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Pittman RN. Regulation of Tissue Oxygenation. San Rafael (CA): Morgan & Claypool Life Sciences; 2011.

Chapter 4Oxygen Transport

Some general comments about gas exchange and diffusion will be made, followed by a description of how oxygen is carried in the blood. The binding of oxygen to hemoglobin will be discussed, including the oxygen saturation (or dissociation) curve and factors (allosteric effectors) which cause it to shift. Next, a discussion of the effects of carbon monoxide on oxygen binding will be presented. Finally, a description of artificial oxygen carriers will be presented. Most of these topics are covered in standard textbooks [6,10,54,113] and monographs on oxygen transport [112].

GAS EXCHANGE AND DIFFUSION

Overall Gas Exchange

Table 2 gives the partial pressures of the four respiratory gases in dry air, moist tracheal air, alveoli and arterial and venous blood.

The composition of alveolar gas depends upon the composition of inspired gas, composition of gas in the functional residual capacity (FRC), minus the O_2 taken up by the blood plus the CO_2 added from blood. Details of how the listed composition arises are discussed in standard monographs of respiratory physiology on the topic of ventilation/perfusion defects [6,10,54,113].

Diffusion

Diffusion takes place in the gas phase by the random motion of gas molecules.

Graham's law of diffusion (1833) states that the rate of diffusion of a gas is inversely proportional to the square root of its molecular weight ($D \sim MW^{-½}$). Thus, the relative rates of diffusion of CO_2 and O_2 are equal to $\sqrt{(32/44)}$ or 0.85. Diffusion coefficients in the gas phase are $D_{gas} \approx 10^{-1}$ cm^2/sec. In the liquid phase, diffusion rates of gases are generally 10,000 times smaller than those in gaseous environments due to the much shorter mean free path between collisions with other molecules (e.g., the solvent); thus, $D_{liquid} \approx 10^{-5}$ cm^2/s [55]. This is not a severe handicap, however, since the distances over which gas transfer must take place in the liquid phase are generally short (about 100 times shorter than that in the gas phase).

Fick's Law of Diffusion

Fick's first law states that the amount of gas transferred per unit time ($\Delta N/\Delta t$) across a membrane of thickness Δx is proportional to the area (A) available for exchange and the partial pressure difference (ΔP) of the gas across the membrane. The constant of

proportionality (K) is called Krogh's diffusion coefficient (see below) to distinguish it from D:

$$\Delta N/\Delta t = KA\,\Delta P/\Delta x \quad (4.1)$$

For gas exchange across an alveolus in the lung, A and Δx are the same for all gases; different transfer rates result from differences in K and ΔP. For the lung, Δx is about 0.5 μm—a very thin barrier; and A is about 70 m^2—a very large surface area. Krogh's diffusion coefficient ($K = aD$) is equal to the diffusion coefficient (D) times the solubility (a) of a gas in the fluid through which the gas diffuses. For example, CO_2 is 24 times more soluble than O_2 in water. Thus, the rate of CO_2 diffusion is $0.85 \times 24 = 20$ times as rapid as that for O_2 given the same partial pressure difference.

Summary of Diffusion Properties

Table 3 summarizes the solubilities and diffusion coefficients for common respiratory gases relative to those factors for oxygen (i.e., the values for a given gas are divided by the value of that variable for oxygen), where α is the solubility (Henry's law coefficient), D is the diffusion coefficient (gas phase), and $K = \alpha D$ is Krogh's diffusion coefficient (liquid phase).

Note that all the D values are about the same since the molecular weights of these gases are similar. Thus, differences in diffusion through the liquid phase are determined primarily by the solubility coefficient.

Gas Exchange Limited by Diffusion and Perfusion

A quantitative description of the gas exchange characteristics of the lungs leads to the conclusion that the exchange of most gases is limited by perfusion (i.e., blood flow). This is the case for oxygen, so that the blood flowing through the pulmonary capillaries comes into equilibrium with the P_{O2} in the alveolar gas after traversing about one-third the length of the pulmonary capillaries. One can carry out an analysis of gas exchange by using Fick's first law to determine the gas transport that takes place between an alveolus and a small volume of blood as it traverses the gas exchange region of the lung. A similar analysis is carried out for oxygen in the peripheral circulation in Chapter 8. For simplicity, gases that only exist in the physically dissolved form (e.g., He, Ar, N_2O) are usually considered, so that one does not have to deal with the complications added by binding to proteins in the blood or carriage in a chemically modified form. This analysis can be found in many monographs on respiratory physiology, as well as the more involved case of oxygen exchange where oxygen binding to hemoglobin inside the red blood cells must be taken into account [47,113].

OXYGEN IN THE BLOOD

Blood: Plasma and Red Blood Cells

For purposes of discussing oxygen transport by the blood, we will consider blood to be composed of two phases: plasma and red blood cells (RBCs). The fractional volume of blood occupied by RBCs is called the hematocrit, and its value is a little less than 50% in human adults (~40% for females and ~45% for males). Oxygen is carried in the blood in two forms:

(1) dissolved in plasma and RBC water (about 2% of the total) and (2) reversibly bound to hemoglobin (about 98% of the total).

