By Adam Hollingworth

ANZCA Introductory Training

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Anaesthetic Machine Check

[1. Basics]
- Anaesthetic machine is connected to electric supply and working
- Check service labels
- Check bulk flow panel on wall

Take manifold apart
Leak test on vent common outlet inner port
Take O2 sensor off
Check monitor analyser system - no water droplets in container
Check alarm settings on monitor (low O2 18%)
- Check frequency of bp measurement

Put filter and sampling line on common gas outlet - watch analysis of O2 and air

- Remove manifold cover
  - Check RA 21%
  - Check 100% o2
  - Check 50% nitrous with O2 mix 2 litres
  - Check anti hypoxia 1:3 ratio and O2 not dropping below 21%
  - Stop O2 check that nitrous stops flowing prior to loss of O2
  -
  - Disconnect piped gas

Check low O2 alarm audible and visual alarm on vent

[3. Gases]
- Reserve Cylinder:
  - Pull out o2 leads
  - Empty machine
  - Switch to O2 cylinder

  ↳ pressure gauges should be 400-500kPa

Check nitrous cylinder

- Reconnect machine then Tug test
-

[4. Gas flows]
Bulk gas pressure for air and O2 (4bar)
Check O2 and air appropriate analyser range
- Bobbin freely and through range
- Check emergency bypass o2 button with test lung. Should fill <5seconds 2 litre bag

[5. Vaporiser]
- Check adequately filled
- Check filling port closed
- Turn on each vaporiser, check O2 does not fall <1 litre
- Each vaporiser correctly seated on back bar

[6. Breathing circuit]
- Inspect configuration of circuit with test lung on

- Vaporiser leak test open common outlet port
  - Use squeeze suction device to check no leak
  - Turn vaporizer on, re-remove air from system & check leak
- Remove scavenger from system
- APL valve closed up, O2 flush until circuit pressures to 30
- Then put scavenger back in and check for leak
- Open APL: check bags not emptying (overactive scavenger)
- Squeeze bag then test lung - check unidirectional valves
- Squeeze bag and test lungs till empty

[7. Vent settings]

turn machine off, with empty belows. **

- Fill belows with o2 then check for leak

turn machine on again with vent on

- Run at 6 litres: Wait for atmospheric pressure reading (<5 pmax) with O2 running at 6 litres
  ↳ turn vent off and off again
- Standard settings: VT 500, RR 12 check getting to target
- High pressure test
- Low pressure test: remove test lung. Await alarm low paw
- Reset vent panel

- Check ambi bag, aux O2 port

[8. Gas Scavenging System:]

- Check CO2 scrubber working correctly
  - Good colour, gauge in green
  - Port closed on side

[9. Ancillary Equip:]

  - Laryngoscope, bougie, forceps, OPA
  - Suction working high and variable pressure with occluded (thumb over end suction holds itself above ground)
  - Check Yanker tube suction
  - Bed/operating trolley working

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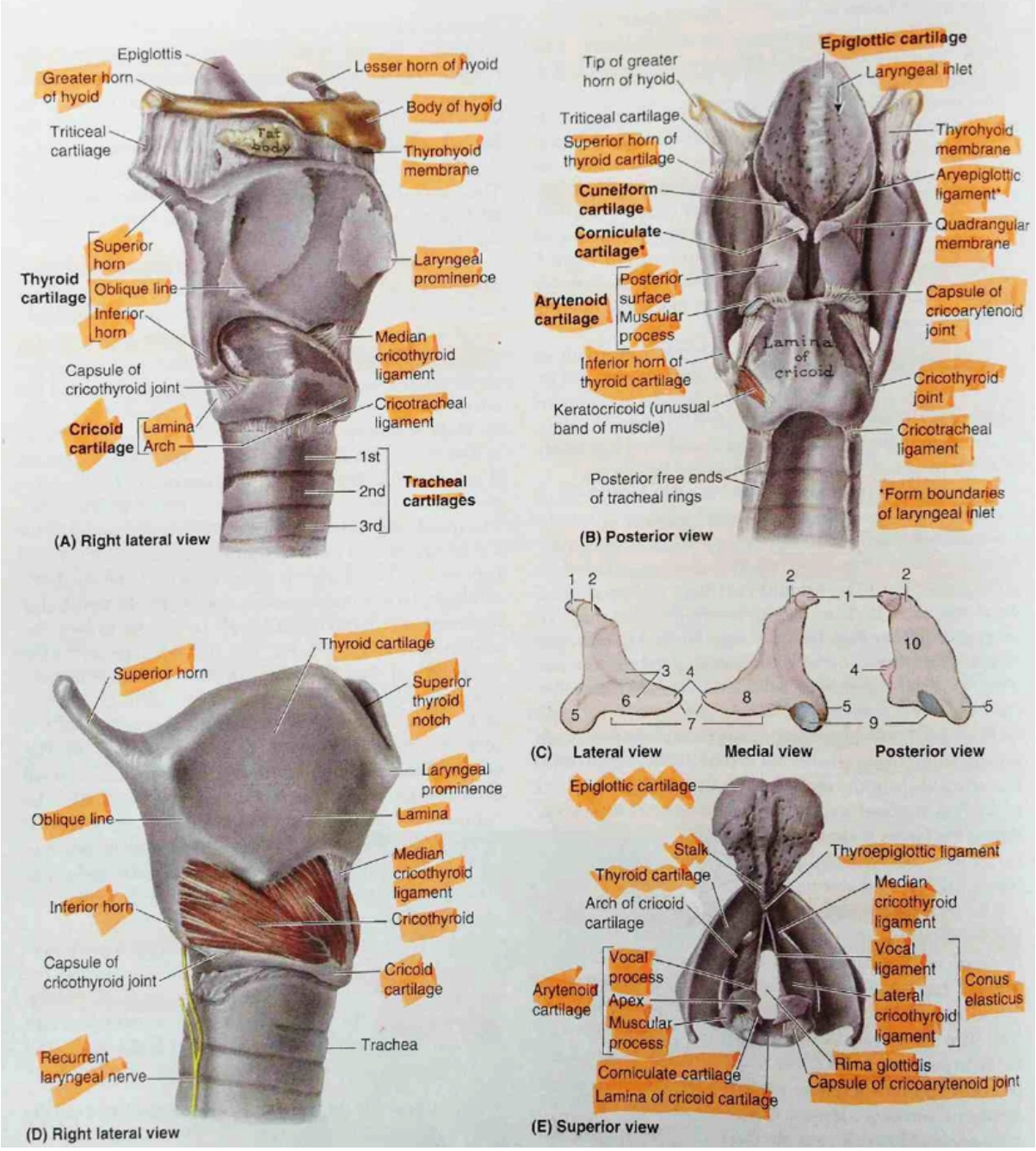
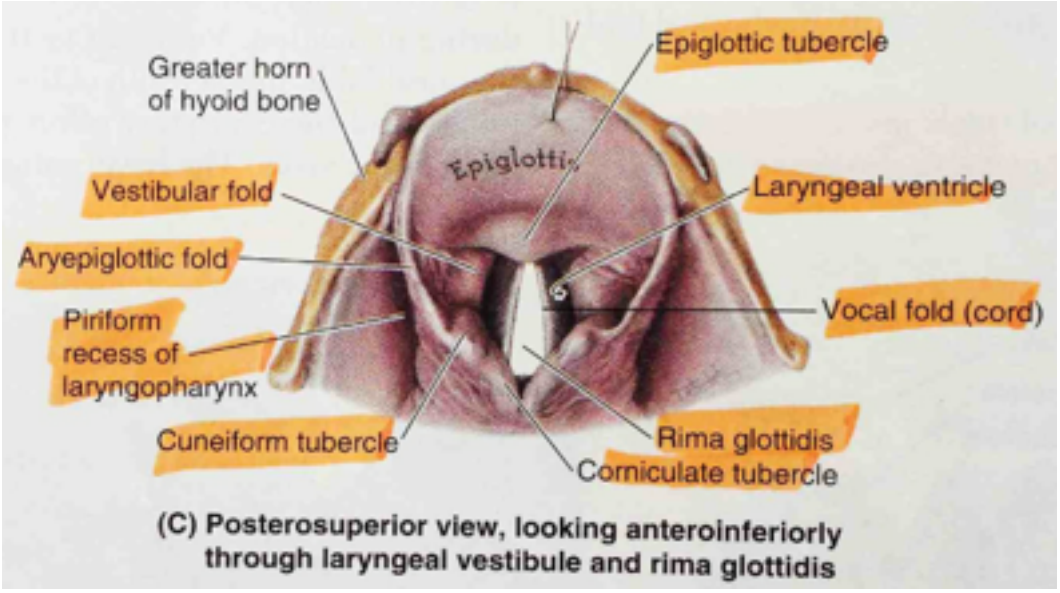
2.1.1 Airway Management

1.1 Basic Structure of Upper Airway incl Larynx





(C) Posterosuperior view, looking anteroinferiorly through laryngeal vestibule and rima glottidis

Nerves of the Larynx

- Superior laryngeal nerve
  - Divides into:
    - Internal branch –
      - Sensory to:
        - Ipsilateral larynx from sup boundary to true cords
        - Pyriform sinus
        - epiglottis
    - External branch –
      - Motor
        - Cricothyroid muscle
      - • Sensory:
        - Ant infraglottic larynx cricothyroid membrane

          ↳ unilat paralysis ⟹ failure of ipsilateral cord closure event with intact RLNs
- Recurrent (inf) laryngeal nerve:
  - Motor:
    - All intrinsic mm of larynx on same side except cricothyroid mm (ext laryngeal from Vagus)
  - ○ Sensory:
    - Ipsilateral mucosa below true cords

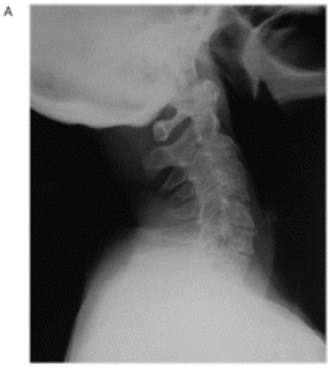
  ↳ L RLN longer course, turing around aortic arch; R RLN turns around subclavian artery

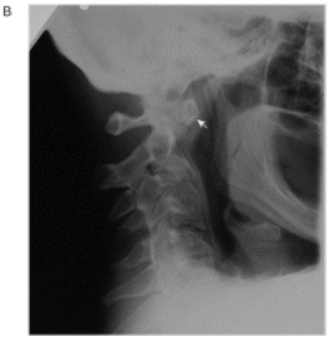
↳ paralysis of RLN ⟹ paramedian vocl cord position due to adduction action of SLN (cricothyroid)

1.2 Airway Assessment

Intro

- Impt - 30% anaesthetic deaths caused by failure of airway management
- Most catastrophe due to unexpected difficult airway
- Prediction of difficult BMV or LMA as important as ETT placement
- Intubation =
  - difficult in 1:50
  - Impossible 1:2000 - ↑'ed to 1:200 for emergencies
- BMV =
  - Difficult 1:20
  - Impossible 1:1500
- Both can't CICO: 1:10000
- Rescue techniques fail 1:20
- Rfs for hypoxemia are important:
  - Pregancy
  - Obesity
  - Children





History

- Congenital airway difficulties:
  - Pierre Robin = micrognathia, small tongue, cleft palate
  - Klippel Feil = congen fusion of >2 Cx vertebrae
    ↳ head displaced ant and inferiorly
  - Down Syndrome =
    - Very large tongue
    - Laryngomalacia = inward collapsing of tissues at laryngeal inlet
    - Tracheomalacia
    - Tracheal bronchus = bronchi come from trachea level
    - Bronchomalacia = colapsing of airways
- Inflamatory:
  - RA -
    - atlanto-axial subluxation (25%) due to deg of transverse ligament
      ↳ types: ↳ ⇒ with risk spinal cord damage
      - Anterior - (80%)
        - C1 moves forward on C2 causing risk spinal cord compression by peg
        - Lat C spine - atlas to peg distance: >44yrs old = >4mm, <44yrs old = >3mm
      - Posterior (5%)
        - Lat extension views
        - Peg is destroyed
      - Vertical (10-20%)
        - Destruction of lat mass of C1 ⇒ peg through foramen magnum & compression cervico-medullary junction
      - Lat or rotatory = degen changes in C1/C2 facet joints ⇒ spinal nerve & vertebral artery compression
    - Subaxial subluxation - uncommon. Occurs below C2
    - Cricoarytenoid joint involvement:
      - Dyspnoea, stridor, hoarseness, severe ⟹ upper airway obstruction
      - Laryngeal amyloidosis & rheumatoid nodules ⇒ obstruction of larynx

    - TMJ joint involvement ⇒ difficult mouth opening
  - Stills disease = (juvenile or adult onset)
    - polyarthritis with sore throat & high spiking fever & salmon pink rash
  - Anky Spond
  - Scleroderma - tight skin & mouth
- Infectious:
  - Epiglottits
  - Submandibular abscesses or Ludwig's Angina
    ↳ cellulitis of submandibular tissues
  - Retropharyngeal abscesses
- Endocrine
  - Acromegaly - hypertrophy of upper airway soft tissues
  - DM - generalised joint and cartilage damage
  - obesity
- Pregnancy
  - Upper airway oedema
  - Incr aspiration risk
- Trauma
  - Foreign bodies
  - Facial or neck trauma
- Iatrogenic Problems:
  - TMJ surgery
  - Cervical fusion
  - Oral/pharyngeal radiotherapy
  - Laryngeal.trachel surgery
- Reported previous anaesthetic problems - check notes, med alerts, databases

Examination

- Unusual anatomy:
  - Small mouth
  - Receding chin
  - High arched palate
  - Large tongue
  - Bull neck
  - Morbid obesity
  - Large breasts
- Acquired problems:
  - Head/neck burns
  - Tumours
  - Abscesses
  - Radiotherapy
  - Scars
- Mechanical limitation
  - ↓mouth opening
  - ↓Ant TMJ movement (protrusion)
  - Poor Cx movement
  - Poor dentition
  - External equipment ie halo traction, C collar, dental wiring
  - Unpatent nasal passages - for nasal intubation

Radiology

- Recent CT/MRi helpful
- Occipito-atlanto-axial disease is more predictive of difficult laryngoscopy than disease below C2
- Plain XRs not that useful:
  - Flex/ext views in RA may be helpful but poor correlation with risk

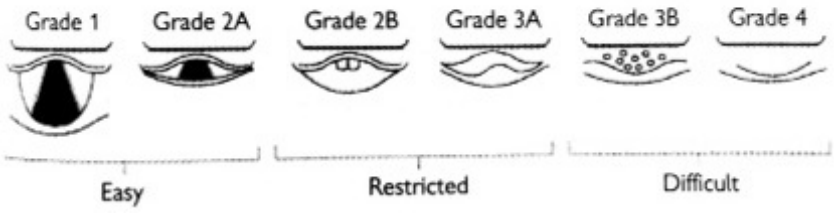
Predictive Tests for Intubation

- For intubation need:
  - Mouth opening
  - Ext upper Cx spine
  - aBility to create submandibular space
- Tests have statistical problems:
  - Low specificity & PPV ie large no of false +ves
    ↳ <10% predicted difficult airways end up being difficult
  - Sensitivity ≈ 50%. Tests quoted high often in specific populations, not in routine practice
  - Combination of tests ⟹ ↑ specificity (↓'ed false positives) BUT ↓'es sensitivity (miss more truely difficult airways)

Laryngeal View Grades

- Restricted = need bougie
- Difficult = advanced techniques

Cormack and Lehane classification of glottic visualisation.



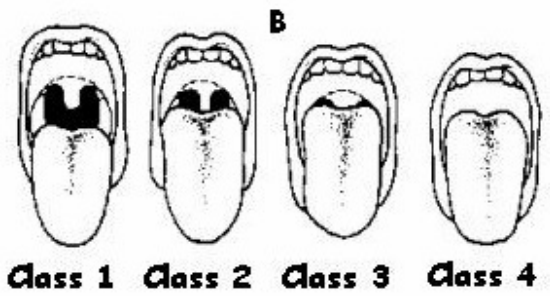
Interincisor Gap

- Distance between incisors with max open mouth
- Affected by TMJ & upper Cx spine mobility
- <3cm ≈ difficult intubation
- <2.5cm ≈ LMA insertion difficult

Protrusion of Mandible

- Class A = lower incisors can protrude beyond upper
- Class B = lower reach margin of uppers
- Class C = lowers cannot reach uppers

↳ class B & C ≈ difficulty



Mallampati Test

- Patient sitting upright, from opposite patient, open mouth maximally and protrude tongue without phonating
- gradings:
  - Class 1 = faucial pillars, soft palate & uvula visible
  - Class 2 = uvula tip masked by bass of tongue
  - Class 3 = soft palate only
  - Class 4 = soft palate not visible
- Class 3 & 4 ≈ difficult intubation BUT:
  - Interobsever variation
  - Sensitivity 50%
  - Low specificity and positive predictive value - 90% false positive rate

Extension of Upper Cx spine

- <90 ≈ difficulty

- Methods:
  - 1:
    - Fully flex head on neck
    - Immobilisin lower Cx spine with one hand, then fuly extend head
    - A pointer on the forehead allows angle to be estimated
  - 2:
    - One finger on chin and one on occiptal protuberance & extend head max
      ↳ norm = chin finger higher; mod limitation = level fingers

Thromental distance (Patil test)

- Neck fully extended, mouth closed: distance tip thyroid cartilage to tip of mandible
- Score:
  - Normal >7cm
  - <6cm ≈ 75% of diff laryngoscopies
- Patil & mallampati tests combined (<7cm & gd 3-4) = specificity 97%, sensitivity 81%

Sternomental Distance (Savva Test)

- Neck fully extended, mouth closed: Upper border of manubrium to tip mandible
- <12.5cm ≈ difficulty (PPV 82%)

Wilson Score

- 5 factors:
  - Weight
  - Upper Cx mobility
  - Jaw movement
  - Receding mandible
  - Buck teeth
- Each gets subjective score 0-2
- Score 2 or >2 ≈ 75% difficult intubations 12% false positives

Predictive Tests for Difficult BMV

- Age >55
- BMI > 26
- Snoring Hx
- Beards
- No teeth

↳ if have 2 of above >70% sensitivity & specificity

- Facial abnormality
- OSA
- Receding or marked prognathism
  ↳ = marked jaw protrusion relative to skull

Predictors of Problems with Back Up Techniques

LMA

- Inability to open mouth >2.5cm
  ↳ impossible if <2cm
- Intraoral/pharyngeal masses

Direct Tracheal Access

- If contemplating need for tracheal access:
  - Position of larynx & trachea
  - Accessibility of cricothyroid membrane & trachea
- Risk factors:
  - Obesity

- Goitre
- Other ant neck masses
- Deviated trachea
- Fixed neck flexion
- Prev radiotherapy
- Surg collar or ext fixator

1.3 Perioperative Fasting Requirements & Aspiration Risk

- Aspiration causes:
  - chemical pneumonitis
  - FB obstruction
  - Atelectasis
- 30-40mls of gastric contents ⟹ sig mortality and morbidity

Gastric Physiology

- Clear fluids - emptied from stomach in exponential manner half life around 10-20mins
  ↳ Thus complete clearance 2hrs
- Solids:
  - High fats/meats 8hrs+
  - Light meals eg toast approx 4hrs
  - Milk = solid as congeals with gastric juice.
    - Cows milk clears approx 5hrs
    - Human milk less fat & protein so clears quicker

Elective Surgery Times

- Adult:
  - Clear liquids 2hrs(<200mls)
  - Light meals 6hrs

Risk Factors

- Full stomach/delayed emptying
  - Causes delayed emptying:
    - Metabolic eg DM, renal failure, sepsis
    - Decr gastric motility eg head injury
    - Pyloric obstruction eg stenosis
  - Delayed emptying of fluids only in very advanced stages
- Known reflux - effects solids not liquids
- Raised intragastric pressure ie obstruction, pregnancy, laproscopic surgery
- Recent trauma
- Peri-op opioids - marked delays
- DM
- Topically anaesthetised airway

↳ anxiety has not been shown to effect gastric emptying

Premeds

- Premeds 1hr prior to surg have no effect on gastric volume of induction anaesthesia
- Oral midaz 30mins prior to surg no link to aspiration risk

Gastric Acidity

- antacids to decr gastric pH in high risk eg pregnancy
  ↳ sodium citrate commonly used
- H2 blocker/PPI:
  - Give evening before, and 2hrs prior
- Gastric motility agents: metoclopramide (better IV) can incr speed of emptying in healthy.
  ↳ ?benefit in trauma patients

Pregnancy

- Elective C section:
  - Ranitidine 150mg evening before (7am on afternoon list) AND 2hr preop
- High risk pt in labour: 150mg 6 hourly
- Emergency case: 50mg IV ranitidine earliest opportunity

↳ all should also have 30ml sodium citrate

Management of Aspiration

Diagnosis

- Clinical:
  - ↑RR, ↑HR, ↓lung compliance, ↓SpO2
  - Ausc: wheeze & creps
  - Tracheal aspirate may be acidic - negative finding does not exclude aspiration
- CXR: diffuse infiltrative pattern esp in R lower lobe
  ↳ late sign

Differential Diagnosis

- Pulmonary oedema
- PE
- ARDS

Management

- 100% O2, minimise further aspiration risk
- Situational Rx:
  - awake or nearly awake: suction in recovery position
  - Unconscious & spont breathing:
    - Apply cricoid pressure (don't if active vomit as risk oesophageal rupture)
    - Place L lat head down position
    - Intubate if tracheal suction & vent indicated
  - Unconscious & apnoeic: intubate immed & ventilate
- Minimise pure vent until airway secured and all aspirates suctioned
- NG tube
- CXR : look for oedema, collapse/consolidation
- Spo2 90-95% try CPAP & chest physio
- Spo2 <90% despite FiO2 1 ≈ food bolus obstructing bronchial tree & consider bronchoscopy
  ↳ should be ICU ref

1.4 Choosing an Airway Strategy

- Procedure:
  - Elective
  - Emergency
- Patient:
  - Age

    - Cooperation
    - Surgery needed
    - Position of patient
    - Trauma
    - Comorbidities
    - Full airway Assessment
        - Predictive tests
        - Fasting
- Own skills
- Equipment & resources available
- Drugs available

Rapid Sequence Induction

- = rapid IV induction mm relaxation to aid tracheal intubation combined with cricoid pressure to ↓ risk of pulmonary aspiration
- Mask ventilation relatively contraindicated
- Consider other techniques if intubation predicted to be difficult ie AFOI

Plan

- 2 laryngoscopes
- Ventilator of anaesthetic machine incl suction
- tipping trolley bed
- Monitoring
- Positioning - tragus of ear above sternum
- Reliable cannulation
- Drugs:
    - Induction agents:
        - Thiopentone 2-5mg/kg
        - Propofol 1-3mg/kg
        - Etomidate 0.3mg/kg
    - Sux 1-1.5mg/kg
    - Emerg drugs
- Equipment for failed intubation (difficult 1:50, impossible 1:200 in emergency)
    - LMA different sizes - with gastric port if possible
    - BM
    - Emerg cricoid kit
    - Video laryngoscopes

Procedure

- Suction on and under pillow
- Preoxygenate until ETO2 >90% or at least 4 vital capacity breaths
- (risks for quick desaturation:
    - Pregnant
    - Obese
    - Septic
    - Anaemic
    - Paediatric
    - Resp disease)
- Apply cricoid pressure 10N
- Administer induction agent, then rapid sux
- At loss of consciousness incr cricoid to 30N

Problems

- Haemodynamic instability:
  - Excessive induction agent ≈ circulatory collapse esp if hypovolaemic
  - Airway instrumentation ≈ tacy, HTN

  ↳ alfentanil 10-30mcg/kg 1min prior may be helpful
- Cricoid pressure:
  - Cartilage held between thumb & finger and pushed post by index finger
  - Poor tolerance eg children
  - Too much pressure makes intubation difficult
  - BURP +/- helpful
  - If vomit with cricoid before loss of consciousness should be releases.

