Physiology week 12 – Respiratory (volumes)

Structure and function of the lungs

Conducting and respiratory zones

Between trachea and alveoli the airways divide 23 times.

Conducting zone

First 16 divisions form the conducting zone
Bronchi, bronchioles, terminal bronchioles.
= dead space (150ml)

Transitional and respiratory zone

Last 7 divisions (17-23)
Respiratory bronchioles, alveolar ducts, alveoli, lung distal to terminal bronchus is acinus

Bronchial tree

Trachea and bronchi

Cartilaginous walls (trachea and bronchi only)
Relatively little smooth muscle
Lined by ciliated epithelium (as far as respiratory bronchioles)
Numerous mucous and serous glands (trachea and bronchi only)
Abundant muscarinic receptors and beta2 adrenoceptors

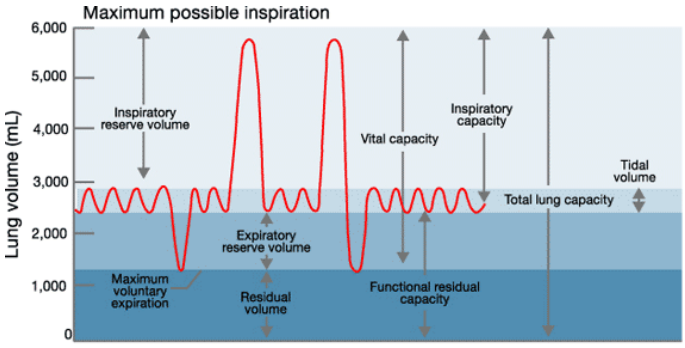
Alveoli

Cross sectional area alveoli 11,800cm2 (300 million alveoli, 70m2 alveolar wall in contact w capillaries).
Surface area 85 m2
Cross sectional area in bronchi 2.5cm2
Type 1 cells - Flat, Large cytoplasmic extensions, Primary lining cells.
Type 2 cells - Thick, Numerous lamellar inclusion bodies, Secrete surfactant.

Pulmonary capillary

Diameter 10µm
Pulmonary artery pressure 15mmHg mean
Each rbc spends 0.75 secs in capillary network

Lung Volumes



TLC - volume air in lungs after max insp effort.
Determined by strength contraction insp muscles in opposition to inward elastic recoil of lungs and chest wall. ~6L

FRC - volume gas in lungs at end of normal tidal expiration.
Balance point between inward elastic recoil of lungs and outward elastic recoil of chest wall. ~3L

TV - volume of air entering or leaving nose or mouth per breath.
During normal, quiet breathing ~500 ml per breath.

VC (Vital Capacity) - volume air expelled from lungs during max forced expiration after max forced inspiration. ~ 4.5L

- Spirometry - must be able to exchange volume to be determined with spirometer.
  - So cannot use spirometry to determine RV, or FRC and TLC, which contain RV.
- Determination of FRC, RV, and TLC
  - Nitrogen washout technique;Helium dilution technique; Body plethysmograph technique
- Gas dilution
  - Closed system - helium measured
  - Compare concs of helium and volumes before and after patient connected to circuit

- So V2(lung volume)=V1(known volume in circuit) (C1-C2)/C2
  - C1 is conc in circuit before patient connected, C2 is after

– Body Plethysmography
  - Essentially in closed box with two measurements made
    - Mention Boyles law – P x V is k at constant temperature
    - So P and V on either side of the equation are the same
    - 1) measure P and V in box when subject breathes against closed mouth piece
      - You want the ΔV P1V1 = P2 (V1-ΔV)
    - 2) measure P and V at mouth piece
      - So P3V2 = P4 (V2 + ΔV)
      - P3 and P4 are pressures at mouth before and after inspiration
      - **V2 = FRC**

Respiration

External respiration

'absorption of oxygen and removal of carbon dioxide from body as a whole'.

Internal respiration

'utilization O2 and production CO2 by cells and gaseous exchange between cells and their fluid medium'

Properties of gases

Ideal gas equation

PV=nRT

the equation of state of a hypothetical ideal gas

good approximation to behaviour of many gases under many conditions

p - absolute pressure of gas; V - volume; n - amount of substance; R - gas constant; T – absolute temp

$R = 8.314472\ \mathrm{J \cdot K^{-1} \cdot mol^{-1}}$

Partial pressure

'pressure exerted by any one gas in mixture of gases equal to pressure X fraction total amount it represents'

Ventilation

Dead space

'volume of lung not available for gas exchange with the pulmonary capillary blood'

Anatomical dead space

'volume of the conducting airways' 150mls (depends on size and posture, incr with inspiration)

Physiological dead space

'volume of conducting airways plus the alveolar dead space'

Anatomical dead space and **physiological** dead space equal in healthy individuals.

