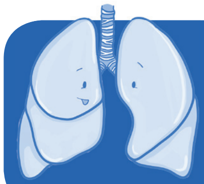

NOTES
GAS EXCHANGE

GAS EXCHANGE & LAWS

- Diffusion of oxygen (O_2), carbon dioxide (CO_2) in lungs, peripheral tissues
- Alveolar O_2 from inhaled gas → pulmonary capillary blood → circulation → tissue capillaries → cells
- CO_2 from cells → tissue capillaries → circulation → pulmonary capillary blood → CO_2 for exhalation from alveoli
- Gas exchange, gas behavior in solution is governed by fundamental physical gas properties → represented by gas laws

FORMS OF GAS IN SOLUTION

Dissolved gas

- All gas in solution are to some extent carried in a freely dissolved form
- For given partial pressure, the higher the solubility of a gas, the higher the concentration in solution
- In solution only dissolved gas molecules contribute to partial pressure
- Of the gases inspired as air, only nitrogen is exclusively carried in dissolved form

Bound gas

- O_2, CO_2, CO are bound to proteins in blood
- O_2, CO_2, CO can all bind to hemoglobin
- CO_2 also binds to plasma proteins

Chemically modified gas

- The ready back and forth conversion of CO_2 to bicarbonate (HCO_3^-) in presence of enzyme carbonic anhydrase allows CO_2 to contribute to gas equilibria despite chemical conversion
- Majority of CO_2 in blood carried as HCO_3^-

IDEAL (GENERAL) GAS LAW

osms.it/ideal-gas-law

- Relates multiple variables to describe state of a hypothetical "ideal gas" under various conditions
  - *Ideal gas:* theoretical gas composed of many randomly moving point particles whose only interactions are perfectly elastic collisions
  - All gas laws can be derived from general gas law
- PV = nRT
  - P = Pressure (millimeters of mercury (mmHg)
  - V = Volume (liters (L)
  - n = Moles (mol)
  - R = Gas constant (8.314 J/mol)
  - T = Temperature (Kelvin [K])
- *In gas phase:* body temperature, pressure (BTPS) used
  - T = 37°C/98.6°F/310K
  - P = Ambient pressure
  - Gas is saturated with water vapor (47mmHg)
- *In liquid phase/solution:* standard temperature, pressure (STPD) used
  - T = 0°C/32°F/273K
  - P = 760mmHg
  - Dry gas (no humidity)
- Ideal gas law can be used to interconvert between properties of same gas under BTPS, STPD conditions
  - E.g. gas volume (V_1) at BTPS → gas volume at STPD (V_2)

$$V_2 = V_1 \times \frac{T_1}{T_2} \times \frac{P_1 - P_{w1}}{P_2 - P_{w2}}$$

$$V_2 = V_1 \times \frac{273}{310} \times \frac{760 - 47}{760 - 0}$$

$$V_2 = V_1 \times 0.826$$

BOYLE'S LAW

osms.it/Boyles-law

- Describes how pressure of gas ↑ as container volume ↓
- $P_1V_1 = P_2V_2$
- For gas at given temperature, the product of pressure, volume is constant
- Inspiration → diaphragm contraction → ↑ lung volume
- If PV constant + lung volume ↑ → pressure ↓
- Pressure ↓ → disequilibrium between room, lung air pressures → air fills lungs to equalize pressure

DALTON'S LAW

osms.it/Daltons-law

- Total pressure exerted by gaseous mixture = sum of all partial pressures of gases in mixture → partial pressure of gas in gaseous mixture = pressure exerted by that gas if it occupied total volume of container
- $P_x = P_B \times F$
  - Px = partial pressure of gas (mmHg)
  - P_B = barometric pressure (mmHg)
  - F = fractional concentration of gas (no unit)
- Partial pressure = total pressure X fractional concentration of dry gas
- For humidified gases
  - $P_x = (P_B - P_{H2O}) \times F$
  - P_{H2O} = Water vapor pressure at 37°C/98.6°F (47mmHg)
  - If the sum of partial pressures in a mixture = total pressure of mixture → barometric pressure (P_B) is sum of the partial pressures of O_2, CO_2, N_2 (nitrogen), and H_2O
  - At barometric pressure (760 mmHg) composition of humidified air is O_2, 21%; N_2, 79%; CO_2, 0%
  - Within airways, air is humidified thus water vapor pressure is obligatory = to 47mmHg at 37°C/98.6°F

