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ICU Summary

- Sepsis - EGDT - ARISE, ProCESS, ProMISE. EGDT vs standard therapy has showed no difference
- fluids:
  ‣ SAFE - albumin is safe except in TBI/Neuro
  ‣ FEAST - Africa - IV fluid did worse
  ‣ CHEST - HES vs saline. ↑ed renal failure
  ‣ 6S - HES vs saline. ↑mortality in HES
  ‣ SPLIT - Saline vs P148 - no diff in outcome
- ARDSNET
  - TTM post OHCA - 36degs for 36hours.
  - brain death
  - DECRA
  - inotropes
  - DM control
  - Ebola & Tamiflu
  - ECMO
- Hb threshold:
  ‣ 70
  ‣ Hb = HCT.
  ‣ acute bleeding will not change Hb
- O2 is bad - normoxyaemia

Diagnostits

Acid Base & ABGs

1. pH – acidaemia or alkalaemia

2. HCO₃⁻ - help with whether there is a metabolic component or not

3. PaCO² – helps with respiratory component

4. A-a gradient = (normal 5-15mmHg)
   • see ↑ed A-a grade with age as CC lies increasingly inside FRC
   • to calculate: predicted - measured
   • (PA02 = PiO₂ – PaCO2/0.8) – PaO2

where PiO₂ = (FiO₂ %/100) * (atmospheric pressure - 47)
   = at sea level 760 - 47 = 713
   = 150 at sea level in RA

4a. PF Ratio=
   • = PaO₂/FiO₂  ie
   • at sea level normal = >500
   • can use as rough guide to whether sig A-a gradient present by rearranging equation:
     ‣ predicted PaO₂ = FiO₂ x 500
     ‣ = 0.21x500
     ‣ = 105mmHg
   • can measure ARDS severity:
     ‣ < 300mmHg – ALI
     ‣ 200-300mmHg - mild ARDS (27% mortality)
     ‣ 100-200 = moderate (32% mortality)
By A Hollingworth & J Fernando

- <100 = severe (45% mortality)

5. **Respiratory Acidosis**
   (Norm HCO3 = 25, Norm PCO2 = 40)

   ACUTE (hours) – 1 for 10 rule = for each 10mmHg rise in CO2, HCO3- goes up by 1mmol/L

   CHRONIC (days) – 4 for 10 rule= for each 10mmHg rise in CO2,HCO3- goes up by 4mmol/L

6. **Metabolic Acidosis**
   - Use either of following to decide if compensated enough:
     - the last two digits of pH should approximately equal the PaCO2 (works well for pH between 7.15-7.45)
     - expected PaCO2 at max compensation = 1.5 x HCO3 + 8
   - PaCO2 rarely falls below 8-10

7. **Anion Gap** = (Na + K) - (Cl + HCO3)

   (NB:
   - unreliable if albumin <15
   - Na needs correcting in ↑ BSL:
     - Corr Na = measured + (BSL -10/3)
   
   - normal = 10 to 15
   - > 30 then metabolic acidosis invariably present,
   - 20-30 then 1/3 will not have a metabolic acidosis)

   **Raised Anion Gap Metabolic Acidosis**
   - MUDPILES
   - causes – accumulation of organic acids or impaired H+ excretion:
     - Methanol
     - Uraemia/renal failure
     - DKA + ketoacids eg starvation
     - Paracetamol
     - Infusion of acid, Iron, Isoniazid
     - Lactate (hypoperfusion or poisoning of electron transport chain)
     - Ethanol/Ethylene Glycol
     - Salicylates
   
   - this metabolic acidosis is normally managed by albumin -> if albumin decreased by 1g then decrease anion gap by 2-3 points.

   **Normal Anion Gap Met Acidosis**
   (USED CARP)
   - Ureto-entric fistula
   - Saline or hyperchloraemia
   - Endocrine eg addisons, spironlactone
   - Diarrhoea
   - Carbonic anhydrase inhibitors
   - Ammonium chloride
   - Renal tubular acidosis
   - Pancreatitis

   **Low Anion Gap Met Acidosis**
   - high lithium, calcium or magnesium

   - lab tests to order = lactate, glucose, creatinine and urea, urinary ketones, serum levels of methanol, ethanol, paracetamol, salicylates and ethylene glycol.
7a. **Osmolal Gap**
- calculate osmolar gap =
  ‣ measured - predicted (ie opposite to A-a gradient)
  ‣ osmolality (from lab) – osmolarity calculated
  ‣ to calculate osmolarity = 2x (Na+K) + glucose + urea
- gap of >10 is abnormal
- causes:
  ‣ DM - ketones
  ‣ ethanol
  ‣ methanol
  ‣ mannitol
  ‣ etylene glycol

8. **BE**
- norm = -3 to +3
- = metabolic component on acid-base disturbance

9. **Respiratory Alkalosis**
(Norm HCO3 = 25, Norm PCO2 = 40)

ACUTE (hours) – 2 to 10 rule = for each 10mmHg drop in PaCO2 the HCO3- goes down 2mmol/L

CHRONIC (days) – 5 to 10 rule = for each 10mmHg drop in PaCO2 the HCO3- goes down 5mmol/L

10. **Metabolic Alkalosis**
- the kidney has a marked capacity for HCO3- excretion
- also, the kidney will avidly retain HCO3- when the plasma concentration is low
- for a metabolic alkalosis to persist there must be a renal process maintaining the initiating disorder
- causes:
  ‣ LOSS OF ACID – diuretics or vomiting/NG losses
  ‣ GAIN OF ALKALI – milk-alkali, metabolism of ketones, lactate, citrated or NaHCO3 infusion
  ‣ REBOUND ALKALAEMIA - chronic resp acidosis but now ventilating normally

- measure urinary Cl- (<15 - > due to loss of Cl-, >25 due to K+ depletion or mineralocorticoid excess)
- expected CO2 with compensation = use either of:
  ‣ 0.7 x HCO3- +20
  ‣ BE +40
  ‣ last 2 digits of pH

**Mixed & Central Venous Saturations**
- O2 flux = (cardiac output x (Haemoglobin concentration x SpO2 x 1.34) + (PaO2 x 0.003)) – oxygen consumption

**MvO2**
- measures the end result of O2 consumption and delivery @ a tissue level
- is used in ICU as a measure of O2 extraction by the body
- normal MvO2 = 60-80%
- measured via a sample of blood from a pulmonary artery catheter (PAC)
- if MvO2 low then either consumption elevated or delivery ↓

**Usefulness**
- marker of how well O2 is being delivered to the peripheral tissues by extrapolation:
  ‣ if MvO2 low & patient in multiorgan failure ⇒ add inotrope ⇒ ↑CO ⇒ ↑MvO2 ie. in severe sepsis
- treatment goal in severe sepsis by Rivers -
if you believe his work decrease mortality and morbidity
- continuous measurement can watch trends with changes in therapy – fluid, inotropes, vasodilators, dialysis
- good information quickly

**Problems**
- must be measured from a PAC: risks of PAC placement;
  ‣ arrhythmia, pulmonary infarction, embolism, bleeding, pneumothorax, line sepsis
- cannot use CVL:
  ‣ SVC sample which different number to MvO2 as draining from high uptake brain
- can be high in a number of situations ie 2 variables:
  ‣ sepsis,
  ‣ liver failure,
  ‣ wedged PAC,
  ‣ administration of high FiO2)
- can be low in a number of situation:
  ‣ multiorgan failure
  ‣ cardiac arrest
- requires calibration for changing haematocrit

**HIGH Svo2**
- increased O2 delivery (increased FiO2, hyperoxia)
- decreased O2 demand (hypothermia, anaesthesia, neuromuscular blockade)
- ↑Q - hyper dynamic circulation

**LOW Svo2**
- decreased O2 delivery:
  1. decreased Hb (anaemia, haemorrhage, dilution)
  2. decreased SaO2 (hypoxaemia)
  3. decreased Q (any form of shock, arrhythmia)

- increased O2 demand (hyperthermia, shivering, pain, seizures)

**Causes of High Svo2 despite evidence of end-organ hypoxia**
- arterial admixture (this is believed to take place in sepsis)
- histotoxic hypoxia
- abnormalities in distribution of blood flow
Practical ICU

Fluids

Types
- Crystalloid:
  - **Isotonic**
    - balanced
      - plasmylate - calcium free, okay for blood carrier
      - Hartmans - must use separate line with rbc
  - **Unbalanced**
    - Saline
- **Hypotonic** - dex
- Colloids:
  - semi-synthetic
    - Dextran - from fungi - anaphylactoid, -ve renal function & coagulopathy
    - Starch - TRRT, coagulopathy
    - Gelofusin - from animals
  - human derived:
    - Albumin - suspended in electrolytes, isotonic
    - rbc

Concepts in Fluid Therapy
- key force to maintain intravascular volume is endothelial glyocalyx:
  - More impt than Starling forces
  - -ve charge lining that repels -ve charge cells (ie rbc, wbc, plt)
    - except albumin which can adhere despite -ve charge
  - Oncotic pressure is felt across glycocalyx not vessel wall
  - endothelial damage ⇒ leaking of all cells eg in sepsis, ischaemia, DM, trauma
- Preventative Rx:
  - Avoid hyper-volaemia/hyper-glycaemia
  - maintain physiological plasma proteins incl albumin
  - no formal Rx's available
- should avoid pre-loading
- open abdo evaporative loss is much smaller than prev thought = 0.5-1ml/kg/hr
- 3rd space does not exist
- fluid therapy affects pt outcome
- treat vasodilation with vasoconstrictors not with fluid

Peri-Op Fluid
- there is an optimum fluid load
- too much & too little is harmful
- correct amount is unknown but possibly restrictive fluid may be better
- no evidence to support goal-directed therapy (EDGT):
  - Tendency to over-infuse
  - Standardising care most important thing
- any fluid given to any patient consider 3 R's:
  - **R esus** fluid:
    - assess response to fluid bolus
  - **R outine** maintenance:
    - adults:
      - 100% balance crystalloid has too much sodium:
        - 24hr needs:
          - 25-30ml/kg water
          - 1mEq/kg Na (1 litre balanced crystalloid = enough salt/day)
          - 1mEq/kg K & Cl
          - 50-100g glucose
- Paeds = 5% dex + crystalloid (balanced or unbalanced)
  - Replacement fluid:
    - replace losses ml/ml

