Respiratory Regulation and Respiratory Disease

Regulation of Respiration

- Nervous system regulation
  - Various levels of activity produce different demands
  - Medulla
  - Regulation of respiratory rate
    - PaCO₂ normal range 35-45 mmHg

Regulation of Respiration

- Nervous system regulation
  - Hyperventilation: increased depth and rate of breathing that exceeds the body’s need to remove CO₂
    - Causes CO₂ levels to decline (hypocapnia)
    - pH increases (alkalosis)
  - Hypoventilation: decreased rate and depth of breathing
    - Causes CO₂ levels to increase (hypercapnia)
    - pH decreases (acidosis)

Regulation of Respiration

- Nervous system regulation
  - Medullary control center
    - Diffuse system of neurons
      - Separate pathways for inspiration and expiration

Regulation of Respiration

- Nervous system regulation
  - Higher brain centers
    - Cerebral cortex
      - Direct signals from the cerebral motor cortex bypass medullary controls
      - Example: voluntary breath holding
    - Hypothalamus
      - Limbic system can modify rate and depth of respiration
      - Examples: breath holding that occurs in anger or gasping with pain, laughing, crying
Regulation of Respiration

• Chemoreceptors
  — Central
  • pCO₂ most potent stimuli
    \[ \uparrow \text{pCO}_2 \text{ (hypercapnia)} \]
    \[ \downarrow \text{pCO}_2 \text{ in the brain} \]
    central chemoreceptor in the medulla stimulated
    \[ \uparrow \text{respiratory rate} \]

• Note that pO₂ has no effect here

Regulation of Respiration

• Nervous system control
  — Peripheral chemoreceptors
  • Carotid and aortic bodies
    \[ \uparrow \text{CO}_2 \text{ levels are the most powerful respiratory stimulant} \]
    • Also respond to \( \downarrow \text{pO}_2 \) and pH

Regulation of Respiration

• High altitude
  — Quick travel to altitudes above 8000 feet may produce symptoms of acute mountain sickness (AMS)
    - Headaches, shortness of breath, nausea and dizziness
    - In severe cases, lethal cerebral and pulmonary edema

Regulation of Respiration

• High altitude
  — \( \text{pO}_2 \leq 60 \text{ mm Hg} \) = major stimulus for respiration
    • Peripheral chemoreceptors sense low \( \text{O}_2 \) = increase respiration rate
      — Hyperventilate \( \rightarrow \) respiratory alkalosis
Regulation of Respiration

- Chronic CO$_2$ retention disorders
  - CSF buffers reduce central chemoreceptor control
  - Rely on paO$_2$
  - Excessive O$_2$ administration = apnea!
  - Example: emphysema

- Exercise
  - Intensity and duration
  - Hyperpnea – increase in depth of breathing
    - Increase in ventilation (10 to 20 fold) in response to metabolic needs
    - Depth of respiration increases more than rate
    - pCO$_2$, pO$_2$, and pH remain surprisingly constant during exercise
      - pCO$_2$ may decrease

- Neural factors cause increase in ventilation as exercise begins
  - Psychological stimuli
    - Anticipation of exercise
      - Simultaneous cortical motor activation of skeletal muscles and respiratory centers
      - Excitatory impulses reaching respiratory centers from proprioceptors

Respiratory Diseases

- COPD
  - Emphysema
  - Asthma
- Pneumonia
- Tuberculosis
- Lung cancer
- Cystic fibrosis
- Smoking
COPD
- Chronic obstructive pulmonary disease (COPD)
- End-stage condition of patients with 2 or more of:
  - Emphysema
  - Asthma
  - Chronic bronchitis

Irreversible decrease in the ability to force air out of the lungs

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COPD
- History of smoking in 80% of patients
- Symptoms
  - Dyspnea
    - Labored breathing (“air hunger”)
  - Coughing
  - Frequent pulmonary infections
  - Respiratory failure (hypoventilation) accompanied by respiratory acidosis

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Peak Flow Meter
Used to assess rate of exhalation in obstructive lung disease

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Emphysema
- Word literally means “inflation”
- Destruction of alveolar walls
  - Leads to large but inelastic alveolar spaces
- Consequences
  1. Must work hard during expiration (enlist accessory muscles)
  2. Bronchioles collapse during expiration (CO₂ trapping)
  3. Pulmonary capillaries damaged → increased pulmonary resistance → decreased blood flow to lung → right ventricular systolic dysfunction

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Emphysema
- Almost exclusively associated with smoking
  - Exception: pre-term infants
- Smoking inhibits production of alpha-antitrypsin which normally stabilizes lysosomes of alveolar macrophages
- Without it, lysosomes rupture and release destructive enzymes
Asthma

- "To pant"
- Active airway inflammation
  - Immune response caused by production of IgE and recruitment of inflammatory cells
- Smooth muscle spasms of bronchioles → reduced air flow
- Often associated with bronchiolar edema
  - Increased wall thickness = impaired diffusion

