Pulmonary circulation

Ventilation/perfusion matching

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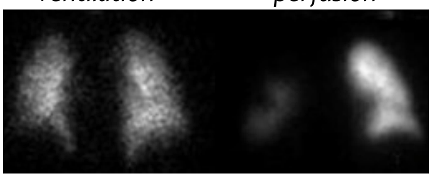
Determinants of lung gas transport

- Pulmonary ventilation
  - how O_2 and CO_2 reach the alveolocapillary membrane
  - what determines the amount of gas that is exchanged between the atmosphere and the alveoli
    - dead space (V_D)
    - functional residual capacity (FRC)
- Pulmonary diffusion
  - determines the passage of O_2 and CO_2 across the alveolocapillary membrane
- Pulmonary perfusion
  - how venous blood is led into lungs form periphery
  - how O_2 - rich blood with little CO_2 is led from lungs to periphery
- Lung ventilation/perfusion ratio



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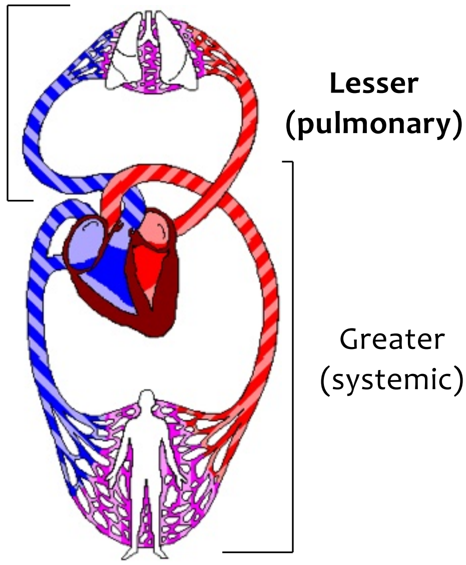
Specifics of the pulmonary circulation

- Function (O_2 into blood)
- ~ whole cardiac output
- Capillaries surrounded by air
  → no support against intravascular pressure
  → pressure has to be low
- High flow at low pressure
  → low vascular resistance



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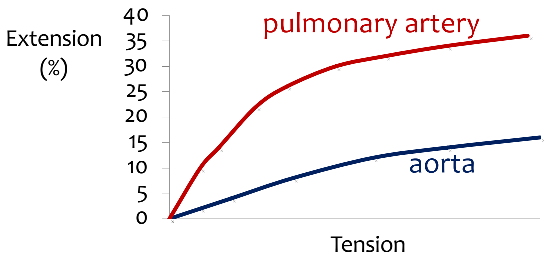
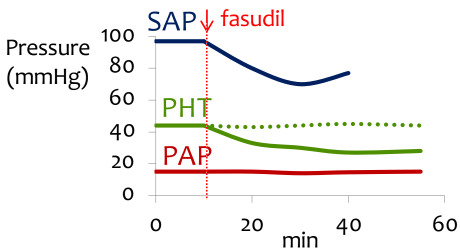
Pulmonary circulation: normally low resting vascular resistance

- Short vessels
  - Hagen–Poiseuille

    $R = 8L\eta / \pi r^4$

- Thin vascular wall (large compliance)
- Minimal resting tone





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Pressures in the pulmonary circulation

mmHg	Pulmonary	Systemic
arterial		
beginning of capillary		
end of capillary		
atrium		
driving pressure		
wedge		

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Methods

- Catheterization
  - ✓ pressures

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*André Frédéric **Cournand** (1895 - 1988)*
*Werner Theodor Otto **Forßmann** (1904-1979)*
*Dickinson Woodruff **Richards**, Jr. (1895-1973)*

Nobel prize 1956

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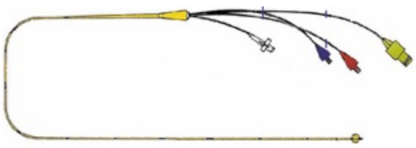
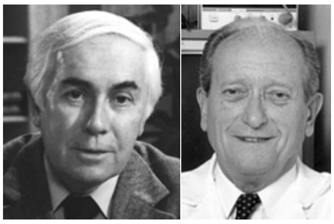
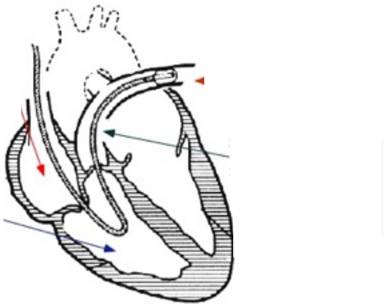
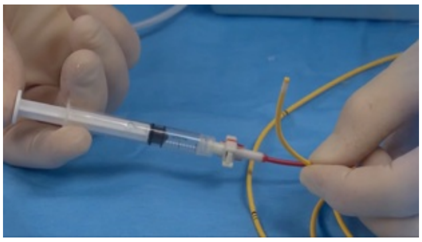


