Physiology of Respiratory System

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3rd year\ Lecture 4

Systemic Gas Exchange

- Systemic gas exchange—the unloading of O_2 and loading of CO_2 at the systemic capillaries

- CO_2 loading
  - CO_2 diffuses into the blood
  - Carbonic anhydrase in RBC catalyzes
    - $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
  - Chloride shift
    - Keeps reaction proceeding, exchanges HCO_3^- for Cl^-
    - H^+ binds to hemoglobin

Systemic Gas Exchange

- Oxygen unloading
  - H^+ binding to HbO_2 reduces its affinity for O_2
    - Tends to make hemoglobin release oxygen
    - HbO_2 arrives at systemic capillaries 97% saturated, leaves 75% saturated
      - Venous reserve: oxygen remaining in the blood after it passes through the capillary beds
  - Utilization coefficient: given up 22% of its oxygen load

Systemic Gas Exchange

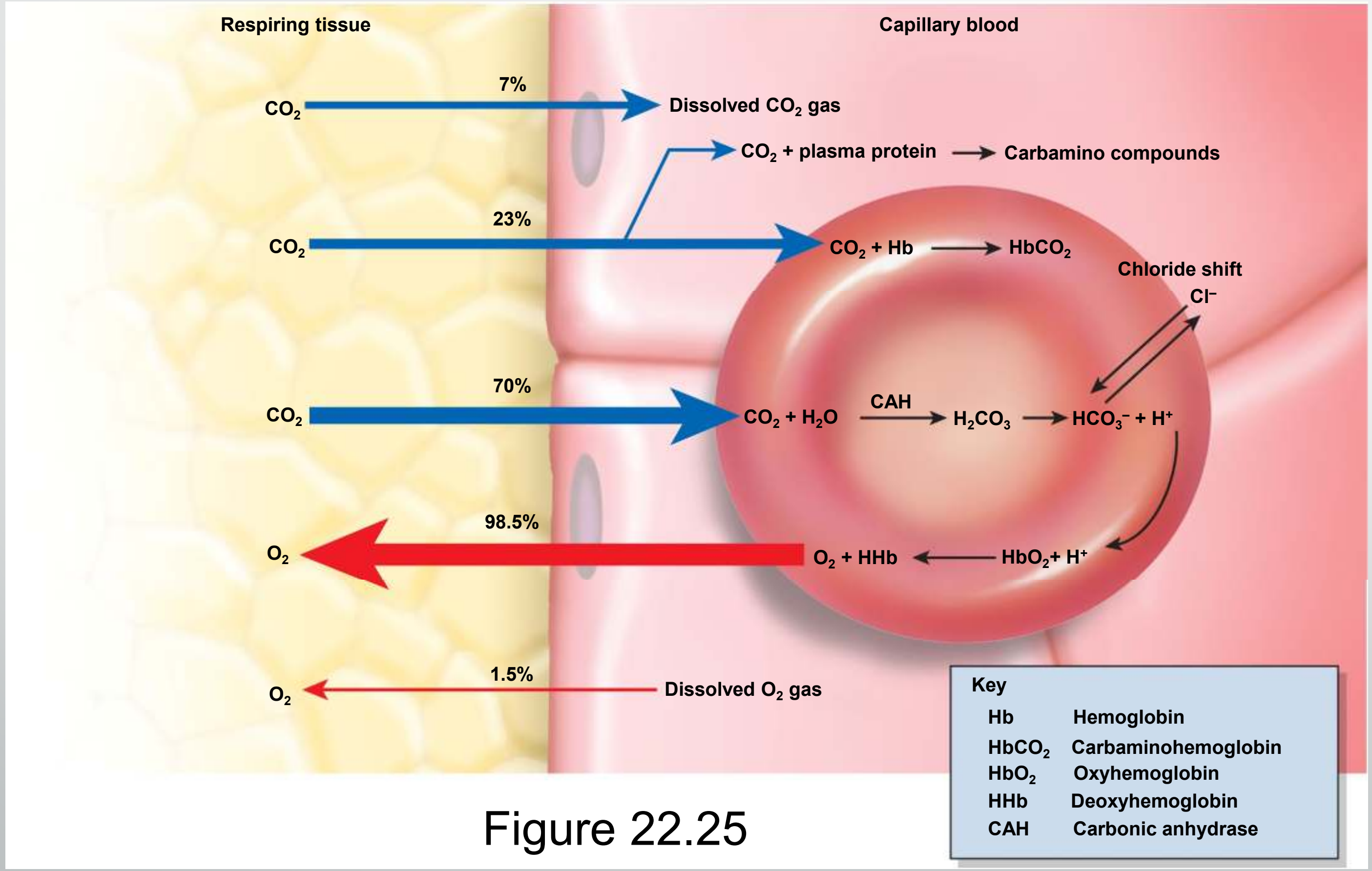


Figure 22.25

Alveolar Gas Exchange Revisited

- Reactions that occur in the lungs are reverse of systemic gas exchange

- CO_2 unloading
  - As Hb loads O_2 its affinity for H^+ decreases, H^+ dissociates from Hb and binds with HCO_3^-
    - $CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$
  - Reverse chloride shift
    - HCO_3^- diffuses back into RBC in exchange for Cl^-, free CO_2 generated diffuses into alveolus to be exhaled

