By Adam Hollingworth

5.Blood Flow & Other Functions

Table of Contents

Mixed Venous Blood

- =represents mixture of all systemic venous blood draining from all tissue capillary beds of the body (including myocardium)
- Comprised of VR from:
    - SVC
    - IVC
    - Myocardium - from coronary sinus
        ↳ myocardium has highest extraction ratio of O_2 (67%) ∴ coronary sinus blood has lowest O_2 content & ∴ PO_2)
- ∴ only place adequate mixing ∴ sampling = pulmonary artery (PA catheter or Swan Ganz)
    ↳ by convention 2.5cm into pulmonary artery
- Normal values:
    - PvO_2 = 40mmHg
    - $PvCO_2$ = 46mmHg
    - CvO_2 = 15mlO_2/100ml blood
    - $CvCO_2$ = 52mlCO_2/100ml
    - SvO_2 75%

Factors Affecting PvO_2 (or $PvCO_2$)

- Factors can effect PvO_2 or $PvCO_2$ as both in equation
- This will be according to Fick principle:

- Normal equation: *Q = flow; V = consumption*

$Q_{/min} = V_{/min} / (A\ content - V\ content)$

- Can rearrange:

$V = Q\,(A\ content - V\ content)$

- Then:

$V\ content = (A\ content - V) / Q$

- In this case:

$CvO_2 = (CaO_2 - VO_2) / Q$

- It is known that PvO_2 proportional to CvO_2 by virtue of oxy-Hb dissociation curve
- So a ↓PvO_2 may be due to:
    - ↓Cao2 ie via ↓Hb (or abnormal Hb), or ↓SpO_2
    - ↓CO (ie Q)
    - ↑VO_2 eg fever, hyperthyroid, MH, exercise, shivering

Another Way of Looking at It:

- Oxygen delivery (or flux) = CaO_2 x CO

∴ PvO_2 depends on balance between oxygen delivery and oxygen consumption

By Adam Hollingworth

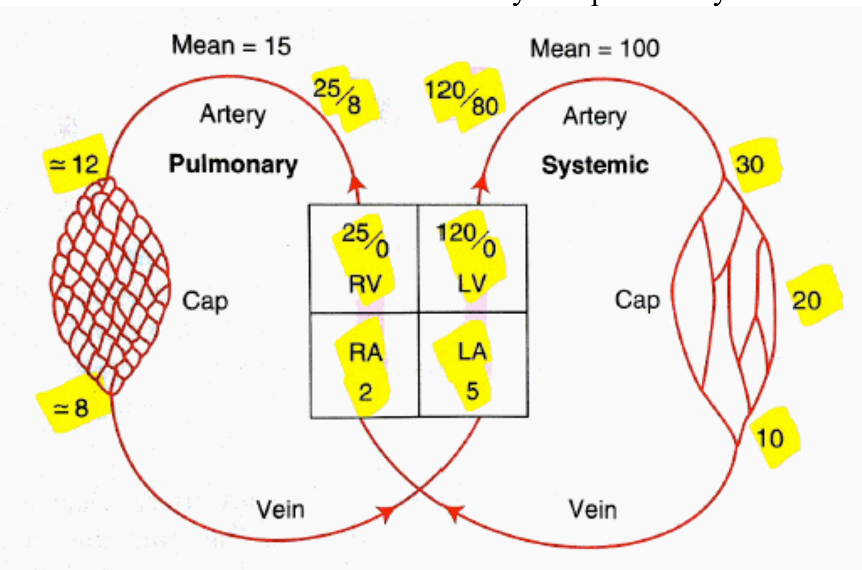
Anatomy

- Pulmonary arteries accompany airways branching as far as terminal bronchioles
- Then ⇒ capillary bed
- Pulmon veins
  - collect oxygenated blood
  - run between lobules
  - unite into 4 large veins into LA

Pressures in Pulmon Vessels

- entire CO from RV flows through the alveoli
- ∴ perfusion vastly exceeds nutritional demands of alveoli (VO2)
  - ↳ ∴ metabolic factors exert no influence on flow
    - ↳ ie no autoregulation either pressure or metabolic exists in pulmon circ