Alveolar ventilation = 350ml; Dead space = 150ml

Measurement of dead space

Fowler's method – measures anatomical dead space

Measures volume of conducting airways down to level where rapid dilution of inspired gas occurs with gas already in lung. Analysis of single breath nitrogen curves.

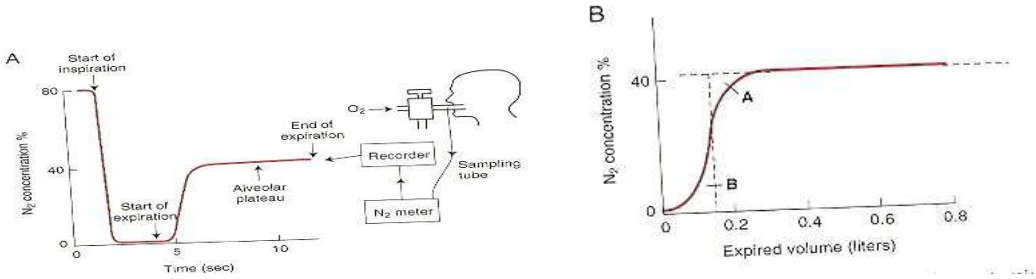
Commence at mid inspiration – single inspiration 100% O2

N2 measured during expiration. Where A=B gives the volume of dead space.

Phase 1 = dead space gas with no nitrogen; Phase 2 = dead space mixed with alveolar gas

Phase 3 = alveolar gas; Phase 4 = between closing volume/residual volume where airways in lower dependent parts of lungs begin to close due to lesser transmural pressure in these areas.

Gas in upper lungs is richer in nitrogen because upper alveoli more distended at start of insp.



Bohr's method – measures physiological dead space

Measures volume of lung that does not eliminate carbon dioxide, a measure of function
Assumes that all expired CO2 comes from alveolar gas and none from dead space.

Therefore dead space calculated from partial pressure of CO2 in expired air, end alveolar partial pressure of CO2 and tidal volume

Bohr equation

$$\frac{V_{D\ Phys}}{V_T} = \frac{PaCO_2 - P_{\bar{E}}O_2}{PaCO_2}$$

normal ratio VD/VT is 0.2-0.35
lung disease - physiological space can be much larger than anatomical
V/Q mismatch – non-perfused alveoli and alveoli with excessive ventilation

Alveolar gas equation

Measures relationship between alveolar O2 partial pressure and alveolar CO2 partial pressure
pAO2 = pIO2 – (pACO2/R) + F
PAO2 = alveolar O2 partial pressure
PIO2 = oxygen partial pressure of inspired air
PACO2 = alveolar CO2 partial pressure
R = respiratory quotient – ratio of CO2 production to O2 consumption (0.8)
F = correction factor 2mmHg compensates for differ between inhaled/exhaled volume
A-a gradient = PAO2 – PaO2
Significance – V/Q mismatch (shunting/dead space)

Regional differences in ventilation

Ventilation increases from top to bottom of the lung
Blood flow increases in the same way, but to a greater extent
– High V/Q at top of lung; V/Q = 1 around rib 3
Intrapleural pressure less negative at base than at apex (- 2.5cm water vs –10cm water) – due to weight of lung.
Base of lung has small resting volume and expands well on inspiration.
Apex has a large resting volume and a small change in volume on inspiration.

Airway resistance

'*the pressure difference between the mouth and the alveoli divided by the flow rate'.*
Greatest at bronchi of intermediate size, in between fourth and eighth bifurcation
(small airways should theoretically offer more resistance but are much more numerous)
Calculated using Ohm's law or Poiseuille's law

Ohm's law

$$R = \frac{\Delta P}{\dot{V}} = \frac{P_{\text{mouth}} - P_{\text{alveoli}}}{\dot{V}}$$

- R = resistance
- P = pressure
- $\dot{V}$ = airflow (dot over letter denotes rate)

Poiseuille's law

$$R = \frac{8nl}{\pi r^4}$$

- R = resistance
- n = viscosity
- l = length
- r = radius

Flow resistance directly proportional to viscosity and length

Inversely proportional to radius to power of 4 (ie half the radius increases resistance 16 fold)

Because of the fourth power in the denominator, resistance increases rapidly as diameter decreases.

