Pulmonary Function Tests

- Forced Vital Capacity (FVC) measures the amt of gas expelled when one takes a deep breath and then forcefully exhales maximally and rapidly.
- Forced Expiratory Volume (FEV) determines the amt of air expelled during specific time intervals of the FVC test.
  - For example, the volume exhaled during the 1st second is the FEV_1. People w/ healthy lungs can exhale about 80% of the FVC in the 1st second.

Obstructive Disease

- Difficult to get air out of the lungs
- Obstruct expiration

- Examples:
  - emphysema
  - chronic bronchitis
  - asthma.

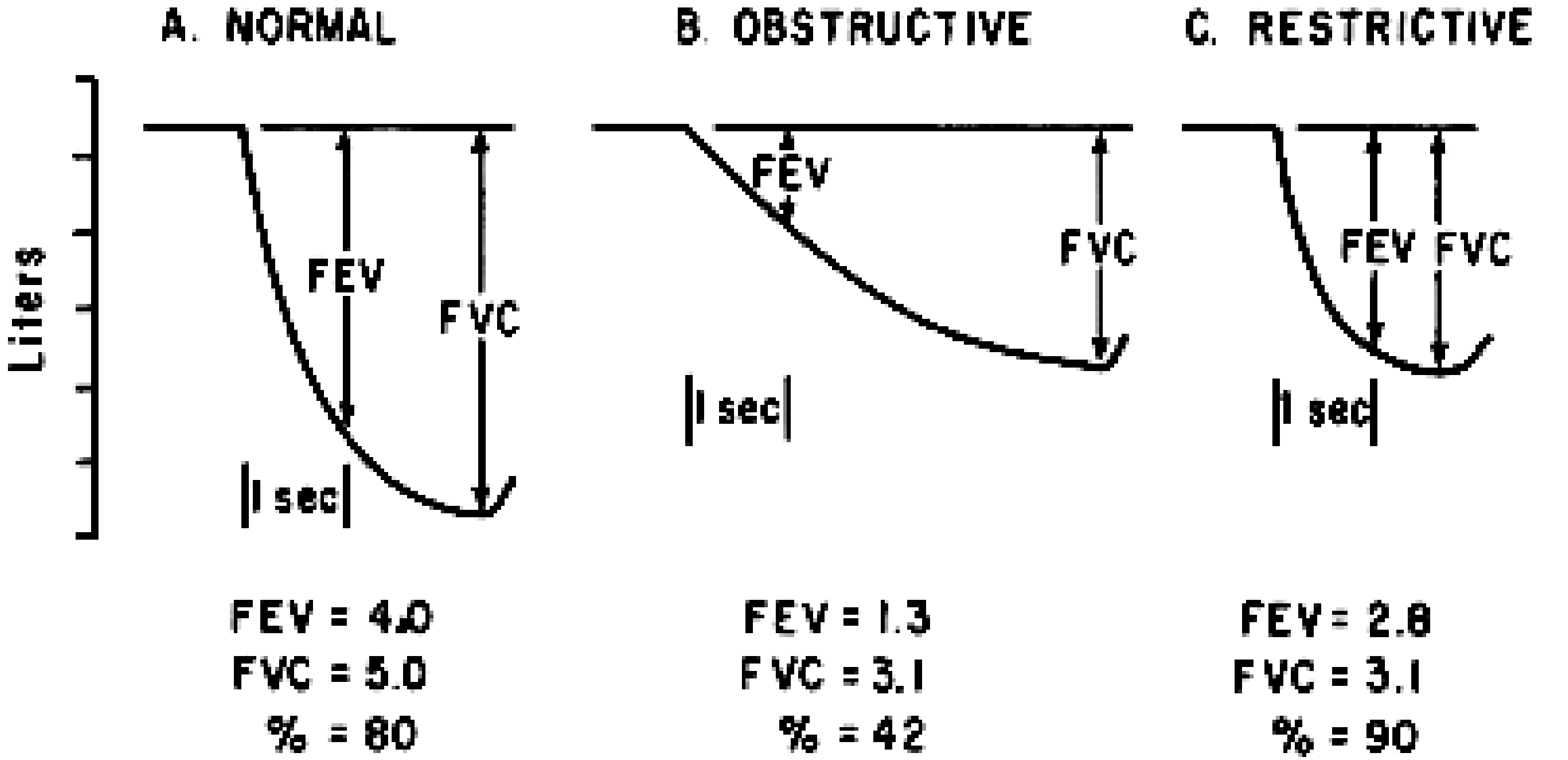
Restrictive Disease

- Difficult to get air in to the lungs
- “Restrict” inspiration
- Examples:
  - intersitial fibrosis
  - muscular diseases
  - chestwall deformities.

