

RESPIRATORY BIOPHYSICS

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RESPIRATORY SYSTEM

- System responsible for exchange of gases utilized and released by cellular metabolism

OUTLINE

- Brief history
- Relevant physical and physical-chemical laws
- Simplified structure of the human respiratory system
- Respiratory function - the respiratory cycle - respiratory work
- Gas exchange
- Relevant pathological conditions

BRIEF HISTORY

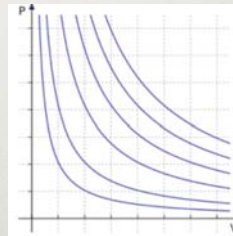
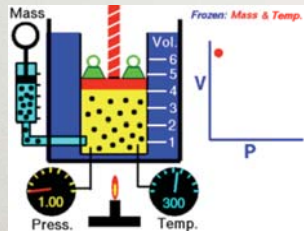
- Aristotle (300 BC): respiration cools the heart and blood
- Galenus (170 BC): breathing adds something to the blood ("*spiritus vitalis*")
- Leonardo da Vinci (1452-1519): animals die in a closed room where air refreshment is blocked.
- Vesalius (1543): the animal dies if its chest is opened, but survives if its lung is rhythmically ventilated.
- Gas laws (17-18. century, Clausius, Clapeyron, Boyle, Mariotte, Gay-Lussac, Charles)
- Black (1754): discovery of carbon dioxide. Priestley (1771): discovery of oxygen.
- "Blood gases": Magnus (1837), Haldane (1900)
- Surfactant: Neergaard (1920s), Pattle and Clements (1950s)

RELEVANT PHYSICAL AND PHYSICAL-CHEMICAL LAWS I.

Ideal gas law (derives from Clausius-Clapeyron's, Boyle-Mariotte's, Charles's laws):
Relationship between the pressure, volume, temperature and amount of gas.

$$PV = nRT$$

P = pressure (Pa)
 V = volume (m^3)
 n = amount (moles)
 R = gas constant ($8.314 \text{ J K}^{-1} \text{ mol}^{-1}$)
 T = absolute temperature (K)



Pressure-volume isotherms

RELEVANT PHYSICAL AND PHYSICAL-CHEMICAL LAWS II.

Dalton's law (John Dalton, 1801):

The total pressure exerted by the mixture of non-reactive gases is equal to the sum of the partial pressures of individual gases.

$$P_{\text{total}} = \sum_{i=1}^n p_i$$

p_i = partial pressure of the i th gas
 n = number of gases in the mixture
 $[p_i = P_{\text{total}} \times r; r = \text{ratio of the gas in the mixture}]$

Henry's law (William Henry, 1803):

At a constant temperature, the amount of a given gas that dissolves in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.

$$p = k_H c$$

p = partial pressure (Pa; atm)
 k_H = Henry's constant ($\text{l} \cdot \text{atm} / \text{mol}$)
 c = concentration of dissolved gas (mol / l)

Young-Laplace equation:

Describes the capillary pressure difference sustained across the interface between two static fluids (e.g., water, air) due to surface tension.

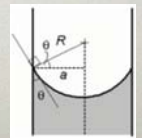
In a sufficiently narrow tube:

$$\Delta p = 2\gamma H$$

p = pressure (Nm^{-2})
 γ = surface tension (Nm^{-1} ; Jm^{-2})
 H = mean curvature (m^{-1})

