Blood Gas Homeostasis

1. **Ventilation**
2. Diffusion
3. Transport
4. Regulation

---

**Table 12-2  Effect of Different Breathing Patterns on Alveolar Ventilation**

<table>
<thead>
<tr>
<th>Breathing Pattern</th>
<th>Tidal Volume (ml/breath)</th>
<th>Respiratory Rate (breaths/min)</th>
<th>Dead Space Volume (ml)</th>
<th>Pulmonary Ventilation (ml/min)</th>
<th>Alveolar Ventilation (ml/min)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quiet breathing at rest</td>
<td>500</td>
<td>12</td>
<td>150</td>
<td>6000</td>
<td>4200</td>
</tr>
<tr>
<td>Deep, slow breathing</td>
<td>1200</td>
<td>5</td>
<td>150</td>
<td>6000</td>
<td>5250</td>
</tr>
<tr>
<td>Shallow, rapid breathing</td>
<td>150</td>
<td>40</td>
<td>150</td>
<td>6000</td>
<td>0</td>
</tr>
</tbody>
</table>

*Equals tidal volume \times respiratory rate.

**Equals (tidal volume – dead space volume) \times respiratory rate.
**Pulmonary Ventilation**

- **Minute ventilation**
- **Volume of air breathed in or out in one minute**

\[
\text{minute ventilation} = \text{tidal volume} \times \text{respiratory rate}
\]

<table>
<thead>
<tr>
<th>(ml/min)</th>
<th>(ml/breath)</th>
<th>x</th>
<th>(breaths/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6000 *BTPS</td>
<td>500 BTPS</td>
<td>x</td>
<td>12</td>
</tr>
</tbody>
</table>

*BTPS = BODY TEMPERATURE PRESSURE SATURATED (with water vapor)*

GAS VOLUME is influenced by pressure, temperature and individual gasses in the mixture

(Boyle’s Law, Charles’ Law, Dalton’s Law)

to standardize gas volumes they are corrected to STPD or BTPS

\[
\begin{align*}
\text{STANDARD TEMPERATURE PRESSURE DRY = STPD} & = (\text{VO2}, \text{VCO2}) \\
\text{BODY TEMPERATURE PRESSURE SATURATED = BTPS} & = (\text{all respiratory volumes}) \\
(37^\circ \text{C} + 100\% \text{ saturated with water vapor} = \text{bigger in body than in air})
\end{align*}
\]

**Alveolar Volume and Alveolar Ventilation**

- **Volume of air exchanged between the atmosphere and the alveoli**
- **In one breath is the ALVEOLAR VOLUME**
  - ALVEOLAR VOLUME = TIDAL VOLUME – DEAD SPACE VOLUME

- **DEAD SPACE VOLUME = anatomical dead space**
  - Volume of air in conducting airways that is not involved for exchange of gasses with blood (no alveolar / capillary interface, i.e. no respiratory membrane)
  - Averages about 150 ml in adults (2 ml/kg)

- **Alveolar ventilation = alveolar volume x respiratory rate**
  - 4200 = 350ml x 12/min

- At this Va, the FRC (2200ml) is “changed” in 2200/4400 minutes = 0.5 = 30seconds or 6 breaths at rest
Blood Gas Homeostasis

1. Ventilation
2. Diffusion
3. Transport
4. Regulation

CONDUCTING ZONE
F = δPR
Warm
Clean
Humidify
Lecture

Exchange Zone
Diffusion by individual $P_{gas}$
Flux = $\frac{(SA \times \Delta P \times K_p)}{Dist}$
Ficks Law of Diffusion
**Diffusion**

- **Definition:** movement of solute molecules from high to low concentration gradient until equilibrium occurs
- **Equilibrium:** no net change in concentration per unit time
- **Fick’s Law of Diffusion** describes factors that dictate FLUX or RATE OF DIFFUSION or TIME TO ACHIEVE EQUILIBRIUM
  - Increased Pressure Gradient, Solubility Coefficient, Surface Area all increase FLUX
  - Increase Distance decreases FLUX
  - Solubility is specific to a solute and a membrane:
    - the membrane solubility for X is high vs. the membrane solubility for Y is low
    - the Z membrane has low solubility for X molecule and high solubility for Y molecule
    - if all other factors are the same for two solutes, one with higher solubility coefficient will achieve equilibrium sooner
      - Solubility coefficient due to molecular nature and molecular weight
      - CO₂ has a higher solubility coefficient that is ~ 20 higher than O₂