Alveolar Gas Exchange

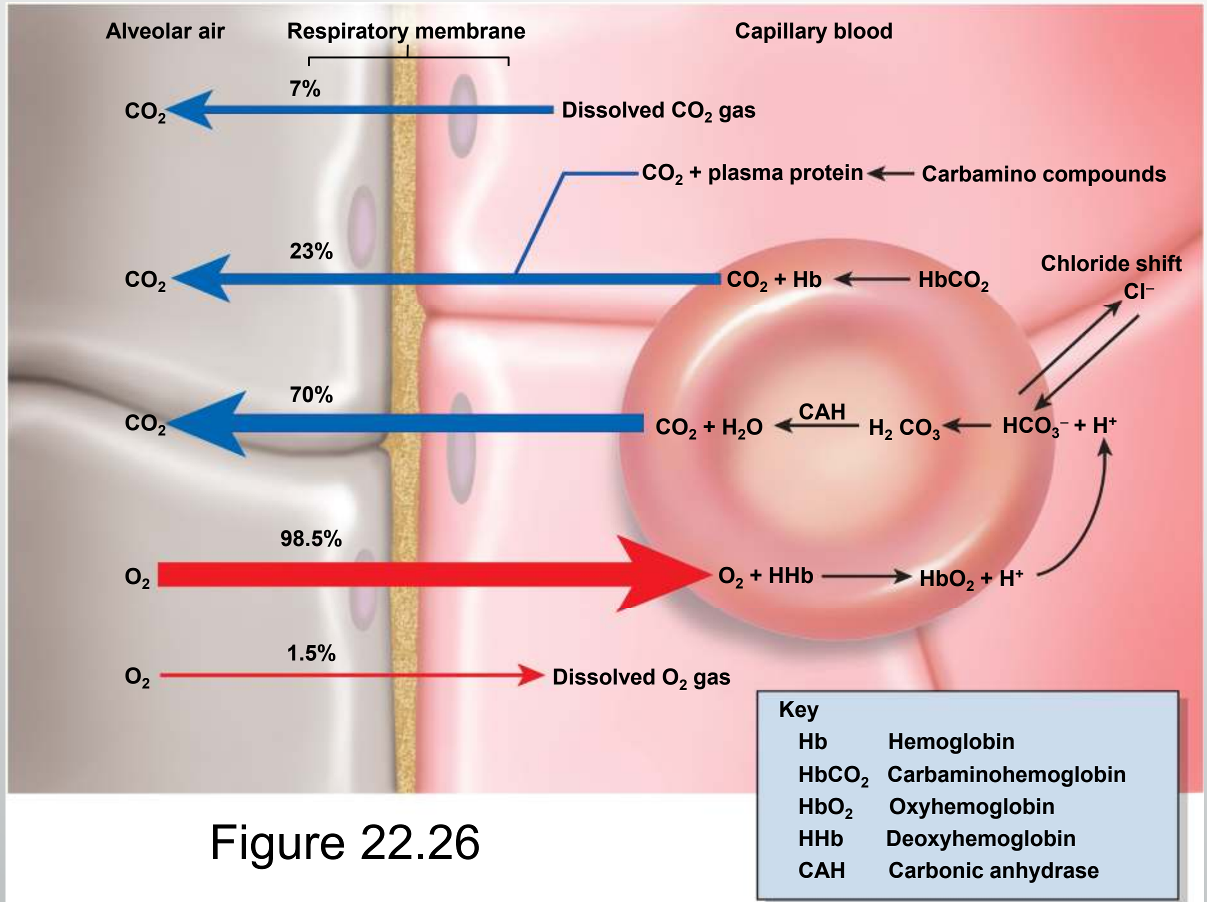


Figure 22.26

Adjustment to the Metabolic Needs of Individual Tissues

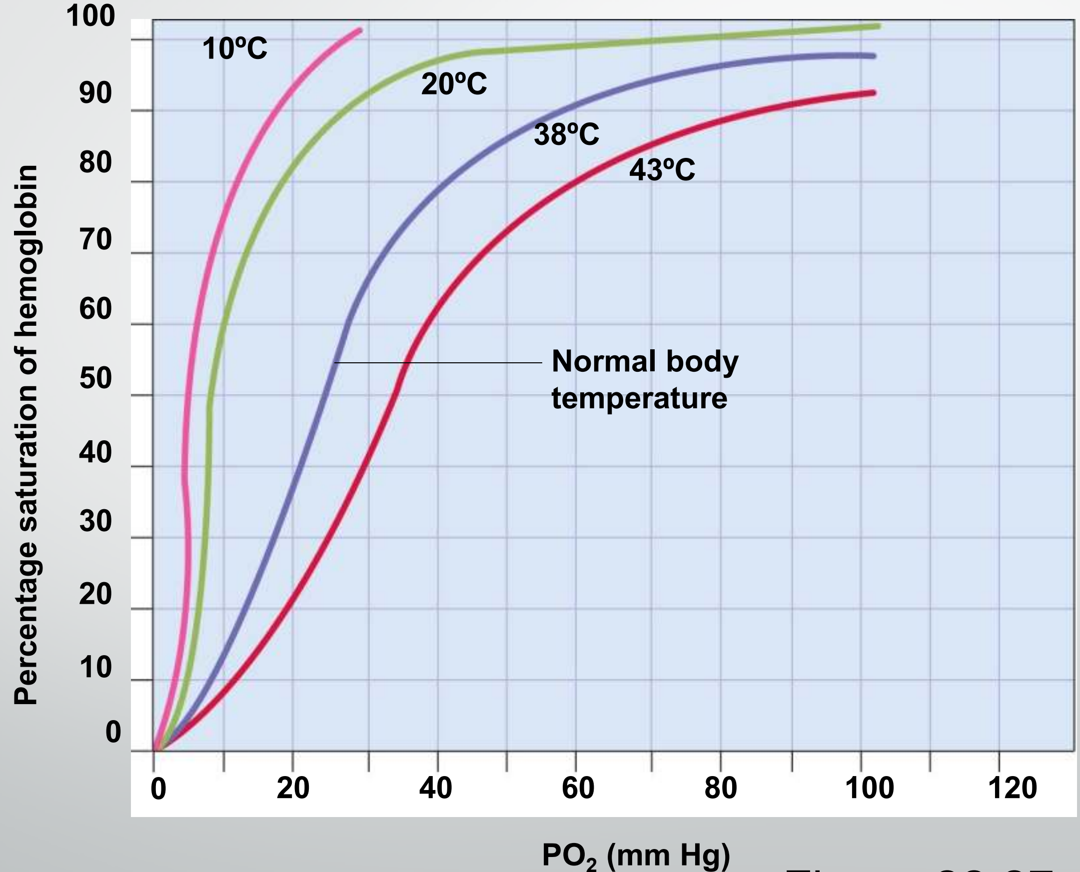
- Hemoglobin unloads O_2 to match metabolic needs of different states of activity of the tissues
- Four factors that adjust the rate of oxygen unloading
  - Ambient PO_2
    - Active tissue has ↓ PO_2; O_2 is released from Hb
  - Temperature
    - Active tissue has ↑ temp; promotes O_2 unloading

Adjustment to the Metabolic Needs of Individual Tissues

Cont.

