PICU Resident Self-Study Tutorial

The Basic Physics of Oxygen Transport

"I was told that there would be no math!"

Christopher Carroll, MD

INTRODUCTION

Physiology of Oxygen Transport

Although cells rely on oxygen for aerobic metabolism and viability, the tissues have no storage system for oxygen. They must receive a continuous supply at a rate that precisely matches changing metabolic requirements. If this supply falls, even for a few minutes, tissue hypoxemia may develop, resulting in anaerobic metabolism and lactic acidosis.

Oxygen transport from environmental air to the mitochondria of individual cells occurs in a series of steps. The heart, lungs, and circulation extract oxygen from the atmosphere and generate a flow of oxygenated blood to the tissues to maintain aerobic metabolism.

In this self-study tutorial, we will go over the basic physics of oxygen transport and delivery. The objective of this tutorial is to introduce the some of the key concepts and underlying mathematical equations underlying oxygen transport and delivery.

OXYGEN UPTAKE IN THE LUNGS

Arterial oxygen tension (PaO_2) is determined by four factors:

1. Inspired Oxygen Concentration and Barometric Pressure
2. Alveolar Ventilation
3. Diffusion of Oxygen from Alveoli to Pulmonary Capillaries
4. Distribution and Matching of Ventilation and Perfusion

Inspired Oxygen Concentration and Barometric Pressure

The percentage of oxygen in dry atmospheric air is a constant 21% of the total dry gas pressure (that is, excluding water vapor). This percentage does not change with altitude. At sea level, the barometric pressure is 760 mmHg, and at the body temperature of 37^{o}C, the water vapor pressure is 47 mmHg. To correct for humidification, the PO_2 of inspired air (PiO_2) can be calculated by

$$PiO_2 = (P_{barometric} - P_{water}) \times FiO_2$$

$$\mathbf{PiO_2 = (760\text{-}47) \times FiO_2}$$

PICU Resident Self-Study Tutorial

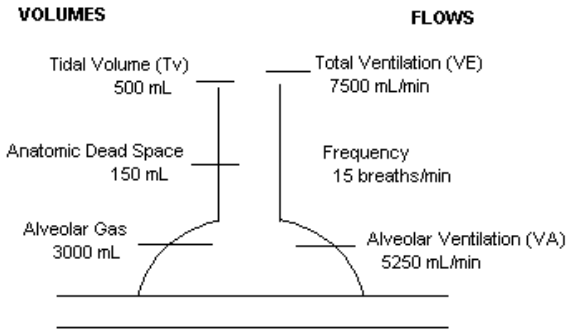
The Basic Physics of Oxygen Transport

Alveolar Ventilation

Ventilation of the alveoli is essential if alveolar oxygen pressure (P_AO_2) is to be maintained and carbon dioxide removed. Alveolar ventilation (V_A) depends on the rate of breathing and the tidal volume (Tv). However, not all the air that is inhaled reaches the alveolar gas compartment where gas exchange occurs. **Dead space** is the part of each breath that does not take part in gas exchange. In normal individuals, about one third of a tidal volume is wasted in the anatomical dead space. (This is a remarkably constant proportion for most animals, even giraffes!) Total ventilation (V_E) is then made up of Alveolar (V_A) and Dead Space (V_D) Ventilation and can be summarized as follows: $V_E = V_A + V_D$

Or re-arranged, we can calculate **Alveolar Ventilation**:

$$\mathbf{V_A = V_E - V_D}$$



So, in the example above, of each 500 mL inhaled, 150 mL remain behind in the anatomic dead space. Thus, the volume of fresh gas entering the respiratory zone (where gas exchange occurs) each minute is (500 – 150) x 15 or 5250 mL/min. This is called the **Alveolar Ventilation** and is the amount of fresh inspired air available for gas exchange.

Note that Alveolar Ventilation can be increased by raising either the tidal volume or respiratory frequency. However, increasing the tidal volume is often more effective because this reduces the proportion of each breath occupied by anatomic dead space.