**Respiratory Membrane: 0.5 µm barrier separating alveolar air and blood in pulmonary capillary**

(a) Alveolus and surrounding pulmonary capillaries

Fig. 12-4a, p. 348
**Surface Area for Gas Diffusion in Lung**

2 lungs per human have:
- 2,400 kilometres (1,500 mi) of airways
- 300 to 500 million alveoli
- total surface area of about 70 square metres (750 sq ft)
- pulmonary capillaries - laid end to end ~1000 kilometres (616 mi).
- each lung 1.1 kilograms (2.4 lb)
- Organ = 2.3 kilograms (5.1 lb)

**Blood Gas Homeostasis**

- Normal Ventilation Rate and Depth = normal $P_AO_2 = 100 \text{ mmHg}$
- $P_{Alveolar}O_2 - P_{Venous}O_2 = \Delta P \text{ mmHg} = 100\text{mmHg} - 40\text{mmHg} = 60 \text{ mmHg}$
- Solubility Coefficient for $O_2 = \sim 1.0 = \text{constant}$
- Surface Area of Lung Constant (large) = $70m^2$
- Distance: Respiratory Membrane thickness constant: .5 $\mu$m
- Cardiac Output constant so transit time of blood in pulmonary capillary constant... perfusion of alveoli constant
- Equilibrium in arterial blood ($PaO_2$) with alveolar air ($P_AO_2$)

$$O_2 \text{ Flux} = (\Delta P \times Kp \times \text{Surface Area}) / \text{Distance}$$

$$O_2 \text{ Flux} = (60\text{mmHg} \times 1.0 \times 70m^2) / .5\mu m$$
Blood Gas Homeostasis

- Normal Ventilation Rate and Depth = normal $P_A CO_2 = 40$ mmHg
- $P_{venous}CO_2 - P_{alveolar}CO_2 = \Delta P$ mmHg, $46$ mmHg $- 40$ mmHg $= 6$ mmHg
- Solubility Coefficient for CO$_2$ = °20.0 = constant
- Surface Area of Lung Constant (large) = 70m$^2$
- Distance: Respiratory Membrane thickness constant: .5 μm
- Cardiac Output constant so transit time of blood in pulmonary capillary constant... perfusion of alveoli constant
- Equilibrium in arterial blood (PaCO$_2$) with alveolar air ($P_A$CO$_2$)

$$CO_2 \text{ Flux} = (\Delta P \times Kp \times \text{Surface Area}) / \text{Distance}$$
$$CO_2 \text{ Flux} = (6 \text{mmHg} \times 20.0 \times 70m^2) / .5 \mu m$$
**O2 diffusion capacity**

Ventilation = 6 liters/min  
Alveolar Ventilation = 4 liters/min  
Cardiac Output = 5 liters/min  

Total Arterial O2 content = 1000 ml O2  
(mostly on Hb)

PAO2 = 100  
PaO2 = 40  
ml O2/mmHg

250 ml O2 diffuses each minute from alveoli to make oxygenated arterial blood, it replaces O2 used in mitochondria.

Oxygen diffusion capacity, ml O2/mmHg/PO2/min

= 250/60 = 4.2 ml O2/mmHg/min

---

**CO2 diffusion capacity**

Ventilation = 6 liters/min  
Alveolar Ventilation = 4 liters/min  
Cardiac Output = 5 liters/min  

Total Arterial CO2 content = 2600 ml  
(most as bicarbonate HCO3⁻)

200 ml CO2 diffuses each minute into alveoli to clear blood of CO2 that was made in mitochondria.

CO2 diffusion capacity is ml CO2/mmHg/min = 200/6 = 33.3 ml CO2/mmHg/min
Healthy Lungs Diffusion to Equilibrium Occurs rapidly compared to transit time available

TISSUE DIFFUSION

Diffusion Capacity is altered if

- Ventilation and Perfusion are mismatched 😞
  - Whole body rest V:P
    - 4 liters alveolar : 5 liters Cardiac Output = 4:5 = 0.8
    - local mismatch 1ml O2 blood flow: 2 ml air flow = 0.5 = “low” blood flow for airflow present or “high” airflow for blood flow “present”
  - Gravity causes V:P in different areas of lungs to be slightly mismatched... smooth muscle responds to try to “fix” imbalance (restore homeostatic “normal”)
    - Adjust Air flow to better match with blood flow (bronchoconstriction/broncho dilation)
    - Adjust Blood flow to better match with air flow (vasoconstriction or vasodilation of pulmonary arterioles)
    - Change smooth muscle contraction force by changing local enviroment
      - Alveolar CO2 influences bronchiol smooth muscle contractile status (bronchoconstriction/brochodilation)
      - Arterial O2 influences arteriole's smooth muscle (vasoconstriction or vasodilation)
Low Airflow due to mucus
Low airway O2
Constriction arteriole
Increase resistance to blood flow
Decrease blood flow
Better ventilation perfusion match in area

