Table of Contents

Changes in Posture .................................................................................................................. 3
  Awake Supine ......................................................................................................................... 3
  Awake Lateral Position .......................................................................................................... 3
  Anaesthetised, closed Chest, Lateral Position ..................................................................... 3
  Anaesthetised, open chest & 1 lung ventilation in lateral position ........................................ 3
Effect of Anaesthetic Drugs on Control of Resp ................................................................. 4
Effect of Anaesthesia on Lung Mechanics/Gas Exchange ..................................................... 4
Effect of IPPV ........................................................................................................................ 4
  CVS Effects ............................................................................................................................. 4
  Resp Effects .......................................................................................................................... 5
  Renal Effects ......................................................................................................................... 5
  GastroIntestinal .................................................................................................................... 6
  CNS ........................................................................................................................................ 6
Effect of PEEP ........................................................................................................................ 6
  Negative Effects of PEEP ...................................................................................................... 6
  Clinical Application of PEEP ............................................................................................... 6
Integrated Cardio-Resp Response to Exercise .................................................................... 7
  Fick Principle ........................................................................................................................ 7
  Cardiovascular Changes in Response To Exercise .............................................................. 8
  Respiratory Changes to Exercise ......................................................................................... 9
  VO2 Max graphs: .................................................................................................................. 9
  Resp & CVS Changes (V/Q) ................................................................................................. 10
  Level of Exercise .................................................................................................................. 10
  Recovery After Exercise ...................................................................................................... 10
  Limits of Exercise Tolerance ............................................................................................... 10
Ageing ....................................................................................................................................... 11
  Cardiovascular Age Changes ............................................................................................ 11
  Respiratory Changes ........................................................................................................... 11
High Altitude .......................................................................................................................... 12
  Demands on body @High Altitude ...................................................................................... 12
  Hyperventilation .................................................................................................................. 12
  Other Resp Changes ............................................................................................................ 12
  Cardiovascular Changes to High Altitude .......................................................................... 12
  Haematological changes ..................................................................................................... 13
  Endocrine ............................................................................................................................... 13
  Mountain Sickness .............................................................................................................. 13
Anaemia ................................................................................................................................. 14
  Compensatory Mechanisms .............................................................................................. 14
O2 Toxicity ............................................................................................................................. 14
  Absorption Atelectasis ........................................................................................................ 14
Space Flight ............................................................................................................................ 15

By Adam Hollingworth
Increased Pressure ................................................................. 15
  Diving ............................................................................... 15
  Decompression Sickness ...................................................... 15
  Inert Gas Narcosis ................................................................. 15
  O2 Toxicity ......................................................................... 16
  Hyperbaric Therapy .............................................................. 16
Polluted Atmospheres ............................................................... 16
  Particulate Matter ............................................................... 16
Liquid Breathing ....................................................................... 16
Perinatal Respiration ................................................................. 17
  Fetal Lung .......................................................................... 17
  First Breath ....................................................................... 17
  Circulatory Changes ............................................................ 17
Hypothermia ........................................................................... 18
Changes in Posture

- Normal distribution of blood flow to lungs:
  - R lung = 55%
  - L lung = 45%

Awake Supine

- ↓ed spread of VQ ratios:
  - Vertical distance for gravity to act on is less in supine (AP distance < apex-base)
- ↓FRC: Diaphragm is ~4cm cephalad displaced
- ↑ed ventilation: diaphragm contracts better from this higher position \(\Rightarrow\) ↑ed ventilation
- ↓lung volume \(\Rightarrow\) ↓lung compliance
- unchanged blood flow distribution

Awake Lateral Position

- ↓ vertical hydrostatic gradient compared to upright \(\Rightarrow\) zone 1 flow in nondependent lung is less
- blood flow - ↑10% to dependant lung over erect flow:
  - R dependant lung = 65% (55% if erect)
  - L dependant lung = 55% (45% erect)
- Ventilation relatively increased in dependant lung:
  - Gravity causes vertical gradient in intrapleural pressures
  - Dependant diaphragm pushed more cephalad \(\Rightarrow\) more efficient spontaneous ventilation
    \(\Leftarrow\) : greater perfusion and ↑ed ventilation to dependant lung \(\Rightarrow\) unchanged V/Q ratios compared to supine

