RESPIRATORY PHYSIOLOGY

Guest Lecture to Biomed Dept.
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Lecture map

Physiology of respiration
- Definitions and structures
- Mechanics of breathing
- Measurements of pulmonary function
- Cellular Respiration, Pulmonary disorders
- Blood gases - Diffusion
- Neural control of respiration
- Hemoglobin (and disorders)
- Transport of CO₂
- Acid/base balance

Anatomy of Respiratory Tree

Longitudinal Section

The Thorax and its contents

What is Respiration?
- Goals:
  - What is the respiratory system?
  - What is respiration?
  - What are the structural features?
  - What are their functions?
Respiration

- Ventilation:
  - Action of breathing with muscles and lungs
- Gas exchange:
  - Between air and capillaries in the lungs.
  - Between systemic capillaries and tissues of the body
- \(O_2\) utilization:
  - Cellular respiration in mitochondria

Functions of the Respiratory System

- Gas Exchange
  - \(O_2, CO_2\)
- Acid-base balance
  - \(CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-\)
- Phonation
- Pulmonary defense
- Pulmonary metabolism and handling of bioactive materials

Inspiratory Movements

- Inspiration
  - Ribs flex out and up
  - Diaphragm pulls down
  - Lung moves with changes in intrathoracic pressure

Thoracic Cavity

- Diaphragm:
  - Sheets of striated muscle divides anterior body cavity into 2 parts.
- Above diaphragm: thoracic cavity:
  - Contains heart, large blood vessels, trachea, esophagus, thymus, and lungs.
- Below diaphragm: abdominopelvic cavity:
  - Contains liver, pancreas, GI tract, spleen, and genitourinary tract.

Mechanics of breathing

- Gas: the more volume, the less pressure (Boyle’s)
- **Inspiration:**
  - Lung volume increases \(\rightarrow\)
- Decrease in intrapulmonary pressure, just below atmospheric pressure \(\rightarrow\)
  - Air goes in!
- **Expiration:** viceversa
Intrapleural space:
- "Space" between visceral & parietal pleurae.
- Visceral and parietal pleurae (membranes) are flush against each other.
- Lungs normally remain in contact with the chest wall.
- Lungs expand and contract along with the thoracic cavity.

Mechanics of breathing

- **Compliance:**
  - This the ability of the lungs to stretch during inspiration
  - Lungs can stretch when under tension.

- **Elasticity:**
  - It is the ability of the lungs to recoil to their original collapsed shape during expiration
  - Elastin in the lungs helps recoil

Inspiration

- **Inspiration** – Active process
- Diaphragm contracts -> increased thoracic volume vertically.
- Intercostals contract, expanding rib cage -> increased thoracic volume laterally.
- More volume -> lowered pressure -> air in.
- Negative pressure breathing

Expiration

- **Expiration** – Passive
  - Due to recoil of elastic lungs.
  - Less volume -> pressure within alveoli is just above atmospheric pressure -> air leaves lungs.
  - Note: Residual volume of air is always left behind, so alveoli do not collapse.

Mechanics of breathing

- **During Quiet breath:**
  - +/- 3 mmHg intrapulmonary pressure.

- **During Forced breath:**
  - Extra muscles, including abdominals
  - +/- 20-30 mm Hg intrapulmonary pressure
**Dynamics of Respiration**

- Simple Mechanical Model
  \[ P = \frac{V}{C} + RV + F \]

- P - pressure
- V - volume
- C - compliance
- R - resistance
- I - inertance

**The Pressures**

- Atmospheric pressure
- Intrapleural pressure
- Transalveolar pressure
- Partial pressure
- Alveolar pressure
- Intrapulmonary pressure
- Collapsing force of lungs

**Respiration**

- It is the process by which the body takes in oxygen and utilizes and removes CO\(_2\) from the tissues into the expired air.
- It comprises of:
  - Ventilation by the lungs
  - Gas exchange across alveolar membrane
  - Transport of gases by blood (haemoglobin)
  - Uptake of O\(_2\) and release of CO\(_2\) by tissues

**Conducting Zone**

- **Conducting zone:**
  - Includes all the structures that air passes through before reaching the respiratory zone.
  - Mouth, nose, pharynx, glottis, larynx, trachea, bronchi.