$$\Delta p = \frac{2\gamma}{R}$$

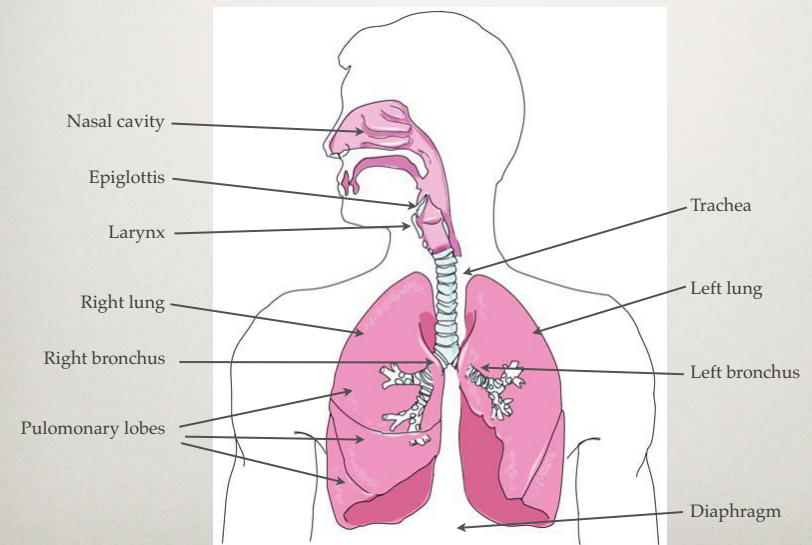
R = radius of curvature



SIMPLIFIED STRUCTURE OF THE RESPIRATORY SYSTEM

- Tube system (air flow)
- Box (volume, pressure, changes thereof, mechanics)
- Surface of gas exchange (area, relative gas pressures, diffusion)

RESPIRATORY SYSTEM



TUBE SYSTEM

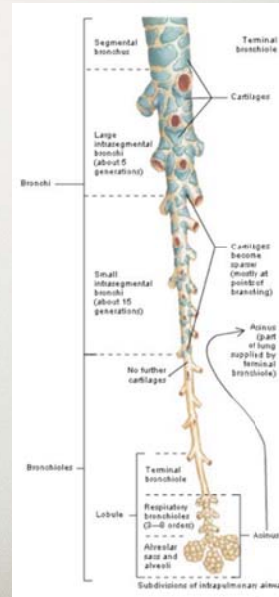
Conducting zone

Trachea
Bronchi
Bronchioli
Terminal bronchioli

Respiratory zone

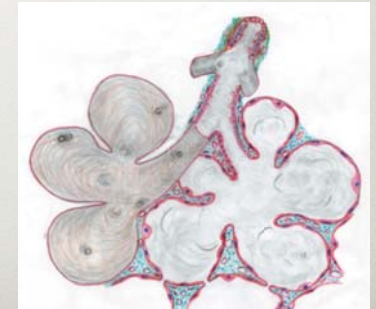
Respiratory bronchioli
Alveolar ducts
Alveoli

23-25 dichotomic divisions!

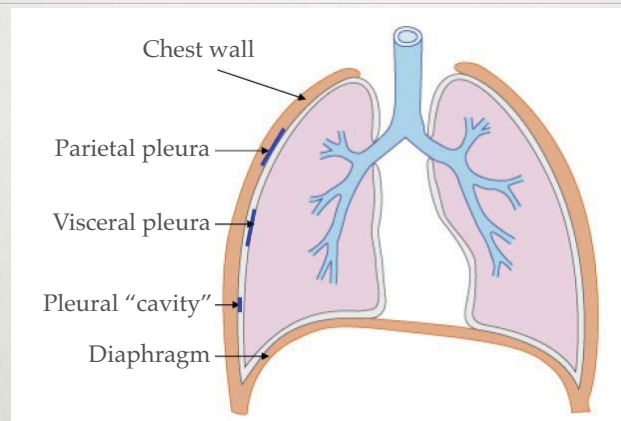


ALVEOLI

- Surface for gas exchange
- Number: ~300 million (N.B.: $2^{25}=33,554,432$)
- Size ($d \sim 200 \mu\text{m}$), area ($5 \times 10^{-7} \text{ m}^2$)
- Total alveolar area ($\sim 100 \text{ m}^2$)
- Wall ($\sim 0.5 \mu\text{m}$):
alveolar epithelium ($\sim 0.2 \mu\text{m}$)
basal membrane ($\sim 0.1 \mu\text{m}$)
endothelium ($\sim 0.2 \mu\text{m}$)

