter's syndrome)
  - Juvenile chronic polyarthropathy
  - Psoriatic arthritis
  - Enteropathic arthritis
- Characterised by:
  - Involvement of spine, especially sacroiliac joints
  - Asymmetrical peripheral arthritis & synovitis
  - Absence of rheumatoid nodules or detectable circulating rheumatoid factor
- Causes unknown but strong association with HLA-B27 (HLA-B27 + children → 33% risk of developing AS)

### Ankylosing Spondylitis

- Autoimmune seronegative spondyloarthropathy
- Painful chronic inflammatory arthritis punctuated by exacerbations ('flares') & quiescent periods
- Primarily affects spine + sacroiliac joints & eventually causes fusion + rigidity of spine ('bamboo spine')
- Associated with ulcerative colitis, Crohn's disease, psoriasis & Reiter's syndrome (uveitis)
- Peak age onset 20-30 years, predominantly men
  - 1% of men (more severe spinal + pelvic disease) & 0.5% of women (more peripheral joint involvement)

### Clinical Features

- History
  - Symptom onset typically 15-40 years
  - Persistent pain & morning stiffness (worse at rest but improves with exercise) in lower spine + sacroiliac joints
  - Visual impairment, photophobia, eye pain
  - Fatigue, weight loss, low-grade fever
  - Family history
- Examination
  - Back + sacroiliac joints:
    - Loss of lumbar lordosis + thoracic kyphosis
    - Severe flexion deformity of lumbar spine
    - Tenderness over lumbar vertebrae
    - Reduction of movement of lumbar spine in all directions
    - Tenderness of sacroiliac joints
    - Measure occiput to wall distance – serial measurements showing an increasing distance indicate worsening deformity
    - Perform Schober's test & test for lateral spine movement by asking patient to run a hand straight down the side of each leg in turn (often severely restricted)
  - Legs:
    - Achilles tendinitis, plantar fasciitis
    - Cauda equina compression (rare) – lower limb weakness, loss of sphincter control, saddle sensory loss
  - Face:
    - Eyes: acute iritis (painful red eye)
    - Temporomandibular joint: limited mouth opening
    - Cricoarytenoid joint: hoarseness
  - Lungs: decreased chest expansion (<5cm), upper lobe fibrosis
  - Heart: signs of aortic regurgitation (1%)
  - Rectum + stool for signs of inflammatory bowel disease
- Investigations
  - FBC – mild normochromic anaemia
  - Elevated serum IgA & ESR
  - Raised alkaline phosphatase in severe disease
  - Spine x-ray – bamboo spine, erosion of sacroiliac joints
  - ECG – conduction defects
  - Echocardiography – aortic regurgitation
  - RFTs – restrictive defect



Bamboo spine: frontal radiograph shows complete fusion vertebral bodies. Extensive facet joint ankylosis & posterior ligamentous ossification produce trolley track appearance.

- Diagnosis made on clinical & radiological criteria:

**Table 1** Modified New York criteria for AS [23]. Diagnosis of AS requires one radiological criterion with at least one clinical criterion. Probable AS > 3 clinical criteria present or radiological criteria.

Clinical criteria
Low back pain > 3 months duration, improves with exercise and is not relieved by rest
Limitation of motion of the lumbar spine in sagittal and coronal planes
Limitation of chest expansion relative to normal values corrected for age and sex
Radiological criteria
Bilateral sacroiliitis – grade 2 (sclerosis with some erosions) or higher
Unilateral sacroiliitis – grade 3 (severe erosions, pseudodilatation of joint space and partial ankylosis) or grade 4 (complete ankylosis)

### Treatment

- Physiotherapy, exercise & education to maintain good posture & function
- Symptomatic treatment (relieve pain + reduce inflammation) – NSAIDs, disease-modifying antirheumatic drugs (methotrexate, sulfasalazine), bisphosphonates, corticosteroids (oral steroids less effective in AS compared to RA)
- TNF  $\alpha$  blockers (infliximab, etanercept) – suppress disease activity, improve physical function, slow disease progression & may achieve remission
- Topical corticosteroid eye drops for uveitis

### Anaesthesia

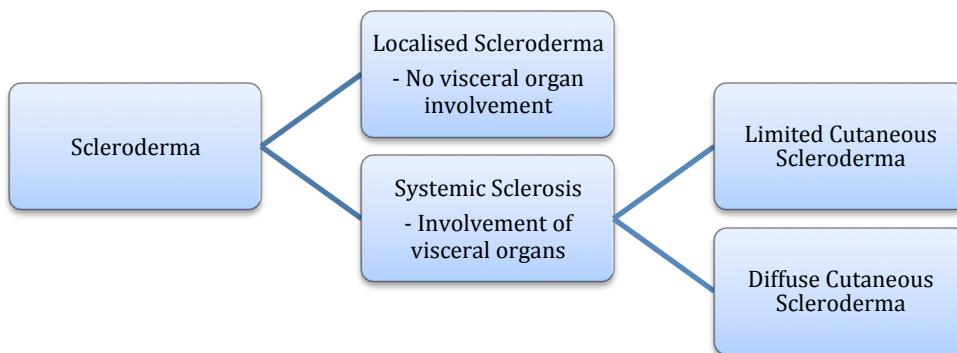
- Potentially difficult airway
  - Limited mouth opening with temporomandibular joint involvement → difficult laryngoscopy & LMA insertion
  - Stiff & deformed spinal column prevents appropriate cervical spine motion for intubation → need fiberoptic or video laryngoscope assistance
  - Excessive neck extension in patients with chronic cervical kyphosis can cause vertebrobasilar insufficiency & neurological injury
  - AFOI – safest option
- Restrictive lung disease from costochondral rigidity & fixed flexion deformity of thoracic spine
- Technically difficult neuraxial blockade – use paramedian approach
- Aortic regurgitation – avoid sudden increases in SVR
- Implications of drug treatment

### Comparison of RA & AS

Characteristic	Rheumatoid Arthritis	Ankylosing Spondylitis
<i>Family history</i>	Rare	Common
<i>Gender</i>	Female (30-50 yrs)	Male (20-30 yrs)
<i>Joint involvement</i>	Symmetrical polyarthropathy	Asymmetrical oligoarthropathy
<i>Sacroiliac involvement</i>	No	Yes
<i>Vertebral involvement</i>	Only cervical	Total (ascending from lumbosacral region)
<i>Cardiac changes</i>	Pericardial effusion Aortic regurgitation Cardiac conduction abnormalities Cardiac valve fibrosis Coronary artery arteritis	Cardiomegaly Aortic regurgitation Cardiac conduction abnormalities
<i>Pulmonary changes</i>	Pulmonary fibrosis Pleural effusion	Pulmonary fibrosis
<i>Eyes</i>	Keratoconjunctivitis sicca (dry eyes)	Conjunctivitis Uveitis
<i>Rheumatoid factor</i>	Positive	Negative
<i>HLA-B27</i>	Negative	Positive

## Systemic Sclerosis (Oxford p198, Stoelting p441)

**Scleroderma** is a connective tissue disease associated with excess production & deposition of collagen, glycosaminoglycans + fibronectins within connective tissues.