**Which Fluid**
- Paeds -
  - maintenance: used balanced crystalloid + 5% dextrose
  - resus: use crystalloid
- choice of fluids based on studies:
  - SAFE:
    - albumin vs saline in ICU
    - Avoid albumin in TBI otherwise is safe
  - ALBIOS: albumin in sepsis is safe but no improvement in mortality
  - Death of starches:
    - CHEST: ↑RRR rate but no change in mortality
    - 6S: 1 death with starch, ↑RRT
- Patient in shock:
  - CRISTAL - ICU trial colloids vs crystalloids = no diff 28day mortality
  - ATLS says use crystalloids but >1.5 litres ⇒ worse outcome
  - MILITARY = replace blood with blood

**Goal Directed Therapy**
- no experimental evidence to show EGDT has any benefit
- Negative trials include PROMISE, ARISE, PROCESS
- perhaps standardised care most imp thing
- Disadvantages of GDT
  - No standard Rx arm in literature
  - Diff protocols
  - run risk of over fluid therapy ⇒ complications eg GI ileus
  - GDT doesn’t ↓variability in fluid admin
  - control groups arguably not standard practise

**Haemodynamic Assessment**
- need assessment tool for GDT
- flaws in Ax methods may explain reason why no successful trials in GDT
- diff types:
  - ECHO
  - CVP
  - PAC
  - Cardiac output measurements
  - Oesophageal doppler

**ECHO**
- Approach:
  - volume
  - Systolic function
  - filling pressures
  - final Ax

**CVP**
- overwhelmingly CVP or change in CVP does not predict fluid responders
- should not use it as a guide
- Reason to give fluid is to ↑DO2 by ↑CO via ↑SV
  - an ↑CVP does not effect this
- an extreme ends risk RV failure from RV overload

**PAC**
- Used Stewart Hamilton equation ⇒ CO measurement
- value averaged over minutes
- risks of line insertion mean only at risk patients should have line inserted
Cardiac Output Measurements
- goal is end organ perfusion
- static variables are too slow ie lactate, pH
- Dynamic variables:
  - HR
  - MAP
  - fluid challenge & Ax bp
  - Passive leg raise - 45deg leg up = 500ml bolus \(\Rightarrow\) response within 1min
  - SPV, PPV, SVV
    - >11% \(\approx\) fluid responder
    - need fixed vent mode, norm RR, norm PEEP, norm intra-abdo pressure, not on vasoactive already
  - oesophageal doppler
    - perhaps best
    - Learning curve
    - probe needs re-positioning
    - underestimates CO (doesnt include cerebral circulation or RUL \(\cdot\) x 1.4)
    - Doesn't measure descending aorta X area \(\cdot\) only a trend not an actual volume of flow measurement
    - some unable to gain window
    - not useful in arrhythmia

Resp Failure
- type 1 = PaO2 <60, PaCO2 <50
- type 2 = PaO2 <60, PaCO2 >50, pH <7.35

Transfer Critically Unwell

Pre-transfer Assessment
- consent (discuss with family)
- formal clinical assessment
- discuss state with intensivists
- check infusions, ventilator settings, monitoring and access
- increase sedation +/- paralyse
- N/G +/- chest drain if being transferred by air
- replace air in ETT with saline
- get all investigations and notes
- discuss procedure & risks with family
- make sure you have adequate skill to deal with problems on the transport
- Communication with team going to

Transport
- invasive monitoring
- hypothermia cares
- remember decreased PaO2 with altitude (@ 1500m PaO2 = 75mmHg)
- acceleration/deceleration can cause haemodynamic instability
- ensure we have enough O2 and batteries
- arrangement of staff

Post-transfer Care
- hand over to ICU stuff
- document how transfer proceeded and any interventions
Specific type II resp failure conditions

COPD - problem:
- acute resp failure caused by dynamic hyperinflation due to ↑airways resistance preventing complete exhalation
causes change in lung mechanics:
- ↑ intrinsic PEEP
- ↑ WOB → early fatigue → ↑ CO2
NIV works by adding
- inspiration: PS helps overcome ↑ airways resistance
- expiration: extrinsic PEEP to offset intrinsic PEEP → ↓ dynamic hyperinflation → ↓ WOB
benefit =
- ↑ VT
- ↓ RR
- ↑ ed clearance of CO2
- normalised pH
criteria to start:
- pH < 7.25
- hypercarbic coma
- type II failure

Asthma
- similar benefit mechanics to COPD
- worth trialling as intubation may be life threatening:
  - severe acidosis
    - barotrauma/volutrauma ⇒ PTX

Morbid obesity
- acute on chronic type II failure

Neuromuscular disorders
- acute (eg GBS, acute myasthenia) not routinely recommended
- chronic (eg NMD) recommended in advanced disease to ease dyspnoea

Specific type 1 resp failure conditions:

Cardiogenic APO -
- CPAP
- mechanism of benefit ⇒ ↓ preload & afterload, ↓ WOB
- 10–12.5 cmH2O causes:
  - ↑ oxygenation
  - ↓ need for intubation
  - shorten ICU stay

Pneumonia
- controversial but can be an effective alternate strategy
- will be 30–40% who will fail & require intubation

ALI/ARDS
- unlikely to be of benefit
  - lung contusion - favourable
  - post op - reintubation carries high risk. Bridging NIV shown to be of benefit

Weaning
- can use a bridging strategy
- support in trials for extubation before meeting standard criteria

Complications of NIV
- minor:
  - air leak
  - mask problems eg discomfort, nasal bridge ulcerations, facial erythema
  - nasal congestion & eye irritation
  - aerophagia - in 25% - suggestion all should have NG placed
- major:
  - aspiration of gastric contents
  - CVS unstable
  - PTX
Feeding in ICU

**Enteral Feeding**
- enteral route is preferred to parenteral route due to:
  - side effects
  - outcome
  - cost
- post pyloric enteral feeding:
  - better at:
    - ↓ aspiration
    - ↑ ed success of achieving target
  - but more problems eg blockage
- target enteral feed = 1ml/kg/hr

**Parenteral Feeding**
- Indications:
  - GI tract not working
  - Unable to meet enteral target
- parenteral side effects:
  - sepsis
  - ↑ BSL
  - ↓ pH
  - dehydration
- additives may be useful:
  - glutamine may be beneficial
  - selenium may ↓ mortality
  - arginine may cause harm

**Combined**
- combined enteral/parenteral feeding is fine

Renal Replacement Therapy

**Indications**
- renal indications:
  - uraemia - coagulopathy or encephalopathy
  - pH <7.1
  - ↑K >6.5
  - fluid overload
non renal:
  - toxicological
  - hyperthermic

- others:
  - endotoxic shock
  - SIRS
  - hepatic failure
  - severe dysnatraemia (<115 or >165)
  - traumatic rhabdo

**Types of therapy**

- continuous therapy:
  - ↓ed risk of hypotension:
    - IHD = hypovolaemia & large fluid shifts ⇒ ↓organ perfusion
    - CRRT ⇒ ↑SVR and MAP due to slow fluid movement drawing fluids into vascular compartment
  - continuous fluid removal ⇒ ↓extravascular lung water
  - improved uraemia control
  - ↓body temp
  - avoidance of dysequilibrium in ICP & CPP
  - use locally drive standard dosing regimes

**Complications**

- include:
  - heparin associated:
    - bleeding
    - HIT
  - catheter related: sepsis thrombosis AV fistula
  - arrhythmia
  - PTX
  - hypothermia
  - anaemia
  - hypovolaemia/hypotension
  - membrane reactions - anaphylaxis
  - electrolyte abnormalities
  - air embolism
  - drug related
Drugs

Propofol
- an IV sedative and anaesthetic agent
- substituted benzene ring structure
- dose = 2mg/kg for induction (adult) or 3-4mg/kg (children)

Advantages in ICU
- characteristically white emulsion mixture (decreased risk of drug errors with multiple infusion in ICU)
- rapid onset
- rapid offset (short context-sensitive half time) -> good for waking up quickly and neurologically +/- extubation
- causes bronchodilation
- anti-emetic
- safe in porphyria
- safe in MH patients
- maintenance of cerebral metabolism and blood flow (unlike volatiles that have been occasionally used in ICU for sedation +/- bronchodilation)
- decrease in ICP
- anticonvulsant (good agent in cerebral oedema and seizures)
- no active metabolites (unlike midazolam and morphine)
- cheap (compared to dexmetidomidine)

Disadvantages in ICU
- painful in injection
- no provision of analgesia (unlike clonidine or dexmetidomidine, need to infuse opioid for analgesia)
- causes vasodilation and negative inotropy -> hypotension (may not be tolerated in patient with severe cardiovascular compromise ie. severe sepsis with multiorgan failure, midazolam and opioid more sensible in this context)
- can cause apnoea and decreased response to PaCO2 and PaO2 -> have to provide controlled ventilation if using boluses.
- decrease renal blood flow and GFR from hypotension
- metabolised by liver (unlike remifentanil which has organ independent metabolism and inactivation)
- doses of >4mg/kg/hr for >48 hours associated with propofol infusion syndrome -> is rare reports of syndrome after 3-5hrs of propofol

† signs:
- severe metabolic acidosis - renal failure & lactic acidosis
- bradycardia
- rhabdomyolysis
- multiorgan failure
- treatment resistant cardiac arrest
† mostly described mainly in children

† pathophys:
- imbalance between energy demand & utilisation
- impairment of oxidative phosphorylation & free fatty acid utilisation
- suppression of cardiac function - via antagonisation of β adrenergic receptor & calcium channel binding

† diagnosis:
- monitor CK & triglyceride levels after 48hrs of propofol
- ↑ing CK => suspect PRIS => stop propofol
- then supportive Rx: renal, cardiac pacing, support, ECMO

† prevention:
- glucose infusion may prevent
- suspect if RFs eg severe head injuries, sepsis, high catecholamines, inborn errors of fatty acid oxidation
- expensive (compared to midazolam and morphine)
- may support bacterial growth if infused over long period of time (>8 hours) although does now have EDTA and sodium metabisulphide
Medical Problems