At physiological P_{O2} (40 < P_{O2} < 100 mm Hg), only a small amount of oxygen is dissolved in plasma since oxygen has such a low solubility. At elevated P_{O2} (breathing 100 % oxygen or during hyperbaric oxygenation), however, the physically dissolved form of oxygen can become significant. Henry's law states that the amount of oxygen dissolved in plasma is directly proportional to P_{O2}: $[O_2] = \alpha P_{O2}$, where $\alpha = 0.003$ ml O_2 (100 ml plasma)$^{-1}$ mm Hg^{-1}. Thus, at a P_{O2} of 100 mm Hg (typical value for arterial blood), 100 ml of plasma contains 0.3 ml O_2 (or 0.3 vol%). Oxygen is carried in two forms inside RBCs: it is dissolved in RBC water (about 70% of RBC volume is water) in accordance with Henry's law, and a much larger amount of oxygen is reversibly bound to the hemoglobin contained within the RBCs.

Hemoglobin (Heme + Globin)

The protein hemoglobin is a molecule which is responsible for carrying almost all of the oxygen in the blood. It is composed of four subunits, each with a heme group plus a globin chain. The heme group is composed of a porphyrin ring which contains an iron (Fe) atom in its center. Normally, the Fe is in the +2 redox state (ferrous) and can reversibly bind oxygen. There are at least six genes that control globin synthesis in humans, resulting in the formation of six structurally different polypeptide chains that are designated α, β, γ, δ, ξ, and ς chains. All normal and most abnormal hemoglobin molecules are tetramers consisting of two different pairs of polypeptide chains, each chain forming a monomeric subunit.

The blood of a normal adult human contains at least six different species of hemoglobin molecules, all of which have the same principal structure and function. Hemoglobin A (A for adult) makes up 92% of the total hemoglobin concentration in a normal adult human. To date, approximately 200 structurally different human hemoglobin variants have been reported. These abnormal hemoglobins (relative to hemoglobin A) often have different oxygen-binding properties.

Hemoglobin A (HbA) is composed of two α chains and two β chains, symbolically written as $\alpha_2 \beta_2$. Its molecular weight is 64,400 Da. Each a chain has 141 amino acids, and each β chain has 146. The concentration of Hb inside red blood cells is 330 g/l (= 33 g%). At a hematocrit of 45%, this yields a blood [Hb] of 150 g/1 or 15 g%. The structure of the Hb molecule has been elucidated by the x-ray crystallographic work of Perutz and his co-workers [14,30]. The α and β chains are arranged in $\alpha\beta$ pairs, and any conformational change in one polypeptide chain is transmitted to the others in the molecule. There are two different arrangements of the subunits within the tetramer that are much more stable than all others. One of these two quaternary conformations predominates when the iron atoms are saturated with oxygen (oxy structure), and the other predominates when these binding sites are vacant (deoxy structure). The deoxy structure is characterized by the presence of inter- and intrasubunit salt bridges which give it a constrained or taut (T) configuration. The oxy conformation is obtained when the salt bonds are broken so as to give the tetramer a relaxed (R) quaternary structure.

When the iron atom in the heme group becomes oxidized (loses an electron), its valence state changes from +2 (ferrous) to +3 (ferric). The hemoglobin is then called methemoglobin (metHb) or ferrihemoglobin (Fe^{+3} will not bind oxygen). Ordinarily, about 1% of the hemoglobin in a red blood cell is in this form. The level of metHb is maintained at this low

level primarily by the enzyme NADH-methemoglobin reductase. It is important that the level of metHb be kept low since it will not reversibly bind oxygen and thus cannot carry oxygen.

Binding of Oxygen to Hemoglobin: Oxygen Saturation (Dissociation) Curve

The hemoglobin molecule has four binding sites for oxygen molecules: the iron atoms in the four heme groups. Thus, each Hb tetramer can bind four oxygen molecules. From the molecular weight of Hb, one can calculate that 1 g of Hb can combine with 1.39 ml of oxygen. Actually, some of the Hb normally in red blood cells cannot bind oxygen (it is either metHb or HbCO), and the empirically determined oxygen-binding capacity of hemoglobin (C_{Hb}) is 1.34 ml O_2 per gram Hb. In 100 ml of blood, there is about 15 g of Hb, so that 100 ml of blood has the capacity to bind 20.1 ml of oxygen. This quantity is called the oxygen-binding capacity of blood (C_B). Note that C_B is proportional to the hematocrit of the blood.

If one begins with a deoxygenated sample of blood and allows it to equilibrate in steps with gas mixtures of increasing P_{O2}, the binding sites for oxygen will become progressively occupied until, at a high enough P_{O2}, all of them will contain oxygen. A curve representing the equilibrium binding of O_2 to blood is shown in Figure 2. The curve is known as the oxygen saturation curve or the oxygen dissociation curve and expresses the relationship between P_{O2} and the bound oxygen content.

