Lecture 10-2023
Respiration Part II:
Diffusion of gases through the respiratory membrane

Chaps. 40+ 41 (Guyton and Hall, 14th Edition)

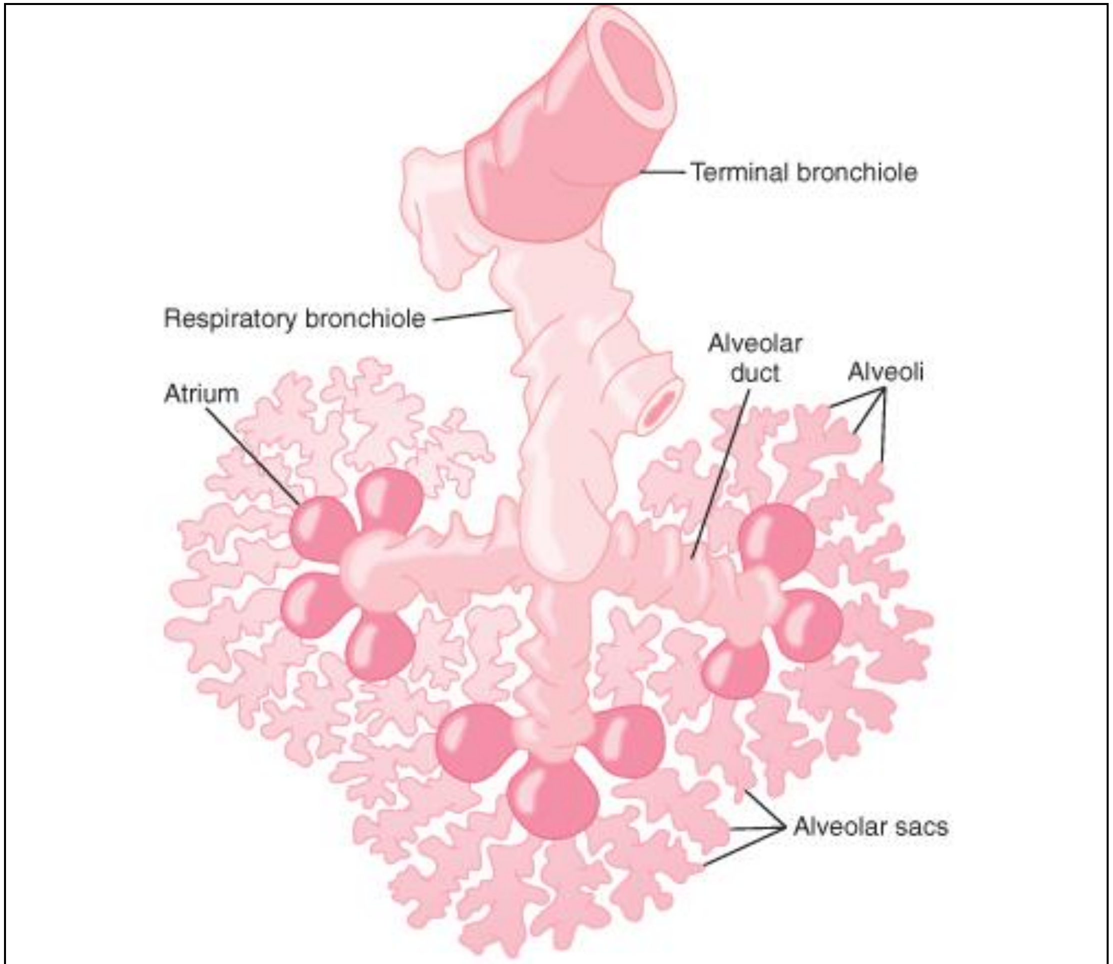
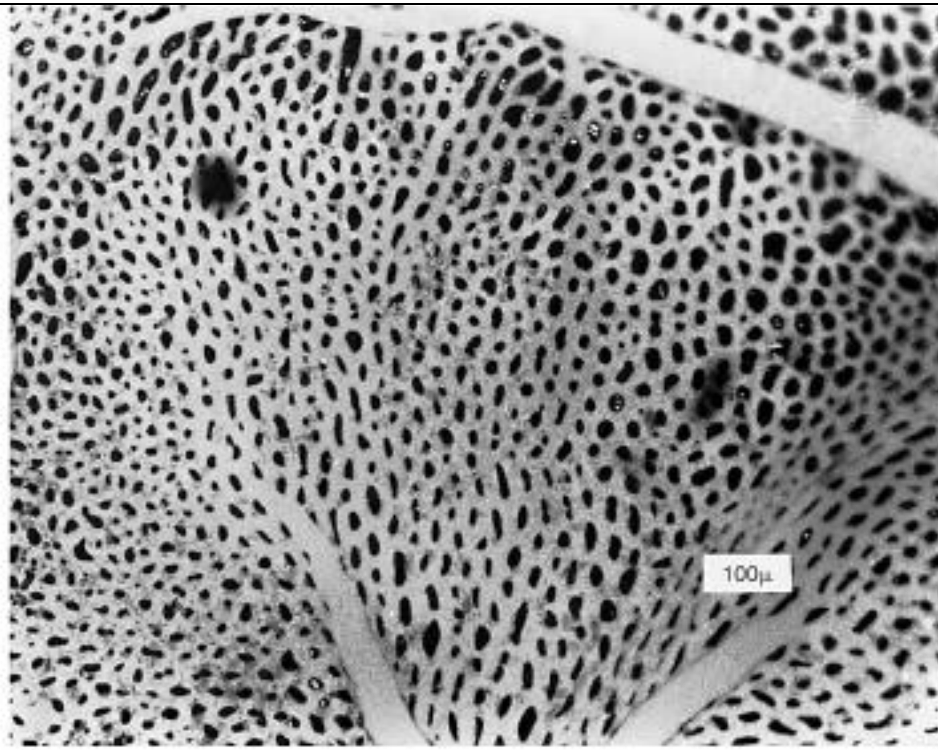


Fig. 39-7 shows the respiratory unit

The alveolar walls are extremely thin, and between the alveoli is an almost solid network of interconnecting capillaries, shown in figure 39-8



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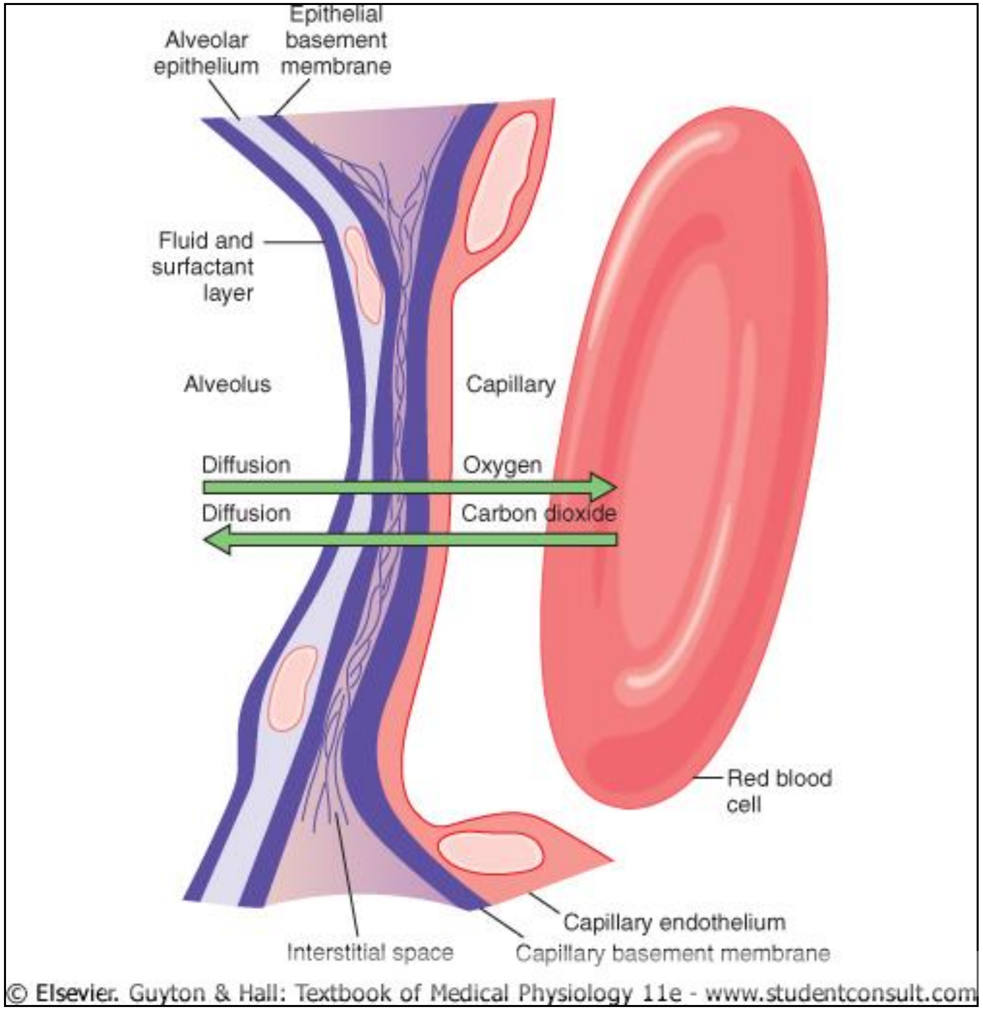
Indeed, because of the extensiveness of the capillary plexus, the flow of blood in the alveolar wall has been described as a sheet of flowing blood. Thus the alveolar gases are in very close proximity to the blood of the pulmonary capillaries