Anaesthetised, closed Chest, Lateral Position

- Regional blood flow does not change awake : anaesthetised in lateral position
- See sig changes in distribution of ventilation:
  - ↑vent to non dependant lung:
    - GA \(\Rightarrow\) ↓FRC of both lungs ie volume loss
      - See a L shift of lung on compliance curve:
        - Dependant lung – moves to less steep part of curve due to volume loss
        - Top lung – moves to steeper part
      - Paralysis and IPPV – higher dome of diaphragm does not add to efficiency
      - Mediastinum compresses dependant lung & physically impedes expansion of that lung
        \(\Leftarrow\) as well as selectively ↓ing FRC
  - \(\therefore\) summary: anaesthetised pt +/- paralysis have ↑ed V/Q mismatch:
    - dependant lung:
      - well perfused
      - poorly ventilated
        \(\Leftarrow\) ↑(A-a)O2 or ↑Qs/QT
    - non dependant lung:
      - poorly perfused
      - better ventilated
        \(\Leftarrow\) ↑V_D/V_T
- PEEP restores some ventilation to dependant lung
  \(\Leftarrow\) by R shifting compliance curve

Anaesthetised, open chest & 1 lung ventilation in lateral position

- Non-dependant chest opened, dependant lung ventilated with double lumen tube \(\Rightarrow\) collapse non-dep lung
  - \(\therefore\) all flow through top lung = shunt ie ~35% L lung top, ~45% R lung top
  - hypoxic pulmonary VC (HPV) starts \(\Rightarrow\) ↓shunt through non-dep lung to ~20-25%
    \(\Leftarrow\) =
      - PAO2 & PACO2 of lung units in areas of shut approach values of mixed venous blood
Small pulmon arteries passing by these units respond to hypoxia by VC (opposite to normal response in rest of body)

- \( \Rightarrow \downarrow \text{shunt} \)
- if breathing norm: airway can also react: bronchial smooth mm would dilate in response to \( \uparrow \text{PACO2} \Rightarrow \downarrow \text{shunt} \)

- techniques to prevent hypoxaemia in 1 lung vent:
  - maintain 2 lung vent as long as possible
  - PEEP to bottom lung
  - High FiO2
  - CPAP to top lung
  - Intermittently vent top lung

**Effect of Anaesthetic Drugs on Control of Resp**

- Volatiles, barbituates, opioids all cause:
  - Depress ventilatory response to hypoxia, hypercapnia, acidosis
  - \( \downarrow \text{ed rate of rise of minute ventilation to } \uparrow \text{ed } \text{PCO2} \)
  - \( \uparrow \text{ed apnoeic threshold ie PaCO2 at which spont vent will resume is higher} \)
  - \( \text{effects persist into early post-op period} \)

**Effect of Anaesthesia on Lung Mechanics/Gas Exchange**

- supine & \( \downarrow \text{muscle tone} \Rightarrow \downarrow \text{FRC} \)
  - \( \Leftarrow \text{irrelevant if paralysed or not} \)
  - \( \downarrow \text{FRC leads to:} \)
    - atelectasis \( \Rightarrow \uparrow \text{shunt} \)
    - \( \uparrow \text{airways resistance} \Rightarrow \uparrow \text{WOB if breathing spont} \)
    - \( \uparrow \text{PVR} \)
    - \( \downarrow \text{compliance} \)

- positioning:
  - lateral position – discussed above
  - prone position - \( \downarrow \text{chest wall compliance} \)
  - sitting - \( \downarrow \text{VR} \Rightarrow \downarrow \text{CO} \Rightarrow \uparrow \text{alveolar dead space ie zone 1} \& 2 \)

- high vent pressures (IPPV +/- PEEP):
  - \( \uparrow \text{zone 1} \& 2 \) (\( \uparrow \text{alveolar dead space} \))
  - potential for barotrauma

- bronchodilation by volatiles

- Compliance: generally \( \downarrow \text{s C}_{\text{Total}} \) (mainly die to \( \text{C}_{\text{lung}} \))

- ETT = slight \( \downarrow \) in anatomical dead space

- IPPV - \( \downarrow \text{WOB} \)

- Hydration & heat loss – depends whether high flow/low flow anaesthetic & if humidifier in circuit

**Effect of IPPV**

- = Intermittent positive pressure pressure ventilation
- = 1 form of controlled ventilation (CV)
- common indications:
  - CPR
  - Resp failure – incl NIV
  - Anaesthesia – ETT vs LMA vs FM +/- Muscle relaxant

**CVS Effects**

- Nearly all effects are from \( \uparrow \text{intrathoracic pressure} \)
  - \( \Leftarrow \Rightarrow \text{degree of effect proportional to insp pressures & pt factors} \)
- Cardiac output effects:
**Preload:**
- [initial] ↑LVEDV as ↑ed blood squeezed from pulmon vessels into heart
- [soon]:
  - ↓VR from body ⇒ ↓LVEDV
  - further ↓LVEDV via RV bulging into LV due to septal shift
  - ↑Pulmon vasc resistance (PVR) ⇒
    - ↓flow thru vascular bed ⇒ ↓LVEDV
    - ↑RV afterload ⇒ ↓RV output ⇒ ↓LVEDV

