• **Physics of Gas Diffusion and Gas Partial Pressures**
  - **Molecular Basis of Gas Diffusion**: Energy provided by non-linear, kinetic motion of molecule
  - **Gas Pressures in a Mixture of Gases - Partial Pressure of Individual Gases**: Pressure caused by impacts of moving molecules against a surface -> direction proportional to concentration of gas molecules
  - **Pressure of Gases Dissolved in Water and Tissues**
    - *Partial Pressure = Henry’s Law*: partial pressure = concentration of dissolved gas / solubility coefficient; CO₂ is 20x as soluble as O₂ -> PCO₂ is 1/20th of PO₂
    - *Diffusion of Gases Between the Gas Phase in the Alveoli and the Dissolved Phase in the Pulmonary Blood*: rate of diffusion of each gas is directly proportional to partial pressure of each gas; net diffusion determined by difference between the two partial pressures
  - **Vapor Pressure of Water**: air is humidified in respiratory passages until it is equilibrium with water (determined by temperature -> affects kinetic energy)
  - **Quantifying the Net Rate of Diffusion in Fluids**
    - Affected by:
      - Solubility of the gas in the fluid: greater solubility -> greater number of molecules available to diffuse
      - Cross-sectional area of the fluid: greater cross-section -> greater total molecules diffuse
      - Distance the gas diffuse across: greater distance -> longer it will take for molecule to diffuse
      - Molecular weight of the gas: inversely proportional to velocity of kinetic movement -> greater velocity -> greater diffusion
      - Temperature of the Fluid: reasonably constant, not considered

\[
D \propto \frac{\Delta P \times A \times S}{d \times \sqrt{MW}}
\]

- **Diffusion Coefficient of the Gas** = \(\frac{S}{\sqrt{MW}}\)

- **Diffusion of Gases Through Tissues**: important gases all highly soluble in cell membranes; limitation to movement of gases is rate at which they can diffuse through tissue water -> diffusion of gases through tissues is almost equal to \(D\) (as calculated above)

• **Composition of Alveolar Air and Atmospheric Air Are Different**
  - Alveolar air is only partially replaced by atmospheric air at each breath
  - Oxygen is constantly absorbed into pulmonary blood from alveolar air
  - Carbon dioxide is constantly diffusing from pulmonary blood into alveoli
  - Dry atmospheric air is humidified in respiratory passages prior to reaching alveoli
  - Humidification of the Air in the Respiratory Passages: totally humidified (adding water to atmospheric air) prior to reaching alveoli
  - **Rate at Which Alveolar Air is Renewed by Atmospheric Air**: only 1/7th of alveolar air is replaced by atmospheric air with each breath -> multiple breaths required to exchange most of the alveolar air
  - **Importance of Slow Replacement of Air**: slow replacement prevents sudden changes in gas concentrations in the blood, making the respiratory control mechanism more stable
  - **Oxygen Concentration and Partial Pressure in the Alveoli**: [O₂] in alveoli (and PO₂) controlled by rate of absorption of O₂ into the blood AND rate of entry of new O₂ into the lungs; increased ventilation can never increase PO₂ over the PO₂ of atmospheric air
  - **Carbon Dioxide Concentration and Partial Pressure in the Alveoli**: CO₂ is continually formed in the body and carried to alveoli AND is continually removed from alveoli by ventilation; alveolar PCO₂ increases as rate of CO₂ excretion increases; alveolar PCO₂ decreases as alveolar ventilation increases
  - **Expired Air is a Combination of Dead Space Air and Alveolar Air**: composition of expired air determined by amount of expired air that is dead space air VS amount that is alveolar air

• **Diffusion of Gases Through the Respiratory Membrane**
  - **Respiratory Unit**: Flow of blood in alveolar wall is thin due to extensive capillary plexus, reducing diffusion
distance; diffusion occurs throughout terminal portions of lungs (not just in alveoli) -> form respiratory (AKA pulmonary) membrane

- **Respiratory Membrane:** 70sq m in normal adult human male -> large surface area and close contact with pulmonary capillary membrane -> rapid diffusion

- **Factors That Affect the Rate of Gas Diffusion Through the Respiratory Membrane**
  - Thickness of the membrane: inversely proportional to rate of diffusion, increases in cases of edema and pulmonary diseases causing fibrosis -> slows gas diffusion
  - Surface area of the membrane: decreases in cases of lung removal, emphysema (alveoli coalesce); 25% impairment can impede diffusion in resting conditions
  - Diffusion coefficient of the gas: inversely proportional to molecular weight of gas
  - Partial pressure difference between 2 sides of membrane: increased diffusion as difference increases