Respiratory membrane. Figure 39-9 shows the ultrastructure of the respiratory membrane drawn in cross section on the left and a red blood cell on the right. It also shows the diffusion of oxygen from the alveolus into the red blood cell and diffusion of carbon dioxide in the opposite direction

Respiratory membrane-2

- Despite a number of layers, the overall thickness of the respiratory membrane in some areas is a little as 0.2 micrometer, and it averages about 0.6 microns, except where there are cell nuclei.
- The average diameter of the pulmonary capillaries is only about 5 micrometers, which means that red blood cells must squeeze through them. The red blood cell membrane usually touches the capillary wall, so that oxygen and carbon dioxide need not pass through significant amounts of plasma as they diffuse between the alveolus and the red cell. This too increases the rapidity of diffusion

Factors that affect the rate of gas diffusion through the respiratory membrane

- 1)Thickness of the membrane;
- 2) surface area of the membrane;
- 3) the diffusion coefficient of the gas in the substance of the membrane;
- 4) the partial pressure difference of the gas between the two sides of the membrane.
- The thickness of the respiratory membrane occasionally increases- for instance, as a result of edema fluid in the interstitial space of the membrane and in the alveoli- so that the respiratory gases must then diffuse not only through the membrane but also through this fluid.
- The surface area of the respiratory membrane can be greatly decreased by many conditions. For example, in emphysema, many of the alveoli coalesce, with dissolution of many alveolar walls. Therefore, the new alveolar chambers are much larger than the original alveoli, but the total surface area of the respiratory membrane is often decreased as much as fivefold because of loss of the alveolar walls.
- The pressure difference across the respiratory membrane is the difference between the partial pressure of the gas in the alveoli and the partial pressure of the gas in the pulmonary capillary blood. – when the partial pressure of a gas in the alveoli is greater than the pressure of the gas in the blood, as is true for oxygen, net diffusion from the alveoli into the blood occurs; -when the pressure of the gas in the blood is greater than the partial pressure in the alveoli, as is true for carbon dioxide, net diffusion from the blood into the alveoli occurs.

Change in oxygen diffusing capacity during exercise

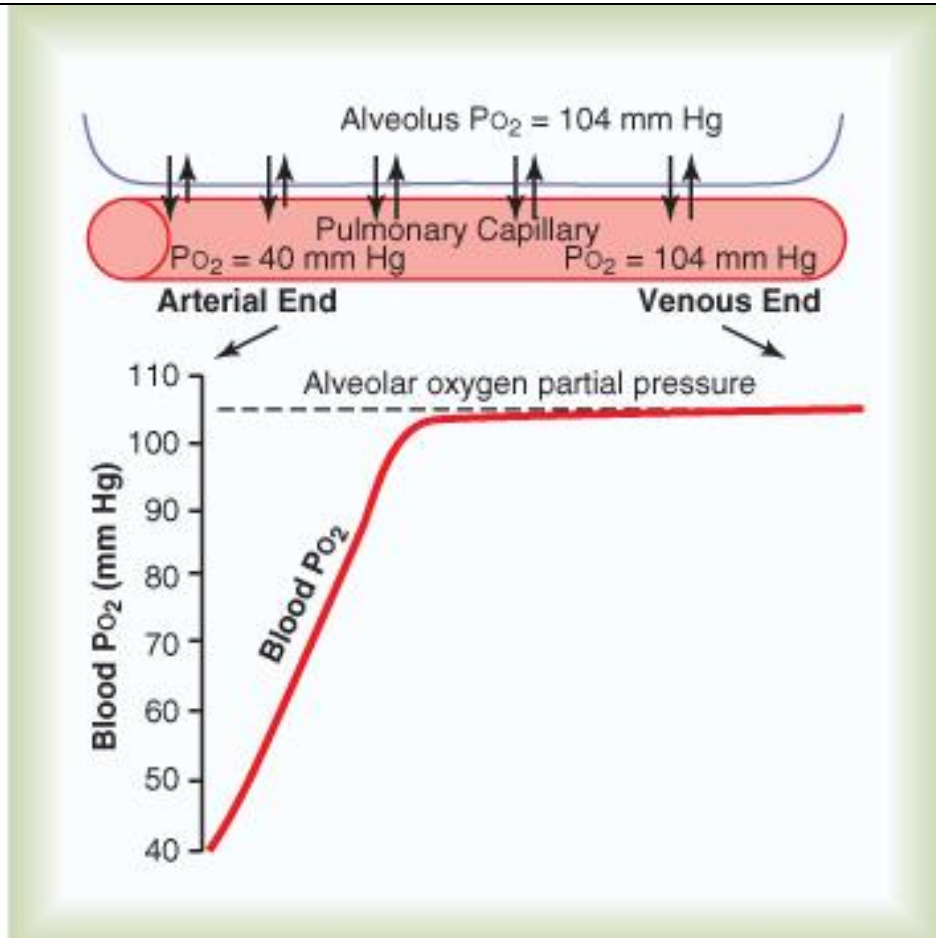
- During strenuous exercise or other conditions that greatly increase pulmonary blood flow and alveolar ventilation, the diffusing capacity for oxygen increases in young men to a maximum of about 65 ml/min/mm Hg, which is three times the diffusing capacity under resting conditions.
- This increase is caused by several factors, including -- opening up of many previously dormant pulmonary capillaries or extra dilation of already open capillaries, thereby increasing the surface area of the blood into which the oxygen can diffuse.

Chapter 41. Transport of Oxygen and Carbon Dioxide in blood and tissue fluids

- Once oxygen has diffused from the alveoli into the pulmonary blood, it is transported to the peripheral tissue capillaries almost entirely in combination with hemoglobin, which allows the blood to transport 30-100 times as much oxygen as could be transported in the form of dissolved oxygen in the water of blood.

Diffusion of oxygen from the alveoli to the pulmonary capillary blood

- The top part of fig. 40-1 shows a pulmonary alveolus adjacent to a pulmonary capillary, demonstrating diffusion of oxygen molecules between the alveolar air and the pulmonary blood.
- PO2 of the gaseous oxygen in the alveolus averages 104 mm Hg; PO2 of the venous blood entering the pulmonary capillary at its arterial end averages only 40 mm Hg, because a large amount of oxygen was removed from this blood as it passed through the peripheral tissues.
- Therefore, the initial pressure difference that causes oxygen to diffuse into the pulmonary capillary = 104-40= 64 mm Hg.
- As the graph shows, PO_2 rapidly rises in the blood as the blood passes through the capillary; the blood PO_2 rises almost to that of the alveolar air by the time the blood has move 1/3 of the distance through the capillary, becoming almost 104 mm Hg.