Factors affecting resistance in airways
- Size of airway (R highest in med sized bronchi, low in very small airways)
- Lung volume (R decreases with expansion as airways pulled open)
- Bronchial smooth muscle tone (controlled by B sympathetics)
- Gas density (eg heliox – low R)
- Forced expiration (intrathoracic pressure compresses airways = "dynamic compression"

Factors affecting radius of airway
- Bronchial smooth muscle tone (sympathetic/parasympathetic activity)
- Lung volume

Factors causing turbulent flow in airways
- Expressed by Reynolds number

Where: ρ is the fluid density;
D is the diameter of the tube;
V is the velocity of flow;
η is the viscosity of the fluid.

$$Re = \frac{\rho D V}{\eta}$$

- Laminar flow only in small airways, transitional most areas, turbulent in trachea (rapid breathing)

Components that make of work of breathing
- **Non-elastic work**
  - Viscous resistance (moving inelastic tissues) 7%
    - Affected by:
      - Higher RR increases flow rate
      - Decr airway radius due to lower lung volumes or bronchoconstrictors
      - Incr air density (SCUBA diving)
      - Incr air viscosity
  - Airway resistance 28%
- **Elastic work** of lungs and chest wall 65%
  - Affected by:
    - Larger tidal volumes
    - Reduced compliance due to:
      - Less lung volume
      - Less during inspiration
      - Incr by incr tissue mass – fibrosis, congestion, chest wall restriction
      - Loss of surfactant

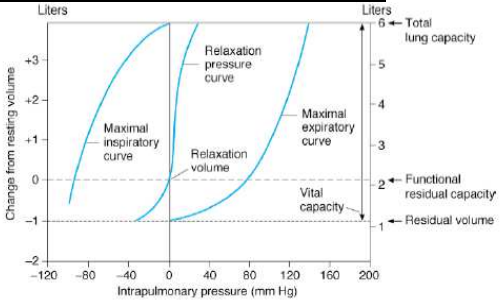
<u>Mechanics of breathing</u>

Inspiration - Active process
- Intrapleural pressure at base lungs reduces –2.5mmHg to – 6mmHg; negative pressure causes airflow into lungs.

Expiration - Passive process at rest.
- Lung recoil pulls chest back to expiratory position; airway pressure becomes positive and air flows out of lungs.

Respiratory muscles
- **Inspiratory muscles** – increase intrathoracic volume
  - **Diaphragm -** Accounts for 75% of change in intrathoracic volume during quiet resp. Moves 1.5-7cm.
  - **External intercostal muscles -** Elevate lower ribs and increase anteroposterior diameter of the chest.
  - **Scalene anterior, medius, posterior; Sternocleidomastoid**
- **Expiratory muscles**
  - **Internal intercostals, Rectus abdominis, Internal oblique, External oblique**

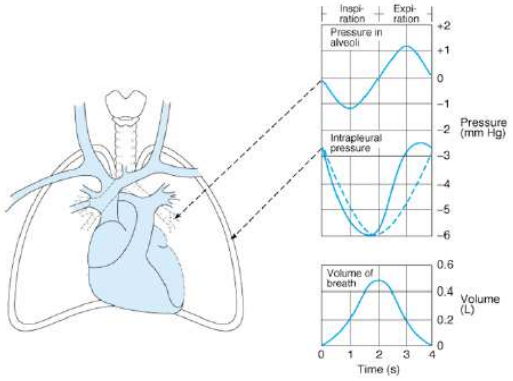
<u>Intrapulmonary pressure vs volume</u>



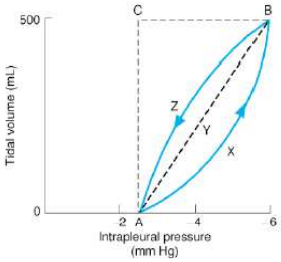
Slope of curve = compliance
Sigmoid curve, does not reach 0% lung volume
Shows lung volume higher during expiration than inspiration for any given pressure = hysteresis
Shows that lung contains residual air without any expanding pressure (due to airway closure)
Shows that compliance decreases at higher lung volumes – lung becomes stiffer due to reaching limits of elasticity

How regional differences in intrapleural pressure affect ventilation:
Intrapleural pressure higher at apex than base – to keep lung expanded against its own weight
Increased compliance at base, so better ability to ventilate base compared with apex

Changes in intrathoracic/intrapleural and intrapulmonary pressure relative to atmospheric



Intrapleural pressure vs volume
AXB – quiet inspiration; BZA – expiration; AYB – compliance



Compliance
'change in lung volume per unit change in airway pressure'
Stretchability of lungs that is a function of recoil of lungs and chest
Slope of pressure volume curve
greatest at moderate lung volumes (reduced at very high and very low volumes)
Higher at base than apex because apex already more distended.
Main determinants:
Surface tension of alveoli (2/3)
Elastin/collagen fibres (1/3)
Alveolar surface tension depends on alveolar pressure, radius and surfactant
(Law of Laplace P = r4T/R)
Compliance in humans = 200ml/cm water – this increases at higher volumes.
Compliance is reduced by:
Fibrosis, Oedema, Atelectasis, loss of surfactant
Compliance is increased by:
Emphysema, Asthma, Ageing

Relaxation volume
'the point where recoil of the chest and recoil of the lungs balance'

Alveolar stability and surface tension
Factors affecting alveolar stability
Supporting parenchymal structure of lungs
Surface tension of the alveoli

Surface tension

'the force acting across an imaginary line 1cm long in a liquid surface'.