P_{50} is defined as the P_{O2} at which oxygen saturation is 50%. The standard conditions under which oxygen binding is measured are T = 37 °C, pH = 7.4 and P_{CO2} = 40 mm Hg. The fractional oxygen saturation of Hb is the amount of oxygen combined with Hb divided by the oxygen-binding capacity of the blood (20.1 vol% at normal Hct). The bound oxygen content is proportional to hematocrit:

$$[O_2]_{bound} = S_{O_2}[Hb]C_{Hb}$$

4.2

where [Hb] is blood hemoglobin concentration and is related to hematocrit (Hct) by

$$[Hb] = Hct\,[Hb]_{RBC}$$

4.3

where $[Hb]_{RBC}$ is the average hemoglobin concentration of a single RBC. It is important to recognize the distinction between oxygen content and oxygen saturation:

$$O_2 \text{ content in bound form} = O_2 \text{ saturation} \times O_2\text{-binding capacity}$$

4.4

The oxygen dissociation curve is said to have a sigmoid shape, which reflects the cooperative nature of oxygen binding to Hb. This curve is highly nonlinear in the normal physiological range of P_{O2} (i.e., 40 to 100 mm Hg). The middle portion of the curve (20–80% saturation) is steeper than the low P_{O2} and high P_{O2} segments. The affinity of Hb for oxygen increases steadily as oxygen saturation goes from 0% to 100% for a given oxygen dissociation curve. For different oxygen dissociation curves, the affinity of Hb for oxygen increases with decreasing P_{50}. A simple quantitative description of the oxygen dissociation is expressed by Hill's equation [3,30]:

$$S_{O_2} = (P_{O_2}/P_{50})^n/[1 + (P_{O_2}/P_{50})^n]$$

4.5

where n is Hill's coefficient and is about 2.7 for human adult hemoglobin and is related to the degree of cooperativity of oxygen binding to hemoglobin. The oxygen-binding characteristic

of myoglobin, a related protein with one heme group that reversibly binds oxygen in striated muscle cells, can also be described by Hill's equation with $n = 1$.

Allosteric Effectors of Oxygen Binding to Hemoglobin

Several factors influence the binding of oxygen to hemoglobin: temperature, pH, P_{CO2} and 2,3 diphosphoglycerate (2,3 DPG). Increasing the temperature of Hb lowers its affinity for O_2 and shifts the oxygen dissociation curve to the right, as shown in Figure 3. This has physiological importance during exercise since the temperature of muscle tissue is higher than 37°C, and oxygen can be unloaded from Hb more easily at the higher temperature (lowered oxygen affinity).

As seen in Figure 4, increased H^+ activity (decreased pH) also lowers the affinity of Hb for O_2. This was originally noticed by Bohr (Bohr effect) and his colleagues (1904) as an effect of increased P_{CO2}, but it has been shown to be primarily an effect of pH inside the red blood cell. CO_2 by itself, at constant pH, also affects the oxygen dissociation curve such that increased P_{CO2} shifts the curve to the right (i.e., lowers the affinity of Hb for oxygen).

2,3 DPG is a glycolytic intermediate produced within the RBC that affects the affinity of Hb for oxygen. Increases in RBC $[H^+]$ cause decreases in [2,3 DPG], and decreases in RBC $[H^+]$ cause increases in [2,3 DPG]. 2,3 DPG is a charged ion that cannot permeate the RBC membrane. Increases in its concentration shift the oxygen dissociation curve to the right. 2,3 DPG is important during respiratory compensation seen in acclimatization to altitude, whereby the hypoxic hyperventilation of high altitude causes P_{CO2} and H^+ to decrease (left shift of oxygen dissociation curve), leading to an increase in 2,3 DPG which shifts the curve back to the right. 2,3 DPG binds to the terminal amino groups of the beta chains and competes with CO_2 for binding at those sites.

Shifts in the oxygen dissociation curve can be summarized as follows. A right shift in the oxygen dissociation curve ($\uparrow P_{50}$ or $\downarrow$ Hb-O_2 affinity) can be produced by increases in any of the following: T, P_{CO2}, $[H^+]$ ($\downarrow$ pH) or [2,3 DPG]. A left shift in the oxygen dissociation curve ($\downarrow P_{50}$ or Hb-O_2 affinity) can be produced by decreases in any of the following: T, P_{CO2}, $[H^+]$ (pH) or [2,3 DPG]. Ordinarily, the Bohr effect is not important except in exercise. In this situation, the oxygen dissociation curve is shifted to the right to allow easier unloading of oxygen from Hb in the tissues. The rightward shift in the oxygen dissociation curve is more important at lower P_{O2}. Although the rightward shift interferes with oxygen loading in the lungs, this never causes a problem in oxygen transport.