Alveolus PO_2 = 104 mm Hg
Pulmonary Capillary
PO_2 = 40 mm Hg
PO_2 = 104 mm Hg
Arterial End
Venous End
Alveolar oxygen partial pressure
Blood PO_2
Blood PO_2 (mm Hg)
110
100
90
80
70
60
50
40

Uptake of oxygen by the pulmonary blood during exercise

- During strenuous exercise, a person's body may require as much as 20 times the normal amount of oxygen. Also, because of increased cardiac output during exercise, the time that the blood remains in the pulmonary capillary may be reduced to less than ½ normal. Yet the blood still becomes almost saturated with oxygen by the time it leaves the pulmonary capillaries. This can be explained by a number of factors:
- 1) the diffusing capacity for oxygen increases almost threefold during exercise, due in part to the increase surface area of capillaries participating in the diffusion process (why?);
- 2) note in fig. 40-1 that under non-exercising conditions, the blood becomes almost saturated with oxygen by the time it has passed through one third of the pulmonary capillary; thus the blood normally stays in the lung capillaries about three times as long as necessary to cause full oxygenation.
- Therefore, during exercise, even with a shortened time of exposure in the capillaries, the blood can still become fully oxygenated, or nearly so.

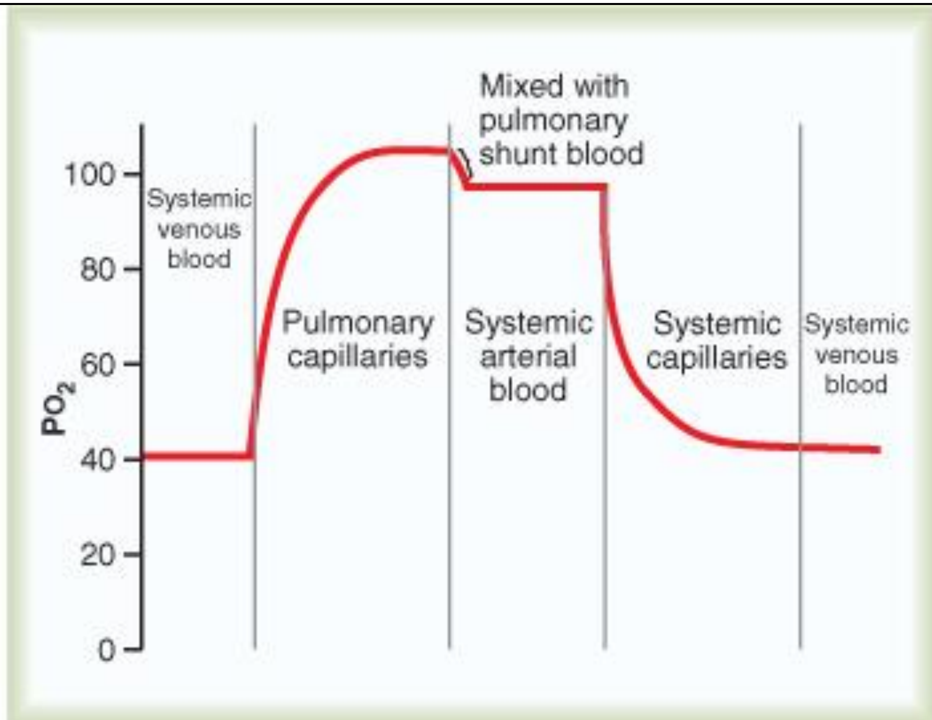
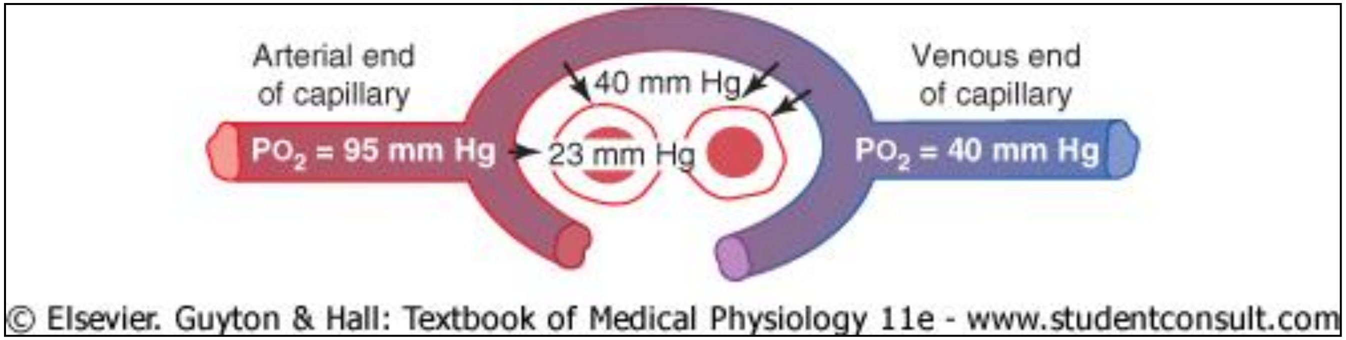


Figure 40-2: changes in PO2 in the pulmonary capillary blood, systemic arterial blood, and systemic capillary blood, demonstrating the effect of "venous admixture"- pulmonary shunt blood

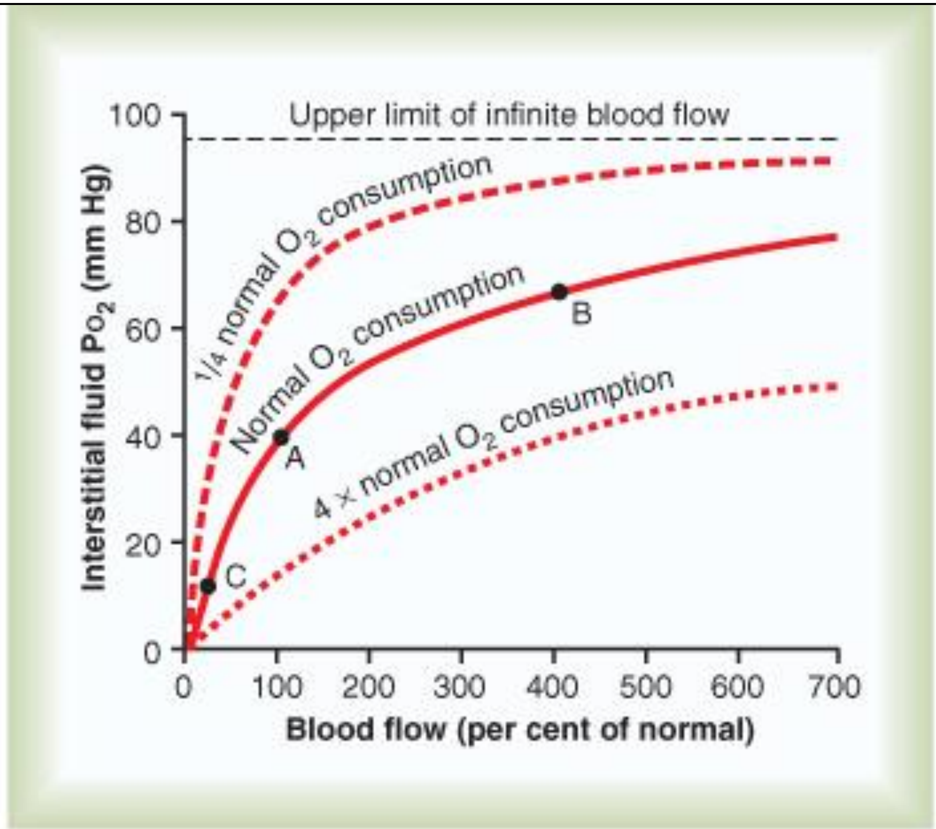


Diffusion of oxygen from the peripheral capillaries into the tissue fluid

- When the arterial blood reaches the peripheral tissues, its PO2 in the capillaries is still 95 mm Hg.
- Yet, as shown in figure 40-3, the PO_2 in the interstitial fluid that surrounds the tissue cells averages only 40 mm Hg. Thus there is tremendous initial pressure difference that causes oxygen to diffuse rapidly from the capillary blood into the tissues.