Surface tension arises because attractive forces between adjacent molecules of liquid are much stronger than between liquid and gas therefore the liquid surface becomes as small as possible.

Surface tension would tend to collapse alveoli if surfactant was not present due to Law of Laplace.

Law of Laplace

Relationship between surface tension of a sphere and resultant pressure:

P=4T/r, where P=pressure, T=surface tension, and r=radius

Surface tension is low at small lung volumes due to production of surfactant by type 2 pneumocytes.

Two bubbles connected (same surface tension), the smaller with higher pressure will blow up the larger with lower pressure, so smaller bubble will collapse – stopped by surfactant

Surfactant

Roles

Increased compliance and reduced work of breathing

Increased alveolar stability – prevents collapse, reduces surface tension

Keeps alveoli dry (opposes transudation of fluid into alveoli)

Mechanism: bipolar molecules oppose normal increasing attacting forces as molecules get closer in a small surface – ends of surfactant molecules repel each other and oppose collapse

Composition:

Dipalmitoylphosphatidylcholine 62%
Phosphatidylglycine 5%
Other phospholipids 10%
Neutral lipids 13%
Proteins 8%
Carbohydrate 2%

Surface tension inversely proportional to conc of surfactant – as alveoli enlarge during insp, conc falls, surface tension increases.

<u>Oxygen Transport from Air to Tissue aka Oxygen Cascade</u>

Purpose O2 - work at mitochondrial level via cytochrome oxidase - enzyme electron transfer chain, produce ATP

PO2 is 20.93%

So if barometric P is 760mmHg (minus 47mmHg which is saturated vapour pressure of water)

Then PAO2 is 20.93/100 x 713 = 149mmHg

But PaO2 is only 100mmHg as it is continuously removed from alveolar gas

The PO2 in mitochondria is vey low and is susceptible to hypoxia

Hypoxia can be secondary to

- Hypoventilation
- Diffusion limitation
- Shunt
- Ventilation perfusion mismatch

Alveolar ventilation (A) = volume of air entering and leaving alveoli per minute. Air ventilating anatomic dead space (VD), where no gas exchange occurs, is not included

So VT = VD + VA (V = volume, T,D,A = tidal, dead and alveolar)

- If you add respiratory frequency you get volume per unit time
- V with a small dot above (can not do with word)
- VA = VE – VD

Alveolar ventilation is increased by increasing tidal volume +/or respiratory rate

To measure alveolar ventilation. Measure CO2 in expired gas (Remember there is no exchange of CO2 in dead space)

$$\dot{V}_A = \frac{\dot{V}_{CO_2}}{P_{CO_2}} \times K$$

If alveolar ventilation is halved then CO2 is doubled

Reaction rate with Hb

- Another factor that contributes to transfer of oxygen from alveolus to rbc is reaction of Hb and oxygen
- This reaction is given by θ x Vc
  - θ rate in ml per minute of O2 that combines with 1ml of blood per mmHg partial pressure of O2
  - Vc volume of capillary blood
- So the factors that influence the uptake are the diffusing capacity of the membrane and the above reaction.
- (Ohms law- Flow (current)=Pressure difference (potential difference)

  Resistance
- So to calculate the resistance to O2 transfer you add resistances which requires them to be inverse, so
- DL=diffusing capacity
- DM=membrane diffusing capacity
- θVC=O2-Hb reaction rate

$$\frac{1}{D_L} = \frac{1}{D_M} + \frac{1}{\theta \cdot V_c}$$

Ventilation-perfusion ratio

Blood flow is also greatest at the base and the relative change from apex to base is greater than ventilation, so Ventilation/perfusion ratio is low at the base and high at the apex.

Impedes exchange of O2 and CO2

Hypoxia cannot be corrected by increased ventilation

Hypercapnia can be corrected by increased ventilation

The O2 dissociation curve is S shaped which means that increased ventilation to units with high V/Q ratios cannot compensate for the shunt causes by low V/Q ratios

The CO2 dissociation curce is more linear so that increasing ventilation will blow off CO2 from the lung units with both high and low V/Q ratios

In clinical practice determine effect of V/Q mismatch on oxygenation by using the A-a gradient

PAO2-PaO2

Oxygen transport from air to tissues

pO2 of inspired air = 150mmHg

pO2 of alveolar air = 100mmHg (due to alveolar replenishment and removal into capillaries)

Causes of hypoxaemia

Hypoventilation

Incomplete diffusion

Shunt

Ventilation/perfusion mismatch

pO2 and pCO2 determined by ratio of ventilation to blood flow.