HENRY'S LAW

osms.it/Henrys-law

- For concentrations of dissolved gases
- When gas is in contact with liquid → gas dissolves in proportion to its partial pressure → greater concentration of a particular gas, in gas phase → more dissolves into solution at faster rate
  - $C_x = P_x$ x Solubility
  - C_x = concentration of dissolved gas (mL gas / 100mL blood)
  - Concentration of gas in solution only applies to dissolved gas that is free in solution
  - Concentration of gas in solution does not include any gas that is presently bound to any other dissolved substances (e.g. plasma proteins/ hemoglobin)
  - P_x = partial pressure of gas (mmHg)
  - Solubility = solubility of gas in blood (mL gas / 100mL blood per mmHg)
- Henry's law governs gases dissolved within solution (e.g. O_2, CO_2 dissolved in blood)
- To calculate gas concentration in liquid phase
  - Partial pressure of gas in gas phase → partial pressure in liquid phase → concentration in liquid
  - Partial pressure of gas in liquid phase (at equilibrium) = partial pressure of gas in gaseous phase
  - If alveolar air has PO_2 of 100mmHg → PO_2 of capillary blood that equilibrates with alveolar air = 100mmHg

HYPERBARIC CHAMBERS

- Hyperbaric chambers employ Henry's law
  - Contain O_2 gas pressurized to above 1 atm → greater than normal amounts of O_2 forced into the blood of the enclosed individual
  - Used to treat carbon monoxide poisoning, gas gangrene due to anaerobic organisms (cannot live in presence of high concentrations of O_2), improve oxygenation of skin grafts, etc.

FICK'S LAWS OF DIFFUSION

osms.it/Ficks-law-of-diffusion

- Describes diffusion of gases

$$V_x = \frac{DA\Delta P}{\Delta x}$$

  - V_x = volume of gas transferred per unit time
  - D = gas diffusion coefficient
  - A = surface area
  - ΔP = partial pressure difference of gas
  - Δx = membrane thickness
- Driving force of gas diffusion is difference in partial pressures of gas (ΔP) across membrane (not the concentration difference)
  - If P_{O2} of alveolar air = 100mmHg
  - P_{O2} of mixed venous blood entering pulmonary capillary = 40mmHg
  - Driving force across membrane is 60mmHg (100mmHg - 40mmHg)
- Diffusion coefficient of gas (D) is a combination of usual diffusion coefficient (dependent on molecular weight) and gas solubility
- Diffusion coefficient dramatically affects

diffusion rate, e.g. diffusion coefficient for CO_2 is approximately 20x greater than that of O_2 → for a given partial pressure difference CO_2 would diffuse across the same membrane 20x faster than O_2

LUNG DIFFUSION CAPACITY (DL)

- A functional measurement which takes into account
  - Diffusion coefficient of gas used
  - Membrane surface area
  - Membrane thickness
  - Time required for gas to combine with proteins in pulmonary capillary blood (e.g. hemoglobin)
- Measured using carbon monoxide (CO) → CO transfer across alveolar-capillary barrier exclusively limited by diffusion process
- Lung diffusion capacity of carbon monoxide (DL_{CO}) is measured using a single breath
  - Individual breathes a mixture of gases with a low CO concentration → rate of CO disappearance is predictable in different disease states
  - Emphysema → destruction of alveoli → decreased surface area for gas exchange → decreased DL_{CO}
  - Fibrosis/pulmonary edema → increase in membrane thickness (via fluid accumulation in the case of edema) → decreased DL_{CO}
  - Anemia → reduced hemoglobin → reduced protein binding in a given time period → decreased DL_{CO}
  - Exercise → increased utilization of lung capacity, increased recruitment of pulmonary capillaries → increased DL_{CO}

GRAHAM'S LAW

osms.it/Grahams-law

- Diffusion rate of gas through porous membranes varies inversely with the square root of its density
- To compare rate of effusion (movement through porous membrane) of two gases → velocity of molecules determine the rate of spread
- Kinetic temperature in kelvin of a gas is directly proportional to average kinetic energy of gas molecules → at the same temperature, molecule of heavier gas will have a slower velocity than those of lighter gas
  - Kinetic energy = ½mv2
  - $\frac{1}{2}m_1v_1^2 = \frac{1}{2}m_2v_2^2$
  - $v_1^2 / v_2^2 = m_2 / m_1$
  - $v_1 / v_2 = \sqrt{(m_2 / m_1)}$
  - Which can be rewritten to give Graham's law

$$\frac{Rate_1}{Rate_2} = \sqrt{\frac{M_2}{M_1}}$$

GAS EXCHANGE IN THE LUNGS

osms.it/gas-exchange-in-lungs

PULMONARY GAS EXCHANGE

- AKA external respiration
- Pulmonary capillaries perfused with blood from right heart (deoxygenated)
- Gas exchange occurs between pulmonary capillary, alveolar gas
  - Room air → inspired air → humidified tracheal air → alveoli
  - O_2 diffuses from alveolar gas → pulmonary capillary blood
  - CO_2 diffuses from pulmonary capillary blood → alveolar gas
  - Blood exits the lungs → left heart → systemic circulation