Effect of rate of blood flow on interstitial fluid PO_2

- If the blood flow through a particular tissue is increased, greater quantities of oxygen are transported into the tissue, and tissue PO_2 becomes correspondingly higher (Figure 40-4).
- increase in flow of 400% of normal increases PO_2 from 40 mm Hg to 66 mm Hg.
- However, the upper limit to which the PO_2 can rise, even with maximal blood flow, is 95 mm Hg, because this is the oxygen pressure in the arterial blood.
- Correspondingly, if blood flow decreases, the tissue PO_2 also decreases, as shown at point C in fig. 40-4.



Upper limit of infinite blood flow
1/4 normal O2 consumption
Normal O2 consumption
4 × normal O2 consumption
A
B
C
Interstitial fluid Po2 (mm Hg)
Blood flow (per cent of normal)
0
20
40
60
80
100
0
100
200
300
400
500
600
700

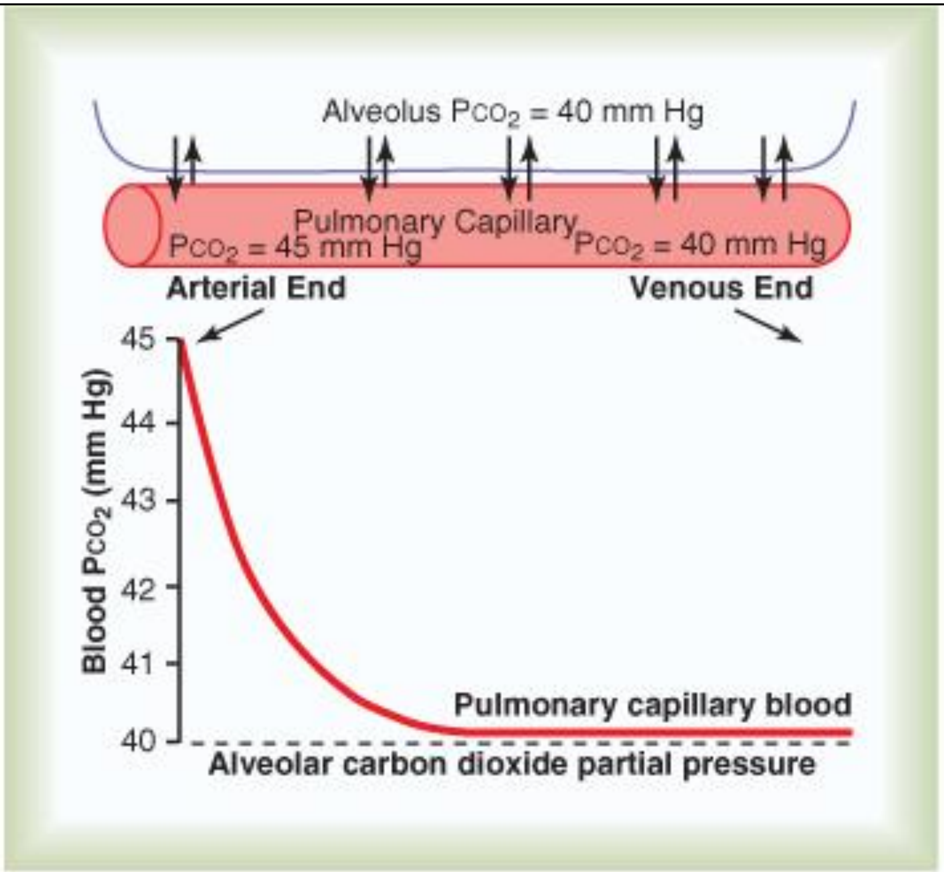
Effect of rate of tissue metabolism on interstitial fluid PO2

- If the cells use more oxygen for metabolism than normal, this reduces the interstitial fluid PO_2. (Fig. 40-4). In summary, tissue PO_2 is determined by a balance between
- 1) the rate of oxygen transport to the tissues in the blood and
- 2) the rate at which the oxygen is used by the tissues.

Diffusion of oxygen from the peripheral capillaries to the tissue cells

- Oxygen is always being used by the cells. Therefore, the intracellular PO2 in the peripheral tissue cells remains lower than the PO2 in the peripheral capillaries.
- The normal intracellular PO2 ranges from as low as 5 mm Hg to as high as 40 mm Hg, averaging 23 mm Hg.
- However, Only 1-3 mm Hg of oxygen pressure is normally required for full support of the chemical processes that use oxygen in the cell, therefore PO_2 of 23 mm Hg is more than adequate and provides a large safety factor for normal cell function.

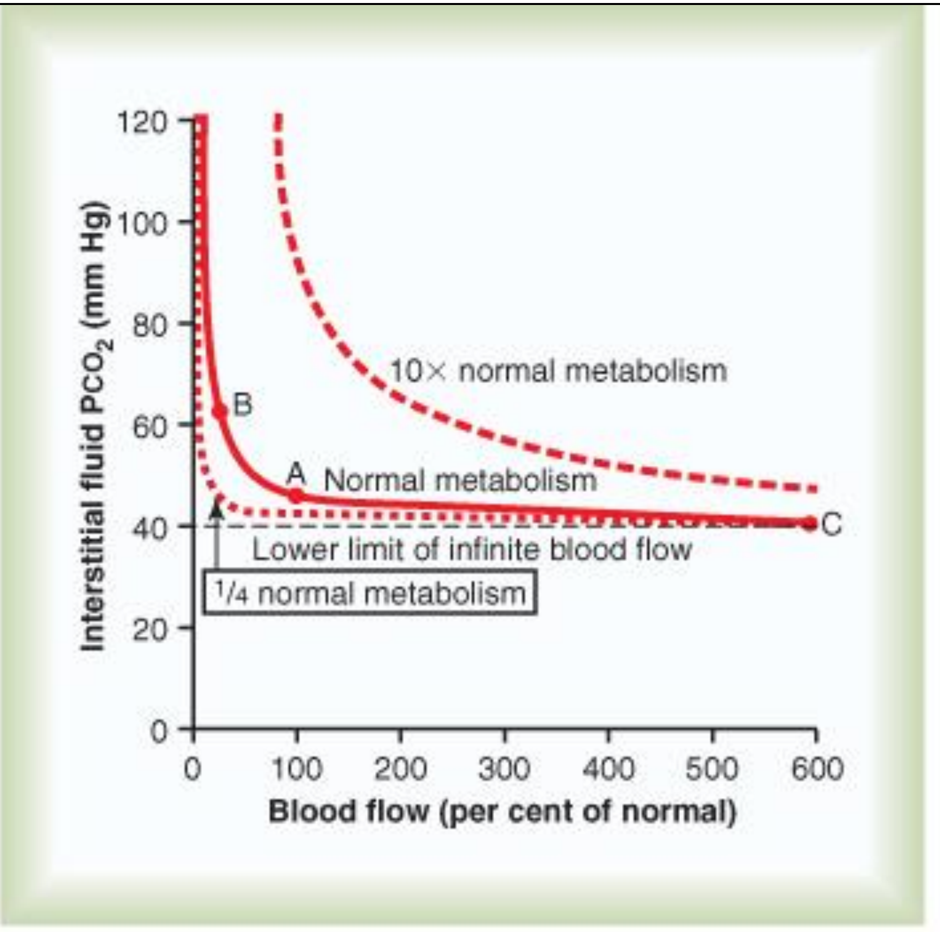
- <u>Diffusion of carbon dioxide from the peripheral tissue cells into the capillaries and from the pulmonary capillaries into the alveoli</u>.
- In the gas transport chain, carbon dioxide diffuses in the direction exactly opposite to the diffusion of oxygen. Since carbon dioxide can diffuse about 20 times as rapidly as oxygen, the pressure differences required to cause carbon dioxide diffusion are, in each instance, far less than the pressure differences required to cause oxygen diffusion.