**Systemic sclerosis** describes a systemic disease characterised by:

- Skin induration & thickening accompanied by various degrees of tissue fibrosis
- Chronic inflammatory infiltration in numerous visceral organs
- Prominent fibroproliferative vasculopathy & humoral + cellular immune alterations

Subdivided into:

- **Limited cutaneous systemic sclerosis**
  - Have long-standing Raynaud's phenomenon before other manifestations appear
  - Subset have CREST syndrome:
    - Calcinoses
    - Raynaud's phenomenon
    - Oesophageal hypomotility
    - Sclerodactyly (thickening + tightness of skin of fingers + toes)
    - Telangiectasia (small blood vessels just below skin surface)
  - Diffuse skin sclerosis does not occur – skin involvement is slowly progressive & remains limited to fingers, distal extremities + face (does not affect trunk)
  - Severe interstitial lung disease does not occur but at high risk of developing pulmonary hypertension
- **Diffuse cutaneous systemic sclerosis**
  - Prominent skin sclerosis – progressive skin induration, starting in the fingers & ascending from distal to proximal extremities, the face & the trunk
  - At risk for early pulmonary fibrosis & acute renal involvement

Unknown cause – likely multifactorial (?autoimmune):

- Human leukocyte antigens, anticentromere & antitopoisomerase antibodies have all been implicated
- Raised levels of endothelial cell antibodies associated with increased disease severity
- Past exposure to CMV, organic solvents, silica, dust, drugs (bleomycin) & aromatic hydrocarbons may also increase risk of developing systemic sclerosis

Typical age at onset is 20-40 years & women are most often affected

Pregnancy – accelerates progression in 50%, incidence of spontaneous abortion, premature labour & perinatal mortality is high

### Clinical Features

- History
  - Ask about symptoms
    - Cutaneous – thickened + dry skin (after initial oedematous phase), itch, dry mouth + eyes, eye burning, painful white lumps under skin
    - Arthritis – joint pain + swelling, muscle pain + stiffness, muscle weakness
    - Gastrointestinal – dysphagia, heartburn (oesophagitis), diarrhea (malabsorption), appetite loss
    - Cardiac – chest pain (pericarditis), palpitations (arrhythmias), symptoms of heart failure (dilated cardiomyopathy), pulmonary hypertension
    - Respiratory – dyspnoea, wheezing, non-productive cough
  - Treatment received & side effects
  - Degree of disability
- Examination
  - General appearance – 'bird-like' facies, weight loss

- Hands
  - Calcinosis, atrophy distal tissue pulp (Raynaud's), sclerodactyly, telangiectasia
  - Dilated capillary loops (nailfolds)
  - Small joint arthropathy, tendon crepitus
  - Fixed flexion deformity
  - Hand function
- Arms – oedema (early) or skin thickening + tightening, pigmentation, vitiligo, hair loss, proximal myopathy
- Head
  - Alopecia
  - Eyes – loss of eyebrows, anaemia, difficulty closing
  - Mouth – puckered ('purse string mouth'), reduced opening
  - Pigmentation
  - Telangiectasia
  - Neck muscles – wasting + weakness
- Chest
  - Tight skin ('Roman breastplate')
  - Heart – pulmonary hypertension, pericarditis, heart failure
  - Lungs – fibrosis, reflux pneumonitis, chest infections
- Legs – skin lesions, vasculitis
- Other
  - Blood pressure (hypertension with renal involvement)
  - Urine analysis (proteinuria)
  - Temperature (infection)
  - Stool examination (steatorrhoea)
- Investigations
  - Blood – ANA positive (40%), anticentromere antibodies in CREST
  - ECG – look for signs of pericarditis, arrhythmias or conduction disturbances
  - CT chest – pulmonary fibrosis
  - Echocardiogram – pericardial effusion indicated by presence of echolucent area adjacent to cardiac structures, abnormal right heart chamber size + motion indicates pulmonary hypertension, note RVSP
  - RFTs – isolated low DLCO + reduced lung volume are common early, abnormal results likely due to interstitial fibrosis or pulmonary hypertension due to vasculopathy



- Diagnosis – according to the *American College of Rheumatology 1980 Classification Criteria* for systemic sclerosis, the presence of either the single major criterion OR two out of three minor criteria, is 97% sensitive for the diagnosis of scleroderma:
  - Major criterion
    - **Proximal scleroderma** – sclerodermatosus (thickening, tautness) involvement of fingers & skin proximal to metacarpophalangeal or metatarsophalangeal joints
  - Minor criterion
    - **Sclerodactyly** – thickening, tautness of skin, limited to fingers
    - **Digital pitted scars of fingertips or loss of substance of distal finger pad**
    - **Bibasilar pulmonary fibrosis**

## Treatment

- Raynaud's phenomenon
  - Preventative – cold avoidance, warming, smoking cessation
  - Calcium channel blockers (nifedipine)
  - α blockers (prazosin)
  - Antiplatelets (aspirin, dipyridamole)
  - Topical nitrates for refractory cases (nitroglycerin ointment)
  - Prostaglandins IV for digit-threatening ischaemia (iloprost)
- Musculoskeletal
  - NSAIDs, prednisone, methotrexate
- Gastrointestinal
  - PPIs for oesophageal reflux
  - Prokinetics for oesophageal hypomotility (metoclopramide, erythromycin)
  - Rotating antibiotics for bacterial overgrowth from small bowel hypomotility
- Respiratory
  - Pulmonary fibrosis – cyclophosphamide (+ prednisone as adjunct), methotrexate, mycophenolate

- Pulmonary hypertension – prostacyclin analogues (iloprost), endothelin receptor antagonists (bosentan), PDE type 5 inhibitors (sildenafil), anticoagulation
- Renal
  - ACE inhibitors
  - Avoidance of high prednisolone doses to reduce risk of developing renal crisis