Dry inspired air

- P_{O2} is approximately 160mmHg
  - Barometric pressure x fractional concentration of O_2 (21%)
  - P_{O2} = 760mmHg x 0.21
  - Assume no CO_2 in dry inspired air

Humidified tracheal air

- P_{O2} of humidified tracheal air is 150mmHg
  - Air is fully saturated with water vapor → "dilution" of partial pressures → calculations must correct for water vapor pressure (subtracted from barometric pressure)
  - At 37°C/98.6°F, P_{H2O} is 47mmHg
  - P_{O2} = (760mmHg – 47mmHg) x 0.21
  - Assume no CO_2 in humidified inspired air

Alveolar air

- Pressures of alveolar gas designated "PA"
- Alveolar gas exchange in lungs sees a drop in O_2 partial pressure, increase in CO_2 partial pressure
- PA_{O2} = 100mmHg
- PA_{CO2} = 40mmHg
- Amount of these gases entering/leaving alveoli correspond to physiological body needs (i.e. O_2 consumption, CO_2 production)

Pulmonary capillaries

- Blood entering pulmonary capillaries is mixed venous blood
- Tissues (metabolic activity alters composition of blood) → venous vasculature → right heart → pulmonary circulation
- P_{O2} = 40mmHg
- P_{CO2} = 46mmHg

Systemic arterial blood (oxygenated)

- Gas partial pressures of systemic arterial blood designated "Pa"
- In a healthy individual, diffusion of gas across alveolar, capillary membrane is so rapid that we can assume equilibrium is achieved between alveolar gases, pulmonary capillaries → P_{O2} and P_{CO2} of blood leaving pulmonary capillaries = alveolar air
- PA_{O2} = Pa_{O2} = 100mmHg
- PA_{CO2} = Pa_{CO2} = 40mmHg
- This blood enters systemic circulation to eventually return to lungs

Physiological shunt

- Small fraction of pulmonary blood flow bypasses alveoli → physiological shunt → blood not arterialized → systemic blood has slightly lower P_{O2} than alveolar air
- Shunting occurs due to
  - Coronary venous blood, drains directly into left ventricle
  - Bronchial blood flow
- Shunting may be increased in various pathologies → ventilation-perfusion defects/mismatches
- As shunt size increases → alveolar gas, pulmonary capillary blood do not equilibrate → blood is not fully arterialized
- *A-a difference:* difference in P_{O2} between alveolar gas (A), systemic arterial blood (a)
  - Physiological shunting → negligible/small differences
  - Pathology → notably increased difference

FACTORS AFFECTING EXTERNAL RESPIRATION

Thickness of respiratory membrane

- In healthy lungs, respiratory membrane → 0.5–1 micrometer thick
- Presence of small amounts of fluid (left heart failure, pneumonia) → significant loss of efficiency, equilibration time dramatically increases → the 0.75 seconds blood cells spend in transit through pulmonary circulation may not be sufficient

Surface area of respiratory membrane

- Greater surface area of respiratory membrane → greater amount of gas exchange
- Healthy adult male lungs have surface area of $90m^2$
- Pulmonary diseases (e.g. emphysema) → walls of alveoli break down → alveolar chambers enlarge → loss of surface area
- Tumors/pneumonia → prevent gas from occupying all available lung → loss of surface area

Partial pressure gradients and gas solubilities

- Partial pressures of O_2, CO_2 drive diffusion of these gases across respiratory membrane
- Steep O_2 partial pressure gradient exists
  - PO_2 of deoxygenated blood in pulmonary arteries = 40mmHg
  - PO_2 of 104mmHg in alveoli
  - O_2 diffuses rapidly from alveoli into pulmonary capillary blood
- O_2 equilibrium (PO_2 of 104mmHg on both sides of respiratory membrane) occurs in around 0.25 seconds of transit through lungs (about ⅓ of the time available)
- CO_2 has smaller gradient → 5mmHg (45mmHg vs 40mmHg), although pressure gradient for O_2 is much steeper than for CO_2, CO_2 is 20x more soluble in plasma, alveolar fluid than O2 → equal amounts of gas exchanged