Asthma

- Affects 1/10 in USA
- More common in children
- Triggers
  - Allergens
  - Stressful state
  - Exercise
  - Viral infection

Asthma

- Treatment
  - Short term relief: inhibit bronchiolar smooth muscle
    - Epinephrine not usually first line
    - Inhaled beta-2 agonists
      - i.e. albuterol
    - Inhaled corticosteroids
  - Long term control
    - Removal of allergen or trigger

Pneumonia

- Infection &/or inflammation within the lung
  - Pathogens
    - Bacterial, viral, or fungal
  - Aspiration
    - Chemicals
    - Ingested material

- Edema/inflammation → increase wall thickness → impaired diffusion

Pneumonia

- Usually treated with antibiotics
- Eighth most common cause of death in U.S.
**Tuberculosis (TB)**

- Caused by the bacterium *Mycobacterium tuberculosis*
  - Related to the organism that causes leprosy
- Airborne
  - Affects lungs but may become systemic
  - May remain dormant in lungs
- Phagocytosis by macrophage $\rightarrow$ *M. tuberculosis*
  - Resists destruction $\rightarrow$ survives in macrophage
  - Phagolysosome $\rightarrow$ carried throughout body $\rightarrow$ infects other organs $\rightarrow$ reactivates during periods of immune suppression

**Symptoms**
- Fever, night sweats, weight loss, racking cough, spitting up blood

**Treatment**
- 12-month course of antibiotics
  - Extensively drug resistant

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**Lung Cancer**

- Leading cause of cancer death

**Most common types**
- Adenocarcinoma
  - From glandular structures in epithelial tissue
- Squamous cell carcinoma
  - From squamous epithelial cells
  - Slow-growing
- Small cell carcinoma
  - Immature, undifferentiated cells of neuroendocrine nature
  - Fast-growing

**Highly metastatic**
- Early detection is crucial

**Most common sites of metastasis**
- Other lung
- Adrenals
- Bone
- Brain
- Liver

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**Lung Cancer**

- Mesothelioma
  - Cancer of the plurae of the lung
  - Almost exclusively caused by exposure to asbestos
    - Naturally-occurring, highly durable fiber
    - Once used for many purposes - fire-proof vests, building insulation, fabric, added to concrete
  - Asbestos fibers are inhaled and become embedded in the lungs
### Cystic Fibrosis

- **Secretion of abnormally viscous mucus**
- **Respiratory**
  - Clogged airways, infections
- **Digestive**
  - Clogged ducts, decreased enzyme function
- **Excretory**
  - Electrolyte imbalances

### Smoking

- **Effects**
  - Nicotine constricts terminal bronchioles
  - Systemic vasoconstriction
  - Increased mucus secretion by goblet cells
  - Impairment of cilia
  - Inhibits alpha-antitrypsin production
  - Carbon monoxide binds Hb
  - Decrease in collagen production

### Acid-Base Disturbances

- **Causes**
  - Abnormal control of breathing
  - Accumulation of acidic or basic chemicals in body
- **Respiratory vs. metabolic**
- **Arterial blood gases**

### Respiratory

- **Acidosis**
  - Hypoventilation → low pH, elevated CO₂
  - **Causes**
    - CNS depression (head injury, drugs)
    - Impaired respiratory muscle function (spinal cord injury, neuromuscular disease, muscle relaxants)
    - Pulmonary diseases

### Cystic Fibrosis

- Most common lethal genetic disease in North America
- Lung disease accounts for most deaths
- Some now living into their 40’s

### Smoking

- Lung cancer leading cause of cancer death in U.S. for men and women
  - Most die within one year after diagnosis
- **COPD**
Respiratory

- Alkalosis
  - Hyperventilation → high pH, low CO₂
  - Causes
    - Psychological (fear, pain, anxiety)
    - Respiratory stimulants
    - Increased metabolic states (fever, pregnancy, sepsis)

Metabolic

- Acidosis
  - Excessive H⁺
    - Organic acid production, loss of base, reduced excretion
      → low pH, low HCO₃⁻
  - Causes
    - Renal failure
    - DKA
    - Starvation
    - Ingestion of salicylates

- Alkalosis
  - Deficient H⁺
    - Loss of acid, low K⁺, Cl⁻, consumption of alkaline substances → high pH, high HCO₃⁻
  - Causes
    - Excessive use of antacids or bicarbonates
    - Protracted vomiting
    - Gastric suction
    - Use of diuretics
    - Excess aldosterone

Compensation

- Respiratory acidosis
  - Kidneys retain base
- Respiratory alkalosis
  - Kidneys excrete base
- Metabolic acidosis
  - Hyperventilation will lower paCO₂
- Metabolic alkalosis
  - Hypoventilation will raise paCO₂