The Respiratory System

Respiration
• Exchange of O₂ and CO₂ gases from exterior air, to lung surfaces, through blood to individual cells
• Involves three distinct activities
  – Pulmonary ventilation - inspiration & expiration
  – External respiration - gas exchange across respiratory surfaces
  – Internal respiration - gas exchange across peripheral capillaries in tissue
• Cellular respiration

Structures of Pulmonary Resp.
• Nasal cavity
• Pharynx
• Larynx
• Trachea
• Left and right bronchi
• Lungs
• Can be divided according to function
  – Conducting portion - nose to bronchi, bronchioles, and terminal bronchioles
  – Respiratory portion - respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli

Structures of Pulmonary Resp. (graphic)

Nasal Cavity
• Functions include filtering, humidifying and warming inhaled air, olfactory reception, and resonation of speech
• Separated left and right by nasal septum (primarily hyaline cartilage, ethmoid and vomer)
• Hair in the anterior portion filters large particulates
• Three medially projecting surfaces of superior, middle (both ethmoid), and inferior nasal conchae
  – Create nearly separated passages - superior, middle and inferior meatuses
• Region covered by mucous membranes - pseudostratified ciliated columnar epithelium
  – Mucous humidifies air and captures particulates
  – Cilia direct mucous toward pharynx where its swallowed or expectorated
  – Other secretions from nasolacrimal ducts and paranasal sinuses contribute to humidification
  – Blood supply warms air
• Separated from pharynx by internal nares

Nasal Cavity (graphic)
Nasal Cavity (graphic)
Pharynx
- Functions include passage of air and food, resonation of speech, and immunological responses (tonsils - MALT)
- Nasopharynx - respiratory only
  - Has two connections to the middle ear - Eustachian tubes
  - Lined with pseudostratified ciliated columnar epithelium
- Oropharynx and laryngopharynx - both respiratory and digestive
  - Lined with nonkeratinized stratified squamous epithelium

Pharynx (graphic)

Larynx
- Group of 9 cartilages that make up the voice box
  - Includes the epiglottis
- Ventricular folds (superior) - seal air in thoracic cavity
- Vocal folds (true vocal cords) - contraction of intrinsic muscles stretch vocal folds
  - As air passes over folds, they vibrate
  - Greater air pressure - louder sound
  - Greater stretch - higher pitch
    - Male hormones affect thickness and length for lower pitch
  - Resonance within pharynx, mouth, nasal cavity and paranasal sinuses
- Whispering sounds generated by oral cavity manipulation only, not vocal folds

Laryngopharynx (graphic)
Larynx -External (graphic)
Larynx - Sagittal (graphic)
Vocal Folds (graphic)
Endoscopic View - Vocal Folds (graphic)
Air Distribution (graphic)

Trachea
- Four primary layers - mucosa (pseudostratified ciliated columnar epithelium), submucosa (areolar connective tissue), hyaline cartilage, and adventitia (areolar connective tissue)
- Cartilaginous C-shaped rings - open portion bound by trachealis muscle and elastic connective tissue
  - Rigidity prevents collapse of air passage

Tracheal Epithelium (graphic)
Ciliated Epithelium (graphic)
Endoscopic View - Trachea (graphic)

Bronchi
- Right and left primary bronchi have similar structure to trachea
  - Right more vertical and thus more susceptible to aspirated objects
- At level of lungs, bronchi → secondary (lobar) bronchi → tertiary (segmental) bronchi → bronchioles → terminal bronchioles
• Transition from pseudostratified ciliated columnar epithelium → non-ciliated simple cuboidal epithelium
  – Macrophages important for particulate removal in the latter
• Transition from cartilaginous C-rings → cartilaginous plates → no cartilage
• Transition to increasing smooth muscle innervated by ANS and sensitive to hormones
  – When active, sympathetic excitation and epi/norepi dilate bronchioles
  – Parasympathetic excitation and histamine constrict them (asthma attack)