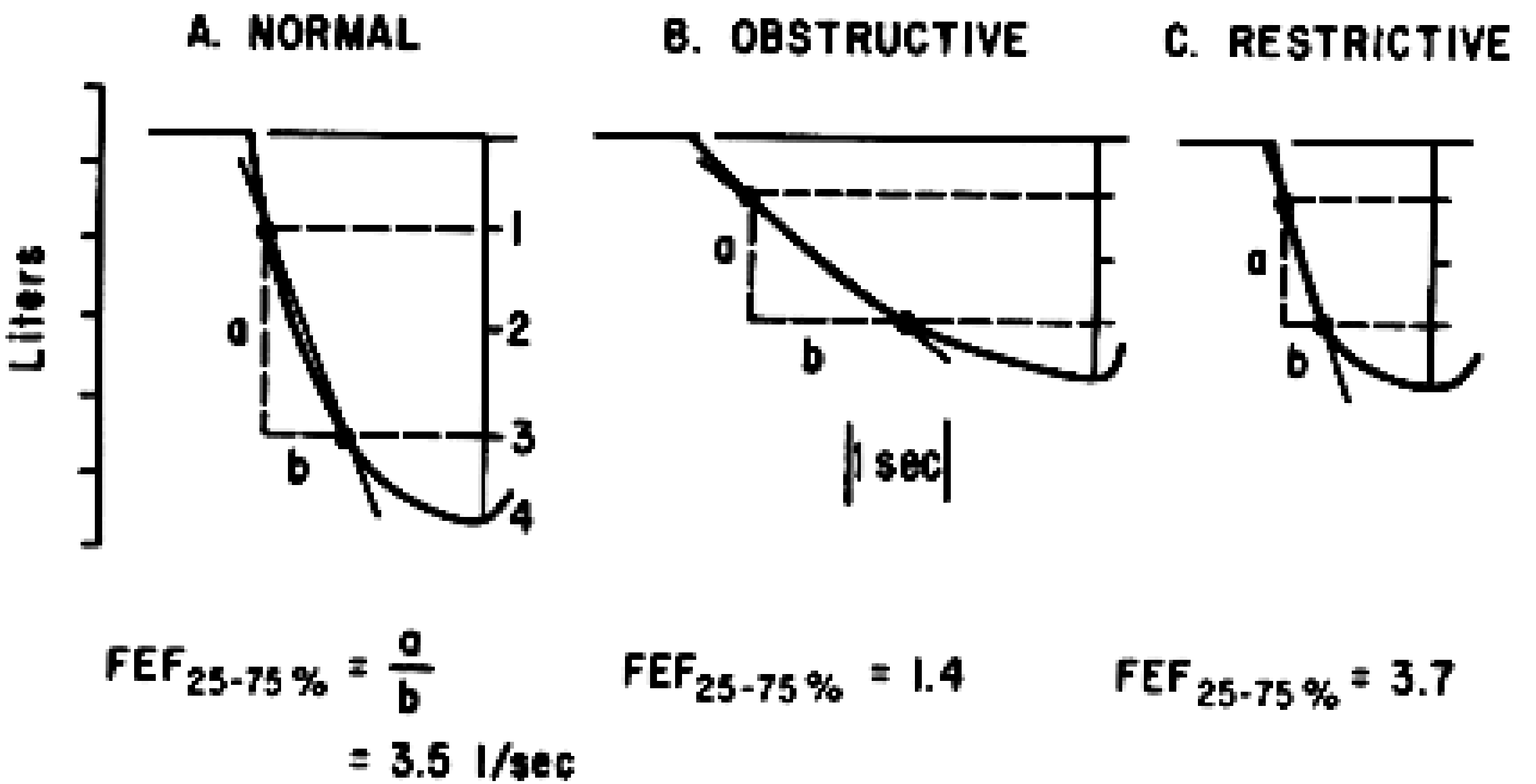
Lung Capacity and Disease—Summary

- Obstructive Disease:
  - Decreased VC
  - Increased TLC, RV, FRC.