- **Conducting Airways**
  - Includes: From Trachea --> Terminal bronchioles
  - Warm and humidifies until inspired air becomes:
    - 37 degrees
    - Saturated with water vapor
  - Filters and cleans:
    - Mucus secreted to trap particles
    - Mucus/particles moved by cilia to be expectorated.
Respiratory Zone

- **Respiratory zone**
  - Region of gas exchange between air and blood
  - Respiratory bronchioles
  - Alveolar ducts, Alveolar Sacs and Alveoli

Respiratory Zone

- **Alveoli**
  - Air sacs
  - Honeycomb-like clusters
  - ~ 300 million.
  - Large surface area (60–80 m²).
  - Each alveolus: only 1 thin cell layer.
  - Total air barrier is 2 cells across (2 μm) (alveolar cell and capillary endothelial cell).

Respiratory Zone

- **Alveolar cells**
  - Alveolar type I: structural cells.
  - Alveolar type II: secrete surfactant.
Branching of Airways

- Dichotomous branching
- ~23 generations
- Can we describe this?
- Can we model this?

Respiratory Zone

Respiratory Zone: Respiratory bronchioles, Alveoli (300 million), Alveolar ducts, Alveolar sacs

Gas Exchange: respiratory membrane
Ventilation

- Mechanical process that moves air in and out of the lungs.
- Diffusion of...
- $O_2$: air to blood.
- $CO_2$: blood to air.
- Rapid:
  - large surface area
  - small diffusion distance.

Bronchial Section - microscopic

Higher magnification of Bronchus

Terminal Bronchioles - bifurcation

Alveoli under microscope

Alveoli - higher magnification
Alveoli

- 8 million alveolar ducts
- 300 million alveoli (diameter 70-300 μm)
- Total alveolar surface area ~ 70 m²
- Alveolar membrane thickness < 1 μm.

The large surface area of alveoli
Bronchoscopy

Blood Vessels of the Lung

- Pulmonary Artery:
  - Deoxygenated (venous) cardiac output.
- Pulmonary capillaries
  - extremely dense
  - underground parking garage
- Pulmonary Veins:
  - Oxygenated (arterial) cardiac output.

Alveolar capillary interface

Alveolar capillary interface - schematic

Surface tension

- **Surfactant**
  - produced by alveolar type II cells.
  - Interspersed among water molecules.
  - Lowers surface tension.
- RDS, respiratory distress syndrome, in preemies.
- First breath: big effort to inflate lungs!
Surface tension

Pulmonary Function

- **Spirometry**
  - Breathe into a closed system, with air, water, moveable bell

  ![Spirometry Diagram](www.drsarma.in)

Lung Volumes

- **Tidal volume (TV):** in/out with quiet breath (500 ml)
- **Total minute volume:** tidal x breaths/min
  - 500 x 12 = 6 L/min
- **Exercise:** even 200 L/min!
- **Anatomical dead space:**
  - Conducting zone
  - Dilutes tidal volume, by a constant amount.
  - Deeper breaths -> more fresh air to alveoli.

Lung Capacities

- **Vital capacity (VC):** the most you can actually ever expire, with forced inspiration and expiration.
  
  \[ VC = IRV + TV + ERV \]

- **Total lung capacity:** VC plus residual volume

Lung Volumes

- **Inspiratory reserve volume (IRV):** extra (beyond TV) in with forced inspiration.
- **Expiratory reserve volume (ERV):** extra (beyond TV) out with forced expiration.
- **Residual volume:** always left in lungs, even with forced expiration.
  - Not measured with spirometer

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Pulmonary disorders

- **Restrictive disorder:**
  - Vital capacity is reduced.
  - Less air in lungs.