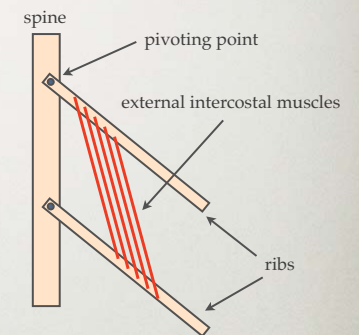
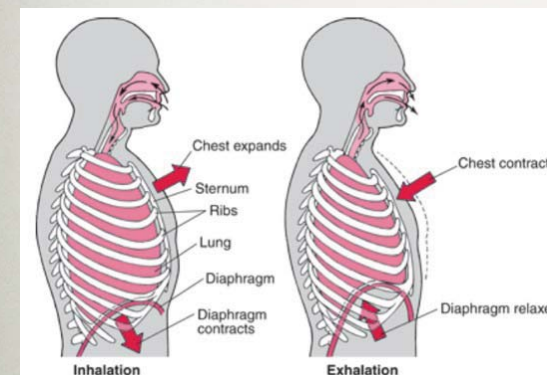


RESPIRATORY SYSTEM AS A BOX



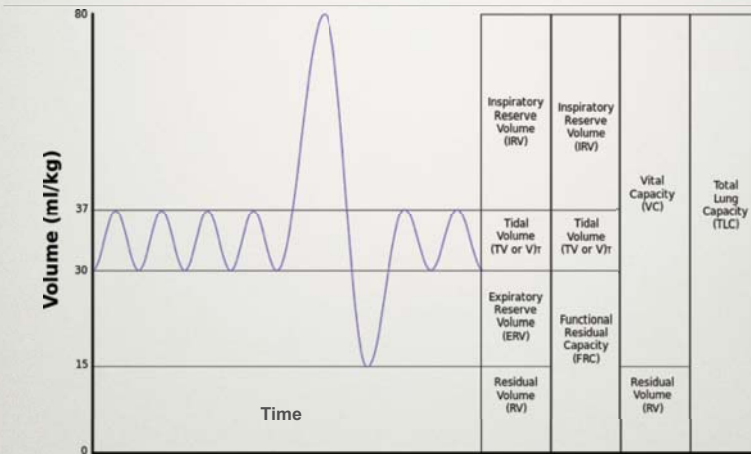
- Intrapulmonary pressure (P_{pulm}): fluctuates around external (atmospheric) pressure
- Intrathoracic or intrapleural pressure (P_{pi}): "negative" (balance between atmospheric pressure, adhesional and contractile forces)
- Transmural (transpulmonary) pressure (P_{tm}): pressure difference across chest wall
- Pneumothorax!

THE BREATHING CYCLE



- Driving forces of breathing: diaphragm, intercostal muscles
- Eupnoe: normal breathing (14-16/min)
- Polypnoe, tachypnoe: number of breaths $>16/\text{min}$
- Dyspnoe: shortness of breath

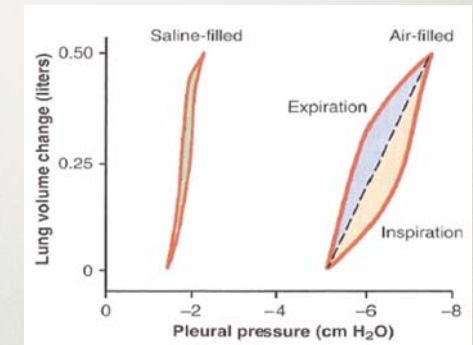
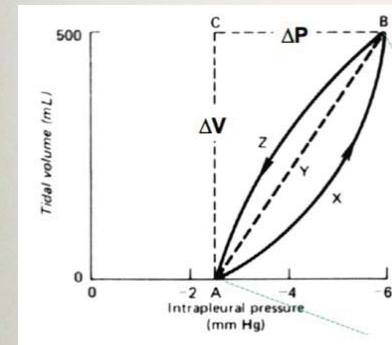
PULMONARY VOLUMES AND CAPACITIES



Volume	Value (litres)		Volume	Average value (litres)		Derivation
	In men	In women		In men	In women	
Inspiratory reserve volume	3.3	1.9	Vital capacity	4.8	3.1	IRV plus TV plus ERV
Tidal volume	0.5	0.5	Inspiratory capacity	3.8	2.4	IRV plus TV
Expiratory reserve volume	1.0	0.7	Functional residual capacity	2.2	1.8	ERV plus RV
Residual volume	1.2	1.1	Total lung capacity	6.0	4.2	IRV plus TV plus ERV plus RV