Lungs
• Within pleural cavities separated by mediastinum
• Serous membranes include parietal and visceral pleura with pleural cavity between
  – Filled with serous fluid for lubrication & adhesion
  – Air (pneumothorax) or blood (hemothorax) can fill cavity as a result of an injury or surgery, may result in collapsed lung
• Divided into 3 right lobes and 2 left lobes supplied by secondary bronchi
• Secondary bronchi further divide into 10 tertiary bronchi per lung
  – Supply air to bronchopulmonary segments - individual segments can be removed without affecting other segments
• Further division of air passages - terminal bronchioles → respiratory bronchioles → alveolar ducts → alveolar sacs and alveoli

Pleural Cavities (graphic)
Lobes of Lungs (graphic)
Lobule of Lung (graphic)
SEM of Lung Tissue (graphic)
Light Microscopy – Lung Tissue (graphic)
SEM - Alveolus (graphic)

Alveoli
• Two cell types (pneumocytes) in wall
• Type I cells (simple squamous epithelial) make up the majority of the wall and contribute to gas exchange
• Type II cells (cuboidal epithelial) are interspersed and secrete moistening alveolar fluid with surfactant
• Additional cells include:
  – Alveolar macrophages (dust cells) - removal of particulates and debris
  – Fibroblasts - surrounding reticular and elastic connective tissue
• Alveolar wall plus capillary wall about 0.5 µm - four layers – respiratory membrane
  – Alveolar wall, epithelial basement membrane, capillary basement membrane, endothelial cells
• Approx. 300 million alveoli total with surface area of 750 sq.ft.
• Unlike blood supply to other tissues, pulmonary circulation reduced by vasoconstriction in response to localized hypoxia (low O₂)

**Alveolus of Lung (graphic)**

**Ventilation**

• Movement of air in and out of lungs
• Boyle’s law - in a closed system, increasing the volume will lower the pressure (dependent on # of gas molecules per unit volume) and vice versa
• Inspiration - expansion of pleural cavity/lungs lowers pressure relative to ambient (alveolar pressure drops 760 → 758 mm Hg)
  – Contraction of diaphragm accounts for 75% of inhaled air
  – Contraction of external intercostals raises ribs and presses sternum anteriorly
  – As parietal plura expands, the visceral plura follows
    • Subatmospheric pressure between them (suction)
    • Surface tension of fluid between them
  – Labored breathing includes other muscles in inspiration (e.g. sternocleidomastoids elevating sternum)
• Expiration - reduction of pleural cavity volume by muscle relaxation and elastic recoil (alveolar pressure increases 760 → 762)
  – Elastic recoil due to elastic fibers and inward collapse caused by surface tension of alveolar fluid (importance of surfactant)
  – Labored breathing includes active expiration - contraction of internal intercostals and abdominal muscles pushing organs against diaphragm
• Compliance - ease of inspiration related to elasticity and surface tension
  – Affected by scar tissue (TB), pulmonary edema, reduced surfactant in alveolar fluid, muscular mobility and reduced elasticity (emphysema)
• Airway resistance - related to cross-section size of passages
  – Inspiration causes increased bronchi and bronchiole diameter
  – Sympathetic bronchodilation
  – Increased resistance caused by asthma and emphysema

**Boyle’s Law (graphic)**

**Inspiration & Expiration (graphic)**

**Rib Cage Involvement (graphic)**

**Muscles of the Rib Cage (graphic)**

**Lung Capacities**

• Tidal volume \((V_T)\) - Minute volume of respiration \((MV)\) = \(V_T \times \text{respiration rate/ min}\)
• Anatomical dead space \((V_D)\) - about 30% of \(V_T)\) - alveolar ventilation rate \((AVR)\) = \((V_T - V_D) \times \text{respiration rate/ min}\)
• Other lung volumes (Figure 23.17)