- metabolic needs of bronchi are met by independent systemic circulation (bronchial circulation)



$$Q_{pulm} = \frac{\Delta P}{PVR}$$

Where Q_{pulm} = RV cardiac output_ = ~ 5l/min or ~ 70ml/kg/min

- ΔP: contrast pressures inlet to outlet systems:
  - systemic (MAP – RA pressure): $90_{(aorta)} - 2_{(RA)}$ = 88mmHg
  - pulmonary (MAP – LA pressure): $15_{(pulmon\ art)} - 5_{(LA)}$ = 10mmHg
  - ↳ ∴ PVR must be very low compared to systemic circulation!
- ∴ low pressures in pulmon system mean little need for vasc smooth mm tone
  - ↳due to:
    - lung must accept all CO all the time
    - no concern over global organ regulation of control
    - less gravity to overcome than ULs/head
- sympathetic vasomotor nerves exist – but have no defined physiological role
- pulmonary capillary pressures:
  - uncertain
  - pressures through pulmon system more linear than systemic system
  - varies considerably through lung due to hydrostatic pressures

Pressures Around Pulmon Blood Vessels

Capillaries

- pulmon capillaries are entirely surrounded by gas
- little or no support to capillary wall ∴ liable to collapse
- alveolar pressure ~ atmospheric pressures
  ↳esp when breathing, glottis open
- effective pressure around capillary = alveolar pressure
  ↳∴ when ↑alveolar pressure > pressure inside cap ⇒ collapse
  ↳this difference = transmural pressure

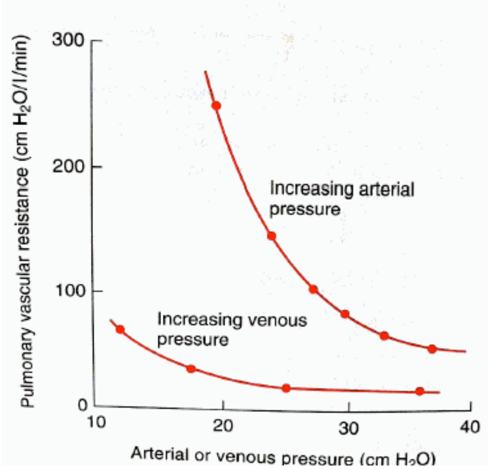
Arteries & Veins

- pressure around large vessels can be much lower than alveolar pressure
  - lung expands ⇒ pulls vessels open by radial traction of lung parenchyma that surrounds them
  - ∴ effective pressure low
- ∴ classified into
  - alveolar vessels:
    - calibre determined by pressure within them & alveolar pressure
  - extra alveolar vessels
    - all art & vein in lung parenchyma
    - calibre greatly affected by lung volume

Pulmon Vasc Resistance

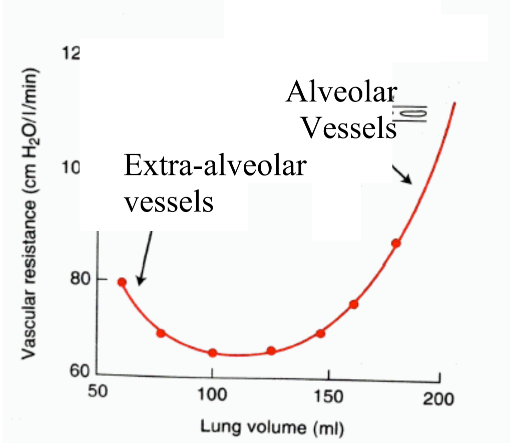
- vascular resistance = $\frac{\text{input pressure - output pressure}}{\text{blood flow}}$
- Mean pulmon artery pressure (MPAP) = 15mmHg
- Pulmon arteries & arterioles are shorter & thin walled compared to systemic system
- systemic vs pulmon pressures = x8
- as blood flow same ∴ resistance must be x8 in systemic system
- pulmon vasc resistance =
  - (15-5)/6
  - = 1.7mmHg/L/min
- systemic =
  - (100-2)/6 = 16.3mmHg/L/min
- PVR made up from:
  - Arterial vessels ~30%
  - Microvascular (arterioles to venules) ~ 50%
  - Veins ~ 20%
- More even spread of PVR ⇒ pulsatile flow through pulmon circ
- Capillary pressure = 8-10mmHg
  ↳ ~ halfway between MPAP & LAP
- ↑LAP to 20-25mmHg ⇒ big enough ↑capillary pressure ⇒ pulmon oedema
- benefit of low PVR is that with any ↑CO see ↓ed relative ↑pulmon vasc pressure
- PVR is lowest at FRC