As shown in Figure 40-6, the PCO2 of the pulmonary capillary blood falls to almost exactly equal the alveolar PCO2 of 40 mm Hg before it has passed more than about 1/3 the distance through the capillaries. This is the same effect that was observed earlier for oxygen diffusion, except that it is in the opposite direction.

Effect of rate of tissue metabolism and tissue blood flow on interstitial PCO2

- Tissue capillary blood flow and tissue metabolism affect the PCO2 in ways exactly opposite to their effect on tissue PO2. figure 40-7 shows these effects as follows:
- 1. a decrease in blood flow from normal (point A) to one quarter normal (point B) increases peripheral tissue PCO2 from normal of 45 mm Hg to an elevated level of 60 mm Hg. Conversely, increasing the blood flow to six times normal (point C) decreases the interstitial PCO2 from the normal 45 to 41 mm Hg, down to a level almost equal to the PCO2 in the arterial blood (40 mm Hg) entering the tissue capillaries.
- 2. note also that a 10-fold increase in tissue metabolic rate greatly elevates the interstitial fluid PCO_2 at all rates of blood flow, whereas decreasing the metabolism to one quarter normal causes the interstitial PCO2 to fall to about 41 mm Hg, closely approaching that of the arterial blood, 40 mm Hg.


120
100
80
60
40
20
0
Interstitial fluid PCO_2 (mm Hg)
0
100
200
300
400
500
600
Blood flow (per cent of normal)
10× normal metabolism
B
A
Normal metabolism
C
Lower limit of infinite blood flow
1/4 normal metabolism

Reversible combination of oxygen with hemoglobin

- The oxygen molecule combines loosely and reversibly with the heme portion of hemoglobin.
- Thus when PO2 is high, as in the pulmonary capillaries, oxygen binds with the hemoglobin, but when PO2 is low, as in the tissue capillaries, oxygen is released from the hemoglobin.
- This is the basis for almost all oxygen transport from the lungs to the tissues.

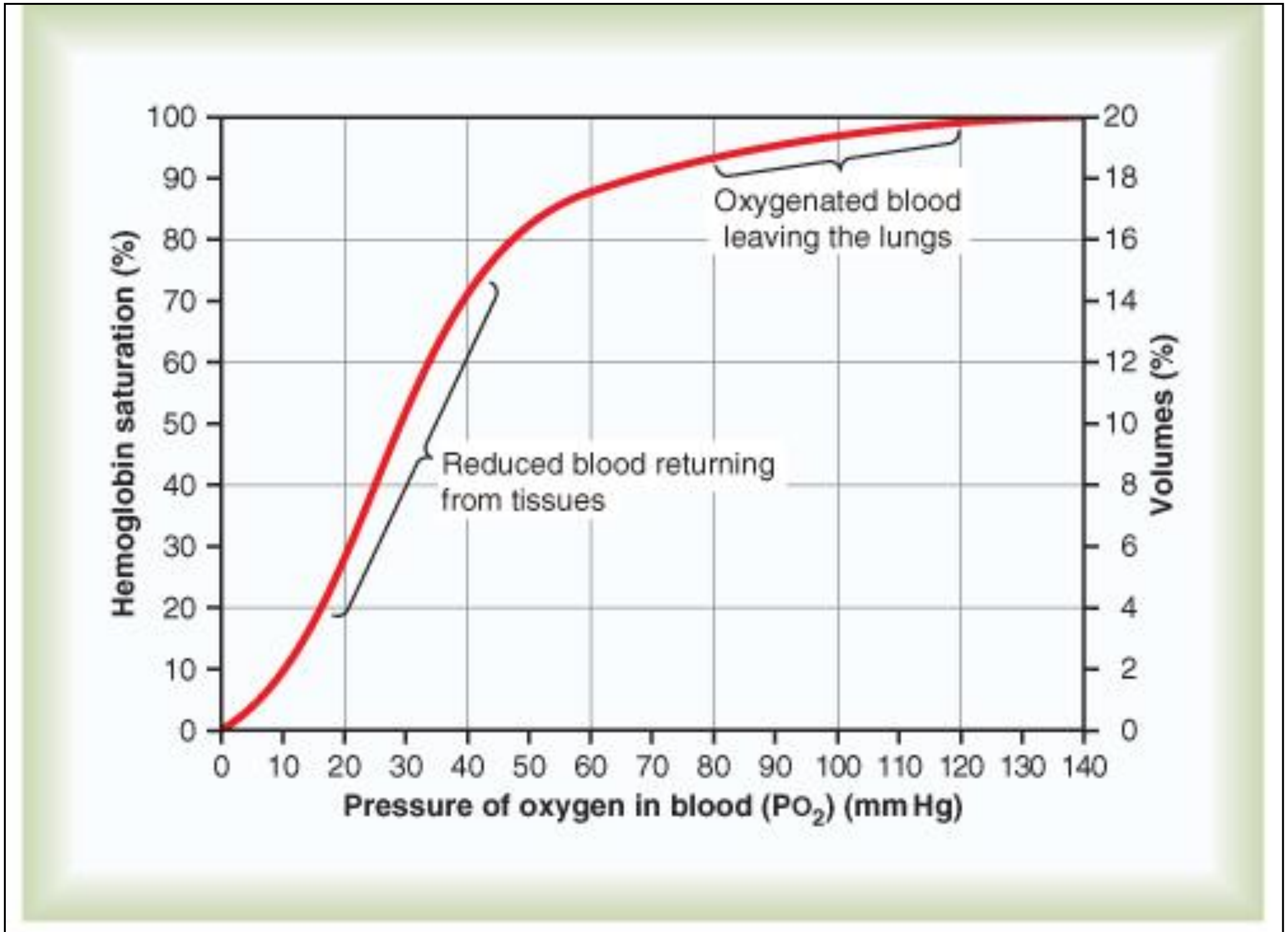


Figure 40-8 Oxygen-hemoglobin dissociation curve.

Figure 40-8 shows the oxygen-hemoglobin dissociation curve, which demonstrates a progressive increase in the percentage of hemoglobin bound with oxygen as blood PO_2 increases, which is called the per cent saturation of hemoglobin.

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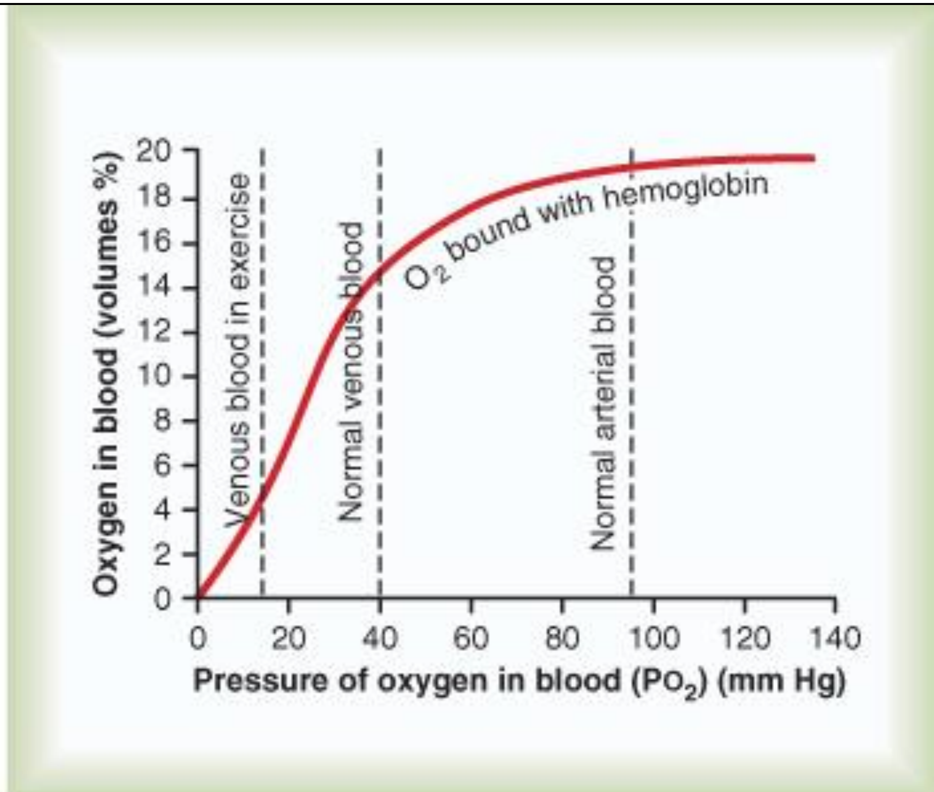


Note:
The slope of
The curve is not
equal in all parts.