Post Cardiac Arrest Care
- post cardiac arrest syndrome common - assoc with marked inflam reponse

Aims
1. prevent further cardiac arrest
2. define the underlying pathology
3. limit organ damage
4. predict non-survivors

Prevention of further cardiac arrest
- O2 - normoxaemia
- assist ventilation via ETT (check placement)
- commence sedation - propofol & opioid
- ventilate to normocarbia
- correct electrolyte abnormalities
- control glucose tightly
- administer appropriate anti-arrhythmic (amiodarone 300mg or 5mg/kg)

Define underlying pathology
- diagnose and treat (may need PCI or thrombolysis)
- treat complications (heart failure, hypotension, rib #, pneumothorax)
- define GCS

Limit organ damage
- if ongoing ST elevation ⇒ reperfusion therapy required ie PCI
- if unconscious despite ROSC ->
  ‣ TTM ie prevent hyperthermia >36
  ‣ ice cold saline, ice blanket
  ‣ 12-24hrs post slowly rewarm
- invasive monitoring
- inotropes/vasopressors

Prediction of non-survivors
- many won’t survive -
  ‣ pre-hospital = 8% survive to d/c
  ‣ in hospital = 18%
- down time key indicator
- often need 72 hours from ROSC to prognosticate neurological outcome (in absence of sedatives)
- generally 3-5days of ICU care in coma following ROSC

Asthma
- benefit of assisted ventilation is external PEEP helps overcome internal PEEP which is high due to gas trapping
- inspiratory augmentation ⇒
  ‣ ↑ VQ match
  ‣ ↑ airspace opening
- NIV:
  ‣ ↓s WOB by equalising pressures
  ‣ ♦ good to use as early trial
  ‣ Contraindications:
    - Arrest
    - severe hypoxia
    - rapid ↓GCS
- facial trauma
- upper GI bleed

Complications of NIV:
- mask/face
- Stomach insufflation
- other - PTX, ↓bp

BiPAP:
- Pinsp 10-20
- PEEP 5-10

IPPV:
- Intubate when:
  - ↑WOB/exhaustion
  - high and rising PCO2 (less reliable)
  - RR >25, paradoxical breathing
  - apnoea on intubation - acidosis
- ↑↑ risk of barotrauma/volutrauma
- long expiratory times
- start with zero PEEP (as can ↓lung volumes) ⇒ otherwise low PEEP (<10)
- watch for auto-PEEP:
  - disconnect and compress chest
  - end exp holds

- use big tube, slow bag with RSI
- VT 5-7/kg, RR 10, I:E 1:4
- allow Pmax up to 55 (alveoli not seeing this pressure)
- Target P plateau <25 (at end insp pause)

### Pulmonary Oedema

**Hydrostatic**
- balance of Starling forces:
  - hydrostatic eg LV failure
  - oncotic pressures eg ALI/ARDS

**Neurogenic Pulmonary Oedema**
- = sudden onset resp failure after injury to CNS
- typically assoc with ↑ICP
- Occurs post:
  - SAH - most common
  - TBI
  - seizues
  - strokes
  - etc
- pathophys:
  - CNS mediated SNS drive ⇒ loss of vasomotor homeostasis ⇒
    - ↑HR & contractility
    - ↑↑ pulmon vasoC
    - secondary myocardial ↑workload ⇒ ischaemia ⇒ failure/Tako-subo cardiomyopathy
  - inflam mediated ↑vasc permeability
- = diagnosis of exclusion
- Rx
  - treat underlying cause
  - supportive care:
    - A - intubate if required
    - B - protective vent strategy but avoid permissive hypercapnia if ↑ICP
    - C - CI >2.5 while avoiding ↑HR, good pHTN care
    - Fluid - many will be fluid deplete ∴ imp to distinguish from cardiogenic APO
- majority should resolve 24-48hrs
Negative Pressure Pulmonary Oedema
- assoc with upper airway obstruction in spont breathing pt
- 50% assoc with laryngospasm
- commoner in younger pts
- pulmon oedema typically described as developing within 2mins of obstruction
- mechanism:
  ‣ obstruction => ↑-ve ITP
  ‣ ↑hypoxia => ↑SNS drive => ↑SVR => ↑pHTN which worsened by hypoxic pulmon vasoC
  ‣ see pressure gradient for fluid pulmon vessel => alveolar
- Rx:
  ‣ CPAP for 2 hours
  ‣ 24 hours of IPPV

HAPE
- SOB >2500m
- HPV central mechanism
- Rx:
  ‣ CCBs
  ‣ steroids
  ‣ descent

Diabetes Insipidus
- = inadequate secretion and action of the anti-diuretic hormone (ADH).
- ADH produced in the hypothalamus & then transported => posterior pituitary gland
- Released in response to
  ‣ thirst,
  ‣ increased plasma osmolarity
  ‣ hypotension.
  ‣ stress
- = key hormone involved in H2O regulation in the body and defence of blood volume.

- post head injury can see ↓production & release of ADH:
  1. direct disruption of the hypothalamus or pituitary
  2. interruption of the blood supply to these parts of the brain
  3. increased ICP or oedema causing herniation of the brain and subsequent compression of the pituitary stalk or gland.

Consequences of decreased ADH action
- decreased H2O reabsorption in the collecting ducts of nephron
- decreased Na+ reabsorption (via AT2/aldosterone)
- increased K+ secretion
- decreased GFR from relaxation of mesangial cells in glomerulus
- ↓intravascular volume (dehydration and hypovolaemia)
- polyuria
- loss of tone in vascular tree => hypotension,

- decreased aldosterone secretion => decreased Na+ reabsorption, increased K+ loss
- decreased angiotensin II => vasodilation, decreased nordrenaline secretion from post-ganglionic sympathetic neurons, decreased thirst sensation, decreased ADH secretion

Diagnosis
- polyuria
- high serum Na+
- low serum K+ (urinary)
- high plasma osmolality
- high urinary Na+ (inappropriate)
- high K+
- low plasma ADH level
- worsening of biochemical markers with fluid restriction
- improvement in biochemical markers and polyuria with desmopressin treatment
- MRI to quantify anatomical integrity of hypothalamus and cerebral blood flow may be required to confirm diagnosis

**Shock Overview**

**Definitions**
- shock = imbalance between o2 supply and demand ⇒ tissue hypoxia
  - NB actual O_2_ delivery to tissues may be ↑ed
- SIRS = 2 or more of
  - Temp <36 or >38
  - HR >90
  - RR >20 or PaCO_2_ <32mmHg
  - WCC <4 or >12 or immature bands of cells (left shift)

**Classification**
- Physiological classification:
  - tissue hypoxia:
    - Hypoxic
    - Anaemic - ↓Hb, ↑HbCO, ↑met-Hb
    - Stagnant – low CO
    - Histotoxic – eg cyanide poisoning
- Clinical classification:
  - **Cardiogenic**:
    - Eg:
      - Infarction ⇒ mechanical ventriculoseptal defect
      - Myocarditis
      - Valvular abnormalities
      - Obstructive
      - = pump failure 2nd to extrinsic obstruction eg PE or tamponade
  - **Obstructive**
  - **Hypovolaemic**:

<table>
<thead>
<tr>
<th>% blood loss</th>
<th>RR</th>
<th>Pulse</th>
<th>SBP</th>
<th>Cap refill</th>
<th>Mental State</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;15</td>
<td>14-20</td>
<td>90-100</td>
<td>Norm</td>
<td>Norm</td>
</tr>
<tr>
<td>2</td>
<td>15-30</td>
<td>20-30</td>
<td>100-120</td>
<td>Norm</td>
<td>&gt;2sec</td>
</tr>
<tr>
<td>3</td>
<td>30-40</td>
<td>30-40</td>
<td>&gt;120</td>
<td>↓</td>
<td>&gt;2sec</td>
</tr>
<tr>
<td>4</td>
<td>&gt;40</td>
<td>&gt;40</td>
<td>&gt;120</td>
<td>↓↓</td>
<td>Undetectable</td>
</tr>
</tbody>
</table>

(T = thready)

- **Distributive**:
  - Septic – difficult to tell pathogen from clinical exam alone
  - Anaphylaxis
- **Neurogenic**
- **Anaphylactic**

**Presentation**
- Not unusual to find combination of different shocks present

**Pathophysiology**
- Oxygen delivery to tissues = D0_2
• oxygen uptake by tissues = VO₂
• ↓DO₂ in shock =
  - hypovolaemic
  - obstructive
  - neurogenic
  - cardiogenic – 2nd to ↓contractility
• ↑DO₂ in shock =
  - septic

**DO₂ vs VO₂**

![Diagram of oxygen uptake vs oxygen delivery](image)

Figure 11.1 Relationship between oxygen uptake (VO₂) and oxygen delivery (DO₂) in cardiogenic, hypovolaemic and septic shock.

- Cardiogenic & hypovolaemic shock:
  - As DO₂ is tissues are able to maintain their VO₂ by ↑ing O₂ extraction from each unit of blood
    \[ \text{↑ in O₂ extraction from each unit of blood} \]
  - Further ↓DO₂ beyond critical value (330ml/min/m²) \( \Rightarrow \) failure compensation \( \Rightarrow \) anaerobic metabolism \( \Rightarrow \) lactic acidosis
    \[ \text{↓ DO₂ beyond critical value} \]
  - supply dependant VO₂

- Septic Shock:
  - ↑DO₂ to ↑CO
  - ↑VO₂ to ↑tissue metabolic activity
  - critical threshold for DO₂ is higher than for other forms of shock \( \Rightarrow \) larger range of supply dependant VO₂
    \[ \text{↑ synthesis of:} \]
    - abnormal microcirculatory perfusion \( \Rightarrow \) local ↓DO₂ compared to global
    - induced mitochondrial dysfunction

**Septic Shock:**

- Microbial components or their toxins bind to cell bound receptors
  - Eg:
    - gram -ve bacteria: LPS \( \Rightarrow \) CD14 & TLR4 (toll like receptor)
    - gram +ve bacteria: peptioglycan \( \Rightarrow \) TLR2
  - release of
    - proinflam cytokines eg TNF α, IL1, IL6
    - antinflam cytokines eg IL10, TNF receptors
    - complement activation
    - activation of coagulation & platelets
  - ↑ synthesis of:
    - arachidonic acid metabolites
    - ROS
    - Nitric oxide

**Result is:**

- vasodilation
- increased capillary permeability
- microvascular thrombosis
- impaired oxygenation utilisation
- lactic acidosis
- myocardial depression
- multi-organ failure

### Anaerobic Metabolism
- switch to anaerobic metab ⇒ ↓ATP stores ⇒ failure cell membrane NaK-ATPase pump⇒cell swelling & influx of water
- worsening lactic acidosis
- mitochondrial Ca loss ⇒ ↓efficiency of oxidation & phosphorylation ⇒ interfere with organ specific functions
- MODS ⇒ frank failure

### Hypodynamic vs Hyperdynamic Shock
- Defined by cardiac index
  \[ \text{CO/BSA Normal } 2.6-4.2 \text{L/min/m}^2 \]
- Hypodynamic = obstructive & cardiogenic
  \[ \text{although may be masked by compensatory mechanisms} \]
- Hyperdynamic = septic. Warm peripheries with bounding pulses.