Overall Oxygen Transport

Figure 5 specifies the normal partial pressures and contents (or concentrations) for oxygen. It also describes the overall transfer of gas between the lungs and blood and between the blood and tissue.

Carboxyhemoglobin

Carbon monoxide has a very high affinity for Hb (200–300 times that of oxygen in normal adults). In situations where there is simultaneously enough oxygen and carbon monoxide to fully saturate the hemoglobin, these two ligands compete for the same binding sites, and the relative amount of each bound to Hb is given by Haldane's first law:

$$\%HbCO/\%HbO_2 = M P_{CO_2}/P_{O_2}$$
4.6
where M lies in the range 220–270 for normal adult hemoglobin. For example, if P_{CO} = 0.08 mm Hg and P_{O2} = 80 mm Hg, about 20% of the Hb is tied up with CO (if M = 250). This represents 20% of the Hb that cannot carry oxygen (i.e., there is one part of HbCO to four parts of HbO_2). Figure 6 illustrates the effect of CO on the oxygen dissociation curve.

The curve labeled “50% Anaemia” represents a sample of blood whose oxygen-binding capacity is one-half the normal value, and none of the hemoglobin is combined with CO. Compare this curve with the one labeled “50% HbCO” just above it (HbCO = 50%) that also has an oxygen-binding capacity of one-half the normal value and note that the blood with HbCO has a left-shifted oxygen dissociation curve.

Carbon monoxide is dangerous for several reasons. When CO binds to one of the binding sites on hemoglobin, the increased affinity of the other binding sites for oxygen leads to a left shift of the oxygen dissociation curve and interferes with unloading of oxygen in the tissues. The presence of CO prevents loading of oxygen due to competition for the same binding sites. Carbon monoxide binds tightly to hemoglobin (high affinity for hemoglobin), and the cumulative effect of its binding up to the limit given above by Haldane's first law shows that very low partial pressures of CO (<1 mm Hg) can effectively block a large fraction of the heme-binding sites from oxygen. Thus, the oxygen content of blood in the presence of carbon monoxide is much lower than normal. Blood remains red because the absorption spectrum for HbCO is similar to that of HbO_2, except that it is shifted slightly to higher wavelengths compared with HbO_2. Finally, there are no obvious physical signs of carbon monoxide poisoning since carbon monoxide is colorless, odorless and tasteless; it does not produce respiratory reflexes like coughing or sneezing; there is no increase in ventilation (thus, P_aO_2 is normal); and no feeling of difficulty in breathing.

ARTIFICIAL OXYGEN CARRIERS

In cases where there is a significant (~30–40%) loss of blood volume (i.e., hemorrhage, see Chapter 9), it is important to restore blood volume as soon as possible, so that the capacity of the blood to carry oxygen to the tissues is not seriously compromised. The natural fluid for such transfusions is whole blood since it contains all the biologically relevant components normally present in blood. Because of concerns about the extent and safety of the blood supply, including adverse transfusion reactions and inadvertent transmission of infectious diseases, there has been a great effort to produce artificial oxygen carriers that can act as substitutes for whole blood transfusions. Two types of fluids have been developed for this purpose, hemoglobin-based oxygen carriers and perfluorocarbon emulsions. Their characteristics in regard to oxygen transport and regulation of tissue oxygenation will now be presented.

Hemoglobin-Based Oxygen Carriers

Since plasma cannot carry much oxygen, due to its low solubility for oxygen, and hemoglobin is the oxygen carrier within RBCs, it is natural to consider hemoglobin when formulating an artificial oxygen carrier. Several hemoglobin-based oxygen carriers (HBOCs) are in various stages of development for the purpose of treating hemorrhagic and hypovolemic shock in trauma patients and other circumstances where there is a compromised

oxygen supply [9,12,116,117]. HBOCs are made from expired human blood or fresh bovine blood which undergoes numerous modifications to make them safe and effective oxygen carriers [12]. The RBCs are first lysed to release their hemoglobin, and then the stroma is removed by a variety of methods, including centrifugation, filtration and chemical extraction [50]. The stroma-free hemoglobin is then purified and undergoes modifications to cross-link, polymerize or conjugate it to other compounds. Without these modifications, the oxygen affinity of the stroma-free hemoglobin is too great to facilitate oxygen release in the tissues due to the reduction in 2,3 DPG. When it is outside the RBC, hemoglobin rapidly dissociates into 32 kDa αβ dimers and 16 kDa α or β monomers, both of which are rapidly filtered in the kidney and can precipitate in the loop of Henle, resulting in severe renal toxicity [36]. For this reason, four different types of HBOCs have been considered: cross-linked hemoglobins, cross-linked and polymerized hemoglobins, hemoglobins conjugated to macromolecules and encapsulated hemoglobins [12].

