For the body to survive, there must be a constant supply of $\text{O}_2$ and a constant disposal of $\text{CO}_2$.

Respiratory System

Respiratory System Overview:

- Protects system (debris / pathogens / desiccation)
- Provides surface area for gas exchange (between air / blood)
- Moves air in / out from gas exchange surface

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Functional Anatomy:

1) External nares
2) Nasal cavity
   - Resonance chamber
3) Uvula
4) Pharynx
   - Nasopharynx
   - Oropharynx
   - Laryngopharynx
5) Larynx
   - Provide open airway
   - Channel air / food
   - Voice production
6) Trachea
7) Bronchial tree
8) Alveoli

Functional Anatomy:

- Conduction of air
- Gas exchange

Conduction of air

Gas exchange

How are inhaled debris / pathogens cleared from respiratory tract?

Macrophages

Nasal Cavity:
- Particles > 10 µm

Conducting Zone:
- Particles 5 – 10 µm

Respiratory Zone:
- Particles 1 – 5 µm

Mucus Escalator
**Respiratory System**

**Functional Anatomy:**

- **Trachea**
  - 15 - 20 cartilages
  - 15 - 20 tracheal cartilages
  - Protect airway
  - Allows for food passage

- **Esophagus**
  - Tough, flexible tube (~1" diameter)

- **Tissue Cells:**
  - Goblet cells: Unicellular mucous secreting glands
  - Pseudostratified ciliated columnar epithelium
  - Goblet cells:
    - Unicellular mucous secreting glands (C-shaped)

- **Brancheal:**
  - Right primary bronchus wider, shorter, & steeper (↑ blockage hazard)
  - 1º = Extrapulmonary bronchi
  - 2º = Intrapulmonary bronchi

- **Trachea:**
  - Allow for food passage

- **Bronchiole:**
  - < 1 mm diameter
  - Pseudostratified ciliated columnar epithelium
  - Thick smooth muscle
  - Cartilage plates?

- **Mucous glands rare - Why?**
  - Allergic attack → Histamine = Bronchoconstriction
  - Synthetic drugs (e.g., albuterol) trigger response

- **Alveoli:**
  - 300 million / lung
  - 0.1 - 0.5 µm thick

- **Pneumocytes:**
  - Type I pneumocytes
  - Type II pneumocytes
  - Alveolar macrophages

- **Respiratory Membrane:**
  - 1) Type I pneumocytes
  - 2) Endothelial cells of capillaries
  - 3) Fused basement membranes

- **Respiratory Physiology:**

  -**Respiration includes:**
  1) Pulmonary ventilation (pumping air in / out of lungs)
  2) External respiration (gas exchange @ blood-gas barrier)
  3) Transport of respiratory gases (blood)
  4) Internal respiration (gas exchange @ tissues)
Pulmonary Ventilation:

Why is the intrapleural pressure negative?

Answer: Interaction of opposing forces

Forces acting to collapse lung:
1) Elasticity of lungs
2) Alveolar surface tension

Force resisting lung collapse:
1) Elasticity of chest wall

Surface tension of serous fluids keep lungs “stuck” to chest wall

Pneumothorax: (“sucking chest wound”)
Puncture of chest wall; results in inability to generate negative pressure and expand the lungs

Pulmonary ventilation is a mechanical process that depends on thoracic cavity volume changes

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 22.13

Pulmonary ventilation is a mechanical process that depends on thoracic cavity volume changes

Boyle’s Law:

\[ P_1 V_1 = P_2 V_2 \]

Example: \( 4 \text{ mm Hg} (2 \text{ mm}^3) = P_2 (4 \text{ mm}^3) \) \( P_2 = 2 \text{ mm Hg} \)

CHANGING THE VOLUME RESULTS IN INVERSE CHANGE OF PRESSURE

Marini et al. (Fundamentals of Anatomy and Physiology, 7th ed.) – Figure 23.13

Pulmonary ventilation is a mechanical process that depends on thoracic cavity volume changes