**Afterload:**
- Raised intrathoracic pressure ⇒ ↑ed pressure gradient thorax:abdomen (ie intrathoracic aorta to abdominal aorta) ⇒↓LV afterload
- [low vent pressures] ↓afterload will balance ↓preload ⇒ preserved CO
- [higher pressures] ↓↓preload will dominate ⇒ ↓CO

↓afterload helps LV emptying (SV)
↑LV venous return by compression of congested pulmon circulation

**Sympathetic nervous system:**
- IPPV in critically ill pts:
  - ↓WOB
  - reverse hypoxaemia/hypercarbia/acidaemia
    -⇒ leads to ↓overall symp n.s. which ⇒ ↓CO, ↓SVR, ↓VR ⇒ ↓MAP

**Cardiac output depressing effects of IPPV will be ↑ed by:**
- PEEP
- Autonomic neuropathy
- Hypovolaemia

**Resp Effects**
- Intrapleural pressure (IPP) (in contrast to spont vent)
  - Inspiration +5cm H20
  - Expiration ~ -5cmH20
    -⇒ the mean IPP ↑+ve compared to SV

**Due to less –ve (+ve) IPP:**
- ↓FRC ⇒ atelectasis ⇒ shunting
  -⇒ more pronounced in dependant areas
- ↓lung compliance
- ↑Dead space (V_D/V_T):
  - ↑zone 1 – esp with high insp pressures ⇒ ↓alveolar perfusion
  - ↓CO ⇒ ↓pulmonary perfusion
- Change in PVR – depends on Vt’s & insp pressures used
  -⇒ ie different influences on intra & extra alveolar vessels
- ↓WOB

**Renal Effects**
- ↓renal perfusion & ↓GFR – due to:
  - ↓CO
  - ↑renal venous pressure
- ↓MAP & ↓GFR ⇒
  - ↑ renin-angiotensin-aldosterone system
  - ↓ANP
  - ↑vasopressin
- overall effect =
  - ↓UO by up to 40%
  - Na retention
**GastroIntestinal**

- Ileus –
  - esp prolonged IPPV
  - causes:
    - possibly: changes to GIT neural activity & pressures
    - more likely: 2nd to concurrent illnesses, surgery, drugs

**CNS**

- ↓VR ⇒ ↑CVP ⇒ ↑ICP

**Effect of PEEP**

- =adjunct to IPPV to achieve ↑FRC ⇒
  - ↓airway collapse
  - ↓shunt
  - ↑lung compliance
- PEEP = maintaining a positive airway pressure during expiration (usually 0)
  - usual 5-20cmH2O
- CPAP = positive pressure throughout spontaneous ventilation

**Negative Effects of PEEP**

- Exhibit same –ve effects of IPPV (except for ↑ing FRC and ↑ compliance)
- But as PEEP ⇒ ↑ed intra-thoracic pressure ⇒ see magnified –ve effects:
  - ↓CO
  - ↑dead space in lungs (zone 1&2)
  - pulmonary barotrauma
  - ↓UO
  - ↑vasopressin secretion
  - ↑ed ICP

**Clinical Application of PEEP**

- obviously conflicting effects of PEEP on DO2:
  - ↓shunt
  - ↑dead space
  - ↓cardiac output

\[
DO2 = CaO2 \times CO
\]

CaO2 = O2 content
DO2 = O2 delivery

∴ PEEP tends to ↑CaO2 but ↓CO

- PEEP definitions:
  - Best PEEP = produces least shunt without sig ↓ in CO
  - Optimum PEEP = produces max DO2 with lowest \( V_D/V_T \)
  - Appropriate PEEP = that with least dead space
Integrated Cardio-Resp Response to Exercise

- Resting O2 consumption (VO2) of 250ml/min can rise (x12-20):
  - Mod fit 3000ml/min (42ml/kg/min)
  - Elite athlete 6000ml/min (85ml/kg/min)
  - fit young adult (~42 mL/kg/min)
  - sedentary 70 year-old (~17 mL/kg/min)

- Co2 output:
  - Rest 240ml/min
  - Mod exercise 3000ml/min

- Mm blood flow ↑s depending on type of mm action:
  - Rest: 2-4ml/100g/min
  - 10% Mm contraction ⇒ part constriction of internal vessels
  - 70% max contraction ⇒ total occlusion of vessels . blood flow stopped
  - rpt isotonic contractions ⇒ x30 ↑blood flow:
    - Exercise: 60-120ml/100g/min

- factors causing ↑mm flow:
  - ↑Pco2; ↓Po2
  - accumulation of K & other metabolites
  - ↑temp ie metabolic autoreg
  - sympathetic n.s. mediated dilation of arterioles & precapillary sphincters:
    - ↑x10-100 number of open capillaries ⇒ ↓SVR
    - .: diffusion distance from open blood vessel to mm cell is decreased
    - ↑’s cross sectional area of vasc bed ⇒ ↓velocity of flow
  - capillary pressure > oncotic pressure ⇒
    - transudation of metabolites
    - ↑lymph flow