Another way of assessing the alveolar ventilation in normal subjects is from the concentration of CO_2 in expired gas. The relationship among alveolar ventilation (V_A), the volume of CO_2 exhaled per unit time, and the alveolar partial pressure of CO_2 is:

$$V_A = (V_{CO2} / PCO_2) \times K \qquad \text{(where K is a constant)}$$

Because in normal subjects, the PCO_2 of alveolar gas (P_ACO_2) and arterial blood ($PaCO_2$) are virtually identical, the arterial PCO_2 can be used to determine alveolar ventilation. **Assuming that CO_2 production remains unchanged, alveolar ventilation is inversely proportional to the arterial PCO_2.** If the alveolar ventilation is halved, for example, the alveolar and arterial PCO_2 will double.

Alveolar Hypoventilation

Alveolar Hypoventilation occurs when there is not enough flow to the alveolar to have adequate gas exchange. This is reflected by a fall in alveolar and arterial PO_2 with increasing $PaCO_2$. Note that alveolar hypoventilation can occur even with a normal minute ventilation in the cases of very low tidal volumes with a large proportion of dead space.

The relationship between the fall in PO_2 and the rise in PCO_2 that occurs in hypoventilation can be calculated from the **alveolar gas equation**. The alveolar gas equation calculates the alveolar PO_2 (P_AO_2) using the composition of inspired oxygen (PiO_2), the alveolar PCO_2 and the respiratory exchange ratio. The respiratory exchange ratio (otherwise known as the respiratory quotient, R) is the ratio of the CO_2 production and O_2 consumption and is determined by the metabolism of tissues at steady state. (normal R = 0.8)

The Alveolar Gas Equation

$$P_AO_2 = PiO_2 - (P_ACO_2/R)$$

If you insert the equation for PiO_2, substitute the normal value for R, and assume that alveolar and arterial PCO_2 are equal you get:

$$\mathbf{P_AO_2 = (713 \times FiO_2) - (PaCO2/0.8)}$$

The Alveolar Gas Equation is important because it explains why a small amount of supplemental oxygen will prevent hypoxia in patients with chronic respiratory failure. Alveolar hypoventilation and increasing $PaCO_2$ will decrease the P_AO_2. However, a small amount of added FiO_2 will prevent a fall in P_AO_2.

Dead Space

There are several components to the dead space:

- Apparatus Dead Space
  - occurs in ventilated patients, from the expanding volume of the ventilator tubing with inspiration
- Anatomical Dead Space
  - from the volume of the conducting passages
- Alveolar Dead Space
  - from alveoli that are well ventilated but poorly perfused, so they effectively contribute to the dead space

Physiological Dead Space (V_D)

the sum of the anatomical and alveolar dead spaces, and represents all components of the tidal volume that do not take part in gas exchange

what is commonly referred to as "dead space"

Physiological dead space (V_D) can be calculated using **Bohr's Equation**. This is derived from the equation for Alveolar Ventilation, and assumes that all of the expired CO_2 comes from the alveolar gas and none from the dead space and also that the alveolar and arterial PCO_2 are identical (which they almost always are). V_T is the tidal volume, $PaCO_2$ is the arterial PCO_2 and P_ECO_2 is the expired PCO_2.

$$\mathbf{V_D / V_T = (PaCO_2 - P_ECO_2) / PaCO_2}$$

Normal V_D / V_T = 0.2-0.3

Diffusion from alveoli to pulmonary capillaries

The partial pressure of oxygen in alveolar blood (P_AO_2) provides the driving pressure for diffusion into the pulmonary capillary blood and in normal conditions is the main determinant of the partial pressure of oxygen in arterial blood (PaO_2). The P_AO_2 - PaO_2 gradient (otherwise known as the **A-a gradient**) describes the overall efficiency of oxygen uptake from alveolar gas to arterial blood in the lungs. It is normally less than 7.5 torr but may exceed 450 torr in severe respiratory failure.