## Anaesthesia

<i>Manifestation</i>	<i>Anaesthetic Consideration</i>
Raynaud's phenomenon	Peripheral vasoconstriction Avoid vasoconstrictors Femoral artery preferred over radial for IAL if significant
Dermal thickening, calcifications, contractures	Difficult peripheral IV access Difficulty with regional techniques Difficult positioning
Skin tightening, microstomia, decreased neck flexibility	Difficult airway management
Telangiectasias	Oral or nasal bleeding Careful TOE monitoring
Oesophageal dilatation, decreased LOS tone	Aspiration
Intestinal malabsorption, malnutrition	Decreased Vit K-dependent clotting factors Altered pharmacokinetics from hypoalbuminemia
Restrictive pulmonary disease	↑ Positive airway pressure, ↑ O <sub>2</sub> concentration, extubation delays
Myocardial fibrosis	Ventricular hypertrophy, diastolic dysfunction, conduction defects, coronary vasospasm
Renal disease (renal artery obstruction from intimal proliferation)	Hypertension, decreased renal clearance
Immunosuppressive therapy	Side effects & drug interactions

## Raynaud's Phenomenon (RP)

- Vasospastic disorder that causes an exaggerated response to cold temperatures &/or emotional stress, resulting in episodic digital ischaemia
- Presents as a cold-induced, symmetric, sharply demarcated white or blue discolouration of the distal fingers or toes, followed by erythema at a variable time after rewarming
- Affects women > men
- Classified as primary or secondary
  - Primary RP – occurs in the absence of any associated disease
  - Secondary RP – associated with an underlying pathologic disorder, use of certain drugs, or related occupation:
    - CREST syndrome (calcinosis, RP, oesophageal involvement, sclerodactyly, telangiectasia)
    - Scleroderma, Sjogren's syndrome, mixed connective tissue disease, polymyositis, dermatomyositis
    - Primary pulmonary hypertension
    - SLE, arteritis
    - Rheumatoid arthritis
    - Thromboangiitis obliterans (Buerger's disease)
    - Drugs - β blockers, ergotamine, vinblastine, bleomycin, OCP, nicotine, caffeine, cocaine, interferon
    - Haematologic disorders – polycythaemia, cryofibrinogenemia
    - Carpal tunnel syndrome
    - Use of tools that vibrate
    - Endocrine disorders – hypothyroidism, carcinoid syndrome, phaeochromocytoma
    - Oestrogen replacement therapy without progesterone
    - Hypercoagulable states
    - Primary biliary cirrhosis
    - Vasospastic disorders – migraines, Prinzmetal angina
    - Malignancy – ovarian cancer, lymphoma

### **Clinical Features**

- Classic description:
  - Digital blanching – vasospasm leads to pallor of fingers + toes, usually bilateral
  - Cyanosis – deoxygenated blood from capillaries + veins
  - Rubor after cold exposure + rewarming
  - Burning + throbbing pain post-episode
- Important to determine if primary or secondary cause

### **Treatment**

- Avoid drugs that may precipitate RP
- Avoid cold exposure & sudden temperature shifts
- Avoid stressful situations
- General measures – rotating arms in a windmill pattern, placing hands under warm water
- Medications:
  - Dihydropyridine calcium channel blockers – nifedipine, amlodipine, felodipine
  - Alpha receptor antagonists – prazosin
  - Topical nitrates – nitroglycerin ointment

### **Anaesthesia**

- No difference between regional or general anaesthesia
- Warm theatre & maintain normothermia
- Really think about the need for an arterial line – if patient has CREST syndrome use larger vessels (femoral over radial)
- Adrenaline in local anaesthetic may provoke vasoconstriction

## Systemic Lupus Erythematosus (SLE) (Oxford p196, Stoelting p456)

- Chronic multisystem inflammatory disease characterised by autoantibody production (95% ANA  $\oplus$ )
- Aetiology unknown
  - Represents regulatory mechanism failure of autoimmune system with multifactorial origin (diet, drugs, toxins, infection, environment, hormones + genetics)
  - Recent evidence suggests that 1° event in pathogenesis may be ↑ oxidative activity with subsequent chemical changes in endogenous DNA
  - Circulation of immune complexes & activation of complement leads to involvement of skin, joints, kidneys, serosal membranes, lungs, GIT & heart
- Affects females > males, peak age of onset 15-40 years
- Highly variable natural history with unpredictable exacerbations + remissions
  - Survival is 95% at 5 years, 90% at 10 years & 78% at 20 years
  - Disability is common due to chronic fatigue, arthritis, pain & renal disease
  - Major causes of death → initially – infection, renal failure; later – thromboembolic events

### Clinical Features

- History
  - General – onset, diagnosis, disease severity (is patient in remission or has acute exacerbation), ability to work/perform ADLs
  - Assess systemic involvement
    - Cardiovascular – conduction abnormalities, non-infective endocarditis, accelerated atherosclerosis + CAD, myocarditis, pericarditis, heart failure
    - Respiratory – pleuritis, pleural effusions, pneumonitis, restrictive lung disease, pulmonary hypertension
    - Renal – nephritis, oedema, dialysis
    - CNS – psychosis, seizures, peripheral neuropathy
    - Hematological – anaemia, leucopenia, thrombocytopenia, thrombosis
  - Treatment & associated complications – NSAIDs, steroids, immunosuppressants, cardiac drugs, plasmapheresis
- Examination
  - General inspection – Cushingoid appearance, weight, mental state
  - Hands – vasculitis, rash, arthropathy
  - Arms – livedo reticularis, purpura, proximal myopathy (active disease or steroids)
  - Head – alopecia, scarring, lupus hairs (short broken hairs above forehead), butterfly rash, cranial nerve lesions
  - Eyes – red & dry (Sjogren's syndrome), pale conjunctiva (anaemia)
  - Mouth – ulcers, infection
  - Chest – pericarditis, pleural effusion, pleurisy, pulmonary fibrosis, collapse or infection
  - Abdomen – hepatosplenomegaly, tenderness
  - Hips – aseptic necrosis
  - Legs – red soles of feet, small joint synovitis, rash, ulcers over malleoli, proximal myopathy, neuropathy, hemiplegia
- Investigations
  - Bloods – electrolytes, urea, Cr, Hb, WCC, platelets, APTT (order lupus anticoagulant if elevated)
  - Plasma cholinesterase level (reduced by plasmapheresis + cyclophosphamide)
  - Antibodies
    - Anti-double-stranded DNA (anti-dsDNA) is highly specific (70% positive)
    - Anti-nuclear antibody (ANA) is highly sensitive (95% positive)
  - ECG – silent ischaemia, conduction abnormalities
  - Echocardiography – valvular dysfunction, Libman-Sacks endocarditis
  - CXR – pleural effusion, pneumonitis, subglottic stenosis
  - RFTs
- Diagnostic criteria – need any 4 of 11:

<b>Criterion</b>	<b>Definition</b>
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences sparing the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling & follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash with sunlight
4. Oral ulcers	Painless oral or nasopharyngeal ulceration
5. Arthritis	Non-erosive arthritis involving 2 or more peripheral joints (tenderness, swelling or effusion)
6. Serositis	Pleuritis or pericarditis