Figure 40-9 Effect of blood Po2 on the quantity of oxygen bound with hemoglobin in each 100 milliliters of blood.

Role of hemoglobin in maintaining nearly constant PO2 in the tissues-2

- During heavy exercise, extra amounts of oxygen (as much as 20 times normal) must be delivered from the hemoglobin to the tissues.
- This can be achieved with little further decrease in tissue PO2 because of
- 1) the steep slope of the dissociation curve and
- 2) the increase in tissue blood flow caused by the decreased PO2—that is, a very small fall in PO2 causes large amounts of extra oxygen to be released from the hemoglobin.
- It can be seen then that the hemoglobin in the blood automatically delivers oxygen to the tissues at a pressure that is held rather tightly between about 15 and 40 mm Hg

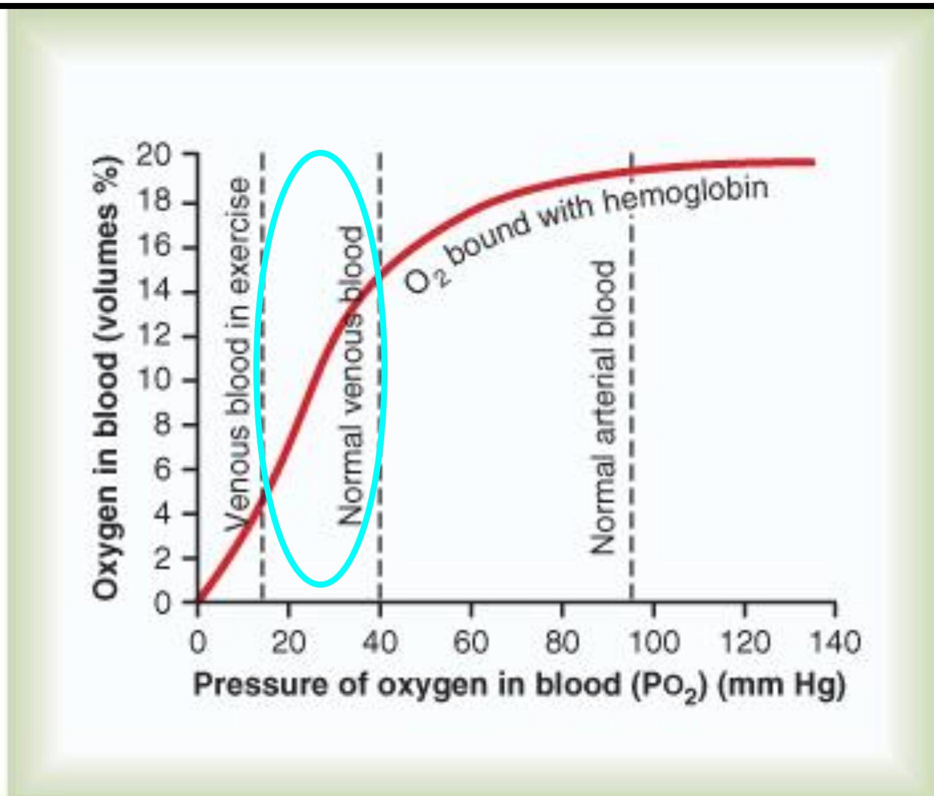
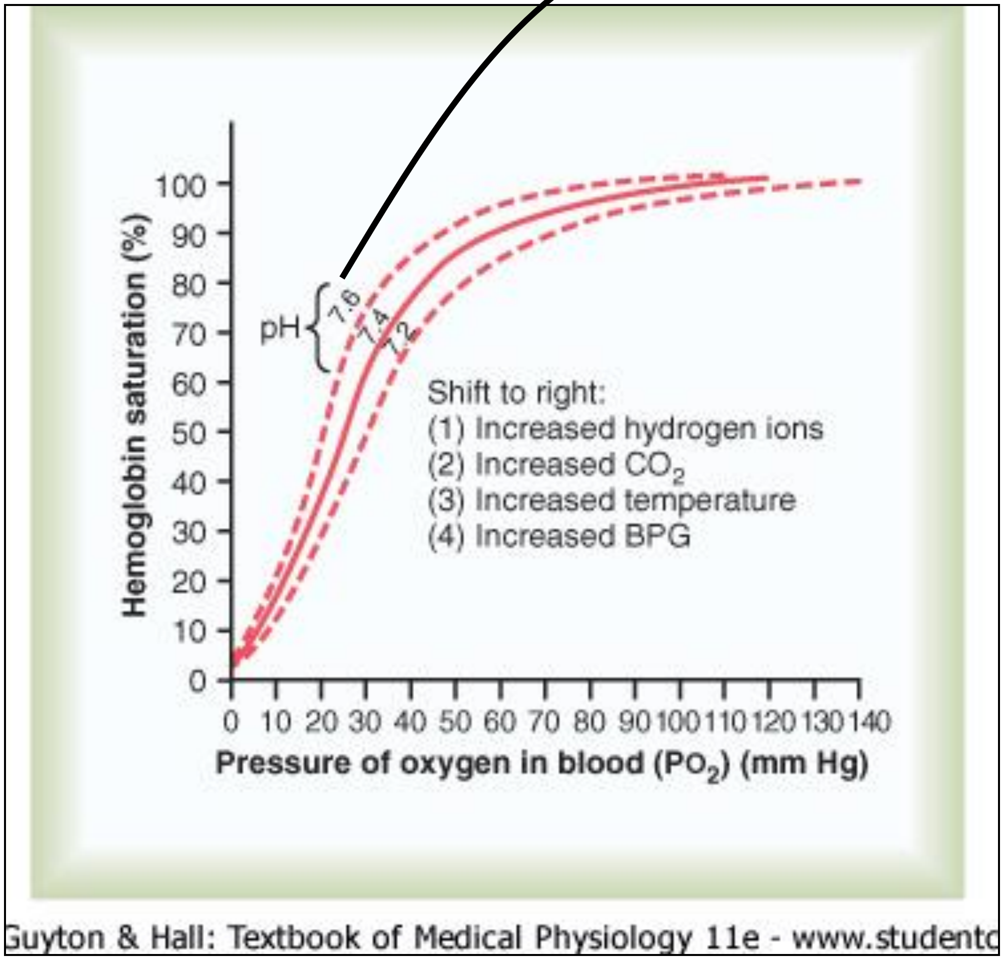


Figure 40-9 Effect of blood Po2 on the quantity of oxygen bound with hemoglobin in each 100 milliliters of blood.

Increased delivery of oxygen to the tissues when carbon dioxide and hydrogen ions shift the oxygen-hemoglobin dissociation curve

- A shift in the oxygen-hemoglobin dissociation curve to the right in response to increases in blood carbon dioxide and hydrogen ions has a significant effect by enhancing the release of oxygen from the blood in the tissues and enhancing oxygenation of the blood in the lungs.
- As the blood passes through the tissues, carbon dioxide diffuses from the tissue cells into the blood.
- This increases the blood PCO_2, which in turn raises the blood H_2CO_3 (carbonic acid) and the hydrogen ion concentration. (more acidic or basic?)
- These effects shift the oxygen-hemoglobin dissociation curve to the right and downward, as shown in fig. 40-10, forcing oxygen away from the hemoglobin and therefore delivering increased amounts of oxygen to the tissues



Exactly the opposite effects occur in the lungs, where carbon dioxide diffuses from the blood into the alveoli. This reduces the blood PCO2 and decreases the hydrogen ion concentration, shifting the oxygen-hemoglobin dissociation curve to the left and upward. Therefore, the quantity of oxygen that binds with the hemoglobin at any given alveolar PO2 becomes considerably increased, thus allowing greater oxygen transport to the tissues.

