



THE MECHANISM OF PULMONARY DIFFUSION

by *Jim Harvey MS, RPFT, RCP*

Diffusing capacity was introduced as a clinical test in 1915 but never caught on because of the difficulty in measuring carbon monoxide. With the introduction of reliable infrared carbon monoxide analyzers in the 1950s, the test was revived, and various testing techniques were developed including single breath, steady state, rebreathing and others. For reasons of simplicity and reliability, the single breath method is in general use today.

As you all know, the diffusion capacity measurement is referred to as DLCO which stands for "diffusion lung carbon monoxide." So we are actually measuring the rate of diffusion for carbon monoxide and not oxygen. We assume that the diffusion for carbon monoxide will be the same as for oxygen, but as we will see later, there is a significant difference.

The term diffusion capacity is actually not accurate because, in conformance with other capacities of the lung, diffusion implies a maximum capacity or transfer of gas. Laboratory tests do not assess the lung's transfer ability at maximum, so the term is incorrect. For this reason, many authors and all Europeans prefer to use the term "transfer factor" to denote the lungs' ability to passively transfer gases across the alveolar capillary membrane.

The diffusion capacity test is one of the most important tests performed by pulmonary function technologists, and its successful completion depends on many factors. It is really a direct measurement of the transfer of carbon dioxide across the alveolar capillary membrane and the physiological process is very interesting and worth a closer look.

The characteristics of the alveolar capillary membrane are indeed the critical component of the cardio-pulmonary system because if the alveolar capillary membrane does not allow sufficient transfer of oxygen and carbon dioxide back and forth, the entire system shuts down. There are approximately 500 million alveoli in the lung separated by thin septae, which contain a

tightly laced network of blood capillaries. There are three types of cells associated with the alveolus.

Type I pneumocytes are squamous or flat cells, which are connected together to form the alveolar hexagonal shape. The transfer of gases takes place through both membranes of these cells. Type II pneumocytes are smaller rounded cells that are responsible for the metabolic functions of the lung. They can turn into macrophages during periods of insult and can also turn into Type I pneumocytes in order to reconstruct the alveolus in healthy, young, non-smokers. Type III pneumocytes are sometimes referred to as hair cells and are thought to have a nerve function in the lung.

Oxygen or carbon monoxide must travel across several barriers on their journey from the alveolar space to the hemoglobin binding site. The actual measurement of diffusion is an estimation of the total resistance to gas transfer. The specific resistances are the alveolar lining of Type I squamous epithelium, the tissue interstitium, the capillary endothelium, the blood plasma layer, the red cell membrane, the red cell cytoplasm and the hemoglobin molecule.

For simplicity, the first four resistances are consolidated into one resistance, which is called the membrane resistance (R_m). The other three resistances are consolidated into one referred to as the red blood cell resistance or (R_{rbc}).


Oxygen, carbon dioxide and carbon monoxide transfer not by active transport but through the law of mass action. When the concentration of a gas is sufficiently higher on one side of the alveolar capillary membrane, the gas will passively follow the concentration gradient at a speed indicated by the concentration difference from one side to the other.

Each of the resistances acts as a barrier to the passive transfer of gases across the alveolar capillary membrane. Because these resistances are in series, the total resistance (RL) is the sum of the partial resistances: $RL = R_m + R_{rbc}$

We will substitute the symbol R for D because D indicates conductance. Because the reciprocal of resistance is conductance, we can rewrite the equation as:

$$\frac{1}{D} = \frac{1}{D_m} + \frac{1}{D_{rbc}}$$

The erythrocyte conductance of carbon monoxide is difficult to measure because it involves a chemical reaction or bonding with hemoglobin. Its conductance has simply been defined as theta (θ), which is a function of the reaction rate of



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carbon monoxide with the erythrocyte, multiplied by the capillary blood volume (Qc). So, the total conductance of the erythrocyte is $Drbc = \theta Qc$

In this case, theta is a constant, relating erythrocyte conductance to capillary blood volume. As such, it is the rate of test gas uptake by whole blood. The units of theta are mlO₂ (STPD)/ml of blood/min/mm Hg. The equation becomes:

$$\frac{1}{D} = \frac{1}{Dm} = \frac{1}{\theta Qc}$$

Therefore, the overall conductance, transfer factor or diffusing capacity of lung is a function of Dm or membrane conductance, which is the ability of the lung's surface area to transfer oxygen and θQc which is the ability of the lung's perfusion to remove oxygen. Ideally, the lung's transfer rate and the perfusion rate, as described above, should be the same throughout the lung but, in reality, the rates are different in various sections of the lung due to the dynamic conditions of respiration, blood flow, effects of gravity and differences in Dm, Qc, and θ .

The relationship between θ and oxygen saturation, or oxygen loading, can be imagined in regard to the rate of the capillary rate of blood flow around the alveolus. Because the alveolar-capillary tension gradient for any test gas is greatest during the early portion of capillary transit, the major portion of oxygen transfer occurs very soon after the blood enters the capillary with equilibrium occurring within 0.2 to 0.3 seconds. The average capillary transit time, which is 0.7 seconds, affects the overall diffusion rate. We will see later that cardiac output has a direct effect on diffusion.

