Chapter 17 The Respiratory System: Gas Exchange and Regulation of Breathing

Chapter Outline

- Overview of Pulmonary Circulation
  - Diffusion of Gases
  - Exchange of Oxygen and Carbon Dioxide
  - Transport of Gases in the Blood
  - Central Regulation of Ventilation
  - Control of Ventilation by Chemoreceptors
  - Local Regulation of Ventilation and Perfusion
  - Respiratory System in Acid-Base Homeostasis

17.1 Overview of the Pulmonary Circulation

- Arterial blood $O_2$ and $CO_2$ levels remain relatively constant
  - Oxygen moves from alveoli to blood at same rate it is consumed by cells
  - Carbon dioxide moves from blood to alveoli at same rate it is produced by cells

17.2 Diffusion of Gases

- The driving force of diffusion across the respiratory membrane is the concentration gradients
- Factors that affect gradients:
  - Partial pressures of gases
  - Solubility of gases in liquids

- **Partial Pressure**
  - Many gases are mixtures of different molecules.
  - Partial pressure of a gas = proportion of pressure of entire gas that is due to presence of the individual gas.
  - Partial pressure of a gas is determined by
    - Fractional concentration
    - Total pressure of the gas mixture

- **Partial Pressure of Gases and Dalton’s Law**
  - Boyle’s Law (Ideal gas law)
    - Pressure (P) of gas depends on temperature (T), number of gas molecules (n), universal gas constant (R) and volume (V)
    - $PV = nRT$
    - $P = nRT / V$
    - If T, R and V are constant, then P is directly proportional to $n$
  - **Dalton’s Law** = Total Pressure of a gas mixture is the sum of the pressures of all gases present in the mixture.
    - $P_{total} = P_1 + P_2 + P_3 + ... P_n$
    - Total pressure of any individual one gas in a gas mixture is calculated by
      - $P_{one \ gas} = \% \ one \ gas \times P_{total}$

- **Gas Composition of Air**
  - 79% Nitrogen
  - 21% Oxygen
Trace amounts carbon dioxide, helium, argon, etc.
Water can be a factor depending on humidity

- **Gas Pressure of Dry Air**
  - $P_{\text{air}} = 760$ mm Hg = $P_{N_2} + P_{O_2}$
  - $P_{N_2} = 0.79 \times 760$ mm Hg = 600 mm Hg
  - $P_{O_2} = 0.21 \times 760$ mm Hg = 160 mm Hg
  - Air is only 0.03% carbon dioxide
  - $P_{CO_2} = 0.0003 \times 760$ mm Hg = 0.23 mm Hg

- **Pressure of Air at 100% Humidity**
  - $P_{\text{air}} = 760$ mm Hg = $P_{N_2} + P_{O_2} + P_{H_2O}$
  - $P_{N_2} = 0.741 \times 760$ mm Hg = 563 mm Hg
  - $P_{O_2} = 0.196 \times 760$ mm Hg = 149 mm Hg
  - $P_{H_2O} = 0.062 \times 760$ mm Hg = 47 mm Hg
  - $P_{CO_2} = 0.00027 \times 760$ mm Hg = 0.21 mm Hg

- **Solubility of Gases in Liquids**
  - Gas molecules can exist in gas form or dissolved in liquid
  - Ability to dissolve depends on properties of gas and properties of liquid
  - Both vaporized and dissolved gases exert partial pressures

- **Henry's Law**
  - $c = kP$
  - $c$ = molar concentration of dissolved gas
  - $k$ = Henry's Law constant
  - $P$ = partial pressure of gas in atmospheres
    - The partial pressure of a gas affects the amount of gas that goes into solution
    - Partial pressures of vaporized and dissolved gases will be equal at equilibrium

- **Oxygen and Carbon Dioxide Solubility**
  - At 100 mm Hg partial pressure in water
  - $[O_2]$ in water = 0.15 mmoles/liter
  - $[CO_2]$ in water = 3.0 mmoles/liter
  - Carbon dioxide is more soluble than oxygen in water (and blood)

17.3 Exchange of Oxygen and Carbon Dioxide

- Gas exchange in the lungs
- Gas exchange in respiring tissue
- Determinants of alveolar $P_{O_2}$ and $P_{CO_2}$

- **Diffusion of Gases**
  - Gases diffuse down pressure gradients from high pressure $\rightarrow$ low pressure
  - In gas mixtures, a particular gas diffuses down its own partial pressure gradient
    - High partial pressure $\rightarrow$ low partial pressure
    - Presence of other gases irrelevant