The most notable effect following administration of HBOCs is a pressor effect, an increase of mean arterial blood pressure (MAP) by as much as 10–35% within 15–30 minutes following administration [36]. The pressure usually returns to baseline within 2 hours following administration in most animal studies. The size of the HBOC appears to play a role in this pressor effect. Smaller HBOCs, such as cross-linked tetramers, produce a larger rise in MAP than do larger polymerized versions, possibly due to extravasation of smaller components of HBOCs from the microcirculation. There are several theories as to why the pressor effect occurs [9,50,89], but the most favored possibility has something to do with the interaction of hemoglobin with nitric oxide (NO). Nitric oxide released from endothelial cells relaxes the smooth muscle in the blood vessel walls. Normally, it is thought that the RBC membrane prevents NO from interacting with hemoglobin. However, the cell-free hemoglobin of HBOCs reacts freely with NO to produce HbNO from deoxyhemoglobin and methemoglobin and nitrate from oxyhemoglobin, resulting in a reduction in NO and leading to an unopposed vasoconstriction [50]. Another mechanism that has been proposed to account for the arteriolar vasoconstriction and elevated MAP considers that the HBOC increases the oxygen-carrying capacity of blood and produces an oversupply of oxygen to the tissues, resulting in a compensatory autoregulatory vasoconstriction [89,116,117]. However, a pressor effect has been observed in cases where small amounts of HBOC have been infused, too small to have an effect on oxygen supply.

In the presence of an HBOC, the total oxygen concentration of blood is given by:

$$[O_2]_{TOTAL} = [O_2]_D + [O_2]_{RBC} + [O_2]_{HBOC}$$

4.7

where $[O_2]_D$ is the dissolved oxygen given by $\alpha_{O2}\, P_{O2}$, $[O_2]_{RBC}$ is S_{O2}^{RBC} Hct $[Hb]_{RBC}$ C_{Hb} and $[O_2]_{HBOC}$ is S_{O2}^{HBOC} (1-Hct) $[Hb]_{HBOC}$ C_{Hb}. $[Hb]_{RBC}$ is the average concentration of hemoglobin in an RBC, and $[Hb]_{HBOC}$ is the concentration of HBOC in the plasma. The assumption is made that the oxygen-binding capacity of hemoglobin is the same for the hemoglobin in the RBC and that making up the HBOC. This assumption can be relaxed if the oxygen-binding capacities are known to be different. Since the oxygen dissociation curves for RBC hemoglobin and the HBOC will generally be different (i.e., different P_{50}s and Hill coefficients, see Eq. 4.5), one would expect the S_{O2} values to be different, even assuming that equilibrium exists for P_{O2} between the RBCs and the HBOC.

Perfluorocarbon Emulsions

Perfluorocarbon-based emulsions (PFCs) are mixtures of fluorocarbons and emulsifying agents that differ greatly in structure and mechanism of action from HBOCs. Fluorocarbons vary in shape and size, but share many of the same general chemical characteristics. These molecules are hydrocarbon chains that are highly substituted with fluorine atoms. The carbon-fluorine bonds give them their unique chemical and biological inertness. Fluorocarbon molecules used in potential artificial oxygen carriers can be linear or cyclic, although it has been shown that linear molecules dissolve greater amounts of oxygen [85,89]. Fluorocarbons have a high gas-dissolving capacity and low viscosity but are highly insoluble in aqueous solutions; they must be emulsified in order to travel through the circulatory system. Surfactants, or surface-active agents, are used as emulsifiers to form small droplets that are 0.1 to 0.3 μm in diameter. They are capable of dissolving large quantities of gases, such as oxygen and carbon dioxide; however, they carry less oxygen than hemoglobin itself [68,95]. They are capable of delivering oxygen to the tissues passively and can carry an amount of oxygen proportional to the ambient P_{O2} without having to rely on the red blood cells [68].

PFCs have a half-life clearance from the body of approximately 2–4 hours and are eliminated unmetabolized through the lungs after being taken up by the reticuloendothelial system (RES) [89]. This short half-life could potentially limit clinical uses in traumatic injury and hemorrhagic shock. The most critical limitation of PFCs is the linear relationship between dissolved oxygen concentration and P_{O2}. Several side effects have been reported for PFCs [89,96], and little is known about the long-term effects of PFC retention.

Unlike hemoglobin molecules, PFCs do not bind oxygen, so that oxygen is carried by PFCs only in the dissolved form. Thus, the concentration of oxygen carried by PFCs is given by Henry's law [85,97]:

$$[O_2]_{PFC} = \alpha_{PFC} P_{O_2}$$

4.8

where α_{PFC} is the solubility of oxygen in the PFC emulsion. The relationship between oxygen concentration and P_{O2} for hemoglobin is sigmoidal in shape, whereas it is linear for PFCs. In contrast to the oxygen bound to hemoglobin, oxygen dissolved in PFCs is not affected by pH, 2,3 DPG or other physicochemical factors [97].