Figure 40-10 Shift of the oxygen-hemoglobin dissociation curve to the right caused by an increase in hydrogen ion concentration (decrease in pH). BPG, 2,3-biphosphoglycerate.

Shift of the dissociation curve during exercise

- During exercise several factors shift the dissociation curve considerably to the right, thus delivering extra amounts of oxygen to the active, exercising muscle fibers.
- The exercising muscles, in turn, release large quantities of CO_2; this and several other acids released by the muscles decrease muscle capillary blood pH, and in addition the temperature of the muscle often rises 2-3 deg. C, which can increase oxygen delivery to muscle even more.
- All of these factors act together to shift the oxygen-hemoglobin dissociation curve to the right, forcing oxygen to be released from the blood hemoglobin to the muscle; then in the lungs, the shift occurs in the opposite direction, allowing the pickup of extra amounts of oxygen from the alveoli.

Metabolic use of oxygen by the cells: Effect of intracellular PO2 on rate of oxygen usage

- Only a minute level of oxygen pressure is required in the cells for normal intracellular chemical reactions to take place.
- ***The main limiting factor is the concentration of ADP in the cells***.
- This effect is demonstrated in Figure 40-11, -- whenever the intracellular PO_2 is above 1 mm Hg, the rate of oxygen usage becomes constant for an given concentration of ADP in the cell.
- –when ADP concentration changes, the rate of oxygen usage changes in proportion to the change in ADP concentration.
- Thus, under normal operating conditions, the rate of oxygen usage by the cells is controlled ultimately by the rate of energy expenditure within the cells- that is, by the rate at which ADP is formed from ATP.

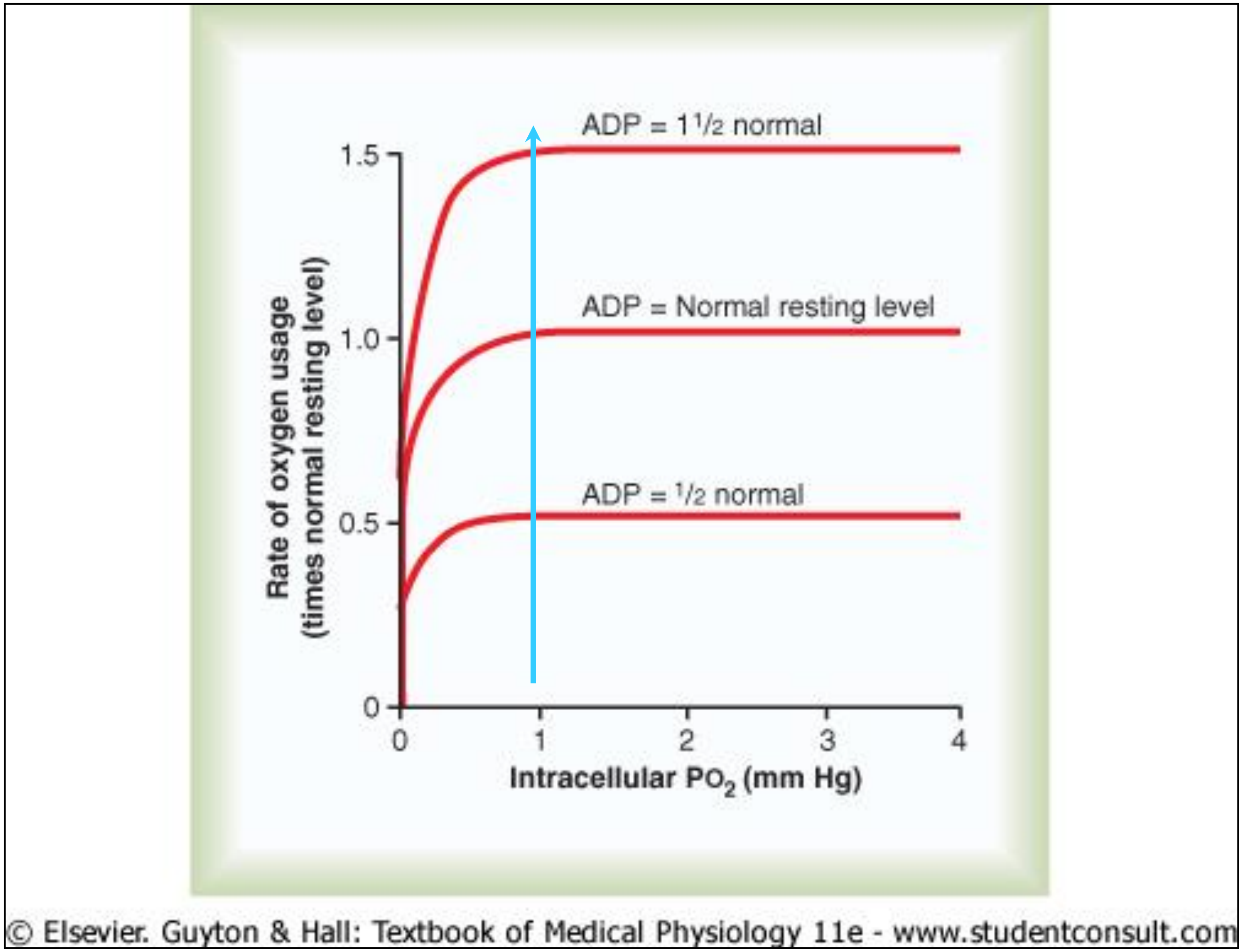


Figure 40-11 Effect of intracellular adenosine diphosphate (ADP) and Po2 on rate of oxygen usage by the cells. **Note that as long as the intracellular Po2 remains above 1 mm Hg**, the controlling factor for the rate of oxygen usage is the intracellular concentration of ADP.

Combination of hemoglobin with carbon monoxide- displacement of oxygen

- Carbon monoxide combines with hemoglobin at the same point on the hemoglobin molecule as does oxygen; it can therefore displace oxygen from hemoglobin, thereby decreasing the oxygen carrying capacity of blood.
- Further, it binds with about 250 times as much tenacity as oxygen, which is demonstrated in Figure 40-12.
- thus a CO partial pressure of only 0.4 mm Hg in the alveoli, 1/250 that of normal alveolar oxygen (100 mm Hg PO2), allows the carbon monoxide to compete equally with the oxygen for combination with hemoglobin and causes half the hemoglobin in the blood to become bound with carbon monoxide instead of with oxygen.
- Therefore a CO pressure of only 0.6 mm Hg can be lethal.

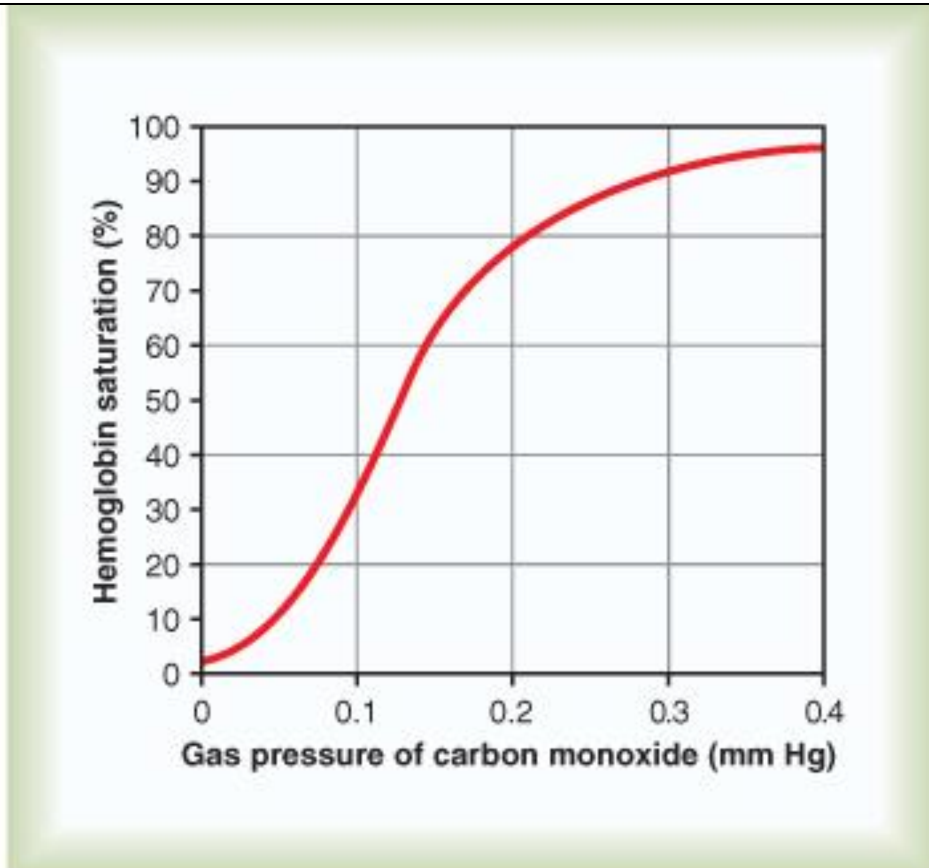


Figure 40-12 Carbon monoxide-hemoglobin dissociation curve. Note the extremely low carbon monoxide pressures at which carbon monoxide combines with hemoglobin.