    ↳ once unconscious vomiting does not occur
  - Unknown force in paeds

1.5 Manual Inline Stabilisation & Implications for Intubation

Indications

- Proven or suspected neck #
- Major mechanism of injury
- Multi trauma unconscious patient

Implications

- Increased difficulty in obtaining intubation
- Increasing failed intubation rate
- Increasing need for adjuncts eg bougie

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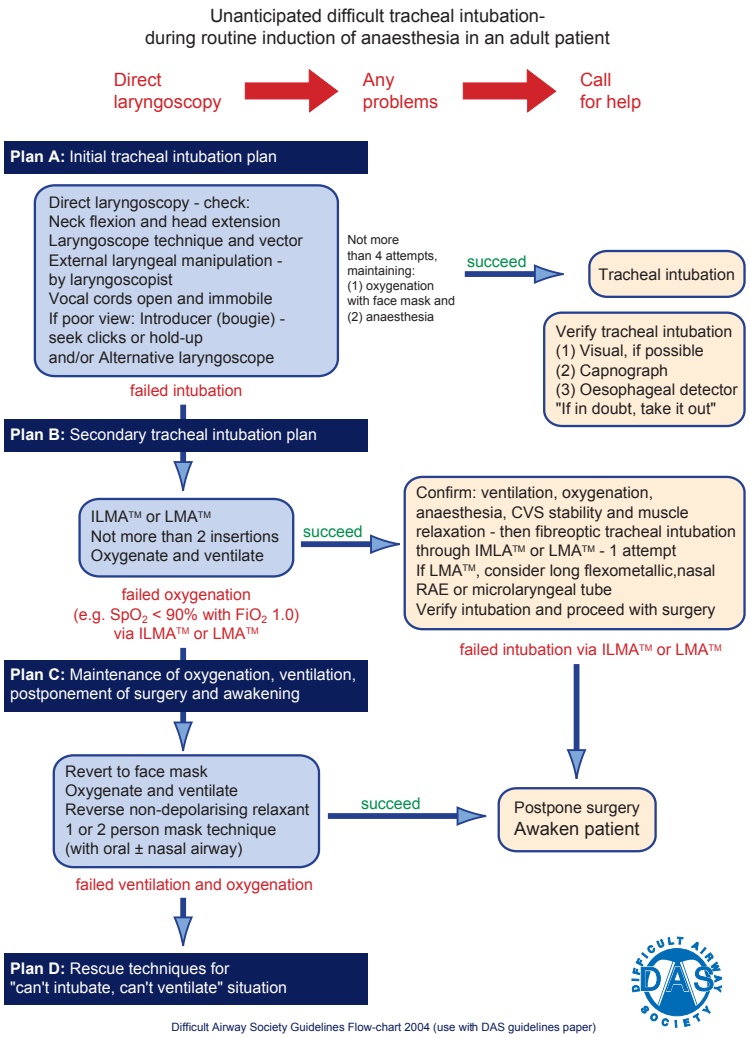
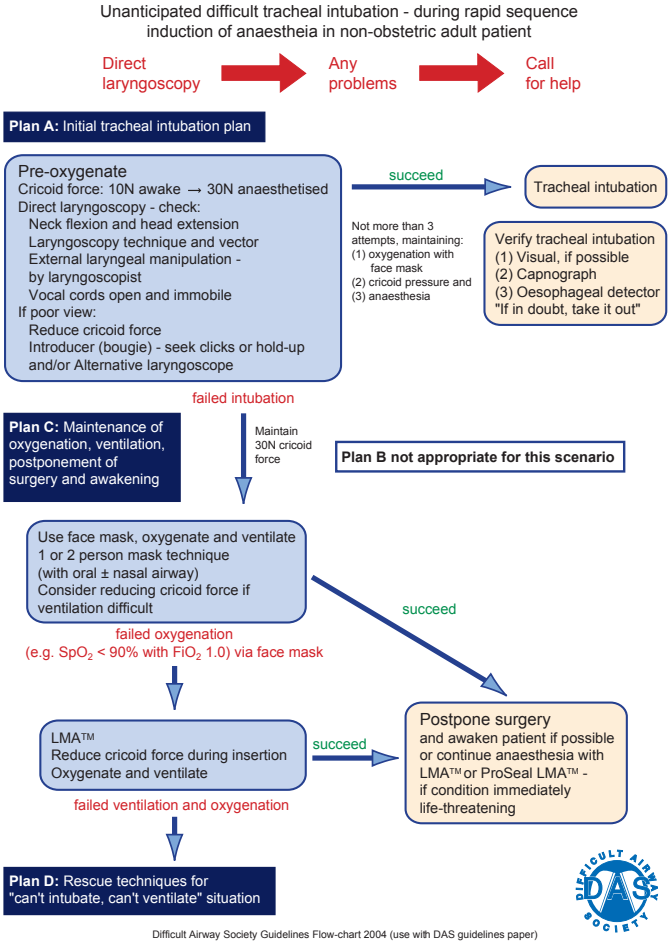
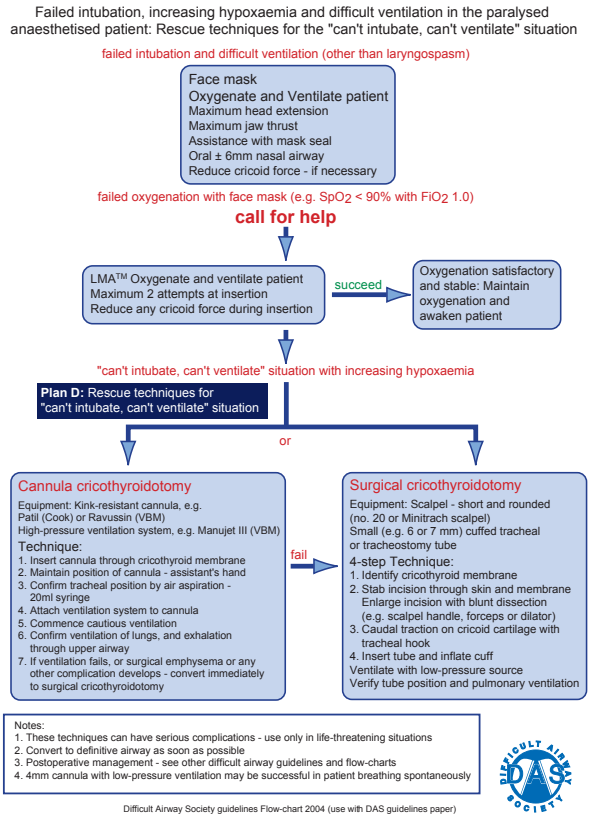
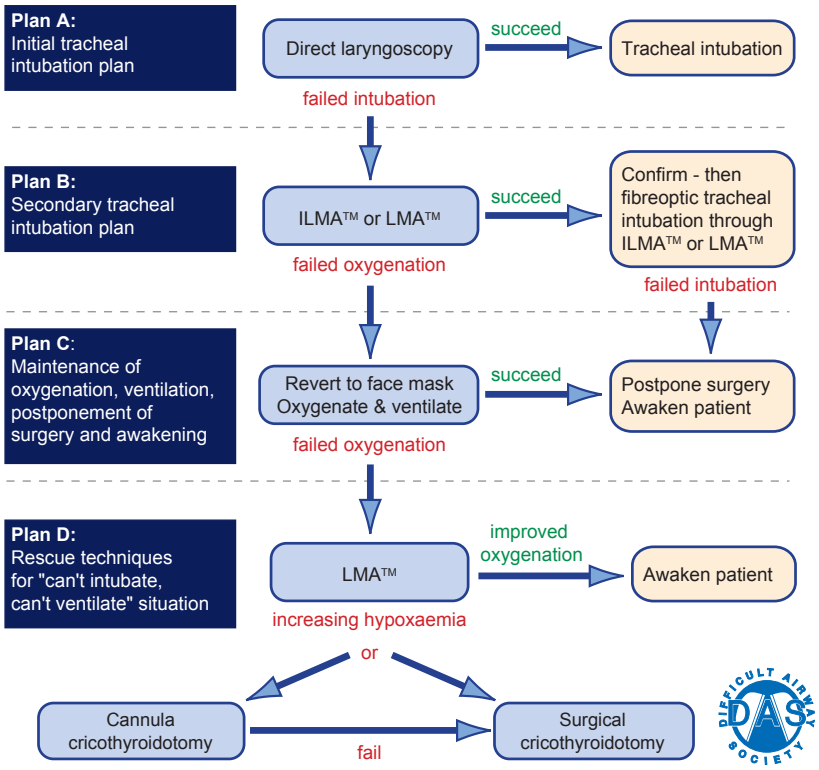
1.6 Can't Intubate, Can't Oxygenate




Unanticipated difficult tracheal intubation - during rapid sequence induction of anaesthesia in non-obstetric adult patient
Direct laryngoscopy
Any problems
Call for help
Plan A: Initial tracheal intubation plan
Pre-oxygenate
Cricoid force: 10N awake → 30N anaesthetised
Direct laryngoscopy - check:
Neck flexion and head extension
Laryngoscopy technique and vector
External laryngeal manipulation - by laryngoscopist
Vocal cords open and immobile
If poor view:
Reduce cricoid force
Introducer (bougie) - seek clicks or hold-up and/or Alternative laryngoscope
succeed
Tracheal intubation
Not more than 3 attempts, maintaining:
(1) oxygenation with face mask
(2) cricoid pressure and
(3) anaesthesia
Verify tracheal intubation
(1) Visual, if possible
(2) Capnograph
(3) Oesophageal detector
"If in doubt, take it out"
failed intubation
Plan C: Maintenance of oxygenation, ventilation, postponement of surgery and awakening
Maintain 30N cricoid force
Plan B not appropriate for this scenario
Use face mask, oxygenate and ventilate
1 or 2 person mask technique
(with oral ± nasal airway)
Consider reducing cricoid force if ventilation difficult
succeed
failed oxygenation
(e.g. SpO2 < 90% with FiO2 1.0) via face mask
LMA™
Reduce cricoid force during insertion
Oxygenate and ventilate
succeed
Postpone surgery
and awaken patient if possible
or continue anaesthesia with LMA™ or ProSeal LMA™ -
if condition immediately life-threatening
failed ventilation and oxygenation
Plan D: Rescue techniques for "can't intubate, can't ventilate" situation
Difficult Airway Society Guidelines Flow-chart 2004 (use with DAS guidelines paper)


Failed intubation, increasing hypoxaemia and difficult ventilation in the paralysed anaesthetised patient: Rescue techniques for the "can't intubate, can't ventilate" situation
failed intubation and difficult ventilation (other than laryngospasm)
Face mask
Oxygenate and Ventilate patient
Maximum head extension
Maximum jaw thrust
Assistance with mask seal
Oral ± 6mm nasal airway
Reduce cricoid force - if necessary
failed oxygenation with face mask (e.g. SpO2 < 90% with FiO2 1.0)
call for help
LMA™ Oxygenate and ventilate patient
Maximum 2 attempts at insertion
Reduce any cricoid force during insertion
succeed
Oxygenation satisfactory and stable: Maintain oxygenation and awaken patient
"can't intubate, can't ventilate" situation with increasing hypoxaemia
Plan D: Rescue techniques for "can't intubate, can't ventilate" situation
or
Cannula cricothyroidotomy
Equipment: Kink-resistant cannula, e.g. Patil (Cook) or Ravussin (VBM)
High-pressure ventilation system, e.g. Manujet III (VBM)
Technique:
1. Insert cannula through cricothyroid membrane
2. Maintain position of cannula - assistant's hand
3. Confirm tracheal position by air aspiration - 20ml syringe
4. Attach ventilation system to cannula
5. Commence cautious ventilation
6. Confirm ventilation of lungs, and exhalation through upper airway
7. If ventilation fails, or surgical emphysema or any other complication develops - convert immediately to surgical cricothyroidotomy
fail
Surgical cricothyroidotomy
Equipment: Scalpel - short and rounded (no. 20 or Minitrach scalpel)
Small (e.g. 6 or 7 mm) cuffed tracheal or tracheostomy tube
4-step Technique:
1. Identify cricothyroid membrane
2. Stab incision through skin and membrane
Enlarge incision with blunt dissection (e.g. scalpel handle, forceps or dilator)
3. Caudal traction on cricoid cartilage with tracheal hook
4. Insert tube and inflate cuff
Ventilate with low-pressure source
Verify tube position and pulmonary ventilation
Notes:
1. These techniques can have serious complications - use only in life-threatening situations
2. Convert to definitive airway as soon as possible
3. Postoperative management - see other difficult airway guidelines and flow-charts
4. 4mm cannula with low-pressure ventilation may be successful in patient breathing spontaneously
Difficult Airway Society guidelines Flow-chart 2004 (use with DAS guidelines paper)


Plan A:
Initial tracheal intubation plan
Direct laryngoscopy
succeed
Tracheal intubation
failed intubation
Plan B:
Secondary tracheal intubation plan
ILMA™ or LMA™
succeed
Confirm - then fibreoptic tracheal intubation through ILMA™ or LMA™
failed oxygenation
failed intubation
Plan C:
Maintenance of oxygenation, ventilation, postponement of surgery and awakening
Revert to face mask Oxygenate & ventilate
succeed
Postpone surgery Awaken patient
failed oxygenation
Plan D:
Rescue techniques for "can't intubate, can't ventilate" situation
LMA™
improved oxygenation
Awaken patient
increasing hypoxaemia
or
Cannula cricothyroidotomy
fail
Surgical cricothyroidotomy
DIFFICULT AIRWAY SOCIETY
DAS

1.8 Common complications of Intubation

- Airway related complications in 4%:
  - Aspiration
  - Oesophageal intubation
  - Dental injury
  - Pneumothorax
  - Laryngospasm
  - Perf trachea or oeseophagus
  - # or dislocation Cx spine/TMJ/arytenoid cartilages
  - Vocal cord damage

1.9 Preoxygenation & Physiology

- = breathing 100% O2 from close fitting mask for 3-5mins (or 4 vital capacity breaths)
- Aim is to denitrogenate lungs $\Longrightarrow$ oxygenation of FRC >1800mls O2
- ↑time to desaturation of 7-8mins
- Best way to measure effectiveness of preoxygenation is measure ET O2 fraction (FEO2)
  - FEO2 ≈ FAO2 (alveolar o2 fraction)
- use alveolar gas equation to understand % of O2 in lung:
  - 149 - 40/0.8 = 100mmHg
  - 100mHg as percentage of 1atmosphere (760mmHg) = 100/760 x 100 = 13%
- ∴ Typical FRC volume = 2.2 litres which in RA contains 13% O2 = 270mls O2
- In norm adult with complete preoxygenation (FAO2 >0.9) lungs should contain around 2000ml O2
- Total body oxygen consumption ≈ 250mls/min
  - ∴ apnoea with norm store takes ~1min (270/250)
- If FRC preoxygenated with FiO2 1:
  - 760 -47 - (40/0.8) = 663
  - 663/760 x 100 = 0.87
  - 2200*0.87 = 1914mls
  - 1914/250 = 7.65mins

Total Ventilation

- Vt = 500ml & RR 15/min:
- Total ventilation: = Vt x RR
- 500 x 15 = 7500ml/min
- ↳volume of air entering is slightly greater as more O2 is taken in than Co2 is given out

Alveolar ventilation:

- = Vt – dead space x RR
- = amount getting to respiratory zone
- anatomic dead space = 150mls ∴ alveolar vent = 500 – 150 x 15 = 5250ml/min

Partial Pressure of Gas

- Partial pressure of gas = concentration x total pressure

  Eg dry air had 20.93% O2

  @ sea level pressure = 760mmHg ∴ Po2 @ sea level = 20.93/100 x760 = 159mmHg
- When air inhaled it is warmed & moistened

  Water vapour pressure = 47mmHg ⇒ total dry gas pressure = 760 – 47 = 713

∴ P_IO2 inspired air = 20.93/100 x 713 = 149mmHg

Alveolar Gas Equation

Allows relationship between fall in PO2 & rise in PCO2 which occurs in hypovent can be calculated

F= small correction factor (~2mmHg)
R = respiratory quotient (~0.8)
↳determined by CO2 production/O2 consumption
↳ie metabolism of tissues in steady state
P_IO2 = composition of inspired gas

$$P_AO2 = \frac{P_IO2 - PACO2}{R} + F$$

Functional Residual Capacity

- FRC = major oxygen store within body
- FRC = balance between tendency of chest wall to spring outwards and tendency of lung to collapse
- Volume changes by many factors
- Decreasing factors:
  - Age
  - Posture - supine
  - Anaesthesia - mm relaxants - diaphragm tone will ↓pull away from lungs
  - Pregnancy - ↑abdo pressure
  - Surgery - laprasocpic
  - Pulmon fibrosis
  - Pulmon oedema
  - Obesity
  - Abdo swelling
- Increasing factors:
  - ↑ing height
  - Erect position
  - Emphysema - less elastic recoil of lungs
  - Asthma - air trapping

1.10 Ventilatory Strategies in Elective and Emergency Patients

IPPV Indications

- Indications:
  - Where neuromuscular blockade is required
  - Abdo or thoracic operations
  - Close control of arterial CO2 is required eg Neuro
  - Resp disease
  - Gross obesity

Ventilators

- Reservoir bag:
  - Hand squeeze ⟹ positive pressure in circuit ⟹ gas forced into lung under positive pressure
- Bag squeezers
  ↳ = flow generator ventilator
  - Bellows are squeezed - usually by intermittently pressurising bellows in fixed jar
  - Gas in circuit are kept separate from compressing air
  - Aka bag in bottle type
  - Deliver constant flow but can create very high airway pressures
- Other flow generators:
  - Fluid logic to divide pressurised gas into smaller volumes
  - Volumes to patient or drive anaesthetic gas from reservoir to patient
  - Often used in paeds or transport vents
- Jet ventilation
  - Used during:
    - Rigid bronchoscopy
    - Upper airway surgery
    - Emerg cricothyrotomy
  - Works on Bernoulli principle: high pressure o2 passed out of narrow tube ⟹ entrainment of air at an area of low pressure around opening
  - Jet of o2 applied intermittently
  - Risk of barotrauma is very high
- Minute volume dividers
  ↳ = constant pressure ventilator
  - Eg Manley series
  - Minute volume of gas is taken from machine and passed under low pressure to ventilator
  - Gas flow divided up into tidal volumes by bellows/lever mechanism and pressuried by small weight
  - Low pressure system causes problems in people with low lung compliance or high airway resistance ie inadequate air flows

Delivering IPPV

- Patients physiological resp drive can be overcome by:
  - Mm relaxants
  - Sedation/anaesthesia
  - Opiates
  - hyperventilation
- Tidal Volume:
  - Without pre-existing lung disease & children: 12ml/kg, 12/min
  - With chronic resp disease: 10ml/kg, 10/min
  - ARDS: 6-8ml/kg & high PEEP upto 15
- I:E ratio:
  - Start with 1:2
  - ↑ inspiration - good with large shunts
  - ↑ expiration - bronchospasm/obstruction

Hyperventilation

$H20+CO2 \leftrightarrow H2CO3 \leftrightarrow H+ + HCO3-$

- Hyperventilation drives equation to L causing

    - Resp alkalosis via decr avaliable H+ ions
- Consequences of hypervent:
    - ↑risk vent disrhytmias
    - Hypokalaemia
    - ↓ionic Ca ⟹ neuromuscular irritability
    - Cerebral VC ⟹
        - ↓ICP (limited to approx 24hrs)
        - ↑risk of regional ischaemia

Physiological Consequences of IPPV & PEEP

cvs

- ↑intrathroacic pressure:
    - ↓filling R heart ⟹ ↓CO ⟹ ↓ bp
- ↑Pulmon vasc resistance ⟹ ↓R ventricular outflow ⟹ RV distension ⟹ bulging of septum ⟹ ↓LV compliance

Renal

- ↓renal perfusion 2nd to hypoperfusion from ↓CO
- Humeral effects:
    - ↓ANP secretion
    - Stim renin-angiotensin axis
    - ↑vasopressin production

↳ all ⟹ ↓urine output & sodium & water retention

Resp

- IPPV much less efficient in maintaing VQ ratio:
    - Atelectasis
    - ↓FRC ⟹ shunting
    - ↑alveolar & anatomical dead space
- Risk of barotrauma
- Long term complications (ie ICU):
    - Bronchopulmonary displasia
    - Oxygen induced lung injury
    - Tracheal stenosis
    - Nosocomial lung infection

Other

- Consequences of ↓VR to heart:
    - ↑ICP
    - Liver dysfunction from hepatic congestion
    -

1.12 Peri-operative Upper Airway Obstruction

- Approach changes based on:
  - Urgency
  - Level of obstruction
  - General condition of patient
- Any airway obstruction always likely to get worse during anaesthesia or airway manipulation:
  - Loss of airway tone
  - Reflex airway responses
  - Trauma
  - Bleeding
- Life threatening complications:
  - Complete obstruction on induction
  - Intra-airway haemorrhage
  - Swelling

↳ always have a back up plan

40mls/kg 60-70ml/kg

Assessment

6-10ml/kg 80

- Preop tests can be useful if have time:
  - Nasoendoscopy 15
  - CT/MRI
  - PFTs with flow volume loops 30
  - ECHO - if pulmon vessel suspected 15
- To consider:
  - What level is it?
    - Oral
    - Supraglottic
    - Laryngeal ≈ insp stridor & voice change
    - Mid tracheal
    - Lower tracheal ≈ exp stridor/wheeze

    ↳ several levels may be effected by 1 pathology
  - Severity:
    - Resp distress & acc muscle use
    - Stridor
    - Hypoxaemia
    - Silent chest
    - Dysphagia
    - Nocturnal panic
  - Lesion - mobile or friable
  - Neck - how easy is it to access trachea as back up plan
  - Effect of positioning
- Management plan for extubation

  ↳ may need to be delayed
- Prolonged instrumentation may cause airway oedema
- Heliox -
  - Premixed helium & O2 21-30%
  - Decr viscocity thus allows improved flow through narrowed tube
  - Note ↓FiO2 BUT can use a Y connector to incr FiO2

Oral, Supraglottic & Laryngeal Lesions

- Eg trauma, burns, tumour, infection
- Semi-elective cases - careful nasoendoxcopy may help in predicting difficult cases
- Cricothyroidotomy will only work if lesion is not obscuring access
- Options:
  - AFOI
  - Inhalational induction ⟹ direct or fibre optic laryngoscopy
  - Elective awake (with LA):
    - Cricothyroidotomy
    - Tracheostomy
    - Trans-tracheal ventilation catheter - back up oxygenation plan
- LMA may be helpful if unexpected obstruction
- if concerns:
  - IV induction with no back up plan should never be done

Mid Tracheal

- Eg tumour or retrosternal goitre
  ↳ may expand suddenly with haermorrhage
- Site of lesion may prevent emerg cric or trachy if needed
- Inhalational induction may be very slow if severe narrowing
- AFOI:
  - Coughing & distress may ⟹ ↑obstruction & cyclic of decline
  - Tube through narrowing may prevent spont vent (= cork in bottle)
- Need to pass through narrowing:
  - ET tube
  - Endobronchial tube
  - Hollow intubation bougie or Cook airway exchange catheter
- Ideal of tube and cuff can sit below obstruction but above corina
- RSI with rigid bronchoscope
- May need TIVA

Lower Tracheal/Bronchial Lesions

- Eg tumour, trauma, mediastinal masses
- Best managed by in tertiary centre
- Cardiopulmonary bypass sometimes necessary eg pulmo artery compression
- RSI, rigid bronchscope may be life saving

1.15 Oesophageal intubation

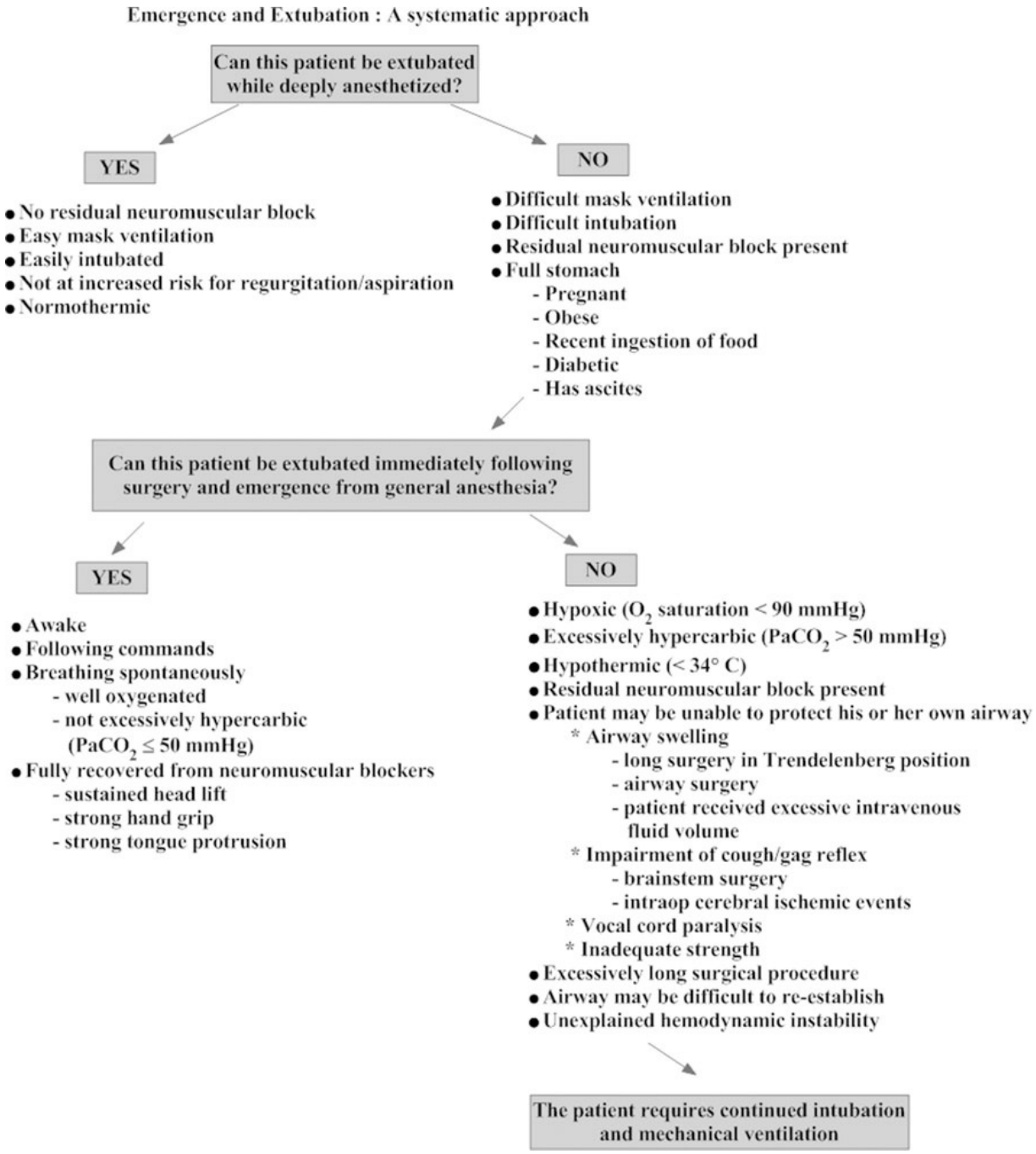
- Direct confirmatory techniques:
  - Fibreoptic bronchoscopy with visualisation of tracheal rings through ETT
  - Visualisation of ETT passing through vocal cords
    ↳ commonly mistaken
- Indirect markers:
  - Auscultation of chest & epigastrium - fail to identify 1:40 oesophageal intubations
  - Condensation on tube: BUT 42:60 oesophageal intubations fogged tube
  - Spo2 - but can have delay of hypoxia up to 8mins with OI
  - CXR - only really useful for identifying bronchial intubation
  - Capnography -
    - Sensitivity 93%, specificity 97% = failed recognition OI in 3% cases
    - False readings possible:

    - Tube in oesophagus but CO shows in trachea: expired alveolar gas introduced into stomach during
        - BMV
        - Ingestion carbonated beverages
        - Antacids
    - Tube in trachea but CO ?in oesphagus:
        - Low cardiac output (Cardiac arrest, Severe hypotension)
        - Severe pulmon disease
        - PE
- Oesophageal Detector Devices
    - Rely on differences in rigidity of tracheal & oesophageal walls
    - Sensitivity & specificity up to 100% although false +ves:

        ↳ controversial paramedic testing 50% sensitivity
        - Prev air insufflation of GI tract
        - COPD
        - Copious secretions
        - COPD
            - Much more useful in low cardiac output states ie arrest

1.17 - 1.20 Extubation

- Resp complications x3 more likely than intubation (4.6 vs 12.6%)
- Main questions:
  - Prev difficulties with controlling the airway
  - What is risk of pulmon aspiration
- Deep vs awake:
  - General rule: extubate when awake
  - Deep ≈ ↓CVS stim, ↓coughing on tube BUT ↑↑complications regardless of operation



Positioning

- Traditional extubate in L lat, head down position:
  - Tongue moved away from post pharyngeal wall
  - Protects airway from aspiration
  - Laryngoscopy & reintubation favourable if skilled in this position
- Supine sitting up position - controversial:
  - No evidence to show less complications that lat position in standard cases
  - Physiological benefits:
    - Facilitates spont rest & diaphragmatic movement
    - Aids cough
    - ↑FRC
    - Encourages from lymph drainage
    - ↓airway oedema
  - May be easier to reintubate esp if expected diff intubation:
    - Obese
    - Chronic resp disease
- Prone:
  - May be necessary after spinal surg
- Children usually extubated in recovery position

Timing Extubation

- ↑threshold to fire of laryngeal adductor neurons during inspiration
  ↳ ∴ extubate at end inspiration when glottis fully open

Method

- Suction post pharynx
- Bite block
- 100% O2
- High flows to washout inhalational agaents
- Positive pressure breath at extubation to prevent atelectasis

Problems with Extubation

Mechanical

- Failure to deflate cuff
- Trauma to larynx
- Cuff herniation
- Adhesion to tracheal wall
- Surg fixation of tube to adjacent structures

CVS Response

- Extubation ≈ 10-30% ↑ bp & HR lasting 5-15mins
- If coronary artery disease ≈ ↓40-50% EF
- Can use drugs to manage:
  - Esmolol 1.5mg/kg 2-5min before extubation
  - GTN
  - Mg
  - Remi/alfentanil infusion
  - Lignocaine 1mg/kg over 2mins
- Can convert to LMA prior to extubation

Resp Complications

- Cough & sore throat - 38-96%

    - Fill cuff with fluid rather than air - less change in pressure via temp & N2O diffusion
    - Lignocaine 2% in cuff - 4-6hrs 45-65% diffusion across cuff
    - Special ETT which has port for topical LA
- Postoperative hypoxaemia:
    - Causes:
        - ↓MV
        - Airway obstruction
        - ↑VQ mismatch
        - Diffusion hypoxia
        - Post hyperventilation hypoventilation
        - Shivering
        - Inhibition of hypoxic pulmon VC
        - Mucocilary dysfunction
        - ↓CO
    - Prevention:
        - 100% preoxygentation prior to extubation
        - Continuous positive pressure vent
        - High inspired O2 during transfer to PACU
- Risk of bronchospasm:
    - Smokers
    - COPD
    - Children upper resp tract infections

Airway Obstruction

- Differential diagnosis of post extubation upper airway obstruction (UAO):
    - Laryngospasm -
        - most common 5% of intubated pts
        - More common kids with upper airway surgery
        - Caused by local irritation of blood/saliva
        - Likely in light planes anaesthesia - no airway reflex or poor cough to clear
        - Leave children in L lat position until they wake up
        - Mg 15mg/kg/20mins or lignocaine 1.5mg/kg over 2mins can help
    - Laryngeal oedema
        - Impt cause in neonates & infants
        - = insp stridor within 6hrs of extubation
        - Supraglottic oedema displace epilgotis post blocking glottis on inspiration
        - Retroarytenoidal oedema below cords limits abduction of vocal cords on inspiration
        - Subglottic oedema of 1mm in neonate ≈ ↓laryngeal cross section by 35%
        - Rfs:
            - Tight tube
            - Trauma at intubation
            - Intubation >1hr
            - Cough on tube
            - Change head/neck position during surg
        - Rx:
            - Humidified air
            - Neb adrenaline 1-5mls 1:1000
            - Dex 0.25mg/kg then 0.1mg/kg 6hrly for 24hrs
            - Heliox 60:40 or 80:20 as temporising measure
            - Reintubation with smaller tube if necessary
    - Haemorrhage

- Trauma:
  - arytenoid cartilage dislocation - voice change or painful swallowing
- Vocal cord paralysis:
  - Rare
  - Trauma to vagus nerve
  - Unilat paralysis ≈ hoarseness - may recover over weeks depending on aetiology
  - Bilat paralysis ≈ UAO ⟹ reintubation
- Vocal cord dysfunction:
  - Uncommon
  - Young females, recent URTI, emotional stress
  - Stridor or wheeze resistant to treatment
  - Paradoxical vocal cord adduction during inspiration

Table 1 Structured approach to the management of laryngospasm[7] (the main aim is to rapidly oxygenate the patient)

Think of
Airway irritation/obstruction
Blood/secretions
Light anaesthesia
Regurgitation
Management
100% oxygen
Visualize and clear pharynx/airway
Jaw thrust with bilateral digital pressure behind temperomandibular joint, oral/nasal airway
Mask CPAP/IPPV
Deepen anaesthesia with propofol (20% induction dose)
Succinylcholine 0.5 mg/kg to relieve laryngospasm (1.0–1.5 mg/kg i.v. or 4.0 mg/kg i.m. for intubation). Be aware of contraindications, for example, neuromuscular problems
Intubate and ventilate

Post Obstructive Pulmon Oedema

- Incidence 1:1000
- Most children or young fit adults
- Presentation:
  - Airway obstruction at emergence ⟹ rapid onset distress ⟹ haemopytsis ⟹ bilat CXR changes consistent with pulmon oedema
- All features usually resove at 24hr with no sequelae
- Pathophys uncertain:
  - Negative intra-alveolapressure
  - ↑cardiac filling
  - Haemorrhage of pulmonvessels
  - Hypoxaemia
  - Catecholamine release on alveolar capillaries ⟹ ↑permeability
- Rx with +ve airways pressure & oxygenation
- Differential = neurogenic pulmon oedema:
  - Similar but more severe onset
  - From severe CNS insult

Tracheomalacia

- Failed extubation with stridor or wheezing may be first signs of tracheomalacia
- Usually erosion of tracheal rings by:
  - Retrosternal thyroid or tumour

    - Enlarged thymus
    - Vascular malformations
    - Prolonged intubation
- Trial deep extubation to avoid coughing
- Maintain CPAP to keep airway patent

Pulmon Aspiration

- ⅓ aspiration occur at extubation
- Swallowing reflex obtunded for approx 4hrs

Recognising High Risk Patients

- Severe heart/lung disease
- Airway pathology
- Obese
- OSA
- Severe GORD
- Multiple attempts at intubation
- Surg factors:
    - Recurrent laryngeal nerve damage (10% thyroids)
    - Haematoma
    - Oedema
    - Post fossa surg
    - Inter-maxillary fixation
    - Drainage neck/dental abscesses

Strategies for Presumed Difficult Extubation

- LMA:
    - Insert when deep
    - Reverse relaxation
    - LMA removed when spont breathing
- Extubation over flex bronchoscope:
    - Used if ?laryngeal paralysis, tracheomalacia, tube entrapment
    - ETT > LMA
    - Bronch passed and cords visualised +/- ETT re placed
- Tracheal Tube Exchange Catheter
    - Useful if expected difficult to reintubate
    - = long hollow catheters with connectors of manual/jet vent
    - Can be left in place for upto 72hrs post
    - Spont breathing, coughing, talking well tolerated

Predicting Unsuccessful Extubation

- Alert test = x4 more likely to succeed:
    - Open eyes
    - Follow with eyes
    - Grasp hand
    - Stick out tongue
- Cuff leak test:
    - Av diff between insp & exp volume after cuff down, 6 consecutive breaths is determined
    - <10% volume difference of delivered Vt ≈ upper airway oedema

2.1.2 General Anaesthesia & Sedation

1.5 Chemical Composition of Fluids and Effects in Volume replacement

	Normal Saline (0.9%)	Dextrose 4% /Saline (0.18%)	Plasmalyte 148 pH 7.4	Gelofusine	Pentastarch	Ringers Lactate/ Hartmans
Na (mM/l)	150	30	140	154	154	130 Na
K (mM /l)			5			4 K
Ca (mM /l)						4 Ca
Mg (mM /l)			1.6			
Cl (mM /l)	150	30	98	120	154	107 CL
Acetate (mM /l)			27			
Gluconate (mM/l)			23			
Glucose (mM /l)		222				29 lactate
Osmolality (mOsm/kg)	300	282	294	274	320	274
Energy (Kilojoules/l)	0	638	66			37.8
Molecular Wt (Daltons)				30 K	250 K	
PH	5.0	4 -5	7.4	7.4	5	6.7

- NSL & pentastarch are significanly hyperchloraemic
- Plasmalyte & ringers lactate = bicarbonate equivalent
- Blood cannot be mixed with
  - Ringers lactate - calcium in ringers
  - Dextrose
  - Haemaccel
- Plasmalyte best for replacement of small bowel or colonic loss or sequestration

1.6 IV Fluid Replacement

IntraOperative Fluid Loss

- <3 litres - Norm saline ok
- >3 litres problems with hyperchloraemic load

Guidelines

- Monitor UO -

    - 1ml/kg AND absence of pulsus paradoxus
      ↳ = abnormally large (>10mmHg) ↓in in SBP during inspiration
    - Response to volume trial with of CVP monitorring- give 5ml/kg over 10min. Result=
      - <2mmHg = hypovolaemia
      - >5mmHg = hypervolaemia
      - 2-5mmHg = reassess or repeat

      ↳ = 2-5 rule
- Fasted patients (no surg losses)
  - Maintenance:
    - 1st hr 5ml/kg/hr
    - Thereafter: 2ml/kg/hr
- Surgical losses - best managed to clinical demand - blood but:
  - Routine - 4-6ml/kg/hr NSL or plasmalyte
  - Open cavity - 6-8ml/kg/hr
- Monitor hyperglycaemia & hyponatraemia

1.7 Anxiolytic or Sedative Premedications

Paediatrics

- Routine premed not required.
- Parents s usefu
- Indications:
  - Very upset
  - Prev unpleasant anaesthetic experience
  - Developmental delay
- Preschool child most at need due to seperation anxiety from parents
- Complications of excessive anxiety include:
  - Sleep disturbance
  - Nightmares
  - Bed wetting
  - Eating disorders

Drugs

- Options:
  - Midaz 0.5mg/kg PO (max 15mg)
    ↳ (Intranasal 0.2mg/kg an option but burns)
    - Onset in 15-30min
    - IV solution is bitter so dilute in pamol
  - Ketamine (0.5mg/kg PO)
    - Action within 15mins
    - May cause ↑salivation & emergence delerium
    - Option for IM (2-3mg/kg if required)
  - Clonidine (5mcg/kg PO)
    - Good induction conditions, good analgesic
    - BUT causes ↓bp & delayed recovery
- Don’t routinely need to coadminister anticholinergics
- Antisialogues (atropine 40mcg/kg PO but variable absorbed) reserved for:
  - Downs & CP
  - +/- ketamine

Contraindications (relative) to Premedications

- New born <1yr
- Elderly
- Decr GCS
- Intracranial pathology
- Severe pulmonary disease
- hypovolaemia

1.8 Physiology of Pneumoperitoneum

- Insuflation of CO2 to av max 20mmHg
- Once intrabdominal pressure (IAP) exceeds physiological thresholds see organ effects

CVS Effects

- ↑SVR:
  - Mechanical compression of abdo aorta
  - ↑release vasopressin and activation of renin-angiotensin-aldosterone axis
- ↓CO:
  - Compression of IVC ⟹ ↓VR ⟹ ↓preload ⟹ ↓CO
    ↳ especially if hypovolaemic
  - Cephelad displacement of diaphragm ⟹ ↑intrathroacic pressure ⟹
    - ↓VR (as above)
    - Compression pulmonary vasculature ⟹ ↑RV afterload

Resp Effects

- ↑IAP ⟹ ↓diaphragmatic excursion ⟹
  - ↑intrathroacic pressure
  - ↓compliance
  - ↓FRC
  - Atelectasis
  - Altered VQ relationships
  - Hypoxaemia
- Absorbed CO2 ⟹ ↑PCO2 which is worsened by VQ mismatching

GI Effects

- ↓kidney & liver blood flow - especially in mod/severe organ disease states
  ↳ IAP 20mmHg = ↓GFR ≈ 25%
  ↳ Mechanism thought to be ↓afferent flow (2nd to low CO) & ↓efferent flow (high venous pressure)
- IAP persistently >20 = ↓40% blood flow to mesenteric & GI mucosa ⟹ ↑acidosis

Neuro Effects

- ↑ICP:
  - ↑IAP ⟹ ↑intrathroacic pressure ⟹ ↓cerebral venous drainage
    ↳ despite ↑ed mean cerebral arterial pressure

1.9 Physiological Effects of Positioning

Supine

- Resp:
  - ↓FRC - abdo contents encroaching on diaphragm
  - ↑VQ mismatch
  - ↓pulmonary compliance
- CVS:
  - ↑VR from LL vasculature
  - ± heart failure in borderline hearts
  - +/-compression of IVC in obese/pregnant ⟹ ↓↓CO & ↓↓ bp
- GI:
  - ↑risk regurgitation
- Eye:
  - Risk of corneal drying in 10mins
- Nerve injury:
  - Supraorbital & facial nerve at risk from tube ties & FMs
  - Brachial plexus (esp C8, T1) - ↑ risk of injury when:
    - Arm abducted >90
    - Hand supinated
    - Head turned away
  - Ulnar nerve (>25% all nerve injuries) - in ulnar groove, medial epicondyle
    (↳ x3 males > female)
- MSK:
  - Loss lumbar lordosis ⟹ ↑chance LBP
  - Pressure sores - heels, occiput, sacrum

Lateral

- VQ mismatch - dependant lung vs non dependant lung
- Greatest amount of ocular complications:
  - Mostly corneal abrasions - either eye
- Nerve damage:
  - Brachial plexus - need good lateral support
  - Saphenous nerve & common peroneal - need padding between legs

Lithotomy

- Very similar to trendelenburg
- Hands and digits at the side of the patient - must be careful to avoid crush when replacing bottom of table
- Nerve damage - bilat flex of hip joints ≈
  - stretch sciatic & obturator nerves
  - Femoral nerve - direct compression under inguinal ligament
- Calf compression ⟹ VTE risk
- Compartment syndrome - mulitple causes of ↓perfusion pressure:
  - Weight of extremity against support ⟹ ↓compartment capacity
  - Elevation above heart

  ↳ stirups no better than combined calf support

  ↳ length of op >5hrs main risk factor

Prone

- Must try and avoid pressure on abdo by good positioning
- Effective positioning can be positive physiologically (approx 70-80% see improvement initially)
  - ↑FRC
  - ↓VQ mismatch
- BUT position assoc with most MSK injuries:
  - Eye & nose
  - UL positions: small ant flex, abducted 90deg and ext rotation

Reverse Trendelenburg

- Beneficial physiological effects:
  - ↑head & neck drainage
  - ↓ICP
  - ↓regurgitation
- Risks:
  - ↓bp
  - ↑risk venous air embolism

Seated

- Venous pooling into LLs & refractory hypotension
- Venous air embolism - esp during craniotomy:
  - Subatmospheric venous pressure & non collapsable dural sinuses

Trendelenburg

- Classic 45deg head down tilt

- CVS system
  - In healthy little long lasting effect due to quick compensation VD to overcome ↑VR
  - No RCT evidence to support trendelenburg position is of benefit in correcting acute ↓bp
  - In elderly or comorbidities with impaired vasomotor control may see ↑bp:
    - Capillaries and most of venous blood above heart
    - Incr VR ⟹ ↑preload ⟹ ↑stroke volume ⟹ ↑CO ⟹ ↑bp
      ↳ effect is marked in
      - deep inhalation: -ve pressure vent ⟹ ↑-ve intrathoracic pressure
      - high spinal/anaesthesia - sympathetic blocking ⟹ ↑VD ⟹ ↑VR
  - Possibility of ↓bp is also argued:
    - ↓VR 2nd to intraabdo and pelvic organs compressing IVC
  - Risk of adverse consequences in people with cormobidities:
    - Obese
    - Compromised RV EF ⟹ R heart failure
    - Pulmonary disorders
    - Head injuries
  - Well leg compartment syndrome - combination of:
    - ↓arterial perfusion to raised LLs
    - Compression of leg vessels by SCDs
    - ↓femoral drainage by +/- pneumoperitoneum

- Resp system:
  - Rasied diaphragm with gravity and weight of abdo cavity organs:
    - ↓VC, ↓FRC, ↑risk basal atelectasis

↳ 20deg head tilt = ↓VC by 15%
  - Hypercarbia 2nd to shunt
  - Incr VQ mismatch: ventilation maximal at bases, perfusion maximal at apex 2nd to gravity
  - Endobronchial intubation - northward movement of pt with fixed position of ETT ⟹ relative southwards migration of tip of ETT further into lungs
  - Upper airway oedema 2nd to orthostatic forces (prolonged positioning)
- Airway/Positioning:
  - Movement of pt with gravity causing soft tissue damage to lips on ETT and tie
  - Danger of patient falling from surg table
- Digestive system:
  - Pooling of secretions in dependant part ie nasopharynx ⟹ ↑risk laryngospasm if not suctionning pre extubation
  - Increased risk of aspiration of gastric contents - if non secured airway
- Neuro:
  - Intra and extra cranial venous congestion ⟹ ↑ICP
  - ↑risk cerebral oedema
- Eye - ↑intraoccular pressure

1.10 Post Operative Nausea & Vomiting

- 20-30% after GA with volatiles
- Up to 70% in high risk patients
- Morbidity:
  - Pt satisfaction, Delayed d/c, Unexpected admission
  - Wound dehiscence
  - Bleeding
  - Pulmon aspiration
  - Oesophageal rupture
  - Fluid & electrolyte disturbance

Physiology Of PONV

- induction of vomiting coordinated response from 2 diff areas:
  - chemoreceptor triggr zone (CTZ) – floor fourth ventricle
  - vomiting/emetic centre – medulla
- emetic centre receives
  - inputs from:
    - CTZ – via neurotrasmitters:
      - ACh, 5HT, Histamine, DA
    - vestibular apparatus/cerebellum
    - higher centres – pain/smell/sight
    - organs eg heart, testes, GI tract
  - efferent to:
    - CN 5, 7, 9, 10, 12
    - Spinal nerves to GI tract, diaphragm, abdo muscles
- CTZ activated by:
  - CSF & blood borne emetics eg chem. toxins & drugs (poor bbb in area)
  - 5HT neurotransmitter from afferent nerves from stomach & small intestine receives input from vestibular apparatus

    - higher centres – smells, emotions, pain
    - ↑ICP
    - endocrine disturbances
    - radiation & chemotherapy
- CTZ cannot initiate vomiting alone
- CTZ very close physically to resp centre ∴ difficult to full abolish vom without effecting RR
- vomiting action via efferent nerves from emetic centre

Risk Factors

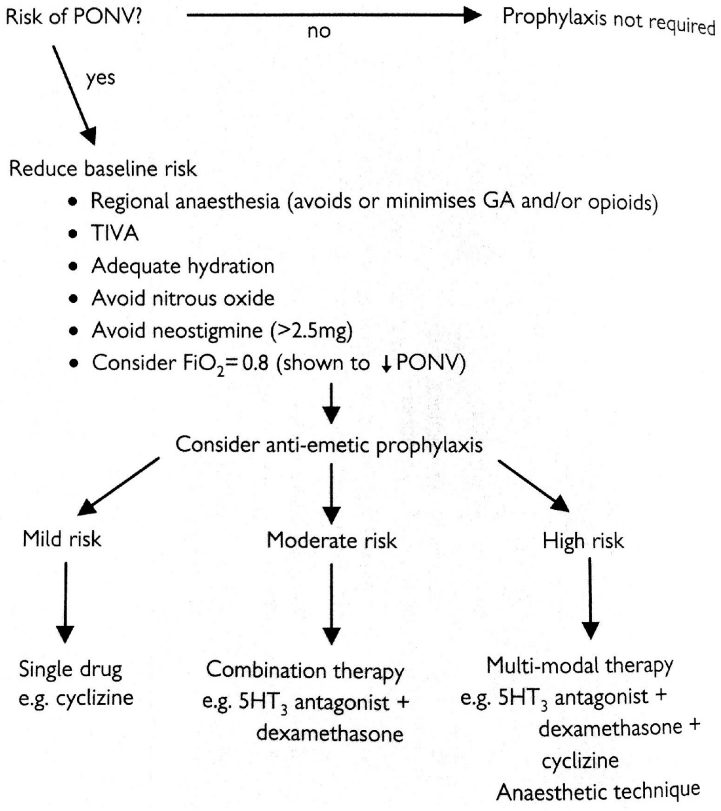
[use a score predictor]

- Patient:
    - Age:
        - ↑children:adult
        - >50 = ↓ risk
        - Female = x3 risk
        - Previous PONV or motion sickness = x2-3 risk
        - Smoker = ↓ 0.6% risk
    - Surgical - high risk procedures = breast, strabismus repair, ENT, gynae, laprascopic, laparotomy, craniotomy (post fossa), genitourinary, shoulder surgery
    - Anaesthetic:
        - Premedication:
            - ↓risk = benzo & clonidine
            - ↑ risk = opiates
        - Type - GA x11 than regional
        - TIVA < volatile
        - Intraop drugs:
            - ↑risk =
                - opiods,
                - NO, volatiles,
                - induction agents of ketamine, etomidate, thio
                - Neostigmine - muscarininc effects on GI tract
            - ↓risk =
                - Propofol
                - Adequate IV hydration

Management

- Multi-modal approach
- Prophylaxis vs treatment is controversial
- High risk patients where PONV >33% ondansetron prophylaxis cost effective
- Combo Rx eg dex & ondansetron
- Look for surgical cause
- Start using different classes:
    - Anticholinergic eg hyoscine or scopoderm
    - Antihistamine - cyclizine
    - Antidopaminergic - prochlorperazine, metoclopramide, droperidol or haloperidol
    - 5HT3 antagonist
    - Steroid - dex

Flow Chart for PONV



1.12 Failure to Wake from Anaesthetic

Causes

1. Pharmacological
2. Metabolic
3. Hypothermia
4. Resp failure
5. Neurological
6. Uncommon

- Pharmacological:

- Benzo's:
  - Elderly
  - In OD
  - In combo with opiates ⟹ ↓resp drive ⟹ ↑CO2 ⟹ coma

  ↳ NB Midaz & alfentanil metabolised by same P450 iso-enzyme which can prolong action of both
- Opiods -
  - major side effects from:
    - Resp depression -

      ↳ opioids direct ↓central chemoreceptors to CO2 ⟹ ↑CO2
    - Direct sedation via opiod receptors
  - Note combination with other sedatives eg benzo's
  - Active metabolites esp in renal failure
- Neuromuscular blockade - mimicks unconsciousness:

- Drug interactions - (as table). Different mechanisms of action:
  - Interfering with Ca - causes Ach release
  - Electolyte disturbances ⟹ cell hyperpolarisation & prolonged block
- Hypothermia ⟹ ↓metabolism of NMBs
- Acidosis ⟹ donation of proton to tertiary amine ⟹ ↑affinity of NMB for receptors
- Deficiency of plasma cholinesterases ⟹ prolonged sux action

Interactions with non-depolarising muscle relaxants	
Drug Interactions	Volatile anaesthetic agents
	Aminoglycosides
	Lithium
	Diuretics
	Calcium channel antagonists
Metabolic Causes	Hypothermia
	Acidosis
	Hypokalaemia
	Hypermagnesaemia
Genetic	Myasthenia gravis
	Eaton Lambert/Myasthenic syndrome
Interactions with depolarising muscle relaxants	
Genetic	Succinylcholine apnoea
	Myotonic Dystrophy
Acquired acetylcholinesterase deficiency	Pregnancy
	Liver Disease
	Renal failure
	Cardiac failure
	Thyrotoxicosis
	Drugs (ecothiopate, ketamine, oral contraceptive pill (OCP), lidocaine, neostigmine, ester local anaesthetics)

- IV anaesthetic agents:
  - Bolus propofol doses terminated by redistribution
  - TIVA - context sensitive half life = time for effect site to ↓ by 50%
    ↳ this depends on length of infusion ie context
    - Need 80% reduction effect site conc before emergence
      ↳ eg 80% reduction in effect site after 2 hrs = 36min (x2 dose = 105min; ½ dose = 10min)
  - Time to wake effected by:
    - Context sensitive half life
    - Amount of drug
    - Other drugs administered
    - Patient factors
- Volatiles:
  - Emergence depends on pulmonary elimination of the drug
  - MACawake = 30% of MAC:
    - Iso 0.39%
    - Des 2.17%
    - Sevo 0.61%
  - Pulmon elimination determined by:
    - Alveolar vent - low vent = longer emergence
    - Blood-gas partition coefficient
      ↳ low coefficient = quicker
    - Dose (MAC-hours) - higher = longer emergence ie incr context sensitive half life