Muscular expansion of thoracic cavity
A) Contraction of diaphragm
   • Lengthens thorax (pushes liver down)
B) Contraction of external intercostal muscles
   • Widens thorax

Muscular expansion of thoracic cavity
A) Contraction of diaphragm
   • Lengthens thorax (pushes liver down)
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   • Widens thorax

Results in:
• Reduced intrapleural pressure \( (P_{ip}) \)
• Reduced intrapulmonary pressure \( (P_{pul}) \)

Results in decreased pressure in thoracic cavity and air enters

Marini et al. (Fundamentals of Anatomy and Physiology, 7th ed.) – Figure 23.13

Atmospheric pressure = ~ 760 mm Hg
(Consider \( P_{atmosphere} = 0 \text{ mm Hg} \))

1) Intrapulmonary Pressure (w/in the alveoli):
   • Static conditions = 0 mm Hg

2) Intrapleural pressure (w/in pleural cavity):
   • Always relatively negative (~ -4 mm Hg)

Inhalation (inspiration) = \( P_{pul} \) slightly negative

Exhalation (expiration) = \( P_{pul} \) slightly positive

Prevents lungs from collapsing
Pulmonary Ventilation:

Pulmonary ventilation is a mechanical process that depends on thoracic cavity volume changes

Expiration:
Retraction of thoracic cavity
A) Passive Expiration
- Diaphragm / internal intercostals relax
- Elastic rebound (lung rebound)
B) Active ("Forced") Expiration
- Abdominal muscles contract
- Internal intercostals contract

Eupnea:
Quiet breathing
(pассивное дыхание)
(динамическое дыхание)

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Lung compliance
It is to expand the lungs at a given pressure
The higher the lung compliance, the easier it is to expand the lungs at a given pressure

Respiratory Distress Syndrome

Several physical factors exist influence pulmonary ventilation

A) Airway resistance

Airflow is directly proportional to pressure difference between outside air and alveoli and inversely proportional to resistance of the airway

B) Surface tension in alveoli

Surface tension generated as neighboring liquid molecules on the surface of alveoli are drawn together by attractive forces

Pressure required to keep alveolus open

Law of Laplace:

Several physical factors exist influence pulmonary ventilation

C) Lung compliance

Measure of change in lung volume that occurs with a given transpulmonary pressure

The higher the lung compliance, the easier it is to expand the lungs at a given pressure

Determined by:
1) Elasticity of lung
2) Surface tension

Emphysema
Increased lung compliance due to loss of elastic fibers

Fibrosis
Decreased lung compliance due to scar tissue build-up

respiratory reading

Respiratory Volumes / Capacities:

Increases with:
• Body size
• Gender
• Conditioning

Vital capacity (~ 4800 ml)
Decreases with:
• Age

Total lung capacity (~ 6000 ml)

(Total lung capacity ~ 6000 ml)

(Female ~ 4200 ml)
Pathophysiology:

**Forced vital capacity (FVC)** is the total volume of air that can be forcibly expired after maximal inspiration; this is a useful measure of lung disease.

**Cardiovascular System**

- **Vessels**

  - **Forced vital capacity (FVC)** is the total volume of air that can be forcibly expired after maximal inspiration; this is a useful measure of lung disease.

  - **Costanzo** (Physiology, 4th ed.) – Figure 5.6

  - **FEV** = Forcefully expired volume

  - **FEV** < 0.8

  - **Both FEV** and FVC low but FEV decreased more than FVC:

  - **Both FEV** and FVC low but FVC decreased more than FEV:

  - **Respiratory System**

  - **Pulmonary Ventilation:**

    - Not all inhaled air participates in gas exchange; this volume is referred to as **dead space**.

    - **Anatomical dead space** in a healthy young adult is equal to 1 ml / pound of ideal body weight.

    - **Physiological dead space**:

      - Anatomic dead space plus any ventilated alveoli that might not participate in gas exchange.