### Surviving Sepsis Bundles

#### New Definitions
- sepsis = life threatening organ dysfunction caused by dysregulated host response to infection as defined by SOFA score
- SOFA score see acute change ≥2 points due to infection:
  - SOFA includes:
    - PF ratio
    - Platelets
    - bilirubin
    - MAP
    - GCS
    - creatinine & UO
  - Quick SOFA:
    - RR >22
    - SBP <100
    - altered mentation
- severe sepsis term no longer used
- septic shock = persisting
  - MAP <65 needing vasopressor
  - lactate >2 despite adequate fluid

#### Outdated terms:
- sepsis = SIRS + presumed or proven infective process
- severe sepsis = sepsis with organ dysfunction:
  - ↑lactate
  - oliguria & AKI
  - deranged LFTs ⇒ ↑↓BSL ⇒ coagulopathy
  - altered mental status
  - ↓↓bp & ↓↓pO2
- septic shock = sepsis with hypotension despite IVF resuscitation

#### Bundles
- protocolised quantitative resus of patients
- poor evidence behind particular aspects eg EDGT
- key philosophies are:
  - Antibiotics a
  - source control - use one with least physiological insult:
    - Drainage
- debridement
- definitive measures

- good routine ICU care

**Resus 3 Hours**
- measure lactate level
- obtain blood cultures - as long as does not delay Abx
- broad spectrum Abx ASAP (within 1 hour)
- 30ml/kg crystalloid if:
  - hypotension
  - lactate >4mmol/L

**Management 6 hours**
- use vasopressors to maintain MAP >65
- if persistent ↓MAP or lactate >4 ⇒
  - either do:
    - re-evaluate volume status carefully
  - or do 2 of these:
    - measure CVP
    - measure ScvO2
    - bedside CVS Ultrasound
    - dynamic Ax fluid responsiveness with passive leg raise or fluid challenge

**Outcome/Endpoints:**
- Targets:
  - CVP ≥8 (or 12 if on vent)
  - MAP ≥65
  - UO ≥0.5ml/kg/hr
  - ScvO2 ≥70 or mixed venous ↓65%
  - Mentation
  - Lactate
- methods:
  - crystalloid or albumin
  - vasopressors
  - transfusion of PRCs to achieve hematocrit >30%

- ScvO2 =
  - norm = >70
  - From central line
  - blood primarily from SVC ie more deoxygenated blood ⇒ ↓O2 sat

- SvO2 (mixed) =
  - norm = 60-80
  - from PAC
  - blood mixed from IVC & SVC: less deoxygenated blood ⇒ ↑O2 sat
- NB in sepsis see reversal where O2 sat of SvO2 ↓s = due to peripheral tissues having to extract more O2 due to ↓DO2

---

Marik PE. Chest 2014 (in press)
Meningococcal Septic Shock

- supportive Rx of ABC
- key points:
  ▶ take blood cultures - do not delay Abx if unable to obtain sample
  ▶ antibiotics as soon as possible - tazocin
  ▶ give steroids prior to antibiotics (as per local protocols)
    ↩ may ↓ neurological sequelae
  ▶ fluid resuscitation:
    - crystalloid max 30ml/kg
    - albumin 10ml/kg of 4%
    - give only if fluid responsive
  ▶ vasopressors:
    - noradrenaline 0.1-1mcg/kg/min
    - adrenaline 0.1-1mcg/kg/min
    - vasopressin 1-4units/hr
  ▶ LP may be contraindicated in presence of coagulopathy
  ▶ routine bloods incl lactate & meningococcal PCR
  ▶ notifiable disease

ALI & ARDS

- ALI = condition diagnosed clinically & radiologically based on presence of non-cardiogenic pulmonary oedema & respiratory failure in critically ill patient
- ARDS = continuum of ALI with worsening hypoxaemia

Diagnosis Criteria
1. Acute onset
2. Bilateral infiltrates on CXR consistent with APO
3. PCWP <18mmHg or no evidence of left atrial hypertension
4. PaO2/FiO2 (PF ratio):
   - ALI 200 - 300mmHg
   - ARDS < 200mmHg regardless of PEEP

- high mortality conditions
- = multifactorial disease which incls environmental trigger on background of genetic predisposition
- environmental causes are multiple & incl
  ▶ direct = pneumonia, aspiration, PE, lung contusion, fat emboli, inhalational
  ▶ indirect = sepsis, blood transfusion, pancreatitis, bypass

Pathphysiology

- 3 stages:
  ▶ acute exudative phase:
    - up to 7 days from onset
    - ↓ pulmon compliance
    - protein rich fluid in alveoli, haemorrhage & neutrophilic alveolar infiltrates ⇒ endothelial & epithelial injury
  ▶ subacute proliferative phase:
    - less persistent hypoxaemia, ↑ dead space & ↓ compliance
    - proliferation of type 2 alveoli cells ⇒ interstitial fibrosis ⇒ microvasular thrombus
  ▶ Chronic fibrotic stage:
    - only some patients transition into this phase:
    - loss of normal lung structure
    - see ↑CO2 retention & improved hypoxaemia
    - may start 14 days - weeks
Ix
- clinical diagnosis
- CXR - no patholognomic findings for ALI
- ABG
- +/- CT

Rx
- treat underlying cause
- good supportive care:
  › glycaemic control
  › DVT prophylaxis
  › prevent VAP & CLAB
  › gastric ulcer prophylaxis/early feeding

Protective Ventilation
- Protective Lung Ventilation in ARDS consists of techniques to minimise
  › barotrauma = high pressure injury
  › ateletrauma = low volume injury
  › biotrauma = injury from local and systemic effects pulmonary inflammatory mediators + translocation of bacteria into circulation from overdistension of pulmonary capillaries
  › volumtrauma = high volume injury
- Techniques include (as per ARDS NET recommendations):
  › permissive hypercapnia (tolerating elevated PaCO2 even up to 90mmHg or pH 7.1)
  › small tidal volume breaths (6mL/kg of IBW)
  › short I:E 1:1, RR <30
  › low plateau pressure (lowest possible, < 30cmH2O); peak <30mmHg
  › high PEEP (5-20cmH2O) – to minimise the amount of distension and collapse of alveoli during respiration, the exact level that is correct for each patient is variable
    ↳ ↑PEEP if ↑ing oxygenation required - look for ↑ed compliance
  › maintenance adequate PaO2 for organ function (70-80mmHg) –
    ‒ variable depending on patient:
      • young healthy = may tolerate a PaO2 of 60mmHg,
      • elderly patient may need higher PsO2 unless may precipitate myocardial ischaemia
- Other techniques that can help with these patients:
  › recruitment manoeuvres (cyclical sighs, CPAP of 30-40cmH2O held for up to 40 seconds)
  › restrictive IVF regime/diuresis
  › O2 toxicity - avoid & target lower SpO2 eg 90%
  › prone positioning
    ‒ improved morbidity:
      • ↑oxygenation
      • ↓VAP
      • no airway problems
    ‒ is now possibly a ↓mortality PROSEVA
  › NO or iloprost -
    ‒ short lived improvement of oxygenation only (24-48hrs)
    ‒ no mortality benefit
  › high frequency ventilation (very small TV, with very large frequency 60/min, can use oscillatory or jet ventilation -> no change in mortality or morbidity)
  › ECMO. ↑ed survival. NNT = 6
  › principles of weaning
    ↳ steroids have been shown to make no difference

Benefits of Protective Strategies
- ↓ed seen:
  › barotrauma complications such as pneumothorax
  › development of auto-PEEP
By A Hollingworth & J Fernando

- breath stacking
- injury related to alveolar distension creating a zone of injury between normal and abnormal lung parenchyma through increased shearing pressure.