- ↑offloading of O2 facilitated by:
  - ↓pH
  - ↑temp
  - ↑2,3 DPG

- Resp exchange ratio (R) = CO2 output/O2 input
  - Changes:
    - Rest 0.8
    - Exercise 1.0
    - reflects ↑reliance on carbohydrate metabolism rather than fat
  - R >1 when strenuous exercise:
    - lactic acid production ⇒ ↑CO2 eliminated from HCO3
    - ↑CO2 elim cos: ↑H+ ⇒ stim periph chemoreceptors ⇒ ↑ventilation

Fick Principle

- VO2 of skeletal mm ↑s x100

- Fick principle:
  - VO2 = CO x (CaO2 – CvO2)

- Thus to meet demand of ↑VO2 need to have:
  - ↑CO
  - ↑(a-v)O2-difference ie larger extraction of O2 in skeletal mm:
    - Spo2 mixed venous normally 75%
    - Can be as low as 20% in heavy exercise
  - ↑ventilation – to maintain CaO2

- physiological changes seen in body are all aimed at meeting ↑ed VO2
Cardiovascular Changes in Response To Exercise

- Stimuli for change:
  - Central – anticipation phase: cerebro-cortical activation of symp n.s. & inhibition of parasymp n.s. ⇒ ↑positive activity on SA node ⇒ ↑tachycardia
  - Reflexes from contracting mms:
    - Afferent: mechano & chemo receptors gp III & IV fibres
    - Efferent: symp nerve fibres
  - Baroreceptor reflex

- Observed changes in isometric exercise:
  - ↑Cardiac output in linearly with ↑ed work level:
    - ↑HR – (210-age)/min
    - ↑SV - ↑10-35%
  - ↑MAP: only slight as ↑ed CO partly offset y ↓SVR
  - ↑VR:
    - mm activity
    - thoracic pump
    - symp mediated VC ⇒ ↑blood return. Vessels include:
      - visceral vessels
      - other periph venous network
    - ↑ in preload only really impt during vigorous exercise
  - targeted blood flow:
    - [initially]: VC in skin. [later]: VD to release temp
    - VC to kidney ⇒ ↓UO
    - VC to splachnic regions
    - VC to inactive mms
- ∴ coordinated response inside heart (HR & SV) and in vasculature (VR & SVR)

Isometric vs Isotonic Exercise

- onset of isometric contraction:
  - ↑ HR 2nd to psychic stimuli ⇒ ↓vagal tone
  - seconds: rapid ↑ systolic & diastolic bp
  - SV mostly unchanged

NB linear ↑ CO, ↑(a-v)O2 to meet ↑VO2
Respiratory Changes to Exercise

- Changes brought about by:
  - Central factors:
    - ↑ventilation at or before exercise eg learned response or anticipation
    - afferent inputs form proprioceptors in mm, tendon, joints
    - chemoreceptors
    - humoral mechanisms ie lactic acidosis
  - result =
    - ventilation ↑instantly and linearly with VO2/work rate (VO2 = Ve x (Fio2 – FeO2))
      ← see graph A.
    - Owles Point = AT where ventilation increases more rapidly
      ← driven by ↑ing lactic acid ~ 21O2/min
    - ↑TV early then ⇒ ↑RR rapidly with ↑ing exercise
    - O2 uptake increases linearly with work rate up to VO2 max
      ← then work rate can only be ↑ed by anaerobic glycolysis (which is self limiting)
  - In periph tissues:
    - Recruitment of capillaries ⇒ ↓diffusion length to mitochondria
    - ↓periph resistance
  - CO : ventilation 1:4
    - Easier to move air than blood
    - MV ↑s to 120L/min (up to 200l/min in athelets) ⇒ resp mm’s consuming 5-10% VO2 max
  - ↑pulmon art & venous pressure ⇒ ↑recruitment & distension in capillaries ⇒ ↓pulmon vasc resistance
  - x3 ↑ diffusion capacity of lung
    - because of:
      - ↑diffusion capacity of membrane
      - ↑volume of blood in pulmonary capillary
      - changes caused by recruitment & distension of pulmon capillaries esp in apices
  - O2 dissociation curve:
    - R shift in exercising mm ⇒ ↑unloading of O2 in tissues
      ← due to ↑PCO2, ↑H+, ↑temp
    - blood returning to lung ⇒ ↓temp ⇒ left shift curve

VO2 Max graphs:

A
- as work rate ↑s, O2 uptake ↑s linearly until certain point where becomes constant
- this = VO2 max
- work above this rate requires anaerobic glycolysis

B
- ventilation also ↑s with work rate or VO2
- at high values, lactic acid production commences ⇒ ↑ed vent stimulus
  ← if clear break in slope = anaerobic threshold
• fitter people take longer to change to anaerobic glycolysis