Methods

- Catheterization (Swan-Ganz)
  - ✓ pressures (incl. wedge)
  - ✓ cardiac output







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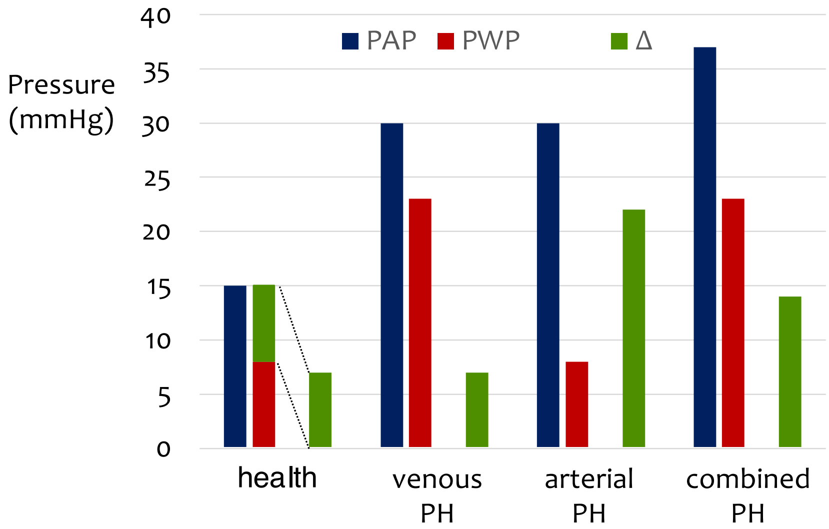
Pulmonary artery wedge pressure



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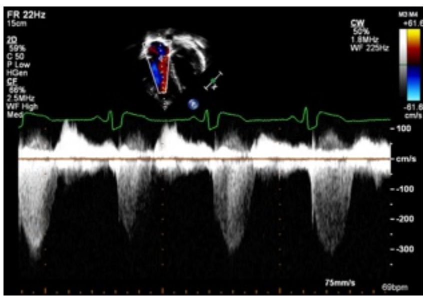
Methods

- Catheterization (Swan-Ganz)
  - pressures (incl. wedge)
  - cardiac output
  - exercise
  - vasodilatory test



- Echocardiography (Doppler)
  - max. tricuspid regurgitation velocity (TR_{max})
    - Bernoulli: $\Delta P = 4 \times TR_{max}^2$

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Bronchial circulation

- Systemic vascular bed
- Nutrition for airways and larger pulmonary vessels
- Some anastamoses into pulmonary veins: "physiological" shunt
  - cca 1% of cardiac output
  - lowers PaO_2 by ~2 mmHg, SaO_2 by ~0.5%
- Can partly replace pulmonary vessels in embolism

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Other functions of the pulmonary vascular bed

- Metabolic
  - ACE (1 & 2)
  - removal of BK, ET, 5-HT…
- Filtering emboli
  - PAP at rest ↑ only when >30% obstructed

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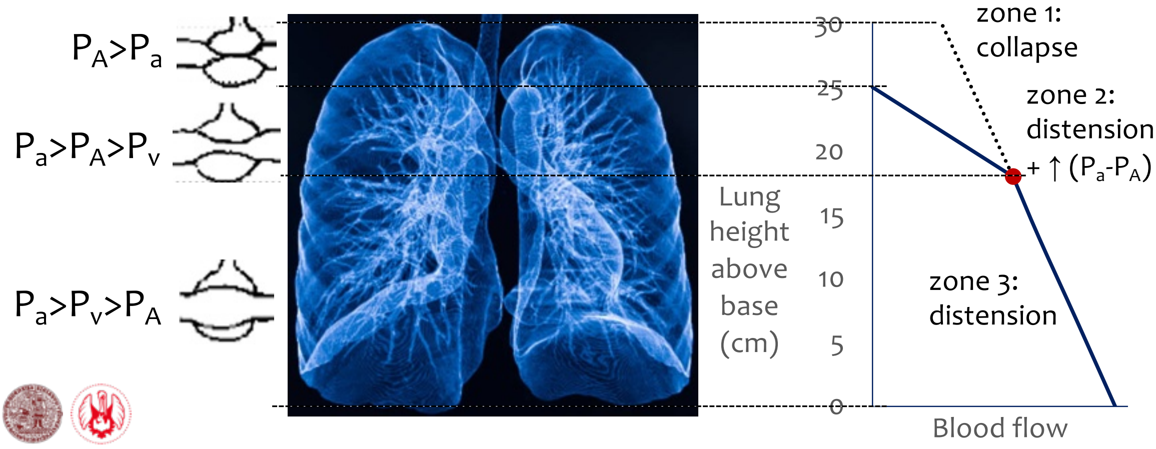
Gravity & lung blood flow



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Consequences of lung blood flow zones

- Small ↑ Pv does not have to ↑ Pa
  - At Pv > PA, Pa rises proportionately to Pv
- Lung edema starts at the bottom (highest pressures)
- **Positive pressure ventilation**: zone 3 reduced, zones 1 & 2 increase