Through studies performed using steady state and single-breath DLCO methods, the ratio for DmO₂/DmCO is 1.23. The higher Dm for oxygen in the pulmonary membrane is determined from Graham's law, which states that the rate of diffusion is inversely proportional to the square rate of molecular weight, and to Henry's law, which states that the rate of diffusion is directly proportional to the solubility coefficient.

Although it has been repeatedly attempted, it is almost impossible to measure diffusion directly for oxygen because oxygen is very difficult to isolate and analyze. Because diffusion for oxygen is significantly different for carbon monoxide, and because carbon monoxide is not a significant physiologic gas, DLCO is a somewhat artificial measurement. But as the ratio of DmO₂/DmCO is constant throughout any lung volume or cardiac output, diffusion using carbon monoxide gives a meaningful indication of the condition of the alveolar capillary membrane.

The crucial factors affecting diffusion are hemoglobin, carboxyhemoglobin, cardiac output and lung inflation. Hemoglobin has a direct effect in θQc , which is the ability of the capillary perfusion to remove oxygen transported across the pulmonary membrane. Any change in hemoglobin causes a change in the amount of oxygen transported.

In anemia, θQc is reduced, resulting in a decrease in diffusion. In polycythemia there is a resultant increase in diffusion. A hemoglobin of 14 g/dL has been found or actually has been chosen to be the standard hemoglobin, and with any values higher or lower, correction factors should be applied. A commonly used correction factor is supplied by the following equation:

$$AdjHb = DLCO \frac{(1 + \%COHb)}{100}$$

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patient can take the device to a certified sleep lab where a sleep tech will review the data and print a comprehensive report.

Another Type III home monitor provides nine channels, exceeding CMS and American Academy of Sleep Medicine requirements for portable monitoring. Handheld and wireless, it increases a patient's comfort by eliminating long lengths of wire that can tangle during sleep and impair mobility. Patient data is saved to a removable memory card for later retrieval.

Both patients and sleep professionals were taken into consideration when the following Type III device went under development. For patients, the sensor hook-up is simplified and easy to use, although it still incorporates accepted PSG sensor technology. For sleep technologists, the device collects data typically associated with Type IV devices such as finger probes and flow for testing. It also autoscores data for quick reporting or gives an option to review waveforms epoch-by-epoch in a full-featured scoring mode.

A different kind of sleep screener uses only respiratory airflow detected by a nasal cannula to detect apneic events. The unit clips to a patient's clothing or rests on his or her pillow. When breathing decreases by 50 percent or more for at least 10 seconds, the device records an apneic event on its readout. In the morning, the device shows all recorded events, and the patient can call them into his or her physician or sleep lab.

Any sleep technologist can see that there is a wide variety of diagnostic equipment available. With a little bit of research, sleep technologists and physicians can select the diagnostic systems that best suits the needs of their practice and patients.

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Normal carbon monoxide saturation or carboxyhemoglobin percent is ≤ 1 , but smokers can have a level as high as 10. Involvement in a traffic jam can result in levels up to 7. The half-life of carboxyhemoglobin is five to six hours while breathing room air and is one to two hours breathing 100 percent oxygen.

Carbon monoxide binds very strongly to the iron atoms in hemoglobin, the principal oxygen-carrying compound in blood. The affinity between CO and hemoglobin is 200 times stronger than the affinity between hemoglobin and oxygen. When CO binds to the hemoglobin, it cannot be released nearly as readily as oxygen would be. The preferential binding of carbon monoxide to heme iron is the main reason for carbon monoxide poisoning.

The decrease in diffusion with a carboxyhemoglobin above 1 percent results from the fact that there is less available hemoglobin for oxygen attachment. It has been found that diffusion decreases about 1 percent for each 1 percent increase in carbon monoxide saturation. A commonly used correction factor is supplied by the following equation:

$$AdjHb = DLCO \frac{(1 + \%COHb)}{100}$$

I noted above that the capillary transit time is approximately 0.7 seconds, and that the oxygen equilibrium time in the capillary is approximately 0.2 to 0.3 seconds. During periods of increased cardiac output, the difference between these two times allows for the proper transfer of oxygen. If the cardiac output was increased three-fold, then the capillary transit time would equal the oxygen equilibrium time. Further increases in cardiac output would result in incomplete equilibration, but that would be more than offset by the additional transport capacity of the increased blood flow.

Diffusion is slightly increased in healthy subjects and that is demonstrated by the slight increase in PaO₂ found after maximum exercise. There are additional factors to consider with exercise, including recruitment of alveoli and the general dynamic effects of increased cardiac output and minute ventilation.

Any technologist performing a diffusion capacity test will appreciate the importance of proper lung inflation in order to obtain the most accurate results. Significant alveolar inflation introduces enough test gas into the alveoli so that effective gas transfer can occur. The American Thoracic Society recommends that during the single breath diffusion maneuver, the patient should be instructed to inspire the test gas to a vital capacity which is at least 85 percent of a previous measured slow or forced vital capacity. Diffusion capacity increases in a linear fashion with increased inspired vital capacity, as well as with increased alveolar volume.

Diffusion capacity is often referred to as an indirect measurement of the condition of the alveolar capillary membrane. In reality, the test produces results that accurately reflect the condition of the membrane, as well as other related physiological factors such as hemoglobin and carboxyhemoglobin. The test has been checked for its significance through many collaborating studies. If testing devices are properly calibrated, and if standard laboratory subjects are regularly tested for proper quality assurance, then the test results can play an important and significant part in pulmonary diagnostics.

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