Metabolic

- Hypoglycaemia:
  - BSL <2.2
  - Effect categories:
    - Sympathetic response

        - Neuroglycopaenia
            - Confusion/abnormal behaviour
            - Seizure
            - Coma
    - Causes:
        - DM
        - Starvation
        - Alcohol consumption - impaired gluconeogenesis in starved pt with poor nutrition & energy reserves
- Hyperglycaemia:
    - Severe can prolong unconciousness
    - BSL >14 ⟹
        - osmotic diuresis & dehydration
        - Hyperosmolality & hyperviscocity ⟹ ↑VTE risk
    - DM micro & macrovascular disease ⟹ ↑chance intra-operative stroke
- Hyponatraemia:
    - Na level
        - <120 ⟹ confusion & irritability
        - <110 ⟹ seizure, coma, mortality
    - Causes:
        - SIADH - 2nd to:
            - Brain trauma
            - SAH
            - Drugs eg opioids, haloperidol, vasopressin
        - Cerebral salt wasting syndrome -
            - in brain injured pt
            - ANP secretion 2nd to intracranial pathology ⟹ salt loss at kidneys
        - TURP syndrome -
            - hypotonic glycine solution absorption
            - Pulmonary oedema
            - Cerebral oedema
- Hypernatraemia:
    - Uncommon postop
- Uraemia

Hypothermia

- <35 = confusion
- <30 = unconsciousness
- <24 = apnoea
- <18 = absent cerebral activity
- CVS effects:
    - ↓CO
    - ↑risk arrhythmia's

Respiratory Failure

- Causes:
    - Neurological ie ↓central drive:
        - Drug overdose
        - Intracranial pathology
        - COPD
        - Sleep apnoea
    - Pulmonary disease:

        - Dead space
        - PE
        - Atelectasis
        - Obstruction
        - Aspiration
        - Consolidation
        - ARDS
        - TRALI
    - Musculature:
        - Primary muscle problem
        - Metabolic imbalance
        - Obesity
        - Residual NMB
- Hypoxaemia:
    - ⟹ cerebral hypoxia ⟹ ↓cerebral function AND ↑ production of:
        - Lactic acid
        - Free radicals
        - Intracellular metabolites
        ↳ ∴ ⟹ cell death
- Hypercapnia:
    - Central chemoreceptors ⟹ ↑resp stim to a point THEN ⟹ ↓ing resp stim & ↓RR
    - Hypoventilation ⟹ acidosis & ↑ing hypercapnic ⟹ cerebral VD ⟹ ↑ICP and 2nd brain injury

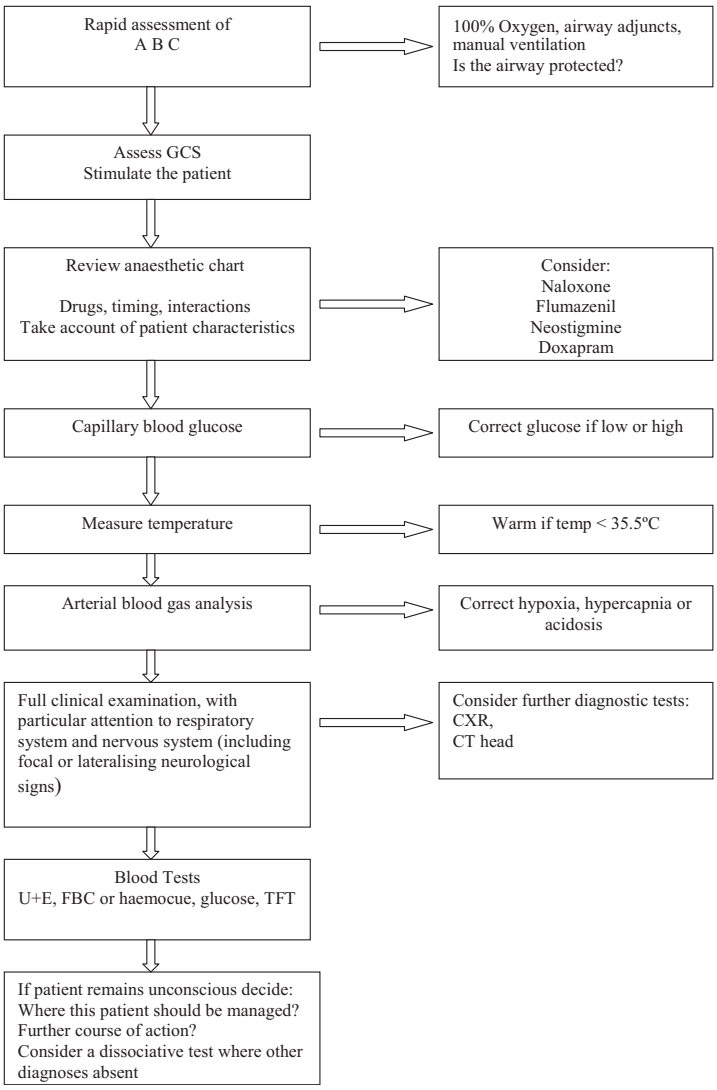
Neurological Causes

- Intraoperative cerebral insult causes are diverse:
    - Ischaemic brain cell death (most common)
        - Inadequate cerebral perfusion 2nd to low MAP
            ↳ (autoreg possible with MAP 60-160)
                ↳ watch for impaired auto reg in hypercapnic/hypoxic/↑metabolism
        - haemorrhage
        - Thrombosis
        - Infarct
    - cerebral hypoxaemia:
        - Prolonged seizure (masked by NMB)
        - Air embolism
    - Intracranial LA toxicity
- Must try and minimise 2nd brain injury by close bp monitoring & strict targets

Uncommon Causes

- Central anticholinergic syndrome:
    - Less common with newer agents
    - Central - irritation, delerium, stupor, coma
    - Peripheral - tachy, blurred vision, dry mouth, urinary retention
    - Reversed by a -stigmine which crosses the bbb
    - Caused by any anticholinergic drug
- Dissociative coma:
    - If organic & pharmacological causes excluded dissociative coma shld be considered
    - 2- 30 hours
- Thyroid failure:
    - Myxoedema coma -
    - Consider Ix thyroid
- LA toxicity

- Valproate toxicity



A stepwise approach to the patient with prolonged unconsciousness.

1.13 Post Op Cognitive Changes

Delirium

- = acute onset of disturbed mental function. Often short lived
- features:
  - Alteration of consciousness
  - Hallucinations
  - Fleeting delusions
  - Anxiety & distress
  - Diurnal variation
- Risk factors for development:
  - Age >65
  - Dementia
  - Functional impairment
  - Anaemia
  - Substance abuse
- 3 different motor types:
  - Hyperactive delirium (rare) = restless, irritable, agitated

    - Hypoactive delirium (71%) = lethargy, ↓activity, unawareness
    - Mixed (29%)
- Diagnosed using scoring systems eg CAM-ICU
- Causes & investigations - need thorough workup for reversible causes:
    - Labs - UEs, phosphate, Mg, Ca, VBGs
    - Infection screen
    - Medications:
        - Top 3 = anticholinergics, opioids, benzo's
        - Others eg dig, diuretics, steroids, warfarin
    - Substance abuse
    - Brain imaging
- Treatment:
    - Prevention -
        - optimise all physiological parameters eg CVS stability, o2, acid base status, electrolyte abnormalities
        - Orientation protocol - repeatedly to surroundings
        - Protected night time sleep
        - Early mobilisation
        - senses:
            - Vision - access to glasses/visual aids
            - Hearing - access to hearing devices
        - Avoid dehydration/hypovolaemia
        - Remove non essential lines & catheters eg urinary catheters
    - Drugs:
        - Haloperidol (better than benzo's & respiridone):
            - Initial: 1-2mg IV/PO/IM
            - Maintenance: 0.25-0.5 IV/PO/IM 4hourly
              ↳can double doses if severe agitation
    - Specific circumstances:
        - Delirium 2nd to substance withdrawal:
            - Down taper dose rather than stopping
            - Alpha 2 agonist eg clonidine
        - Central anticholinergic syndrome - dramatic delirium (hypo or hyper)
            - Use physostigmine 10-30mcg/kg

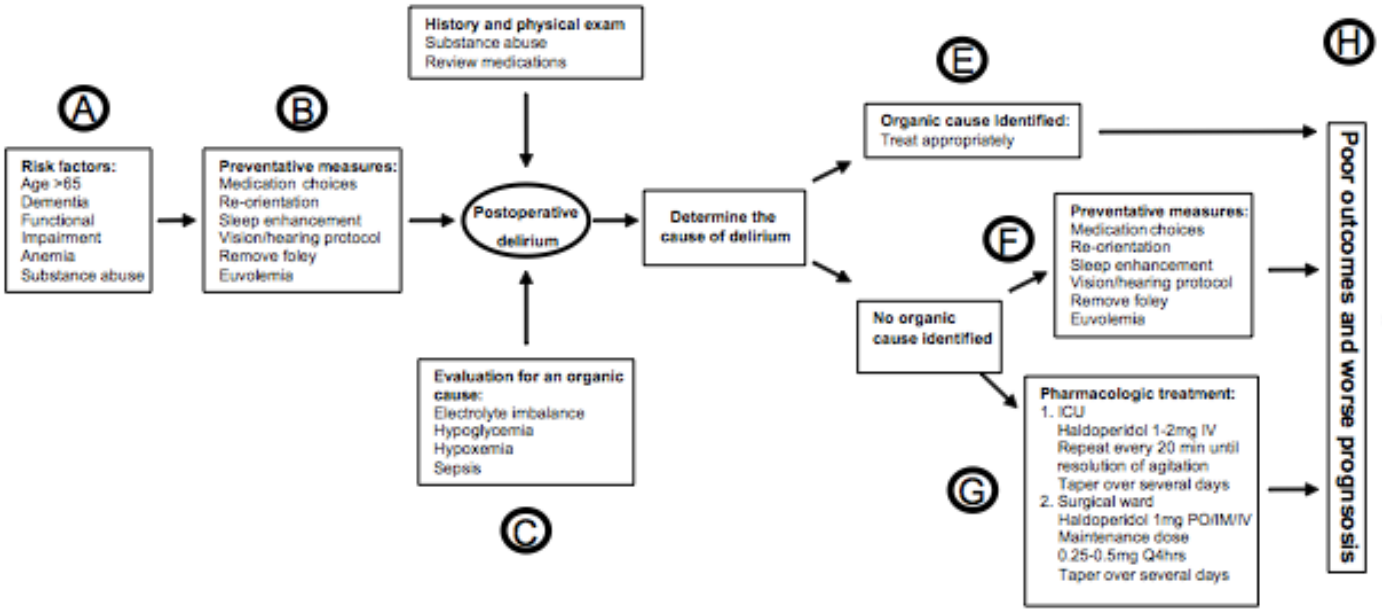


Figure 1 Postoperative delirium in the elderly – A diagnostic and treatment algorithm.

Dementia

- Defined as:
  - series of chronic organic brain syndromes with irreversible pathology
  - Global deterioration of cognitive function without clouding of consciousness
- Frequent misdiagnosis of delirium vs dementia. Both can occur together
- Many causes of dementia assoc failure cholinergic transmission
  - ↳ ∴ anticholinesterases can be used to ↑cognitive function

Postop Cognitive Dysfunction

- Definitions:
  - = deterioration in formal neuropsychological testing that would be expected in <3.5% of controls
    - ↳ doesnt define clinical features or severity
  - Disorder of thought processes which effect memory, comprehension, attention
- Difficult trial to do
- 1 study 1200 >60yrs old incidence of POCD:
  - 25% at week 1
  - 10% at 3 months
  - ↑incidence in age: 33% of 80+ group
- Known causes:

Table 2 Predisposing factors for POCD

Early POCD
Increasing age
General rather than regional anaesthesia
Increasing duration of anaesthesia
Respiratory complication
Lower level of education
Re-operation
Postoperative infection
Prolonged POCD (months postoperatively)
Increasing age only

- Theorised causes:
  - multiple emboli - especially following bypass
  - Periop physiological disturbances - eg

    - Hyponatraemia
    - Hypoxaemia/hypotension - although no evidence to support this
  - Pre-existing cog impairement - ↑risk with pre-existing issues

Conduct of Anaesthesia to ↓POCD

- Regional vs GA:
  - POCD incidence in 1st week: regional (12.7%) vs GA (21.2%)
    ↳ but difference does not persist at 3 months
  - Overall no difference in POCD between regional & GA
    ↳ but early differences may have large effect on recovery/length of stay/mobility

2.1.3 Pain Medicine

1.1 Pain Definitions

- Pain = an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
- Duration of pain defines acute (<30d - 6months) ⟹ subacute (1-6months) ⟹ chronic (>6-12months)
  ↳ arbitrary lengths

1.2 Basic Pain History

- SOCRATES:
  - Site
  - Onset
  - Character
  - Radiation
  - Associations
  - Timing
  - Exacerbating/Relieving factors
  - Severity

1.3 Multimodal & Pre-emptive Analgesia

Multimodal Analgesia

- =use of number of drugs/analgesics/adjuvants in combo to achieve best pain relief possible
- Pain complex construct with sophisticated transmission pathways through nervous system
- Main targets of modulating pain transmission:
  - Peripheral receptors:
    - LA's
    - NSAIDs
  - ascending pathways
    - Opiates
    - NSAIDs
    - NMDA receptor antagonists
    - gabapentinoids
  - Descending pathways
    - Tramadol
    - Clonidine
    - 5HT3 antagonists

    - Central perception
        - Opioids
        - paracetamol
- Combination of drugs means can reduce total dose of any one drug

Pre-emptive Analgesia

- Transmission of pain signals evoked by tissue damage leads to sensitisation of complex peripheral & central pain pathways
- Pre-emptive analgesia given before surgery aims to limit this sensitisation
- Theory that preventing cascade of sensitisation will limit subsequent doses of analgesia
- Theory holds for nociceptive stimuli associated with tissue damage
    ↳ this leads to
        - Peripheral (nociceptors) sensitisation - by inflam response - substance P/prostaglandins/ serotonin/bradykinin/histamine
        - Central sensitisation - by sustained afferent activation & upregulation of transmission ⟹ 'pain memory'
- Drugs & evidence:
    - Opioids - no evidence for pre-emptive
    - Ketamine - no evidence
    - Epidural -
        - single shot - some evidence reduction in analgesic demand postop
        - Continuous - no change post op analgesic demand
    - Caudal block - no evidence
    - Peripheral LA's:
        - Pre-op incisional LA - no evidence compared to post op LA infiltration
        - Nerve blocks - very limited evidence
- Pre-emptive analgesia & chronic pain:
    - 1 trial pre vs post incisional treatment showed sig ↓ chronic pain at 6months
- Summary: limited evidence to support pre-emptive analgesia at all but limited side effects & good scientific rationale

1.4 Analgesic Agents

Opioids

Morphine

MOA

- still not entirely clear
- diff actions at diff levels:
    - spinal cord level:
        - stim opioid receptors ⟹ ↓release of substance P from dorsal horn neurons ⟹ ↓afferent transmission of pain
    - supraspinal levels:
        - opioid receptors widely distributed in CNS esp limbic, thalamus, hypothalamus, midbrain
            ↳ ⟹ altered perception of pain

Opioid Receptors

- receptors where endogenous opioid peptides function (enkephalins & endorphins)
- action at these receptors classified:
    - agonists – natural or synthetic
    - antagonists
    - partial agnoists eg buprenorphine – less than max effect at mu receptors

- opioid receptors are GPCRs. Activation ⇒
  - inhibit adenylate cyclase ⇒↓cAMP levels
  - ↑opening K channels ⇒ ↑K out
  - ↓opening of Ca channels ⇒ ↓Ca in

  ↳∴ overall effect ↓neuronal excitability & ↓release of excitatory pain transmitters
- tolerance due to:
  - loss inhibitory functions
  - ↑excitatory signalling
- withdrawal due to rebound ↑cAMP levels via delta opioid receptors
- recptors:
  - μ (mu): (endogenous = B endorphins)
    - strong agonists – morphine & fentanyl
    - partial agonist – buprenorphine
    - weak agonist – pethidine
    - response:
      - supraspinal analgesia & euphoria
      - resp depression & sedation
      - constipation
      - Miosis
      - bradycardia
      - dependance
  - κ (kappa): (endogenous = dynorphins)
    - agonist – morphine
    - little/no acivity – methadone, pethidine
    - response:
      - spinal & periph analgesia
      - resp depression & sedation
      - dysphoria
      - miosis
  - δ (delta):
    - agonist – (endogenous enkephalins)
    - response:
      - spinal analgesia
      - resp depression & constipation
      - rebound in withdrawal
  - σ (sigma):
    - stim by partial agonists eg buprenorphine
    - only –ve response: dysphoria, hallucinations, confusion
- receptor summary:
  - analgesia & constipation assoc with all three
  - euphoria = μ
  - dysphoria = κ & δ

Agonists & Antagonists of Receptors

- agonist analgesics =
  - morphine, pethidine
  - activate μ & κ
- partial agonists =

  - buprenorphine
  - only activate 1 receptor & minimal effects at others
  - may induce undesirable σ receptor
- antagonists – naloxone & naltrexone antagonise all receptors

Pharmacokinetics

- generally not well absorbed
- low & variable bioavailabilty due to extensive 1st pass metab in liver
- in IV dosing remains variable plasma conc, rates of metab & elim
- morphine protein bound (35%)
- main metabolites of morphine:
  - morphine-6-glucuronide (M6G)
  - morphine-3-glucuronide (M3G)
- wide volume of distribution
- small fraction cross bbb
- excreted :
  - primarily by kidneys
  - 10% enterhepatic circulation ⇒ prolonging half life
- mean elim half life 2-3hrs
- onset of action:
  - morphine = hydrophilic ∴ only slow entry to CNS
  - fentanyl = highly lipophillic ∴ rapid onset & short duration action
    ↳can also give transdermally
- liver damage:
  - may accumulate active drug
  - sensitive to depressant effects of drug
  - pethidine ⇒ toxic metabolite norpethidine may ⇒ seizures
  - methadone may be safer in liver disease
- renal disease:
  - extend half life of opioids excreted in an active form ⇒ resp depression
    ↳eg methadone, pethidine, M6G

Equivalent Dosing

- 30mg oral morphine = 10mg IV

Uses

- CNS effects:
  - analgesia
  - suppression cough reflex
  - suppression resp centre
  - sedation & sleep
  - euphoria
  - dysphoria – hallucinations & nightmares
  - miosis – pinpoint pupils
  - N&V via CTZ
  - prolongation of labour
  - ↓bp & bradycardia in large doses via medulla
  - tolerance & dependence via μ receptors

- PNS effects:
  - GIT effects: ↓motility & ↑smooth mm tone ⇒ constipation
    ↳loperamide = weak opioid
  - spasm of smooth mm ⇒ delayed gastric emptying, bilary colic, urinary retention
  - suppression of some spinal reflexs
  - release of histamine ⇒ bronchoconstriction & severe itching

Adverse Reactions

- main incl:
  - resp depression
  - excessive sedation
  - dysphoria
  - constipation
  - N&V
  - tolerance & dependence
    ↳tolerance to dosing but no tolerance to SEs

Cautions/Contraindications

- elderly & infant <1 – dose needs reduced due to ↑CNS sensitivity & ↓ed clearance
- hypovolaemic pts – IM absorb ↓ed
- avoid in:
  - acute resp depression
  - acute alcoholism
  - HI
- caution in:
  - acute asthma
  - COPD
  - elevated ICP – morphine small ↑ICP
  - pancreatitis/bilary colic
- Rx in preg – risk of fetal withdrawal in labour

Interactions

- alcohol or other CNS depressants –
  - additive effect on CNS
  - ↓RR
  - ↓bp
- buprenorphine given with full agonist:
  - additive effect on ↓RR if given concurrently with full agonist
  - ↓analgesic effect of full agonist
  - precipitate withdrawal symptoms
- MAOIs:
  - intensify opiod effects – esp tramadol & pethidine
  - risk of serotonin syndrome
- diltiazem, erythromycin, fluconazole:
  - inhibit metab of alfentanil ⇒ ↑conc
- rifampicin ⇒ ↑metab of morphine, codeine, & alfentanil

Dose

standard dose 10mg IV/IM; 30mg oral

Other Opiates

Codeine

- =prodrug of morphine
- metabolised to morphine & norcodeine; metabolites excreted in kidneys
- 5-10% of whites lack enzyme (CYP2D6) to metab codeine ∴ no analgesic effect
  ↳rapid metaboliser may reach toxic concs

Fentanyl

- potent opioid
- short duration of action
- good adverse effect profile ∴ popular in anaesthetics
  ↳↓ed constipation
- varies preparations of administration incl patch
- patch:
  - duration of action 3days ∴ not easily reversed
  - heat ⇒ ↑uptake of drug from patch
  - rash & itching from site
  - after 3days patches still contain 50% activity

Methadone

- duration of action 4-6hrs; but with repeated doses may extend to 72hrs

Tramadol

- centrally acting synthetic analgesic which not chemically related to opioids
- MOA:
  - agonist of μ receptors (<50% of action)
  - inhibit reuptake of NA & 5HT

  ↳∴ called opioid-SSRI analgesic
- used for mode-severe pain & neuropathic pain
- less effective than morphine
- prodrug which requires activation by liver metab (CYP2D)
  ↳∴ multiple interactions esp with drugs effect serotonin levels
- Excreted by kidney
- SEs: nausea, dizziness, HTN, seizures

Pethidine

- only IV/IM
- less effect than morphine on histamine release or to ↑smooth mm contraction
  ↳∴ good for acute asthma, bilary colic/pancreatitis
- has a toxic metabolite = norpethidine:
  - from liver metab
  - can accumulate ∴drug only suitable for short term
- MAOIs ⇒ severe SEs incl serotonin syndrome
- used highly in drug seekers

Oxycodone

- synthetic opioid x10 more powerful than codeine
- well absorb rectal mucosa if required

Heroin

- =prodrug rapidly metabolised to morphine on administration

is more lipophilic than morphine ∴ greater CNS penetration ⇒ 'rush'

Paracetamol

- safer than aspirin because:
  - adverse effects & allergic reactions rare with therapeutic doses
  - low risk gastric upset
  - plasma protein binding negligible ∴ no displacement & less drug interactions
  - no sig drug interactions eg can take concurrently with anticoagulants
  - safe in children – no Reye's syndrome
  - safe in preg & lactation

MOA

- inhibition of some COX isoenzymes ⇒ ↓PGs at site of injury
- exact MOA are not clear
- does inhibit COX in some tissues in some species
- ??acts as prodrug with one of its active metabolites activating cannabinoid receptors in CNS

Pharmacokinetics

- orally – rapidly absorbed – peak plasma 15-60mins
- elim half life 1-3hrs
- metabolised in liver:
  - norm pathway: metabolised to glucuronide & sulfate derivatives
  - high dose/toxic pathway:
    - saturation of normal pathway
    - metabolised to benzoquinone intermediates (BQI)
    - BQI has 2 pathways of metab depending on available glutathione:
      - enough glutathione ⇒ paracetamol-mercapturic acid derivative (non toxic)
      - depleted glutathione ⇒ formation protein derivatives, lipid perioxidation, oxidative stress ⇒ liver cell death

↳N acetylcysteine is a synthetic analogue of glutathione

Uses

- effective
  - antipyrexic
  - analgesic
- very limited anti-inflammatory

Adverse Reactions

- rare at normal levels
- nausea & rash have been reported
- overdose can lead to serious liver/renal damage

NSAIDs

MOA

Analgesic

- inhibition of COX isoenzymes ⇒ ↓breakdown of arachidonc acid ⇒ ↓PGs, ↓prostacyclins & ↓Thromboxane A2 at site of injury
- PGs sensitise nociceptors to actions of bradykinin & other pain mediators
- COX1 & COX2 catalyse synthesis of PGs involved in pain
  ↳also GI side effects of which COX2 shows less of
- analgesic action is peripheral & central

- Opiod sparing effect of 20-40%

Antipyrexic

- inhibition of PG synthesis in hypothalamus

Side Effects

- GI side effects:
  - due to ↓synthesis of mucoprotective PGs by systemically absorbed NSAIDs
  - incl: dyspepsia, N&V, gastritis, constipation/diarrhoea
- renal damage:
  - ↓ed vasodilator PGs
  - esp in elderly on long acting NSAIDs
- asthma
- skin reaction – uritcaria
- Na retention ⇒ heart failure & HTN

Comparison of NSAIDs and COX-2

	NSAIDs	COX-2
Efficacy for moderate to severe acute pain (numbers needed to treat—NNT)	Diclofenac 50mg (2.3) Ibuprofen 400mg (2.4) Ketorolac 10mg (2.6)	Celecoxib 200mg (4.5) Parecoxib 20mg (3.0) Valdecoxib 20mg (1.7)
Renal function	Can affect renal function postoperatively	Similar adverse effects on renal function
Gastrointestinal	Acute gastroduodenal damage and bleeding can occur. Risk increased with higher doses, history of GI ulceration, long-term use, and elderly	Less clinically significant peptic ulceration than NSAIDs (VIGOR and CLASS studies)
Platelet function	Inhibit platelet function but do not significantly increase surgical blood loss in normal patients. Associated with higher incidence of post-tonsillectomy haemorrhage	Do not impair platelet function
Aspirin-exacerbated respiratory disease	10–15% of asthmatics affected when given aspirin. Cross-sensitivity with NSAIDs	Do not produce bronchospasm
Bone healing	Impaired in animal models. No good evidence that clinically important	Similar to NSAIDs

Ketamine

- has certain benefits over other GA/analgesic agents:
  - bronchodilator
  - minimal cardiovascular depression
  - minimal resp depression
  - amnesia

MOA

- non competitive NMDA receptor antagonist:
  - receptor opens in response to glutamate
  - ketamine blocks channel ⇒ analgesic effects
- at high doses: also binds to opioid μ (mu) & σ (sigma) receptors
- also effects on other receptors:
  - potent D2 partial agonist
  - dopamine reuptake inhibitor
  - NA reuptake inhibitor
- produces dissociative anaesthesia

↳MOA of these hypnotic effects under debate

Pharmacokinetics

- onset of anaesthesia 15-30sec
- recovery time 15-30min
- metab in liver
- frequent dosing ⇒ tolerance due to induction of hepatic enzymes

Uses

- GA – induction & maintenance
- analgesia

Side Effects

- tachycardia & HT
- ↑ICP
- ↑intraocular pressure
- hypersalivation
- laryngospasm
- hallucinations – thus often also give benzodiazepines. Worse in adults
- re-emergence phenomena – disagreeable dreams, hallucination on awakening