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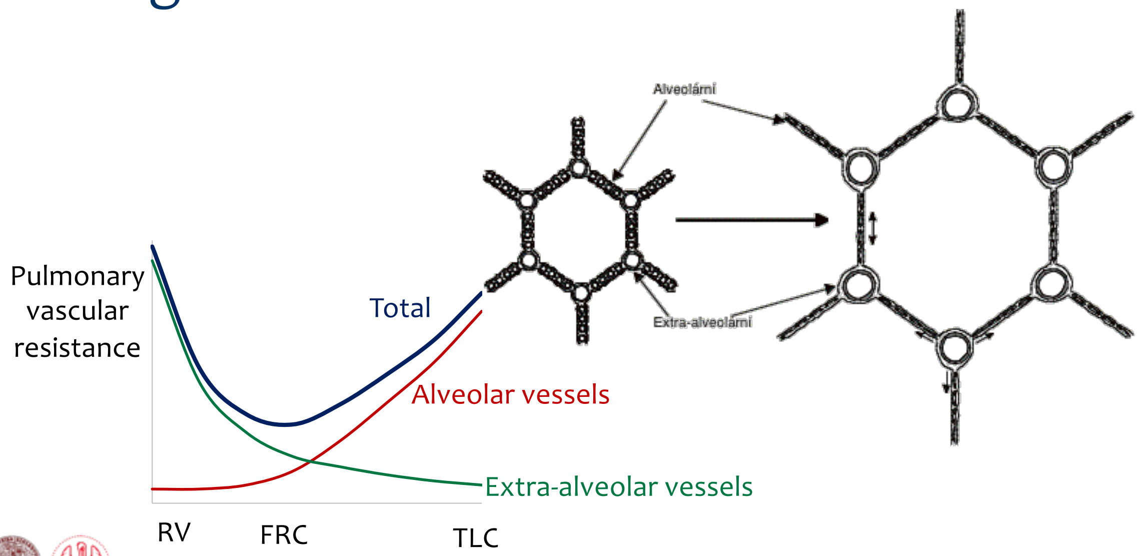
Lung volume & vascular resistance



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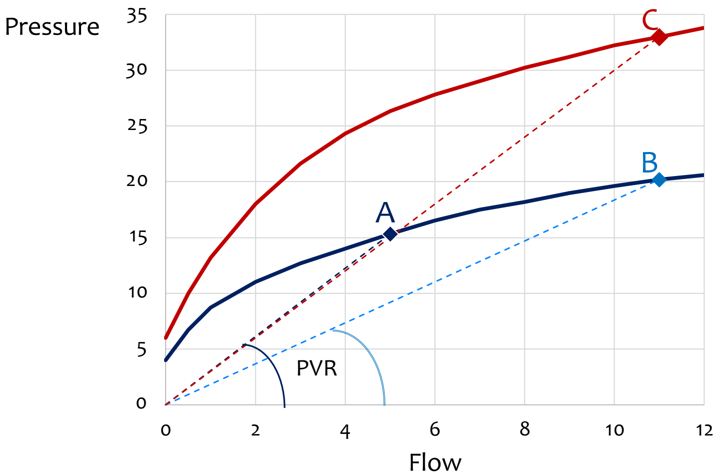
Pulmonary vascular resistance



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↑ cardiac output (e.g. exercise)

- ↓ PVR (mainly microcirculation):
  - distension
  - recruitment (zones, critical opening pressure)
- → only minimal ↑ pressure
  - saves heart work, prevents edema
  - extreme exercise: „stress failure“ of lung capillaries
  - RBC passage through lung capillary shortens from ~0.8 sec to ~0.3 sec

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Regulation of the pulmonary circulation

- Blood flow = cardiac output
- Minimal neural regulation
  - only ↑ venous return - SNS
- Humoral influences:
  - platelets, macrophages, endothelium,...
  - TxA_2, PGI_2, NO, ET, 5-HT,...
  - mainly pathology (pulmonary hypertension, edema, embolism,..)
- Local regulation
  - intra-organ flow distribution ($\dot{V}/\dot{Q}$ matching)

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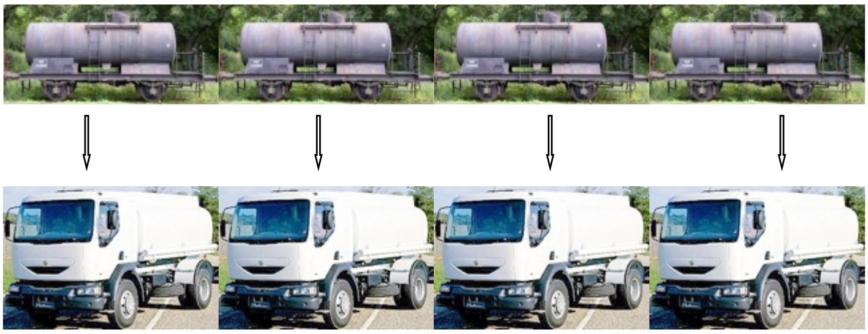
Ventilation/perfusion ratio ($\dot{V}/\dot{Q}$)



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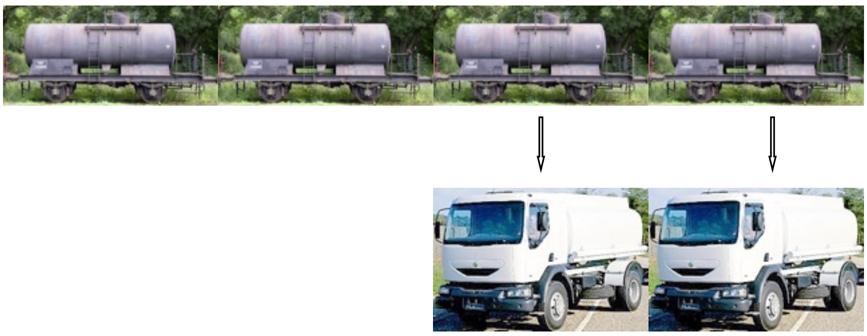
$\dot{V}/\dot{Q}$