PULMONARY COMPLIANCE

("deformability", "stretchability", "distensibility")



$$C = \frac{\Delta V}{\Delta P}$$

C = compliance (mN⁻¹; N.B.: inverse of stiffness)
 ΔP = change in pressure (Pa, Nm⁻²)
 ΔV = change in volume (m³)

ROLE OF SURFACE TENSION

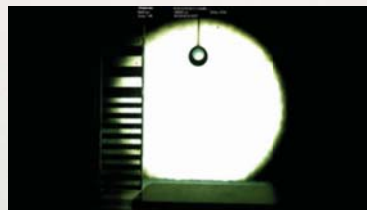
Surface tension: contractive tendency of the liquid that resists external force.
 Imbalance of cohesive forces in the bulk versus the surface of the liquid.



Chemical	Surface tension (mN/m)
Ethanol	24.4
Methanol	22.7
Acetone	23.7
Chloroform	27.1
Benzene	28.5
Water	72.9

Large surface tension

Consequences on **hydrophobic** surface



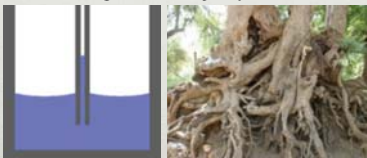
Persisting droplet on a superhydrophobic surface

Consequences in macroscopic living systems



Water striders

Consequences on **hydrophilic** surface



Capillary action (model)

Capillary action aiding plant root function



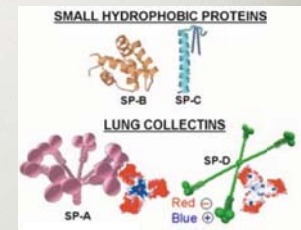
"Jesus Christ lizard" (basilisk)

SURFACTANT

Young-Laplace equation: $\Delta p = \frac{2\gamma}{R}$

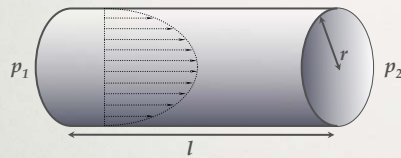
p = pressure
 γ = surface tension
 R = radius of curvature

- Pulmonary surfactant:** surface-active lipoprotein complex (phospholipoprotein) formed by (type II) alveolar cells.
- Composition:** 90 % lipids, 10 % proteins ("surfactant protein" SP-A, SP-B, SP-C, SP-D)
- Function:** reduces surface tension
- Effect:** the smaller the surface tension, the less pressure needed to keep alveoli open (for a given pressure, smaller alveoli can be opened).
- Restrictive diseases:** pulmonary compliance is reduced (fibrosis, lack of surfactant, etc.).



ROLE OF AIR FLOW

Hagen-Poiseuille's law

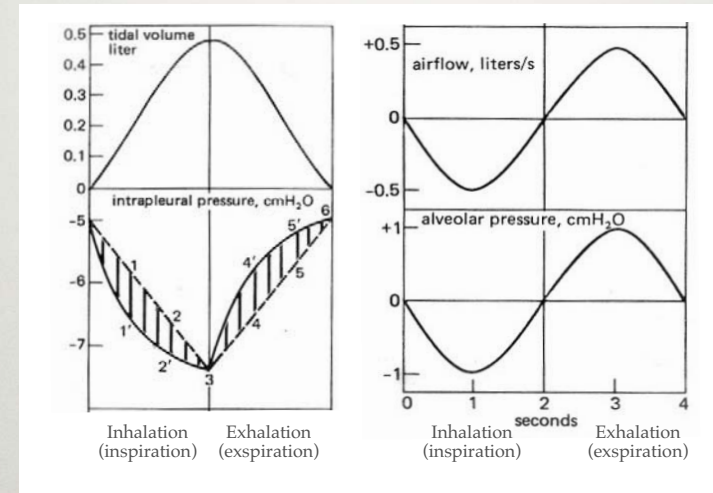


$$\frac{V}{t} = \frac{\pi r^4}{8\eta} \frac{dp}{dl}$$

V = volume
 t = time
 $(V/t = Q = \text{flow intensity})$
 r = tube radius
 η = viscosity
 p = pressure
 l = length of tube
 $(dp/dl = \text{pressure gradient, maintained by } p_1 - p_2)$