- Restrictive Disease:
  - Decreased VC
  - Decreased TLC, RV, FRC.

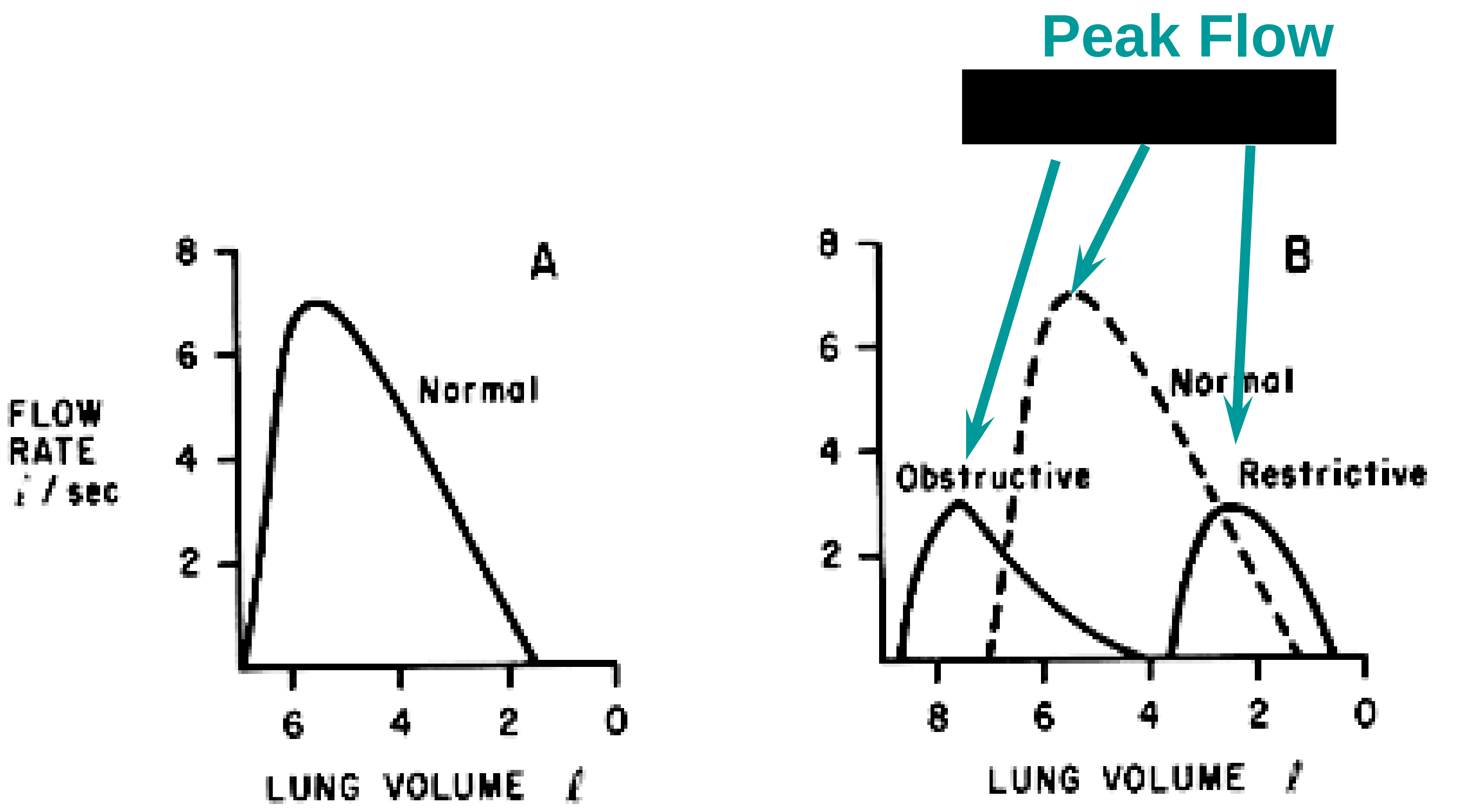
Forced Vital Capacity
$FEV_{1.0}$ / FVC Ratio