Figures

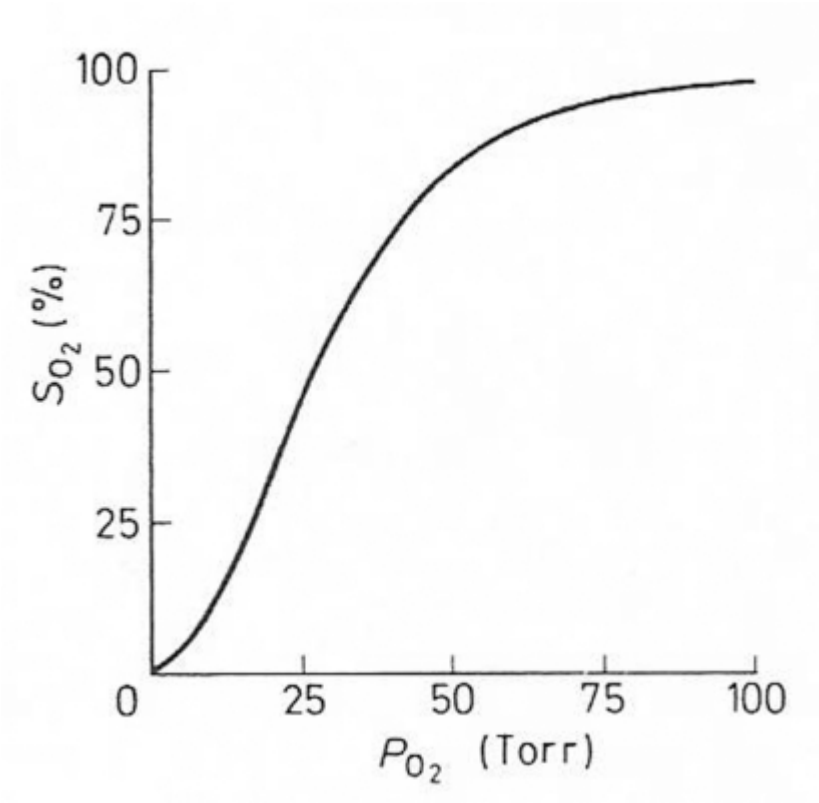

FIGURE 2

Oxygen dissociation curve-relating oxygen bound to hemoglobin (oxygen saturation, S_{O2}) as a function of partial pressure of oxygen (P_{O2}). From CC Michel, The transport of oxygen and carbon dioxide by the blood, in *Respiratory Physiology*, eds. AC Guyton, JG Widdicombe, Baltimore: University Park Press, pp. 67–104, 1974. Used with permission of the publisher.