**Permissive Hypercapnia**
- Associated respiratory acidosis surprisingly not major problem:
  - may protect lung against reperfusion or ischaemic injury (proven in rabbits)
  - decreases likelihood of inflammatory mediator release
  - less pulmonary oedema
  - improved lung compliance
  - less oxygen and nitrogen species damage
  - less pulmonary apoptosis

**Ventilator Associated Pneumonia (VAP)**
- hospital acquired infection in those on ventilation >48hrs
- <48hr community organism
- >5days often multi resistant eg MRSA, pseudomonas, klebsiella
- no gold standard diagnosis criteria
- 10-60%
- most common hosp acquired infection in ICU (50%)

**Pathogenesis**
- sources:
  - oropharynx:
    - colonised with aerobic Gram -ve bacilli & staph
    - in healthy people salivary fibronectin protects this build up of bacteria
    - ↓ed fibronectin in critically ill ⇒ micro aspiration of infected secretions into distal bronchi
  - nasal sinuses:
    - NG tubes ⇒ sinusitis ⇒ micro-aspirations
  - upper GI tract:
    - PPIs or H2 blockers ⇒ non-acidic environment ⇒ proliferation of gram -ve organisms ⇒ microaspirations
  - ETT:
    - bacteria through folds in cuff
    - colonise tube and grow down it
    - +ve pressure carries bacteria into lungs

**Risk Factors**

| Table 1 Risk factors for the development of ventilator-associated pneumonia |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| Severity of illness (APACHE score > 16) | Severe burns | Acute or chronic respiratory conditions | Supine body position | Mechanical ventilation for > 7 days |
| Enteral nutrition | Glasgow coma scale < 9 | Chronic lung disease | Excessive sedation | Cigarette consumption |

**Diagnosis**
- standard diagnosis of pneumonia: fever, ↓gas exchange, ↑WCC, purulent sputum, infiltrates on CXR
- all poor specificity
- ideally culture organisms:
By A Hollingworth & J Fernando

- sterile suction
- broncho-alveolar lavage -
  - encouraged as best method as soon as suspect disease
  - bronchoscope wedged in distal airway
  - 120ml saline injected & then aspirated
- protected specimen brushing
  - through bronchoscope - brush with protective gelatin plug

**Treatment**
- empirical broad spectrum Abx which changed asap to targeted narrow spectrum
- very uncommon to need to Rx anaerobic organisms

**Prevention**
- generic sterility & hand washing
- avoid nasal intubation if possible
- 30deg head up - ↓GORD
- NG feeding - careful rate control & prevention of aspiration
- cuff pressure checks - >20cmH2O
- good oral hygiene care
- avoid failed extubations/reintubation
- Avoid over-sedation. do early trashy
- selective decontamination of digestive tract (SDD) - non-absorbable antimicrobial paste to oropharynx
- nil evidence based:
  - Use sucralfate instead of H2 blockers or PPI
  - chest physio

---

**TCA Overdose**

**PROBLEMS**
1. anticholinergic effects
2. inhibition of catecholamine reuptake (initial increase in sympathetic tone - > prolonged decrease)
3. profound alpha-adrenergic blockade
4. myocardial toxicity

**HISTORY**
- having taken a large quantity of TCA (patients may be asymptomatic for 2-3 hours post ingestion)

**EXAMINATION**
CVS - dry mucous membranes, tachycardia, hypertension - > hypotension - > cardiovascular collapse (arrhythmia), postural hypotension, dehydration

CNS - nystagmus, dizziness, agitation, decreases level of consciousness, unconscious/coma, seizures, increase in tone, clonus, tremor, hyporeflexia, pupillary dilation, blurred vision

GI - N+V, abdominal pain, dry mouth

METABOLIC – severe metabolic acidosis, fever

GU – urinary retention

SKIN - flushed
INVESTIGATIONS
ABG - metabolic acidosis
ECG – Sinus tachycardia, PR prolongation, prolonged QT interval (>430ms), QRS prolongation (>100ms), VF/VT/asystole, 2nd or 3rd HB, RBBB.
Bloods – renal impairment

MANAGEMENT
- supportive care of airway, breathing, circulation and electrolytes
- admission to ICU
- IV NaHCO₃ + hyperventilation to ensure pH is >7.5 (decreased myocardial binding of the TCA)
- some advocate lipid emulsion

Cervical Cord Injury
- multi system impact

Respiratory
- depends greatly on level
- loss:
  ‣ intercostals - loose AP expansion with paradoxical chest sucking on inspiration
  ‣ diaphragm ⇒ rapid shallow breathing
    - loose piston effect
    - cephehalad movement ⇒ ↓ thoracic space
  ‣ abdo muscles ⇒ unable to forcefully cough
- 30% will need intubation:
  ‣ sux only used within 48hrs of injury
- C1-3 quadraplegia may require domicillary ventilation
- ≥C4 weanable from ventilator:
  ‣ intercostals will become spastic helping make chest wall rigid

<table>
<thead>
<tr>
<th>Level of injury</th>
<th>Effect on respiration</th>
<th>Clinical consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1–3</td>
<td>Complete paralyis of all respiratory muscles</td>
<td>Apnoea and immediate death unless mechanical ventilation is applied. Ventilator-dependent unless a diaphragm stimulator is used</td>
</tr>
<tr>
<td>C3–5</td>
<td>Varied impairment of diaphragmatic contraction (see text)</td>
<td>Ventilation often necessary in the acute stages. Vast majority will wean from mechanical ventilation depending upon functional descent of injury level, recovery of function in incomplete lesions, and improvement in respiratory mechanics over time</td>
</tr>
<tr>
<td>C6–8</td>
<td>Diaphragm and accessory cervical inspiratory muscles intact. Intercostals and abdominal muscles paralysed</td>
<td>Expiration entirely passive. Secretion retention is a problem. Respiratory failure rarely seen unless co-existent chest/lung injury, pre-existing lung disease, or the need for surgery</td>
</tr>
</tbody>
</table>

- Weaning strategies:
  ‣ PS weaning - slowly reducing level of PS until conversion to CPAP
  ‣ T piece weaning -
    - = progressive vent free breathing
    - PS at 12-15 then disconnect from vent for short periods which slowly increase
    - aka sprint weaning
CVS System
- neurogenic shock:
  - lesion above T6 ⇒ loss of SNS output ⇒
    - loss of vasoC
    - loss of cardiac accelerator fibres ⇒ ↓HR
  - duration variable, postural hypotension may persist
  - Rx with IVF resus
  - Induction of GA ⇒ ↓↓hypotension
  - in first 72hrs should aim for MAP 80 to ensure spinal cord perfusion pressure sufficient
- VTE - common, prevent
- Sympathetic hyperreflexia:
  - = life threatening condition triggered by somatic/visceral stimuli below level of injury
  - commonly bladder/rectal distension
  - manifests 4-6wks post injury once neurogenic shock resolved
  - common in lesion T6-T10
  - loss of descending inhibition means an any trigger ⇒ ascending SNS drive unopposed ⇒
    - profound vasoC below injury
    - compensatory baroreceptor mediated vasoD above injury
    - vasomotor center ⇒ ↓HR
  - .. clinically see:
    - malignant HTN with bradycardia
    - restless & agitated
    - LOC
    - seizures & +/- death
  - prevention impt
  - Rx of crises = α blockers

GI System
- delayed gastric emptying & ileus common - last for 2-3weeks
- gastric stress ulcer
- constipation

Metabolic
- ↓ed temp regulation
  - ↑BSL - due to stress response. Should keep <10
  - steroids not recommended

Other
- Psych aspects
- pain management:
  - acute pain
  - chronic pain =
    - neuropathic pain
    - hyperesthesia & allodynia common
  - spasticity

Pulmonary Embolism
- classification:
  - massive (>50% obstruction):
    - 5%
    - ↓↓bp or frank cardiac arrest
    - tend to be proximal saddle emboli with R heart dysfunction
  - sub-massive (30-50% obstruction):
    - 25%
    - haemodynamically stable
    - ECHo shows R heart strain & RV dysfunction
- ↑BNP or TNT as well
  - non-massive (<30% obstruction):
    - 70%
    - any other PE with norm R heart

**Treatment**
- non massive:
  - LMWH & warfarin
  - continue warf for 3-6months
  - acute PE occurring within 6 weeks after surgery has negligible recurrence rate
    - shorter warf time ie 6 weeks -12 weeks
- Massive:
  - thrombolyis
  - then as above
- sub massive:
  - controversial but some advocate thrombolysis
  - may reduced chronic pHTN & R heart failure & SOB
- vena cava filters - recent evidence questions efficacy

**Diagnostics**
- CTPA
- Pulmonary angiography (gold standard)
- ECHO
- VQ scan - better in pregnant as higher sensitivity than CTPA
- ECG - signs:
  - sinus tachy
  - R heart strain:
    - R axis deviation,
    - St depression/T wave inversion anteriorly (V1-4) & inferiorly inferiorly 9II, III, aVf)
Sodium Disorders After TBI

Hyponatraemia

Table 2 Common causes of hypotonic hyponatraemia

<table>
<thead>
<tr>
<th>Hypovolaemic hyponatraemia</th>
<th>Normovolaemic hyponatraemia</th>
<th>Hypervolaemic hyponatraemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSWS</td>
<td>SIADH</td>
<td>SIADH</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
<td>Subarachnoid haemorrhage</td>
<td></td>
</tr>
<tr>
<td>Other central nervous system pathology</td>
<td>Drug induced</td>
<td>Pulmonary pathology</td>
</tr>
<tr>
<td>Diuretics (including osmotic)</td>
<td>Thiazide diuretics</td>
<td>Congestive cardiac failure</td>
</tr>
<tr>
<td>Ketonuria</td>
<td>Adrenal insufficiency</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Diarrhoea/vomiting</td>
<td>Hypothyroidism</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Sweating</td>
<td>Iatrogenic</td>
<td>Acute renal failure</td>
</tr>
<tr>
<td>Blood loss</td>
<td></td>
<td>Iatrogenic</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- <135mmol/L
- Rx underlying cause
- correction should be gradual to avoid central pontine myelinolysis
- correct no more than 0.5mmol/l/hr or 10mmol/l/day
- end point should be resolution of symptoms

Table 1 Symptoms and signs of hyponatraemia and hypernatraemia

<table>
<thead>
<tr>
<th>Hyponatraemia</th>
<th>Hypernatraemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Lethargy</td>
<td>Thirst</td>
</tr>
<tr>
<td>Nausea, vomiting, and anorexia</td>
<td>Irritability</td>
</tr>
<tr>
<td>Irritability</td>
<td>Restlessness</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Muscle weakness/cramps</td>
<td>Hyporeflexia</td>
</tr>
<tr>
<td>Severe</td>
<td>Ataxia</td>
</tr>
<tr>
<td>Hyporeflexia</td>
<td></td>
</tr>
<tr>
<td>Drowsiness and confusion</td>
<td>Seizures</td>
</tr>
<tr>
<td>Seizures</td>
<td>Coma</td>
</tr>
<tr>
<td>Coma</td>
<td>Death</td>
</tr>
<tr>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

SIADH

- common neuro causes:
  - SAH
  - TBI
  - tumour
  - meningitis
  - drug related
- ADH inappropriately high
- diagnostic criteria:
  - hypotonic hyponatraemia (<135, osmolality <280)
  - urine osmolality > serum osmolality
  - urine sodium concentration >18mmol/l
normal thyroid, adrenals & renal function
- euvolaemic - very imp to differentiate it from cerebral salt wasting syndrome
- Rx:
  - electrolyte free water restriction to 1000ml/day
  - hypertonic saline - restricted to severe disease & stopped once Na at 120-125
  - frusemide with Na supplementation
  - demeclocycline - inhibits kidneys response to ADH