<i>7. Renal disorder</i>	Persistent proteinuria or cellular casts
<i>8. Neurologic disorder</i>	Seizures or psychosis
<i>9. Haematologic disorder</i>	Haemolytic anaemia, leukopenia, lymphopenia or thrombocytopenia
<i>10. Immunologic disorder</i>	Anti-dsDNA antibody (specific), anti-Sm antibody or positive finding of antiphospholipid antibodies with either (i) abnormal serum IgG or IgM anti-cardiolipin antibody levels or (ii) positivity for lupus anticoagulant or (iii) false positive serological testing for syphilis
<i>11. Antinuclear antibody</i>	Abnormal ANA titer (sensitive) in absence of lupus causing drugs

### Treatment

- Avoid sunlight & use high-SPF sunscreen
- Screening & counseling for modifiable cardiovascular risk factors (like smoking cessation) for prevention of atherosclerotic disease
- Counseling for pregnancy planning
- NSAIDs for arthritis/arthralgia
- Antimalarials (hydroxychloroquine) often reduce dermatitis, arthritis & fatigue
- Calcium carbonate & vitamin D3 supplementation for prevention of early osteoporosis
- Hypercoagulability treated with warfarin
- Corticosteroids (prednisone, methylprednisolone, topical preparations)
  - Effectively suppress glomerulonephritis & cardiovascular abnormalities
  - Limited & defined courses for control of acute/subacute symptoms
  - Caution – corticosteroids accelerate coronary atherosclerosis
- Immunosuppressive drugs (methotrexate, azathioprine, cyclophosphamide)
  - Steroid-sparing drugs for severe SLE
  - Indications:
    - Involvement of major organs or extensive involvement of non-major organs (skin) refractory to other agents
    - Failure to respond to or inability to taper corticosteroids
    - Specific organ involvement
      - Renal – proliferative or membranous nephritis
      - Haematologic – severe thrombocytopenia, thrombotic thrombocytopenic purpura-like syndrome, severe haemolytic or aplastic anaemia, immune neutropenia
      - Respiratory – lupus pneumonitis, alveolar haemorrhage
      - Cardiac – myocarditis with depressed LVEF, pericarditis with impending tamponade
      - Gastrointestinal – abdominal vasculitis
      - Nervous – transverse myelitis, cerebritis, optic neuritis, psychosis refractory to corticosteroids, mononeuritis multiplex, severe peripheral neuropathy
- Dialysis or renal transplant for renal failure
- Splenectomy if thrombocytopenia does not respond to medical therapy

Drug	Indication	Anesthetic implications
Anti-malarials (hydroxychloroquine)	Cutaneous SLE Pleuritis/pericarditis Arthritis Reduced renal flares	Retinotoxicity Neuromyotoxicity Cardiotoxicity
Corticosteroids (prednisone, methylprednisolone, topical preparations)	Cutaneous SLE Arthritis Nephritis Pleuritis/pericarditis Diffuse alveolar hemorrhage NPSLE Mesenteric vasculitis SLE pancreatitis Antiphospholipid syndrome SLE arthritis	Hyperglycemia Hypercholesterolemia Hypertension Osteoporosis
Aspirin/NSAIDs		Peptic ulceration Platelet inhibition Renal impairment Fluid retention/electrolyte disturbance Hepatic dysfunction Bronchospasm
Cyclophosphamide	Nephritis NPSLE	Myelosuppression Pseudocholinesterase inhibition Cardiotoxicity Leucopenia Hemorrhagic cystitis
Azathioprine	Arthritis	Myelosuppression Hepatotoxicity
Methotrexate	Arthritis Cutaneous SLE	Myelosuppression Hepatic fibrosis/cirrhosis Pulmonary infiltrates/fibrosis
Mycophenolate mofetil	Nephritis Hemolytic anemia, thrombocytopenia	GI upset Pancytopenia

## Anaesthesia

Management Issue	Comment
<b>Preoperative</b>	
History	Review disease activity index, accrued organ damage, and drug history.
Examination	Thorough examination of cardiovascular, respiratory, and neurological systems, including testing for atlantoaxial subluxation symptoms and signs.
Full blood count	Test for anemia, thrombocytopenia, and leucopenia. Consider further testing for hemolysis if anemia is present.
Serum electrolytes, creatinine, urea	Any abnormality requires further investigation for lupus nephritis.
Liver function tests	Abnormalities should prompt review for autoimmune or drug hepatotoxicity.
Coagulation studies	Elevated aPTT requires investigation for the presence of lupus anticoagulant.
Anti-dsDNA, complement levels	May reflect lupus activity after comparison with previous baseline measurements.
Urinalysis	Proteinuria, red cells, white cells, and cellular casts may indicate clinically silent disease and prompt further investigation.
Electrocardiogram	Silent ischemia, myocarditis, pericarditis, and conduction abnormalities may be identified.
Chest radiograph	Pleural effusion, interstitial pneumonitis, pericardial effusion, or subglottic stenosis may be seen.
<b>Intraoperative</b>	
5-lead electrocardiography	Accelerated coronary artery disease, conduction abnormalities.
Intra-arterial blood pressure monitoring	Case dependent, consider in presence of myocarditis, conduction abnormalities, valvular abnormalities, or autonomic dysfunction. Special care to be taken in the presence of Raynaud's phenomenon.
Laryngeal mask airway if appropriate	Minimize airway manipulation due to risk of inflammation and postextubation airway edema.
Difficult airway precautions with immediate access to smaller-size endotracheal tubes	Vocal cord paralysis, subglottic stenosis, or laryngeal edema may make intubation difficult.
Standard antibiotic prophylaxis	Innate susceptibility to infection and immunosuppressive therapy predispose to infection risk.
Caution with muscle relaxants	Azathioprine and cyclophosphamide may interact with muscle relaxants.
Renal protective strategies	Maintain urine output, avoid hypoperfusion and hypotensive states, and use nephrotoxic drugs cautiously because of possibility of subclinical lupus nephritis.
Careful patient positioning	Predisposition to peripheral neuropathies and osteoporosis.
Antithrombotic prophylaxis	Institute mechanical and pharmacological measures early, especially in the presence of antiphospholipid antibodies. Patients with confirmed lupus anticoagulant and previous thromboembolic events warrant therapeutic anticoagulation in discussion with a hematologist.
Eye protection and artificial tears/lubrication	Sjögren's Syndrome may predispose to corneal abrasions despite adequate eye taping.
Temperature monitoring	Hypothermic states may induce vasospasm in patients with Raynaud's phenomenon.
Pain management	Consider side effects of systemic analgesics; regional techniques may be helpful if neuropathies, myelitis, and coagulopathies are excluded.
Corticosteroid cover	Adrenal suppression may have resulted from long-term corticosteroid therapy with the need for a "stress dose" perioperatively.
<b>Postoperative</b>	
Pain management	Regular review and input by a specialist pain service to minimize systemic side effects.
Antithrombotic prophylaxis	Early institution of mechanical and pharmacological prophylaxis dependent on surgical factors.

