Respiratory System

The goal of these lectures is to discuss basic respiratory physiology. This lecture will discuss gas transport, control, hypoxia and non-respiratory functions of lungs.

The sections for this lecture are:

- Transport of gases
  - PO2, PCO2, H+ conc, t°C, DPG, Hb saturation
  - Bhor, Haldane, respiratory acidosis / alkalosis

- Neural control of ventilation
  - Rhythmic breathing, PO2, PCO2, and H+ conc
  - Exercise, other ventilatory responses

- Hypoxia and non-respiratory functions of lungs
  - Hypoxia and acclimatization to high altitude
  - Non-respiratory functions of the lungs

Life is a series of chemical reactions occurring in compartmentalized environments. The main purpose of life is to keep itself alive.

Physiology, the study of how life works, is based on the simultaneous occurrence of the following three concepts:

- Levels of organization
- Structure / function relationship
- Homeostatic regulation

Life is a series of chemical reactions occurring in compartmentalized environments. The main purpose of life is to keep itself alive.

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Neural control of ventilation

Rhythmic breathing, PO2, PCO2, and H+ conc

Exercise, other ventilatory responses

Hypoxia and non-respiratory functions of lungs

Hypoxia and acclimatization to high altitude

Non-respiratory functions of the lungs

PCO2

PO2

pH

Pa

Inputs

Outputs

Neural CV center

Cardio +

Cardio -

Vasoconstriction

Extrinsic

Intrinsic

Heart

Periphery

Lung

Baroreceptor mechanism (e.g. carotid sinus)

Where we would like to be at the end of the cardiovascular and respiratory sections, by the end of this week.
Respiratory System

Introduction, last lecture
- Structure / function, gas laws, lungs / chest wall relations, pressures / forces

Lung mechanics, last lecture
- Ventilation, inspiration / expiration, compliance / resistance
- Lung volume / capacities, alveolar ventilation / dead space
- Partial pressures of gases and their diffusion in liquids
- Alveolar gas pressures and alveolar - blood exchange
- Matching alveolar ventilation and alveolar blood flow
- Gas exchange in tissues

Transport of O2, CO2 and H ions in blood, this lecture
- Hemoglobin (Hb), effect of PO2 on Hb saturation
- Blood PCO2, H+ conc, t°C, DPG on Hb saturation
- Carbamino compounds and carbonic anhydrase
- Total blood carbon dioxide and the Haldane effect
- Respiratory acidosis and respiratory alkalosis

Control of respiration, this lecture
- Neural generation of rhythmical breathing
- Control of ventilation by PO2, PCO2, and H+ conc
- Control of ventilation during exercise
- Other ventilatory responses

Hypoxia and non-respiratory functions of lungs, this lecture
- Hypoxia and acclimatization to high altitude
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Transport of gases

Effect of Added Hemoglobin on Oxygen Distribution

<table>
<thead>
<tr>
<th>PO2</th>
<th>PO2</th>
<th>PO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>A</td>
</tr>
</tbody>
</table>

- Hemoglobin (Hb), effect of PO2 on Hb saturation
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Transport of gases

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Effect of Added Hemoglobin on Oxygen Distribution

Oxygen Content at Systemic Arterial Blood at Sea Level

1 liter (L) arterial blood contains

3 ml O2 physically dissolved (1.5%)

197 ml O2 bound to hemoglobin (98.5%)

Total 200 ml O2

Cardiac output = 5 L/min

O2 carried to tissues/min = 5 L/min × 200 ml O2/L

= 1000 ml O2/min

Transport of gases

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Gas exchange as function of capillary length

Pulmonary capillary PO2, (nmHg)

Systemic venous PO2

% of capillary length
Transport of gases

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Oxygen-Hemoglobin Dissociation Curve

- Systemic venous
- Systemic arterial

Transport of gases

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Oxygen Movement in Lungs and Tissues
Transport of gases

Hemoglobin (Hb), effect of PO2 on Hb saturation

Blood PCO2, H+ conc, t°C, DPG on Hb saturation

Carbamino compounds and carbonic anhydrase

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Respiratory acidosis and respiratory alkalosis

\[ \text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\text{H}_2\text{CO}_3} \]
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Transport of gases

Hemoglobin (Hb), effect of PO2 on Hb saturation

Blood PO2, H⁺ conc., t°C, DPG on Hb saturation

Carbamino compounds and carbonic anhydrase

Total blood carbon dioxide and the Haldane effect

Respiratory acidosis and respiratory alkalosis

Effects of Various Factors on Hemoglobin

The affinity of hemoglobin for oxygen is decreased by:
1. Increased hydrogen ion concentration
2. Increased $P_{CO_2}$
3. Increased temperature
4. Increased DPG concentration

The affinity of hemoglobin for both hydrogen ions and carbon dioxide is decreased by increased $P_{O_2}$; that is, deoxyhemoglobin has a greater affinity for hydrogen ions and carbon dioxide than does oxyhemoglobin.