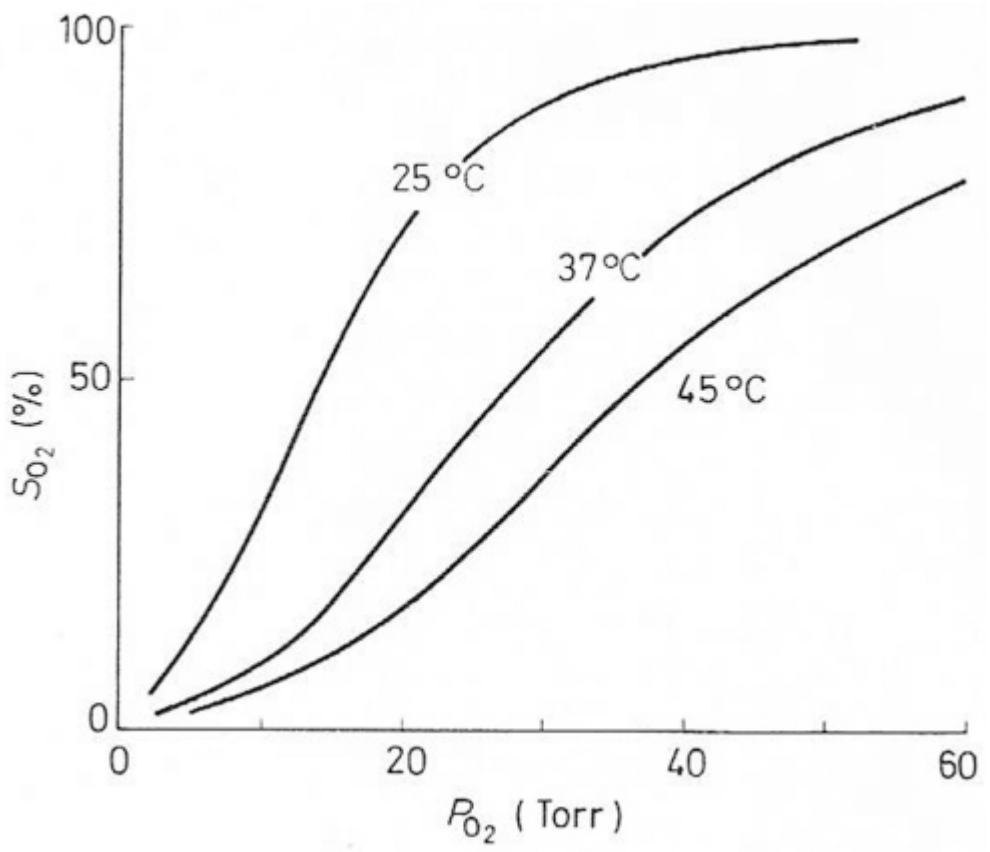

FIGURE 3

Shifts in the oxygen dissociation curve due to changes in temperature. From CC Michel, The transport of oxygen and carbon dioxide by the blood, in *Respiratory Physiology*, ed. AC Guyton, JG Widdicombe, Baltimore: University Park Press, pp. 67–104, 1974. Used with permission of the publisher.

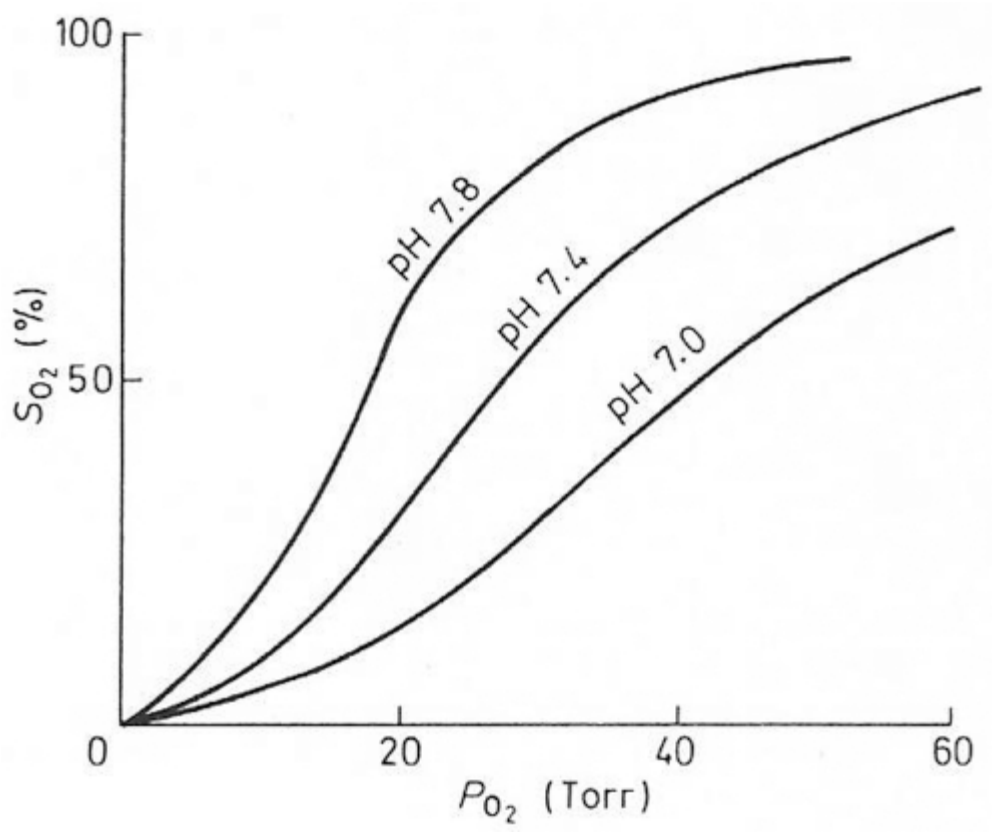

FIGURE 4

Shifts in the oxygen dissociation curve due to changes in pH. From CC Michel, The transport of oxygen and carbon dioxide by the blood, in *Respiratory Physiology*, eds. AC Guyton, JG Widdicombe, Baltimore: University Park Press, pp. 67–104, 1974. Used with permission of the publisher.

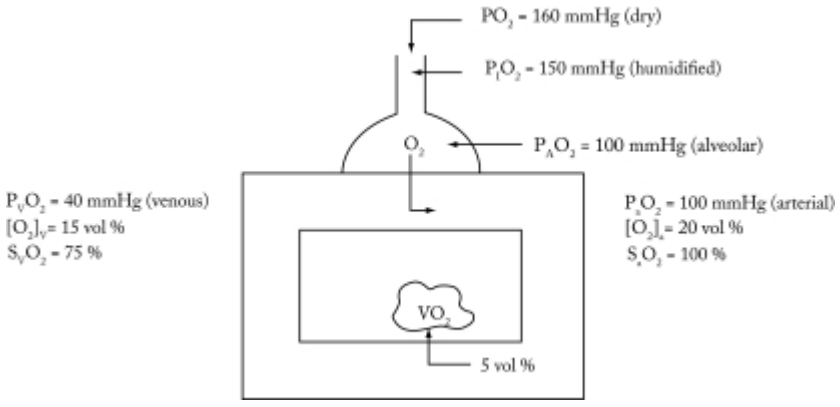

FIGURE 5

Overall oxygen transport. The partial pressure of oxygen is shown in the dry air, humidified tracheal air (P_IO_2) and the alveolar compartment (P_AO_2). After pulmonary gas exchange takes place, the composition of arterial blood is shown (P_aO_2, $[O_2]_a$ and S_aO_2). Following uptake of 5 vol% of oxygen from the arterial blood by the peripheral tissues (resting conditions), the composition of venous blood is shown (P_vO_2, $[O_2]_v$ and S_vO_2).

