2.1 Introduction

Organic evolution has been essentially linked to oxygen (O\(_2\)) since it was first introduced in the earth’s atmosphere by photosynthesis of early cyanobacteria species some 2.5 billion years ago. In the steady state (i.e., normoxia), most of the oxygen consumed by a cell is used by mitochondria in the generation of adenosine triphosphate (ATP) via oxidative phosphorylation, providing eukaryotic cells with a highly sophisticated survival advantage. Whereas a total of 38 molecules of ATP are generated per molecule of glucose via oxidative phosphorylation, only 2 are produced via anaerobic metabolism. In fact, more than 90% of the oxygen consumption of the body is used for oxidative phosphorylation. Thus, since the chemical reduction of molecular oxygen is the primary source of metabolic energy for most eukaryotic cells, a constant oxygen supply is critical for continued cell function and survival.

Therefore, it is not surprising that dysoxia (i.e., inadequate supply of tissue oxygenation at levels impairing mitochondrial respiration)\(^1\) and oxygen debt are major factors in the development and propagation of multiple-organ failures, especially in critically ill patients. Dysoxia is the result of an abnormal relationship between O\(_2\) supply and O\(_2\) demand. In mammals, the function of the lungs, heart, and vasculature must ensure a continuous and adequate supply of oxygen and nutrients to the tissues to maintain cellular integrity and function.

2.2 Oxygen Delivery

The respiratory system allows gases to transfer by convective and diffusive processes between the atmospheric air and the blood. Furthermore, it also plays a central role in the maintenance of the acid–base balance and is related to other functions associated with the immune system and metabolism. This chapter focuses on the respiratory mechanisms that avoid tissue hypoxia by means of the analysis of the determinants of lung function.

The most important function of the respiratory and circulatory systems is the supply of oxygen to the cells of the body in adequate quantity and at satisfactory partial pressure.\(^2\) On the one hand, the respiratory system allows appropriate partial oxygen pressure for the diffusion of gases through the alveolar-capillary barrier. On the other hand, the cardiovascular system favors an appropriate sanguineous flow to optimize the delivery, at the tissue level, of the oxygen already incorporated into the blood. The oxygen delivery (\(\dot{D}_{O_2}\)) expresses this joint function of both systems. The quantity of oxygen made available to the body in 1 min is the product of the cardiac output (CO) and the arterial oxygen content (\(CaO_2\)):\(^3\)

\[
\dot{D}_{O_2} = CO(l/\text{min}) \times CaO_2(\text{dl/ min}) \times 10
\]

Under normal physiological conditions, the amount of oxygen delivered to the tissues is approximately 1,000 mL/min. Anaerobic metabolism occurs when \(\dot{D}_{O_2}\) falls below about 3.03 ± 1.08 mL/kg/min (dysoxia), when oxygen demands exceed oxygen supply and
tissue extraction to meet that need (e.g., beyond $V_{\text{O}_2} \text{max}$ with severe exercise), or when the mitochondria are unable to utilize the oxygen. The essential feature of hypoxia is the cessation of oxidative phosphorylation when the mitochondrial $P_{\text{O}_2}$ falls below a critical level. That is, hypoxia occurs when there is a reduction of DO$_2$ due to hypoxemia (i.e., a reduced amount of oxygen being carried in the blood), to a restriction of the blood supply to the tissues, or to both.

Oxygen is carried by the blood in two forms: as solution (i.e., dissolved in the plasma) and as oxyhemoglobin. The quantity of hemoglobin (Hb) in solution in plasma at 37°C is defined by the capacitance coefficient, which is approximately 0.003 mL \( \text{O}_2 / \text{dL} \text{ blood} \times \text{mmHg} \). The amount of oxygen that can be transported into the blood can be expressed by the equation describing CaO$_2$:

$$CaO_2 = [1.39 \times \frac{mL(O_2)}{g Hb} \times Hb(frac{v}{d}) \times SaO_2] + [Pa_{O_2} (mmHg) \times 0.003[L(O_2)/al.minHg)]$$

(2.2)

where 1.39 (Huffner’s constant) is the amount of \( mL \) O$_2$ (mL) carried per gram of Hb at sea level. Therefore, CaO$_2$ could be impaired by a decrease in the Hb concentration or in the arterial oxygen pressure (Pa$_{O_2}$).

The function of the lung and its control system allows the maintenance of CaO$_2$ and avoids the hypoxia throughout four processes:

- The generation of a pressure gradient between the alveolar space and either the mouth or the airway opening, transairway pressure\(^3\) to maintain an adequate alveolar oxygen pressure (PA$_{O_2}$) and alveolar pressure of carbon dioxide (PA$_{CO_2}$) by the cyclic ventilation of alveolar gas with atmospheric air.
- Gas exchange across the blood–air barrier. This requires a large, thin, moist exchange surface; a pump to move air; and a circulatory system to transport gases to the cells.
- Perfusion as the process by which deoxygenated blood passes through the lung and becomes reoxygenated, given an appropriate ventilation–perfusion ratio \( V_A / Q \).\(^1\)
- The maintenance of a control system that allows permanent “sensing” of specific chemical and physical conditions of the blood, especially gas pressures and acid–base status, which must follow the actual requirements of the body.

### 2.3 Pulmonary Ventilation

Ventilation is the process by which fresh gas moves in and out of the lung. Minute ventilation \( (\dot{V}E) \) or total is the volume of air that enters or leaves the lung per minute and can be expressed by the equation

$$\dot{V}E = f \times VT$$

(2.3)

where \( f \) is the number of breaths per minute, and \( VT \) is the tidal volume or volume of air inspired (or exhaled) with each breath. Tidal volume varies with age, gender, body position, and metabolic activity. In an average-size adult, \( VT \) is 500 mL (6–7 mL/kg). In children, the tidal volume is 3–5 mL/kg.\(^5\) The initial portion of the tidal volume is directed into the alveoli to effect gas exchange. However, the last portion remains in the airway conducts and is commonly referred to as anatomical dead space \( (V_{D(\text{anat})}) \). Therefore, the volume that enters the alveoli per breath \( V_A \) is

$$V_A = V_T - V_{D(\text{anat})}$$

(2.4)

and the alveolar ventilation can be expressed as

$$\dot{V}_A = \dot{V}_T \times f - V_{D(\text{anat})} \times f$$

(2.5)

or

$$\dot{V}_A = f[V_T - V_D]$$

(2.6)