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$\dot{V}/\dot{Q}$

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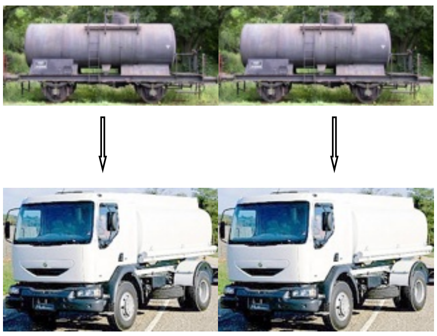
$\dot{V}/\dot{Q}$



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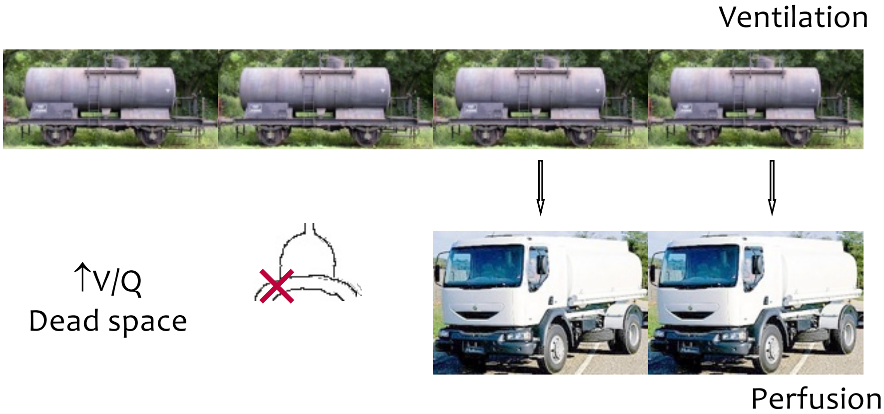
$\dot{V}/\dot{Q}$



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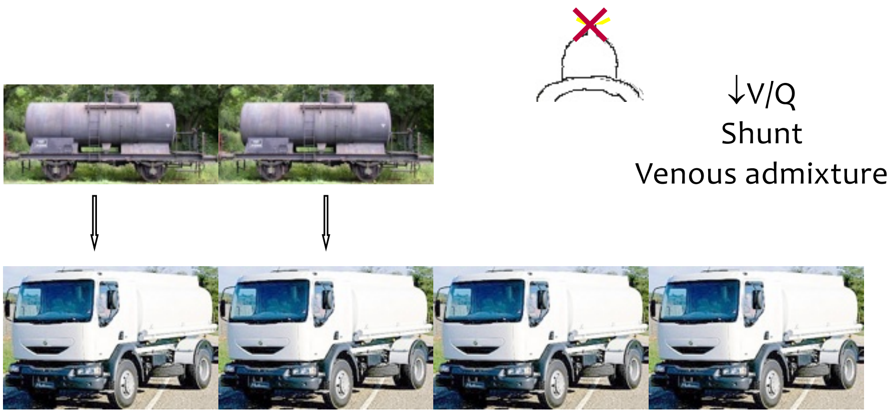
$\dot{V}/\dot{Q}$



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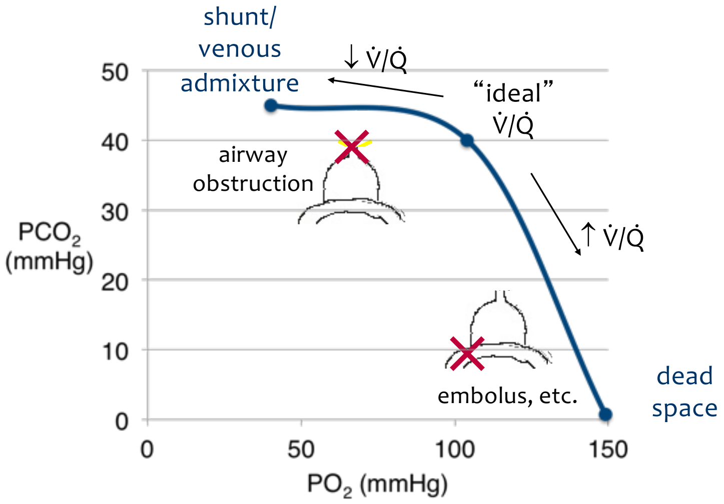
Rahn-Fenn diagram (local PO_2-PCO_2)



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V̇/Q̇ mismatch →↓PaO_2

- Main cause of hypoxemia in lung diseases
  - ↓ V̇/Q̇ → venous admixture
  - ↑ V̇/Q̇ → Q̇ only through unaffected parts → relatively ↑ Q̇ there → venous admixture

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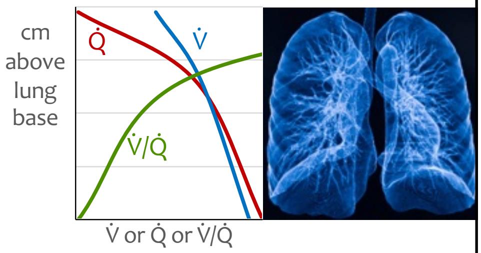
$\dot{V}/\dot{Q}$ mismatch



- Some even in health
  - effect of gravity: $\dot{Q} > \dot{V}$
  - mucus
  - variability in resistance & compliance of airways & alveoli