- pulmon vasc resistance can become even smaller as pressure within it rises:
  ↳2 processes:
  - recruitment:
    - ↑pressure ⇒ ↑flow or opening of shut down vessels ⇒ ↓resistance
    - chief mechanism in ↓pressure in pulmon artery at low starting pressures
  - distension:
    - in higher starting pressures
    - = change in shape from nearly flat to more circular
      ↳strong evidence cap wall resists stretching
  ↳can both occur together also



- lung volume also effects pulmon resistance:
  - extra-alveolar vessels – large lung volume ⇒↓ resistance
    - high volume lung pulls vessels open
    - @low volume – smooth mm ⇒ ↑resistance
    - lung collapsed – critical opening pressure not reached

  - alveolar vessels – large lung volume ⇒ ↑vasc resistance
    - depends on transmural pressure ie alveolar : vasc pressure
      - during large insp: ↓vasc pressure ⇒ ↑transmural pressure ⇒ squash vessel
    - also see stretching & thinning of alveolar walls ⇒ direct affect on calibre of capillaries
- Drugs that affect smooth mm will effect pulmon resistance:
  - VCs ⇒ ↑resistance = serotonin, histamine, NA
    ↳esp good when lung volume is low
  - VDs eg Ach



Measurement of Pulmon Blood Flow

- Use Fick principle:

$$\text{Blood flow/min} = \frac{\text{O2 consumption/min}}{\text{Conc of O2 in pulmon artery} - \text{Conc O2 in pulmon vein}}$$

- O2 consumption measured with spirometer.
- Direct vein & arterial sampling with catheters

Pulmonary vs Systemic Circulation

Blood Volume

- Erect: 15% circulating volume = central:
  - Pulmonary Circ (Lungs) ~500ml:
    - *3% is in the **pulmonary** capillaries*
  - Heart ~250ml
- Supine: ↑to ~25% of circulating volume = central

Anatomical

- Pulmon circulation:
  - Dual circulation – pulmon arteries & bronchial arteries
  - ~30cm short
  - thin walled vessels – large pulmon arteries only 30% of aorta wall thickness
  - pulmon post capillary venules contain smooth mm (systemic do not)

Functional Differences
- pulmon =
  - gas exchange
  - metabolic functions – is exposed to whole of CO
- systemic = delivery of O2 & nutrients to tissues

Vascular Resistance
- PVR =
  - 1/10th systemic
  - Minimal at FRC
  - Evenly distributed along whole circulation ∴ flow pulsatile throughout
    ↳systemic max at arterioles ∴ non pulsatile distal to arterioles
  - Opposite stimuli for VC/VD compared to systemic:
    - ↑VC: hypoxia, hypercarbia, acidaemia

Pressures (P pressure: S pressure)
- systolic= 25:120
- diastolic 8:80
- mean = 15:90
- Perfusion pressure:
  - Pulm: 25-5 = 10mmHg
  - Systemic: 90-2 = 88mmHg

Vascular Tone
- Systemic circulation:
  - ↑ed resting vasomotor tone
  - ↑ed response to endogenous & exogenous stimuli
    ↳ ∴ with ↑ed tone blood volume shifts from periph to central

Gravity
- erect ⇒ supine: shift volume centrally
- vertical pressure gradient in pulmon vessels in combo with effect of alveolar pressure = Starling resistor

Filtration
- pulmon circ good at filtering:
  - clots
  - air
  - debris
  ↳ preventing systemic emobolisation

hypxic pulmonary vasoconstriction
see later

metabolic functions
see later

Passive Distribution of Blood Flow

- Upright/supine lung – blood flow ↓s in linear fashion from dependant to nondependent (bottom to top)
- During exercise ↓ in regional differences
- Explained by hydrostatic pressures:
  - Pulmon system = Low pressure
  - Vertical Column of blood exerts 23mmHg difference from top to bottom 2nd to gravity
  - Alveolar vessels are exposed to gravity AND alveolar pressure
    ↳ = a 'starling resistor'
    ↳ defines 'pressure heads' which prevent flow
  - Lung split into zones
    - Zone 1 – top region ($P_A > P_a > P_v$)
      - Pulmon art pressure falls close/below atmospheric ⇒ little/no flow

- Only occurs under pathological conditions eg
  - ↓art pressure eg haemorrhage OR
  - ↑alveolar pressure eg positive pressure vent
- ventilated but unperfused lung ∴ physiologic (alveolar) dead space