Ventilation perfusion ratio reduces from apex to base due to regional differences in ventilation and blood flow.

pO2 changes by over 40mmHg from apex to base (132 at apex, 89 at base)

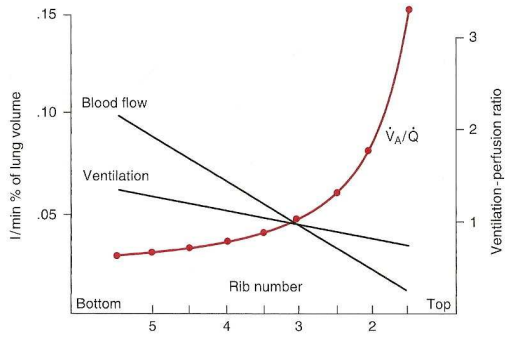
pCO2 changes by 14mmHg from apex to base (28 at apex, 42 at base)

These difference result in alveolar-arterial oxygen difference because the best perfused region of the lung is the most poorly oxygenated therefore overall pO2 will never reach alveolar pO2.

In lung unit with normal V/Q ratio the PO2 = 100 and the PCO2 = 40mmHg

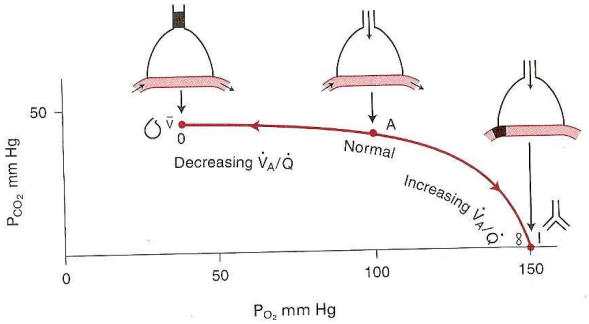
In lung unit with no ventilation the V/Q ratio is 0 with a PO2 = 40 and PCO2 = 45 i.e. mixed venous gas

In lung unit with no perfusion, V/Q ratio is ∞ with a PO2 =150 and PCO2 = 0 mmHg i.e. inspired gas



$$\frac{\dot{V}_A}{\dot{Q}} = 8.63 \cdot R \cdot \frac{(Ca_{O_2} - C\bar{v}_{O_2})}{PA_{CO_2}}$$

What effect does V/Q have on PO2 and PCO2?



PO2

- V/Q mismatch will cause a large difference between alveolar gas and arterial blood as
  - High V/Q areas will have a PO2 between inspired gas (150) and ideal alveolar gas (100), but
    - There are few of these areas and the flow is too low to contribute to actual PaO2
  - Low V/Q areas have a PO2 between ideal alveolar gas (100) and mixed venous (40)
    - These areas have a relatively high flow and so contribute more
    - Shape O2 dissoc curve means low PO2 in low V/Q units dramatically decr O2 content

PCO2

- V/Q mismatch causes a small difference between alveolar gas and arterial blood as
  - as above, but low V/Q PCO2 diff between alveolar gas (40)/mixed venous blood (45) small

<u>Diffusion</u>

Volumes

End expiratory volume **-** 2200ml **-** Volume of gas present in alveoli at end of expiration

Alveolar volume **-** 350ml **-** Alveolar volume small proportion FRC therefore O2 and CO2 content alveoli constant

Follow Ficks law of diffusion

Gas flow α A/T x D x (P1 – P2)

- A= area, T= thickness, D= diffusion constant, P= pressure
- D α solubility / square root of molecular weight

Diffusion proportional to tissue area and conc gradient of gas, and inversely proportional to tissue thickness x R

R = diffusion constant (relates to gas and tissue solubility)

Gases diffuse across alveolocapillary membrane

Composed of

Pulmonary epithelium; Capillary endothelium; Fused basement membranes.

Blood in pulmonary capillary has 0.75s for gas exchange

Ability to reach partial pressure equilibrium depends on reaction with substances in the blood

If no reaction in blood then gas dissolves only in plasma – rapid equilibrium, so gas uptake limited by perfusion

- Diffusion limited gas uptake

Equilibrium not achieved and is not limited by flow of blood.