Resp & CVS Changes (V/Q)
• change in VQ mismatch:
  o moderate exercise:
    ▪ ↓VQ mismatch due to more uniform distribution of blood flow
  o elite exercise:
    ▪ VQ mismatch develops due to mild interstitial pulmon oedema

level of Exercise
• moderate ex – PO2, PCO2, pH little change
• high work level:
  o ↓PCO
  o ↑PO
  o ↓pH – lactic acid

Recovery After Exercise
• symp activity ↓ ⇒ ↓CO ⇒ ↓SVR ⇒ activation of baroreceptor reflex ⇒ bp return to pre exercise levels
• can sometimes see transient hypotension awaiting baroreceptor reflex
• VO2 remains elevated after severe exercise for ~90mins

Limits of Exercise Tolerance
• Do2 (O2 delivery) to active mm major limiting factor ie Cardiac output
• Feelings of distress & exhaustion:
  o ↑symp activity ⇒ cutaneous VC ⇒ ↑temp ⇒ distress
  o once O2 demand > DO2 then ⇒ anaerobic glycolysis ⇒ lactate ⇒ ↑pH ⇒ muscle pain & exhaustion
• trained athletes:
  o ↑ed ability to delivery O2:
    ▪ ↑ed SV with larger heart
    ▪ ↑ed resting HR thus ↑variability
    ▪ in mm:
      • ↑capillary density
      • ↑no of mitochondria
      • ↑oxidative enzyme activity in mitochondria
    ▪ ↑ed (a-v)O2 difference ie ↑ed ability to extract more O2 from blood flow
    ↓: ↑ed VO2 max
  o lactate:
    ▪ liver may remove more circulating lactate
    ▪ ↑ed tolerance to high serum lactate levels
Ageing
- natural physiological process beginning from 20’s
- theories as to why occurs – none good eg apoptosis
- WHO definitions:
  - 45-59 = middle aged
  - 60-74 = elderly
  - 75-89 = old
  - >90 = very old

Cardiovascular Age Changes
- general:
  - ~50-65% coexisting CVS disease >60yrs eg atherosclerosis, silent ischaemia,
- Cardiac output:
  - HR:
    - Resting HR +/- unchanged
    - ↓ed Max HR 200 ⇒ 160
    - intrinsic (with no autonomic input) HR ↓ed
    - ↑ incidence of arrhythmias – fibrous infiltration of SA Node
    - physiological downregulation of B1 receptors ie ↓response to ephedrine
  - Preload:
    - ↓ compliance ⇒ ↑diastolic dysfunction:
      - general stiffening of myocardium (amyloid, LVH)
      - fibrosis of endocardium
      - ie elderly heart becomes preload dependant but also volume intolerant
  - Afterload - ↑ed due to ↑MAP which then ⇒ LVH
    - ↑SBP & ↑MAP due to stiffened arteries
    - ↓DBP due to more rapid run off from stiff arteries
  - Contractility: unchanged or ↓ed

End result in 25-80yrs is no sig ↓ in CO during rest or mod exercise BUT max CO is ↓ed
- Baroreceptor mechanism: ↓ed sensitivity ie more prone to syncope moving to erect posture

Respiratory Changes
- ↓ alveolar surface area
- ↑V_D/V_T = ratio of dead space to tidal volume
  - both alveolar & anatomical increase
- ↑Q_S/Q_T (shunt equation):
  - mostly due to loss of lung elastic tissue ⇒ ↑C_L (as well as C CW) ⇒ more +ve intrapleural pressure ⇒ ↑Closing capacity ⇒ atelectasis of dependant lung areas ⇒ shunting
  - occurs at different ages in diff positions in normal tidal breathing:
    - 44 = supine
    - 66 = erect
- ↑D(A-a)O2 – mainly due to shunting ⇒ ↓PaO2
  - rough rule: PaO2 ~ 105 – (age/3)
- ↓chest wall compliance ⇒ ↑total work of breathing
  - Nb C_total = normal
- ↓ neural response to hypoxia & hypercapnia
- ↑frequency & duration of sleep apnoeic episodes
- volumes:
  - ↓FEV1
  - ↓VC
  - normal TLC – due to air trapping
High Altitude

- pressure ↓s exponentially with distance from earth
- sea level pressure = 1 bar
- pressure at 5800m = ½ of normal (760 mmHg)
  \[ \text{PO2 of moist inspired gas} = (380 - 47) \times 0.2093 = 70 \text{mmHg} \]
- @ Mt everest 8848m PO2 = 43
- @ 19200m PO2 = 0

Demands on body @High Altitude

- low PAO2 ⇒ low PaO2 ⇒ hypoxaemia
  \[ \text{PO2 <90mmHg} \Rightarrow \text{↓ing Spo2 & CaO2} \]
- colder ambient temps
- ↓relative humidity ⇒ ↑insensible water loss from skin & lungs
- ↑ed exposure to solar radiation due to thin atmosphere