$$\mathbf{A\text{-}a\ gradient = P_AO_2 - PaO_2}$$

Using the alveolar gas equation to calculate P_AO_2, you get another **formula for A-a gradient**:

$$\mathbf{A\text{-}a\ gradient = [(713 \times FiO_2) - (PaCO2/0.8)] - PaO_2}$$

GETTING THE OXYGEN TO THE TISSUES

Oxygen Carrying Capacity of the Blood

Most oxygen is carried in the blood bound to hemoglobin with only a small amount dissolved in the plasma. The formula for calculating the oxygen content of blood is:

$$\mathbf{Oxygen\ Content\ (CO_2) = (1.34 \times Hb \times Saturation) + (0.003 \times PO_2)}$$

This formula can be used to calculate the oxygen content of arterial or venous blood. SvO_2 is the venous oxygen saturation and SaO_2 is the arterial oxygen saturation

$$\mathbf{CaO_2 = (1.34 \times Hb \times SvO_2) + (0.003 \times PaO_2)}$$

$$\mathbf{CvO_2 = (1.34 \times Hb \times SaO_2) + (0.003 \times PvO_2)}$$

Oxygen Delivery

The major function of the central circulation is to transport oxygen from the lungs to the peripheral tissues at a rate that satisfies overall oxygen consumption requirements. Failure to meet these needs results in circulatory shock.

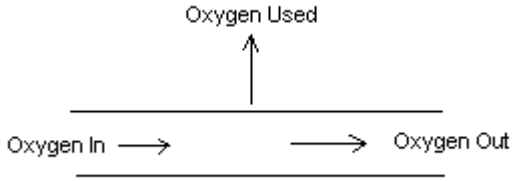
Under normal conditions, the total oxygen delivery is more than adequate to meet the total tissue requirements for aerobic metabolism. Only 25-30% of delivered oxygen is used. Accordingly, venous blood is usually 70-75% saturated when it returns to the heart.

Oxygen delivery (DO_2) is defined as the product of cardiac output (Q) and the oxygen content of blood.

$$\mathbf{DO_2 = Q \times CaO_2}$$

Oxygen Consumption

In 1870, the German physiologist Adoph Fick contrived the first method for measuring cardiac output in intact animals and people. The basis for this method, called the **Fick Principle**, is simply an application of the law of conservation of mass. **It states that the amount of a substance that goes into an organ in a given period of time minus the amount that comes out, must equal the tissue utilization of that substance.**



As applied to oxygen, the amount transported to the peripheral tissues per unit time (DaO_2) minus the amount of oxygen that leaves the peripheral tissues per unit time (DvO_2), equals the oxygen consumption (VO_2) of the peripheral tissues. Or in equation form:

$$VO_2 = DaO_2 - DvO_2$$

Now, if we replace DaO_2 and DvO_2 using the equation for oxygen delivery,

$$VO_2 = (Q \times CaO_2) - (Q \times CvO_2)$$

And by mathematically re-arranging we arrive at what is referred to as the **Fick Equation.** (Note: The factor of 10 is added to correct for unit conversion)

$$\mathbf{VO_2 = Q \times (CaO_2 - CvO_2) \times 10}$$

The Fick Equation can be used to calculate cardiac output when the oxygen consumption is known, or to calculate oxygen consumption when the cardiac output is known.

To perform these calculations, we need to replace CaO_2 and CvO_2 with their respective equations for oxygen content (Note: conventionally, the proportion of oxygen dissolved in blood is left out of the equations, since that amount usually contributes very little to the total oxygen content)

$$\mathbf{VO_2 = Q \times [(1.34 \times Hb \times SaO_2) - (1.34 \times Hb \times SvO_2)] \times 10}$$

RELATIONSHIP BETWEEN OXYGEN DELIVERY AND CONSUMPTION

The importance of oxygen delivery in the management of critically ill patients depends on its relation with oxygen consumption. The sum of the oxygen consumptions by the various organs is the global oxygen consumption (VO_2), which can be measured directly or derived from the Fick Equation with measures of cardiac output (Q) and arterial and venous oxygen contents.