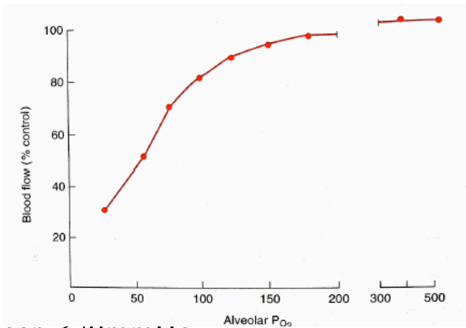
▪ Zone 2 – middle section ($P_a > P_A > P_v$) (driving pressure = Pa-P_A)
- Pulmon art pressure > alveolar pressure
- Venous pressure still < alveolar pressure
- ∴ blood flow is determined by arterial:alveolar pressures
  ↳NOT a-v difference as in systemic situation
  ↳venous pressure only influence if > alveolar pressure
- just below zone 1
- capillary recruitment occurs as move down zone

▪ zone 3: bottom section ($P_a > P_v > P_A$) (driving pressure = Pa – Pv)
- venous pressure > alveolar pressure ∴ flow determined in usual way
- blood flow determined by distension of capillaries
  ↳pressure within ↑s as go downwards
  ↳alveolar pressure constant ∴ ↑ing transmural pressure
- distension & recruitment ⇒ ↓s resistance to flow ($Q = \Delta P/R$)
  ↳zone where should measure PAWPs form

▪ (zone 4)
- @ low lung volume – resistance of extraalveolar vessels becomes impt
- ↓in regional blood flow seen starting at base lung where parenchyma least expanded

NB zones 1-3 = alveolar vessles (pulmon capillaries) responsible for distribution of blood flow
Zone 4 = extra-alveolar vessels responsible

Other Causes of Uneven Blood Flow
- some regions intrinsically higher vasc resistance
- peripheral regions of lung receive less blood than central
- random arrangement of vessels & capillaries ⇒ inequalities of flow



Active Control of Circulation
- hypoxic pulmonary vasoconstriction
- contraction of smooth mm in arterioles in hypoxic region
- response to P_AO2
  ↳not PaO2 of pulmon artery
- also see response to PACO2 ⇒ vasodilation
- stimulus response curve non linear ie plateau above 100mmHg P_Ao2; steep < 70mmHg
- precise mechanism unknown but does not require neural control
- theory's :
  - perivascular tissue releases VC substance in response to hypoxia
  - inhibition of voltage K channels ⇒ ↑Ca [in] ⇒ smooth mm contraction
- NO does play a role:
  - eNOS (endothelial) ⇒ NO ⇒ GTP to cGMP ⇒ smooth mm relaxation
    ↳inhibitors of NOS ⇒ pulmonary VC
- endothelin 1 (ET-1) & thromboxane A2:
  - released by endothelium
  - potent VCs
  - blockers of ET-1 receptor can Rx pulmon HTN
- hypoxic VC ⇒ directs blood away from hypoxic lung segments⇒decreases V/Q mismatch

↳ impt in thoracic surgery to divert blood away from collapsed lung ⇒ better V/Q match than would expect

- chronic hypoxia (eg COPD) ⇒ ↑PVR ⇒ cor pulmonale
- @high altitidue see generalised pulmon VC ⇒ ↑pulmon art pressure
- @birth:
  - fetal life –
    - pulmon VC very high partly due to hypoxic VC
    - only 15% CO through lungs
  - 1st breath oxygenates alveoli ⇒ dramatic ↓vasc resistance 2nd to VD of smooth mm
- other active processes on pulon resistance:
  - low pH ⇒ VC esp if hypoxia also present
  - autonomic ns – ↑symp output ⇒ VC

Water Balance in the Lung

- must keep alveoli free of fluid
- fluid exchange across endothelium obey's Starlings Law

net fluid out = $(Pc - Pi) - o(\pi c - \pi i) \times k$

Pc = capillary hydrostatic pressure
Pi = interstitial pressure
O = reflection coefficient ie effectiveness of capillary in preventing proteins across it
πc (~28mmHg)= osmotic force of blood
πi = osmotic force of interstitium