## Potential Questions

*What is antiphospholipid syndrome (APS)?*

- APS is characterised by clinical features of arterial or venous thrombosis *and/or* pregnancy morbidity *and* the presence of at least one type of antiphospholipid antibody
  - Can occur with or without associated rheumatic disease, the most common being SLE
  - Affects all organ systems & includes venous thrombosis (DVT, PE), arterial thrombosis (TIA/CVA, MI, leg ulcers, retinal artery thrombosis, multi-infarct dementia), recurrent foetal losses & thrombocytopenia
- Antiphospholipid antibodies (aPL) are antibodies directed against serum proteins bound to anionic phospholipids
  - Autoantibodies inhibit the fibrinolytic system & bind to antigenic anticoagulants, which activate endothelial cells, monocytes & trophoblasts, resulting in complement-mediated thrombosis
  - Three types of aPL have been characterised:
    - Anticardiolipin antibodies (most common)
    - Lupus anticoagulant
    - Anti-β2-glycoprotein-1 antibodies
- Treatment includes use of heparin, LMWHs, warfarin, novel oral anticoagulants, aspirin, clopidogrel & hydroxychloroquine

## **Marfan's Syndrome (MFS)** (Oxford p317, Stoelting p154+443)

- Autosomal dominant, multisystem connective tissue disease
- Caused by a mutation in fibrillin-1 gene which codes for fibrillin (an important connective tissue protein in the capsule of the ocular lens, arteries, lungs, skin & dura mater) +/- a mutation in transforming growth factor β 1 or 2 (a cytokine that regulates cell morphogenesis)
- Incidence 4-6 per 100,000 live births
- Mean survival 32 years

### **Clinical Features**

- History
  - How was diagnosis made?
  - Ask about lens subluxation or dislocation, dilated aorta, valvular heart disease, pneumothorax, exercise tolerance
  - Family history (26% have no family history – 'sporadic cases')
  - Treatment – drugs & surgery
- Examination
  - Cardiovascular
    - Aortic dilation, dissection or rupture with associated AR
    - Valve dysfunction/prolapse – MR resulting from MVP is common, look for AR
    - Heart failure, pulmonary hypertension
    - Conduction abnormalities
  - Respiratory
    - Restrictive defect due to pectus excavatum/kyphoscoliosis
    - Emphysema, bronchogenic cysts & honeycomb lung lead to pneumothorax
  - Skeletal – high arched palate, long tubular bones → tall stature, pectus excavatum, kyphoscoliosis, joint hyperextensibility
  - Ocular – lens dislocation, myopia, retinal detachment
- Investigations
  - ECG – bundle branch block
  - Echocardiography – MVP, MR, tricuspid valve prolapse, AR, dilatation of aortic root
  - CXR – apical bullae, pneumothorax, cardiomegaly, pulmonary oedema
  - TOE, chest CT/MRI or aortography for suspected dissection
  - Genetic testing for FBN1 mutation

### **Diagnosis by Ghent 2 Criteria (2010)**

#### **In the absence of family history:**

1. Aortic root diameter (Z-score  $\geq 2$ ) and ectopia lentis = MFS\*
2. Aortic root diameter (Z-score  $\geq 2$ ) and causal *FBN1* mutation = MFS
3. Aortic root diameter (Z-score  $\geq 2$ ) and systemic score  $\geq 7$  points = MFS\*
4. Ectopia lentis and causal *FBN1* mutation with known aortic root dilatation = MFS

#### **In the presence of family history:**

5. Ectopia lentis and family history of MFS (as defined above) = MFS
6. Systemic score  $\geq 7$  points and family history of MFS (as defined above) = MFS\*
7. Aortic root diameter (Z-score  $\geq 2$  above 20 years old,  $\geq 3$  below 20 years) and family history of MFS (as defined above) = MFS\*

\*Caveat: without discriminating features of Shprintzen–Goldberg syndrome, Loeys–Dietz syndrome or vascular form of Ehlers–Danlos syndrome AND after *TGFBR1/2*, collagen biochemistry, *COL3A1* testing if indicated.

#### **Scoring of systemic features of MFS**

1. Wrist and thumb sign – 3 points (wrist or thumb sign – 1 point)
2. Pectus carinatum deformity – 2 points (pectus excavatum or chest asymmetry – point)
3. Hindfoot deformity – 2 points (plain pes planus – 1 point)
4. Protrusio acetabuli – 2 points
5. Reduced upper segment/lower body segment ratio and increased arm/height and no severe scoliosis – 1 point
6. Scoliosis or thoracolumbar kyphosis – 1 point
7. Reduced elbow extension – 1 point
8. Facial features (3/5) – 1 point (dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia)
9. Pneumothorax – 2 points
10. Skin striae – 1 point
11. Myopia  $> 3$  diopters – 1 point
12. Mitral valve prolapse (all types) – 1 point
13. Dural ectasia – 2 points

The systemic features number 1–13 are used for the systemic score in the Ghent-2 nosology, where a maximum total score points of 20 points can be obtained. We number the systemic features as 1–8 and address these as "skeletal score", and the systemic features as 9–12 and address these as "non-skeletal score".<sup>73</sup>

- Briefly, in the absence of a family history, MFS is diagnosed in the presence of aortic root dilatation combined with ectopia lentis, or a causative FBN1 mutation, or a systemic score  $\geq 7$  points, or with the combination of ectopia lentis with an FBN1 mutation known to cause aortic dilatation
- In the presence of a family history, MFS is diagnosed with the demonstration of ectopia lentis, or a systemic score  $\geq 7$  points, or aortic root dilatation

### **Treatment**

- Regular cardiac & aorta monitoring by echocardiography
- Endocarditis prophylaxis
- Restriction of contact sports, weight lifting & overexertion
- $\beta$  blockers (standard therapy)
  - Prescribed to slow rate of aortic root dilation by reducing aortic wall stress + HR
  - All patients who can tolerate  $\beta$  blockers should be treated regardless of the presence or absence of aortic dilatation
- ACE inhibitors
  - Slow rate of progressive aortic root dilatation independent of haemodynamic effects
  - Inhibit TGF $\beta$  signaling & reduce vascular smooth muscle apoptosis
- Genetic counseling
- Monitor aorta during pregnancy because of increased risk of dissection
- Surgery
  - Better outcome with early aortic root surgery than with an emergency or later surgery
  - Prophylactic surgery recommended when the diameter at the sinus of Valsalva exceeds 5.5cm in adults
  - Need lifelong anticoagulation post aortic root repair