Cerebral Salt Wasting Syndrome (CSWS)
- renal loss of sodium ⇒ polyuria, hyponatraemia & hypovolaemia
- often mistaken for SIADH
- common after SAH/TBI
- precise pathology is unknown
- criteria:
  - ↓ Na
  - high or normal serum osmolality (diff to SIADH)
  - high or norm urine osmolality
  - hypovolaemic (diff to SIADH)
- see overall negative sodium intake:output balance
- Rx:
  - volume & saline resus
  - refractory: fludrocortisone

Hypernatraemia
- uncommon ~1%
- causes:
  - drugs - too much mannitol or conc saline
  - hypovolaemic ↑Na:
    - DI - high urine output
    - dehydration - low urine output
  - hypervolaemic ↑Na:
    - excessive salt intake

Diabetes Insipidus
- Di post TBI is a sign of impending pre-terminal cerebral oedema
- criteria:
  - >2000ml urine/24hr
  - serum Na >145
  - serum osmolality >305mmol/kg
  - low urine osmolality <350mmol/kg
- Rx:
  - replace & retain water - free water via NG
  - replace ADH:
    - if UO >250ml/hr then give DDAVP 100-200mcg intranasally or 0.4mcg IV

Management of Haematological Malignancy
- commonest types admitted to ICU:
  - acute myeloid & lymphoblastic leukaemias
  - non-Hodgkins lymphoma
- less common:
  - Hodgkins
  - myeloma
  - chronic leukaemias

Chemotherapy
- Bleomycin: risk of resp failure if high FiO2 given
By A Hollingworth & J Fernando

Stem Cell Transplant

Table 1 Some common complications associated with chemotherapy agents

<table>
<thead>
<tr>
<th>Complications</th>
<th>Associated chemotherapy agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic interstitial pneumonitis</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>Bleomycin; high-dose methotrexate</td>
</tr>
<tr>
<td>Haemorrhagic cystitis</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Cyclosporin</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
<td>Cyclosporin, tacrolimus</td>
</tr>
</tbody>
</table>

Table 2 Complications of stem cell transplant

<table>
<thead>
<tr>
<th>Early complications (usually &lt;100 days)</th>
<th>Late complications (usually &gt;100 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>Infections</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>Chronic GVHD</td>
</tr>
<tr>
<td>Acute GVHD</td>
<td>Chronic pulmonary disease</td>
</tr>
<tr>
<td>Graft failure (especially aplastic anaemia)</td>
<td>Autoimmune disorders</td>
</tr>
<tr>
<td>Haemorrhagic cystitis</td>
<td>Cataract</td>
</tr>
<tr>
<td>Interstitial pneumonitis</td>
<td>Infertility</td>
</tr>
<tr>
<td>Others, including veno-occlusive disease, cardiac failure</td>
<td>Second malignancies</td>
</tr>
</tbody>
</table>

- sub categorise stem cell transplant (likelihood of ICU admision):
  - origin of cells:
    - peripheral
    - bone marrow
  - donor of cells
    - Allograft = transplant of cells/tissue/organ to a recipient from non-identical donor of same species
    - Xenograft = graft from different species
    - Isograft = transplant from genetically identical donor ie identical twin
    - Autograft = own tissue transplanted from one site to another on same pt
  - intensity of conditioning:
    - myeloablative (40% - complete destruction of endogenous bone marrow)
    - reduced intensity conditionning (18%)

Neutropaenia

- Practise = <1x10⁹/L
- high risk of atypical infections eg fungal & viral
- often on prophylactic antiviral/fungals
- must cover pseudomonas
- anti-fungals often used as part of broad spectrum cover
- GCSF often used to promote neutrophil recovery
  - rare risk of splenic rupture

Resp Failure

- Causes:
  - infection (most likely)
  - APO
  - GVHD
  - pulmon haemorrhage
- infection may be hard to prove
- if intubation required is assoc with worse outcomes
Thrombocytopaenia
- spontaneous bleeding <5
- targets for counts:
  - >50 = if active bleeding or surgery planned
  - >10 = background count
  - >20 = insertion of CVL

Tumour Lysis Syndrome
- most assoc with:
  - acute leukaemias
  - high grade lymphomas esp Burkitts
- most common after treatment (can be spontaneous) esp dexamethasone
- signs:
  - ↑↑K
  - renal failure
  - acidosis
  - ↑↑phosphate & ↓↓Ca
  - ↑serum uric acid
- treatment:
  - fluid hydration
  - Rx of ↑↑K
  - rasburicase = recombinant urate oxidase enzyme
treatment: allopurinol can be used as prophylaxis

Other Organs
- Neuro:
  - seizures ➔ CT head
  - hypercoagulable state ➔ infarction/venous thrombosis
  - hyperviscosity syndrome ➔ drowsiness ➔ LOC
- GI:
  - GVHD
  - typhilitis =
    - neutropaenic enterocolitis 10-14days post chemo
    - presents similar to C diff/appendicitis
- Renal:
  - failure
  - often assoc with hepatic failure

GVHD
- acute GVHD
  - = <100days post HSCT
  - grade of problem predicts mortality
  - signs:
    - skin rash
    - diarrhoea
    - hepatitis
    - others:
      - ↓↓platelets
      - conjunctivitis
      - haemolysis
  - treatment =
    - steroids
    - immunosuppressants eg cyclophosphamide
    - parental nutrition to rest gut
    - octreotide for severe diarrhoea
- chronic GVHD = multiorgan syndrome with very varied presentation
Drug Toxicology

**Blood Tests**
- paracetamol & other checkable drugs (AEDs) @ 4hrs
- other routine bloods

**Initial Management**
- not recommended:
  - gastric decontamination = lavage, emesis then AC
  - induced emesis
  - lavage - especially if >1hr since drug ingestion
- activated charcoal:
  - 50g or 1g/kg in child
  - time dependant: 90% ↓ absorption if 30mins post ingestion ⇒ 30% ↓ absorption at 1hr
  - beneficial in paracetamol up to 2hrs post
  - repeated doses if slow release drug
- whole bowel irrigation:
  - useful for sustained release or enteric coated tablets
  - where AC not useful ie alcohols, cyanide, iron, lithium, acids & alkalis
  - in non drugs ie batteries, body packers
- alkaline diuresis:
  - good for salicylates & some herbicides
- haemodialysis:
  - good for ethylene glycol, methanol, lithium, theophylline, salicylate poisoning

**Specifics**
- paracetamol:
  - NAC
- salicylates:
  - rehydration
  - correction of pH
  - close monitoring of acid-base disturbance
  - haemodialysis
- benzo's:
  - flumazenil rarely indicated due to SEs:
    - VT
    - ↑ICP
    - withdrawal in chronic abusers ⇒ seizures
  - supportive Rx esp securing airway
- TCAs:
- signs = tachy, mydriasis, coma, hyper-reflexia, wide QRS, ↓bp
- Rx:
  - AC
  - sodium bicarb (even in absence of ↓pH)
  - benzo’s to Rx seizures

- SSRIs:
  - bad if SSRIs if given with other seroto-mimetic drugs ie cocaine, MAOIs, MDMA
  - serotonin syndrome = altered mental status, clonus autonomic instability
- Rx:
  - AC
  - benzo’s for seiures
  - cryoheptadine may be useful

- methanol & ethylene glycol:
  - high anion gap met acidosis
  - Rx with ethanol
  - fomepizole cleaner solution

---

**Diabetic Ketoacidosis**

- paeds mortality 2nd to cerebral oedema
- pathophysiology:
  - absolute lack of insulin
  - relative lack ie Tcounter reg hormones eg catecholamines, glucagon, cortisol, growth hormone
  - leads to classic trifecta:
    - hyperglycaemia
    - hyperketonaemia
    - hyperosmolality
- diagnosis:
  - BSL >11
  - pH <7.3
  - ketonaemia

**Treatment**

- summary:
  - IVF
  - exogenous insulin
  - replacement electrolytes

- Airway:
  - any drowsiness may indicate cerebral oedema
  - intubate if required but avoid hyperventilation
  - give Abx if febrile paed

- fluid -
  - resus: guarded fluid therapy based on local guidelines (not >20ml/kg in first 4hrs)
  - replacement:
    - normal maintenance + calculated dehydration (often assume 10%)
    - give over min 48hrs
    - normotonic solutions
  - electrolyte replacement:
    - sodium:
      - total body sodium may be ↓ed due to ↑excretion with water
      - pseudohypoNa: ↑BSL draws water out of cells ⇒ ↓serum Na
        ⟷ ↓ should calculate corrected Na
    - potassium:
      - total body K generally always low despite any serum K result
      - due to ↓insulin, vomiting, diuresis, 2nd aldosteronism
      - only defer giving K if serum >5.5
  - aims:
    - normalise anion gap or remove measured ketones

**Cerebral Oedema**

- give IV osmotherapy asap eg hypertonic saline or mannitol
- can use scoring systems to grade likelihood of cerebral oedema (can just use GCS)
- biggest cause of morbidity or mortality in paeds
- Better to use hypertonic saline (3% 3-5ml/kg):
  - plasma sodium easy to monitor in all labs
  - plasma sodium primary driver osmolality
  - Na 150-158 effective at preventing & treated clinical signs of cerebral oedema
  - mannitol
    - rapidly excreted
    - diuretic \( \Rightarrow \) fluid loss
    - effect short lived
    - rapidly swings osmolality which can be more harmful
    - can no longer use plasma corrected sodium due to presence of another osmole (mannitol)
Surgical Problems

Pneumothorax
- = presence of air in pleural cavity with associated lung collapse

Classification
- 3 main types:
  ‣ spontaneous (most common in medicine)
    ‣ primary spontaneous (PSP) ie no obvious lung disease
    ‣ secondary spontaneous (SSP) ie pre-existing underlying lung disease
  ‣ traumatic (most common in Anaesthesia):
    ‣ barotrauma
    ‣ direct trauma from intervention
  ‣ iatrogenic