- Values unknown but likely net Starling flow is outward ~10-20ml/hr into lymph
- Fluid which leaks out into interstitium of alveolar wall tracks to
  - perivascular & peribronchial space = low pressure areas sucking fluid into them
  - ⇒ hilar lymph nodes
- Pulmon oedema = engorgement of these spaces
  ↳aka interstitial oedema
- If pulmon oedema persists ⇒ alveolar oedema
  - fluid cross alveolar epithelium into alveolar space
  - no gas exchange possible
  - alveoli fill one by one
  - ?exact cause of fluid into space. Perhaps =
    - interstitial route drainage exceeded ⇒ ↑ed pressure to threshold
  ↳∴ alveolar oedema more serious than interstitial oedema
- ∴ Mechanism to prevent pulmonary oedema:
  - lymph:
    - interstitial fluid movement towards hilum
    - interstitial pressure more –ve towards hilum ∴ gradient for flow
    - lymphatic flow promoted by rhythmic external compression occurring in respiration
      ↳ (& presence of valves in central lymph)
  - ↓ interstitial oncotic pressure
    - 2 mechanisms:
      - when filtration ↑s the NET albumin loss across membrane in filtrate ↓s
      - ↑lymph flow to wash albumin out of interstitium
    - = oncotic buffering mechanism
    - it will fail if capillary is damaged
  - high interstitial compliance:
    - large volume of fluid can accumulate in interstitium without much ↑pressure

        - until threshold where interstitium full ⇒ sharp ↑P ⇒ alveolar flooding
    - surfactant:
        - opposes movement of water from pulmon interstitium into alveolar spaces
        - 2 forces which encourage transudation of fluid into alveoli:
            - surface tension causes pressure within alveolar lining fluid < alveolar pressure
            - pulmon cap pressure (in most of lung) > alveolar pressure
        - surfactant ↓s surface tension!
    - Active removal:
        - fluid in alveolar space actively pumped out by NaK ATPase in epithelial cells
- mechanisms quite effective at preventing at counteracting ↑ing pulmon cap hydrostatic pressures
    ↳ P_c can ↑x3 before alveolar flooding
- Rate of lymph flow from lung ↑s if capillary pressure is high over long period

Non-Respiratory Functions of Lungs

- Blood reservoir
    - ~ 450mls
    - Can ↑ with larger pulmonary artery pressure
    - This volume can be mobilised to ↑LVEDV (LV preload) with:
        - IPPV
        - PEEP
        - Straining
        - Valsalva eg (↓to 250ml)
- Any ↑in lung blood volume ⟹ ↓lung compliance

[central blood volume (800ml) = volume of:
- Blood in heart (350ml)
- Blood in lungs (450ml)]

- Filter blood –
    - small thrombi removed before reach vital organs eg brain
    - wbc's trapped ?why
    - Also particles/fat emoblism

Metabolic Functions of Lung

- lung only organ apart from heart which receives all blood
- vascular ECs responsible for metabolic properties
- endothelium actively produces NO
- number of vasoactive substances metabolised in lung:

Substances Effected
- Angiotension I – converted to angiotensin II by ACE
- located in small pits in surface of capillary ECs
- Bradykinin – 80% inactivated by ACE
- Serotonin – 98% removed by uptake & storage
- NA - ~30% removed by uptake
- Leukotrines – almost completely removed
- Carbohydrate metabolism
- Proteases - removed

Substances not Effected
- Adrenaline –
- Angiotensin II
- Vasopressin (ADH)
- Histamine & dopamine not effected

AA metabolites

- membrane bound phospholipid AA by phospholipase A2
- lot of AA metabolism and release under certain circumstances:
    - lipoxygenase:
        - ↳ leukotrienes ⟹ airway constriction
    - COX pathway:
        - ↳ Prostagladins – potent VDs or VCs
            - PGE2 – helps relax ductus arteriosus in fetus

Other Roles

- Clotting mechanism:
    - Large no of mast cells containing heparin in intersitium
- Defense mechanism – lung secretes IgA in bronchila mucus, pulmonary macrophagues
- Synthetic functions:
    - Production of surfactant
    - Protein synthesis – collagen & elastin
- Heat regulation - esp upper resp tract
- Facilitate speech
- Pharmacologic:
    - Pharmacokinetic mainly ie
        - route of administration eg volatiles
        - Effect site - eg bronchodilators
        - Route of elimination eg volatiles & 1st pass uptake of fentanyl

Summary

- Capillaries are exposed to alveolar pressure; extra alveolar vessels have lower pressure
- Pulmon vasc resistance is low. It ↓s with ↑CO.
- Pulmon vasc resistance ↑s at low & high lung volumes
- Hypoxic pulmonary VC ↓s blood flow to poorly ventilated regions
    - ↳release of this at birth ⇒ ↑blood flow to lung in baby
- Many metabolic functions of lung – most impt angiotensin I ⇒ II by ACE