Respiratory Physiology

• Functions of Respiratory System
• Organization of Respiratory system
• Ventilation and Lung mechanics: Boyle’s Law, Surfactant
• 5-steps of respiration: Ventilation, external respiration, transport in blood, internal respiration and utilization of O₂ and production of CO₂ in cells
• Lung volumes and capacities
• Anatomical Dead Space
• Hemoglobin and transport of gases
• Oxygen Hemoglobin dissociation curve
• Regulation of breathing: chemoreceptors and breathing center
• Lung diseases
  • Main Functions of Respiratory System
    • Supplies O₂ and removes CO₂
    • Joins kidney to Regulate pH of blood
    • Produces sounds for speech
    • Defends against microbes
    • Traps and dissolves systemic blood clots
  • Organization of Respiratory system
  • Respiratory system is organized as below:
    • **Upper Airways**: external nares → nasal cavity → internal nares → nasopharynx → oropharynx → laryngopharynx → larynx
    • **Lower Airways**: trachea → bronchi → bronchioles → terminal bronchioles → respiratory bronchioles → alveolar ducts → alveoli (main portion of gas exchange)
    • **Conducting zone**: From external nares → terminal bronchioles
    • **Respiratory Zone**: respiratory bronchioles → alveolar ducts → alveoli (main portion of gas exchange)
      • Conducting zone
      • Provides a low resistance path to alveoli
      • Bronchioles are the main site of air flow regulation by ANS and hormones. Bronchodilation versus bronchoconstriction
      • Macrophages, mucous and cilia lining it defend against microbes and harmful particles
      • Epithelium secretes a watery fluid for easy movement of mucous. **Cystic Fibrosis** is genetic disease in which patient fails to secrete watery fluid and mucous narrows down the airways.
      • In **chronic smokers** cilia get damaged leading to mucous accumulation and chronic coughing
    • Respiratory zone
      • Main site of exchange of gases is Alveoli = air sacs
      • Each alveolus is surrounded by large # of pulmonary capillaries. Gases need to pass through 1 layer of very flat alveolar cells and 1 layer of endothelium of capillary wall
      • Type 1 Alveolar cells: very flat, simple squamous epithelium, used for exchange of gases.
      • Type 2 Alveolar cells: are thick cells and secrete detergent like Surfactant that prevents lung alveoli from collapsing.
        • Lung Mechanics
          • **Ventilation** is exchange of air between lungs and atmosphere. It is done by breathing. Breathing has 2 phase inspiration and expiration.
          • **Flow of air** \( F = \frac{\Delta P}{R} \) where \( \Delta P = P_{\text{alv}} - P_{\text{atm}} \)
            • **Inspiration**: Air moves in when \( P_{\text{atm}} > P_{\text{alv}} \)
            • **Expiration**: air move out when \( P_{\text{atm}} < P_{\text{alv}} \)
          • **Boyle’s Law**: for same # of gas molecules pressure is inversely proportional to volume of gas.
• P = 1/V or P₁V₁ = P₂V₂ It means increase in volume decreases pressure and decrease in volume increases pressure.

• Volume of lungs

• Volume of lungs depends on Transpulmonary pressure and lung compliance = strechability
• Transpulmonary Pressure = P₁p is the difference in pressure inside (alveolar) and outside (intrapleural) lungs.
• Alveolar Pressure = P₁v is pressure inside lung
• Intrapleural Pressure = P₁p is pressure outside lungs or pressure between 2 pleural membranes, visceral and parietal

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• Pressure changes in normal, quiet breathing:
  • P₁v mm/Hg: inspiration = -3 expiration = +3
  • P₁p mm/Hg: inspiration = -6 expiration = -3
  • P₁p mm/Hg: inspiration = +3 expiration = +6

• Lung Compliance = Capacity to stretch is compliance. It is decreased by surface tension of water molecules lining the alveoli. Surfactant lining the alveolar surface lowers the surface tension and makes the lungs more expandable.

• Law of Laplace: is P = 2T/r where P = pressure, T = surface tension and r = radius. If the surface tension is equal in 2 alveoli but larger alveolus has double radius than smaller alveolus, pressure in smaller alveolus is double than the larger alveolus. It will make it empty its air to larger alveolus and smaller alveolus collapses.

• Lung volumes and Capacities: Residual Volume is the air in lungs present at the end of a forceful expiration (we cannot empty the lungs). It is about 1200mls.
• Tidal Volume is about 500mls inspired and expired during relaxed Quiet breathing.
• Expiratory Reserve Volume is 1200mls, the air we can expire after tidal expiration.
• Inspiratory Reserve Volume is 3500mls and is the air forcefully inspired in after tidal inspiration.
• Vital Capacity of lungs = Inspiratory Reserve Volume + Tidal Volume + Expiratory Reserve Volume (4.7L)
• Total Lung Capacity = Vital Capacity + Residual Volume (5.9L) All lung volumes vary from person to person
• Anatomic Dead Space is the conducting zone and has 150mls of air in it. Out of 500mls of tidal volume 150mls remain in anatomic dead space and 350mls enter into Respiratory zone (alveoli and respiratory bronchioles) where exchange of gases takes place.
• Alveolar Dead Space is due to the fact that some alveoli may not have blood supply. It is very small in normal humans but may be large in several diseases.
• Physiological Dead Space = anatomical dead space + alveolar dead space.