    - **Alveolar Ventilation**:

      - Available for gas transfer:

        \[
        \text{Minute Volume} = f (\text{breaths / minute}) \times (V_T - V_D) \]

        \[
        = 12 \text{ breaths / minute} \times (500 \text{ mL} - 150 \text{ mL}) \]

        \[
        = 4200 \text{ mL / minute} \]

        \[
        = 4.2 \text{ liters / minute} \]

    - **Respiratory System**

      - **Pulmonary Ventilation:**

        - **Minute Volume:**

          \[
          V_M = f (\text{breaths / minute}) \times V_T (\text{tidal volume}) \]

          \[
          = 12 \text{ breaths / minute} \times 500 \text{ mL} \]

          \[
          = 6000 \text{ mL / minute} \]

          \[
          = 6.0 \text{ liters / minute} \]

          - **Alveolar Ventilation**:

            \[
            V_A = f (\text{breaths / minute}) (V_T - V_D) \]

            \[
            = 12 \text{ breaths / minute} \times (500 \text{ mL} - 150 \text{ mL}) \]

            \[
            = 4200 \text{ mL / minute} \]

            \[
            = 4.2 \text{ liters / minute} \]

    - **Respiratory System**

      - **Gas Exchange:**

        - Gas exchange in the respiratory system refers to diffusion of O₂ and CO₂ in the lung and in the peripheral tissues.

        - **Basic Properties of Gases:**

          - **Dalton’s Law of Partial Pressures:**

            - The total pressure of a gas is equal to the sum of the pressure of its constituents.

            - For dry gases:

              \[
              P_X = P_B \times F \]

              \[
              P_O_2 = 760 \times 0.21 \]

              \[
              P_O_2 = 160 \text{ mm Hg} \]

            - For humidified gases:

              \[
              P_X = (P_B - P_{H_2O}) \times F \]

              \[
              P_O_2 = (760 - 47) \times 0.21 \]

              \[
              P_O_2 = 150 \text{ mm Hg} \]

        - **Respiratory Physiology:**

          - **Respiration includes:**

            1. Pulmonary ventilation (pumping air in / out of lungs)

            2. External respiration (gas exchange @ blood-gas barrier)

            3. Transport of respiratory gases (blood)

            4. Internal respiration (gas exchange @ tissues)

        - **Randall et al. (Ecker t Animal Physiology, 5th ed.) – Figure 13.19**

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Gas Exchange:

Gas exchange in the respiratory system refers to diffusion of \( \text{O}_2 \) and \( \text{CO}_2 \) in the lung and in the peripheral tissues.

### Basic Properties of Gases:

- \( \text{CO}_2 \gg \text{O}_2 \gg N_2 \)
- Solubility: How much of a gas will dissolve in a liquid at a given partial pressure

#### Henry's Law

Gases in a mixture dissolve in a liquid in proportion to their partial pressures.

\[
C_X = P_X \times \text{Solubility}
\]

- \( C_X \) = Concentration of dissolved gas (mL X / 100 mL blood)
- \( P_X \) = Partial pressure of gas (mm Hg)
- Solubility = Solubility of gas in blood (mL X / 100 mL / mm Hg)

\[
[O_2] = P_{O_2} \times \text{Solubility}
\]

\[
[O_2] = 150 \times 0.003
\]

\[
[O_2] = 0.45 \text{ mL} / 100 \text{ mL blood}
\]

Total gas concentration = Dissolved gas + Bound gas + Chemically modified gas

### Diffusion

The transfer of a gas across a cell membrane depends on the driving force, gas solubility, and the surface area available for transport.

\[
V_X = \frac{DA \Delta P}{\Delta X}
\]

- \( V_X \) = Volume of gas transferred per unit time
- \( D \) = Diffusion coefficient of the gas (includes solubility)
- \( A \) = Surface area
- \( \Delta P \) = Partial pressure difference of the gas
- \( \Delta X \) = Thickness of the membrane