- Bohr effect
  - Active tissue has ↑ CO_2, which lowers pH of blood; promoting O_2 unloading
- Bisphosphoglycerate (BPG)
  - RBCs produce BPG which binds to Hb; O_2 is unloaded
  - Haldane effect—rate of CO_2 loading is also adjusted to varying needs of the tissues, low level of oxyhemoglobin enables the blood to transport more CO_2
  - ↑ body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and cause O_2 unloading
  - ↑ metabolic rate requires ↑ oxygen

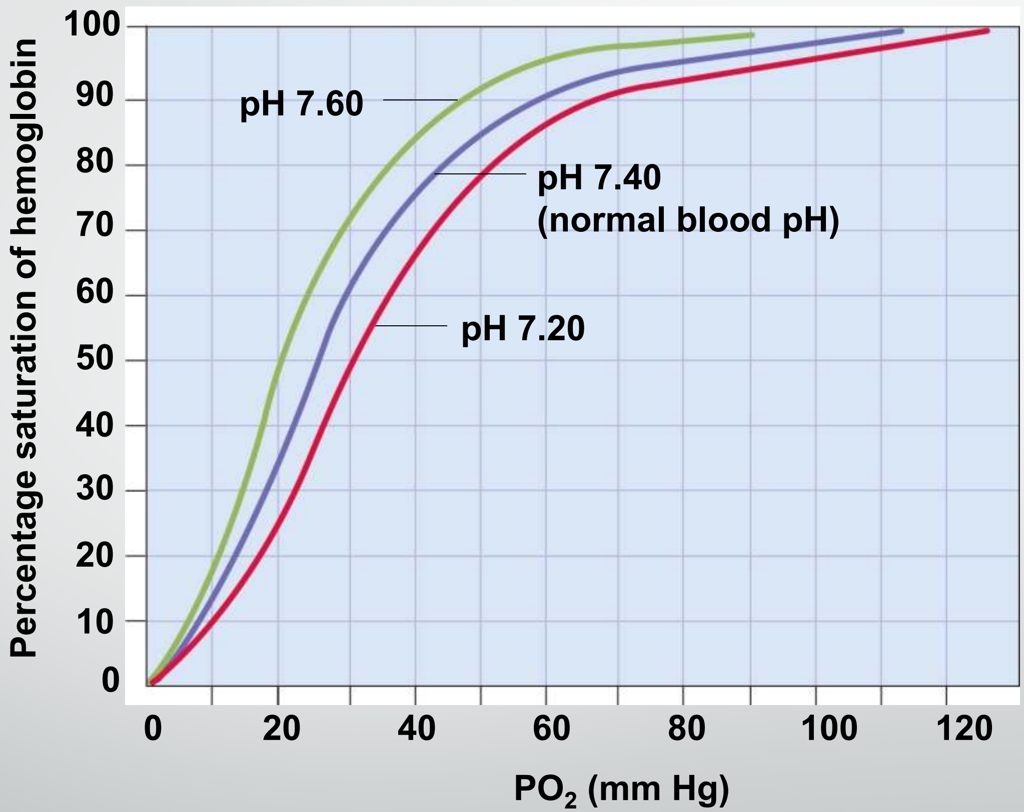
Effects of Temperature and pH on Oxyhemoglobin Dissociation



(a) Effect of temperature

Figure 22.27a

Effects of Temperature and pH on Oxyhemoglobin Dissociation



(b) Effect of pH

Figure 22.27b

Bohr effect: release of O_2 in response to low pH

Blood Gases and the Respiratory Rhythm

- Rate and depth of breathing adjust to maintain levels of:
  - pH 7.35 to 7.45
  - P_{CO_2} 40 mm Hg
  - P_{O_2} 95 mm Hg
- Brainstem respiratory centers receive input from central and peripheral chemoreceptors that monitor the composition of blood and CSF
- Most potent stimulus for breathing is pH, followed by CO_2, and least significant is O_2

Hydrogen Ions

- Pulmonary ventilation is adjusted to maintain pH of the brain
  - Central chemoreceptors in the medulla oblongata produce about 75% of the change in respiration induced by pH shift
  - H^+ does not cross the blood–brain barrier very easily

Hydrogen Ions

Cont.

