5. Blood Flow & Other Functions

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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:
  o SVC
  o IVC
  o Myocardium - from coronary sinus
    ↓ myocardium has highest extraction ratio of O2 (67%) ∴ coronary sinus blood has lowest O2 content & ∴ PO2

• ∴ only place adequate mixing ∴ sampling = pulmonary artery (PA catheter or Swan Ganz)
  ↓ by convention 2.5cm into pulmonary artery

• Normal values:
  o $P_{vO2} = 40mmHg$
  o $P_{vCO2} = 46mmHg$
  o $C_{vO2} = 15mlO2/100ml blood$
  o $C_{vCO2} = 52mlCO2/100ml$
  o $SvO2 75\%$

Factors Affecting $P_{vO2}$ (or $P_{vCO2}$)

• Factors can effect $P_{vO2}$ or $P_{vCO2}$ 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:

    $C_{vO2} = (CaO2 - VO2) / Q$

• It is known that $P_{vO2}$ proportional to $C_{vO2}$ by virtue of oxy-Hb dissociation curve

• So a ↓$P_{vO2}$ may be due to:
  o ↓$CaO2$ ie via ↓Hb (or abnormal Hb), or ↓SpO2
  o ↓CO (ie Q)
  o ↑VO2 eg fever, hyperthyroid, MH, exercise, shivering

Another Way of Looking at It:

• Oxygen delivery (or flux) = CaO2 x CO
  ∴ $P_{vO2}$ depends on balance between oxygen delivery and oxygen consumption
Anatomy

- Pulmonary arteries accompany airways branching as far as terminal bronchioles
- Then $\Rightarrow$ 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
- $\therefore$ perfusion vastly exceeds nutritional demands of alveoli (VO2)
  - $\Leftarrow$ metabolic factors exert no influence on flow
  - $\Leftarrow$ ie no autoregulation either pressure or metabolic exists in pulmon circ

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

\[ Q_{\text{pulm}} = \frac{\Delta P}{\bar{P}_{\text{V}}} \]

Where $Q_{\text{pulm}} = \text{RV cardiac output} = \sim 5 \text{l/min or } \sim 70 \text{ml/kg/min}$

- $\Delta P$: contrast pressures inlet to outlet systems:
  - systemic (MAP – RA pressure): $90_{\text{(aorta)}} - 2_{\text{(RA)}} = 88 \text{mmHg}$
  - pulmonary (MAP – LA pressure): $15_{\text{(pulmon art)}} - 5_{\text{(LA)}} = 10 \text{mmHg}$
  - $\Leftarrow$: PVR must be very low compared to systemic circulation!

- $\therefore$ 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 \(\therefore\) liable to collapse
- alveolar pressure \(\sim\) atmospheric pressures
  \(\leftarrow\) esp when breathing, glottis open
- effective pressure around capillary = alveolar pressure
  \(\leftarrow\): when \(\uparrow\)alveolar pressure > pressure inside cap \(\Rightarrow\) collapse
  \(\leftarrow\) this difference = transmural pressure

**Arteries & Veins**
- pressure around large vessels can be much lower than alveolar pressure
  - lung expands \(\Rightarrow\) pulls vessels open by radial traction of lung parenchyma that surrounds them
  - \(\therefore\) effective pressure low
- \(\therefore\) 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 = \(\frac{\text{input pressure} - \text{output pressure}}{\text{blood flow}}\)
- 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 \(\therefore\) resistance must be x8 in systemic system
- pulmon vasc resistance =
  - \(\frac{(15-5)}{6}\)
  - \(= 1.7\text{mmHg/L/min}\)
- systemic =
  - \(\frac{(100-2)}{6} = 16.3\text{mmHg/L/min}\)
- PVR made up from:
  - Arterial vessels \(~30\%\)
  - Microvascular (arterioles to venules) \(~50\%\)
  - Veins \(~20\%\)
- More even spread of PVR \(\Rightarrow\) pulsatile flow through pulmon circ
- Capillary pressure = 8-10mmHg
  \(\leftrightarrow\) halfway between MPAP & LAP
- \(\uparrow\)LAP to 20-25mmHg \(\Rightarrow\) big enough \(\uparrow\)capillary pressure \(\Rightarrow\) pulmon oedema
- benefit of low PVR is that with any \(\uparrow\)CO see \(\downarrow\)ed relative \(\uparrow\)pulmon vasc pressure
- PVR is lowest at FRC
Blood Flow & Other Functions