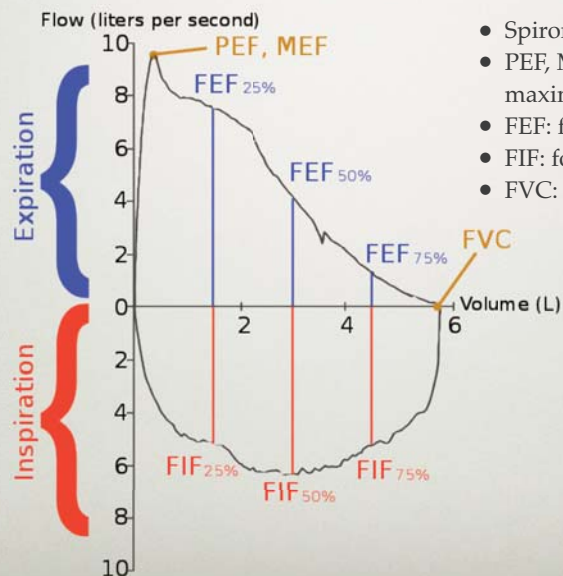
- **Normally (eupnoe):** flow is laminar.
- **Tachypnoe or disease:** turbulent airflow
- **Obstructive diseases:** pulmonary airflow is compromised (COPD - "chronic obstructive pulmonary disease").

RESPIRATORY CYCLE



• 1 cmH₂O = 0.1 kPa = 0.7 mmHg

DYNAMIC ANALYSIS OF BREATHING CYCLE

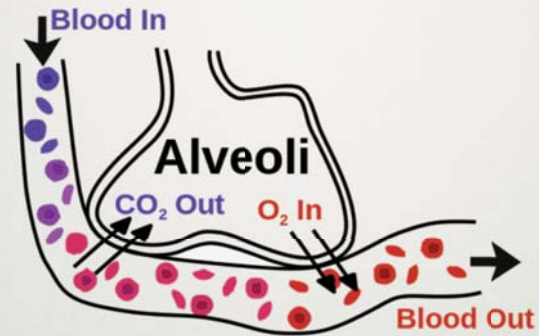


- Spirometry
- PEF, MEF: peak expiratory flow, maximal expiratory flow
- FEF: forced expiratory flow
- FIF: forced inspiratory flow
- FVC: forced vital capacity

RESPIRATORY WORK

- Volume change against average transmural pressure
- Minute volume (MV) = 7 l
- Breathing rate (BR) = 14 / min
- Pressure (P_{tm}) = 0.7 kPa
- Respiratory volume (V) = 0.5 l ($5 \times 10^{-4} \text{ m}^3$)
- Work (W) = $P_{tm} \times V = 0.35 \text{ J/inspiration}$ (294 J/h)
- At great loads it may reach 8400 J/h

PULMONARY GAS EXCHANGE



- Alveolus: open thermodynamic system
- Partial gas pressures in gas phases
- Dissolved gas tensions in liquid (plasma)
- Driving forces: gas diffusion (gas exchange driven by partial pressure gradient)

PARTIAL PRESSURES

	Alveolar gas	Inhaled gas (air)	Exhaled gas
Oxygen	100 mmHg	158 mmHg	116 mmHg
CO ₂	40 mmHg	0.2 mmHg	29 mmHg
Nitrogen	573 mmHg	597 mmHg	568 mmHg
Water vapor	47 mmHg	5 mmHg	47 mmHg

	pO ₂	pCO ₂	pN ₂
Alveolar gas	100 mmHg	40 mmHg	573 mmHg
Arterial blood	95 mmHg	40 mmHg	573 mmHg
Venous blood	5.3 mmHg	46 mmHg	573 mmHg

- Alveolar gas exchange: defines partial pressures (~350 ml/breath)
- Apparent diffusivity: amount of exchanged gas / (surface area x layer thickness x pressure difference)
- Normal conditions: gas exchange takes place within ~0.25 s

PATHOLOGIC CONSIDERATIONS

- Pneumothorax
- Restrictive diseases (compliance)
- Obstructive diseases (airflow)
- Coughing (sudden airflow increase)
- Decompression disease (Caisson, dissolved gases)