O_2 transport/perfusion inhomogeneity probably also in other organs

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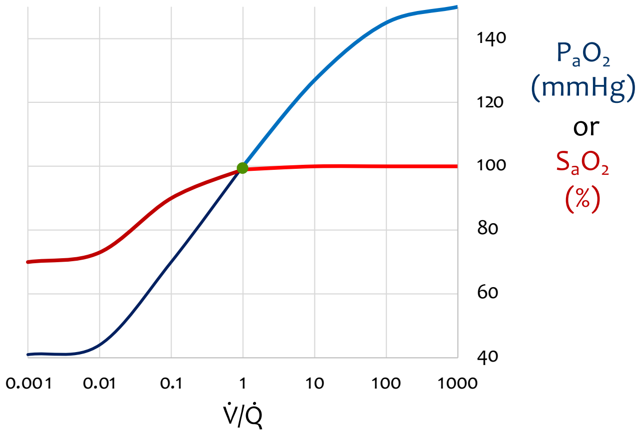
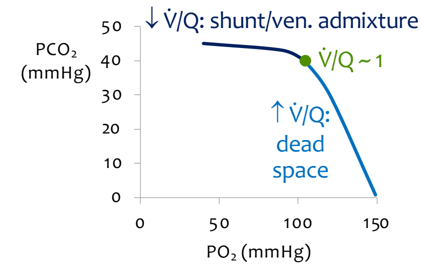
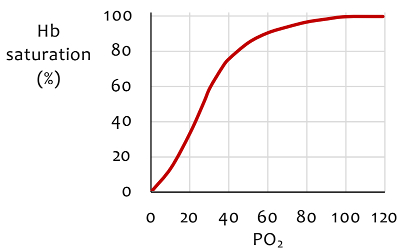
Effect of $\dot{V}/\dot{Q}$ on Pa_{O2} & Sa_{O2}







↑ $\dot{V}/\dot{Q}$ in one part of lung can't compensate for ↓ $\dot{V}/\dot{Q}$ elsewhere

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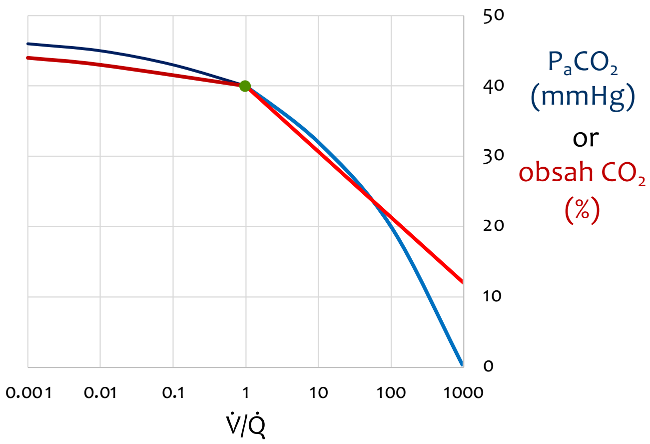
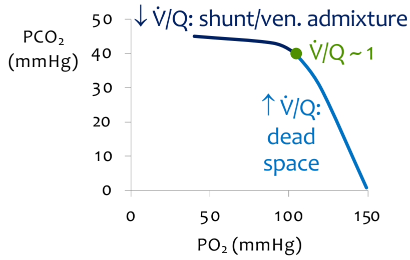
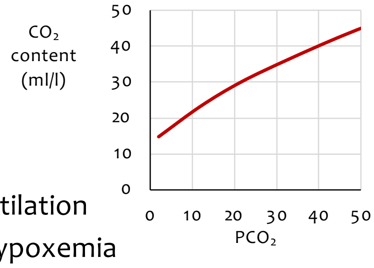
Effect of V̇/Q̇ na Pa_{CO_2} & CO_2 transport







- ↓V̇/Q̇ little effect on CO2 → correction: ↑ ventilation
- ↑V̇/Q̇ → ↓CO2 → ↓ventilation → worsens hypoxemia
- therefore effect of V̇/Q mismatch: $O_2 > CO_2$

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Why to detect V̇/Q̇ (in)equality?

To determine the causes of hypoxemia:

- Intrapulmonary
  - shunts
  - dead space
- Extrapulmonary
  - hypoventilation
  - anemia
  - cardiac failure
  - A-B disbalance

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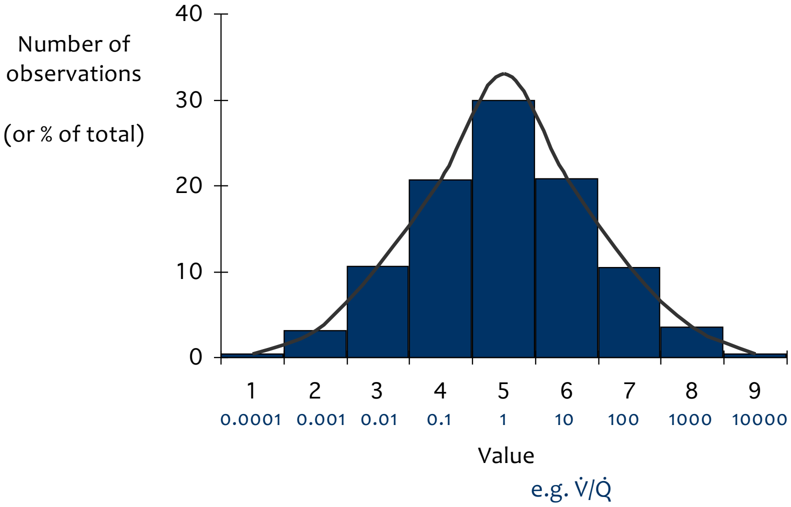
Quantification of V̇/Q̇ matching: Distribution