- **Obstructive disorder:**
  - Rate of expiration is reduced.
  - Lungs are “fine,” but bronchi are obstructed.

Disorders

- **Air/ Fluid in the pleural space**
  - Pneumothorax
  - Hydrothorax
  - Pyothorax
  - Hydropneumothorax

- **Restrictive disorder:**
  - Black lung from coal mines.
  - Pulmonary fibrosis: Tuberculosis
  - Too much connective tissue.

Pneumothorax – collapse lung

Obstructive Sleep Apnea

- Normal

Pulmonary Disorders

- COPD (chronic obstructive pulmonary disease):
- Smoking is the main cause for COPD
  - Asthma
  - Emphysema
  - Chronic bronchitis

Disorders

- **Asthma:**
  - Obstructive
  - Inflammation, mucus secretion, bronchial constriction.
    - Provoked by: allergic, exercise, cold and dry air
    - Anti-inflammatories, including inhaled epinephrine (specific for non-heart adrenergic receptors), anti-leukotrienes, anti-histamines.
Disorders

- Emphysema:
  - Alveolar tissue is destroyed.
  - Chronic progressive condition
    - Cigarette smoking stimulates macrophages and WBC to secrete enzymes which digest proteins.
    - Or: genetic inability to stop trypsin (which digests proteins).

Blood Gases

- Barometers use mercury (Hg) as convenience to measure total atmospheric pressure.
- Sea level: 760 mm Hg (torr)

Blood Gases

- Total pressure of a gas mixture is = to the sum of the independent, partial pressures of each gas (Dalton’s Law).
- In sea level atmosphere:
  - \( P_{STP} = 760 \text{ mm Hg} = P_{N_2} + P_{O_2} + P_{CO_2} + P_{H_2O} \)

Blood Gases

- Partial pressures: % of that gas x total pressure.
- In atmosphere:
  - \( O_2 \) is 21%, so \( (0.21 \times 760) = 159 \text{ mm Hg} = P_{O_2} \)
  - Note: atmospheric \( P_{O_2} \) decreases on a mountain, increases as one dives into the ocean.

Blood Gases

- But inside you, the air is saturated with water vapor.
  - \( P_{H_2O} = 47 \text{ mm Hg} \) at 37 degrees
  - So, inside you, there is less \( P_{O_2} \):
  - \( P_{O_2} = 105 \text{ mm Hg} \) in alveoli.
  - In constrast, alveolar air is enriched in \( CO_2 \), as compared to inspired air.
  - \( P_{CO_2} = 40 \text{ mm Hg} \) in alveoli.

Blood Gases

<table>
<thead>
<tr>
<th>Gas</th>
<th>Partial Pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( H_2O )</td>
<td>Variable</td>
</tr>
<tr>
<td>( CO_2 )</td>
<td>60.3 mmtlg</td>
</tr>
<tr>
<td>( O_2 )</td>
<td>159 mmtlg</td>
</tr>
<tr>
<td>( N_2 )</td>
<td>601 mmtlg</td>
</tr>
<tr>
<td>Total Pressure</td>
<td>760 mmtlg</td>
</tr>
</tbody>
</table>

Inspiried air Alveolar air
Blood Gases

- Gas and fluid in contact:
- Gas dissolved in a fluid depends directly on its partial pressure in the gas mixture.
- With a set solubility, non-changing temp.
- (Henry’s law)
- So...
- $P_{O_2}$ in alveolar air $\sim = P_{O_2}$ in blood.

Blood Gases

- O$_2$ electrodes can measure dissolved O$_2$ in a fluid. (also CO$_2$ electrodes)
- Good index of lung function.
- Arterial $P_{O_2}$ is only slightly below alveolar $P_{O_2}$
- Arterial $P_{O_2}$ = 100 mm Hg
- Alveolar $P_{O_2}$ = 105 mm Hg
- $P_{O_2}$ in the systemic veins is about 40 mm Hg.