Thus, the alveolar ventilation depends on the breathing pattern and the volume of dead space. This dead space is called anatomic dead space because it represents the wasted ventilation of the airways that do not participate in gas exchange. The total volume of gas in each breath not participating in gas exchange is called the physiological dead space \( V_{D(\text{physiol})} \). Normally, \( V_{D(\text{physiol})} \) is approximately equal to \( V_{D(\text{anat})} \) and accounts for 25–30% of the \( V_T \). It includes two separate components: (1) the anatomical dead space and (2) the dead space secondary to ventilated, but not perfused, alveoli or alveoli overventilated relative to the amount of perfusion. The physiological dead space may be determined by de Bohr’s equation:

$$\frac{V_{D(\text{physiol})}}{V_T} = \left( \frac{Pa_{CO_2} - P_{*CO_2}}{Pa_{CO_2}} \right)$$

(2.7)

\(^1\)The special symbols in respiratory physiology compiled by Pappenheimer et al.\(^4\) are used throughout this chapter.
where $p_{E_{\text{CO}}}$ is the mixed expired $P_{\text{CO}}$. It is assumed that the $P_{\text{CO}}$ of the exchanging (i.e., perfused) alveoli equals the $P_{\text{CO}}$ of the arterial blood. As a consequence, a decrease in ventilation out of proportion to any decrease in metabolic $V_{\text{CO}_2}$ (amount of CO$_2$ evolved from the body each minute) results in a high arterial $P_{\text{CO}_2}$. Hence, increase in dead space is a cause of hypercarbia.

At any given rate of metabolic CO$_2$ production, the steady-state value for $P_{A_{\text{CO}}}$ is therefore inversely related, in a hyperbolic fashion, to the rate of alveolar ventilation. The determinants of $V_{A}$ were expressed in (2.6).

### 2.3.1 Lung Volumes

The amount of gas in the lungs at different levels of inflation is represented as volumes (when they are single components) and capacities (when they are composed of two or more components). The balances between the elastic recoil properties of the lung and the properties of the chest wall and its muscles determine lung volumes. All lung volumes are subdivisions of the total lung capacity (TLC), and they are measured in liters. The static volumes of the lungs are shown in Fig. 2.1.6

The functional residual capacity (FRC) is the resting volume of the lung. It is determined by the balance between the lung elastic recoil pressure, which operates to decrease the lung volume, and the pressure generated by the chest wall to become larger. At FRC, the pressure difference across the respiratory system is zero, and it is approximately 50–60% of TLC (see the forces shown in Fig. 2.2 at resting volume). The interaction between elastic recoil forces of the chest wall, which pull the chest wall outward, and the elastic recoil forces of lung, which pull inward, creates a negative pressure in the intrapleural space with respect to atmospheric pressure (see section 2.3.2).

Vital capacity, tidal volume, inspiratory reserve, and expiratory reserve can all be measured with a simple spirometer. Total lung capacity, FRC, and residual volume (RV) all contain a fraction that cannot be measured by simple spirometry. However, RV and TLC can be measured using other methods: body plethysmography, nitrogen washout, or helium dilution or using imaging techniques. The methods more commonly used are nitrogen (N$_2$) washout (in its modern form, an open-circuit method) and helium (He) dilution (a closed-circuit method). The former method uses nitrogen washout by breathing 100% oxygen. Total quantity of nitrogen eliminated is measured as the product of the expired volume collected and the concentration of nitrogen. For example, if 4 L of nitrogen are collected and

![Fig. 2.2 Siting pressure–volume curve of lung ($P_t$), thoracic cage ($P_c$), and the result of these two forces, the total respiratory system ($P_r$). Diagrams on the right side indicate direction and magnitude of forces for the two elastic systems of the chest at various lung volumes. Dotted arrows indicate lung tensions and solid arrows the thoracic-cage tension. Average vital capacity was 4,730 cm$^3$ ATPS (Ambient temperature, ambient pressure, saturated with water vapor conditions of a volume of gas) at 26°C. Standard errors are indicated by brackets unless smaller than width of the line. (From 7 with permission)
the initial alveolar concentration was 80%, the estimated initial lung volume is 5 L. The latter method uses wash-in of a tracer gas such as helium (preferred for its low solubility in blood), which can be measured by katharometry. For example, if 50 mL of helium are introduced into the lungs and the helium concentration is then found to be 1%, the estimated lung volume is 5 L.

Measurements of lung volumes by radiographic, plethysmographic, gas dilution, or washout techniques produce on average similar results when normal subjects are tested. In contrast, the results of these techniques can differ significantly when ill patients are evaluated.12

### 2.3.2 Forces Involved in Breathing (Gradient Pressures)

Airflow in any system is directly proportional to the gradients of pressure and inversely related to the resistance to airflow, as expressed by Ohm’s law:

$$\dot{Q} = \frac{P_1 - P_2}{R}$$  \hspace{1cm} (2.8)

where $P_1$ is the circuit initial pressure, $P_2$ is the pressure at the end, and $R$ is the flow resistance. In the lung, the pressure gradient of concern is the difference between atmospheric (barometric) and alveolar pressure:

$$\dot{Q} = \frac{P_B - P_{alv}}{R_{aw}}$$  \hspace{1cm} (2.9)

where $P_B$ is the barometric pressure, and $P_{alv}$ is the alveolar pressure. Alternatively, it is described as the pressure gradient between the alveolar space and either the mouth ($P_m$) or the airway opening ($P_{aw}$), the transairway pressure. $R_{aw}$ represents the airway resistance.

If the subject is breathing ambient air, atmospheric pressure ($P_{atm}$) does not change. This means that gas flow in the lungs results from changes in alveolar pressure; this is brought about by changes in the dimension of the thorax. Inspirations lead to expansion of the thorax, causing a fall in alveolar pressure sustained until the end of inspiration, when alveolar pressure equals atmospheric pressure. During expiration, the inspiration muscles relax, and the intrapleural pressure ($P_pl$) becomes less negative with respect to the atmospheric pressure. The elastic recoil of the lung then compresses the alveolar gas and raises its pressure above that of the mouth. If $P_{alv} > P_{atm}$, then, air flows out the lung (Fig. 2.3). During quiet breathing in the supine position, the process occurs passively without much participation of the expiratory muscles because the energy required is provided by the elastic recoil of the lungs aided by the weight of the abdominal contents pushing the diaphragm in the cephalad direction. In the upright posture and during stimulated ventilation, the internal intercostal muscles and the abdominal wall muscles are active in returning the rib cage and diaphragm to the resting position.

**Barometric pressure ($P_B$):** Dalton’s law (also called Dalton’s law of partial pressures) states that the total pressure exerted by a gaseous mixture is equal to the...
sum of the partial pressures of each individual component in the mixture. This empirical law was observed by John Dalton in 1801 and is related to the ideal gas laws. Thus, the barometric pressure at a given location depends on the weight of the column of atmosphere directly over that point. Hence, places closer to sea level have “higher columns” of air above them and consequently greater “atmospheric” or “barometric” pressures. The air density and pressure decrease almost linearly with increasing altitude. It should be remembered that the atmospheric air is a mixture of gases, mostly nitrogen (78.09%), oxygen (20.95%), and small amounts of other gases. This remains largely unchanged around the globe. In other words, at high altitude the air contains the same percentage of oxygen as at sea level. However, since the air is less dense, a given volume of air contains fewer gas molecules, including oxygen. Thus, the partial pressure of oxygen (P\text{O}_2) is lower at high altitude due to the reduced barometric pressure.