Cautions/Contraindications

- caution in:
  - CVS disease- although tends to maintain or ↑CO
- crosses placenta:

Interactions

- additive effect with other sedatives incl benxo's, barbituates, opiates, alcohol

Dose

- induction dose 1-2mg/kg
- paeds dose for minor procedure 2-2.5mg/kg IM (0.5mg-1mg/kg IV)

1.6 Principles of Acute Pain Management (PS41)

Principles

- Adverse physiological & psychological effects result from unrelieved severe acute pain
- Effective post op pain relief will:
  - ↓morbidity
  - ↓hosp length of stay

    - ↓chronic pain
- Requiring tailoring of Rx regimes to individual patients
- Requires close liaison with all staff & education of patient & carer
- Effective acute pain Rx depends on formal protocols & guidelines at local institutions & quality assurance programs to evaluate effectiveness of these regimes
- Special pt groups:
    - Children
    - Pregnant
    - Elderly
    - Indigenous peoples
    - OSA pts
    - Liver & renal disease
    - Opioid tolerant pts/substance abuse patients
    - Cognitive behavioural pts

Assessment of Analgesic Efficacy

- Regular assessment of pt needing including checking for side effects
- Patients should be involved in self assessment of their pain including effects of different interventions
- Pain should be assessed at rest & during activity
- Pain which suddenly increasing may signal development of new medical/surg/psych diagnosis
- All side effects & complications should be recorded

Pharmacological Therapies

- Agents to use:
    - Opioids
    - NSAIDs
    - La's
    - Adjuvants:
        - Antidepressants
        - Anticonvulsants
        - Membrane stabilisers
- Use careful titration & individualisation of dosing
- Multimodal analgesia (use of diff classes) is good
- Specialist routes require expertise:
    - PCA
    - Epidural & intra-thecal
    - Regional LA's
    - Continuos infusions opioids/LA's/ketamine

Non Pharmacological

- Complimentary:
    - Psych interventions
    - Acupunture
    - TENS
    - Physio

Acute Pain Service Guidelines

- For all patients with complex medical/psych problems:
- Features:
    - Med personal: anaesthetists & specialist nurses
    - Liaison with MDT

    - Develop protocols & guidelines for Rx & monitoring
    - Review all patients at least daily
    - Consultation service for pts with acute/acute on chronic pain
    - After hours service
    - Discharge analgesia plans
    - Research
    - Education

1.7 Management of pain in Recovery

- Nurse controlled IV opiate titration

1.8 Pain Management plan for Day Surgery Procedures

Summary

- Patient education - starting at pre-assessment
- Written information about analgesics & the regimen eg:
    - Description of drug
    - When taken
    - For how long
    - Side effects
    - Who to contact if problems
- Detailed drug history and allergies:
- Pain assessment:
    - Verbal rating - none, mild, mod, severe
    - Visual analogue - <3cm acceptable
- Peri-operative techniques:
    - Early planning - from pre-assessment
    - Multimodal:
        - NSAIDs - always if able
        - Opiates - use shorter acting if able (if using morphine use <0.1mg/kg)
    - Regional blocks - bupivocaine max 2mg/kg
    - Spinal anaesthesia - time to mobilisation may be increased. Full recovery prior to d/c
- Paeds patients:
    - Pain assessment harder in young children
    - Paracetamol 90mg/kg/day
    - Distraction therapy

1.9 & 1.12 PCA's & Opioid Infusions

- PCA helps overcome the marked variability in response to post op opioids
- Patients titrate their own plasma opioid concentration into the therapeutic window:
    - > minimum effective analgesic concentration (MEAC)
    - < minimum toxic concentration (MTC)
- Safety of PCA is that if excessive doses of opioid given pt will become sedated and thus stop pressing button

PCA Regimes

- Most common is morphine although greater incidence of pruritis than other fentanyl
- Regime:

    - No loading dose - pts should be comfortable before starting PCA
    - Bolus - morphine 1g, fentanyl 10mcg, tramadol 10mg
    - Concentration - standardised to institution
    - Lock out - 5mins
    - Background infusion - use with extreme caution
    - Dose limit - often not used. Eg 30mg morphine in 4hrs
- Paeds regime - local protocols
- PCA been shown to be effective in as low as 6yr olds

Complications

- Equipment malfunction:
    - Battery failure
    - Electricity surges
    - Failure of anti-reflux vlave led to resp depression
- Operator error:
    - Programming errors
    - Drug errors
- Side effects to opiates:
    - N&V
    - Pruritis
    - Sedation
    - Resp depression
    - Urinary retention
    - Confusion
    - Constipations
    - Hypotension
- Continuous infusions very dangerous and should be used very sparingly due to context sensitive half live of drugs

Troubleshooting

- N&V:
    - Add antiemetic to bag eg ondansetron, cyclizine, haloperidol
    - Prescribe reg antiemetic
    - Change opioid
- Prutitis:
    - Ondansetron
    - Anti-histamine
    - Change opioid
- Breakthrough pain:
    - Multi-modal analgesia
    - Incr bolus dose
    - (consider background infusion)
- Resp depression:
    - Best indicator of resp depression is sedation level
        - 0 = wide awake
        - 1= easy to rouse (mild drowsy)
        - 2= easy to rouse (mod drowsy)
        - 3= difficult to rouse
        - S = asleep but easy to rouse
    - Decrease dosing
    - Use titrated naloxone if required

1.9 Regional Anaesthesia Risks & complications

- Major risks:
  - Direct trauma to nerve - needle/suture/instrument
  - Neurotoxicity of LA's
  - Ischaemia from compression (haematoma/abscess)
  - Infection
  - Unknown cause

Direct Trauma

- Good technique & anatomy knowledge
- Use short bevelled needle
- Use ultrasound (although nerve stim though to be no better)
- If severe resistance or pain on injection ≈ stop. Suggests intraneural or intrafasicular injection
- Symptoms within hours = extra/intra-neural haematoma or oedema
- Symptoms within weeks = tissue reaction or scar formation

LA Toxicity

- High plasma levels from:
  - Drug overdose
  - Direct IV injection
  - Rapid absorption from highly vascular area
  - Cumulative effect from multiple injections
- Thus consider:
  - Site & vascularity of injection
  - Acidosis, hypoxia, hypercarbia all potentiate =ve ionotropic/chronotropic effects of LA
  - Keep to max doses

Maximum recommended doses of common agents (BNF)

Agent	Maximum recommended doses	Maximum recommended doses with vasoconstrictor
Bupivacaine	2mg/kg	2mg/kg
Levobupivacaine	2mg/kg	2mg/kg
Ropivacaine	3mg/kg	3mg/kg
Lidocaine	3mg/kg	6mg/kg
Prilocaine	6mg/kg	8mg/kg
Cocaine	1.5–3mg/kg	

Signs of toxicity

- Mild:
  - Perioral tingling
  - Metallic taste
  - Tinnitus
  - Visual disturbance
  - Slurred speech
- Moderate:

    - Altered consciousness
    - Seizures
    - Coma
- Fatal:
    - Cardiovascular collapse
    - Resp arrest

Treatment of Toxicty

- Stop injection
- ABC
- Mild symptoms - consider midaz or small doses of propofol to ↑seizure threshold
  ↳ NB hypoventilation & acidosis will worsen toxicity
- Moderate to severe toxicity:
    - Conventional therapies to Rx hypotension/tachy/bradycardia
    - Early use of 20% intralipid:
        - 1.5ml/kg bolus over 1min
        - Start infusion 15ml/kg/hr
        - @5mins: if CVS still unstable
            - repeat bolus (can do total of 3 boluses)
            - Double infusion rate
    - Continue CPR - arrythmias may be very refractory to treatment
- Methaemoglobinaemia Prilocaine toxicity
    - Specific to prilocaine
    - Hb oxidated to metHb by o-toluidine
    - O-toluidine formed by metabolism of prilocaine in liver
      ↳ in high doses >600mg
    - MetHb has ↓O2 carrying capacity ⟹ cyanosis
    - ∴ avoid prilocaine in pregnancy and anaemia
    - Rx: methylene blue 1mg/kg IV

1.10 Actue Pain patients who are Previously opioid Dependent

- Tolerance = ↓sensitivity to opioids to same dose
- Dependence = physiological phenomenon characterised by withdrawal reaction when drug is withdrawn or antagonist administered
- Addiction = pattern of drug abuse characterised by compulsive use to experience a psychological effect & to avoid withdrawal reaction
- Pseudoaddiction = iatrogenic drug seeking behaviour normally due to under-treatment of acute pain by physician
- Signs of withdrawal:
    - Yawning
    - Sweating
    - Anxiety
    - Rhinorrhoea
    - Lacrimation
    - Tachy
    - Hypertension
    - Diarrhoea
    - N&V
    - Abdo pain

    - Cramps
- Symptoms peak at 36-72hrs
- Aims of treatment:
    - Provide analgesia
    - Prevent opioid withdrawal
    - Manage abnormal behaviour
- PCA settings may need to replace usual opioid dose eg ↑bolus dose or background infusion
- Aim to d/c pt on no more opioid than was on at admission
- Dose reduction of 20-25% every day towards pre-admission opioid will avoid withdrawal
- Oral or s/c clonidine 50mcg tds can be used to Rx opioid withdrawal
- Objective assessment of function ie ability to cough better guide than pain scores
- Use regional techniques wherever possible

1.13 Management of hypotension assoc with a central neuraxial block

- Order of Rx:
    - Volume resuscitation with IV fluids
    - Posture - legs up if possible
    - Consider wide bore access
    - Vasopressors - especially if unresponsive to volume bolus

2.1.4 Perioperative Medicine

PO 1.1 ASA status

- American Society of Anaesthesiologists:
    - 1 = healthy with no systemic disease
    - 2 = Mild to mod systemic disease
    - 3 = severe systemic disease imposing functional limitation on patient
    - 4 = severe disease with constant threat to life
    - 5 = moribund pt who not expected to survive ± operation
    - 6 = brainstem dead pt for organ donation
- Incidence of death in ASA
    - 1 & 2 = 1:100,000
    - 3 & 4 ± emergency surgery = ↑x5-10 risk

PO 1.2 & 1.3 Functional Assessment

- Exercise tolerance (cardiovascular fitness)= major predictor of risk
- Physiological response to major surgery ⟹ ↑o2 demand by 40%
- Fitness defined by metabolic equivalents (METs)
- Scale defined by Duke Activity Status Index:
    - 1-3 METS = light activities:
        - 1 = Watching tv
        - 2 = strolling very slowly
        - 3 = walking at 4k/hr
    - 3 -6 METS = moderate intensity activities
        - 3 = Static bike very slowly
        - >4 = climbing a flight of stairs

    - 4 = leisure bicycle <10 mph
    - 4 = climbing flights of stairs,
  - >6 METS = vigorous activities
    - 7 = jogging
    - 8 = pushups, situps
    - 10 = rope jumping

Cardiopulmonary exercise testing (CPET)

- Risk of survival depend on:
  - Age
  - Sex
  - Organ dysfunction: brian, heart, kidney, periph artry disease
  - Fitness
- Fitness only variable not routinely quantitatively measured and documented
- CPET used to define resp & cardiac variables of pt
- Requirements for CPET:
  - Exercise machine
  - Computer controlled ramped ↑workload
  - Calibrated pneumotachograph to measure gas flow & composition
  - Continuous 12 lead ECG
  - Someone trained to perform and analyse results
- Survival correlates with:
  - Peak O2 consumption
  - Power
  - HR
  - Anaerobic threshold
  - O2 uptake slope
  - Oxygen pulse
  - HR recovery
- Early work showed anaerobic threshold to be most important factor:

Anaerobic threshold	Mortality rate		
	Test ECG: no ischaemia	Test ECG: ischaemia	Total
>11ml O_2/kg/min	0/107 (0%)	1/25 (4%)	1/132 (0.8%)
<11ml O_2/kg/min	2/36 (5.5%)	8/19 (43%)	10/55 (18%)
All	2/143 (1.4%)	9/44 (20%)	11/187 (6%)

- CPET helpful to provide:
  - Individual estimation of survival
  - Informed decision making
  - Peri-op management - HDU/ICU need
  - Risk reduction by guiding interventions
- Used as standard before AAA surgery & heart transplants

PO 1.4 Treatment of life threatening arrhythmias

- ….insert brady & tachy arrhythmia algorithms

PO 1.5 Perioperative Risk & Anaesthetic Implications

Respiratory Infection

Adult

- Current resp tract infections with:
  - Fever AND
  - Cough
  - ± chest signs

  ↳ should not have elective procedure 2nd to ↑risk post op resp complications
- Adult pts with coryza not at ↑risk unless :
  - have other chronic resp problems OR
  - Major abdo/thoracic surgery
- Laryngospasm more likely if recent URTI but currently asymptomatic

Paeds

- Pre-school kids 6-8 URTIs/yr
- 25% kids have chronic runny nose
- GA with concurrent URTI assoc ↑risk of:
  - Excess secretions
  - Airway obstruction
  - Laryngospasm
  - Bronchoconstriction

  ↳ risk x5 with LMA; x10 with intubation
- Children to postpone
  - Productive cough
  - Purulent sputum or nasal secretions
  - Fever
  - Constitutional symptoms eg D&V
- Child with mild URTI borderline decision:
  - Hx: if now post viral, apyrexial, no chest signs & systemically well = prob ok for surg even runny nose
- Length of time to postpone:
  - Significant URTI - postpone 2wks
  - LRTI - 4 weeks
  - Bronchiolitis - 6wks

COPD

- If element of reversibility of airflow obstruction then Rx as asthma
- BiPAP very helpful post op if needed

Preop Ax

- Exercise tolerance eg METs
- Rx all potential reversibility - consider trial oral pred/resp r/v
- Pulmon HTN & R vent failure possibility - optimise heart failure Rx

Ix

- Spirometry
- ABGs - if:
  - difficulty climbing 1 flight stairs
  - Cyanotic

    - Spo2 <95% on RA
    - Periph oedema
- CXR
- ECG

Anaesthesia

- Severe COPD ≈ likely post op NIV needed ≈ elective HDU/ICU admission
- Avoid ETT if able although pts with marked secretions may benefit from endotracheal toilet
- Vigilance for pneumothorax
- Avoid histamine releasing drugs
- Premed B agonists
- ↑risk bronchospasm - consider potent opiods/LA to cords
- Use short acting potent opiods if post op pain will allow

Post Op

- Extubate in sitting position

OSA

- Sleep apnoea syndrome = cessation of airflow for >10 seconds
- Develop hypoxaemix & resp arrest during REM sleep
- Hypoxia ⟹ restart of resp
- Symptoms:
    - Overweight snorers
    - Disturbed sleep
    - Excessive daytime drowsiness
    - Headache
- 2 types of sleep apnoea syndrome:
    - OSA 85%
    - Central apnoea 10% - loss of central drive
- Long term complications of undiagnosed apnoea's:
    - Systemic & pulmon HTN
    - RV hypertrophy ⟹ failure
- Pts at ↑risk peri-op airway obstruction & resp failure post drugs

PreOp Ax

- Undiagnosed in 80%
- Ask about daytime sleepiness & snoring from partner
- Ensure HTN & failure maximally managed
- Consider resp opinion if periph oedema & Spo2 <92%
- Bring own CPAP machine to hosp for op
- All children presenting for adenotonsillectomy should be considered to ± sleep apnoea

Ix

- FBC
- ECG - ?R heart strain ⟹ ECHO
- ABG baseline

Anaesthesia

- Avoid sedative premeds
- Anticipate intubation & BMV may be difficult
- Regionals good
- Short acting opiates if able

Post Op

- Extubate sitting
- ?HDU/ICU

- ?few hours of ventilation post op of benefit
- Aim for preop spo2
- Watch for CO2 retention

Heart Failure

- Commonest cause of admission to hosp in >65
- 50% 5 yr mortality
- Characteristics:
  - Decr ex tolerance & fatigue
  - Orthopnoea
  - SOB
  - Ventricular arrhythmias
- Uncontrolled failure & emergency laparotomy = morality of 20-30%

Medical Management

- Drugs:
  - Diuretics:
    - Spiro & ACEI ↓'s mortality if ECF <25%
    - Vasodilators - ACEI, AIIRB, nitrates
    - Bblockers - ↓arrhythmia's & ↓myocardial o2 demand
    - Inotropes - dig useful if concurrent atrial arrhythmia
    - Anticoags - indicated in:
      - Atrial arrhythmia
      - Intracardiac thrombus
      - LV aneurysm
      - Hx of VTE

PreOp

- Hx - any decompensating episodes last 6/12
- Optimise med management & continue meds
- Rx metabolic abnormalities
- Aggressive Rx of arrhythmias - esp AF

ECHO

- EF:
  - 60-80% = norm
  - 40-50 = mild
  - 30-40 = mod
  - <30 = severe

Anaesthesia

- If severe heart failure:
  - Dependant on preload for vent filling
  - Rely on sympathetic tone
  - Poorly tolerant of any change in physiology
  - Use regional techniques if able
- Give all anti-failure meds that day
- ACEI - resume as soon as poss post op. If >3days then resume at lower dose
- Decompensating pts may need inotropes or phosphodiesterase inhibitors
- Watch Uo carefully as renal perfusion and GFR will be borderline
- Good analgesia regime to avoid symp stresses of pain
- Low threshold for ICU admission

Arrhythmias

Sinus Brady

- Causes:
  - Drugs - BB's, dig, anticholinesterases, sux
  - Cardiogenic - MI, sick sinus
  - ↑ICP, hypothyroid, hypothermia
- Rx:
  - Stop surg stim
  - Antimuscarinic
  - Chronotropes - isoprenaline or adrenaline
    ↳ also consider glucagon

SVT/Nodal Re-entry

- Sinus massage
- Adenosine
- Bblockers - esmolol/metoprolol
- Ca channel blockers - verapamil can be useful if relapse post adenosine
  ↳ avoid co-use with BB's
- Amiodarone
- (avoid dig - facilitate accessory pathway and WPW

VT

- May be triggered intra-op by:
  - MI, hypoxia, hypotension
  - Fluid overload
  - Electrolyte imbalance
  - Ionotropes
- Rx:
  - Sync shock - 200-360J (approx 100% success)
  - If relapse use lignocaine or amiodarone
  - Lignocaine -
    - bolus 100mg (30-40% success)
    - Maintenance 4mg/min for 30min; 2mg/min 2 hr, then 1mg/min
  - Other drugs:
    - Amiodarone
    - Procainamide

Heart Block

- Bi/tri-fasicular block rarely progress to complete heart block during anaesthesia thus not normal to pace unless episode of syncope:
  - RBBB with L ant hemiblock = V1 RSR AND L axis dev (more common)
  - RBBB with L post hemiblock = R axis dev (non specific)
- 1st deg block ok
- 2nd degree block - consider need for pacing
- Intraoperative heart block:
  - Atropine - rarely effective but try
  - Isoprenaline
  - Transcutaneous/oesophageal/invasive pacing

Pacemakers

- Pacemaker codes:
  - 5 positions - 1st 3 antibrady functions and are always stated

    - Position 1 = chamber paced
        - O - none
        - V - ventricle
        - A - atrial
        - D - dual
    - Position 2 = sensing chamber - OVAD (as above)
    - Position 3 = response to sensing:
        - O - no action in response to sensing. ie will pace no matter what.
        - I - inhibit
        - D - dual
    - Position 4 - rate modulation:
        - O - none
        - P - simple program
        - M - multi-program
        - R - rate modulation
    - Position 5 - anti-tachy functions
        - O - none
        - P - pacing
        - S - shock
        - D - dual
- emergency mode = DOO
- ideal ICU mode = DDI
- ICD codes:
    - Pos 1 = shock chamber: OAVD
    - Pos 2 = chamber to which antitachycardia pacing is delivered: OAVD
    - Pos 3 = means of detection of tachy:
        - E - intracardiac electrogram
        - H - haemodynamic means
    - Pos 4 = 3-5 letter code for pacemaker function

Anaesthesia

- Preop battery check & function
- ECG to confirm function eg AV synchronicity, polarity of pacing, baseline rate
- Concern about electromagnetic interference
    ↳ diathermy - if a must - plate position so current flows away from pacemaker
- Bipolar diathermy is safe
- In emergency magnet over box ⟹ asynchronous vent pacing (VOO) on next cardiac cycle
    ↳ note if in severe heart failure loss of A-V synchrony may ⟹ ↓↓CO
        ↳ may need technician to help!

Venous Thromboembolism

- PE responsible for ≈ 10% hosp deaths
- Without prophylaxis 40-80% high risk pts will develop DVTs
- Incr VTE present 2nd to:
    - Hypercoagulable 2nd to surg/cancer/hormone therapy
    - Venous stasis
    - Interferenance with VR eg pregnancy, pelvic surg, pneumoperitoneum
    - Dehydration
    - ↓Cardiac output

Risk Factors

- Duration and type surg:

    - >30mins = high risk
    - Surg to abdo/pelvis/joint replacement
- Pts factors:
    - Hypercoagulable RFs eg prev DVT, thrombophilia
    - Obstetric eg preg, OCP
    - >40yrs
    - Obese
    - Vvs
- Assoc diseases:
    - Malignancy
    - Trauma
    - Heart disease
    - Sepsis
    - Haem diseases

↳ split into low, moderate, high risk

Prophylaxis

- Heparin ↓s incidence of fatal VTE by 66%
- LMWH:
    - Give 1800 so >12hrs prior to surg allowing neuraxial blocks
    - Check renal function and local dosing policy
    - Start post op
- Unfractionated heparin:
    - Bridging heparin in high risk. Local protocol
- Graduated compression stockings:
    - ↓DVT risk, but not PE risk
    - May be better with LMWH
    - Advisable for all laparoscopic procedures
- Intermittent pneumatic compression devices:
    - Compress leg 35-40mmHg for 10secs/min
    - As good as heparin in preventing DVT
- Warfarin - good evidence in ortho ops

Choice of Anaesthetic

- Regional is protective esp in LL joint replacement

OCP use & VTE

- OCP may ↑risk 3-4x VTE periop
- Risk may ↓longer been on OCP
- Progesterone only OCPs do not change risk
- Poor evidence means:
    - Decide on individual basis for people undertaking major operations and other individual RFs
    - Need to stop 4/52 prior to surg

HRT & VTE

- HRT ⟹ ↑risk VTE
- BNF suggests to stop HRT 4-6weeks before major surgery but balanced decision

Electrolyte Abnormalities

Acid-Base Abnormalities

Chronic Renal Impairment

- CRF = multisystem disease
- Renal failure when GFR <35
- Dialysis usually when <15
- ESRF GFR <5
- Main causes:
  - DM 30%
  - HTN 24%
  - GN 17%
  - Unknown 20%

Preoperative

- Check for HTN/DM/anaemia/IHD
  ↳ consider ECHO - higher risk valve disease & LVF
- Type of dialysis
- Residual UO
- Fluid status: hyper vs hypo-volaemic
- Allow 4-6hr post haemodialysis before surg
- Indications for urgent dialysis:
  - Hyperkalaemia
  - Fluid overload
  - Acute acidosis
  - Symptomatic uraemia
- Plan for ICU

Ix's

- FBC: aim 80-100
- K - aim <6
- Coags:
  - ↓platelets - consider cryo or DDAVP

PeriOp Care

- vessels:
  - Avoid fistula arm for all lines/monitoring
  - Cannulate back of hand to save other vessels
  - Use A lines sparingly - and radial only
- Fluids:
  - Aim for normovolaemia
  - Avoid hypotension
  - Use NaCl 0.9%.avoid any fluid with K+
  - Use CVL line if big fluid shifts expected
- Sux - ↑'s serum K by 0.5mmol.
  ↳ ↑K also worsened by acidosis so avoid hypovent & hypercarbia
- Delayed gastric emptying likely. But reserve RSI for normal indications
- Careful aseptic technique for all lines - immunosupressed
- Universal precautions - Hep B & C are common

Post Op

- Liaise with renal unit for next dialysis
- Close fluid balance - if oliguric:
  - Hourly fluids to replace losses + 30mls/hr for insensible losses
- Avoid nephrotoxics
- Avoid hypotension

Drugs in CRF

- Loading doses unchanged, maintenance doses ↓ed
- Hypoalbuminaemia & acidoses ⟹ ↑active available drugs which norm protein bound eg induction agents
- Drug classes:
  - analgesics:
    - Fentanyl - inactive metabolites but still may accumulate if prolonged use
    - Remi & alfentanyl fine
    - Tramadol has active metabolites
  - Induction agents: ↓by 30% dosage
  - Volatiles - no change
  - Muscle relaxants:
    - Sux as above
    - Plasma cholinesterase unchanged
    - Avoid vec & roc infusions
    - Neo/glyco excretion is prolonged
  - La's:
    - ↓max dose by 25%
    - Consider ↑ed risk of spinal haemorrhage & haematoma with neuraxial blocks

Steroid Dependance

- Endogenous cortisol (hydrocortisone) = 25-30mg/24 in circadian pattern
- During stress = 75-100mg/day
  ↳ can remain elevated up to 72hr following major surgery
- Pred (vs hydrocortisone):
  - X3-4 more potent in glucocorticoid & anti inflam
  - Much less active mineralocortocoid
    ↳ thus why hydrocort often used peri-op
- Expect HPA suppression if taking >10mg pred daily
- HPA suppression Ix'ed by short Synacthen test
- Fludrocortisone:
  - Oral tab only
  - Withhold if being given IV hydrocort

Rx Regime

- <10mg - no change
- >10mg:
  - Minor surg (eg hernia)- routine steroid that day or hydrocort 25mg IV @ induction
  - Mod surg (eg hysterectomy) -
    - routine pre op steroid
    - Hydrocort 25mg Iv @ induction AND 6hrly for 24hrs
  - Major surg -
    - Routine preop steroid
    - Hydrocort 25mg @ induction and then 6hrly for 48-72hrs
- High dose immunosupression:
  - Convert usual oral steroid dose to hydrocort, then revert back to oral dose when able
- If taking steroids until <3months ago ⟹ Rx as if on steroids