Ventilation-perfusion coupling

- *Ventilation:* amount of gas reaching alveoli
- *Perfusion:* amount of blood flow in pulmonary capillaries
- These are regulated by local autoregulatory mechanisms → continuously respond to local conditions → some control in blood flow around lungs
- Arteriolar diameter controlled by P_{O2}
  - If alveolar ventilation is inadequate → blood taking O_2 away faster than ventilation can replenish it → low local P_{O2} → terminal arteriole restriction → blood redirected to respiratory areas with high P_{O2}, oxygen pickup more efficient
  - In alveoli where ventilation is maximal → high P_{O2} → pulmonary arteriole dilation → blood flow into pulmonary arterioles increases
  - Pulmonary vascular muscle autoregulation is opposite of that in systemic circulation
- Bronchiolar diameter controlled by P_{CO2}
  - Bronchioles connecting areas where PA_{CO2} high → dilation → allows CO_2 to be eliminated from body
  - Those with low CO_2 → constrict
- Independent autoregulation of arterioles, bronchioles → matched perfusion, ventilation
- Ventilation-perfusion matching is imperfect
  - Gravity → regional variation in blood, air flow (apices have greater ventilation but lesser perfusion, bases have greater perfusion, lesser ventilation)
  - Occasionally alveolar ducts may be plugged with mucus → unventilated areas

INTERNAL RESPIRATION

- Capillary gas exchange in body tissue
- Partial pressures, diffusion gradients are reversed from lungs however physical laws governing the exchanges remain identical
- Cells in body continuously use O_2, produce CO_2
  - PO_2 always lower in tissue than arterial blood (40mmHg vs 100mmHg) → O_2 moves rapidly from blood → tissues until equilibrated
  - CO_2 moves rapidly down its pressure gradient (P_{CO2} of 40mmHg in fresh blood arriving at capillary beds beds vs. P_{CO2} of 45mmHg in tissues) → venous blood → right heart

- Gas exchange at tissue level driven by partial pressures, occurs via simple diffusion

DIFFUSION-LIMITED & PERFUSION-LIMITED GAS EXCHANGE

osms.it/diffusion-limited-perfusion-limited-gas-exchange

Diffusion-limited gas exchange

- Diffusion is limiting factor determining total amount of gas transported across alveolar-capillary barrier
- As long as partial pressure gradient is maintained, diffusion continues
  - Gas readily diffuses across permeable membrane
  - Blood flow away from alveoli/chemical binding → partial pressure of gas on systemic end does not rise → partial pressure maintenance
  - Given a sufficiently long capillary bed diffusion will continue along entire length as equilibrium is not achieved
- Examples include
  - CO across alveolar-pulmonary capillary barrier
  - Oxygen during strenuous exercise/emphysema/fibrosis

Perfusion-limited gas exchange

- Perfusion (blood flow) is the limiting factor determining total amount of gas transported across alveolar-capillary barrier
- Increasing blood flow → increasing amount gas transported; examples include
  - Nitrous oxide (N_2O): not bound in blood → entirely free in solution; PA_{N2O} is constant, Pa_{N2O} = zero at start of capillary → initial large A-a difference → because no N_2O binds to any other components of blood, all of it remains free in solution → partial pressure builds rapidly → rapid equilibration, most of capillary length does not participate in gas exchange; new blood must be supplied to partake in further gas exchange with alveolar N_2O → "perfusion-limited gas exchange"
  - O_2 at rest
  - CO_2

Limitations of O_2 transport

- Under physiological conditions O_2 transport into pulmonary capillaries → perfusion-limited
- Diseased or abnormal conditions → diffusion-limited
- Perfusion-limited O_2 transport
  - PA_{O2} is constant = 100mmHg
  - At beginning of capillary Pa_{O2} = 40mmHg (mixed venous blood) → large partial pressure gradient → drives diffusion
  - As O_2 diffuses into pulmonary capillary blood → increase in Pa_{O2}
  - Hemoglobin binds O_2 → resists increase in Pa_{O2} → initially gradient is maintained; eventually equilibrium is achieved → perfusion-limitation
  - Therefore pulmonary blood flow determines net O_2 transfer (changes in pulmonary blood flow will affect net O_2 transfer)

Diffusion-limited O_2 transport

- Fibrosis → thickening of alveolar walls → increased diffusion distance for O_2 (decreases DL) → slowed rate of diffusion → prevents equilibration → partial pressure gradient maintained along length of capillary
- Increasing capillary length allows for more time for equilibrium to occur → diffusion-limitation

O_2 transport at high altitude

- High altitude reduces barometric pressure → reduced partial pressures
- Reductions in Pa_{O2} → reduce oxygen amount available to diffuse into blood → reduced rate of equilibration at capillary → more time required for gas exchange, lower peak oxygen concentration reached once equilibrated