Maximal inspiratory (P_{\text{I,mo,max}}, MIP, or P_{\text{I,max}}) and expiratory pressure (P_{\text{E,mo, max}}, MEP, or P_{\text{E,max}}) at the mouth. Both of these are simple indexes of ventilatory or respiratory muscle endurance. They are the most widely used measures of global inspiratory and expiratory muscle strength. MIP decreases with age independent of gender. However, the decline is larger in men than in women. The measurement is the maximal sustained pressure over 1 s, and the result is the maximal value of three measures. The result is compared with standardized values that take into account age, height, gender, and body mass. Typically, an MIP value that does not reach −80 cm H\text{O} is likely to be abnormal. Diaphragm contraction force can be estimated from the transdiaphragmatic pressure P_{\text{di}}, which is the difference between pressure above and below the diaphragm, measured as intragastric and intraesophageal pressure, respectively. Maximal contraction of the diaphragm is obtained by performing a maximal sniff maneuver or by phrenic nerve stimulation. Inspiratory muscle strength is often better reflected by esophageal pressure during a maximal sniff (sniff P_{\text{oes}}). Sniff P_{\text{oes}} is performed from FRC without a nose clip. In such a case, the volume increases about 500 mL, and diaphragm contraction is therefore relatively isometric. The normal mean sniff P_{\text{oes}} is 93±20 cm H\text{O}, ranging between 74 and 135 cm H\text{O}.

Alveolar pressure (P_{\text{alv}}): Boyle’s law describes pressure–volume relationships of gases. Thus, in the alveolar space the pressure is determined for the size of the container (i.e., the alveolus). If the size of the container is reduced, the collisions between gas molecules and the walls become more frequent, and the pressure rises (i.e., at expiration, P_{\text{alv}} becomes greater than P_{\text{pl}}, and the air flows out of the lungs). Therefore, the alveolar pressure depends on the alveolar volume, and the alveolar volume is determined by the relationship between forces involved in elastic lung and chest wall recoil. Hence, P_{\text{alv}} is simply the sum of the intrinsic recoil pressure (P_{\text{recoil}}) of the lung (at that volume) and the applied intrapleural pressure (P_{\text{pl}}). Therefore, to develop a change in P_{\text{alv}}, it is necessary to adjust the amount of P_{\text{recoil}}, P_{\text{pl}}, or both.

Causes of lung recoil: The lung tends to recoil to a lower volume even after a maximal volitional exhalation (i.e., at residual volume). Two basic factors account for this retractive, or recoil, force: elastic recoil and lung surface tension.

1. Elastic recoil: Elastic and collagen fibers are present in the alveolar walls and bronchial tree and, when distended, tend to return to equilibrium configuration. During inspiration, contraction of respiratory muscles stretches the elastic and collagen tissue network of the lungs and pleura, also overcoming the surface tension that is present at the interfaces between the air and alveoli, and the fluid lines alveolar walls. These features constitute an elastic hindrance to inspiration. At most lung volumes, the hindrance is mainly due to surface tension, but if lungs are nearly fully distended the recoil of the elastic and collagen fibers contributes as well. The work that is done in stretching the lung is not dissipated as heat. Instead, the energy is stored in the stretched structures and then spent in driving the subsequent expiration. This entails shrinking the lungs back to their previous volume. Hence, normal expiration is affected by the elastic recoil of the lung tissue. The energy applied to the lung in inspiration is not recovered in expiration. The property of dissipating energy is called hysteresis. Lung hysteresis can be quantified because it applies to the area between the ascending and descending portions of the pressure–volume curve and depends specifically on surface tension as discussed in item 2 19 (see also Fig. 2.4).

The network of fiber confers stability on the lungs because a local change in volume causes enlargement or shortening of collagen or elastic fibers in the immediate surrounding area. This is defined as interdependence.
Interdependence mitigates the effect of local stress. The lung parenchyma, the airways, and the pulmonary and bronchial vascular systems are continuously subjected to a wide range of passive and active physical forces as a result of the dynamic nature of lung function. These forces include changes in stress (i.e., force per unit area) or strain (i.e., any forced change in length in relation to the initial length) and shear stress (i.e., the stress component parallel to a given surface). The response to stress will be further analyzed in chapter number four.

2. Lung surface tension: In 1929, Kurt von Neergaard evacuated air from an isolated porcine lung, which he then filled with an isotonic gum solution to eliminate surface tension of the air tissue interfaces. Von Neergaard then obtained pressure–volume measurements and constructed curves based on the induced expansion of the lungs with air and liquid. From these experiments, he arrived at two main conclusions: (1) Surface tension is responsible for the greater part of total lung recoil compared to tissue elasticity. (2) A lower surface tension would be useful for the respiratory mechanism because without it pulmonary retraction might become too great, interfering with adequate expansion. Surface tension is a measure of the force acting to pull a the surface molecules of a liquid together at an air–liquid interface. Alveolar surface tension is similar to that existing in a spherical bubble. The surface tension created by the thin film of fluid is directed toward the center of the bubble and creates pressure in the interior. The law of Laplace is an expression of this pressure.

If the surface tension of the fluid was the same in the small and large alveoli, then small alveoli would have higher inwardly directed pressure than larger alveoli and consequently an increased resistance to stretch. As a result, more work would be needed to expand smaller alveoli. However, a surfactant reduces the surface tension, especially in the smaller alveoli, where higher concentrations are accumulated. Alveolar surfactant is well known for its ability to reduce minimal surface tension at the alveolar air–liquid interface to values below 5 mN/m. Hence, surfactant avoids collapse of the smaller alveoli. For this reason, alveoli with different diameters would have the same pressure (Fig. 2.5).
Production of surfactant is reduced when the lung parenchyma is damaged by breathing oxygen-enriched air, by severe shock, and by diversion of pulmonary blood flow through an extracorporeal circulation.

The surface tension also occurs in the airways. The airway surfactant existence reduces surface tension at the air–liquid interface of conducting airways. This decreases the tendency of airway liquid to form bridges in the narrower airway lumen (film collapse). In addition, a low surface tension minimizes the amount of negative pressure in the airway wall and its adjacent liquid layer, which in turn decreases the tendency for airway wall (compliant) collapse. According to the law of Laplace, it becomes obvious that the smaller the airways, the higher the pressure would increase if surface-active material lowering the value of $\gamma$ were absent. Surface tension in the conducting airways has been shown to be in the range between 25 and 30 mN/m.