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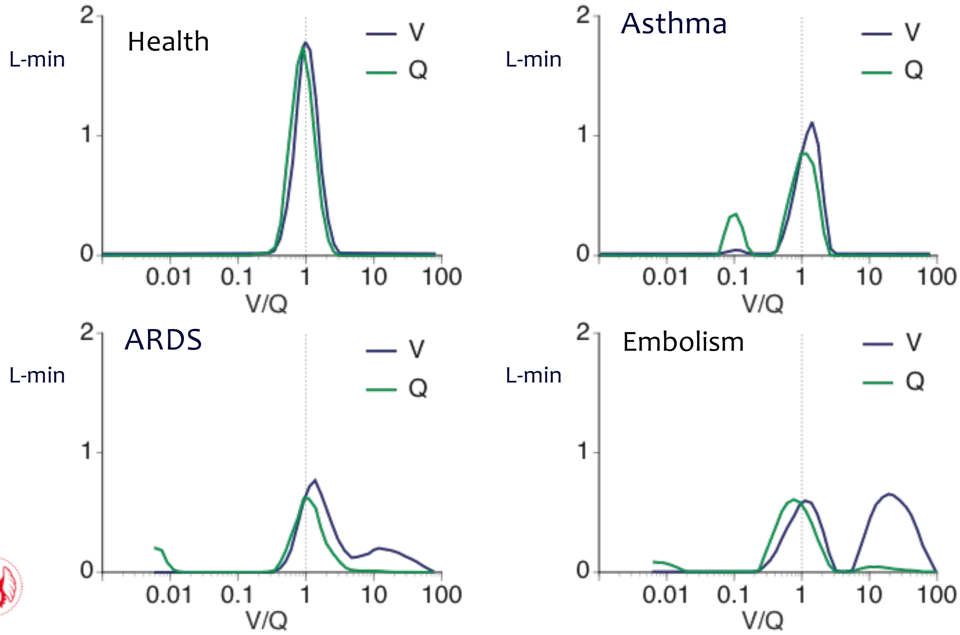
Multiple Inert Gas Elimination Technique (MIGET)



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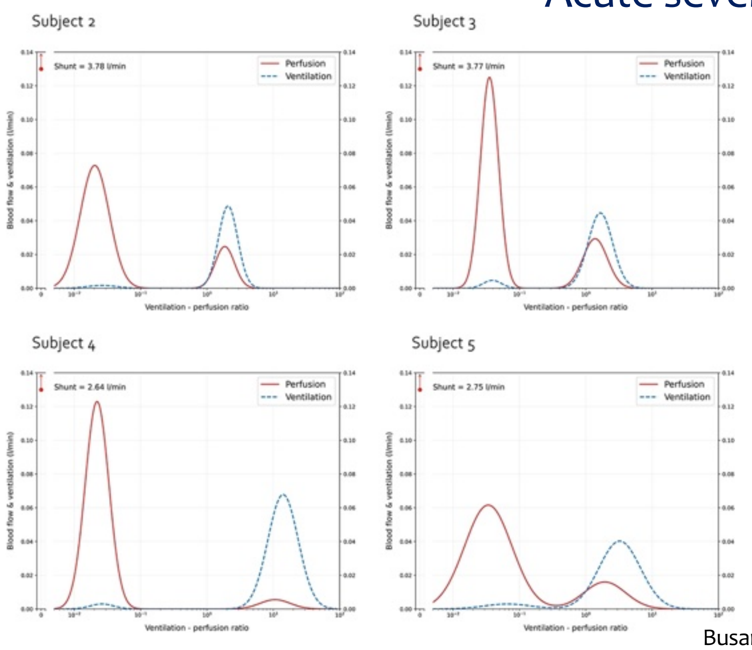
Acute severe COVID-19



Busana et al: *J Appl Physiol* 2021

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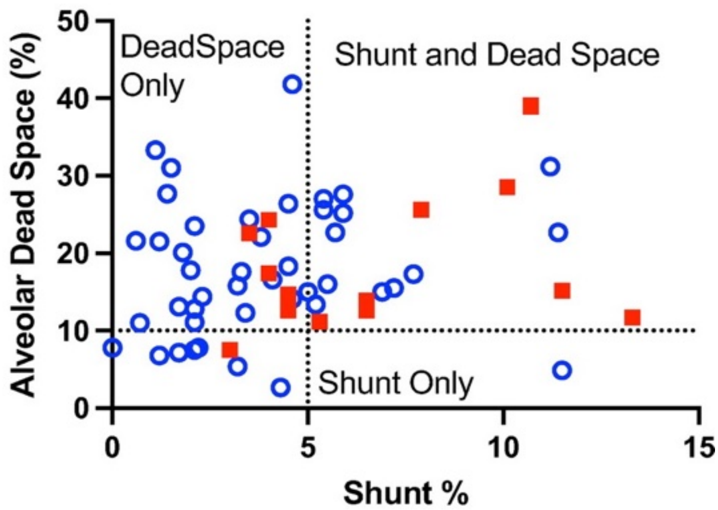
Post Covid-19: ↑ shunt, ↑ dead space



Farrow et al: *J Appl Physiol* 2023

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Doing MIGET

- I.V. infusion of solutions of variably dissolving gases
  - ✓ Acetone (most dissolving)
  - ✓ Ether
  - ✓ Enflurane
  - ✓ Cyklopropane
  - ✓ Ethane
  - ✓ SF6 (least dissolving)
- Detection in exhaled air & in arterial blood