Management
- observed if:
  ‣ Small PSP's AND asymptomatic:
    ‣ high flow O2 ⇒ ↑ ed speed of absorption via de-nitrogenation
    ‣ rate reabsorb = 1.25-1.8% volume/24hrs
- aspiration if:
  ‣ primary PTX
  ‣ small <2cm
  ‣ minimally breathless
- chest drain:
  ‣ secondary PTX
  ‣ only remove when bubbling/swinging stopped
  ‣ if on suction should have underwater seal 10-20cm H2O

Bronchopleural Fistula
- = communication between bronchial tree & pleural space
- clinically = persistent air leak despite ICD for 24hrs
- causes incl trauma, iatrogenic, chest drain in lung parenchyma, mechanical ventilation
- prevent weaning from vent
- vent strategies:
  ‣ add more ICDs with bigger drain size
  ‣ ↓ insp pressure
  ‣ ↓ VT
  ‣ ↓ RR
  ‣ ↓ PEEP & insp times
  ‣ permissive hypercapnia & accept lower Sats
- surgical repair an option

Pancreatitis
= proteolytic enzymes are activated and cause haemorrhagic necrosis of the pancreatic parenchyma.
- complications: SIRS, sepsis -> MODS
- endocrine cells form Islets of Langerhans:
  ‣ A cells = glucagon
  ‣ B cells = insulin
  ‣ D cells = somatostatin
  ‣ F cells = pancreatic polypeptide
- clinical course 2 phases:
  ‣ 1st: 1-2 weeks of SIRS & organ dysfunction +/- necrosis
  ‣ 2nd: >2 weeks = sepsis & MODS
HISTORY
- severe epigastric pain -> back
- N+V
- anorexia
- fever/chills
- steatorrhoea

Causes
I diopathic
G all stones
E thanol
T rauma
S teroids
M umps and other viruses (EBV, CMV)
A utoimmune diseases (SLE, polyarteritis nodosa)
S nake or scorpion bites
H yper - calcaemia, lipidaemia, Hypothermia
E RCP
D rugs (SAND – sulphasalazine, azathioprine, NSAIDS, diuretics)

EXAMINATION
- haemorrhagic discolouration of flanks and umbilicus (Grey Turners & Cullens sign)
- epigastric tenderness
- hypotension
- oliguria
- respiratory failure

INVESTIGATIONS
- amylase - x3>normal ~ pancreatitis
- lipase - remain high for 14days & more sensitive (>600IU/L)
- severity score assessment:
  › Glasgow Pancreatitis Score = (PANCREAS)
    - PaO2,
    - Age,
    - Neutrophilia,
    - Calcium (↓Ca)
    - Renal function (urea)
    - Enzymes (LDH, AST)
    - Albumin
    - Sugar (BSL)

- CXR: raised hemidiaphragm, pleural effusion, ALI, atelectasis
- CT: haemorrhagic and oedema of pancreas, CBD diameter
- U/S: gall stones and obstruction

MANAGEMENT
- primarily supportive
- O2
- IVF
- ETT + V
- N/J feeding -
  › enteral feeding is cheaper, safer & ↓infective complications with better outcome
  › gastric feeding often fail due to duodenal ileus
  › move to PN if failure of feeding after 5-7days
- insulin
- electrolyte management
- treat cause
- radiological drainage of areas of necrosis
- antibiotics are controversial (imipenem or meropenem) - use if suspect necrotic infected pancreas
- analgesia
- surgery:
  - aims:
    - relieve biliary obstruction - ERCP within 72hrs
    - minimise regional/distal organ damage
    - remove infected pancreatic necrotic material - should delay until ≥3rd week
  - surgery within 1-2 weeks assoc with high mortality

**Intra-Abdominal Hypertension**

- normal IAP = zero or negative pressure
- mild ↑ IAP:
  - seen during IPPV or post surgery
  - can compensate with fluid resus
  - = 3-15mmHg
- IAP HTN = >25mmHg
  - although can vary with fluid status
  - syndrome of CVS, renal, pulmon dysfunction
- Rx:
  - prompt recognition
  - fluid resus
  - surgical decompression

**Measurement**

- several but most used = trans-bladder measurement:
  - bladder wall = passive diaphragm for abdo pressure measurement between 5-70mmHg
  - pt must be ventilated then apnoec & paralysed
  - 50-100ml saline into bladder through IDUC
  - column of fluid allowed to drain down catheter tube and then clamped (excluding air)
  - insert 16G needle through culture aspiration port & transduced
  - zero point is symphysis pubis
- can see indirect markers on CT

**PathoPhys**

- acute rise in pressure is key step eg trauma, haemorrhage, oedema, DIC
- chronic rise can be overcome by abdo wall compliance changes

**Table 1**  Factors predisposing to intra-abdominal hypertension

<table>
<thead>
<tr>
<th>因素</th>
<th>Traumatic haemorrhage</th>
<th>Ruptured aortic aneurysm</th>
<th>Ascites</th>
<th>Pancreatitis</th>
<th>Blunt abdominal trauma</th>
<th>Pancreatitis</th>
<th>Post haemorrhagic Sepsis</th>
<th>Laparoscopy</th>
<th>Visceral rupture</th>
<th>Gastric dilatation</th>
<th>Bowel obstruction</th>
<th>Ileus</th>
<th>Intractable constipation</th>
<th>Neoplasms</th>
<th>Surgical packs</th>
<th>Loss of domain after hernia repair</th>
<th>Pelvic fracture</th>
<th>Retroperitoneal haemorrhage</th>
<th>Burn excision</th>
<th>Morbid obesity</th>
<th>Towel clip closures</th>
</tr>
</thead>
</table>

ICU - 38
Systemic Effects of ↑IAP

- CVS:
  - ↓VR from compression of IVC
  - ↓CO:
    - ↑afterload - due to ↑SVR & ↑PVR
    - changes in ventricular compliance - diaphragm elevation ⇒ distorts ventricle
    - acidosis
  - ↑bp:
    - ↑SVR
    - ↑CVP due to ↑ITP
  - ↑VTE risk - stasis of blood in femoral venous flow due to ↑IAP

- Resp effects:
  - atelectasis ⇒ ↑shunt fraction ⇒ ↓PF ratio
  - ↑CO2
  - ↑insp pressure to ventilate⇒ ↓pulmon & ↓chest wall compliance

- Renal effects:
  - AKI & oliguria:
    - ↓renal plasma flow & ↓GFR
    - ↑renal vasc resistance
    - ↑ADh release & ↓ANP due to ↓VR

- CNS:
  - ↑ICP via transmission through body cavities & ↓VR

- GI:
  - gut mucosal oedema
  - ↓tissue oxygenation
  - bacterial translocation
  - breakdown of surg anastomosis & abdo wound dehiscence

Management

<table>
<thead>
<tr>
<th>Measured IAP</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>10–15 mmHg</td>
</tr>
<tr>
<td>Grade II</td>
<td>16–25 mmHg</td>
</tr>
<tr>
<td>Grade III</td>
<td>26–35 mmHg</td>
</tr>
<tr>
<td>Grade IV</td>
<td>&gt; 35 mmHg</td>
</tr>
</tbody>
</table>

- Aggressive fluid resus
- paralysis
- may have to leave bowel open:
  - slight ↑fluid requirement
  - enteral feeding remains fine

Abdominal Decompression Syndrome

- 3 potentially dangerous changes:
  - sudden ↓SVR:
    - aggressive volume loading
    - vasopressors
  - ↓ITP:
    - pre decompression common to need PIP ~50cmH2O
    - on decompression must ↓pressures to avoid trauma
  - toxic product washout:
    - decompression ⇒ sudden VR of vasodilating metabolites
    - see arrhythmia, myocardial decompression, vasoD, cardiac arrest seen in up to 25%
- some advocate reperfusion cocktail:
  - 2 litres crystalloid
  - 50g mannitol
  - 50mEq sodium bicarb
Death

Pathophysiology of Brainstem Death

- early, short lived massive SNS outflow during brainstem herniation ⇒
  - ↑ bp & ↑ HR
  - myocardial dysfunction
  - ↓ organ perfusion & ischaemia
- CVS:
  - Autonomic nervous system collapse ⇒
    - ↓ CO with ↓ bp & ↓ HR (which is atropine resistant)
    - circulatory collapse will follow if not untreated
- Coagulopathy - due to release of fibrinolytic agents & plasminogen activators from necrotic brain
- Resp:
  - neurogenic pulmon oedema
  - Acute lung injury
- Endocrine:
  - ↓ T3 & T4 with compensatory ↑ ed peripheral conversion of T4 to T3 ⇒ global shift to anaerobic metabolism
  - ↑ BSL - caused by ↓ circulating insulin & insulin resistance
  - ↓ ADH secretion ⇒ neurogenic DI ⇒ polyuria and hypovolaemia
  - electrolyte changes: ↑ Na, ↓ K, ↓ phosphate, ↓ Ca
- Neuro:
  - ↓ Temp - due to hypothalmic dysfunction

Brain Death & DBD

- 2 med practitioners (1 specialist) & 2 separate exams
  - none member of transplant team
  - same procedure in paeds >2months but need 1 paeditrician
- formal time of death = end of 2nd examination
- commonest causes of brainstem death =
  - head injury
  - ICH
  - cerebral tumours
  - hypoxic brain injury
- to diagnose brainstem death need:
  - fulfil certain preconditions
  - absent brainstem reflexs

Preconditions:

- unconscious - caused by known & irreversible cause
- apnoeic & dependent on mechanical ventilation
- diagnosis considered:
  - >4hrs after onset apnoeic coma
  - >24hrs after restoration of circulation eg cardiac arrest
  - >24hrs after induced hypothermia
- GCS =3
- need a cause/diagnosis to coma eg tbi/arrest

Exclusion:

- reversible causes of brainstem depression have been excluded:
  - sedatives
  - mm relaxants - TOF =4
  - alcohol
  - hypothermia
  - hypotension
  - metabolic & endocrine disorders - TFTs, Na, K
Procedure:
- cannot use standard tests if high C spine injury, or hypoxic cause of death
- only test once preconditions are fulfilled:
  - pupil testing:
    - fixed
    - non direct or consensual response to light
  - corneal reflex = absent
  - CNs =
    - no VII motor response applied peripherally or centrally to pain
    - (local unilateral reflex allowed, but not contralateral)
  - Oculo-vestibular reflex
    - No response to 50mls ice cold water into ext auditory meatus
    - Observe for 1min after each injection
    - Must ensure direct access to TM with scope
  - Gag/Cough reflex:
    - suction catheter in pharynx or down ETT to carina
  - Apnoea:
    - present on disconnection from mech vent
    - done last to avoid ↑CO2 which may impact on other reflexes
    - steps:
      • preoxygenated with 100% O2 prior
      • PaCO2 at 45mmHg
      • disconnect & place ambubag on ETT & monitor SpO2
      • observe for any movement or EtCO2 in next 5mins
      • at 5mins measure PaCO2 to ensure >60mmHg (if previously normal individual)
Alternate to clinical testing:
- if any doubt to exam or pre-conditions can't be met then can perform adjunct tests:
  - 4 vessel cerebral angiography
  - Marginal tests:
    - EEG,
    - brainstem evoked potentials - SSEPs
    - cerebral perfusion scan
    - CTA/MRA
Potential donors:
- Identify potential for organ donation after 2nd brain stem testing
- Should consider all comers as very few exclusions in modern practise
- General criteria:
  - **No age limit anymore***
  - Vent with intact circulation
  - No active invasive cancer within last 3yrs (excluding non-melanoma skin Ca & primary brain tumour)
  - No haematological malignancy
  - No untreated systemic infection
  - No HIV, CJD
Comms
- Can access driver licence donor information
- Use 'dead', 'die' in communication.
- describe facts leading up to death
- fact brain death has occurred
- what brain death means
- ask questions
- allow time before organ donation 'did x ever talk about organ donation', 'what would x have wanted?'
- Must involve coroner and police if required.
Physiology of death
- coning - cushings response
- neurogenic pulmonary oedema
- hypothermia

Ix required
- CXR
- Bloods, hepatitis, HIV, grouping
- Echo, ECG
- Tissue typing & serology

DBD Organs
- DBD is not physiologically neutral
- significant inflammatory process begins on death
- effects immunogenic organs ie lungs - outcome worse than DCD
- but overall improved outcome as led warm ischaemic time for organ harvest
- kidneys - better short term outcome in DBD
  ➔ but DCD kidneys long term equivocal

DCD (Donation after Circulatory death)
- For when does not fulfil brain death criteria but no hope of recovery & in best interest of patient to withdraw
- Historically DCD came before DBD but then people realised DBD organs could be retrieved without suffering hypoxic time
- DCD difference = organs suffer warm ischaemic time which starts when:
  › SBP <50mmHg
  › SpO₂ <70%
  › or both
- Phases:
  › Warm ischaemia Time =
    - Criteria above until initiation of cold perfusion
    - DCD only
    - minimised as much as possible
  › Cold ischaemia time =
    - initiation of cold preservation until warm circulation after transplant
    - DCD & DBD
    - protective to organs preventing irreversible ischaemic damage

Selection criteria
- consider all who active therapy to be withdrawn from
- 2 types DCD:
  › controlled:
    - organ retrieval plan prior to death
  › uncontrolled:
    - already died prior to consideration for organ donation

Table I Modified Maastricht classification of DCDs

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Controlled/Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>Dead on arrival at hospital</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Category II</td>
<td>Unsuccessful resuscitation</td>
<td>Uncontrolled</td>
</tr>
<tr>
<td>Category III</td>
<td>Awaiting cardiac arrest</td>
<td>Controlled</td>
</tr>
<tr>
<td>Category IV</td>
<td>Cardiac arrest in a brain-dead donor</td>
<td>Controlled</td>
</tr>
<tr>
<td>Category V</td>
<td>Unexpected cardiac arrest in a critically ill patient</td>
<td>Uncontrolled</td>
</tr>
</tbody>
</table>

- in ICU mostly type III controlled
- other categories while possible to get organs from are logistically very difficult
- thus given warm ischaemic times - for successful donor:
  › need prediction that post withdrawal of support ventilation will stop within 60mins
Organs from DCD
- improved outcome seen for immunogenic organs:
  - lung
  - kidney - slow to start working (↑morbidity) but 10yr survival same as DBD
- warm ischaemic times for different organs:
  - kidney <2hr
  - liver <30min
  - pancreas <30min
  - lung <1hr

Practical Process of DCD
- difficult communication with family:
  - timescales post death
  - family will not have much time with pt after death
  - if death does not occur quickly organ donation may not proceed
  - family can stop donation at anytime
- withdrawal of treatment:
  - tissue type donor prior to withdrawal
  - retrieval team & family ready
  - withdraw treatment in way independent of transplant process
  - in some pts respiration will continue after withdrawal of support ⇒ loss of organ viability
- confirmation of death:
  - independent doctor
  - loss of cardiorespiratory function for 5mins prior to certification:
    ↳ use A line or asystole on ECG
    ↳ palpation of pulses is not acceptable
  - if return of cardioresp in that 5 mins then restart clock after further cessation
  - post certification of death family get 5 min with patient
    then → operating room
  - retrieval of organs starts not before 10min post circulatory arrest
- if lung donation & extubated:
  - will need reintubating after death confirmation
  - x1 recruitment manoeuvre 10min after death allowed
  - otherwise only allowed to restart ventilation after cerebral circulation been isolated (clamping)

Ethical Problems
- conflict of interest between decision making of futility & subsequent organ donation
- concern about adjusting end of life care pathway to allow organ donation
- uncertainty about how soon post circulatory death can organ retrieval begin:
  - never been evidence spontaneous:
    - circulation returned after 7min of asystole post resus
    - circulation return post asystole without resus
  - ⇒ 5+5 min gives grace period

Organ Retrieval after Brain Death
- organs usually taken via long midline incision & median sternotomy
- absolute CIs to organ donation:
  - Infectious diseases eg CJD, HIV, active TB
  - recent malignancy
- ↑ common to see donation after brain death (DBD) in older people 2nd to ICH rather than TBI

Preoperative
- check confirmation of brainstem death
- change in Rx strategy from cerebral resuscitation to optimal organ perfusion & oxygenation
- large blood loss likely - X match units
- CVP - avoid >6mmHg to prevent ↑physiological shunt & ↓lung donation
• vasopressin is first line vasoactive +/- noradrenaline
  ≣ should replace desmopressin used for DI - vasopressin has ↓ed effect on myocardium
• follow local protocols on hormone resuscitation:
• Correct electrolytes:
  › Na <155 ⇒ use DDAVP +/- free water
  › Maintain norm BSL
• Correct clotting disorders with products & platelets
• target physiological parameters:
• Access preferred - as L innominate vein & R subclavian artery are ligated early:
  › R IJ CVL
  › L rad A line
• CXR, ECG, ECHO & 4hrly ABGs for potential donors

**Perioperative**

• Induction
  › CVP, A line, core temp, Urine output
  › R upper limb big access - may need up to 8litres fluid resus
• Maintenance
  › keep temp >35
  › GA controversial - need to control reflex pressor responses during surgery:
    - volatile up to 1 MAC
    - fentanyl or remi infusions
    - labetalol or GTN
  › NDNMBs used to prevent reflex muscular contractions - panc or vec = cardiostable
  › large haemodynamic fluctuations are common
  › broad spectrum Abxs used
  › heparinisation (300IU/kg) prior to cannulation of major vessels
  › If lung harvest: epoprostenol (5-20ng/kg/min) via PA catheter may be needed for 10mins
    ≣ prostacyclin used for PAH
  › remove CVLs before ligation of SVC
  › aortic X clamp time = beginning of organ ischaemic time

**Table 16.3 Hormone resuscitation during organ retrieval**

<table>
<thead>
<tr>
<th></th>
<th>Bolus</th>
<th>Infusion</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liothryonine (tri-iodothyronine, T₃)</td>
<td>4 micrograms</td>
<td>3 micrograms/hr</td>
<td>Reverses myocardial dysfunction and reduces inotrope requirements</td>
</tr>
<tr>
<td>Vasopressin (ADH)</td>
<td>1U</td>
<td>0.5-2U/hr</td>
<td>Treats diabetes insipidus and restores vascular tone. Titrated to MAP &gt;60mmHg or SVR 800-1200 dyn.s/cm²</td>
</tr>
<tr>
<td>Insulin</td>
<td>Sliding scale</td>
<td></td>
<td>To maintain blood sugar 6-9 mmol/L</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>15mg/kg</td>
<td>±</td>
<td>Improves oxygenation and increases donor lung procurement by reducing cytokine-mediated cellular injury</td>
</tr>
</tbody>
</table>

• Extubation
  › remove ETT after lung inflation & trachea cross clamping
  › surg team continue in circulatory arrest
### Table 16.4 Target parameters for organ retrieval

<table>
<thead>
<tr>
<th>Target parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP</td>
<td>4–10mmHg (&lt;6mmHg for potential lung donors)</td>
</tr>
<tr>
<td>MAP</td>
<td>60–80mmHg</td>
</tr>
<tr>
<td>PAOP</td>
<td>10–15mmHg</td>
</tr>
<tr>
<td>Cardiac index</td>
<td>&gt;2.2–2.5L/min/m²</td>
</tr>
<tr>
<td>Hb</td>
<td>100g/L (Hct 30%)</td>
</tr>
<tr>
<td>SpO₂</td>
<td>&gt;95% (with lowest FiO₂ and PEEP)</td>
</tr>
<tr>
<td>Vₜ</td>
<td>6–8mL/kg</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>4.5–5.5kPa (34–41mmHg)</td>
</tr>
<tr>
<td>Urine output</td>
<td>1–3mL/kg/hr</td>
</tr>
<tr>
<td>Peak inspiratory pressure</td>
<td>&lt;30cmH₂O</td>
</tr>
</tbody>
</table>

### Special Points
- Quality of care of donor can effect >6 recipients
- If cardiac arrest: CPR should be commenced in DBD:
  - Liver & kidneys quick to remove with aortic cross clamping of aorta at diaphragm & infusion of cold preservation solution into distal aorta & portal vein