**Pleural (intrapleural) pressure** ($P_{pl}$) depends on the elastic and chest wall recoil interaction forces. The recoil of the lung causes it to attempt to retract to its equilibrium volume (effectively that of a gas-free lung). The elastic properties of the chest wall cause it to expand to adopt its own equilibrium point (which is half the volume of the fully expanded state). Thus, at the same time elastic recoil of the lungs creates an inwardly directed force that tends to pull the lungs away from the chest wall. As a consequence, at the end of normal (passive) expiration (FRC), the combination of the outward pull of the thoracic cage and inward recoil of the elastic lungs creates a subatmospheric intrapleural pressure of about $-3$ mmHg. When a person is in the upright position, the weight of the lungs pulls the lungs away from the chest wall at the top of the lungs and squeezes them against the chest wall at the base of the lungs. This means that intrapleural pressure is more negative at the top of the lungs and less negative at the bases. Consequently, the alveolar volume is different between apex and bases because the alveolar volume is determined by transpulmonary pressure ($P_{alv} - P_{pl}$). In any posture, the pleural fluid pressure with respect to atmospheric pressure is more negative at the top than at the bottom of the lung (Fig. 2.6).

The pleural space does not contain gas. This is because the sum of the tissue gas tensions is considerably less than atmospheric pressure, leading to the reabsorption of any gas in the pleural space. Also, the concentration of protein in the pleural fluid is low (1–2%), leading to a lower osmotic pressure than in the plasma. Therefore, the fluid is reabsorbed, and as a result the pleural space is relatively dry.

**Respiratory muscles and $P_{pl}$**: At FRC, neither the lung nor the chest wall are in equilibrium. However, the combined chest wall system adopts an equilibrium position due to the absence of volitional contraction of muscles of breathing applied to the chest wall. However, when respiratory muscles are contracted, the $P_{pl}$ changes. The fall in $P_{pl}$ obtained in response to a given stimulation of the phrenic nerves decreases rapidly as the lung volume is passively increased above

---

**Fig. 2.6** Correlation between percentage total lung capacity (% TLC) and regional lung volume. Abscissa lower axis is the overall lung volume expressed as percentage TLC, and the upper axis is the overall lung volume expressed as percentage vital capacity (VC). The broken line (line of identity) indicates percentile degree of expansion of the regions equal to that of the entire lungs. The vertical distance ($D$) from the top of the lungs (in centimeters) to the center of each counter is indicated (From [26], with permission).
FRC, and muscle length is decreased. Inspiration is effected by three groups of muscles, diaphragm, external intercostals, and some accessory muscles (e.g., scalenes, sternocleidomastoids, and trapezius come into play at high rates of ventilation). When the diaphragm contracts, it loses its dome shape and drops down toward the abdomen. In quiet breathing, the diaphragm moves about 1.5 cm. This movement increases thoracic volume by flattening its floor. Contraction of the diaphragm causes between 60 and 75% of inspiratory volume change during normal breathing. Movement of the rib cage creates the remaining 25–40% of the volume change (Fig. 2.7). During inhalation in the upright position, the external intercostals and scalene muscles contract and pull the ribs upward and out.

Weakness of inspiratory or expiratory muscles reduces inspiratory capacity and expiratory reserve volume, respectively. That weakness can be caused by mechanical derangement, in association with critical or chronic illness and as a result of a neurological or muscular disorder. For this reason, on both accounts the vital capacity and TLC are reduced. If the reduction in vital capacity exceeds 50%, the hypoventilation is likely to occur with hypercapnia, and it can lead to hypoxemia.

Lung compliance \( (C) \) is the capability of the lungs to distend under pressure, as measured by pulmonary volume change per unit pressure change. The distending pressure across the lung is the difference in pressures between the inside and outside of the lung, that is, the transpulmonary pressure \( (P_{\text{alv}} - P_{\text{pl}}) \):

\[
C = \frac{\Delta V_{\text{ml}}}{\Delta P_{\text{pl}}} \Rightarrow C = \frac{\Delta V_{\text{ml}}}{\Delta(P_{\text{alv}} - P_{\text{pl}})} (\text{cmH}_2\text{O}) \tag{2.10}
\]

The measurement of lung compliance under conditions of no airflow (i.e., under static conditions) allows establishing the intrinsic elasticity or stiffness of the lungs without the confounding influence of needing additional pulmonary pressures to overcome the resistance to airflow. At the end of inspiration and expiration, \( P_{\text{alv}} \) must be exactly equal to \( P_{\text{atm}} \), because the airflow is zero. Thus, to measure static lung compliance only, the changes in the lung volume and intrapleural pressure are needed. The lung volume can be readily measured with a simple spirometer, and the pleural pressure is normally estimated by measuring the intraesophageal pressure. For normal adults, a change of \( P_{\text{pl}} \) from \(-4\) to \(-6\) cm H\(_2\)O would induce a volume change, a tidal volume, of approximately 600 mL. The compliance in this case would be 200 mL/cm H\(_2\)O. In a normal adult, it has a mean value of 240 mL/cm H\(_2\)O (Fig. 2.8). Recent studies have found that regular use of pressure–volume curves provides useful physiological data that help to optimize mechanical ventilation at the bedside and, more interestingly, to improve outcome.\(^2\) In a normal subject on mechanical ventilation, compliance should

\(^2\)A positive transpulmonary pressure is needed to increase the lung volume.
be greater than 50–100 mL/cm H₂O. Lower values are obtained in children and in women compared with men, mainly due to absolutely smaller lungs. However, when the lung volume is considered in relative terms (e.g., as a fraction of the TLC), no significant differences are found due to age and gender. This has the effect that the compliance per liter of lung volume, which is the specific compliance \( sC \), is effectively constant.

\[
sC = \frac{C_{\text{measured}}}{V_{C}}
\]  

(2.11)

The specific compliance is usually reported for expiration at FRC; it then has a value in normal subjects of 0.08 cm H₂O (range 0.03–0.14 cm H₂O). Loss of compliance increases the work of breathing (WOB).

Measurements of transpulmonary pressure and volume also can be recorded continuously during tidal breathing. Then, the so-called dynamic compliance \( \left( C_{\text{dyn}} \right) \) can be obtained – usually on a plot of pressure vs. volume – by measuring the slope of a line crossing values of esophageal pressure and volume at end expiration and end inspiration as determined by zero airflow at the mouth. In normal subjects, dynamic compliance is only slightly less than static compliance. In patients with airway disease, redistribution of air continues through narrowed intrapulmonary airways even when flow at the mouth ceases. Consequently, some of the transpulmonary pressure apparently overcoming elastic forces is dissipated against resistive forces, and the apparent compliance is less than estimated statically. This effect goes along with increases in breathing frequency. Thus, in patients with even mild diffuse airway disease, the dynamic compliance falls as frequency increases.