Transport of carbon dioxide in the blood.

Chemical forms in which carbon dioxide is transported.

- To begin the process of carbon dioxide transport, carbon dioxide diffuses out of the tissue cells in the dissolved molecular carbon dioxide form.
- On entering the tissue capillaries, the carbon dioxide initiates a host of almost instantaneous physical and chemical reactions, shown in Fig. 40-13, which are essential for carbon dioxide transport.

- ***A small portion*** (7%) of the CO_2 is transported in the dissolved state to the lungs.
-
- <u>Transport of CO2 in the form of bicarbonate ion</u>.
- Reaction of CO2 with water in the red blood cells- effect of carbonic anhydrase.
- The dissolved CO2 in the blood reacts with water to form carbonic acid.
- This reaction is catalyzed with a reaction rate up to 5000-fold by the enzyme carbonic anhydrase; this allows tremendous amounts of CO2 to react with the red blood cell water even before the blood leaves the tissue capillaries

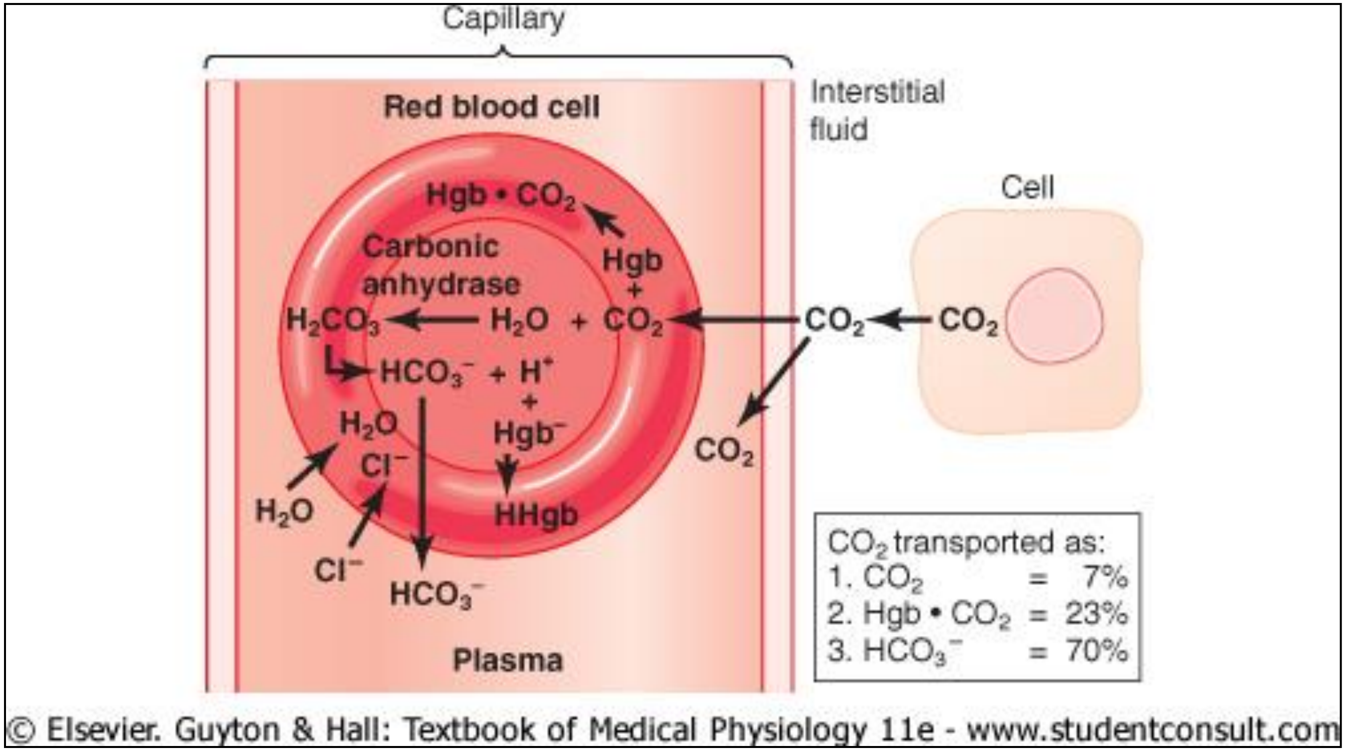


Figure 40-13 Transport of carbon dioxide in the blood.

Dissociation of carbonic acid into bicarbonate and hydrogen ions

- In another fraction of a second, the carbonic acid (H_2CO_3) dissociates into hydrogen (H+) and bicarbonate ions (HCO3-).
- Most of the H+ then combine with the hemoglobin in the red blood cells, because the hemoglobin protein is a powerful acid-base buffer.
- In turn, many of the bicarbonate ions diffuse from the red blood cells into the plasma, while chloride ions diffuse into the red blood cells to take their place.
- This is made possible by the presence of a special bicarbonate-chloride carrier protein in the red blood cell (RBC) membrane that shuttles these two ions in opposite directions at rapid velocities.
- Thus the chloride content of venous RBCs is greater than that of arterial RBCs, ***a phenomenon called the chloride shift***.
- The reversible combination of CO_2 with water in the RBCs under the influence of carbonic anhydrase ***accounts for about 70%*** of the CO_2 transported from the tissues to the lungs.
- The other 30% of CO_2 transported is through combination with hemoglobin and plasma proteins.

When oxygen binds with hemoglobin, CO_2 is released, to increase CO_2 transport

- Increase in CO_2 in the blood causes oxygen to be displaced from the hemoglobin (the Bohr effect), which is an important factor in increasing oxygen transport.
- The reverse is also true: binding of oxygen with hemoglobin tends to displace CO_2 from the blood (Haldane effect).
- The effect results from the simple fact that the combination of oxygen with hemoglobin in the lungs causes the hemoglobin to become a stronger acid.
- This displaces CO_2 from the blood and into the alveoli in 2 ways:
- 1) more highly acidic hemoglobin has less tendency to combine with CO_2, thus displacing much of the CO_2 that is present in the carbamino form from the blood and
- 2) the increased acidity of the hemoglobin also causes it to release an excess of hydrogen ions, and these bind with bicarbonate ions to form carbonic acid; this then dissociates into water and CO_2, and the CO_2 is released from the blood into the alveoli, and finally, into the air.

Change in blood acidity during CO_2 transport

- The carbonic acid formed when CO_2 enters the blood in the peripheral tissues decreases the blood pH.
- However, reaction of this acid with the acid-base buffers of the blood prevents the hydrogen ion concentration from rising greatly.
- Ordinarily, arterial blood has a pH of about 7.41 and as the blood acquires CO_2 in the tissue capillaries, the pH falls to a venous value of about 7.37.
- in heavy exercise or other conditions of high metabolic activity, or when blood flow through the tissues is sluggish, the decrease in pH in the tissue blood can be as much as 0.5, about 12 times normal, causing significant tissue acidosis.

End!