Hyperventilation

- most impt feature of acclimatization
- starts at 3000m and reaches max at 6000m
- alveolar gas equation:
  
  \[
  \text{if climber PACO2 = 40 & resp exchange ratio 1:} \\
  \text{PAO2 = 43 - (40/1) = 3 mmHg} \\
  \text{BUT climber ↑vent x5 ⇒ ↓PCO2 to 8:} \\
  \text{PAO2 = 43 - (8/1) = 35 mmHg}
  \]
  
- hypervent created by hypoxic stim of periph chemoreceptors
- initially ↓PCO2 and ↑pH limit the ↑RR
  \[ \text{BUT after a day CSF pH is normalised by extrusion of HCO3}\]
  
  resp centre gets reset to function at lower PaCO2 ⇒ L shift & ↑ed slope of CO2 curve
  
  after 3 days renal compensation normalises blood pH by excreting HCO3
  
  @3-4km after 1-2 weeks hypervent again reaches a maximum & persists

Other Resp Changes

- O2 transfer becomes diffusion limited
  - Especially during exercise
  - max O2 uptake declines rapidly over 4600m
  - can be corrected if breathe 100% O2
- hypoxic pulmonary VC ⇒ pulmonary HTN
- ↑sensitivity of carotid bodies to hypoxia during acclimatisation
- ↑maximum breathing capacity
  - ↓density of air assists high ventilations
- pulmon HTN ± ⇒ pulmon oedema
  - pulmonary venous pressure still normal
  - caused by uneven arteriolar VC ⇒ leakage in protected damaged capillaries
  - oedema is an exudate not transudate

Cardiovascular Changes to High Altitude

- HR- ↑in hours due to ↑symp n.s. activity
- SV – initially unchanged but within days ↓s
- CO –
o Initial: slight ↑ due to ↑HR  
o Days: return to normal: ↑HT, ↓SV  
o Reduction in max CO during exercise due to limitation of ↓SV  
o Redistribution of CO:  
  ▪ ↓skin & splanchic flow  
  ▪ ↑vital organs  
• coronary blood flow: ↑ed due to metabolic autoreg from hypoxia  
• ↑ work by R heart ⇒ hypertrophy:  
  o pulmon VC ⇒ pulmon HTN  
    ⇣response to alveolar hypoxia  
  o ↑viscosity ⇒ ↑resistance to flow ⇒ ↑R heart work  
    ⇣no known benefit from RVH except blood flow becomes more uniform  
• Angiogenesis ⇒ ↑number of capillaries/unit volume in periph tissues  
• ↑cellular oxidative enzymes

**Haematological changes**  
**Polycythaemia**  
• ↑rbc concentration ⇒ ↑Hb concentration ⇒ ↑O2 carrying capacity ⇒ ↑ O2 concentration of blood  
  ⇣despite ↓PaO2 & ↓SaO2  
• stimulus for ↑rbc's = hypoxaemia ⇒ ↑EPO from kidney ⇒ stim bone marrow production of rbc's  
• NB although polycythaemia ⇒ ↑O2 carrying capacity it also ↑s viscosity of blood & ↓ resistance  
  ⇣can be bad ⇒ ↓perfusion of organs

**OHDC**  
• At moderate altitude:  
  o R shift of O2 curve at moderate altitudes ⇒ ↑unloading of tissues in tissue  
  o Hypoxia ⇒ ↑2,3-DPG production effecting R shift  
    ⇣ok but in severe hypoxia R shift will impede O2 loading in lungs & L shift actually better for DO2  
  o Resp alkalosis ⇒ L shift effect (partially offsets R shift as above)  
• At higher altitude:  
  o L shift of curve  
  o Caused by ↑ing resp alkalosis  
  o Assists with loading of O2 in pulmon capillaries  
    ⇣O2 loading in lungs takes priority over tissue PO2  
    ⇣similar to foetus (P50 17mmHg) where PO2 is very low and curve is markedly L shifted

**Endocrine**  
• ↑catecholamines, glucocorticoids, thyroid hormones, & ADH  
  ⇣within 1 week due to hypoxia  
• fluid changes:  
  o [initial] fluid retention  
  o [within 1wk]: ↓ed ADH & ↓aldosterone in response to ↑ed volume  
    ⇣initial fluid retention can contribute to HAPO/HACO esp with exertion

**Mountain Sickness**  
• acute –  
  o hypoxeaemia & alkalosis  
  o headache, fatigue, dizzy, palps, insomnia, ↓apetite, nausea  
• chronic –  
  o more ill defined  
  o ↑↑polycythaemia, fatigue, ↓ex tolerance & severe hypoxaemia
Anaemia

