5. Oxygen transport

Partial Pressures of Alveolar Gases
In the alveoli, the partial pressures of oxygen and carbon dioxide vary during the respiratory cycle. As gas exchange occurs, the alveolar partial pressure of carbon dioxide will rise and the alveolar partial pressure of oxygen will fall. Because these fluctuations are small (a few mm Hg) as compared with the 3000 ml present at the end of tidal exhalation, they are generally ignored and only **mean values PO_2 and PCO_2 are considered.**

The relationship between PO_2 and PCO_2 in the alveoli is described by the **alveolar gas equation**:

$$\mathbf{PAO_2 = (P_{atm} - P_{H2O}) \times FiO_2 - PACO_2/RQ}$$

Because diffusion is so rapid and complete in the lung, the $PACO_2$ and PAO_2 in the alveoli normally determine these gas pressures in arterial blood ($PaCO_2$ and PaO_2). But there is a slight difference between alveolar and arterial gas pressures even in normal subjects such that PAO_2 and PaO_2 differ by 5-15 mm Hg. This difference is due to anatomical shunting of blood (reduced perfusion) and to the mismatch between ventilation and perfusion that exists even in normal lungs. Both of these conditions will be discussed later in detail.

Normal values for **arterial PaO_2 and $PaCO_2$** are:
PaO_2 = 100 mm Hg
$PaCO_2$= 40 mm Hg.

The PaO_2 and $PaCO_2$ can be measured directly from arterial blood draws. PAO_2 is calculated by the alveolar gas equation. For a patient breathing room air at sea level, this equation simplifies to:

$$\mathbf{PAO_2 = 150 - PaCO_2/0.8}$$

Notice that alveolar PO_2 is determined by three factors:
1. PO_2 of atmospheric air
2. Alveolar ventilation rate
3. Rate of tissue O_2 consumption (RQ).

Each of these factors can change independent of another. For example, a decrease in either PO_2 of the atmospheric air (changes with altitude) or in alveolar ventilation (hypoventilation) will decrease the amount of fresh air entering the alveoli per unit time. Likewise, an increase in the rate of total body O_2 consumption will decrease PO_2 in the alveoli.

Because there is essentially no PCO_2 in inspired air, only the rate of ventilation and the rate of tissue metabolism affect the PCO_2 levels in the alveoli. In this instance, hypoventilation and/or increased cellular metabolism will increase PCO_2 in the alveoli.

Hypoventilation exists when there is an **increase in the ratio of CO_2 production to alveolar ventilation.** That is the alveolar ventilation cannot keep up with CO_2 production resulting in a rise in alveolar **$PACO_2$ > 40 mm Hg**. Hypoventilation can be caused by drugs such as barbiturates that depress the part of the central nervous system that drives breathing, or by damage to the chest wall, lungs, or respiratory muscles and when the movement of the chest wall is limited (e.g., caused by arthritis or deformation of the thoracic cavity).

Hyperventilation exists when there is a **decrease in the ratio of CO_2 production to alveolar ventilation**. That is the alveolar ventilation is too great for the CO_2 produced resulting in **$PACO_2$ < 40mmHg.** Hyperventilation will occur in response to hypoxia, high altitude, or some drugs such as cocaine which can cause anxiety attacks.

***Notice that **hyperventilation is not "increased ventilation**" that accompanies mild to moderate aerobic exercise. In aerobic *exercise the increase in production of CO_2 is matched to increased alveolar ventilation (depth and rate of breathing).*

Transport of Oxygen and Carbon Dioxide
To enhance delivery and transport of O_2 and CO_2 to and from tissues, specialized mechanisms (O_2-hemoglobin and bicarbonate transport of CO_2) have evolved.

OXYGEN TRANSPORT
Oxygen is not very soluble in water and therefore requires the carrier, hemoglobin (Hb), for transport in blood. Blood normally contains about 15 g of Hb per 100 ml. This effectively raises the solubility of O_2 from 3ml/L of plasma (blood minus the red blood cells) to 200 ml/L plasma. Since oxygen consumption ranges from 250 to 1500 L/min, this extra O_2 carrying capacity of Hb enables the heart and lungs to provide for the O_2 needs of the body.

Hemoglobin binds up to 4 molecules of O_2 tightly, cooperatively, and reversibly. Normally Hb is almost completely saturated (96%) when exposed to room air (FiO_2 = 21%). This occurs because of the transit time (0.75 seconds) for the red blood cell through the alveolus-capillary unit and the rapid equilibration (0.3 seconds) for both carbon dioxide and oxygen within this region of the lung.

This rapid equilibration reflects the driving pressure for diffusion and the solubility of the gas. The driving pressure for diffusion of CO_2 in the alveolus-capillary unit is lower ($PMVCO_2$-$PaCO_2$ = 46 mm Hg - 40mm Hg = 6 mm Hg) than that for O_2 (PaO_2 - $PMVO_2$ = 100 - 40 = 60 mm Hg), but the solubility of CO_2 in plasma is much greater. The net result is that the rates of diffusion for CO_2 and O_2 are approximately equal in the alveolus-capillary unit. This means that **there is ALWAYS adequate time to saturate Hb with O_2 regardless of ventilatory rate.**

Oxygen concentration in the blood is dependent on the **Hb concentration** in the red blood cells, the number of red blood cells (**hematocrit**), and on the adequacy of **perfusion** of the lungs rather than on diffusion rate itself.

Not all of the O_2 bound to Hb is released in the tissues. At rest only about 25% of the O_2 in blood is released. This provides a large driving force for diffusion and a large reservoir of O_2 to be called upon when needed as in exercise.

The Hb-O_2 dissociation curve is **S-shaped** because the interaction of oxygen with hemoglobin is **cooperative**. That is, when one oxygen molecule binds, it increases the affinity of the hemoglobin for the next oxygen molecule. Each hemoglobin molecule can bind four oxygen molecules.

The plateau of the Hb-O_2 dissociation curve is called the "**association part"** of the curve, because oxygen is loaded in the lungs at relatively high partial pressures. Increasing the partial pressure above 100 or down to about 80 mm Hg, ***does not result*** in a large change in the % saturation. This tends to stabilize arterial O_2 content, making it relatively insensitive to moderate changes in breathing or altitude.

The "**dissociation part"** of the curve is the steep part of the curve. In this region a small change in PO_2 results in a large change in % saturation which allows for large quantities of oxygen to be dumped in the tissues.

The P50 is the partial pressure of oxygen required to saturate 50% of the hemoglobin. A normal P50 is about 26-27 mm Hg. This value is a useful measure of the affinity of hemoglobin for O_2.

Oxygen-Hb binding and association is affected by a number of parameters including temperature, the red blood cell metabolite 2,3 diphosphoglycerate (DPG), and pH. Elevated temperature, low pH and increased 2,3 DPG shift the curve to the right (**decrease affinity**) which **enhances unloading of O_2 from Hb**. Note that these are conditions found within the interstitial tissue surrounding actively contracting muscle. Hypoxic conditions also result in increased formation of 2,3-DPG by the red blood cells.

Conversely, a decrease in temperature, high pH and a decrease in 2,3, DPG shifts the O_2-Hb dissociation curve to the left (**increase affinity**) which **promotes loading of O_2 onto Hb**.