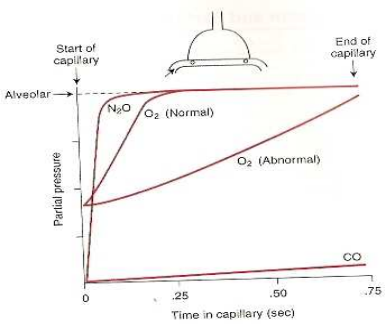
Carbon monoxide rapidly crosses capillary membrane, taken up by Hb therefore partial pressure in plasma remains low and no opportunity to equilibrate

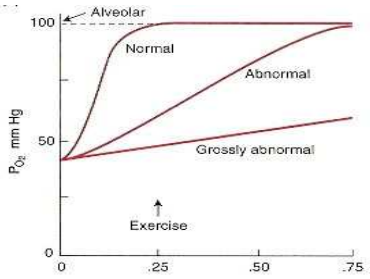
Such great affinity that PCO in capillary falls rapidly – slow equilibrium, diffusion limited

Uptake of carbon dioxide also diffusion limited.

- Perfusion/flow limited gas uptake
  Nitrous oxide reaches equilibrium in 0.1s (less than 0.75s it takes for blood to traverse pulmonary capillaries)
  As it crosses capillary membrane, there is no binding with Hb so partial pressure rises rapidly
  Rate for diffusion determined by blood flow and independent of diffusion properties.

- Oxygen is between the two but perfusion limited
  - Normal PO2 as blood enters capillary is 40 mmHg with alveolar PO2 of 100 mmHg.
  - Diffusion of oxygen is generally complete by the time the red cell has passed one third along the capillary
  - Uptake of oxygen also involves reaction of oxygen with haemoglobin but this is extremely rapid (0.3s)
  - Diffusion of carbon dioxide is 20 times faster as it is 20 times more soluble than oxygen
  - During heavy exercise reduced time for combination with Hb (0.25s), possible reduced O2Hb saturation
  - At altitude less O2 partial pressure in atmosphere so takes longer
    - Also, at lower PO2, steep slope of O2 dissociation curve means uptake slower





Diffusing capacity of the lung

Diffusing capacity of a gas is proportional to surface area of alveolocapillary membrane, a diffusion constant and the difference in partial pressure and inversely proportional to its thickness – **diffusing capacity** is A/T x D
Carbon monoxide used
Normal value 25ml/min/mmHg
Hence $DL_{CO} \quad \frac{\dot{V}_{CO}}{P_{ACO}}$
Diffusing capacity of CO = amount of CO entering blood/partial pressure CO in alveoli
Diffusing capacity limited by
Increased membrane thickness - Fibrosis
Decreased membrane surface area - Emphysema
Decreased partial pressure difference across membrane
Anaemia; pulmonary hypertension; interstitial lung disease
pO2 of blood entering the capillary is normally about 40mmHg.
pO2 of alveolar air is normally about 100mmHg.
Oxygen diffuses down its partial pressure gradient to reach 97mmHg by time it is 1/3 way down capillary.
This drops to 95mmHg in the aorta due to shunt.
In severe exercise the whole capillary length is required.

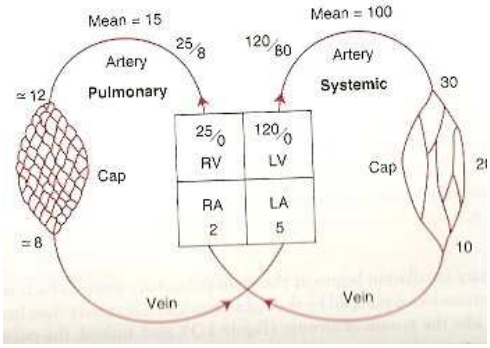
Other important factors in diffusion

Diffusion from alveolar wall to haemoglobin
Reaction rate with haemoglobin (0.01s)

Pulmonary Circulation

Pressure around pulmonary vessels
Pulmonary capillaries are surrounded by gas so alveolar pressure can affect their calibre
- Pressure across capillary = transmural pressure

Pulmonary arteries and veins
- As lung expands are pulled open; Alveolar pressure has no effect so called extra alveolar vessels.