- Pulmonary vascular 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 pulmonary 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 affects pulmonary 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 ⇒ ↑ vascular resistance
      - Depends on transmural pressure ie alveolar : vascular pressure
        - During large inspirations: ↓ vascular pressure ⇒ ↑ transmural pressure ⇒ squash vessel
      - Also see stretching & thinning of alveolar walls ⇒ direct affect on calibre of capillaries
  - Drugs that affect smooth mm will affect pulmonary resistance:
    - VCs ⇒ ↑ resistance = serotonin, histamine, NA
      - Especially good when lung volume is low
    - VDs eg Ach

Measurement of Pulmonary Blood Flow

- Use Fick principle:
  - Blood flow/min = O2 consumption/min
    - Cone of O2 in pulmonary artery – Cone O2 in pulmonary 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

- Pulmonary circulation:
  - Dual circulation – pulmonary arteries & bronchial arteries
  - ~ 30cm short
  - Thin walled vessels – large pulmonary arteries only 30% of aorta wall thickness
  - Pulmonary post capillary venules contain smooth mm (systemic do not)
Functional Differences
• pulmon =
  o gas exchange
  o metabolic functions – is exposed to whole of CO
• systemic = delivery of O2 & nutrients to tissues

Vascular Resistance
• PVR =
  o 1/10th systemic
  o Minimal at FRC
  o Evenly distributed along whole circulation ∴ flow pulsatile throughout
    ↑systemic max at arterioles ∴ non pulsatile distal to arterioles
  o 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:
  o Pulm: 25-5 = 10mmHg
  o Systemic: 90-2 = 88mmHg

Vascular Tone
• Systemic circulation:
  o ↑ed resting vasomotor tone
  o ↑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:
  o clots
  o air
  o debris
    ← preventing systemic embolisation

hypoxic 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:
  o Pulmon system = Low pressure
  o Vertical Column of blood exerts 23mmHg difference from top to bottom 2nd to gravity
  o Alveolar vessels are exposed to gravity AND alveolar pressure
    ← = a ‘starling resistor’
    ← defines ‘pressure heads’ which prevent flow
  o 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 – P_v)
  - 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 = ΔP/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 vessels (pulmon capillaries) responsible for distribution of blood flow
Zone 4 = extra-alveolar vessels responsible

Other Causes of Uneven Blood Flow
  - some regions intrinsically higher vase 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 <10mmHg
  - 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
    - poten 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 altitudue 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 =  \((P_c – P_i) – o(\pi_c – \pi_i) x k\)

\[ P_c = \text{capillary hydrostatic pressure} \]
\[ P_i = \text{interstitial pressure} \]
\[ O = \text{reflection coefficient ie effectiveness of capillary in preventing proteins across it} \]
\[ \pi_c (~28\text{mmHg}) = \text{osmotic force of blood} \]
\[ \pi_i = \text{osmotic force of interstitium} \]

- 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
    - \(\therefore\) alveolar oedema more serious than interstitial oedema
- \(\therefore\) 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:
  o opposes movement of water from pulmon interstitium into alveolar spaces
  o 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
  o surfactant ↓s surface tension!

• Active removal:
  o 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
    ⇐ Pc 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
  o ~ 450mls
  o Can ↑ with larger pulmonary artery pressure
  o 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:
  o Blood in heart (350ml)
  o Blood in lungs (450ml)]

• Filter blood –
  o small thrombi removed before reach vital organs eg brain
  o wbc’s trapped ?why
  o Also particles/fat embolism

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
• Leukotrienes – 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:
  o lipoxygenase:
    ↓ leukotrienes \(\implies\) airway constriction
  o COX pathway:
    ↓ Prostagladins – potent VDs or VCs
    ▪ PGE2 – helps relax ductus arteriosus in fetus

Other Roles
• Clotting mechanism:
  o Large no of mast cells containing heparin in intersitium
• Defense mechanism – lung secretes IgA in bronchila mucus, pulmonary macrophagues
• Synthetic functions:
  o Production of surfactant
  o Protein synthesis – collagen & elastin
• Heat regulation - esp upper resp tract
• Facilitate speech
• Pharmacologic:
  o 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
  \(\leftarrow\) release of this at birth \(\Rightarrow\) ↑blood flow to lung in baby
• Many metabolic functions of lung – most impt angiotensin I \(\Rightarrow\) II by ACE