**Measurable Lung Volumes (graphic)**

**Foundation of Gas Exchange**
• Passive diffusion based on partial pressure of gas
• Dalton's Law - each gas in a mixture exerts pressure according to its proportion
  – Atmospheric pressure at sea level = 760 mm Hg = \( p_{O_2} + p_{CO_2} + p_{N_2} + p_{H_2O} \)
  – Air we breathe is 79% \( N_2 \), 21% \( O_2 \) and 0.04% \( CO_2 \), water vapor depends on humidity
• Gas diffuses from area of high partial pressure to area of low partial pressure
  – Alveolar air is 14% \( O_2 \) and 5.2% \( CO_2 \)
  – Expired air is 16% \( O_2 \) and 4.5% \( CO_2 \)
• Water vapor increases in alveolar and expired air due to humidification
• Henry’s Law - the amount of gas that can dissolve in a liquid is proportional to its partial pressure and its solubility coefficient at constant temperature
  – Solubility coefficients are 0.57 \( CO_2 \), 0.024 \( O_2 \), and 0.012 \( N_2 \)
  – Even though \( p_{N_2} \) is high, low solubility coefficient means little dissolves in body fluids (except when diving with SCUBA - nitrogen narcosis and decompression sickness)

Gas Comparisons
(At rest)

<table>
<thead>
<tr>
<th>In mm Hg</th>
<th>( p_{O_2} )</th>
<th>( p_{CO_2} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atmosphere (sea level)</td>
<td>159</td>
<td>0.3</td>
</tr>
<tr>
<td>Alveoli</td>
<td>105</td>
<td>40</td>
</tr>
<tr>
<td>Oxygenated blood</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Tissue cells (rest)</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>Deoxygenated blood</td>
<td>40</td>
<td>45</td>
</tr>
</tbody>
</table>

External & Internal Respiration
• Blood flow slow enough to allow equilibrium
• Oxygenated blood, \( p_{O_2} \) is slightly lower than alveoli value because of mixing
• Rate of gas diffusion dependent on individual partial pressure gradients (effects of atm. pressure), surface area (effects of emphysema), diffusion distance (effects of edema), gas solubility (\( CO_2 \) 24x> \( O_2 \)), and molecular weight (\( CO_2 \) 1.2x> \( O_2 \))
  – Thus \( CO_2 \) moves 20x > \( O_2 \) (any limitation of ext. respiration likely to cause hypoxia before hypercapnia)

Internal and External Gas Exchange (graphic)

O₂ Transport
• 98.5% of \( O_2 \) carried by hemoglobin, rest is dissolved in plasma
• Only the dissolved \( O_2 \) diffuses, implications for binding and dissociation of \( O_2 \) with hemoglobin
• \( Hb + O_2 \rightleftharpoons HbO_2 \) (Hb=dexoyhemoglobin, HbO₂=oxyhemoglobin)

Gas Transport (graphic)

Hb Characteristics
• Percent saturation = percent of HbO2 of total hemoglobin
  – Increases with increasing \( pO_2 \) to saturation
  – At \( pO_2 \) of tissues (40 mm Hg), Hb is 75% saturated

• Other factors besides \( pO_2 \) affect saturation of hemoglobin - affinity
  • Increased acidity decreases affinity - Bohr effect - \( H^+ \) ions bind in amino acids in hemoglobin reducing its \( O_2 \) carrying capability
    – Effect of lactic acid

• Increased \( pCO_2 \) decreases affinity - Either direct interaction between \( CO_2 \) and Hb or \( CO_2 \) converted to carbonic acid by carbonic anhydrase
  – Effect of high \( pCO_2 \) at tissues

• Increased temperature decreases affinity
  – Heat a byproduct of metabolism

• Increased BPG (bisphosphoglycerate) in RBCs decreases affinity
  – BPG formed as a byproduct of glycolysis in RBCs
  – Thyroxine, hGH, epi, norepi and testosterone increase BPG formation
  – BPG higher when living at high alt.