Compliance is different from elastance (elasticity). The fact that a lung stretches easily (high compliance) does not necessarily mean that it will return to its resting volume when the stretching force is released. For example, when destruction of elastin occurs, the lungs exhibit high compliance and stretch easily during inspiration. However, these lungs also have decreased elastance, so they do not recoil to their resting position during expiration. Thus, people with emphysema have more difficulty exhaling than inhaling.

Chest wall compliance is the relationship of the pressure change across the chest wall to thoracic volume. In normal subjects, it is on average 230 mL/cm H₂O. It can correlate negatively with age, disease of chondrovertebral joints, damage to thoracic vertebrae, scarring of the skin of the chest, large bosom, or central obesity.

Closing volume \( (CV) \) is the lung volume at which the dependent lung zones cease to ventilate, presumably as a result of airway closure (Fig. 2.9). At the point of maximal closure, the volume of gas remaining in the lungs is the residual volume. This volume is reached when the pleural pressure is greater than the airway pressure in the terminal bronchi (in normal subjects). Premature closure increases the residual volume; the most common cause is the loss of lung elasticity.
J.A. Sánchez-Godoy

Increased compliance, which occurs with increasing age and with emphysema. Premature generalized closure can also occur as a consequence of narrowing of airways from other causes, including contraction of bronchial muscles and thickening of air walls. Several factors as well as the elastic recoil of the lungs and the chest wall must be overcome to move air into or out of the lungs. These factors include the inertia of the respiratory system and the frictional resistance of the airways to the flow of air. Inertial forces are of negligible magnitude except when a high-frequency oscillation is applied for mechanical ventilation or in experimental conditions. Pulmonary tissue resistance \( (R_t) \) is caused by the friction encountered as the lung tissues move against each other during lung expansion. The \( R_t \) itself is bigger in pulmonary fibrosis and other conditions in which the quantity of interstitial lung tissue is increased.

Pulmonary tissue resistance \( (R_t) \) plus the pulmonary tissue resistance is often referred to as the pulmonary resistance \( (R_l) \). Pulmonary tissue resistance normally contributes about 10–20% of the pulmonary resistance, with airways resistance responsible for the rest. Pulmonary tissue resistance can be augmented in such conditions as pulmonary sarcoidosis and fibrosis. Since airways resistance is the major component of the total resistance, this chapter concentrates on airways resistance.

\[ R \propto L \eta / r^4 \]  

**Fig. 2.9** The proposed mechanism for the closing volume (CV) maneuver with a tracer gas. A The lung is at residual volume (RV), and a bolus of tracer gas is inspired, passing into lung regions served by airways that remain open. Lung regions with closed airways do not receive any tracer gas. B The tracer gas bolus is followed by unlabeled air. As this unlabeled air is inspired, it dilutes the tracer gas according to the regional ventilation pattern of the lung. Regions previously closed are then open and receive air. C Total lung capacity (TLC) is reached. The alveoli that were open at RV contain tracer gas; the alveoli that were closed, and the airways, contain air only. D Expiration has started, and airway gas containing no tracer is exhaled; this is dead-space gas. E The “alveolar plateau” contains slightly varying contributions from different lung regions (partly because of cardiac movement). The exhaled concentration represents this variation in contributions from different regions. F As airway closure starts, the lung regions that contain less or no tracer gas cease to contribute to expired gas. Consequently, the tracer gas concentration in the expired gas increases as it is now only emerging from labeled lung regions. The lung volume at which airway closure starts is called the closing capacity (CC), and the difference between CC and RV is the CV (From 32, with permission)
In normal conditions, the length and viscosity are constant; then, the radius of the airways becomes the primary determinant of $R_{aw}$. However, the work needed by a normal subject to overcome resistance of the airways to airflow is much less than work needed to overcome the resistance of the lungs and thoracic cage to stretch.

Because the airways behave like a circuit in parallel, the resistance at each level of the airways depends on the cross-sectional area. For this reason, the resistance is greater in the proximal airway (e.g., trachea 2–2.5 cm$^2$) than in the distal airway ($5 \times 10^3$ cm$^2$). The first eight airway generations are the major site of airway resistance. $R_{aw}$ varies with lung volume because the airways diameter, as well as the alveoli, depends on the changes in the pleural pressure. The resistance is lower at large volumes when the airways are expanded; it rises during expiration as the airways diminish in size and becomes infinite at residual volume when some airways close.

The $R_{aw}$ also depends on the pattern of flow. The airflow resistance is the sum of its laminar and turbulent components. The determinants of this pattern were described by Reynolds:

$$\text{Re} = \frac{\dot{V} D \rho}{\eta A} \quad (2.13)$$

where $\dot{V}$ is the bulk flow gas, $A$ is the cross-sectional area, $D$ is the diameter, $\rho$ is the gas density, and $\eta$ is the gas viscosity. Re numbers less than 100 and more than 4,000 are associated, respectively, with completely laminar and fully turbulent flow. With other values, Re would be intermediate. Thus, on the trachea it is intermediate, and in the bronchioles it is nearly laminar.

**Work of breathing:** The two main components of the WOB are the elastic recoil of the lungs and chest wall and the resistance to airflow. The inertia of the airway is also part of impedance, but its contribution is negligible in respiratory physiology. Impedance can be estimated through measurements of the WOB. In respiratory physiology, WOB describes the energy required as the flow begins to perform the task of ventilation. Breathing requires the use of respiratory muscles (diaphragm, intercostals, etc.), which expend energy. In general, the work performed during each respiratory cycle depends on the resistance to airflow as well as the force required to overcome the elasticity of the lungs and chest wall. The calculation of the WOB is usually associated with inspiratory effort because expiration is generally a passive process. However, in patients with air trapping or acute respiratory failure, expiration can be an active process and can require significant work. Although ventilation normally requires 5% of total oxygen delivery, this requirement increases during lung pathological states, such that the metabolic demand for oxygen may reach 25% of total oxygen delivery.

### 2.3.3 Alveolar Gas Pressures

The levels of oxygen and carbon dioxide in alveolar gas are determined by the altitude ($P_B$), the composition of the inspired air, the alveolar ventilation volume ($VA$), the rate of oxygen consumption ($\dot{V}O_2$), and the carbon dioxide production of the body ($\dot{V}CO_2$). The partial pressure of oxygen changes as it flows through the airway. The partial pressure of oxygen in the ambient air is determined by $P_B$. Hence, the dry $P_{O_2}$ can be calculated from the fraction of oxygen ($F_{O_2}$) in the gas mixture times the total or ambient (barometric) pressure. At sea level, that is,

$$P_{O_2} = P_B \times F_{O_2} \Rightarrow P_{O_2} = 760 \text{ mmHg}$$

$$\times 0.21 \Rightarrow P_{O_2} = 159.6 \text{ mmHg} \quad (2.14)$$

Evidently, $P_{O_2}$ will be altered if the subject is at altitude or if using supplemental oxygen.