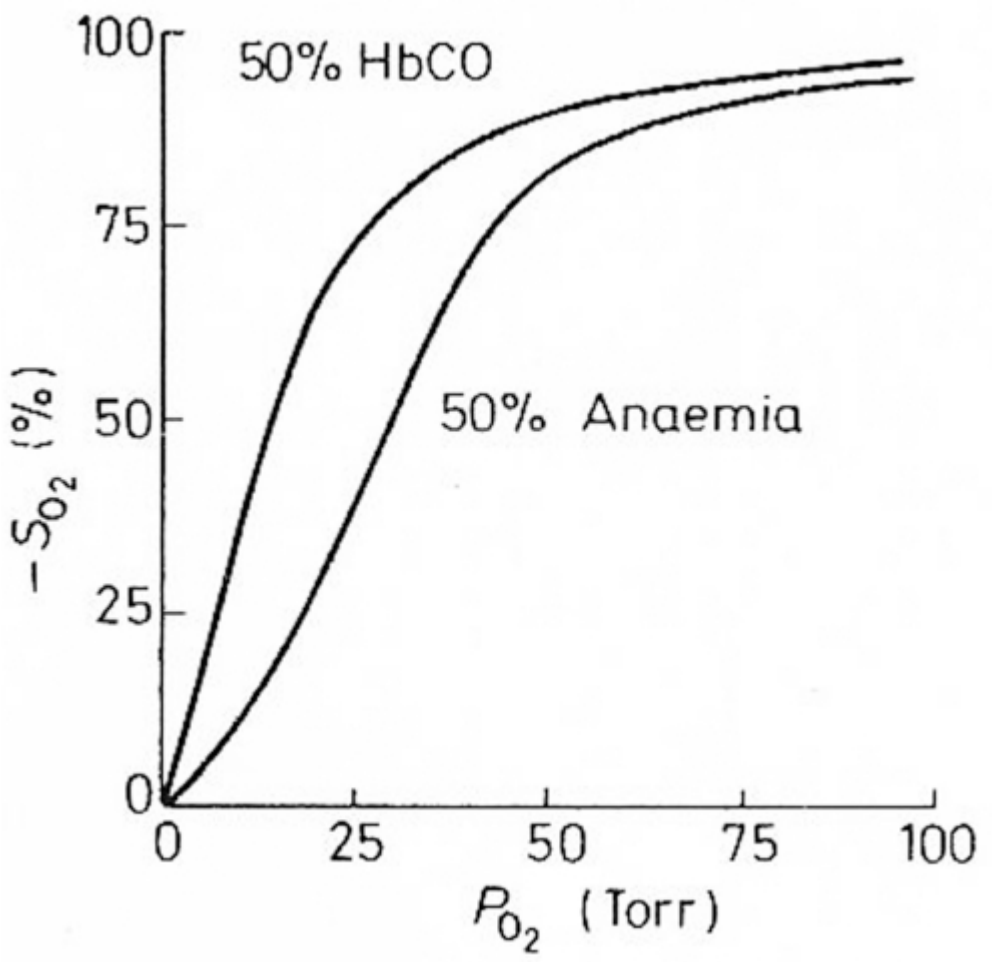

FIGURE 6

Effect of carbon monoxide on the oxygen dissociation curve. From CC Michel, The transport of oxygen and carbon dioxide by the blood, in *Respiratory Physiology*, eds. AC Guyton, JG Widdicombe, Baltimore: University Park Press, pp. 67–104, 1974. Used with permission of the publisher.

Tables

Table 2Partial pressures of gases in gas and blood phases.

	TOTAL AND PARTIAL PRESSURES OF GASES (mm Hg)				
	DRY AIR	MOIST TRACHEAL AIR	ALVEOLAR GAS	ARTERIAL BLOOD	MIXED VENOUS BLOOD
P_{O2}	159.1	149.2	104	100	40
P_{CO2}	0.3	0.3	40	40	46
P_{H2O}	0.0	47.0	47	47	47
P_{N2}	600.6	563.5	569	573	573
P_{TOTAL}	760.0	760.0	760	760	706

Table 3Solubility, diffusion coefficient, and Krogh's diffusion coefficient for various gases relative to values for oxygen

gas	α	D	$K = \alpha D$
O_2	1	1	1
CO_2	24	0.85	20
CO	0.8	1.07	0.86
N_2O	16	0.85	14
N_2	0.5	1.07	0.53