Lung Perfusion and Ventilation

Ventilation – Perfusion Matching

System Overview
Perfusion
- Geometry of vascular tree
  - \( R = \frac{\eta}{r^4} \)
- Passive factors affecting PVR
  - PA pressure
  - LA pressure
  - effect of lung volume on PVR
- Local factors regulating Q and matching V/Q
  - HPV
  - pH/pCO2

Capillary Sheet
- Capillaries appear in septal walls between alveoli
- Coverage is approx. 90% of alveolar surface area
- Effective coverage is less allowing for recruitment

Capillary Recruitment
- We don’t perfuse all capillaries all the time
- Increased CO (e.g., exercise)
  - Spatially increased in Hb/P
  - Recruit unperfused capillaries
  - Dilate all capillaries

Tissue Respiration
- Oxygen release and CO\(_2\) pick up at the tissue level.
Cellular Respiration

Blood gases
- Most $O_2$ is in hemoglobin
  - 0.3 ml dissolved in plasma +
  - 19.7 ml in hemoglobin
  - 20 ml $O_2$ in 100 ml blood!
- But: $O_2$ in hemoglobin $\rightarrow$ dissolved $\rightarrow$ tissues.
- Breathing pure $O_2$ increases only the dissolved portion.
  - insignificant effect on total $O_2$
  - increased $O_2$ delivery to tissues

Pulmonary Circulation
- Left ventricle pumps to entire body,
- Right ventricle only to lungs.
- Both ventricles pump 5.5 L/min!
- Pulmonary circulation: various adaptations.
  - Low pressure, low resistance.
  - Prevents pulmonary edema.
  - Pulmonary arteries dilate if $P_{O_2}$ is low (opposite of systemic)

Neural control
- I neurons = inspiration
- E neurons = expiration
- I neurons $\rightarrow$ spinal motor neurons $\rightarrow$ respiratory muscles.
- E neurons inhibit I neurons.

Neural control
- Also
  - voluntary breathing controlled by the cerebral cortex.
**Chemoreceptors**

- Oxygen: large “reservoir” attached to hemoglobin.
- So chemoreceptors are more sensitive to changes in $P_{CO_2}$ (as sensed through changes in pH).
- Ventilation is adjusted to maintain arterial $PCO_2$ of 40 mm Hg.
- Chemoreceptors are located throughout the body (in brain and arteries).

**Chemoreceptors (CTZ)**

**Hemoglobin**

- Each hemoglobin has 4 polypeptide chains (2 alpha, 2 beta) and 4 hemes (colored pigments).
- In the center of each heme group is 1 atom of iron that can combine with 1 molecule $O_2$.
- (so there are four $O_2$ molecules per hemoglobin molecule.)
- 280 million hemoglobin molecules per RBC!

**Hemoglobin**

- **Oxyhemoglobin:**
  - Ferrous iron ($Fe^{2+}$) plus $O_2$.

- **Deoxyhemoglobin:**
  - Still ferrous iron (reduced).
  - No $O_2$.

**Hemoglobin**

- **Carboxyhemoglobin:**
  - Carbon monoxide (CO) binds to heme instead of $O_2$
  - Smokers
Hemoglobin

**Loading:**
- Load $O_2$ into the RBC.
- Deoxyhemoglobin plus $O_2$ -> Oxyhemoglobin.

**Unloading:**
- Unload $O_2$ into the tissues.
- Oxyhemoglobin -> deoxyhemoglobin plus $O_2$.

Loading/unloading depends on:
- $P_02$
- Affinity between hemoglobin and $O_2$
  - $pH$
  - Temperature

Dissociation curve: % oxyhemoglobin saturation at different values of $P_0$.
- Describes effect of $P_0$ on loading/unloading.
  - Sigmoidal
  - At low $P_0$, small changes produce large differences in % saturation and unloading.
  - Exercise: $P_0$ drops, much more unloading from veins.
  - At high $P_0$, slow to change.