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MIGET principle

- Admixture of air <u>from dead space</u> (where the injected gas couldn't penetrate from the blood) "dilutes" the total exhaled air
  → with higher $\dot{V}/\dot{Q}$, less injected gas appears in exhaled air
- Admixture of <u>blood from shunt</u> (where the injected gas couldn't escape from blood) prevents a decrease in injected gas concentration in arterial blood
  → with lower $\dot{V}/\dot{Q}$, more injected gas appears in arterial blood

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Compensation of $\dot{V}/\dot{Q}$ inequality

- $\uparrow\dot{V}/\dot{Q} \rightarrow$ local hypocapnia $\rightarrow \uparrow$ pH $\rightarrow$ local bronchoconstriction - weak
- $\uparrow\dot{V}/\dot{Q} \rightarrow \downarrow$ surfactant $\rightarrow \downarrow$ compliance $\rightarrow \downarrow$ volume
- $\downarrow\dot{V}/\dot{Q} \rightarrow \uparrow CO_2 \rightarrow \uparrow$ ventilation
  - improves CO_2 > O_2 (dissociation curves)
- $\downarrow\dot{V}/\dot{Q} \rightarrow$ **hypoxic pulmonary vasoconstriction**

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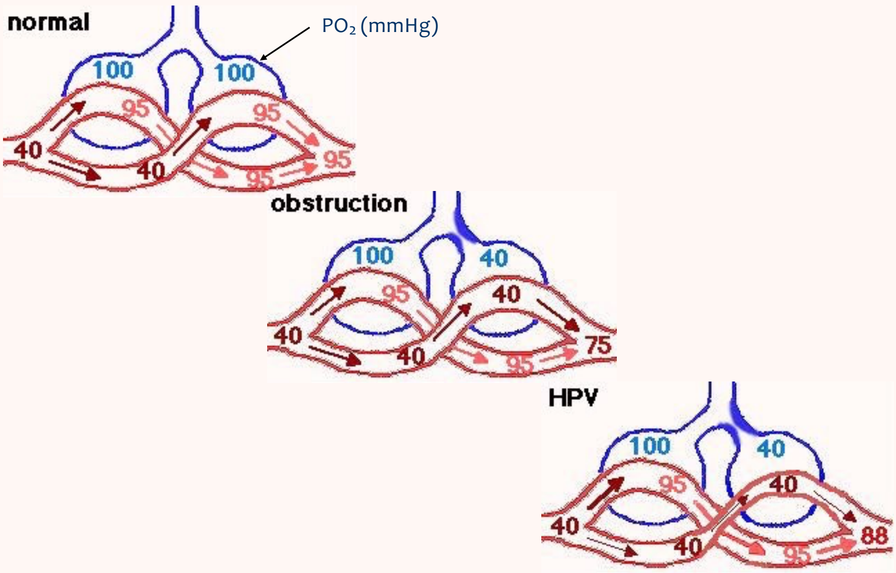
Hypoxic pulmonary vasoconstriction maintains $\dot{V}/\dot{Q}$



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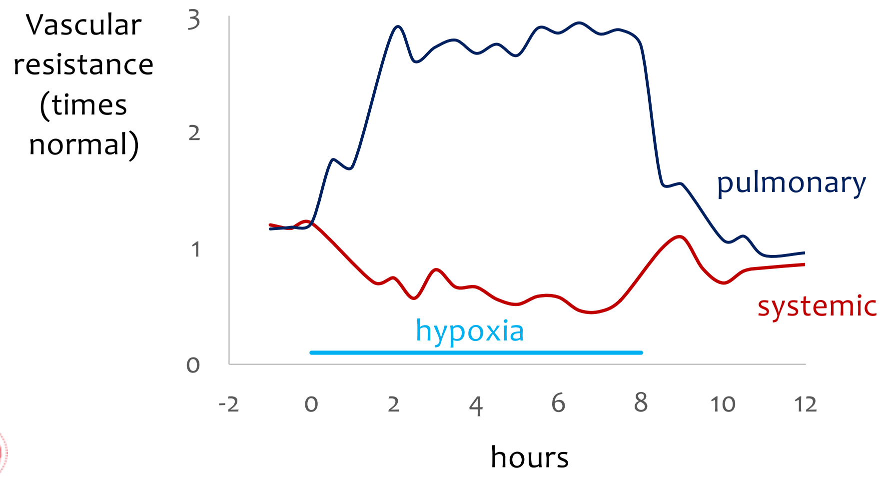
HPV: fast, sustained, reversible



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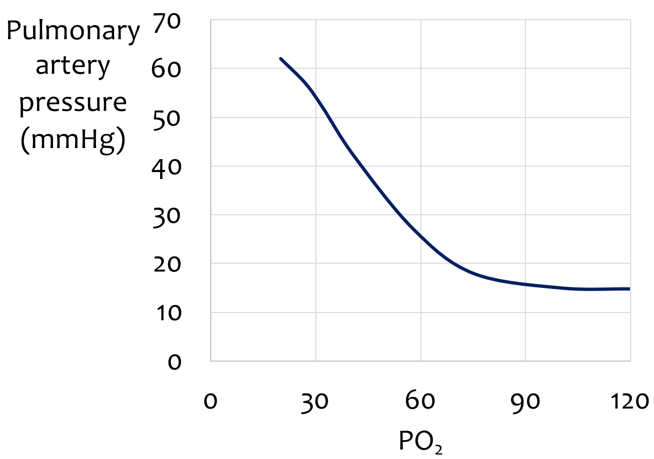
HPV: depends on degree of hypoxia