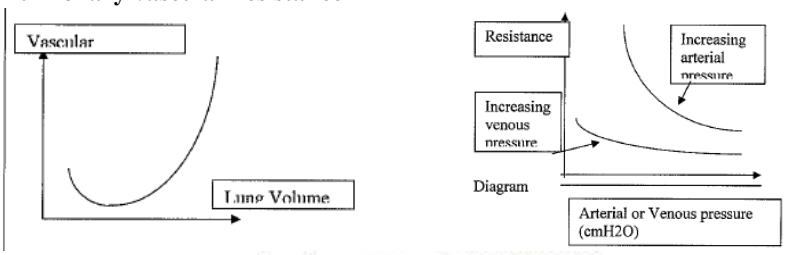
Pulmonary blood pressure

Arterial pressure low - Pressure = 24/9, mean pressure 15mmHg.
Flow is pulsatile
Volume of blood in pulmonary vessels is 1000ml, 100ml of which is in the capillaries.
Lung is obliged to accept whole blood volume.
Entire circulation passes from left ventricle to right atrium and right ventricle with 2 exceptions:
- Anastomoses between bronchial capillaries and pulmonary capillaries and veins - bypassing rt ventricle.
- Blood flow direct from coronary arteries to chambers of the left side of the heart.

Pulmonary blood vessels

Pulmonary artery 30% as thick as the wall of the aorta.
Smaller arteries have very little smooth muscle.
Some post capillary vessels have some smooth muscle.
Pulmonary capillary networks are large with multiple anastomoses

Pulmonary vascular resistance



$$\text{Vascular resistance} = \frac{\text{input pressure} - \text{output pressure}}{\text{blood flow}}$$

So R = 1.7mmHg/liter/min ~ 100 dyne/s

Pulmonary vasculature has one tenth the resistance of the systemic circulation (low resistance system)
- Pressure just enough to reach apex only standing (dependent lung may collapse)

Resistance falls as blood pressure (both pulm art and pulm venous) rises due to
- **Recruitment** of capillaries (with rises in pressure at low levels)
- **Distension** of capillaries (with rises in pressure at higher levels)

Then rises at very large lung volumes (capillaries resistant to stretch)
- A collapsed lung has a high PVR

At very low lung volumes (eg lung collapse), pressure needed to re-expand = CRITICAL OPENING PRESSURE to enable any flow
At very high volumes, when alveolar pressure > pulmonary capillary pressure, PVR increase (vessels squashed)

Measurement of pulmonary blood flow

Fick principle
- '*Oxygen consumption per minute is equal to the amount of oxygen taken up by the lungs'*
- Q = flow of blood/minute
- VO_2 = O_2 consumption, equal to amount O_2 taken up by blood/minute
- CVO_2 and CaO_2 are the O_2 concentrations in blood entering and leaving the lung

$$\dot{V}_{O_2} = \dot{Q}\,(Ca_{O_2} - C\bar{v}_{O_2})$$

or

$$\dot{Q} = \frac{\dot{V}_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}}$$

Flow equals amount O2 taken up by lung divided by arterial minus venous partial pressure of O2
Or can be measured by indicator dilution using dye or temperature

Regulation of pulmonary blood flow/PVR

Passive factors

Obligatory receipt of cardiac output (arterial pressure > venous pressure)
Recruitment and distension
Gravity and its effect on regional blood flow/positional change

Active factors

Hypoxic pulmonary vasoconstriction

Contraction of smooth muscle in arteriole walls in response to alveolar hypoxia.
Blood is then shunted away from the area of hypoxia.
Marked vasoconstriction occurs below 70mmHg.
Hypoxia results in opening of smooth muscle potassium channels, causing a potassium efflux and depolarization of the cell to cause contraction.
Very important mechanism for newborn infant

Other local factors

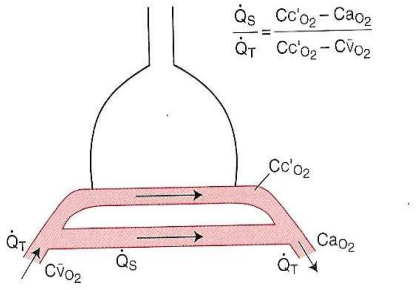
Lung volume (J shaped curve)
Chemical factors - Carbon dioxide, Potassium, Lactate, Histamine
Substances released by endothelium - Nitric oxide
Systemic regulation by hormones – affect vascular smooth muscle tone
Vasoconstrictors - Adr/NA, Angiotensin II, Vasopressin/ADH, Endothelins
Vasodilators - Kinins, Serotonin, Histamine, Prostaglandins, TXA2, ANP
Systemic regulation by the nervous system

Shunt

When alveoli are perfused, but not ventilation - ventilation/perfusion ratio is zero
Shunt is blood that enters the arterial side of the circulation without being oxygenated
Hence mixed venous blood enters arterial side and this drops the PO2 as predicted by the shunt equation

- small degree of shunt is normal and may be described as 'physiological shunt'
  - PAO2 > PaO2 in healthy person.
  - Reasons:
    - Atelectasis
    - Bronchial arterial blood flows to pulmonary veins without being oxygenated
    - Coronary artery blood flows to coronary veins then thebesian veins in left ventricle
    - With aging shunt increase because harder for O2 to diffuse from alveolus to capillary