- **Diffusion in Lungs**
  - Diffusion between alveoli and blood is rapid
    - Small diffusion barrier
    - Large surface area
    - Gases diffuse down partial pressure gradients in respiring tissue
Determinants of Alveolar $P_{O_2}$ and $P_{CO_2}$
- Factors affecting alveolar partial pressures
  - $P_{O_2}$ and $P_{CO_2}$ of inspired air
  - Minute alveolar ventilation
  - Rates at which respiring tissue use O$_2$ and produce CO$_2$
- Most critical is rate of alveolar ventilation relative to rate of oxygen use and carbon dioxide production

Table 17.2 Some Terms Used in Respiratory Physiology

17.4 Transport of Gases in Blood
- Oxygen
- Carbon dioxide

I. Oxygen Transport in the Blood
- Oxygen not very soluble in plasma
  - Thus only 3.0 mL/200 ml arterial blood oxygen dissolved in plasma (1.5%)  
- 98.5 % arterial blood oxygen is transported by hemoglobin
  \[ Hb + O_2 \leftrightarrow Hb\cdot O_2 \]
  - Hb = deoxyhemoglobin
  - Hb\cdot O$_2$ = oxyhemoglobin

- Oxyhemoglobin and Deoxyhemoglobin
- Saturation of Hemoglobin
  - Saturation of hemoglobin is a measure of how much oxygen is bound to hemoglobin
  - Binding of oxygen to hemoglobin follows law of mass action
    - More oxygen $\rightarrow$ more binds to hemoglobin
  - Non-linear relationship: Positive cooperativity

- Saturation of Hemoglobin with O$_2$ (Figure 17.7)
- Oxygen-Carrying Capacity of Blood
  - When 100% saturated, 1 gram hemoglobin carries 1.34 mL oxygen
  - Normal blood hemoglobin levels = 12–17 gm/dL
  - Oxygen-carrying capacity of hemoglobin in blood = 200 mL oxygen per liter blood

- Oxygen Dissociation Curve (Figure 17.8)
- Effects of O$_2$ Affinity Changes (Figure 17.9)
  - $\uparrow$ affinity = Less oxygen unloaded

- Temperature Effects: O$_2$ Saturation (Figure 19.10 a)
  - Higher temperature
    - Active tissues
    - Curve shifts right
    - More O$_2$ unloading in tissues
    - More O$_2$ delivery to tissues

- pH Effects: O$_2$ Saturation (Figure 17.b)
  - Bohr effect: Lower pH increases O$_2$ unloading
  - Active tissues
    - Produce more acid pH decreases in tissues
- Decreased pH causes shift right in saturation curve
- More O₂ is unloaded to tissues

**Effects of CO₂ — Carbamino Effect**
- Carbon dioxide reacts with hemoglobin to form carbaminohemoglobin
  - Hb + CO₂ ↔ HbCO₂
- Carbon dioxide binds amino acids in a hemoglobin
- HbCO₂ has lower affinity for oxygen than Hb
- Increased metabolic activity → increases CO₂
- Increases oxygen unloading in active tissue

**Effect of 2,3-DPG**
- 2,3-DPG = 2,3-diphosphoglycerate
  - Produced in red blood cells under conditions of low oxygen such as anemia and high altitude
  - Synthesis inhibited by oxyhemoglobin
- 2,3-DPG decreases affinity of hemoglobin for oxygen enhancing oxygen unloading

**Carbon Monoxide**
- Hemoglobin has greater affinity for carbon monoxide (CO) than for oxygen
- Prevents oxygen from binding to hemoglobin
- Carbon monoxide poisoning

II. Carbon dioxide Transport in the Blood

- **Table 17.3 Carbon Dioxide Transport in Blood**
  - Most carbon dioxide is dissolved as bicarbonate.

- **Carbonic Anhydrase (CA):** Enzyme that converts carbon dioxide and water to carbonic acid
  - CA
  - \( \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \)
  - Law of Mass Action: An increase in CO₂ causes an increase in bicarbonate and hydrogen ions

- **CO₂ Exchange: Tissues (Figure 17.11)**
  - **Chloride shift : CO₂ Exchange: Lungs**

- **PO₂ Effect on CO₂ Transport (Figure 17.12)**
  - Increased PO₂ in blood decreases the affinity of Hb for carbon dioxide (Haldance effect)

- **Tissues: CO₂ Loading/O₂ Unloading (Figure 17.13 a)**
- **Lungs: CO₂ Loading/O₂ Unloading (Figure 17.13b)**