As inspiration begins, inspired gases become saturated with water vapor, which exerts a partial pressure (47 mmHg at normal body temperature). Because the total pressure remains constant at $P_B$, water vapor dilutes the total pressure of the other gases. Hence, in the conducting airways the partial pressure of oxygen may be calculated as

$$P_{O_2} = F_{l_{O_2}} \times (P_B - P_{H_2O})_{at \text{ sea level}} \Rightarrow P_{O_2}$$

$$= 0.21 \times (760 - 47)_{\text{mmHg}} \quad (2.15)$$

At the end of inspiration or expiration, with the glottis open, the total alveolar pressure is equal to $P_B$. The gas...
exchange decreases the $P_{O_2}$ and increases the $P_{CO_2}$. Therefore, the alveolar oxygen pressure ($PA_{O_2}$) is slightly lower than $PI_{O_2}$ and can be calculated by the alveolar gas equation:

$$PA_{O_2} = PI_{O_2} - \frac{PA_{CO_2}}{R} \Rightarrow PA_{O_2}$$

$$= FI_{O_2} (P_B - P_{H_2O}) - \frac{PA_{CO_2}}{R}$$

(2.16)

The respiratory exchange ratio is the ratio of the rate at which carbon dioxide leaves the lung in expired gas ($V_{CO_2}$) to the rate of oxygen consumption ($V_{O_2}$). Under steady-state conditions, such a ratio is representative of the metabolism of the subject and is called the respiratory quotient ($R$). $R$ varies between 0.7 and 1.0 when the metabolism is exclusively from fatty acid or when there is exclusive carbohydrate metabolism, respectively. $R$ in a mixed diet is approximately 0.8.

The concentration of carbon dioxide in the alveolar gas is dependent on $VA$ and on $VCO_2$ (and its delivery to the lung in the mixed venous blood). The volume of carbon dioxide expired per unit of time ($VE_{CO_2}$) is equal to $VA$ times the alveolar fractional concentration of $CO_2$ ($FA_{CO_2}$). No carbon dioxide comes from the dead space. This relationship is defined by the alveolar carbon dioxide equation:

$$V_{CO_2} = VA \times FA_{CO_2}$$

(2.17)

since the $PA_{CO_2}$ is defined by

$$PA_{CO_2} = FA_{CO_2} \times (PB - PH_2O)$$

(2.18)

then,

$$PA_{CO_2} = \frac{V_{CO_2} \times (PB - PH_2O)}{VA}$$

(2.19)

Therefore, there is an inverse relationship between $PA_{CO_2}$ and $VA$. $PA_{CO_2}$ is tightly regulated to remain constant around 40 mmHg at sea level via a ventilatory control system. In a normal subject, $PA_{CO_2}$ is in equilibrium with arterial carbon dioxide pressure ($Pa_{CO_2}$). Thus, when $VA$ decreases (hyperventilation), $Pa_{CO_2}$ becomes greater, causing respiratory acidosis. Hyperventilation has the opposite effect (Fig. 2.10).

**Fig. 2.10** $PA_{O_2}$ and $PA_{CO_2}$ are inversely related due to the converse effects of ventilation. Hyperventilation ($Pa_{CO_2}$<40 mmHg) results in increased $Pa_{O_2}$ and decreased $Pa_{CO_2}$. Hypoventilation ($Pa_{O_2}$>40 mmHg) causes decreased $PA_{O_2}$ and hypoxemia (From 37, with permission)

When the alveolar oxygen equation and alveolar carbon dioxide equation are related to each other, it is possible to demonstrate that $Pa_{O_2}$ and $Pa_{CO_2}$ are inversely related due to the converse effects of ventilation. Hyperventilation ($Pa_{CO_2}$<40 mmHg) results in increased $Pa_{O_2}$ and decreased $Pa_{CO_2}$. Hypoventilation ($Pa_{O_2}$>40 mmHg) causes decreased $PA_{O_2}$ and hypoxemia. $Pa_{O_2}$ is in equilibrium with arterial carbon dioxide pressure ($Pa_{CO_2}$). Thus, when $VA$ decreases (hyperventilation), $Pa_{CO_2}$ becomes greater, causing respiratory acidosis. Hyperventilation has the opposite effect (Fig. 2.10).

4This is because the pleural pressure is lower at the apex than at the base because the weight of the lungs tends to pull it downward, away from the chest wall. If the pleural pressure is decreased, the transpulmonary pressure must be increased, and the alveolar volume increases in this area.
are less compliant and consequently change their volume less than alveoli of the bases despite the same fall in the P\textsubscript{pl} (Fig. 2.6). Therefore, the weight of the lungs sets alveoli at different initial volumes, which affects how much their volume can be increased during a breath. Those at the base are ventilated more than those at the top of the lung.

In a theoretically constructed model of the lung, complete gas exchange equilibrium is reached between alveolar gas and pulmonary capillary blood, and partial pressures for CO\textsubscript{2} and O\textsubscript{2} in arterial blood are equal to those in alveolar gas. In fact, under basal conditions, most O\textsubscript{2} transfer across the alveolar–capillary membrane occurs within one third of the transit time for blood in the pulmonary capillaries.

In real lungs, partial pressure differences between alveolar gas and arterialized blood – an alveolar-to-arterial \textit{PO\textsubscript{2}} difference (A\textsubscript{a}DO\textsubscript{2}) and arterial-to-alveolar \textit{PCO\textsubscript{2}} difference (aADCO\textsubscript{2}) – are found. In the conventional model analysis of alveolar gas exchange, these differences are attributed to three mechanisms: (1) unequal distribution of alveolar ventilation to pulmonary blood flow; (2) shunt; and (3) diffusion limitation.