### Gas Transport in the Lungs

- Unlike alveolar air, where there is only one form of gas, blood is able to carry gases in addition forms.
- Bound gas
  - Gases bind directly to plasma proteins or to hemoglobin
- Dissolved gas
  - The higher the solubility of a gas, the higher the concentration of the gas in solution
- Chemically modified gas
  - Gases react with blood components to form new products

### Gas Transport in the Lungs

- Systemic tissues undergo reversal of pattern observed at lung
- Partial pressure gradients maintained across entire length of capillary (gas does not equilibrate)

#### Diffusion-limited

The total amount of gas transported across the alveolar / capillary barrier is limited by the diffusional process.

Example: Carbon monoxide

#### Parfusional-limited

The total amount of gas transported across the alveolar / capillary barrier is limited by blood flow.

Example: Nitrous oxide
Respiratory System

Gas Exchange:

Under normal conditions, O₂ transport into pulmonary capillaries is a perfusion-limited process.

Recall:

\[ \text{PO}_2 \text{ equilibrium never reached} \]

Outcome:

Decreased \( \text{PO}_2 \) in systemic arterial blood, especially during physical activity.

Respiratory Physiology:

Driving force:

\[ \Delta P = \frac{D A \Delta P}{\Delta x} \]

Oxygen Transport in Blood:

O₂ is carried in two forms in blood: dissolved and bound to hemoglobin

A) Dissolved O₂:

- Accounts for 2% of total O₂ content of blood

\[ \text{Henry's Law:} \]

\[ \text{C}_g = \frac{\text{P}_g}{\text{S}} \]

\[ \text{C}_g = \text{Concentration of dissolved gas (mL X / 100 mL blood)} \]

\[ \text{P}_g = \text{Partial pressure of gas (mm Hg)} \]

\[ \text{S} = \text{Solubility of gas in blood (mL X / 100 mL / mm Hg)} \]

\[ \text{[O}_2\text{]} = \text{P}_\text{O}_2 \times \text{S} \]

\[ \text{[O}_2\text{]} = 100 \times 0.003 \]

\[ \text{[O}_2\text{]} = 0.30 \text{ mLL X / 100 mL blood} \]

B) O₂ bound to hemoglobin:

- Accounts for remaining 98% of total O₂ content of blood

\[ \text{Oxyhemoglobin} = \text{O}_2 \text{ bound to hemoglobin} \]

\[ \text{Deoxyhemoglobin} = \text{No O}_2 \text{ present} \]

\[ \text{Methemoglobin} = \text{Iron in ferric (Fe³⁺) state} \]

\[ \text{Should \ O}_2 \text{ oxidize iron ferric state (Fe³⁺) of} \]

\[ \text{Not} \text{ -- nitrogen bonds present then} \]

\[ \text{BUT} \text{ -- it does happen:} \]

\[ \text{Methemoglobin reductase} = \text{reduces Fe³⁺ to Fe²⁺} \]
Oxygen Transport in Blood:

O₂ is carried in two forms in blood: dissolved and bound to hemoglobin

B) O₂ bound to hemoglobin:

Hemoglobin structure demonstrates a developmental shift

The O₂ saturation of hemoglobin is a function of the PₐO₂ of blood

The actual amount of O₂ delivered to tissues:

\[ O₂ \text{ content} = (O₂ \text{ binding capacity} \times \% \text{ saturation}) + \text{O₂} \text{ dissolved} \]

\[ O₂ \text{ delivery} = \text{Cardiac output} \times O₂ \text{ content of blood} \]

Oxygen Transport in Blood:

O₂ is carried in two forms in blood: dissolved and bound to hemoglobin

B) O₂ bound to hemoglobin:

Amount of O₂ bound to hemoglobin determined by the hemoglobin concentration and by the O₂ binding capacity of that hemoglobin