TIA/Strokes

- Causes of death in developed world = heart disease > Ca > stroke

TIA

- Causes by emobolism of platelet & fibrin from atherosclerotic plaques
- Risk of stroke post TIA = 5%/yr with mortality 30%/episode
- Ix with doppler studies in defined service
- Should delay all but emerg surgery for workup
- Indications ref for carotid surgery:
  - >80% stenosis
  - Ragged plaque

Stroke

- Assoc with:
  - HTN
  - DM
  - Obesity
  - Smoking
  - ↑age
- Look for renal & herat disease

Timing of operation

- Op within 6 wks of stroke ⟹ ↑x20 risk post-op stroke
- Hemiplegia <6-9months ⟹ ↑ed K response to sux
  - ↳ ∴ wait 3-6 months before elective surg

PreOp Ax

- Aim for stable bp & BSL
- Bridging LMWH is required
- Document carefully neuro baseline - allows Ax new lesions
- Consider VBI symptoms - can they extend neck without any symptoms

Anaesthesia

- Cont antiHTN's (except ACEIs)
- Maintain normotension:
  - Pressors
  - Opiods/labetalol/esmolol/GTN
- Neutral neck position
- Cover intubation with strong opiod to prevent HTN spikes
- Avoid hypocarbia ⟹ ↓CPP
- Close examination in PACU

Plasma cholinesterase Deficiency

- Aka pseudo-cholineterase deficiency
- Capable of hydrolysing variety of esters
- No physiological function found for enzyme yet
- Synthesized in liver, half life 5-12d
- Metabolised 70% 100mg sux <1min
- Several variant genes:
  - Atypical -
    - heterozygotes no issue unless concurrent illness
    - Homozygous - 1:3000 - paralyse for 2-3hrs
  - Silent gene:
    - Heterozygote - mild prolongation sux
    - Homozygote - prolonged apnoea - 3-4 hrs but upto 24hrs
  - Flouride resistant gene:

        - Homozygote very rare - 1:150000, moderatly sensitive to sux
    - Other variants also seen with varying effects
- Can lab test for activity
- Also see ↓plasma cholinesterase activity in:
    - Hepatic/renal disease/burns/malignancy/malnutrition
    - Drug interactions:
        - Esmolol, MAOI, MTX - all compete for metabolism ∴ ⟹ prolonged sux action
        - Anticholinestareases - inhibit plasma cholinesterase as well
    - Pregnancy - ↓activity by 25%
    - Plasmapheresis & bypass

Diagnosis

- Unable to sustained head off pillow for 5 secs
- TOF - adductor policis
- DBS - more accurate than TOF

- (non depolarising) Post tetanic count:
    - Use when TOF = 0
    - 50Hz tetanic stim applied for 5 secs then single stim every second
    - Reversal possible if count >10

Anaemia

- Causes:
    - Blood loss - acute vs chronic
    - Bone marrow failure
    - Megaloblastic anaemias - b12 or folate deficiency
    - Complex anaemias:
        - Renal failure
        - RA
        - Hypothyroid
    - Haemolytic anaemias:
        - Inherited - thallasaemia or sickle cell
        - Acquired - autoimmune, drugs, infections
        - Physical - mechanical valves, DIC
- Always ask about NSAIDs and alcohol

Ix

- Pre-op Hb in major surg or those at risk
- Anaemia screen:
    - Iron studies
    - B12/folates
    - TSH
    - Renal/liver function
    - Direct Coombs test

Rx

- Check FBC weeks before elective surgery to allow for corrective Rx:
    - IV iron/oral iron
    - B12/folate supplementation

Periop Transfusion

- Restrictive approach to transfusion becoming more evidence based
    - If Hb ↓s then CO↑s due to a ↓in viscosity of blood ⟹ maintenance of O2 delivery
- Use of HaemoCue - to check Hb intra-op

- Threshold 70-80.
- Consider higher levels if majore systemic disease but this is only a historical theory

Transfusion Reactions

- Types:
  - Actue haemolytic transfusion reaction:
    - ABO incompatibility due to clerical error
    - Recipient antibodies bind to transfused red cell antigens ⟹ haemolysis
    - Shock, ARF ± death
  - Bacterial contamination:
    - Rapid onset of CVS instability, rigors, collapse
    - Rare but more common with platelets stored at room temp
  - TRALI:
    - Antibodies in transfusion unit reacting with antigens in recipitent
    - 1:5000 to 10,000 of plasma products ie FFP, whole blood
    - Leuco-deplete rbcs is ↓s frequency
    - Should be considered if pt develops APO within 6hrs of transfusion
    - Manage as would ARDS/ALI
  - Acute transfusion reactions (ATR)
    - Up to 24hrs post transfusion
    - Anaphlyaxis to febrile non haemolytic reactions
  - Delayed heamolytic transfusion reactions (DHTR):
    - >24hrs post transfusion
    - 2nd to development of red cell alloantibodies
  - Transfusion assoc graft vs host disease (TA GvHD)
    - Usually in immuncomprimsed
    - Engraftment & proliferation of transfused lymphocytes
    - Damage cells with HLA antigens in skin, liver, spleen, bone marrow
    - Fever, skin rash, diarrhoea, dermatitis
    - Usually fatal
    - Leucodepletion also reduced incidence
  - Infections transmissible by transfusion:
    - Eg HIV/HCV/syphillis, vCJD

Acute Blood Loss

- Establish percentage of circulatory loss:

Classification of hypovolaemic shock according to blood loss (adult)

	Class I	Class II	Class III	Class IV
Blood loss (%)	<15	15–30	30–40	>40
Blood loss (ml)	750	800–1500	1500–2000	>2000
Systolic blood pressure	Unchanged	Normal	Reduced	Very low
Diastolic blood pressure	Unchanged	Raised	Reduced	Unrecordable
Pulse (bpm)	Slight tachycardia	100–120	120 (thready)	>120 (very thready)
Capillary refill	Normal	Slow (>2s)	Slow (>2s)	Undetectable
Respiratory rate	Normal	Tachypnoea	Tachypnoea (>20/min)	Tachypnoea (>20/min)
Urine output (ml/hr)	>30	20–30	10–20	0–10
Extremities	Normal	Pale	Pale	Pale, cold, clammy
Complexion	Normal	Pale	Pale	Ashen
Mental state	Alert	Anxious or aggressive	Anxious, aggressive, or drowsy	Drowsy, confused, or unconscious

- If no antibodies on G&S - compatible blood can be electronically issued in 5mins
- If antibodies present then delay up to 2hrs

Processes for Red Cell or blood Product Transfusion

- Confirm identity to pt or by wrist band
- Check blood compatibility label with the blood bag
- Check expiry date & unit
- Inspect bag integrity & evidence of red cell clumping
- If blood out of fridge >30min needs to transfused within 4hrs of discarded
- Meticulous documentation

Thrombocytopaenia

- = platelet count <150
- Spont bleeding uncommon unless <10-20
- Causes:
  - Failure production:
    - Selectively:
      - Hereditary
      - Drugs
      - Alcohol
      - Viral
    - General marrow failure:

        - Aplasia
        - Cytotoxics
        - Infiltration/fibrosis
        - Myelodysplasia
    - ↑ed consumption:
        - With immune basis:
            - ITP
            - Drugs
            - Viral infections
            - SLE
            - Lymphoproliferative disorder
        - Without immune basis:
            - DIC
            - TTP
            - Bypass
    - Dilution - massive transfusions
    - Splenic pooling - hypersplenism
- If unexpected results - rpt sample

Preop Preparation

- Ix unexpected thrombocytopaenia preop
- Bone marrow biopsy can be done without platelet cover
- Acceptable counts:
    - >50=
        - Major procedures eg laparotomy
        - CVLs
    - >100
        - LP/epidurals
        - Special ops eg brain/eye
- If ITP - reserve platelet T/Fs for major surgery & use high dose steroids

Post Op

- If microvascular oozing despite platelets >50 ≈ DIC
  ↳ if so give cryo & FFP
- Avoid all IM injections
- Desmopressin 0.3mcg/kg in 100mls NAcL/30min may help in certain situations:
    - ARF/CRF
    - Haemophilia
    - vWF disease

Coagulation Disorders

- Extrinsic & intrinsic pathways now thought only in vitro
- Now common pathway:
    - TF release from vascular beds
    - TF combines with VIIa ⟹ activation IX, X ⟹ generation IIa (thrombin)
    - Process amplified causing activation V & VIII ⟹ massive amounts of thrombin ⟹ fibrin
- Causes coagulation disturbance:
    - Acquired:
        - Lack synthesis of factors
        - Consumption of factors eg DIC
        - Massive blood loss
    - Hereditary:
        - Haemophilia A -

    - X linked defect in VIII activity
    - Levels:
        - <2% = severe - spont bleeding
        - 5-30% = mild - bleed after trauma
    - Elective cases get level day prior to surg & aim for 50-100% levels AND for 2/7 post op
    - Avoid all drugs effecting platelet function
- Haemophilia B - sex linked recessive IX
- vWD -
    - autosominal dominant
    - 3 subtypes
    - Desompressin trial can be undertaken to see if a responder
    - Responders can have desompressin for surg (prophylactically or bleeding)
    - Non responders - give
        - VIII concentrate - includes vWF
        - cryo
- Concurrent medical problems may be relevant:
    - Liver disease
    - Malabsorption - vit K deficiency
    - Infection
    - Malignancy (DIC)
    - Autoimmune disease - RA/SLE
    - Medications - NSAIDs

Disorder	Platelet count	INR	APTT	TT	Fibrinogen	Other
Haemophilia A	Normal	Normal	↑	Normal	Normal	↓ VIII
Haemophilia B	Normal	Normal	↑	Normal	Normal	↓ IX
von Willebrand's disease	Normal (usually)	Normal	↑	Normal	Normal	↓ VIII, vWF, ↑ bleeding time
Liver disease	Normal or ↓	↑	↑	Normal	Normal or ↓	↓ V
Vitamin K deficiency	Normal	↑	↑	Normal	Normal	↓ II, VII, IX, X
DIC	Normal or ↓	↑	↑	↑	Normal or ↓	↑ FDPs, D-dimers, ↓ II, V, VIII
Massive transfusion	↓	↑	↑	Normal or ↑	Normal or ↓	Normal FDPs
Heparin (unfractionated)	Normal (rarely ↓)	Normal or ↑	↑	↑	Normal	↑ anti-Xa
Heparin (LMWH)	Normal (rarely ↓)	Normal	Normal	Normal	Normal	↑ anti-Xa
Warfarin	Normal	↑	↑	Normal	Normal	↓ II, VII, IX, X
Lupus anticoagulant	Normal	Normal or ↑	↑	Normal	Normal	DRVVT +ve, cardiolipin antibody

AntiCoagulants

Warfarin

- Interferes with vit K metabolism ⟹ liver produces non functioning factors (II, VII, IX, X, protein C &S)
- Reversal:
    - Need depends on INR - >5 consider reversing
    - Vit K - oral vs IV
        ↳ if emergency always give as adjunct
    - FFP

    - Prothombin complex
- Surgery INR threshold:
    - <1.5 - norm surgery
    - <1.2 high risk surg
        ↳ once <2 consider need for bridging anticoagulation
- Need to stop warfarin for operation controversial - can be based on scoring system
        ↳ eg CHADS (heart failure, HTN, >75yrs, DM, stroke x2 points) 0-2 low, 3-4 mod, >5 high)
- 10% peri-op major bleeding risk if don't stop warf (33% of them need blood transfusion)
- Risks without anticoagulation of VTE:
    - Mechanical heart valve = annual 17% or 0.4% for 8day periop period
    - AF = 8day perip op = 1%
    - Previous VTE = embolic stroke significant neuro deficit in 70% of cases & fatal in 4-9%
        ↳ bridging VTE effective for VTE
- Warf should be stopped 5d prior to surgery
- Bridging:
    - Unfractionated heparin - by protocol. Stop 6hr prior to surg
    - LMWH
    - IVC filter - very high risk
- Restart warf 12-24hrs post op

Heparin

- Potentiates antithrombin
- Unfractionated heparin monitored by APTT
- Half life is 1-2hrs but complex pharmacokinetics and narrow therapeutic window mean strict protocols are important
- Stop 6 hours prior to surgery
- Protamine reversal - give slowly to avoid hypotension.
- Complications of heparin:
    - HIT ⟹ serious venous & arterial thrombosis
        ↳ less of a problem with LMWH
- LMWH renally excreted

Anti-platelet Agents

- Decrease platelet aggregation
- May inhibit thrombus formation in arterial circulation
        ↳ anticoagulants have little effect

Aspirin

- Irreversible binding to platelets ⟹ ↓thromboxane A2 production
- Need new platelets to reverse effect (7-9days)
- Aspirin use peri-op In
    - CABGs:
        - ↑peri-op bleeding
        - ↑graft patency
    - TURPs - significant ↑peri-op bleeding
- Defo need to stop if:
    - Retinal surgery
    - Intracranial surgery
    - TURP

Dipyridamole

- Needs to be stopped at least 7d prior to surgery
- Less clinically significant effect than aspirin

Clopidogrel
- Binds irreversibly with ADP receptor on platelets
- prodrug
- Stop 7d prior surg
- Can try platelet transfusion but should be >24hr after last dosing

Immunosuppressed patient
- 3 classes of drug:
  - Immunophilin binding drugs - prevent cytokine mediated T cell activation & proliferation
    ↳ eg ciclosporin A, tacrolimus
  - Nucleic acid synthesis inhibitors - block lymphocyte proliferation
    ↳ eg azathioprine
  - Steroids -
    - block production inflam cytokines
    - Lyse T lymphocytes
    - Alter function remaining lymphocytes
- Ciclosporin -
  - associations:
    - Renal dysfunction - Often causes HTN
    - Prolongs non depolarising muscle relaxants
  - Ca channel blockers $\Longrightarrow$ ↑ciclosporin levels $\therefore \Longrightarrow$ ↓dosing regimes
- Tacrolimus:
  - Renal dysfunction
- Steroids - supplementation may be required. See above
- Must use strict asepsis in all invasive procedures

Rheumatoid Arthritis
- =chronic systemic inflam disorder involving mainly joints but with extra articular effects
- Peak onset 30-55
- Higher than av mortality due to both disease & concurrent disorders
- Stills disease in children

PreOp Ax
- See airway Ax
- Non articular:
  - CVS:
    - Assoc IHD
    - Vasculitis & raynauds
    - Pericarditis & pericardial effusions common
    - Aortic incompetence & endocarditis rare
  - Resp:
    - Costo-chondral disease gives ↓ed chest wall compliance
    - Fibrosing alveolitis or acute pneumonitis
    - Pleural effusions
  - Anaemia:
    - NSAID assoc blood loss or anaemia of chronic disease
    - DMARD assoc bone marrow suppression
    - Felty's syndrom = splenomegaly, neutropaenia, anaeamia & thrombocytopaenia
  - Nervous system:
    - Periph & compression neuropathies
    - Cx cord compression

- Infections - common 2nd to disease or iatrogenic
- Renal & Hepatic -
  - Iatrogenic CRF
  - ↓albumin, ↑fibrinogen & ↑a - acid glycoprotein

Ix

- Routine blood tests
- Cx spine XRs - flex & ext views:
  ↳ only mandatory if neuro signs or symptoms or persistent neck pain
  ↳ MRI better test
  ↳ consider inline stabilisation/AFOI

Peri-Op

- Drugs:
  - Steroid supplement if required
  - NSAIDs- only stop if:
    - Bleeding risk
    - Hypotension
    - ↓ing renal function
  - DMARDs - little evidence effects risk of wound infection thus continue
  - TNF-a blockers - suggestions of potential ↑post op infection risk but no consensus whether to stop
  - Use gastro prophylaxis esp if on NSAIDs
- Good positioning on the table
- Regional techniques may be difficult because of pain while remaining immobile
- Norothermia
- Strict asepsis techniques

PostOp

- PCA may be difficult due to hand function
- Early mobilisation
- Maintain fluids
- Restart DMARDs early

Smoking

- Contains nicotine and at least 43 known carcinogenic compounds
- Long term assoc ⟹ ↑risk:
  - COPD
  - Lung cancer
  - IHD
  - Vascular disorders
- Effects of smoking:
  - ↑resp tract mucus
  - ↓mucocilary clearance
  - ↑anaesthesia susceptibility :
    - resp events:
      - Post op atelectasis
      - Desat during induction
      - Post op pneumonia
        ↳ these risk specifically ↑ed with abdo/thoracic surgery or obesity
    - ↑ed airway irritability:
      - Coughing

    - Laryngospasm
        ↳ can avoid by using less irritant volatile eg sevo & deepening anaesthesia slowly
        ↳ if spont breathing required may have to LA vocal cords or use high dose opioids
- COHb may be up to 15% in heavy smokers
    ↳ falsely reassuring Spo2 readings

Risk Reduction

- Total abstinence from smoking for 8weeks ⟹ ↓morbidity from resp complications to non smoking level
- If stop for 12hrs prior to surg still get benefit
    ↳ ↓ed nicotine activated ↑coronary vasc resistance (via symp system) AND ↓COHb levels

2.15 Regional & Local Anaesthesia

RA 1.1 College Document on Major Regional Analgesia

- Informed consent should include discussion of risks including:
    - Nerve injury
    - Drug toxicity
    - Haemodynamic changes
    - Bleeding or bruising
    - Infection
    - Failure of technique
    - Post dural puncture headache
- Problems with informed consent in labour ward of PACU understood
- Should have qualified help when doing technique - tech or midwife
- preparation:
    - Need full infection control
    - Skin prep must be dried to avoid contaminating equipment or drugs
    - Coagulation status must be assessed before all blocks
    - IV access prior & maintainned during duration of technique
- Monitoring:
    - During insertion:
        - ECG, SPo2, RR, conscious state, frequent bp
        - Continue that level until 30mins after vitals stable
    - Person doing block must be around to assess satisfaction of block or until immediate complications have passed
    - May then delegate responsibility to other MDT members eg pain team
- Full record keeping incl prescription charting
- Equipment:
    - Catheters & giving sets must be well labelled and specifically a diff colour
    - Dedicated pumps with set protocols to avoid OD
- Post procedure r/v:
    - Local protocols to r/v for complications, effectiveness, side effects, timing of removal
    - Daily r/v

    - MRI preferred to CT for nerve injury
    - Remove catheters if suspected infection and send for culture
- Late complications of neuraxial analgesia:
    - Postdural puncture headache
    - Epidural abscess
    - Epidural haematoma
    - Spinal cord or nerve root compression

Neuraxial Anatomy

- Spinal cord terminates L1 adults (L3 infants)
- Iliac crests = Tuffers line = L4 level
- Subarachnoid space
    - ends S2 in adults (lower in children)
    - Extends laterally along nerve roots to dorsal root ganglia
- Subdural space = potential space inbetween dura & arachnoid mater
- Epidural space =
    - lies between walls of vertebral canal & ligamentum flavum & spinal dura mater
    - Low pressure area occupied areolar tissues, loose fat & internal vertebral venous plexus
- Ligamentum flavum maximal thickness in Lx region 2-5mm

Technique

- Midline
- Paramedian:
    - 1-cm lateral to upper border of spinous process
    - Insert needle perpendicular to contact lamina of vertebra
    - Withdraw slightly reinserting 15 deg medial, 30deg cephelad to pass over lamina through interlamina space until pop through dura

Coagulation Disorders & Regional Techniques

- Haemorhage can be brisk ⟹ haematoma ⟹ nerve compression
  ↳ in/around spinal cord ⟹ permamnent paralysis
- Coagulopathy relative contraindication depending considerably on context
- Numbers:
    - Platelets >80
    - INR <1.5

Epidural Analgesia

- Can provide complete analgesia for 3-5days

Benefits

- Efficacious
- ↓ed atelectasis & pulmon infection, better cough
- ↓post op ACS:
    - ↓sympathetic stress thus ↓myocardial oxygen requirement
- ↓hypercoagulable states & fibrinolytic function is improved
  ↳ proven benefit in graft survival in vascular surgery
- Quicker post op mobility ⟹ ↓post op DVT

- ↑gut action by ↓pain & ↓opiate need
- Intraop epidural ↓s post op blood transfusions

↳ BUT no ↑survival benefit in high risk patients

Contraindications

- Patient refusal
- Untrained staff
- Contraindications to needle placement:
  - Local or general sepsis
  - Hypovolaemia
  - Coag disorders:
    - Platelets <80
    - INR >1.5
  - Concurrent anticoag drugs
  - Central neurological diseases

Tips

- Breakthrough pain:
  - Add oral paracetamol or NSAID
  - Bolus dose 3-5ml then ↑infusion rate
  - Check all connections and infusion site
  - Check block - if patchy withdraw catheter to 2cm in space
  - Bolus fentanyl 50-100mcg only
- Pruritis:
  - Give naloxone 50-100mcg & consider adding 300mcg to infusion fluids
  - Remove opioid from infusion
  - Try antihistamines or ondansetron
- Hypotension:
  - Check fluid status
  - Check block height $\Longrightarrow$ ↓infusion rate
  - Ephedrine/metaraminol
- Motor block -
  - ↓infusion rate
  - ↓LA concentration

Complications

Complications of epidural anaesthesia[4] (see also pp746–51)

Complication	Incidence (%)	Management
Dural puncture	0.16–1.3	Bed rest, analgesia, hydration, blood patch (see p748)
Headache	16–86	Bed rest, analgesia, hydration, suspect dural puncture
Nerve or spinal cord injury	0.016–0.56	Immediate neurological assessment (see p32 and p1178)
Catheter migration	0.15–0.18	Remove catheter and resite if appropriate
Epidural haematoma Epidural abscess	0.0004–0.03 0.01–0.05	MRI or CT scan. Immediate neurosurgical assessment. Antibiotics (see also p1105 and p1171)
Respiratory depression	0.13–0.4	Decrease in opioid concentration may be required
Hypotension	3–30	IV fluids ± vasopressors. Temporarily reduce or stop infusion
Pruritus	10	Naloxone IV (50–100μg) ± antihistamine
Urinary retention	10–30 (in males)	Catheterisation
Motor block	3	Check for catheter migration. Temporarily cease infusion. Consider epidural haematoma (p1171 and p1174)
Other		Possible increased risk of anastomotic leakage after bowel surgery. No evidence to support this

- Spinal infection:
  - Classic triad of epidural abscess (0nly seen together in 13%):
    - Fever (66% on own)
    - Backache (75% on own)
    - Neurological signs (very late sign)
  - Normal bloods mean nothing
  - If suspect should remove immediately and send line tip to lab
  - 90% infections are bacterial (mostly staph aureus)
  - MRI early before neurology develops
  - Once muscle weakness develops:
    - only 20% will regain full function even after surgery
    - Better prognosis: <36hrs, extent compression, younger
  - Mortality 10%
  - Needs percutaneous abscess & Abx

Drugs in Epidural

- Standard protocols used in different institutions:
  - Light mix - bupivacaine 0.125% & fentanyl 5mcg/ml
- Infusion rates:
  - 8-15ml/hr adult
  - 4-8ml/hr >70yr olds

Spinal Anaesthesia

Dosing

- Older & pregnant need less
- 2.5 - 3mls of hyperbaric will reach T6-T10 in most non pregnant young if placed in lying shortly after injection
- If isobaric LA given dose needs to be higher
- Lignocaine not used
- Ropivocaine not licensed for intrathecal use
- Hyperbaric solutions:
  - Used to get higher block
  - More hypotension
- Isobaric:
  - Produce lower lock height
  - Less hypotension

Contraindications

- Absolute:
  - Local sepsis
  - Refusal
  - Anticoagulation (see epidural)
- Relative:
  - Aortic or mitral stenosis
  - Hypovolaemia/hypotension
  - Prev back surgery - possibly technically difficult
  - Neurological disease
  - Systemic sepsis - ↑ed risk of meningitis/epidural abscess

Complications

- Hypotension
- Bradycardia -
  - block into mid thoracic region
  - Can progress to cardiac arrest
- High block ⟹ compromised breathing ⟹ total spinal
- Urinary retention
- Nerve damage -
  - permanent injury 1:25,000 to 1:50,000
  - Paraplegia or death 1:50,000 to 1:140,000
- Post dural puncture headache
- Infection
- Bleeding

RA 1.6 & 1.11 Complications of Neuraxial Block

Hypotension

- Avoid aortocaval occlusion (pregnancy) ⟹ move to full lateral position
  - ↳ measure bp on dependant arm
- IV fluid bolus

- Vasopressor/inotrope - ephedrine vs metaraminol

Subdural block

- When epidural catheter placed between dura mater & arachnoid mater
- Less than 1:1000 BUT may be indistinguishable from epidural placement
- Definitive diagnosis is radiological
- Characteristics of subdural block:
  - Slow onset 20-30min which is much more extensive than volume should dictate
    ↳ may extend to Cx dermatomes with Horners syndrome
  - Patchy & asymmetrical block with sparing of motor fibres to LLs
  - Total spinal with top up dose
    ↳ due to ↑volume ⟹ rupture of arachnoid mater
- Rx by stopping infusion and re-siteing catheter

Total Spinal

- If initial plan is epidural incidence = 1:5,000 - 1:50,000
- Features:
  - Rapid onset BUT can be delay upto 30mins
    ↳ change maternal position or migration of catheter
  - Rapid rising block
  - Impaired coughing
  - Loss hand/arm strength
  - Difficulty talking, breathing & swallowing
  - Cardiovascular depression ⟹ resp paralysis ⟹ unconsciousness ⟹ fixed dilated pupils
- Rx:
  - Maintain airway & ventilation
    ↳ may need intubation if if not fully unconscious in order to protect airway
  - Avoid aortocaval compression (pregnant)
  - Ventilation for 1-2hours may be required

IV injection of LA

- IV or partial IV catheter positioning occurs in at least 5% epidurals
- Every dose is a test dose
- Strategies to reduce risk:
  - Always check for blood in catheter
  - Always think of LA poisoning with ever dose even if prev had no issues
  - Divide all large LA doses into smaller aliquots
  - Use low toxicity LAs
  - LA toxicity algorithm