• Fetal Hb is molecularly different than maternal
  – Hb-F has a higher \( O_2 \) affinity

• CO poisoning due to high affinity of Hb for CO (200x greater)
  – When \( pCO=0.5 \) mm Hg, capacity of Hb reduced by 50% (hypoxia)

\( O_2 \) Dissociation Curve (graphic)

Effects of pH (graphic)
Fetal \( O_2 \) Exchange (graphic)

Hypoxia
• Low \( pO_2 \) in arterial blood - hypoxic hypoxia

• Low functioning hemoglobin - anemic hypoxia

• Insufficient blood flow - stagnant (ischemic) hypoxia

• Inability of tissues to use \( O_2 \) (e.g. cyanide) - histotoxic hypoxia

\( CO_2 \) Transport
• 9% of \( CO_2 \) dissolved gas in plasma
• 13% carried by hemoglobin
  – \( Hb + CO_2 \leftrightarrow Hb\cdotCO_2 \) (Hb-CO\(_2 \) = carbaminohemoglobin)
  – As \( pO_2 \) increase, affinity for \( CO_2 \) decreases - Haldane effect

• 78% transported as bicarbonate ions
  – \( CO_2 \) converted to carbonic acid by carbonic anhydrase (within RBC’s)
  – \( H_2CO_3 \leftrightarrow H^+ + HCO_3^- \)
  – \( H^+ \) binds with Hb, HCO\(_3^-\) diffuses out into plasma while Cl\(^-\) diffuses in (chloride shift)

Mechanisms of \( CO_2 \) Transport (graphic)
Respiratory Control
• Between rest and strenuous exercise, O₂ use can increase 15-20x (30x - athletes)

• Respiratory center composed of three primary CNS locations
  – Medullary rhythmicity area with both inspiratory and expiratory areas - normal breathing consists of autorhythmic excitation from inspiratory centers for 2 sec per ventilation (inactive for 3 sec)
  – Pneumotaxic area in pons - inhibits inspiratory area as lungs fill
  – Apneustic area in pons - stimulates inspiratory area to activate and prolong inspiration but is overridden by activity from pneumotaxic area

• Cortical control - voluntary
  – Holding breath ultimately increases pCO₂ and H⁺ to level where voluntary control is not effective (inspiratory area strongly stimulated)

• Chemoreception control
  – Central receptors in medulla/CSF- CO₂ is lipid soluble and passes blood-brain barrier and may be sensed as pCO₂ or H⁺ (response is significant since there are no buffers)
  – Peripheral receptors in major arteries (aortic and carotid bodies) sensitive to pCO₂, H⁺, and particularly to pO₂ (extreme hypoxia depresses central chemoreception and respiratory centers causing a positive feedback situation)

• Many other factors
  – Proprioception - exercise stimulates inspiratory area
  – Inflation reflex - stretch receptors in bronchi & bronchioles (over inflation) inhibit inspiratory and apneustic areas
  – BP - rapid decline increases resp. rate and vice versa
  – Limbic system - anxiety increases resp. rate and depth
  – Temperature - increased body temperature increases resp. rate and vice versa
    • Sudden cold causes apnea
  – Severe pain - causes brief apnea followed by increased resp. rate
  – Stretching of anal sphincter - increases resp. rate
  – Mechanical or chemical irritation of airway - reduces resp. rate. plus coughing or sneezing

CNS Respiratory Control (graphic)
More CNS Respiratory Control (graphic)
CO₂ Homeostasis (graphic)
Effect of Hypoxia (graphic)
Effects of Exercise
• As cardiac output increases, pulmonary perfusion increases, O₂ diffusing capacity inc. by 3x due to maxed perfusion of pulmonary capillaries
• Ventilation increases during moderate exercise mostly by resp. volume
  – Increases rapidly at first, then more gradually
– 1st part due to anticipation, proprioceptive input, motor cortex
– 2nd part due to $pO_2$, $pCO_2$, $H^+$ and temperature values
• Increase during more strenuous exercise by increased frequency of ventilation

**Effects of Smoking**
• Nicotinic constriction of terminal bronchioles
• CO component in smoke
• Irritants increase mucous production in bronchial tree
• Irritants inhibit ciliary movement
• Destruction of elastic fibers

**Carbon from Smoking (graphic)**

**Respiratory Diseases**
• On your own