17. 5 Central Regulation of Ventilation

- Voluntary control by motor neurons
- Involuntary control by autonomic neurons (most of time)
- The mechanism of the central control is not well understood

**Neural Control of Breathing**
- Respiratory muscles = skeletal muscles are controlled by motor neurons
Inspiration:
- Phrenic nerve → diaphragm
- External intercostal nerve → external intercostal muscles

Expiration:
- Internal intercostal nerve → internal intercostal muscles

• Components that Generate the Breathing Rhythm (Figure 17.15)
  - Respiratory control centers
    - medulla
    - pons
    - Two types of neurons
      - inspiratory
      - expiratory

• Neurons
  - Inspiratory neurons: Depolarize during inspiration followed by a termination of at the end of inspiration
  - Expiratory neurons: Depolarize during expiration
  - Mixed neurons: Have properties of both inspiratory and expiratory neurons

• Activity of Inspiratory Neurons

• Output to Motor Neurons
  - Inspiratory neurons hypothesized to control motor neurons to inspiratory muscles
  - Expiratory neurons hypothesized to control motor neurons to expiratory muscles and/or inhibit inspiratory neurons

• Central Pattern Generator (CPG)
  - Is a network of neurons that generates the respiratory rhythm or cycle
  - Location and mechanism of action unknown (most likely in medulla).
  - Two hypotheses
    - CPGs have pacemaker activity
    - The neuron network generates rhythm

• Model of Quiet Breathing (Figure 17.17)

17.6 Control of Ventilation by Chemoreceptors
- Chemoreceptors detect blood levels of O₂ and CO₂
  - Two types of chemoreceptors
    - Peripheral chemoreceptors
    - Central chemoreceptors

• Peripheral Chemoreceptors (Figure 17.8)
  - Located in carotid bodies near carotid sinus
  - Direct contact with arterial blood
  - Respond mainly to changes in blood pH

• Ventilation Effects of P₀₂ (Figure 17.9)
  - Little effect before dropping less than 60 mmHg
  - Low P₀₂ ↑ the sensitivity of the peripheral chemoreceptors to carbon dioxide

• Ventilation Effects of P₇⁰₂ (Figure 17.9)
  - ↑ P₇⁰₂ has large effects on minute ventilation
• Central Chemoreceptors (Figure 17.20)
  • Located ventral surface of medulla
    o Respond to changes in pH of the cerebrospinal fluid (CSF)
    o Not directly responsive to CO₂
    o Responds indirectly to CO₂ via pH
    o Not responsive to changes in [O₂]
• Chemoreceptor Reflexes (Figure 17.21)
  • The effects of hypoventilation and hyperventilation on minute ventilation (Figure 17.22)

17.7 Local Regulation of Ventilation and Perfusion (Figure 17.24)
• Ventilation-perfusion ratios
  o Ventilation = rate of air flow
  o Perfusion = rate of blood flow
• Local control of ventilation and perfusion
• Ventilation-Perfusion Ratios (Figure 17.23)
  o Local ventilation and perfusion are regulated to match
  o Ventilation-perfusion ratio = \( \frac{V_{A}}{Q} = 1 \) (normal lung)
• Mechanisms of Matching Ventilation to Perfusion
  o If ventilation to certain alveoli decreases
    ▪ Increased \( P_{CO₂} \) and decreased \( P_{O₂} \) in blood and air
    ▪ Increased \( P_{CO₂} \) in bronchioles \( \rightarrow \) bronchodilation
    ▪ Decreased \( P_{O₂} \) in P. Arterioles \( \rightarrow \) vasoconstriction
  o If perfusion to certain alveoli decreases
    ▪ Increased \( P_{O₂} \) and decreased \( P_{CO₂} \) in blood and air
    ▪ Increased \( P_{O₂} \) in P. Arterioles \( \rightarrow \) vasodilation
    ▪ Decreased \( P_{CO₂} \) in bronchioles \( \rightarrow \) bronchoconstriction
• Local Control of Ventilation and Perfusion
  o Figure 17.24
  o Table 17.4

17.8 The Respiratory System in Acid-Base Homeostasis
• Normal blood pH = 7.4 (range 7.3 – 7.42)
• Respiratory and renal systems regulate blood pH
  o Hemoglobin functions as a buffer
    ▪ Deoxyhemoglobin has greater affinity for H⁺
      \( Hb + H^+ \leftrightarrow HbH \)
    ▪ Bicarbonate ions as a buffer
      \( HCO₃^- + H^+ \leftrightarrow H₂CO₃ \leftrightarrow CO₂ + H₂O \)
• Respiratory system can regulate pH by regulating CO₂ levels