• a reduced O2 carrying capacity of the blood due to either a reduced Hb concentration +/- the presence of abnormal Hb
  ⇐ NB conditions ⇒ dyshaemoglobinaemias eg carboxyhaemoglobin = functional anaemia

• normal Hb:
  o female - <12g/dl
  o male <13g/dl

• aetiology – many classifications
  o ↑loss – eg bleeding, haemolysis
  o ↓production – eg Fe deficiency
  o abnormal Hbs

• anaemia ⇒ ↓CaO2 & ∴ ↓DO2
  \[
  \text{CaO}_2 = (\text{Hb} \times 1.39 \times \text{SpO}_2) + (\text{PaO}_2 \times 0.03) \\
  \text{DO}_2 = \text{CaO}_2 \times \text{CO}
  \]

• anaemia ⇒ ↓viscosity of blood ⇒ ↓flow resistance
  ⇐ but can ⇒ ↑tubulant flow

Compensatory Mechanisms

• depend on nature and onset of anaemia:
  o acute hypovolaemic anaemia – see notes on shock in CVS
  o acute normovolaemic anaemia – only mechanism =
    ▪ ↑CO – methods of doing this:
      * metabolic autoregulation:
        o tissue hypoxia ⇒ generalised VD ⇒ ↓SVR ⇒ ↑CO
      * ↓viscosity ⇒ ↓flow resistance through arterioles ⇒ ↓afterload ⇒ ↑CO
      ▪ +/- some redistribution of CO
    o chronic anaemia:
      ▪ ↑CO
      ▪ redistribution of CO to impt organs (brain & heart)
      ▪ ↑O2 extraction:
        * lower tissue PO2 causes ↑ed gradient for diffusion
        * ↑rbc 2,3 DPG (R shift OHDC) ⇒ ↑offloading O2 to tissues
      ▪ ↑EPO from kidney ⇒ ↑rbc production
      ▪ ↑ventilation – although of little help as Spo2 usually already high

O2 Toxicity

• evidence of toxic damage >30hrs
• toxic O2 causes:
  o damage to pulmon endothelium
  o substernal distress – aggravated by deep insp
  o ↓vital capacity of 500-800ml
    ⇐ by absorption atelectasis
  o Po2 >760mmHg ⇒ CNS stim ⇒ Nausea, tinnitus, facial twitching
    ⇐ then seizure
  o in neonates:
    ▪ local VC ⇒ retrolental fibrosis ⇒ blindness
    ⇐ kep PO2 <140mmHg

Absorption Atelectasis

• airway blocked by mucus (A)
• total pressure in trapped gas close to 760mmHg
massive PAO2 in trapped air which dissolves into pulmon blood ⇒ collapse of alveolar
then ↑ed work to reopen alveoli as must overcome ↑surface tension in smaller units

absorption also occurs in inspired air with trapping (B)
process slower as is limited by N2 absorption
N2 has a low solubility .: acting as a splint to alveoli
Collapse most common at base of lung
parenchyma most poorly expanded ± small airway collapse

Space Flight
Lack of gravity ⇒ ↑ingly uniform VQ
Deposition of sediment altered because no sedimentation
↓periph venous pooling blood in legs ⇒ ↑thoracic blood volume ⇒ ↑pulmon capillary blood ⇒ ↑diffusing capacity
on return to earth:
  o cardiovascular deconditioning – post hypotension
  o bone & mm atrophy
  o ↓rbc mass

Increased Pressure
Diving
↑pressure by 1 atmosphere for every 10m of descent
↑ed density of gas at depth ⇒ ↑WOB ⇒ CO2 retention especially on exercise

Decompression Sickness
during dive high partial pressure of N2 forces the poorly soluble gas into solution in tissues
lot of N2 driven into fat:
  o poor blood supply
  o blood can carry little N2
  o N2 diffuses slowly due to poor solubility
  equilibrium of N2 tissue:environment takes hours
During ascent:
  o N2 slowly removed from tissues
  o Too rapid ⇒ bubbles of N2 formed
  o Symptoms:
    ▪ Pain – bends
    ▪ Deafness
    ▪ ↓vision
    ▪ CNS paralysis
Treatment = recompression:
  o ↓s bubble size ⇒ force N2 back in solution
prevent
  o with slow staged ascent
  o helium – O2 mixture
    ▪ helium is
      • even more unsoluble (½) than N2
      • 1/7 molecular weight of N2 .: ↑rapid diffuser through tissue
      • lower density gas ⇒ ↓WOB

Inert Gas Narcosis
N2 generally inert BUT at high pressure ⇒ CNS effect
• ~50m depth ⇒ euphoria
• >depths ⇒ ↓coordination & coma
• mechanism not entirely understood
• helium & hydrogen avoid these