- **Diffusing Capacity of the Respiratory Membrane**
  - Volume of gas that will diffuse through membrane each minute for a partial pressure difference of 1mm Hg
  - **Diffusing Capacity for Oxygen:** diffusing capacity (230mL/min) approximately equals rate at which resting body uses oxygen
  - **Increasing Oxygen Diffusing Capacity During Exercise:** increased pulmonary blood flow and alveolar ventilation increases diffusing capacity by opening up previously dormant pulmonary capillaries or extra dilation of open capillaries (increases surface area) AND better matching the ventilation-perfusion ratio -> during exercise, oxygenation of the blood increases by alveolar ventilation AND greater diffusing capacity of the respiratory membrane
  - **Diffusing Capacity for Carbon Dioxide:** never directly measured because it diffuses too rapidly to cause measurable differences in PCO2 on each side of the membrane
  - **Measurement of Diffusing Capacity - Carbon Monoxide Method:** physiologists measure CO (with PCO2 being 0 in the blood b/c it binds to hemoglobin instantly and use it to calculate diffusing capacity and calculate diffusing capacity for carbon dioxide and oxygen

**Effect of Ventilation-Perfusion Ratio on Alveolar Gas Concentration**

- **Alveolar Oxygen and Carbon Dioxide Partial Pressure When Va/Q = 0**
  - Va (alveolar ventilation) is 0, but Q (perfusion of alveolus, AKA capillary blood flow) exists -> alveolus equilibrates with blood oxygen and carbon dioxide -> blood flow exists, but no ventilation

- **Alveolar Oxygen and Carbon Dioxide Partial Pressure When Va/Q = infinity**
  - No capillary blood flow -> alveolar gases equilibrate with humidified inspired air -> no blood flow exists AND no ventilation

- **Gas Exchange and Alveolar Partial Pressures When Va/Q is Normal**
  - Normal alveolar ventilation and normal alveolar capillary blood flow -> oxygen and carbon dioxide exchange through respiratory membrane is nearly optimal

- **PO2-PCO2, Va/Q Diagram (Figure 39-11)**

- **Concept of Physiologic Shunt when Va/Q is Below Normal**
  - Shunted blood: fraction of venous blood through pulmonary capillaries does not become oxygenated
  - Physiologic shunt: Shunted blood AND blood through bronchial vessels (versus pulmonary capillaries)

\[
\frac{Q_{PS}}{QT} = \frac{C_{iO2} - C_{aO2}}{C_{iO2} - C_{VO2}}.
\]

- Greater shunt -> greater amount of blood that fails to be oxygenated as it passes through lungs

- **Concept of Physiologic Shunt when Va/Q is Above Normal**
  - Ventilation of alveoli is great, but blood flow is low -> more oxygen is available than can be transported away by the flowing blood -> ventilation in these alveolar is “wasted” AND anatomical dead space in respiratory passages is wasted (sum of two wasted spaces is physiologic dead space
\[
\frac{V_{D_{phys}}}{VT} = \frac{PaCO_2 - PeCO_2}{PaCO_2},
\]
where \(V_{D_{phys}}\) = physiologic dead space, \(VT\) = tidal volume, \(PaCO_2\) = partial pressure of carbon dioxide in the arterial blood, \(PeCO_2\) = average partial pressure of carbon dioxide in expired air

- Great physiologic dead space -> work of ventilation is wasted b/c ventilating air never reaches blood

- Abnormalities of Ventilation-Perfusion Ratio
  - Abnormal \(Va/Q\) in the Upper and Lower Normal Lung: at top of lung, \(Va/Q\) is 2.5x ideal value = physiologic dead space; at bottom of lung, \(Va/Q\) is 0.6x ideal = physiologic shunt; decrease the lungs effectiveness; during exercise, blood flow to upper lung increases and effectiveness approaches optimum
  - Abnormal \(Va/Q\) in Chronic Obstructive Lung Disease: smokers develop bronchial obstruction -> serious alveolar air trapping -> emphysema -> alveolar walls are destroyed; abnormal \(Va/Q\) because alveoli beyond obstructions are unventilated AND alveoli coalescence causes ventilation to be wasted b/c of inadequate blood flow to transport blood gases -> some areas of lung exhibit physiologic shunt AND some areas exhibit physiologic dead space -> effectiveness of lungs is reduced