### **Anaesthesia**

- Preoperative evaluation should focus on cardiorespiratory abnormalities
- Proper positioning & limb support to avoid joint trauma/dislocation
- Prepare for a potentially difficult intubation due to high arched palate, jaw protrusion, teeth crowding & cervical spine bony/ligamentous abnormalities
- Avoid excessive traction on jaw during laryngoscopy to prevent temporomandibular joint dislocation
- Control airway pressure to prevent barotrauma + pneumothorax
- Tracheomalacia has been reported as a potential complication
- Invasive monitoring – IAL, TOE
- Avoid measures that can lead to tachycardia or hypertension – blunt sympathetic response to laryngoscopy + intubation, analgesia for painful surgical stimulation
- “Full, fast, forward” if MVP/MR/AR – maintain preload, avoid bradycardia (aim high-normal HR), reduce afterload
- Consider antibiotic prophylaxis for bacterial endocarditis & perioperative  $\beta$  blockade
- Adequate postoperative pain management to avoid detrimental effects of hypertension & tachycardia

## Ehler's-Danlos Syndrome (EDS) (Oxford p306, Stoelting p 155+443)

- Heterogeneous group of inherited connective tissue disorders characterized by joint hyperlaxity, skin hyperextensibility & tissue fragility
- Affects males + females of all ethnic backgrounds & 1 in 5,000 people
- Pathophysiology – generally abnormal collagen synthesis resulting in reduced strength of collagen in numerous tissues
- Six major types, with EDS types I (classic) + III (hypermobility) accounting for 90% of all cases
- Only form associated with an increased risk of death is type IV (vascular) syndrome – life expectancy 48 years

### Clinical Features – highly variable & depend EDS type

- All forms:
  - Joint hypermobility (shoulder, elbow, ankle, TMJ)
    - Beighton score assess degree of joint hypermobility – (1) passive dorsiflexion of little fingers beyond 90°, (2) passive apposition of thumb to flexor aspect of forearm, (3) hyperextension of elbow beyond 10°, (4) hyperextension of knees beyond 10°, & (5) forward flexion of trunk with knees fully extended so that palms of hand rest flat on floor
  - Skin hyperelasticity, fragility + bruising
  - Impaired wound healing & inappropriate scarring
  - Musculoskeletal discomfort
  - Osteoarthritis
- Typical facial appearance in vascular type – slender face, sunken cheeks, thin or pinched nose, thin upper lips, prominent eyes with periorbital pigmentation & firm, lobeless ears
- Ophthalmologic features – strabismus, ptosis, keratoconus, blue sclerae, glaucoma, photophobia, lens subluxation, globe rupture & blindness from recurrent retinal haemorrhages
- Cardiovascular anomalies – multiple aneurysms (rarely of aorta) & rupture + dissection of arteries, varicosis, MVP (common), orthostatic hypotension & acrocyanosis
  - Vascular type – arterial rupture occurs in 25% of patients before age 20 years & 80% before age 40 years
- Gastrointestinal anomalies – gastro-oesophageal/inguinal/umbilical hernias, anal prolapse & spontaneous intestinal organ rupture

EDS Type	Former Type	Inheritance	Major Criteria	Minor Criteria	Pathogenesis
Classic	Gravis type (EDS type I) Mitis type (EDS type II)	Autosomal dominant	Skin hyperextensibility Wide, atrophic scars Joint hypermobility	Smooth, velvety skin Subcutaneous spheroids Molluscoid pseudotumors Easy bruising Manifestations/complications of joint hypermobility (dislocations/subluxations), tissue hyperextensibility, and fragility (hiatal hernia, anal prolapse) Surgical complications (postoperative hernias) Muscle hypotonia with delayed motor development Positive family history	Abnormal electrophoretic mobility of the proα1(V) or proα2(V) chains of collagen type V Mutations on COL5A1 and COL5A2 Abnormal electron microscopic findings in the collagen fibril structure ("cauliflower" deformity of collagen fibrils)
Hypermobility	Hypermobile type (EDS type III)	Autosomal dominant	Hyperextensible, smooth, velvety skin Generalized joint hypermobility	Recurring joint dislocations Chronic joint/limb pain Positive family history	Unknown In some cases anomalies of collagen V have been described
Vascular	Arterial-ecchymotic type (EDS type IV)	Autosomal dominant	Thin, translucent skin Arterial/intestinal (colon)/uterine fragility or rupture Extensive bruising Typical facial appearance	Acrogeria Hypermobility of small joints Tendon and muscle rupture Taipes equinovarus Early-onset varicosis Arteriovenous, carotid-cavernous sinus fistulas Pneumo(haemo)thorax Gingival recession Positive family history Sudden death in close relative	Structural anomalies in the proα1(III) chain of collagen type III encoded by the COL3A1 gene
Kyphoscoliosis	Ocular-scoliotic type (EDS type VI)	Autosomal recessive	Generalized joint laxity Severe muscle hypotonia and progressive scoliosis at birth Scleral fragility and rupture of the ocular globe after minor trauma	Tissue fragility, including atrophic scars Easy bruising Arterial rupture Marfanoid habitus Microcornea Radiologically osteopenia Positive family history	Lysyl hydroxylase deficiency
Arthrochalasia	Arthrochalasis multiplex congenital type (EDS types VIIA + VIIB)	Autosomal dominant	Severe joint hypermobility with recurrent subluxations Congenital bilateral hip dislocation	Skin hyperextensibility Tissue fragility and atrophic scars Easy bruising Muscle hypotonia Kyphoscoliosis Mild osteopenia	Mutations of COL1A1 or COL1A2 result in defects of proα1(I) (type A) or proα2(I) (type B) chains of collagen
Dermatosparaxis	Human dermatosparaxis type (EDS type VIIC)	Autosomal recessive	Severe skin fragility Sagging, redundant skin	Soft, doughy skin texture Easy bruising Premature rupture of fetal membranes Large hernias (umbilical, inguinal)	Procollagen I N-terminal peptidase deficiency