High Airflow due bigger breath
Higher airway O2
Dilate arteriole
Decrease resistance to blood flow
Increase blood flow
Better ventilation perfusion match in area

Low Airflow = High CO2
High airway CO2
Dilate Airway
Decrease resistance to air flow
Increase blood flow
Better ventilation perfusion match in area

High Airflow = Low CO2
Low airway CO2
Constrict Airway (Bronchoconstriction)
Increase resistance to air flow
Decrease air flow
Better ventilation perfusion match in area
Predict Change to Fix Problem

Assume that ventilation to an alveolar sac is low, due to a small tumor.
- \( \text{PO}_2 \) decreases because \( \text{O}_2 \) is not replenished
- \( \text{PCO}_2 \) increases because \( \text{CO}_2 \) is not diminished

Predict the response of the arterioles and bronchioles, and click the correct button.

Low \( \text{O}_2 \) = arterial constrict
High \( \text{CO}_2 \) = airways dilate

Smoking Acutely and Chronically Decreases O2 diffusion capacity

- **ACUTE: sudden**
  - Carbon Monoxide causes acute vasoconstriction and decreases pulmonary capillary volume
  - Carbon Monoxide replaces \( \text{O}_2 \) on Hb binding site and is not released at tissue
    - Most \( \text{O}_2 \) is transported on Hb so diffusion capacity is low

- **Chronic: long term**
  - Structural Damage
    - Emphysema
      - Loss of surface area
      - Fick’s LAW: Surface Area x Kp x \( \Delta P \)
      - Increased Distance (change in alveolar epithelial structure)
    - Heart Failure (left congestive heart failure) lung interstitial space fills with fluid filtered out of pulmonary capillary by high pulmonary artery pressure (increase diffusion distance)
1. Ventilation
2. Diffusion
3. Transport
4. Regulation
Gas Transport

- Most oxygen in the blood is transported bound to hemoglobin.

\[ \text{Hb} + \text{O}_2 \leftrightarrow \text{HbO}_2 \]

(reduced hemoglobin) (oxyhemoglobin)

- Hemoglobin combines with oxygen to form oxyhemoglobin.
  - This is a reversible process, favored to form oxyhemoglobin in the lungs.
    - \[ \text{Hb} + \text{O}_2 \rightarrow \text{HbO}_2 \]
  - Hemoglobin tends to combine with oxygen as oxygen diffuses from the alveoli into the pulmonary capillaries.

- A small percentage of oxygen is dissolved in the plasma.
  - .03 ml/mmHg ΔP/ dl blood
    - at normal PaO₂ 100mmHg = .3ml O₂/dl blood
    - at normal PVO₂ 40mmHg = .12ml O₂/dl blood
O2 transport on Hemoglobin

1 gram Hb  100% Saturated with 1.34 ml O2
% Saturation is altered by
(1) pO₂ mmHg
(2) At any pO₂
   (1) Temperature
   (2) pH
   (3) PCO₂
   (4) DPG
Gas Transport

Hemoglobin promotes the net transfer of oxygen at both the alveolar and tissue levels.

- There is a net diffusion of oxygen from the alveoli to the blood. This occurs continuously until hemoglobin is as saturated as possible (97.5% at 100 mm of Hg).
- At the tissue cells hemoglobin rapidly delivers oxygen into the blood plasma and on to the tissue cells. Various factors promote this unloading.
- An increase in carbon dioxide from the tissue cells into the systemic capillaries increased hemoglobin dissociation from oxygen (shifts the dissociation curve to the right).
Gas Transport

- Increased acidity has the same effect.
- This shift of the curve to the right (more dissociation) is called the Bohr effect.
- Higher temperatures also produces this shift, as does the production of BPG.
- Hemoglobin has more affinity for carbon monoxide compared to oxygen.
Gas Transport