Arteries: 97% saturated (i.e. oxyhemoglobin)
Veins: 75% saturated.
Arteries: 20 ml $O_2$/100 ml blood.
Veins: ~5 ml less
Only 22% was unloaded!
Reservoir of oxygen in case:
- don’t breathe for ~5 min
- exercise (can unload up to 80%)
Hemoglobin

- Fetal hemoglobin (F):
- Gamma chains (instead of beta)
- More affinity than adult (A) hemoglobin

Hemoglobin

- Anemia:
  - Hemoglobin below normal.
- Polycythemia
  - Hemoglobin above normal.
  - Altitude adjustment.

Disorders

- Sickle-cell anemia:
  - fragile, inflexible RBC
  - inherited change: one base pair in DNA -> one aa in beta chains
  - hemoglobin S
  - protects vs. malaria; african-americans
- Thalassemia:
  - defects in hemoglobin
  - type of anemia

RBC

- RBC
  - no nucleus
  - no mitochondria
  - Cannot use the O₂ they carry!!!
  - Respire glucose, anaerobically.

C₀₂ Transport

- C₀₂ transported in the blood:
  - most as bicarbonate ion (HCO₃⁻)
  - dissolved C₀₂
  - C₀₂ attached to hemoglobin (Carbaminohemoglobin)

C₀₂ Transport

Carbonic anhydrase in RBC promotes useful changes in blood P₀₂:

\[
\begin{align*}
\text{CA} & : & H₂O + C₀₂ & \rightarrow & H₂C₀₃ & \rightarrow & HCO₃⁻ & \text{ high P₀₂} \\
\text{CA} & : & H₂O + C₀₂ & < & H₂C₀₃ & < & HCO₃⁻ & \text{ low P₀₂}
\end{align*}
\]
C0₂ Transport

- Chloride shift:
  - Chloride ions help maintain electroneutrality.
  - HCO₃⁻ from RBC diffuses out into plasma.
  - RBC becomes more +.
    - Cl⁻ attracted in (Cl⁻ shift).
  - H⁺ released buffered by combining with deoxyhemoglobin.
  - Reverse in pulmonary capillaries

Acid-Base Balance

- Normal blood pH: 7.40 (7.35 - 7.45)
- **Alkalosis:** pH up
- **Acidosis:** pH down
  - H₂O + C0₂
  - Hypoventilation:
    - PCO₂ rises, pH falls (acidosis).
  - Hyperventilation:
    - PCO₂ falls, pH rises (alkalosis).

Acid-Base Balance

- Hyperventilation -> PCO₂ down -> pH of CSF up -> vasoconstriction -> dizziness.
- If hyperventilating, should you breath into paper bag? Yes! It increases PCO₂!
- Metabolic acidosis can trigger hyperventilation.
- Diarrhea -> acidosis.
- Vomit -> alkalosis.

Other Functions of the Respiratory System

- BEHAVIORAL - talking, laughing, singing, reading
- DEFENSE - humidification, particle expulsion (coughing, sneezing), particle trapping (clots), immunoglobulins from tonsils and adenoids, α-1 antitrypsin, lysozyme, interferon, complement system
- SECRETIONS - mucus (goblet cells, mucus glands)

Other Functions: cont

- METABOLIC - forms angiotensin II, prostacyclin, bradykinin, serotonin and histamine
- ACID - BASE BALANCE - changes in ventilation e.g., acute acidosis of exercise
- MISCELLANEOUS - lose heat and water, liquid reservoir for blood, force generation for lifting, vomiting, defaecation and childbirth

Best of Luck to all of you !!!

- CD of my lectures is made available
- Contact us for any clarifications or needs
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