The amount of oxygen consumed (VO_2) as a fraction of oxygen delivery (DO_2) defines the oxygen extraction ratio. Normally, oxygen consumption is 25% of oxygen delivery. In other words the normal oxygen extraction ratio is 25%.

Oxygen saturation in blood draining from different organs varies widely (hepatic venous saturation is 30-40% and renal venous saturation about 80%) and reflects the balance of oxygen delivery and metabolic demands of these tissues.

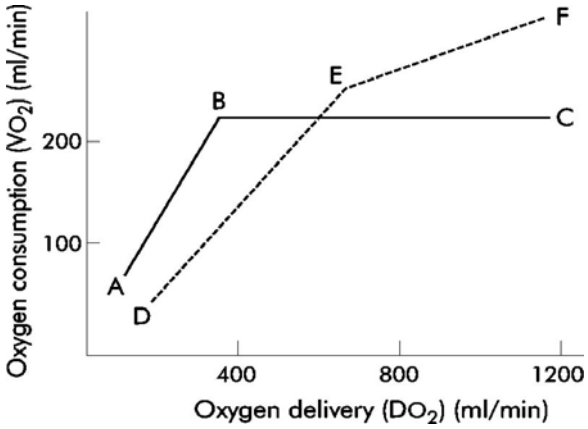
The normal 70 kg adult undertaking normal daily activity has a VO_2 of approximately 250 ml/min, with an oxygen extraction ratio of 25%. The oxygen not extracted by the tissues returns to the lungs and the mixed venous saturation (SvO_2) measured in the pulmonary artery represents the pooled venous saturation from all organs. SvO_2 will be influenced by changes in both DO_2 and VO_2, but provided that regional perfusion and the mechanisms for cellular oxygen uptake are normal, it will remain >65% if the supply matches demand.

PICU Resident Self-Study Tutorial

The Basic Physics of Oxygen Transport

As metabolic demand (VO_2) increases or supply (DO_2) diminishes, the oxygen extraction ratio rises to maintain aerobic metabolism. However, once the maximum extraction ratio is reached (at 60-70% for most tissues) further increases in demand or falls in supply lead to tissue hypoxia and anaerobic metabolism. In critically ill patients, however, the slope of maximum oxygen extraction ratio is less steep, reflecting the reduced extraction of oxygen by tissues, and does not plateau so that consumption remains supply dependent even at "supranormal" levels of oxygen delivery.

The following figure shows the relation between oxygen delivery (DO_2) and oxygen consumption (VO_2) in a normal subject (solid line) and in a critically ill patient (dotted line).



CONCLUSION

And there you go! Now you know why you had to take all that physics and math in college!

Oxygen Delivery is the fundamental concept in critical care. Almost all of our interventions in critically ill patients are designed to alter oxygen delivery. This tutorial has hopefully provided an introduction to this very interesting and expansive topic.

For further reading, I would highly recommend:

West JB. Respiratory Physiology: The Essentials. 6th edition. Baltimore, MD: Lippincott Williams & Wilkins, 2000. *(Concise and to the point. A must-have for anyone interested in Critical Care or Pulmonology)*

Mohrman DE, Heller LJ. Cardiovascular Physiology. 4th edition. New York, NY: McGraw-Hill, 1997. *(Another concise review book. A must-have for anyone interested in Critical Care or Cardiology)*

West JB. Respiratory Pathophysiology: The Essentials. 5th edition. Baltimore, MD: Lippincott Williams & Wilkins, 1997.

Berne RM, Levy MN. Cardiovascular Physiology. 7th edition. St. Louis, MO: Mosby, 1997