## AAnaesthesia

- Preoperative assessment
  - Thorough history of complications with previous surgeries & ask about excessive bleeding after minor trauma
  - Determine degree of cardiorespiratory compromise associated with kyphoscoliosis (restrictive lung disease, cor pulmonale)
  - Consider RFTs, ABG, ECG & echocardiography
    - ECG – RBBB, left anterior hemiblock
    - AR + MR may be associated with classic & vascular type
  - Excessive bleeding (classic & vascular types) – may manifest as increased bleeding time rather than abnormal coagulation tests; cross-match blood prior to surgery
  - Check for difficult airway management due to mandibular hypoplasia, recurrent TMJ dislocations, gingival anomalies +/or atlanto-axial instability (vascular type)
- Anaesthetic considerations
  - Careful positioning to prevent damage to delicate skin & avoid joint dislocations
  - Adequate venous access to cope with potential heavy blood loss
  - Invasive monitoring only when essential to patient management
    - CVL may be complicated by mediastinal or pleural hematomas
    - IAL may be complicated by aneurysm formation or excessive hematoma formation
  - Regional techniques allowed but neuraxial blocks associated with higher risk of hematoma formation
  - Local anesthesia may have an insufficient effect (hypermobility type)
  - General anesthesia should be accomplished using minimal airway trauma
    - Mask anesthesia is management of choice, but when appropriate, airway intubation & extubation should be performed as gently as possible to minimise airway bruising
  - Avoid TMJ dislocation/subluxation & cervical spine subluxation
  - Peak airway pressure must be kept as low as possible to reduce risk of pneumothorax
  - Avoid wide swings in BP to reduce risk of hemorrhage & aneurysm rupture
  - Risk of cerebral hemorrhage from intracranial aneurysms is considered low but should be kept in mind for patients with vascular type
  - Pregnancy
    - High risk of uterine rupture in vascular type
    - Maternal mortality up to 25% secondary to uterine, aortic, pulmonary artery or vena cava rupture
    - Severe hemorrhage may occur in early postpartum period
    - Epidural anesthesia has been used successfully
    - Large-bore IV access & availability of blood products is recommended
  - Pharmacology
    - No strict contraindications, but agents interfering with blood coagulation & haemostasis should be used with caution
    - IE prophylaxis recommended if MVP associated with thickened leaflets +/or MR

## Sarcoidosis (Oxford p124, Stoelting p200+272)

- Chronic multisystem granulomatous disease characterised histologically by presence of nonspecific, non-caseating granulomas with unknown aetiology
- Granulomas occur in multiple organ systems – lung, lymphatics, bone, liver, nervous system
  - Lung – airway granulomas, restrictive (+/- obstructive) disease, alveolar fibrosis, pulmonary hypertension, ↓ diffusion capacity
  - Airway – laryngeal + nasal mucosal sarcoidosis
  - Heart – heart block, pericardial disease, restrictive cardiomyopathy
  - Spleen + Liver – splenomegaly, hepatomegaly, progressive liver disease leading to portal hypertension with variceal bleeding + hepatopulmonary syndrome (rarely)
  - Kidney – granulomatous interstitial nephritis, renal tubular dysfunction, obstructive uropathy
  - CNS – dementia, encephalopathy, seizures, headache, facial nerve neuropathy, uveitis
  - Eye – lacrimal gland enlargement, conjunctival nodules, uveitis
  - Skin – sarcoid lesions, erythema nodosum, lupus pernio
  - Bone + Joint – arthralgias, arthritis
  - Aberrant calcium + vitamin D metabolism – renal stones, nephrocalcinosis with renal insufficiency, hypercalciuria, hypercalcemia
- Form of chronic restrictive intersitital lung disease (others include – hypersensitivity pneumonitis, eosinophilic granuloma & alveolar proteinosis)

## Clinical Features

- History
  - Ask about symptoms – fatigue, weight loss, night sweats, dyspnoea, dry cough, hoarse voice, stridor, chest pain, syncope, seizures, headache, blindness, joint pain
  - Diagnosis
    - Presentation may be acute or chronic & 50% detected incidentally on abnormal CXR
      - Acute sarcoidosis (Lofgren's syndrome) = arthritis, erythema nodosum + bilateral hilar adenopathy
      - CXR, CT, bronchoscopy, mediastinoscopy, lymph node biopsy
  - Exercise tolerance, SOBOE
  - Treatment to date & complications
  - Positive family history
- Examination
  - Skin – raised red or purple nodules most common on lower limbs
  - Joints – non-deforming arthritis
  - Respiratory – end-inspiratory crackles, commonly no signs
  - Cardiovascular – pulse, right heart failure, pericardial rub
  - Abdomen – hepatosplenomegaly
  - Systemic complications of steroids used in treatment
- Investigations
  - Electrolytes, calcium, ABG (normal CO<sub>2</sub>, ↓pO<sub>2</sub>), LFTs,
  - ↑ACE level 2° ↑production by cells within granuloma – no useful diagnostic or prognostic significance
  - CXR – bilateral adenopathy of hilar + paratracheal nodes, pulmonary infiltration
    - Classified into four groups:
      1. Bilateral hilar lymphadenopathy
      2. Bilateral hilar lymphadenopathy with pulmonary infiltration
      3. Pulmonary infiltration alone
      4. Advanced fibrosis with evidence of honeycombing, hilar retraction, bullae, cysts + emphysema
  - RFTs – restrictive defect with ↓FVC, ↓DLCO, or both, & normal FEV<sub>1</sub>/FVC ratio
    - VC <15ml/kg = severe disease
  - CT chest – indicated if CXR atypical or haemoptysis, ground-glass appearance when active alveolitis present but not specific for sarcoidosis
  - ECG – conduction abnormalities, RVH
  - Echocardiography – cardiomyopathy, pulmonary hypertension

## Treatment

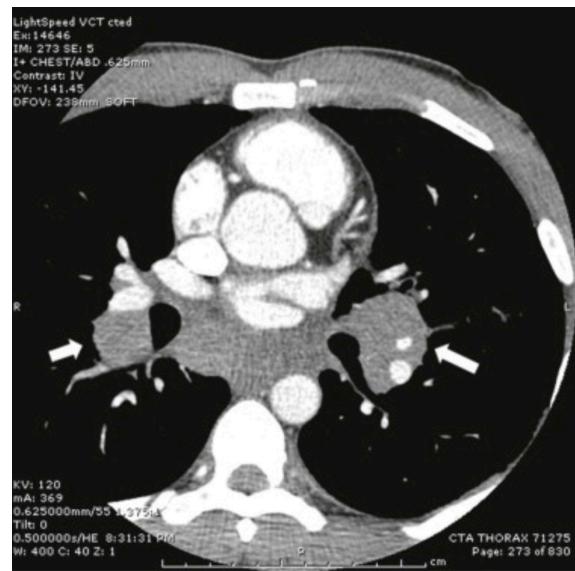
- Smoking cessation, treatment of infection & sputum clearance
- Corticosteroids – suppress manifestations of sarcoidosis & treat hypercalcemia
- Immunosuppressants (methotrexate, azathioprine, hydroxychloroquine) & radiation for severe steroid-resistant disease