NB shunt can NOT be reversed with O2



Distribution of blood flow

Blood flow increases from top to bottom of lung
Normal conditions flow almost ceases at apex - pulm artery pressure only just sufficient to maintain perfusion

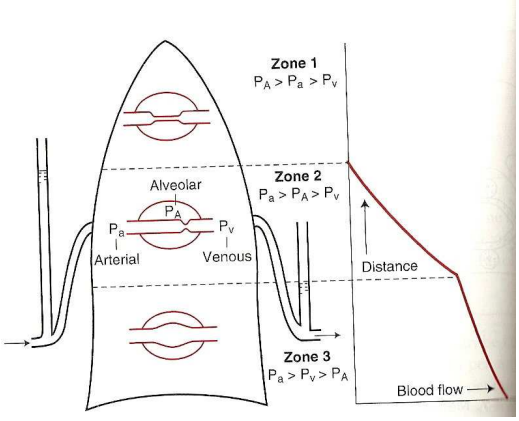
Factors influencing distribution of pulmonary blood flow:

1. GRAVITY

Due to hydrostatic pressure

With mild exercise, difference decreases

- 3 zones explained by hydrostatic P +/- zone 4 (only at very low lung volumes)
  - Lung 30cm tall, so pressure difference between top and bottom is 23mmHg
- Gives rise to West's zones
- Slow increase in ventilation from top to bottom but not as much as perfusion. Highest V/Q at apex
- When supine distribution changes – blood flow from apex to base almost uniform but flow in posterior segments exceeds anterior segments



Zone 1(apical) not present in normal conditions = alveolar dead space – pulm P so low that alveolar P squashes capillaries

Therefore ventilated but not perfused

PA>Pa>Pv

Zone 2 (middle) recruitment – capillaries collapse at venous end, called a "Starling resistor" – intermittent flow, mainly systole; usually 7-10cm above heart to apices

Pa>PA>Pv

Zone 3 (basal) distension + recruitment – blood flow determined by arterial-venous difference

Blood falls into pulm veins and alveolar pressure lower than all parts of vasculature - **waterfall effect**

Pa>Pv>PA

Zone 4 – only at low lung volumes; blood flow decreases because lung poorly ventilated and squashed

Zones 1-3 due to capillaries, zone 4 due to extra-alveolar vessels (which tighten at low volumes)

2. ALVEOLAR HYPOXIA

Hypoxic pulmonary vasoconstriction

- Alveolar PO2 not arterial important
- Affects smooth muscle of small arterioles
- Effect starts at 70mmHg PAO2 and is non linear
- Mechanism unknown: Nitric oxide, Endothelin, Thromboxane

Causes blood to divert from non ventilated lung

3. VASCULAR RESISTANCE

Pulmonary HTN/PE

4. PULMONARY DISEASE

Asthma, COPD, infection, infarction, cancer, fibrosis, PTX, chest trauma

5. VASOACTIVE SUBSTANCES

NO, endothelin, prostaglandins/TXA2

6. ACIDOSIS

pH drop causes vasoconstriction

7. SYMPATHETIC STIMULATION

Causes stiff pulmonary arteries – vasoconstriction

Extra-pulmonary factors influencing pulmonary blood flow

- Blood volume
- Cardiac output
- Atmospheric pressure
- Temperature
- Pathology (anaemia, cancer, infection)
- Exercise
- Posture

Other functions of the respiratory system

- **Blood reservoir -** Pulm blood volume incr by 400ml lying - volume discharged into general circulation standing
- **Blood filtering -** Removes small thrombi
- **Metabolic and endocrine functions**
  - Production of surfactant
  - Production and release into blood - Prostaglandins, Histamine, Kallikrein
  - Activated in the lungs (ACE is located in capillary endothelial cells) - Angiotensin I > angiotensin II
  - Partially removed/inactivated - Prostaglandins, Bradykinin, Adenine nucleotides, Serotonin, NA, Ach
- **Lung defense mechanisms**
  - **Temperature control of inspired air**
  - **Particle removal**
    - Hairs remove particles greater than 10 micrometres
    - Remaining particles settle on mucus membranes, particularly near the tonsils and adenoids
    - Particles 2-10 micrometres fall onto the walls of the bronchi as airflow slows and are then removed by ciliary action at a rate of 16mm/min
    - Particles less than 2 micrometres reach the alveoli and are ingested by macrophages
  - **IgA secretion**
  - **Nitric oxide production -** Epithelia of paranasal sinuses contain NO which is bacteriostatic.
  - **Pulmonary alveolar macrophages -** Ingest bacteria and small particles, help process inhaled antigens.