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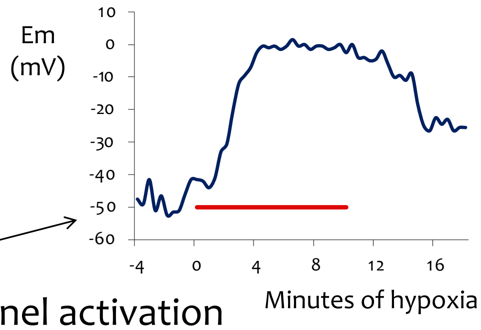
Mechanisms of HPV



- redox changes???
- K^+ channel inhibition
- depolarization
- voltage-gated Ca channel activation
- Ca^{2+} influx
- Ca^{2+} release from intracellular stores
- contractile apparatus activation

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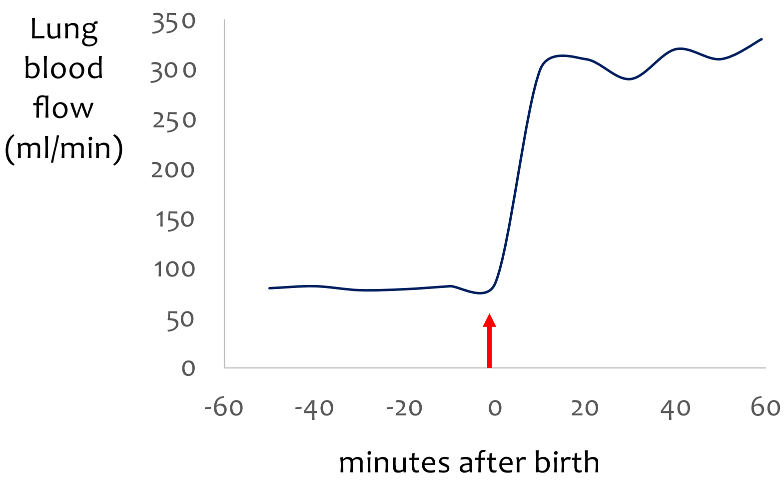
Lung blood flow at birth



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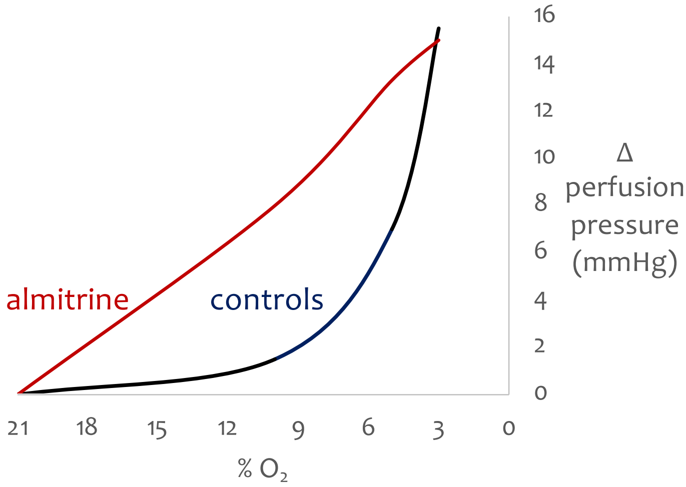
Almitrine sensitizes HPV

stimulates
carotis bodies



Falus, Herget, Hampl: *Eur Respir J* 1991

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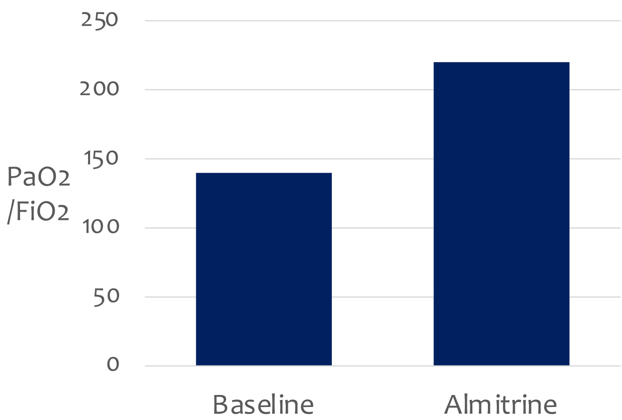
Almitrine can help in COVID-19



Losser et al: *Anaesth Crit Care Pain Med* 2020

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Filtration in lung capillaries

- capillary pressure: 7 mmHg
- negative interstitial pressure: 8 mmHg
- osmotic pressure of the interstitial fluid: 14 mmHg

Σ TOTAL FORCE OUTWARD: 29 mmHg

- osmotic pressure of plasma: 28 mmHg

Σ TOTAL FORCE INWARD: 28 mmHg

Σ Net filtration pressure (outward): 1 mmHg

- drained by the lymphatic system

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Diseases

- Pulmonary hypertension
  - idiopatic
  - secondary
    (L ♥ failure, hypoxia [COPD], thrombi, schistosomas,...)

- Lung edema
  - ARDS
  - cardiogenic
  - HAPE
- Lung embolism

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