$\text{HCO}_3^- \quad \text{pH} = pK + \log \frac{\text{HCO}_3^-}{\text{H}_2\text{CO}_3}$

$\text{pH} = pK + \log \frac{\text{HCO}_3^-}{\text{PCO}_2}$

In the tissue
Transport of gases

- Hemoglobin (Hb), effect of PO2 on Hb saturation
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### Transport of gases

**Hemoglobin (Hb), effect of PO2 on Hb saturation**

**Blood PCO2, H+ conc, t°C, DPG on Hb saturation**

**Carbamino compounds and carbonic anhydrase**

**Total blood carbon dioxide and the Haldane effect**

**Respiratory acidosis and respiratory alkalosis**

<table>
<thead>
<tr>
<th>Form</th>
<th>Systemic Arterial Blood</th>
<th>Systemic Venous Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CO2 volume (mL/L)</td>
<td>% of total CO2 in LDL</td>
</tr>
<tr>
<td>Dissolved in LDL</td>
<td>37</td>
<td>5.3</td>
</tr>
<tr>
<td>Dissolved in Lockwood</td>
<td>403</td>
<td>51.0</td>
</tr>
<tr>
<td>Bound to hemoglobin</td>
<td>24</td>
<td>4.9</td>
</tr>
<tr>
<td>Total</td>
<td>460</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mechanism for B & C: ???
Transport of gases

Hemoglobin (Hb), effect of PO2 on Hb saturation

Blood PCO2, H+ conc, t°C, DPG on Hb saturation

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\[ \text{pH} = \text{p}K + \log \left( \frac{\text{HCO}_3}{\text{PCO}_2} \right) \]

Control of respiration

- Neural generation of rhythmical breathing
- Control of ventilation by PO2, PCO2, and H+ conc
- Control of ventilation during exercise

stimulatory inhibitory PONS pneumotaxic apneustic MEDULLA other inputs control of respiration means control of amplitude and frequency lung stretch receptors inspiratory muscles expiratory muscles

Inspiratory center is tonically active

Expiratory center is active only when stimulated

SPINAL CORD
Control of respiration

- Neural generation of rhythmical breathing
- Control of ventilation by PO2, PCO2, and H+ conc
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Major Stimuli for the Central and the Peripheral Chemoreceptors

Peripheral chemoreceptors—that is, carotid bodies and aortic bodies—respond to changes in the arterial blood. They are stimulated by:

1. Decreased $P_{O_2}$ (hypoxia)
2. Increased hydrogen ion concentration (metabolic acidosis)
3. Increased $P_{CO_2}$ (respiratory acidosis)

Central chemoreceptors—that is, located in the medulla oblongata—respond to changes in the brain extracellular fluid. They are stimulated by increased $P_{CO_2}$ via associated changes in hydrogen ion concentration. (See Equation 13-11.)
Control of respiration

• Neural generation of rhythmical breathing

• Control of ventilation by PO2, PCO2, and H+ conc

• Control of ventilation during exercise
**Control of respiration**

- Neural generation of rhythmical breathing
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**Factors That Increase and Decrease Ventilation**

- Increase PCO2 → increases Va decrease PCO2 → decrease Va
- Increase H → increase Va decrease H → decrease Va
- Increase Po2 → decrease Va decrease PO2 → increase Va
Control of respiration

Factors That Stimulate Ventilation

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- Control of ventilation by PO2, PCO2, and H+ conc
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Control of respiration

- Neural generation of rhythmical breathing
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Hypoxia

Causes of a Decreased Arterial PO2 (Hypoxic Hypoxia) in Disease

1. Hypoventilation may be caused (a) by a defect anywhere along the respiratory control pathway; from the medulla through the respiratory muscles, (b) by severe thoracic cage abnormalities, and (c) by major obstruction of the upper airway. The hypoxemia of hypoventilation is always accompanied by an increased arterial PCO2.

2. Diffusion impairment results from thickening of the alveolar membranes or a decrease in their surface area. In turn, it causes failure of equilibration of blood PO2 with alveolar PO2. Often it is apparent only during exercise. Arterial PCO2 is either normal, since carbon dioxide diffuses more readily than oxygen, or reduced, if the hypoxemia reflexly stimulates ventilation.

3. A shunt is (a) an anatomic abnormality of the cardiovascular system that causes mixed venous blood to bypass ventilated alveoli in passing from the right side of the heart to the left side of the heart, or (b) an intrapulmonary defect in which mixed venous blood perfuses unventilated alveoli (ventilation/perfusion = 0). Arterial PCO2 generally does not rise since the effect of the shunt on arterial PCO2 is counterbalanced by the increased ventilation reflexly stimulated by the hypoxemia.

4. Ventilation-perfusion inequality is by far the most common cause of hypoxemia. It occurs in chronic obstructive lung diseases and many other lung diseases. Arterial PCO2 may be normal or increased, depending upon how much ventilation is reflexly stimulated.

Hypoxia

Acclimatization to the Hypoxia of High Altitude

1. The peripheral chemoreceptors stimulate ventilation.

2. Erythropoietin, a hormone secreted by the kidneys, stimulates erythrocyte synthesis, resulting in increased erythrocyte and hemoglobin concentration in blood.

3. DPG increases and shifts the hemoglobin dissociation curve to the right, facilitating oxygen unloading in the tissues. However, this DPG change is not always adaptive and may be maladaptive. For example, at very high altitudes, a right shift in the curve impairs oxygen loading in the lungs, an effect that outweighs any benefit from facilitation of unloading in the tissues.

4. Increases in capillary density (due to hypoxia-induced expression of the genes that code for angiogenic factors), mitochondrial, and muscle myoglobin occur, all of which increase oxygen transfer.

5. The peripheral chemoreceptors stimulate an increased loss of sodium and water in the urine. This reduces plasma volume, resulting in a concentration of the erythrocytes and hemoglobin in the blood.
Other lung functions

NON-RESPIRATORY FUNCTIONS OF THE LUNGS

(in addition to gas exchange and regulation of H+ concentration)

“sieve” for small blood clots
endothelial cells lining lung capillaries
(eg. histamine, ACE, exogenous GnRH & cocaine ??)

Respiratory System
Homeostasis, or constancy of the internal environment, is needed for chemical reactions underlying life to occur. It is maintained, predominantly, through negative feedback mechanisms. Integrators compare what it should be with what it actually is and generate an error signal.
Respiratory System

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AT THE MIDDLE OF THE ROAD

I wonder how will I look after the next section

???

I’D RATHER BE AT THE BEACH