O2 Toxicity
• pure O2 at >4atmospheres ⇒ convulsions within 30mins
• O2 concentration progressively ↓ed as diver deeper

Hyperbaric Therapy
• ⇒ artificial high PaO2
• useful in:
  o CO poisoning:
    ▪ ↑PO2 to >3 atmospheres ⇒ ↑dissolved O2 in blood to ~6ml/100ml
      ↓this level can meet tissue needs without any Hb loading
  o Rx gas gangrene – organism cannot live in high Po2 environment
  o Decompression sickness
• Chamber filled with air, O2 given with mask

Polluted Atmospheres
• Pollutants
  o Oxides of nitrogen, hydrocarbons, CO – from combustion engines
  o Sulphur oxides – fossil fuels
  o Ozone - sunlight
  o Particulate matter
    ↓concentration ↑ed by temp inversion which traps pollutants at breathing level
• Symptoms of pollution:
  o Nitrogen Oxides
    ▪ Inflam of upper airways
    ▪ Eye irritation
  o Sulphur oxides & ozone –
    ▪ Bronchial inflam
    ▪ Pulmon oedema
  o Hydrocarbons – carcinogetic
  o CO – irreversible Hb binding

Particulate Matter
• Fate of aerosols depend on size of particles:
  o Large particles = impaction:
    ▪ Weight of particle cannot turn corner ⇒ stuck on nasal mucosa
  o Medium sized = sedimentation:
    ▪ Deposit in small airways where flow suddenly ↓s due to ↑in cross sectional area of tubes
      ↓.: terminal & resp bronchioles
  o Smallest (<0.1 micron) reach alveoli:
    ▪ Exhaled in next breath
    ▪ Deposit on alveoli wall by diffusion ⇒ phagocytosis

Liquid Breathing
• Possible to live on fluid if liquid has high solubility for O2 & CO2
• Liquids = much higher density ⇒ ↑↑WOB
• Adequate oxygenation of arterial blood possible if O2 concentration is high enough
• CO2 retention & acidosis very common:
  o Diffusion rate in liquid of CO2 much slower
    ↓means need much bigger pressure difference to drive elimination of CO2
Perinatal Respiration

- Fetal life – placental & periph tissues lie in parallel circuits
- Adult – pumon & peripheral tissue series
- Placenta:
  - Maternal blood ⇒ uterine artery ⇒ intervillous sinusoids
  - Fetal blood ⇒ capillary loops ⇒ protrude into intervillous spaces
  - Gas exchange across 3.5um thick blood-blood barrier
  - Less efficient than lungs:
    - Large differences in PO2
    - Fetal blood leaving placenta ~30mmHg
- Arterial blood in descending aorta ~22mmHg

Fetal Lung

- Lung inflated with liquid to ~40% total lung capacity
- Fluid
  - secreted by alveolar cells
  - low pH

First Breath

- ↓placental gas exchange ⇒ hypoxaemia & hypercapnia
- ↑sensitivity of chemoreceptors - ?mechanism
  - first gasp:
    - fetus in uterus already makes small rapid breathing motions pre birth
    - some fluid squeezed out lung during passage of baby
    - preinflation with fluid ↓s surface tension required to create 1st breath
      - but still see intrapleural pressure -40 to -100 cmH2O
      - also to overcome ↑ed viscosity of fluid: gas
    - expansion of lung uneven at first
    - surfactant stabilises alveoli
    - lung fluid reabsorbed by lymph & capillaries
- takes only a few moments for FRC at normal level to be achieved
- days before uniform ventilation

Circulatory Changes

- dramatic ↓pulmon vasc resistance after birth due to:
  - first breaths ⇒ ↑volume of lung ⇒ wider extralveolar vessels
  - ↑PAO2 ⇒ ↓hypoxic VC
- pulmon arteries v sensitive to
  - VC agents eg:
    - hypoxaemia
    - acidosis
    - serotonin
  - VD agents eg Ach
- ↑pulmon blood flow & ↑aortic bp from switch to series (from parallel) circulation ⇒ ↑LA pressure ⇒ closure of flap covering foramen ovale
- ↓RA pressure as umbilical flow ceases
- ductus arteriosis constricts in minutes due to:
  - high PO2 action on smooth mm
  - ↓prostaglandins
Hypothermia

- Henrys law states with ↓temp:
  o Solubility coefficient ↑
  o Partial pressure ↓
- ∴ .....  
  o ↑ solubility for O2 & CO2  
  o ↓ppO2 & Co2  
- OHDC will shift to L with ↓ ⇒ Hb ↑ed affinity for O2:  
  o At high PO2 level – Hb already fully saturated so wont see much effect  
  o At low PO2 level - ↑ed affinity means ↑ed O2 to binding to Hb ⇒ ↓pO2 
    ↓ on top of the ↑ed solubility of O2  

NB in all these states total oxygen content will NOT change