## Anaesthesia

- Avoid GA & use local/regional where possible if impaired respiratory function
  - Tolerate apnoeic episodes poorly due to ↓FRC & low O<sub>2</sub> stores – GA, supine position + mechanical ventilation further ↓FRC
  - Poor lung compliance needs ETT & ventilation with low airway pressure to minimise barotrauma
- Appropriate steroid cover if needed



CXR demonstrating stage 1 disease



CT scan showing typical hilar adenopathy (stage 1)

## Haemophilia (Oxford p218, Stoelting p421)

- Haemophilia A – X-linked recessive deficiency or defective factor VIII
- Haemophilia B – X-linked recessive deficiency or defective factor IX (Christmas disease)
- Haemophilia C – autosomal dominant/recessive deficiency or defective factor XI

Key points in history:

- Presentation depends on severity but usually early in life or following surgery or trauma
- X-linked so males are affected + females are carriers
- Can present with spontaneous bleeding into joints leading to arthritis or into muscle causing hematomas
- Can also get compartment syndromes + nerve palsies from hematomas/bleeds
- History of disease + complications
- Treatments received
- Usually well known to local haemophilia/haematology team

Key points in examination:

- Signs of bleeding, arthritis + complications from ongoing treatments/transfusions

Key investigations:

- Prolonged APTT + normal prothrombin time
- Normal platelet count, INR + fibrinogen
- Reduced factor level

**Table 2** Grading of severity of haemophilia

Haemophilia (A, B, or C)	Mild	Moderate	Severe
% activity of factors	5–40	1–5	<1
Factor levels (IU ml <sup>-1</sup> )	0.05–0.40	0.01–0.05	<0.01

Medical management + optimisation before surgery:

- Patients with haemophilia need 80-100% correction of their factor VIII before any major surgical procedure & this must be confirmed before surgery
- Postoperatively, levels should be maintained for up to 6 weeks after orthopaedic procedures & 1-2 weeks for other procedures
- Mild haemophilia with low risk of bleeding – use desmopressin infusion of 0.3mcg/kg in 50-100ml of normal saline over 30 minutes & tranexamic acid
- Recombinant factors VIII + IX are available – should be given 30-60 minutes before surgical procedure
  - Lyophilized powder
  - Free from risk of disease transmission as seen with blood products
  - Limiting factor = cost
  - Dosage
    - Factor VIII
      - Each factor VIII unit per kilogram of body weight infused IV will raise the plasma factor VIII level by 2% ( $t_{1/2}$  FVIII = 8-12 hours)
      - Number of units of FVIII required = weight of patient x % factor level desired x 0.5
    - Factor IX
      - Each factor IX unit per kilogram of body weight infused IV will raise the plasma factor IX level by 1% ( $t_{1/2}$  FIX = 18-24 hours)
      - Number of units of FIX required = weight of patient x % factor level desired
- Patients must be screened for the presence of inhibitors to factor VIII or IX
  - Depending upon the amount of inhibitors present, patients are classified as low risk (inhibitor level <5 Bethesda units/ml) or high risk (>5 Bethesda units/ml)
  - Low risk group requires a higher dose of the deficient factor
  - High risk group requires approved alternative regimes like recombinant activated factor VIII (rFVIIIa) or factor eight inhibitor bypassing activity (FEIBA)
- Cryoprecipitate (contains factor VIII) & FFP (contains factor IX) should only be used to correct clotting factors in an emergency due to their chance of transmitting infection

## Complex Regional Pain Syndrome (CRPS)

Described as a 'strange pain in a strange looking limb'

- Pain is "strange" because its severity is out of keeping with the often minor & transient nature of the inciting event
- Affected part also looks "strange" (swollen, red, white or blue) & responds in a "strange" manner (hot, cold, sweaty, tremulous or weak)
- Dysfunction of cortical, sensory, motor & autonomic components of the nervous system along with peripheral inflammatory changes (neurogenic inflammation, tissue ischaemia) may be the pathophysiological basis for CRPS
- Psychological & social problems such as anxiety, depression, fear avoidance (of painful movements) & loss of employment may develop

### **Classification**

CRPS type I (reflex sympathetic dystrophy) – diagnosed where there is no evidence of a precipitating nerve injury

CRPS type II (causalgia) – nerve injury is present

#### *CRPS type I*

1. The presence of an initiating noxious event, or a cause of immobilization.
2. Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event.
3. Evidence at some time of oedema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain.
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Note: criteria 2-4 must be satisfied.

#### *CRPS type II*

1. The presence of continuing pain, allodynia, or hyperalgesia after a nerve injury, not necessarily limited to the distribution of the injured nerve.
2. Evidence at some time of oedema, changes in skin blood flow, or abnormal sudomotor activity in the region of the pain.
3. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

Note: all three criteria must be satisfied.

### **History**

- Women > men
- Usually minor trauma, e.g. sprain, colles #, carpal tunnel release
- Can follow stroke, damage to musculoskeletal tissue
- Adults: upper limb > lower limb
- Kids: lower limb > upper limb
- Pain – neuropathic, with mechanical/thermal/somatic hyperalgesia

### **Examination**

1. **Sensory changes**
  - a. Spontaneous pain, mechanical/thermal/somatic hyperalgesia
2. **Vascular changes**
  - a. Vasodilation, skin colour changes, asymmetric skin temp
3. **Oedema/sweating abnormalities**
  - a. Swelling, hyper/hypohidrosis
4. **Motor/trophic changes**
  - a. Hair/nail changes
  - b. Tremor
  - c. Skin atrophy

### **Relevant Investigations**

Diagnosis is clinical, imaging can be used to support diagnosis

X-ray, CT, MRI – show changes to bone mineralisation/oedema

Bone scan – show abnormalities of blood flow

### **Anaesthetic implications**

Patient will be on multiple analgesia, treat as per chronic pain

Perioperative steroids and ketamine role is unclear, but potential benefit may outweigh harm

Prevention with vitamin C (500mg daily for 1 month) showed to reduce CRPS in colles # from 10-2%

### **Treatment**

Multimodal analgesia including heavy allied health involvement, medication only form one part of the treatment

Successful use of **graded motor imagery** (also use in phantom limb pain):

1. Lateral recognition – Phase ONE

2. Imagined movements – Phase TWO

3. Mirror movements – Phase THREE

Sympathetic blockade

- Stellate ganglion block, lumbar sympathetic block
- Permanent sympathectomy

- IV regional guanethidine (bier's block)

None show promise in Cochrane review, but still use clinically

Spinal cord stimulators