### 2.3.4 Unequal Distribution of Ventilation to Perfusion

**Perfusion:** The systemic and pulmonary circulations differ significantly with regard to blood flow and pressure–volume relationship. The pulmonary circulation is a low-pressure and low-resistance system with a driving pressure that is almost a 13th of the systemic circulation. This difference is partially caused by greater compliance of the pulmonary vessels than the systemic vessels. In contrast to systemic arterial vessels, the anatomical structure of pulmonary arteries is characterized by a thinner media and fewer smooth muscle cells surrounding precapillary resistance vessels. The pulmonary vessels are seven times more compliant than the systemic vessels. Hence, increased vascular distensibility causes decreased pulmonary vascular resistance (PVR) when compared with systemic vascular resistance despite an equal blood flow. This resistance is about ten times less than in the systemic circulation. Using an equation like Ohm’s law, PVR can be calculated as the difference between mean pulmonary artery pressure (MPAP) and pressure of left atrium (PLA) divided by the cardiac output. PLA can be replaced with pulmonary artery wedge pressure (PAWP):

\[
R_{\text{pulmonary}} = \frac{\text{MPAP} - \text{PLA}}{\text{Cardiac output}} \Rightarrow R_{\text{pulmonary}} = \frac{\text{MPAP} - \text{PAWP}}{\text{Cardiac output}}
\]

Lung volume can affect PVR through its influence on alveolar vessels, mainly on the capillaries. At the end of inspiration, the fully distended air-filled alveoli compress the alveolar capillaries and increase PVR. In contrast to the capillary beds in the systemic circulation, the capillary bed in the lung has a major influence on PVR, and it accounts for about 40% of the resistance. This stretching effect during inspiration has an opposite effect on larger extra-alveolar vessels, which increase in diameter due to radial traction by the connective tissue and alveolar septa holding the larger vessels in place in the lung (Fig. 2.11). The extra-alveolar vessels are not influenced by alveolar pressure changes, but they are affected by intrapleural and interstitial pressure changes. As lung volume is increased by making the intrapleural pressure more negative, the transmural pressure gradient of the larger arteries and veins increases, and they distend.

![Fig. 2.11](image-url) The mechanism of radial traction on blood vessels. When the lungs are expanded (a) the capillaries in the alveolar walls are attenuated, and the volume of blood that they contain is less than when the lung is partially deflated. (b) By contrast, the alveolar corner vessels and the extra-alveolar vessels in the interstitial spaces are increased in size due to traction from surrounding structures (From 38, with permission)
PVR usually decreases with increases in pulmonary blood flow, pulmonary artery pressure, left atrial pressure, or pulmonary capillary blood volume because of distention of already open blood vessels, recruitment of previously unopened vessels, or both. Therefore, recruitment of physiologically collapsed pulmonary vessels at rest provides constant PVR even in the presence of increased cardiac output during exercise (Fig. 2.12). This effect is due to a decrease of the PVR occurring when the blood vessels are recruited and distended. Alveolar hypoxia (or hypercapnia) can cause constriction of precapillary pulmonary vessels, diverting blood flow away from poorly ventilated or unventilated alveoli. However, local hypoxia does not alter PVR. Approximately 20% of the vessels need to be hypoxic before a change in PVR can be measured. Low inspired oxygen levels due to exposure to high altitude will have a greater effect on PVR.

Regional perfusion changes because of gravity: In upright, resting subjects, blood flow increases linearly from the apex of the lung to the base of the lung, where the flow is the greatest. The marked effect of gravity on pulmonary circulation stems from the low arterial pulmonary pressure and the very different densities of blood and air. Because there is a hydrostatic gradient in blood but practically none in alveolar air, the transmural pressure in pulmonary vessels increases vertically from top to bottom, leading to distension of vessels and increased blood volume and blood flow in the lower (dependent) lung regions. The interplay of alveolar pressure, flow rate, and vascular resistance is best considered by dividing the lung field into four zones. Zone 1 represents the apex region, where blood does not flow under certain conditions. Under normal conditions, zone 1 does not exist; nevertheless, this state is reached during positive-pressure mechanical ventilation and conditions with severe decrease of the arterial pressure (Pa). In zone 2, which comprises the upper one third of the lung, Pa is greater than the PA, which is greater than venous pressure (Pv). In zone 3, Pa is greater than Pv, which is greater than Pa, and blood flow in this area parallels the pressure gradients. In zone 4, in the most dependent part of the lung the intravascular hydrostatic pressure is relatively high. This can lead to fluid passing into the interstitial tissue. In normal circumstances, the quantity of fluid is small. It can increase dramatically if pulmonary venous pressure or the permeability of the pulmonary capillary membrane is increased or if the plasma osmotic pressure is reduced, thus causing alveolar interstitial edema (Fig. 2.13).

It has been known for many years that the distribution of ventilation–perfusion ratios (VA/Q) is uneven in the lungs of normal subjects. The 1953 work of Martin, Cline, and Marshall demonstrated interlobar differences in O₂ and CO₂ concentrations best explained by regional differences in ventilation and blood flow. On average, VA/Q is approximately 1. However, as described in previous sections, the effect of gravity produces differences in ventilation and perfusion from the top to the bottom of the lungs. Relative to the top of the lung, the base of the lung is ventilated (approximately 3 times) and perfused (18 times) better. However, because the change in ventilation from the top to the bottom of lungs is not as great as the change in blood flow, VA/Q decreases from the top to the bottom of the lungs (approximately five times). This means that the top of the lungs is overventilated relative to its blood flow, and the base of the lung is overperfused relative to its ventilation. In other words, VA/Q is high at the top of the lung and low at the base of the lung. This imbalance between alveolar ventilation and blood flow is also called VA – Q mismatch.

Regional differences in VA/Q result in regional differences in gas exchanges from the top to the bottom of the normal lung. Thus, blood leaving the top of the lung has a higher PₐO₂ and a lower PₐCO₂ than the blood leaving the base of the lung.
Ventilation and perfusion must be matched on the alveolar–capillary level for optimal gas exchange. The alveolar–arterial $P_\text{A}-P_\text{A}$ difference ($\Delta P_{\text{a}}$) due to $V_{\text{A}}/Q$ inequality may amount to 10–15 mmHg in normal individuals, the alveolar-arterial $P_\text{CO}_2$ difference to 2–4 mmHg. The extreme cases are of particular interest.

$V_{\text{A}}/Q = 0$ means lack of ventilation and therefore absence of gas exchange, its perfusion constituting shunt or venous admixture. $V_{\text{A}}/Q = \infty$, due to $Q = 0$, designates the presence of ventilated but unperfused alveoli (Fig. 2.14). Again, there is no gas exchange, and the ventilation of such a compartment is functionally a dead space ventilation. It is called parallel or alveolar dead space ventilation, as distinguished from conducting airway ventilation, which is series or anatomic dead space ventilation. The sum of both is equivalent to total ventilation not contributing to gas exchange. It is termed physiologic dead space ventilation. It can be calculated from Bohr’s equation as described previously. Ventilation–perfusion ratios close to 1.0 result in alveolar $P_\text{O}_2$s of approximately 100 mmHg and $P_\text{CO}_2$s close to 40 mmHg (at sea level); ventilation–perfusion ratios greater than 1.0 increase the $P_\text{O}_2$ and decrease the $P_\text{CO}_2$; ventilation–perfusion ratios lower than 1.0 decrease the $P_\text{O}_2$ and increase the $P_\text{CO}_2$.