- CO_2 does cross, and once in CSF it reacts with water and produces carbonic acid
  - Dissociates into bicarbonate and hydrogen ions
  - Most H^+ remains free and greatly stimulates the central chemoreceptors
- Hydrogen ions are also a potent stimulus to the peripheral chemoreceptors which produce about 25% of the respiratory response to pH change

Hydrogen Ions

- Acidosis—blood pH lower than 7.35
- Alkalosis—blood pH higher than 7.45
- Hypocapnia—PCO_2 less than 37 mm Hg (normal 37 to 43 mm Hg)
    - Most common cause of alkalosis
- Hypercapnia—PCO_2 greater than 43 mm Hg
    - Most common cause of acidosis

Hydrogen Ions

- Respiratory acidosis and respiratory alkalosis—pH imbalances resulting from a mismatch between the rate of pulmonary ventilation and the rate of CO_2 production
- Hyperventilation is a corrective homeostatic response to acidosis
  - "Blowing off" CO_2 faster than the body produces it
  - Pushes reaction to the left:
    CO_2 (expired) + $H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + \downarrow H^+$
  - Reduces H^+ (reduces acid), raises blood pH toward normal

Hydrogen Ions

- Hypoventilation is a corrective homeostatic response to alkalosis
  - Allows CO_2 to accumulate in the body fluids faster than we exhale it
  - Shifts reaction to the right:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$

  - Raising the H^+ concentration, lowering pH to normal

Hydrogen Ions

- Ketoacidosis—acidosis brought about by rapid fat oxidation releasing acidic ketone bodies (diabetes mellitus)
  - Induces Kussmaul respiration: hyperventilation cannot remove ketone bodies, but blowing off CO_2, it reduces the CO_2 concentration and compensates for the ketone bodies to some degree

Carbon Dioxide

- Indirect effects on respiration
  - Through pH, as seen previously
- Direct effects
  - ↑ CO_2 at beginning of exercise may directly stimulate peripheral chemoreceptors and trigger ↑ ventilation more quickly than central chemoreceptors

Oxygen

- PO_2 usually has little effect on respiration
- Chronic hypoxemia, PO_2 less than 60 mm Hg, can significantly stimulate ventilation
  - Hypoxic drive: respiration driven more by low PO_2 than by CO_2 or pH
  - Emphysema, pneumonia
  - High elevations after several days

Respiration and Exercise

- Causes of increased respiration during exercise
  - When the brain sends motor commands to the muscles
    - It also sends this information to the respiratory centers
    - They increase pulmonary ventilation in anticipation of the needs of the exercising muscles
  - Exercise stimulates proprioceptors of the muscles and joints
    - They transmit excitatory signals to the brainstem respiratory centers
    - Increase breathing because they are informed that the muscles have been told to move or are actually moving
    - Increase in pulmonary ventilation keeps blood gas values at their normal levels in spite of the elevated O_2 consumption and CO_2 generation by the muscles

Respiratory Disorders

- Expected Learning Outcomes
  - Describe the forms and effects of oxygen deficiency and oxygen excess.
  - Describe the chronic obstructive pulmonary diseases and their consequences.
  - Explain how lung cancer begins, progresses, and exerts its lethal effects.

Oxygen Imbalances

- Hypoxia—a deficiency of oxygen in a tissue or the inability to use oxygen
  - A consequence of respiratory diseases
- Hypoxemic hypoxia—state of low arterial PO_2
  - Usually due to inadequate pulmonary gas exchange
  - Oxygen deficiency at high elevations, impaired ventilation: drowning, aspiration of a foreign body, respiratory arrest, degenerative lung diseases
- Ischemic hypoxia—inadequate circulation of blood
  - Congestive heart failure

Oxygen Imbalances

- Anemic hypoxia—due to anemia resulting from the inability of the blood to carry adequate oxygen
- Histotoxic hypoxia—metabolic poisons such as cyanide prevent the tissues from using oxygen delivered to them
- Cyanosis—blueness of the skin
  - Sign of hypoxia

Oxygen Imbalances

- Oxygen toxicity—pure O_2 breathed at 2.5 atm or greater
  - Safe to breathe 100% oxygen at 1 atm for a few hours
  - Generates free radicals and H_2O_2
  - Destroys enzymes
  - Damages nervous tissue
  - Leads to seizures, coma, death
- Hyperbaric oxygen
  - Formerly used to treat premature infants, caused retinal damage, was discontinued