• Gas transport in blood: Oxygen – 98.5% of O₂ binds with hemoglobin inside RBC’s and travels as Oxyhemoglobin. 1.5 % oxygen travels dissolved in plasma. Carbon Dioxide – Most of CO₂ enters RBC’s and joins with water to form Carbonic Acid by the action Carbonic Anhydrase. Carbonic acid ionizes to form H⁺ and HCO₃⁻ ions. Then most HCO₃⁻ = bicarbonate ions enter plasma and travel as sodium bicarbonate (70%). Some CO₂ molecules combine with hemoglobin and travels as Carbaminohemoglobin (23%). Some CO₂ travels physically dissolved in plasma (7%).
• **Internal Respiration: Blood-tissue gas exchange**: Pulmonary veins carry O₂ to heart and arteries carry O₂ to body tissue via blood capillaries with thin walls. O₂ enters interstitial fluid and finally into cells. Mitochondria use O₂ and produce CO₂ which leaves cells and enters into blood capillaries through interstitial fluid. Capillaries join to form veins which carry CO₂ to heart which sends the blood to lungs for gas exchange.

• **Hemoglobin** is formed of globin = formed of 4 polypeptide chains each joined to a heme group having Fe²⁺ at its center that can combine to 1 O₂ molecule. Therefore, 1 hemoglobin can carry 4 molecules of O₂.

• **Oxygen – hemoglobin dissociation Curve** explains why in presence of high O₂ hemoglobin has high affinity for oxygen but in tissues its affinity for oxygen declines and it releases oxygen there. Therefore hemoglobin is a oxygen transporting molecule different from myoglobin which continuously has a high affinity for oxygen and is a better oxygen storing molecule. 2,3 DiPhosphoGlycerate or BPG, H⁺ or acidity, PCO₂ and temperature move the dissociation curve to right and decrease affinity of hemoglobin for oxygen.

• **Regulation of Breathing**:
  
  • **Ventral Respiratory Group = VRG** lies in medulla and sets the basic rhythm of breathing.
  
  • **Dorsal Respiratory Group = DRG** lies posterior to VRG and receives inputs from carotid bodies – glossopharyngeal nerve, aortic bodies – vagus nerve, central chemoreceptors in medulla, PRG in pons and higher brain centers. It modifies the basic rhythm set by VRG. It sends instructions to spinal integrating centers. Spinal integrating centers send impulses to diaphragm, intercostal and other accessory muscles.

  • **Pontine Respiratory Group = PRG** lies in pons and receives inputs of higher brain centers to modify rhythm of breathing.

  • **Peripheral Chemoreceptors**: Carotid bodies in internal carotid and aortic bodies in aortic arch have chemoreceptors that detect Hypoxia = low PO₂, High H⁺ = metabolic acidosis and High PCO₂ = respiratory acidosis and send afferent information to brain stem to increase ventilation.

  • **Central Chemoreceptors** are present in breathing center in medulla. These respond to high PCO₂ and resulted [H⁺].

• **Regulation of breathing**:
  
  Breathing is regulated by respiratory centers present in Brain Stem. The center is more sensitive to changes in CO₂ concentration than O₂ concentration. 70% stimulus is the pH of cerebrospinal fluid – directly affected by CO₂ concentration. 30% stimulus is regulated by impulses from receptors inside Carotid and Aortic bodies. **Hypoxia** is less supply of oxygen and **Hypercapnia** is greater retention of CO₂. Metabolic Acidosis is the increase in H⁺ by reasons other than addition of CO₂. Metabolic Alkalosis if H⁺ decreases due to factors other than removal of CO₂.

  • **Sleep Apnea** is cessation of breathing during sleep, may be by obstruction of air passage.

• **Lung disease**: SO₂ sulfur dioxide, CO carbon monoxide and O₃ like pollutants damage lungs but the worst is tobacco smoke which carries more than 4000 chemicals attached to smoke particles. Many of these molecules are toxic and others are carcinogenic = cause cancer. So **lung cancer** is more common in smokers than non-smokers. In addition tobacco smoke inactivates cilia lining the lung passages so that harmful particles remain in lungs and make alveoli inelastic. This enlargement of alveoli due to broken walls and loss of elasticity is called **Emphysema**. **Chronic Bronchitis** is the constant irritation of lungs by inhaled irritants and leads to formation of excessive mucus and is the cause of smoker’s cough.

• **Asthma** is intermittent constriction of bronchioles due to hypersensitivity of smooth muscle fibers caused by chronic inflammation of airways due to several causes like allergy, environmental factors, and viruses etc. In allergic asthma eosinophil count gets very high. Also mast cell count goes high. Inhalers act on beta receptors for epinephrine and cause bronchodilation.