### 2.3.5 Shunt or Venous Admixture

A short circuit of blood passing gas-exchanging regions of the lungs leads to admixture of venous blood to arterialized blood and thus to a decrease of $P_\text{O}_2$ and increase of $P_\text{CO}_2$ in the arterial blood. *Shunt* refers to a condition in which $V_{\text{A}}/Q$ tends to zero because of no ventilation. The lack of ventilation may occur for two reasons: either the vasculature does not have access to alveoli or alveoli do not permit gas exchange because they are either physically plugged (not ventilated) or impermeable to gas. There are two types of shunts, anatomic and absolute. *Anatomic (extrapulmonary) shunt* refers to the amount of systemic venous blood that mixes with the pulmonary end-capillary blood on the arterial side of the circulation. In a normal healthy adult, about 2–5% of the cardiac output, including venous blood from the bronchial veins, the Thebesian veins, and the pleural veins, enters the left side of the circulation directly without passing through the pulmonary capillaries. In contrast, mixed venous blood perfusing pulmonary capillaries, associated with totally unventilated or collapsed alveoli, constitutes an
absolute shunt because no gas exchange occurs as the blood passes through the lung. Absolute shunt is sometimes also referred to as true shunt, alveolar shunt, or intrapulmonary shunt. Alveolar–capillary units with low $V_{A}/Q$ also act to lower the arterial oxygen content because the blood draining these units has a lower $PO_2$ than blood from units with well-matched ventilation and perfusion. These are referred to as “shuntlike states.” The combined effect of anatomical shunt, alveolar shunt, and “shuntlike” states is called physiological shunt and can be calculated by the shunt equation:

$$\dot{Q}_s / \dot{Q}_t (\%) = \frac{Cc'O_2 - CaO_2}{Cc'O_2 - CvO_2} \times 100$$  \hspace{1cm} (2.22)

where $C$ is content of oxygen; $c'$, $a$, and $\bar{v}$ refer, respectively, to the end-capillary, arterial, and mixed venous blood. In a healthy young adult at rest, 2% of cardiac output does not participate in gas exchange. At age 60, the average proportion is approximately 4%. Among the intrapulmonary causes for an increased venous admixture effect, an enlarged anatomical shunt occurs in some cases of bronchiectasis, atelectasis, and pulmonary edema. Extrapulmonary causes include cyanotic congenital heart disease and portal cirrhosis.

According to experimental results, a substantial part of the $V_{A}/Q$ inequality appears not to be due to gravity but to anatomical heterogeneity of airways and blood vessels. The gravitational model of ventilation–perfusion distribution might fail to explain adequately several important observations regarding the distribution of ventilation and perfusion: heterogeneity at the same vertical level, postural inequality, and the persistence of heterogeneity in the absence of gravity. The underlying structure of the bronchial and pulmonary vascular anatomy with nonsymmetrical branching is now considered an important factor in causing heterogeneity in pulmonary perfusion and ventilation in both health and disease.

### 2.3.6 Gas Diffusion

Diffusion is important for gas movement from the smaller airways to the alveoli and for gas movement across the alveoli into the blood and from the blood to the tissue and mitochondria (oxygen) and conversely from the tissue to blood, from the blood to the alveoli, and from alveoli to the smaller airways (carbon dioxide). Four factors determine the amount of gas diffusing through a sheet of tissue over time, but only one changes under normal conditions, the pressure gradient. Fick’s law states that the rate of diffusion ($V$) of a gas across a sheet of tissue is directly related to the surface area $A$ of the tissue, the diffusion constant $D$ of the specific gas, and the partial pressure difference $P_1 - P_2$ of each gas on each side of the tissue, and it is inversely related to the tissue thickness $T$. Thus,

$$V_{\text{gas}} = \frac{(P_1 - P_2) \times A \times D}{T}$$  \hspace{1cm} (2.23)

Two properties of the gas contribute to the diffusing capacity of the lungs $D_L$: solubility $S$ and molecular weight $MW (S/MW)$. First, the mobility of the gas should decrease as its molecular weight increases. Indeed, Graham’s law states that the diffusion is inversely proportional to the square root of $MW$. Second, Fick’s law states that the flow of the gas across the wet barrier is proportional to the concentration gradient of the gas dissolved in water. According to Henry’s law, these concentrations are proportional to the respective partial pressures, and the proportionality constant is the solubility of gas. Therefore, poorly soluble gases like $N_2$ and helium diffuse poorly across the alveolar wall. The ratio $A \times D/T$ represents the conductance of a gas from alveolus to the blood. The physical properties of oxygen and carbon dioxide enable them to diffuse rapidly between the alveolar air and the blood. Therefore, the amount of these gases in the blood is not limited by diffusion. Nevertheless, the amount of these gases in the blood is limited by blood flow. As carbon monoxide has a low solubility in the capillary membrane, it is limited by diffusion across the alveolar–capillary membrane. For this reason, CO is a useful gas for calculating $D_L$, also named the transfer factor, as follows:

$$DL = \frac{\dot{V}_{\text{CO}}}{P_{\text{ACO}}}$$  \hspace{1cm} (2.24)

\*If the partial pressure of a gas in the plasma equilibrates with the alveolar partial pressure of the gas within the amount of time the blood is in the pulmonary capillary, its transfer is perfusion limited; if equilibration does not occur within the time the blood is in the capillary, its transfer is diffusion limited.
The oxygen-diffusing capacity of the lung \( (DL_{O_2}) \) is its conductance \( (A \times D/T) \) when considered for the entire lung; thus, applying Fick’s equation, the \( DL_{O_2} \) can be calculated (theoretically) as follows:

\[
DL_{O_2} = \frac{\dot{V}_{O_2}}{PA_{O_2} - P_{\text{al}}}
\]

(2.25)

where \( \dot{V}_{O_2} \) is the net diffusion of \( O_2 \), and \( PA_{O_2} \) is the mean pulmonary capillary \( O_2 \) pressure. But, as \( DL_{O_2} \) cannot be calculated directly, \( DL_{CO} \) is most frequently used in determinations of the diffusing capacity because the mean pulmonary capillary partial pressure of carbon monoxide is virtually zero when nonlethal alveolar partial pressures of carbon monoxide are used.

Although diffusion per se involves no expenditure of energy, the body must do work, in the form of ventilation and circulation, to create the concentration gradients under which \( O_2 \) and \( CO_2 \) diffuse as discussed.

References


Principles of Pulmonary Protection in Heart Surgery
Gabriel, E.A.; Salerno, T. (Eds.)
2010, XX, 453 p., Hardcover