Most CO\(_2\) (about 60%) is transported as the bicarbonate ion
- CO\(_2\) combines with H\(_2\)O to form carbonic acid
  - The enzyme carbonic anhydrase facilitates this in the erythrocyte
  - Carbonic acid dissociates into hydrogen ions and the bicarbonate ion
- 2-step, reversible process is favored at the tissue cells
  - The reverse of this process occurs in the lungs
- 30% of the CO\(_2\) is bound to hemoglobin in the blood
- About 10% of the transported CO\(_2\) is dissolved in the plasma
- By the chloride shift, the plasma membrane of the erythrocyte passively facilitates the diffusion of bicarbonate ions and chloride ions
- By the Haldane effect the removal of O\(_2\) from hemoglobin at the tissue cells increases the ability of hemoglobin to bind with CO\(_2\)
Tissue cells

Alveoli

1. Dissolved CO₂ → O₂ + Hb
2. CO₂ + Hb → HBCO₂
3. CO₂ + H₂O + ca → H⁺ + HCO₃⁻

Red blood cell

From systemic circulation to pulmonary circulation

HbO₂ ← O₂ + Hb

HbO₂

Hb + CO₂ → HbCO₂

Hb + CO₂ + H⁺ → HbH

HbO₂ + CO₂ → HbO₂ + CO₂

H₂O + CO₂ → HbO₂ + CO₂

Dissolved CO₂

Plasma

ca = Carbonic anhydrase

Table 12-4  Miniglossary of Clinically Important Respiratory States

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea</td>
<td>Transient cessation of breathing</td>
</tr>
<tr>
<td>Asphyxia</td>
<td>O₂ starvation of tissues, caused by a lack of O₂ in the air, respiratory impairment, or inability of the tissues to use O₂</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>Bluiness of the skin resulting from insufficiently oxygenated blood in the arteries</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Subjective sensation of shortness of breath, often accompanying labored or difficult breathing</td>
</tr>
<tr>
<td>Eupnea</td>
<td>Normal breathing</td>
</tr>
<tr>
<td>Hypercapnia</td>
<td>Excess CO₂ in the arterial blood</td>
</tr>
<tr>
<td>Hyperpnea</td>
<td>Increased pulmonary ventilation that matches increased metabolic demands, as in exercise</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>Increased pulmonary ventilation in excess of metabolic requirements, resulting in decreased P₄ CO₂ and respiratory alkalosis</td>
</tr>
<tr>
<td>Hypocapnia</td>
<td>Below-normal CO₂ in the arterial blood</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>Underventilation in relation to metabolic requirements, resulting in increased P₄ CO₂ and respiratory acidosis</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Insufficient O₂ at the cellular level</td>
</tr>
<tr>
<td>Respiratory arrest</td>
<td>Permanent cessation of breathing (unless clinically corrected)</td>
</tr>
<tr>
<td>Suffocation</td>
<td>O₂ deprivation as a result of an inability to breathe oxygenated air</td>
</tr>
</tbody>
</table>
Blood Gas Homeostasis

1. Ventilation
2. Diffusion
3. Transport
4. Regulation

Control of Ventilation

- Respiratory centers in brain stem establish a rhythmic breathing pattern
  - Medullary respiratory center
    - Dorsal respiratory group (DRG)
      - Mostly inspiratory neurons
    - Ventral respiratory group (VRG)
      - Inspiratory neurons
      - Expiratory neurons
  - Pre-Bötzinger complex
    - Widely believed to generate respiratory rhythm
  - Pneumotaxic center
    - Sends impulses to DRG that help “switch off” inspiratory neurons
    - Dominates over apneustic center
Control of Respiration

- Apneustic center
  - Prevents inspiratory neurons from being switched off
  - Provides extra boost to inspiratory drive
- Hering-Breuer reflex
  - Triggered to prevent overinflation of the lungs
- Chemical factors that play role in determining magnitude of ventilation
  - $\text{Pa}_\text{CO}_2$
    - Via central chemoreceptors
    - Via peripheral chemoreceptors
  - $\text{H}^+$
    - Via peripheral chemoreceptors
  - $\text{Pa}_\text{O}_2$
    - Via peripheral chemoreceptors

Fig. 12-25, p. 374
Arterial $P_{CO_2}$ relieves central chemoreceptors. Peripheral chemoreceptors (when arterial $P_{CO_2}$ > 70–80 mm Hg) increase brain ECF $P_{CO_2}$, which combines with water ($CO_2 + H_2O \xrightarrow{ca} H^+ + HCO_3^-$) to form carbonic acid ($H_2CO_3$) and releases $H^+$. This increases brain-ECF $H^+$, which stimulates ventilation and decreases arterial $P_{CO_2}$.

$ca = $ Carbonic anhydrase