IT 1.120 Plan B for a Regional technique

- Steps:
  - Consider technique - US vs periph nerve stim
  - Reattempt if dosing allows
  - Get help, another operator
  - If partial:
    - Co-sedation an option - midaz/propofol/remi
  - GA
  - Postpone surgery
  - Consider placing indwelling catheter - epidural/periph nerve catheter/indwelling intrathecal catheter

IT RT 1.1 Systematic Approach to Identifying Problems

C - circulation, capnograph & colour
O - oxygen supply & oxygen analyser
V - ventilation & vaporisers
E - ETT, & eliminate the machine
R - review monitors & equipment

A - airway
B - breathing
C - circulation
D - drugs

SWIFT CHECK - of patient, surgeon, process, & responses

Four levels of intensity:
S - scan (every 5mins)
C - check (when not going to plan)
A/R - alert/ready
E - emergency

Severe Hypoxia

- Causes:
  - Gas mixture:
    - Incorrect flowmeter settings
    - Second gas effect - NO (especially on extubation)
    - O2 failure
    - Machine error
  - Failure to ventilate:
    - Vent depression or narcosis
    - Inadequate IPPV
    - Disconnection
    - Misplaced ETT - oesophageal/endobronchial
    - Airway obstruction - patient to machine
    - ↑airway resistance eg bronchospasm/laryngospasm
    - ↓FRC - Ptx, ↑intra-abdominal pressure, morbid obesity
  - Shunt:
    - Atelectasis
    - Airway secretions
    - ↓hypoxic pulmonary VC
    - Heart failure & APO
    - Gastric aspiration
    - Pre-existing pathology - VSD/ASD
  - Poor o2 delivery in body:
    - Systemic hypoperfusion - hypovolaemia/sepsis
    - Embolus

    - Regional problems - Raynauds/vascular problems
  - ↑O2 demand -
    - Sepsis
    - Malignant hyperthermia
- Rx:
  - 100% o2
  - Check Fio2
  - Expose pt & check for central cyanosis
  - Check vent bilaterally
  - Hand ventilate on simple system - 4 large breaths for recruitment
  - Secure airway
  - Endotracheal suction
  - Initially remove PEEP (consider brief disconnection of circuit) then trial more
  - Adrenaline if losing pulses

Hypocarbia

- Causes:
  - shock:
    - Cardiogenic shock
      - Ischaemia
      - emboli
    - Distributive - septic
    - Anaphylactic
    - Hypovolaemic
  - ↑Ventilation -
    - Pain
    - Too much IPPV
- Check ABC

Hypoventilation/Hypercarbia

- Causes:
  - Anaesthesia:
    - Coughing/breath holding/light anaesthesia ⟹ rapidly deepen with IV agent (10%-20% dose)
  - Airway obstruction
  - Position:
    - Lithotomy/trendelenburg
  - Surgical factors:
    - Distended abdo
    - Loss integrity chest wall or diaphragm
  - CNS depression - drugs eg opioids or sedatives
  - Drugs:
    - High spinal
    - relaxants
  - Muscle weakness
  - Pre-existing conditions:
    - Primary - myopathies
    - Secondary - drugs/electrolytes
    - Trauma/neuropathy/stroke
  - Equipment problems -
    - Disconnection/leaks/obstructions
- Signs:

    - Desat
    - Hypercarbia
    - Tachy/bradycardia
- Rx:
    - Rx primary cause
    - Control airway and ventilate lungs

High Airway Pressures

- Causes:
    - Misplaced ETT - listen to chest
    - Obstruction to airway/filter/mount/circuit ⟹ isolate with ambi bag
    - ↑airway resistance - listen to chest
        - Laryngospasm
        - Bronchospasm
        - Anaphylaxis
        - Pulmonary oedema
        - Airway secretions
        - Aspiration gastric contents
    - ↓FRC:
        - Morbid obesity
        - ↑intraabdominal pressure - check with surgeon

Bradycardia

- Causes:
    - Vagal stimuli:
        - Peritoneal tension
        - Abdo distension
        - Visceral retraction
        - Airway stim
        - Extraocular muscle retraction
    - airway:
        - Severe hypoxia/hypoventilation
    - Primary cardiac problems:
        - Rhythmn ie Av blockade
        - Ischaemia
    - Electrolytes:
        - hypokalaemia
    - Drugs:
        - Neostigmine
        - Propofol
        - Volatiles
        - Sux
        - Vasopressors
        - phenytoin
        - High Neuraxial LA blockade
- Signs - obvious
- Rx:
    - Stop all vagal stimuli
    - If cardiovascular unstable:
        - Atropine in 500mcg boluses up to 3mg
        - Adrenaline/isoprenaline/glucagon/glyco

    - Transcutaneous pacing
- Be concerned if:
    - Recent asystole
    - Mobitz II/type 3
    - Vent pauses >3secs

Tachycardia

- If sinus tachy ⟹ consider hypotension and Rx
- If tachy arrhythmia choose Rx based on severity of hypotension:
    - Severe ⟹ sync shock
    - Mild ⟹ drugs
- Reversible causes:
    - Hypovolaemia:
        - Dehydration
        - Diuresis
        - Sepsis
        - Blood loss
    - Drugs:
        - Anaesthetic agents
        - Atropine
        - LA toxicity
    - Airway:
        - Hypoventilation/hypoxia
    - Anaphylaxis
    - Reflex stim
        - Pain!
    - Cardiopulmonary problems:
        - Obstructive lesions:
            - Tension
            - Tamponade
            - Massive haemothorax
        - Sepsis
        - Embolism - gas/amniotic/thrombus
        - Myocardial irritability - drugs/ischaemia/trauma
- Rx - based on diagnosis
- Rx of arrhythmias based on:
    - Pulse ⟹ no ⟹ ALS
        - Narrow
            - Patient stable ⟹ no ⟹ ALS (DC shock)
            - Regular or irrgeular
                - Regular:
                    - Vagal
                    - Adenosine
                - Irregular:
                    - AF - onset <48hrs:
                        - Rate control
                        - Rhythm control
        - Broad:
            - Stable ⟹ no ⟹ ALS (DC shock)
            - Regular:
                - Pulsatile VT ⟹ drugs vs shock

    - Irregular:
        - AF with BBB - as AF
        - Pre-excited AF - amio
        - Polymorphic VT - Magnesium & rpt

Severe Hypotension

- Causes:
    - Patient:
        - Hypovolaemia - HR >100, RR >20, ↑CRT, narrow pulse pressure, swing arm line
        - Obstructed venous return
        - Raised intrathoracic pressure eg tension Ptx - examine chest
        - Anaphylaxis
        - Embolism -
            - Suspect if pre-existing low CVP & open venous bed
            - Signs:
                - Sudden ↓ETCO2
                - ↓Spo2
                - Cardiovascular collapse ⟹ PEA
        - Pump failure -
            - Ischaemia
            - Failure - worsening Spo2 with fluid challenge, distended neck veins
            - Arrhythmia
        - Sepsis - warm peripheries
    - Technique
        - Measurement error - check pulse when cuff up
        - Excessive depth anaesthesia
        - High spinal block:
            - Horners syndrome - small pupil/ptosis/anhydrosis/stuffy nose)
        - Drug error eg LA toxicity, barbituates
- Rx:
    - ABC
    - Optimise preload -
        - Fluid challenge with pressure infusion
        - Lift legs - very acute temporising measure (↑preload & afterload)
    - ↑contractility - ephedrine, adrenaline, Ca
    - ↑SVR - vasopressors

Severe Hypertension

- Causes:
    - Inadequate depth of anaesthesia - check TIVA/volatiles
    - Inadequate analgesia - trial alfentanil 10-20mcg/kg
    - Measurement error - palpate pulse/check transducer height
    - Hypoxia/hypercapnia
    - Drug error
    - Pre-eclampsia - >20wks, check platelets, proteinuria, LFTs, clotting
    - Raised ICP - Cushings
    - Thyroid storm
    - Phaeochromocytoma
    - Surgical techniques:
        - Aortic x clamp
- Rx:

    - ABC
    - Vasodilators (may cause tachycardias)
        - ↑volatiles
        - GTN infusion
        - MgSo4 bolus 10mmol then infusion 5mmol/hr
        - clonidine
    - B blockade (↑HR or dysrhythmia):
        - Esmolol
        - Labetalol - b:a blockade 7:1
    - a blockade (normal or ↓HR):
        - Phentolamine

Oliguria/Anuria

- Causes:
    - Surgical factors
    - Hypovolaemia/hypotension
    - Fluid status
    - Cardiovascular/renal perfusion

IT RT 1.2 Management of Life Threatening Conditions

Cardiac & Respiratory Arrest

- ALS protocols
- Consider naloxone post op
- ABCD
- Post arrest care:
    - Optimise oxygenation
    - Ventilate to normalise CO2
    - Correct electrolytes
    - Keep BSL <10
-

Shock

- Hypovolaemic - fluids, blood, stop bleeding
- Distributive - fluids, adrenaline or other vasopressors
- Cardiogenic -
    - normalise cardiovascular parameters
    - Consider anti-thrombotics
    - Consider intubation if appropriate
    - Monitoring especially post op
- Obstructive - Rx underlying cause

Cardiac Tamponade

- Diagnose with ultrasound
- Classically:
    - Muffled heart sounds
    - Distended neck veins
    - Hypotension
- Rx with pericardiocentesis
- Call CT surgeon!

Acute Myocardial Ischaemia

Perioperative MI:

- Usually day 3-4 post op
- Causes:
  - acute plaque rupture (50%)
  - Oxygen supply/demand imbalance
- Rx:
  - Move to CCU/HDU
  - Aspirin/morphine/GTN
  - Consider B blockers to decr myocardial o2 demand
  - Angio relatively contraindicated - D/W cardiologist
  - Rx APO

Acute Pulmonary Oedema

- Causes:
  - ↑hydrostatic pressure
  - ↑vascular permeability
  - ↓colloid pressure
  - -ve interstitial pressure
  - Obstructed lymph drainage
- Presents:
  - Frothy sputum
  - ↑HR
  - ↑RR
  - ↓SPo2
  - ↑CVP
- Rx:
  - 100% o2
  - If awake:
    - Sit up right if able - ↑s FRC and offloads pulmon vasculature
    - CPAP
  - If intubated:
    - ↑PEEP to at least >5cmH20
    - 15deg head up - ↓s atelectasis & improves FRC
    - Aspirate free fluid from trachea
  - Use GTN via spray/infusion or patch in either

Aortic Dissection

- Aim to reduce:
  - HR - to 60-70
  - Bp SBP 100-120 mmHg
- Use labetalol initially as has alpha action
- Cautious GTN as can cause reflex tachy

Aspiration of Gastric Contents

See pg 19

Bronchospasm

- Identify causes:
  - APO
  - Analphylaxis

    - Asthma
    - ETT obstruction
- Rx:
    - Suction or place bougie down ETT
    - ↑volatile - sevoflurane least irritant. Considering stopping dex
    - IV salbutamol
    - Inhaled salbutamol:
        - Aersol spray in 50ml syringe with fine bore tubing fed directly down ETT
    - Ketamine
    - Aminophylline - 250mg (max 5mg/kg) slow IV injection

Tension Pneumo

- Decompress

Massive Haemoptysis

- Early cardiothoracic involvement
- 100% o2
- Place pt in recovery position with bleeding lung down
- Plan RSI
- Consider need for double lumen tube to isolate bleeding lung
- IV access ⟹ CVL
- Flexible bronchoscopy later

Raised ICP

- Normal ICP 5-12mmHg
- Initial compensatory mechanisms by ↓ing volume of CSF & ↓blood volume
- Then after marked ↑in ICP per intracranial volume
- Causes of raised ICP:
    - ↑ed brain substance
    - ↑ed CSF volume
    - ↑ed blood volume
    - ↑ied ECF
- Autoregulation maintains cBF between MAP 50-140mmHg
    ↳ if chronic HTN then all limits increase
- Rx:
    - Avoid ↑ing CBF further by avoiding:
        - hypercarbia
        - Hypoxia
        - HTN
        - Hyperthermia
    - Good anaesthetic depth
    - Good Analgesia
    - Avoid ↑venous pressure - tube ties, head 30deg up, avoid coughing on tube
    - Avoid hypotonic fluids
    - Maintain CPP - avoid hypotension. Aim CPP >70mmHg
- Specific measures to ↓ICP:
    - Diuretics - mannitol 0.25-1g/kg over 15mins
    - Aim PaCO2 30-35 mmHg- effect for 24hours
    - Dexamethasone (if NOT trauma)
    - CSF drainage
    - Head up

- Conc NaCL 25% 20ml boluses

Prolonged Seizures

- Benzo's - lorazepam (0.1mg/kg) or midazolam (0.2mg/kg)
- Phenytoin 15-18mg/kg load
- Sodium valproate 20mg/kg slow push
- Clonazepam
- Intubate & sedate - thiopentone better than propofol

LA Toxicity

- see earlier

Anaphylaxis

- Adrenaline 50-100mcg boluses IV or 500mcg IM
- IVF
- Anti Hs and steroids later
- Refer for testing
- Reverse roc & vec with suggamadex

Malignant Hyperthermia

Aetiology

- = pharmacogenetic disease of skeletal mm
- Induced by exposure to:
  - Volatile agents
  - Depolarising mm relaxant ie sux
- Inherited autosomal dominant condition
- Caused by loss normal Ca homeostasis within excitation-contraction coupling process on exposure to trigger
- Any defect along complex process can trigger MH
- Most likely site:
  - Junction between T tubules
  - Voltage sensor of dihydropyridine receptor (DHPR) & Ryanodine receptor (RYR)
    - ↳ = efflux Ca channel in sarcoplasmic reticulum
    - ↳ 70% families RYR1 gene linkage

Epidemiology

- Rare 1:10,000. All races
- Mortality fallen from 70-80% to 2-3% due to awareness & dantrolene
- Young adults; males>females
- Previous uneventful anaesthetic does not prevent occurrence

Signs & Symptoms

- Varied presentation:
  - Florid & life threatening vs insidious onset
  - Acutely vs 2-3d postop with massive myoglobinuria & rhabdomyolysis
- Signs:
  - ↑metabolism:
    - Tachy/Arrhythmia ⟹
    - ↑ed CO_2 production ⟹ most important early sign
    - Met acidosis
    - Fever (late) - ↑temp 2 deg/hr
    - DIC
  - Muscle signs:

- Masseter muscle spasm (MMS) after sux
  - = spasm impeding intubation persisting for around 2mins
  - 30% pts with MMS alone & otherwise normal anaesthetic ⟹ MH susceptible
  - If present:
    - Abandon surgery - possible OR
    - TIVA - volatile free surgery
    - Consider A line
  - Investigations:
    - Initial and 24hr CK
    - First void urinary myoglobinuria
  - Consider neurological opinion
- Generalised rigidity
- ↑K
- High CK
- Myoglobinuria ⟹ renal failure

Differential

- Rebreathing
- Sepsis
- Awareness
- Neuroleptic malignant syndrome
- Ectasy
- Thyroid storm

Treatment

- ABC. Stop volatiles
- Hyperventilate - 100% O2 to flush volatiles from system
- Declare problem to team and get help
- Use fresh breathing circuit machine if able
- Dantrolene 2-3mg/kg IV (20mg ampoules - so about 4)
  ↳ up to 10mg/kg
- Stop surgery or use TIVA
- Reduce core temp:
  - Ice to groin & axilla
  - Cold fluid into
    - bladder via catheter
    - Veins
    - Stomach via NG tube
- ABG - correct acidosis & potassium
  ↳ beware bicarb as will produce more CO2
- Call for surg team help to conclude operation as quickly as possible

Peri-MH Treatment

- Invasive monitorring
- Clotting screen & CK
- Urine samples
- Monitor renal function ⟹ diuretics and IVF

Post Episode Care

- Ref to MH investigation unit for mm biopsy & testing
- Warn pt & family
- Pt & family should be offered screening

Anaesthesia for known MH

- MH safe technique - TIVA with no sux may be safe - but balance risks
- All LA's are safe
- Dantrolene should not be given prophylactically
- Standard monitoring
- Baseline temp recorded 2hr preop & temp monitored for 4 hrs post op
- Use vapour free machine
    - ↳ if unable: remove soda lime, vaporisers and purge for 30mins with O2

Anaesthesia for suspected FHx

- Establish goof Fhx and d/w MH centre for contact tracing & diagnoses
- If case urgent then proceed with MH safe technique

General Anaesthesia

- GA drug = produces reversible state of unconsciousness with absence of pain sensation over entire body
- drugs need rapid onset of action and to be reversible
- usually
    - induced by injection of anaesthetic agent eg propofol or thiopentone
    - maintained by inhalational of a gas (nitrous oxide) mixed with volatile liquid eg halothane/sevoflurane

Stages of Anaesthesia

- 4 stages:
    - 1-2 = induction
        - ↳stage 2 dangerous ∴ rapid induction to stage 3, with maintenance there
    - 3 = surgical anaesthesia
    - 4 = medullary paralysis

Stage 1 Analgesia

- beings with onset of anaesthetic administration
- lasts until LOC
- order of effects:
    - ↓smell & pain ↓ed first
    - auditory or visual hallucinations
    - speech difficult
    - hearing last sense lost

Stage 2 Excitement

- varies greatly individuals
- depends on
    - amount & type of premeds
    - anaesthetic agent
    - levelof external stimuli
- most reflexs still present & exaggerated esp noise
- swallowing risk abolished ⇒ risk aspiration
- signs:
    - increase in:
        - autonomic activity

        - mm tone
        - eye movement
        - dilation of pupils
    - irreg breathing – uneven inhalation of anaesthetic
    - vomiting

Stage 3 Surg Anaesthesia

- surgery generally done in plane 2 – upper plane 3
- subdivided into 4 planes:
    - plane 1:
        - resp incr shallow & rapid until paralysis & requires assisted ventilation
    - plane 2:
        - loss of reflexs in cephalocaudal direction
        - conjunctival reflex lost
        - pupil constrict ⇒ reaction to light lost ⇒ dilate
        - gag & laryngeal reflexs lost
    - plane 3:
        - ↓mm tone – need flaccid abdo wall for surgery
        - ↓body temp: skin cold, wet & pale
    - plane 4: ↓ing bp & weaker pulse

Stage 4 – Medullary Paralysis

- toxic stage
- impending overdose, resp arrest & vasomotor collapse
- artificial resp required to reverse this stage

Mechanisms of Action of GA's

- assumed no one anaesthetic receptor
- potency of anaesthetic effect strongly correlated with lipid solubility
  ↳very lipid soluble = very potent
- MAC =
    - minimal alveolar concentration to prevent movement to standardised surg stimuli in 50% of people breathing 100% oxygen
    - inverse correlation between lipid solubility and dose (MAC)
- Awake MAC = concentration in alveolar which permits voluntary response to command in 50% of patients
  ↳ approximately 1/3 MAC
- any GA has narrow band of conc at which LOC

Factors Effecting MAC

- Increasing MAC:
    - Young
    - Chronic alcohol abuse
- Factors decreasing MAC:
    - Elderly
    - N20, sedatives, analgesics
    - ↓bp
    - ↓temp
    - low brain sodium
    - pregnancy

Membrane Theory

- = anaesthetic agent dissolves into hydrophobic sites on the CNS nerve cell membrane & expands these sites
- ⇒ ↓nerve conduction by physical disruption of channels permiting ion transport accros membrane
- anaesthesia depends on concurrent list of factors
    - membrane site sufficiently expanded
    - no. of molecules of agent in membrane
    - partial pressure of anaesthetic in tissues
    - p.p. of anaesthetic in bood
    - alveolar p.p. of anaesthetic
    - ↳ ∴ alveolar pp of anaesthetic determines the CNS pp & onset of anaesthesia

↳ but now thought not correct. Instead direct target of actions on receptors

Targets for GA Actions

- theories
- are protein targets which are impt
- best theory of GA action is modulate transmitter gated ion channels
- 3 main targets:
    - $GABA_A$ receptors –
        - at synapses & extrasynaptic receptors
        - GA binding ⇒ opening Cl channels ⇒ ↑ depressant action of GABA
    - K channels – 2 pore domain channels
        - opening of these mediates effects of some volatile GAs
    - NMDA receptors
        - mediate slow components of synaptic transmission
        - inhibited by most inhlational Gas
- other possible targets:
    - glycine receptrs
    - cyclic nucleotide-gated cation channels
    - presynaptic Na channels
- overall effect of GAs is LOC by
    - ↓ing excitatory neurotransmitters:
        - ACh – nicotinic
        - 5HT
        - glutamate
        - NMDA
    - ↑ing inhibitory neurotransmitters:
        - GABA
        - glycine
    - ?interacting with
        - peptidergic transmission:
        - opiod receptors
        - NO-cGMP transduction pathway
        - ROS
- sensitive areas of CNS:
    - sensory pathways thalamus - cortex ⇒ potentiation of sleep & LOC
    - hippocampus ⇒ amnesia of GA
    - multiple molecular targets in spinal cord ⇒ immobility

Pharmacokinetics

- conc of anaesthetic in lung/blood needs to rapidly equilibrate with CNS levels
  ↳∴ depth of anaesthetic depends on partial pressure or conc of drug in brain
- variables involve:
  - high inspired anaesthetic concentration
  - high alveolar ventilation
  - oil-gas partition coefficient = solubility of agent in lipids
  - low blood-gas partition coefficient = solubility of agent in blood & tissues
  - low cardiac output
  - 2nd gas effect with N2O
- general rules of GA pharmacokinetics:
  - high lipid solubility ⇒ ↑potency
  - high lipid solubility delays recovery:
    - agent forms depot in fat tissues = 2 compartment pharmacokinetic model
    - take hrs to be cleared – hangover effect
  - high blood-gas partition coefficient & high CO ≈ longer time for equilibrium of gas to tissues
    - if agent is highly soluble and large CO ⇒ agent washed away from alveolar ⇒ longer time for alveolar partial pressure of agent to build ∴ tissues would be receiving a lot of anaesthetic but at a low partial pressure
  - low blood-gas partition coefficient ≈ faster equilibration of agent ∴ quick onset and recovery time
  - alveolar ventilation = most impt factor in equilibration of gas agent into blood
    ↳esp if have high blood solubility
  - low blood flow to fatty tissues ⇒ slow equilibration of drugs to them

  ↳∴optimal agent = low blood & tissue solubility with high lipid solubility (potency)
  ↳eg sevoflurane

  NO = rapid but weak (low blood solubility but less lipid solubility). Cannot produce anaesthesia alone except in hyperbaric conditions

  ether = slow but potent (high blood solubility but very lipid soluble)

Elimination

- routes of elimination:
  - exhalation (most)– esp for agents low blood-gas partition coefficient
    - eg desfluorane faster than sevo
    - NO not metabolised at all
  - Hepatic metabolism – halothane (20%), des 0.02%

Halothane Hepatitis

- Mild form =
  - Common
  - Direct hepatocellular damage
  - Norm of no clinical consequence
- Fulminant form:
  - Immune reaction to reactive metabolite of halothane via reductive pathway
  - Risk factors:
    - Repeated halothane exposure
    - Hypoxia
    - Obesity
    - Concomitant drugs inducing liver enzymes
- Other inhalational agents can also cause but halothane most severe

Systemic Effects of Inhalational Agents

Cardiovascular

- All [except halothane]:
  - myocardial depression
  - vasodilation
- halothane:
  - tachycardia in face of decreased vascular resistance
    ↳ due to sensitising myocardium to catecholamines ⇒ fatal ventricular arrhythmias (esp with hypoxia & light anaesthesia)
- desflurane – pungency of smell ⇒ sympathetic stimulation

Respiratory

- All:
  - ↓ Vt
  - ↑RR
  - ↓response to hypoxia and ↑CO2
  - bronchodilators
- desflurane:
  - airway irritant
  - if high concentrations too early ⇒ laryngospsm & bronchospasm

CNS

- all [except halothane]:
  - dose dependant depression EEG
  - ↓cerebral vascular resistance
  - ↓cerebral metabolic rate of O2 consumption
  - ↑cerebral blood flow
  - ↑ICP

- enflurane & sevoflurane = assoc with epileptiform activity
  ↳ should not be used in epileptics

Other

- all:
  - mm relaxation
  - potentiate neuromuscular blockers
  - N&V 1:4
  - Uterine muscle relaxation

Adverse Effects & toxicity of GA

- common SEs:
  - post op convulsions
  - headache
  - N&V
  - kidney/liver toxicity
  - hepatotoxicity – esp with chloroform & halothane
  - malignant hyperthermia

Drug Interactions

- anticoags eg hep/warf: stopped 6/24hrs prior to surg
- CNS depressants eg alcohol, antiHs, antianxiety, opiods, sedatives:
  - all ↑ CVS, resp & CNS depressant effects of GA
  - reduce GA dose as required
- antiayyhythmics: may ↑CVS depression & hypotension from GA
- Ca & β blockers: ↑CVS depression & ↑arrhythmias. ↓GA
- chronic steroids: adrenal suppression ⇒ ↓bp during surg due to lack stress response. ↑steroids
- inhibitors of CYP3A4 eg azole antifungals, protease inhibitors, macrolides:
  - inhibit metab of midazolam ⇒ ↓midaz dose
- drgs which affect bp or HR: interact with ketamine which ↑s bp & HR

Special Considerations

- young:
  - halothane & NO commonly used as incidence of hepatitis low in kids
  - neonates more sensitive to non-depolarising mm relaxing agents
- old:
  - ↑ed and longer drug effect
- preg & childbirth:
  - lipid solubility means drugs will cross placenta
  - careful monitoring of drugs
  - avoid GA if possible
  - epidural with lignocaine & fentanyl
- obesity:
  - obtaining desired depth anaesthesia & mm relaxation may be difficult
  - highly fat soluble anaesthetics should be avoided
- smoke: post op complications x6 more common
- high alcohol:
  - liver/stomach/pancreas problems