O₂ binding capacity:

\[ \text{O₂ binding capacity} = 15 \text{ g / 100 mL} \times 1.34 \text{ mL O₂ / g HbA} \]

Under normal conditions:

- 1.0 g of hemoglobin can bind 1.34 mL O₂
- [hemoglobin A] = 15 g / 100 mL

This results in:

- 2.1 mL O₂ / 100 mL blood

O₂ Delivery to tissues:

The actual amount of O₂ delivered to the tissues

Costanzo (Physiology, 4th ed.) – Figure 5.22

Oxygen Transport in Blood:

O₂ is carried in two forms in blood: dissolved and bound to hemoglobin

B) O₂ bound to hemoglobin:

The O₂/hemoglobin dissociation curve can shift to the right or the left depending on local conditions in the blood

Right shift = Decreased Hb affinity for O₂

Left shift = Increased Hb affinity for O₂

The O₂/hemoglobin dissociation curve can shift to the right or the left depending on local conditions in the blood

Costanzo (Physiology, 4th ed.) – Figure 6.32

Oxygen Transport in Blood:

O₂ is carried in two forms in blood: dissolved and bound to hemoglobin

B) O₂ bound to hemoglobin:

Hemoglobin structure demonstrates a developmental shift
Respiratory System
Pathophysiology:
Carbon monoxide poisoning is catastrophic for O₂ delivery to tissues

Carbon monoxide poisoning

1) CO decreases O₂ bound to Hb
   - CO binds to Hb with an affinity that is 250x greater than that of O₂ (forms carboxyhemoglobin)

2) CO causes left shift of dissociation curve
   - Heme groups not bound to CO have an increased affinity for O₂

Example: “cherry red”

Respiratory System
Carbon Dioxide Transport in Blood:
CO₂ is carried in three forms in blood: dissolved, bound to hemoglobin, and as bicarbonate (HCO₃⁻)

A) Dissolved CO₂:
   - Accounts for 5% of total CO₂ content of blood

   \[ CO_2 = P_{CO_2} \times \text{Solubility} \]

   \[ [CO_2] = 40 \times 0.07 \] (Arterial blood)

   \[ [CO_2] = 2.80 \text{ mL} / 100 \text{ mL blood} \]

Respiratory System
Carbon Dioxide Transport in Blood:

B) CO₂ bound to hemoglobin:
   - Accounts for 3% of total CO₂ content of blood

Carbon dioxide combines with water (H₂O) to form carbonic acid (H₂CO₃)
- Reaction catalyzed by carbonic anhydrase (CA)

\[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \]

\[ \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]

Diffuses into RBCs

1) Carbon dioxide (CO₂) combines with water (H₂O) to form carbonic acid (H₂CO₃)
- Reaction catalyzed by carbonic anhydrase (CA)

2) H₂CO₃ dissociates into hydrogen ion (H⁺) and bicarbonate ion (HCO₃⁻)
   - HCO₃⁻ released into plasma
   - H⁺ buffered in RBC by deoxyhemoglobin

IN TURN

When less O₂ is bound to Hb, the affinity of Hb for CO₂ increases (the Haldane effect)

Respiratory System
Carbon Dioxide Transport in Blood:

C) CO₂ converted to HCO₃⁻:
   - Accounts for remaining 92% of total CO₂ content of blood

To maintain charge balance in RBCs, a Cl⁻ is exchanged with a HCO₃⁻ as the HCO₃⁻ leaves the cell

Chloride shift:
- Band three protein functions as passive transporter
Ventilation / Perfusion Relationships:

The distribution of pulmonary blood flow with the lung is uneven due to the effects of gravity.