- ↑liver enzymes ⇒ ↑drug doses required
- alcohol withdrawal post GA

Premedication

- no longer essential as less use of ester & chloroform
- some uses still:
  - ↓anxiety ⇒ ↓GA doses needed eg opiates, benzos
  - ↓secretions eg salivary, gastric, bronchial eg anticholinergics atropine
  - ↓post op vomiting eg phenothiazines ie prochlorperzine, promthezine
  - prophylactic analgesia & sedation eg opiates, benzoes, phenothiazones

Inhalational Anaesthetics

- gases or volatile liquids
- rapid reach conc in blood & brain
- following chars:
  - complete anaesthesia ∴ abolish superficial & deep reflexs
  - controllable anaesthesia – depth can be varied quickly
  - lung function critical to administration & excretion
  - may not have analgesic action
  - rapid recovery with removal of drug
  - allergc reactions uncommon

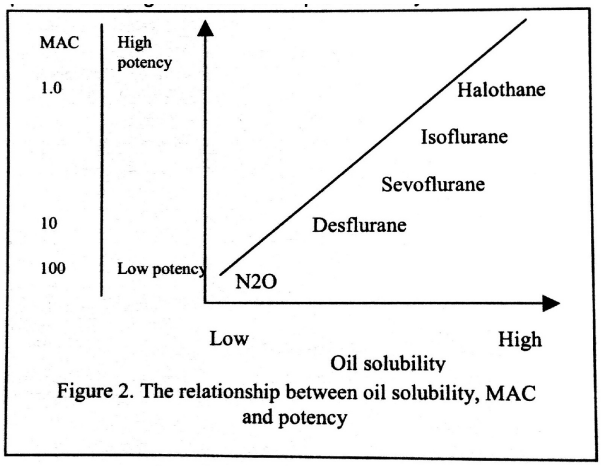


Figure 2. The relationship between oil solubility, MAC and potency

Volatile Liquid Anaesthetics

- ether & chloroform first used
- halothane – assoc with hepatic failure
- now use halogenated hydrocarbon series eg sevoflurane

Nitrous Oxide

- simple inorganic molecule N20
  ↳NB not NO (nitric oxide)
- at room temp = vapour, >36.5 = gas

MOA

- 2 main actions:
  - analgesic action similar to opioids ?mediated by opioid receptors
  - anxiolytic action: ⇒ enhanced GABA mediated CNS depression

Pharmacokinetics

- inhaled & absorb by lungs
- 2nd gas effect: rapid uptake into blood from alveoli ⇒ ↑concentration of other agent in alveoli ⇒ ↑more rapid onset anaesthesia
- low solubility in blood & tissues ∴ rapid onset and offset
- 100% excreted unchanged via lungs

Uses

- powerful analgesic
- useful anxiolytic
- weak anaesthetic – MAC value 105

↳∴ often use as carrier gas with O2 for other volatile anaesthetics to enhance effects in major surgery

- eg entonox 50:50 O2:N20

Adverse Reactions

- non irritant with no odour
- Primary probs
  - Mild ↑CBF & cerebral O2 consumption ⇒ ?avoid in neuroanaesthesia
  - Diffusion hypoxia:
    - at termination of gas administration rapid movement of N2O from circ into lungs
    - occurs faster than N2 can move back into blood
    - may dilute O2 in lung
    - avoid by 3-5mins 100% O2 cover this period
  - expansion air filled spaces:
    - N2O is x40 more soluble than N2
    - If N2O containing blood perfuses tissue adjacent to air filled space ⇒ N2O diffusion faster than N2 returning from air ⇒ expansion
    - Problem in bowel & PTx & head injuries
  - Haematopoetic System
    - N2O alters valency of central cobalt atom of vit B12
    - Prolonged exposure N2O ⇒
      - altered DNA synthesis,
      - megaloblastic & suppressed bone marrow,
      - subacute combined degen of spinal cord
  - Pollution:
    - N20 + UV light ⇒ free radicals ⇒ ozone break down
    - Chronic effects on health care workers:
      - Fatigue, malaise
      - ?abortions, marrow suppression, teratogenicity
  - post op nausea & vomit
- safe in pregnancy

Cautions/Contraindications

- altered mental state
- recent scuba
- v cold conditions (<-6deg)
  ↳gases may separate
- Severe pulmonary disease may alter elimination of NO

Interactions

- nil

Dose

- GA:
  - induction 70:30 N20:O2
  - maintenance 30:70 N20:O2
- obstetrics: entonox 50:50
- dental procedures 25:75% mixture

Sevoflurane

Compound A

- = vinyl ether produced by degredation of sevo
- in rats shown to produce ATN
- debate about effect in humans but likely little clinical effect

- compound A production
  - directly related to
    - sevo concentrations
    - absorbent temp
  - inversely related to fresh gas flow rate (FGF)
- manufacture recommends sevo not used in FGF <1L/min and for no longer than 2 MAC hours
- for anaesthetic >2hrs FGF should be at least 2L/min

Characteristics that influence the choice of an agent

Agent	Useful	Problems
Halothane	Cheap Low pungency makes induction tolerable Bronchodilation	Cardiac depression Arrhythmias 'Halothane hepatiis' *
Isoflurane	Rapid onset and elimination Cardiac stability Little increase in ICP, marked reduction in $CMRO_2$	Pungent Tachycardia ± Coronary steal *
Enflurane	Few major problems	Seizure promotion Respiratory depression Product of metabolism toxic to renal tubules
Sevoflurane	Pleasant, rapid induction	Apnoea, laryngospasm more common than with halothane Compound A production Expensive
Desflurane	Very rapid elimination	Pungent Sympathetic stimulation at induction because of the above Requires special type of vaporiser Expensive

* Although hepatitis and coronary steal are *classically* associated with halothane and isoflurane, the problems are described with all inhalational agents.

Intravenous Induction Anaesthetics

- major gps:
  - ultrashort acting:
    - barbituates – thiopentone
    - non-barbituates – propofol & ketamine
  - midazolam – actually a benzo but has benefits & common adjunct
- benefits of IV anaesthetics:
  - rapid onset
  - controllable
  - amnesic effects
  - ↓amount of inhalational agent required
  - prompt recovery with small doses
  - no risk of explosion
- disadvantages of IV anaesthetics:
  - minimal mm relaxation & analgesic properties
  - subject to liver & renal excretion
  - common hypersensitivity reactions
  - tissue reactions if extravasation
  - hypotension/laryngospasm & resp failure a risk

Pharmacokinetics

- high lipid solubility ⇒ high potency & rapid onset
- short duration of action as drug quickly redistributed into fat deposits
- 2 compartment distribution of drug:
  - obese people have shorter effect of single IV dose
  - saturation of fat ⇒ prolonged action of drug as drug slow release back into circulation

Pharmaceutics

- 2 problems:
  - need high lipid solubility ⇒ to cross bbb
  - water soluble to be formulated as a solution for safe IV injection
- ∴ formulated as oil in water emulsions (milk)
- propofol in soya oil/egg lecithin/glycerol emulsion

Total IV Anaesthesia

- GA using only IV anaesthesia & no inhlaational drugs
- bolus dose then maintenance

Ultrashort Barbituate – Thiopentone

- CNS depressant produces hypnosis & anaesthesia without analgesia
- combine with mm relaxant & analgesia

MOA

- suppression of RAS

Pharmacokinetics

- high lipid soluble ⇒ rapid onset
- slow metabolism as moves out of adipose tissue slowly

Uses

- good emerg anaesthesia drug:
  - anticonvulsant properties
  - ↓ICP

Adverse Reactions

- serious:
  - ↓CO (↓SV) & ↑venous capacitance ⇒ ↓bp
  - cardiac arrhythmias
  - emergence delirium – excitability, confusion, hallucinations
  - resp depression
  - allergy
- during recovery:
  - shivering & trembling
- prolonged fatigue & headache

Non- Barbituates: Propofol

MOA

- rapidly acting non barbiturate hypnotic
- formulated in an emulsion for IV use
- no analgesic properties
- MOA not known- ?CNS depression via GABA receptors

Pharmacokinetics

- rapid onset of action – 40seconds
- duration of effect 3-5mins
- majority liver metab +/- extrahepatic metabolism
- almost completely metabolised to glucuronide

↳inactive metab; half life 3-8hrs

Uses

- induction & maintenance of GA
- PSA

Adverse Reactions

- resp & CVS depressant:
  - apnoea
  - bradycardia & ↓bp
- N&V
- involuntary mm movement common

Cautions/Contraindications

- pain & thrombophlebitis on injection

- potential for abuse

Interactions

- sedative effects of other CNS depressants ↑ed
- no other sig interactions

Dose

- IV dose 2-2.5mg/kg
- PSA 0.5-2mg/kg

Somatic NS

- aka voluntary ns
- primary motor area of cerebral cortex initiate voluntary movement
- impulse through UMN which decussate in medulla oblongata
- UMN terminate in ant grey horn of spinal cord at each spinal segment
- often interneurons which then connect to LMN
- LMN = final common pathway which connects CNS to skeletal mm

Targets to Block Neuromuscular Transmission

- incl:
  - block AP generation in motor neuron
  - inhibition of release of Ach
    ↳eg botox
  - inhibition of breakdown of Ach
  - blockade of postsynaptic receptors

Neuromuscular Junction

- @NMJ motor neuron divides into cluster of synaptic end bulbs containing Ach
- Ach released on arrival AP ⇒ diffuses cleft ⇒ postsynaptic nicotinic receptors on end plate
- NMJ norm in centre of mm fibres
- impulses radiate out from NMJ over mm
- action of Ach rapidly terminated by AChE (acetylcholinersterase) which attached to collagen fibres

Motor End Plate Nicotinic Receptors

- receptor 5 subunits with ion channel in centre:
  - α x2
  - β
  - δ
  - ε epsilon
- bulk of receptor faces extracellularly
- 2 molecules of Ach bind onto each α subunit ⇒ channel opens ⇒ Na flow through ⇒ depolarisation end plate ⇒ contraction

Neuromuscular Blocking Drugs

- 2 types:
  - competitive or non depolarising drugs:
    - block action of Ach at
      - postsynaptic nicotinic
      - presynaptic nicotinic ⇒ blocks normal feedback loop which ⇒ ↑Ach under conditions of enhanced stimulation
    - action can be reversed by anticholinesterase
    - eg pancuronium, curare
  - depolarising drugs:
    - nicotinic receptor agonists ⇒ maintain depolarised state of motor end plate ∴ no further APs
    - eg suxamethonium

Non Depolarising Blocking Drugs

- rapid blockade with motor weakness ⇒ total flaccid paralysis
- small muscles (eye,jaw) ⇒ limbs ⇒ trunk ⇒ diaphragm
  ↳recovery is generally opposite order
- can cause histamine release from mast cells:
  - flushing & rash ⇒ anaphylactic reaction
  - not due to receptor action but acidic nature of drug
  - risk varies inbetween drugs

Pancuronium

MOA

- non depolarising competitive blockade of nicitonic receptors at motor end plate
- interruption requires >70% of N receptors; blockade >95%

Pharmacokinetics

- wide volume of distribution within 5mins post injection
- highly water soluble ∴ urinary excretion begins immed
- clearances:
  - 25% renal unchanged
  - rest hepatic metab ⇒ bilary excretion
- half life 30mins

Uses

- adjunct to GA for surgery/ICU

Adverse Reactions

- slight ↑HR, ↑CO, ↑bop
- ↑intragastric pressure ⇒ risk of vomiting
- anaphylactoid reaction small risk (1 in 10,000)
  ↳histamine release

Cautions/Contraindications

- care in:
  - HTN
  - liver/kidney failure

Interactions

- additive effect with:
  - inhalational anaesthetics

    - sux
    - aminoglycosides (also cause blockade themselves)
    - benzo's
    - Ca channel blockers
    - lithium
    - propanaolol
- ↓effect with:
    - adrenaline
    - carbamazepine
    - anticholinesterase agents eg neostigmine
    - high dose steroids
    - Ca, Na, K salts

Dose

- initial 0.04-0.15mg/kg in adults & children >1month
- maintenance dose 0.01-0.02mg/kg

Post Op Reversal

- sugammadex
    - modified cyclodextrin
    - forms a complex with neuromuscular blocker ⇒ ↓binding to nicotinic receptors
    - rapid effect within 5mins (compared to 50min effect of neostigmine
    - SEs: taste sensations & allergic reactions
    - interacts with some drugs – fluclox, progesterones (take extra contraceptive precautions)

Depolarising Blocking Drugs

Suxamethonium

MOA

- agonist of N receptors on motor end plate
- ⇒ persistent stim & maintenance of depolarisation of MEP
- Na channels remain open ∴ no further response to elec stimulus
- during onset of action see mm fasciculation's:
    - as each MEP is depolarised ⇒ local AP to motor units without total mm contraction
    - x1 fasciculation/Motor unit then blockade
- short acting mm relaxant
- reversal by anticholinesterase not possible:
    - will prolong depolarisation

Pharmacokinetics

- rapid onset of action
- half life 2-4mins
- blockade persists for ~10mins
- hydrolysed by butyrylcholinesterase (aka pseudo-cholinesterase) to
    - choline
    - succinyl monocholine ⇒ hydrolysed to choline & succinic acid

    ↳if atypical pseudo-cholinesterase see extended blockade

Uses

- brief mm relaxation eg
    - ECT

  - tracheal intubation
  - surg procedures

Adverse Reactions

(M myalgia
A apnoea
R raised ICP & IOP
K hyperkalaemia
E vent Ectopics & bradys
T MH
& ↑gastric pressure and ↑salivation)

- profound & complex effects on CVS system:
  - bradycardia
  - tacchy/arrhythmia's
  - HTN
  - cardiac arrest
- ↑ICP
- ↑Intra-occular pressure – avoid in eye surg if anterior chamber needs to be opened
- ↑gastric pressure ⇒ vomit risk
- ↑serum K:
  - release of K from MEP
  - caution in burns & massive trauma
- malignant hyperthermia – mm spasm & rapid rise in body temp
- low pseudo-cholinesterase levels ⇒ prolonged mm paralysis
  ↳seen with liver disease ↳anticholinesterase drugs inhibit pseudo-C action
- anticholinergic effects ⇒ excessive salivation:
  - muscarinic like action of sux
  - prevented by atropine

Cautions/Contraindications

- care if:
  - electrolyte disturbance
  - low pseudo-C levels
  - renal disease
  - digoxin
- contraindicated:
  - malignant hyperthermia or FH
  - extensive burns or multiple trauma

Interactions

- additive effect (many):
  - lignocaine
  - non penicillin Abx
  - βblockers
  - lithium
  - steroids
- metoclopramide - ↓s inactivation of sux ⇒ prolonged NMJ blockade

Dose

- 1mg/kg loading; maintenance 0.5mg/kg
- IV or IM
- not to conscious person

Anticholinesterase Agents

- AChE (acetylcholinesterase) hydrolses Ach ⇒ choline & acetate
- enzyme bound to postsynaptic membrane
- active site of enzyme contains 3 amino acids:
  - } = esteratic site — serine
  - histidine
  - glutamate = anionic site
- 2 broad categories of drugs:
  - short acting eg donepezil
    - bind reversibly to anionic site
    - eg alzhemiers
  - medium acting eg neostigmine, pyridostigmine:
    - bind to both anionic & esteratic sites
    - hydrolysed more slowly
    - eg myasthenia & alzheimers
  - irreversible :
    - bind to esteratic
    - eg pesticides & chem. warfare

Neostigmine

MOA

- reversible inhibitor of AChE
- forms a carbamylated enzyme at active site
- complex slowly hydrolysed by AChE over 3-4hours

Pharmacokinetics

- poorly absorbed from GI tract
- doesn't cross bbb
- plasma half life 0.5-1.5 hours
- excretion:
  - faeces >50%
  - urine 30%
- metab by plasma cholinesterases
  - ↳∴ liver disease has no effect on drug

Uses

- used for reversal of non depolarising competitive NMJ blockers eg pancuronium
- Rx myasthenia gravis

Adverse Reactions

- best seen in overdose situation which ⇒ cholinergic crisis ie ↑↑Ach action at synapses:
  - NMJ – fasciculation's, weakness, paralysis, depressed vent
  - postganglionic parasympathetic synapses:
    - salivation, tears, ↑Gi & bronchial secretions, ↑bowel activity
    - bronchonconstriction
    - brady & hypotension
    - constricted pupils
    - D&V & urination

- CNS –
  - stim ⇒ depression with larger doses
  - irritability
  - ataxia, fatigue, amnesia
  - ↓GCS & resp depression
- CVS –
  - reflex ganglionic & postganglionic effects of Ach accumulation
    - initial – excitation
    - later – ganglionic blockade through persistent depolarisation ∴ inhibitory
  - ↑parasymp vagal tone ⇒
    - bradycardia
    - ↑refractory period & conduction time SAN/AVN

Cautions/Contraindications

- care in
  - asthma
  - heart disease
  - ↓bp
  - peptic ulceration

Interactions

- ↓effect:
  - steroids
- any drugs with anticholinergic activity will ↓effect of neostigmine & vice versa

Dose

- reversal of NMJ blockade 50-70mcg/kg to max 5mg over 1min
  ↳give after or with atropine 0.6-1.2mg

Local Anaesthesia

- ideal LA
  - target sensory nerves only
  - rapid reversible
  - non toxic
  - rapid painless onset
- 2 commonest used =
  - lignocaine
  - bupivacaine
- rapid evaporation ⇒ cooling can provide similar LA effect
  ↳eg ethyl chloride
- = membrane stabilisers or ion channel modulators

Chemistry of LAs

- generally have
  - aromatic (phenyl gp) at one end:
    - makes this end lipid soluble
  - amine (nitrogen containing) gp at other end
    - makes this end hydrophilic

  ↳joined by intermediate chain of carbons
- different solubilities at either end of molecule allows chemical to align & act in nerve cell membranes

↳in the phospholipid bilayer

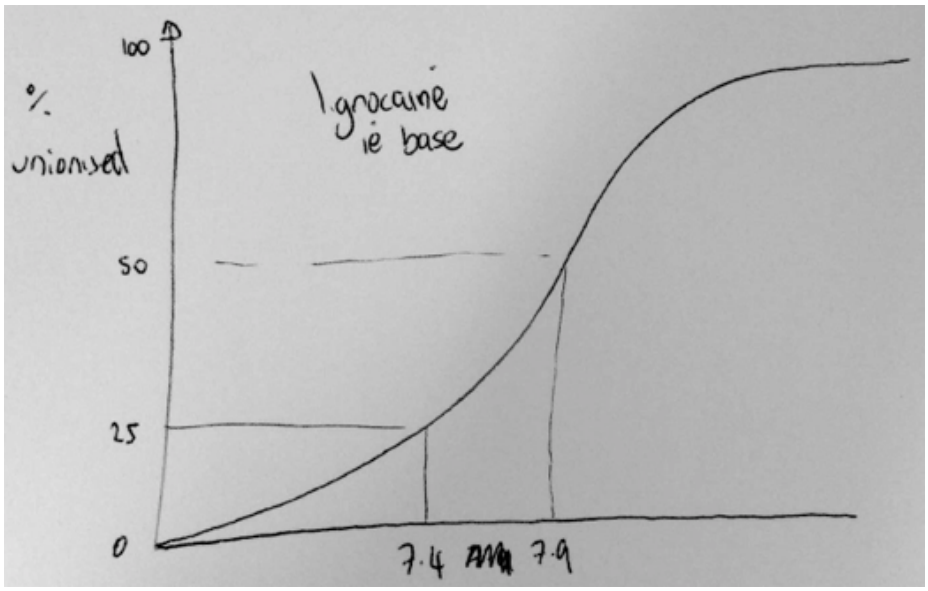
- intermediate carbon chain contains a link which defines subgroup of molecules; either:
  - ester link CO-O
    - = ester LAs - cocaine, procaine, amethocaine
    - metab'ed rapidly by plasma esterase enzymes ⇒ PABA metabolites
    - PABA metabs responsible for allergic reactions
    - less common to use this gp
  - amide link CO-N
    - eg lignocaine, prilocaine, bupivacaine
    - not metab'ed to PABA metabolites ∴ allergy less common
- all LAs are amines ∴ can exist as either: (R=any radical)
  - uncharged amine form (NR_3)
  - charged quaternary amine form (N^+R_3H)

  ↳move in equilibrium: $H+ + NR3 \longleftrightarrow N^+R_3H$
- balance of equilibrium depends on:
  - chemistry of individual LA drug
  - pH of solution
- extent of ionisation determined by pH of environment:
  - strength of acid = tendency to dissociate into H+ & anions
  - dissociation defined by pKa:

    ↳ = pH at which half the chemical is in its ionised form (pH – pKa = 0)
  - degree of unionised depends on

    ↳ whether drug is
    - acid: if pKa < physiological pH (7.4) = <50% unionised
    - base: if pKa < 7.4 = >50% unionised (all LAs are bases)

      curves drawn differently for acid/base drugs– for all LA's:



MOA

- enter cell by diffusion through membranes
- bind to modulatory site in voltage dependant Na channel ⇒ block it by preventing transient opening
- ∴threshold potential not reached ⇒ not depolarisation & no AP
- LAs effect all membranes eg ANS, motor nerves, mm cells, CNS neurons
- Susceptibility of nerve to LA depends on (better):
  - fibre diameter & myelination – order of block (first to last):
    - small myelinated
    - unmyelinated (C)
    - large myelinated (A delta)
  - tissue pH (physiological – alkaline)
  - length nerve fibre
- ∴ autononmic & sensory fibres effected first – thinner & unmyelinated
  ↳motor fibre can be effected with big enough dose
- sequence of anaesthesia:
  - loss pain
  - loss temp sens
  - loss proprioception
  - loss touch/pressure

Pharmacokinetics

- injection ⇒ local dispersion
- onset of action determined by movement into nerve cells which determined by:
  - lipid solubility which depends on
    - pH tissue
    - degree ionisation of LA molecules (function of pKa of drug)
- protein binding & vasoconstrictor in solution help to retain drug in tissue for longer
- local action terminated by:
  - diffusion away
  - dilution & uptake into vessels

  ↳determined by lipid solubility & ?VC present in solution
- bupivocaine have a longer duration of action#
  ↳as ↑ed lipid solubility & ↑protein bound

Comparisons

- short acting: (30-60mins)
  - procaine:
    - least toxic LA
    - low lipid solubility ∴ slow onset
    - potency 0.5
- intermediate acting (30mins- 4hrs)
  - lignocaine:
    - potency 1
    - more cardiotoxic than prilocaine
  - prilocaine:
    - products of liver metab may ⇒ methaemoglobinuria

  - EMLA (lignocaine/prilocaine)
    - local irritation
    - toxic if swallowed
    - <6months risk of metharmoglobinaemia
- long acting (3-10hrs):
  - bupivacaine:
    - potency 4
    - ↑cardiotoxic than lignocaine
    - slow onset
    - less motor blockade
  - amethocaine (tetracaine):
    - topical LA
    - potency 5
    - slow onset

Vasoconstrictors

- most LAs ⇒ VD by
  - direct action on blood vessels
  - action on sympathetic VC nerve fibres ⇒ VD
- risk of rapid systemic absorb: if absorb>rate of elimination then toxicity
- ∴ adrenaline or phenylephrine ⇒ VC ⇒ drug stays local longer
  ↳α adrenoceptor agonist in nasal spray with lignocaine

Toxicity

- order of toxicity (less > more):
  - procaine >prilocaine>lignocaine>bupivocaine>amethocaine>cocaine
- reactions:
  - specific to drug eg prilocaine = metHb ⇒ cyanosis
  - allergies eg bronchospasm & anaphylaxis (more common with esters)
  - systemic effects of LA:
    - numb tongue
    - CNS stim: tremor, visual disturbance, convulsions
    - CNS depression: relax smooth mm & skel mm; CVS/resp depression, ↓bp

Reversal

- recovery of sens can be accelerated with phentolamine:
  - α receptor antagonist
  - infiltrate into same site as LA ⇒ VD ⇒ ↑clearance of lignocaine

  ↳good in dental surg

Types of Block

- epidural:
  - injection into extradural space between dura & lig flavum
  - space filled with loose adipose & lymph & blood vessels
  - injection C7-T10
  - injection stays local to level
  - post op urinary retention common 2nd to block of parasymp nerves
- spinal anaesthesia
  - injection into CSF in subarach space

- below spinal cord level ie >L2
- onset action 1-2mins
- duration 1-3hrs
- specific gravity of LA & position of pt is important to prevent LA rising though spinal cord
- SEs:
  - include hypotension; ↓CO; resp depression 2nd to depression symp pathways & medullary centres
  - Rx with sympatomimetics eg ephedrine & metaraminol

Lignocaine

MOA

- amide –type LA
- blockade of Na channel ⇒ prevents initiation & propogation of nerve impulses
  ↳also stabilises all potentially excitable membranes incl heart

Pharmacokinetics

- rapid onset action 5-10mins
- Peak blood level usually occur 10-25min post injection
  ↳when toxicity most likely to occur
- duration blockade 1-1.5hrs
- once absorb into gen circulation rapid redistribution to all tissues esp heart
- large 1st pass metab in liver – CP450 hydrolyses amide link
  ↳why cant take orally
- excretion via kidneys - <10% unchanged
- half life 90-120 mins

Uses

- LAf
- Rx or prevent ventricular arrhythmias
-

Adverse Reactions

- toxic depressant effects in CNS/ANS/PNS & CVS & resp systems if:
  - ↑↑dose
  - rapid absorb
  - delayed elimination
- allergy rare

Cautions/Contraindications

- ↓dose: children, elderly, CVS, Neuro, hepat-renal disease
- contraindicated if:
  - infection at site injection
  - severe shock
  - hypotension
  - SVTs

Interactions

- other anti-arrhythmics/phenytoin/alcohol ⇒ ↑CVS effects of lignocaine
- ↓clearance of lignocaine:
  - β-blockers
  - cimetidine
  - erythromycin

Dose

- lowest effective dose
- Max safe dose 3mg/kg(adults & child) (6mg/kg with adrenaline)
  Thus 70kg man = 210mg. 1% contains 10mg/ml thus 20mls contains 200mg
  2% contains 20mg/ml thus 10mls contains 200mg
- anti-arrhythmic dose: not more 300mg/1hr