1. Apex of lung: Low blood flow
   - $P_{\text{aerial}} > P_{\text{venous}} > P_{\text{arterial}}$
   - Pulmonary capillaries compressed by surrounding alveoli

2. Middle of lung: Medium blood flow
   - $P_{\text{aerial}} > P_{\text{venous}} > P_{\text{arterial}}$
   - Minimal compression; blood flow driven by $P_{\text{aerial}} - P_{\text{arterial}}$ difference

3. Base of lung: High blood flow
   - $P_{\text{aerial}} > P_{\text{venous}} > P_{\text{arterial}}$
   - The greatest number of capillaries open; high arterial and venous pressures

Mechanisms of Regulation:

- **A)** Partial pressure of alveolar $O_2$ ($P_{\text{A}}O_2$)
  - Reduces pulmonary flow to poorly ventilated alveoli
- **B)** Vasoactive Chemicals
  - Hypoxic vasoconstriction
    - If $P_{\text{A}}O_2$ falls below 70 mm Hg, blood flow to more ventilated alveoli

Control of Breathing:

Breathing is regulated so the lungs can maintain the $PaCO_2$ and $PaO_2$ within a normal range.

1. Medullary Respiratory Centers:
   - **Ventral Respiratory Group**
     - Inspiratory center: Oscillating rhythm of neuronal firing / quiescence
   - **Dorsal Respiratory Group**
     - Inspiratory center: Active during forced exhalation
     - Expiratory center: Triggers prolonged inspiratory gasps

2. Pontine Respiratory Centers:
   - **Apneustic Center**
     - Triggers prolonged inspiratory gasps
   - **Pneumotaxic Center**
     - Limits size of tidal volume

Control of Breathing:

Depth and rate of breathing can be modified in response to changing demands on the body.

Most important factors regulating ventilation are chemical.

1. Hypoxia: Increased $P_{\text{A}}O_2$ in arterial blood
2. Hypercapnia: Decreased $P_{\text{A}}CO_2$ in arterial blood

- Most potent respiratory stimulant (maintained @ $P_{\text{A}}CO_2 = 40$ mm Hg)
- Mediated via central / peripheral chemoreceptors

Chemical Factors:

- $P_{\text{A}}CO_2$
  - Mediated via central / peripheral chemoreceptors
Control of Breathing:
Chemical Factors:
A) $P_{CO_2}$
- Most potent respiratory stimulant (maintained at $\pm 3$ mm Hg)
- Mediated via central / peripheral chemoreceptors

B) $P_O_2$
- Minor respiratory stimulant ($O_2$ lacks respiratory drive)
- Mediated via peripheral chemoreceptors
- Stimulated by $P_{CO_2} < 60$ mm Hg in arterial blood

C) Arterial pH
- Independent of changes in arterial $P_{CO_2}$
- Compensatory mechanism for metabolic acidosis
- Mediated by peripheral chemoreceptors (central body is not involved)

If respiratory distress occurs:
- Mediated by peripheral chemoreceptors (carotid body only)
- Chemoreceptor stimulation by $P_{CO_2}$ in system results in $P_{O_2}$ taking over regulation

Addition factors contribute to ventilation regulation
- Nasal cavity + Sinus
- Lower conduction system + Cough
- Agress (assault of breathing)
- Epiglottic closure: thoracic cavity shrinks
- Epiglottic opens; air forcefully released (~ 100 mph)

Respiratory System
Control of Breathing:
Depth and rate of breathing can be modified in response to changing demands on the body

Addition factors contribute to ventilation regulation
- Hypoventilation: Decrease breathing rate / depth
- Hyperventilation: Increase breathing rate / depth

Pain / emotional stimuli acting through hypothalamus
Higher control centers; voluntary control over breathing

Hering-Breuer Reflex:
- What lung / arterial stretch inspiratory center initiates
- Lung stretch receptors:
- Aortic arch (X)
- Carotid body
- Vagus (X) nerve

Joint / muscle stretch receptors
Function in anticipatory response to exercise

Addition factors contribute to ventilation regulation
- Lung stretch receptors
- Infradiaphragmatic receptors
- Central chemoreceptors
- Peripheral chemoreceptors
- Carotid body (IX)
- Aortic arch (X)

Respiratory System
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