Small Airways Disease
$FEF_{25\text{-}75}$



Flow -Volume Curves



Dead Space

Anatomical dead space – volume of the conducting respiratory passages (150 ml)

Alveolar dead space – alveoli that cease to act in gas exchange due to collapse or obstruction

Total dead space – sum of alveolar and anatomical dead spaces

Alveolar Ventilation

- Alveolar ventilation rate (AVR) – measures the flow of fresh gases into and out of the alveoli during a particular time

AVR	=	frequency	X	(TV – dead space)
(ml/min)		(breaths/min)		(ml/breath)

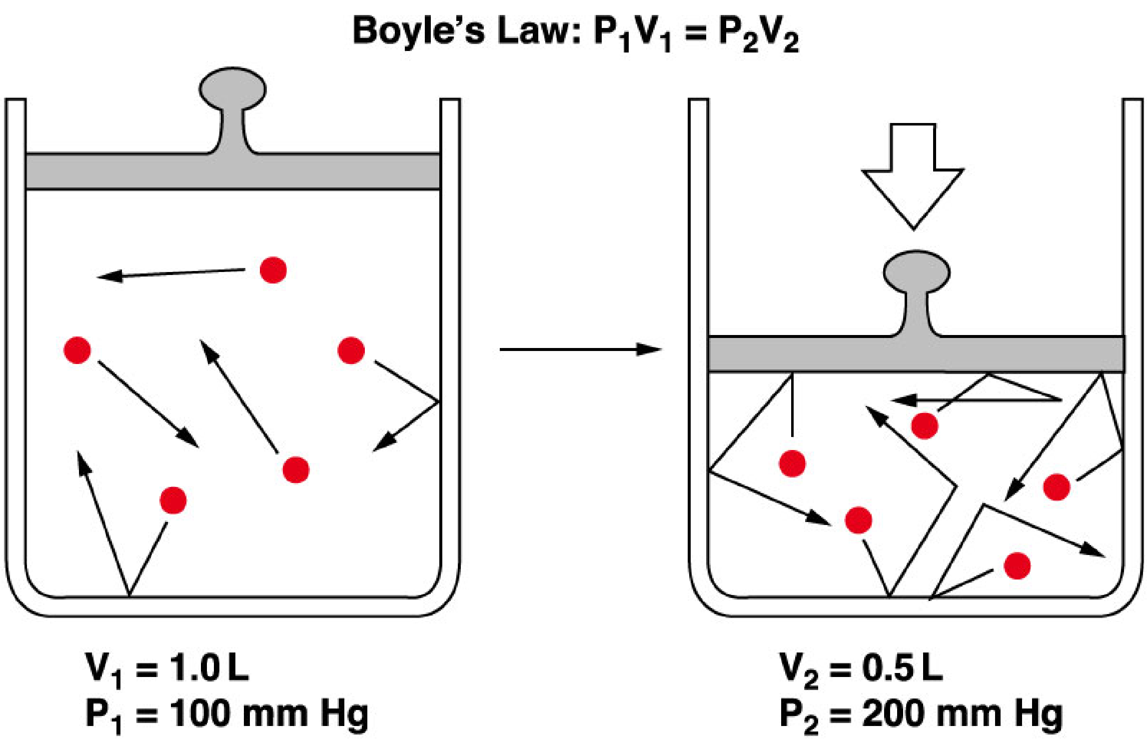
- Slow, deep breathing increases AVR and rapid, shallow breathing decreases AVR

Gas Laws Govern O2 and CO2 Saturation of Blood

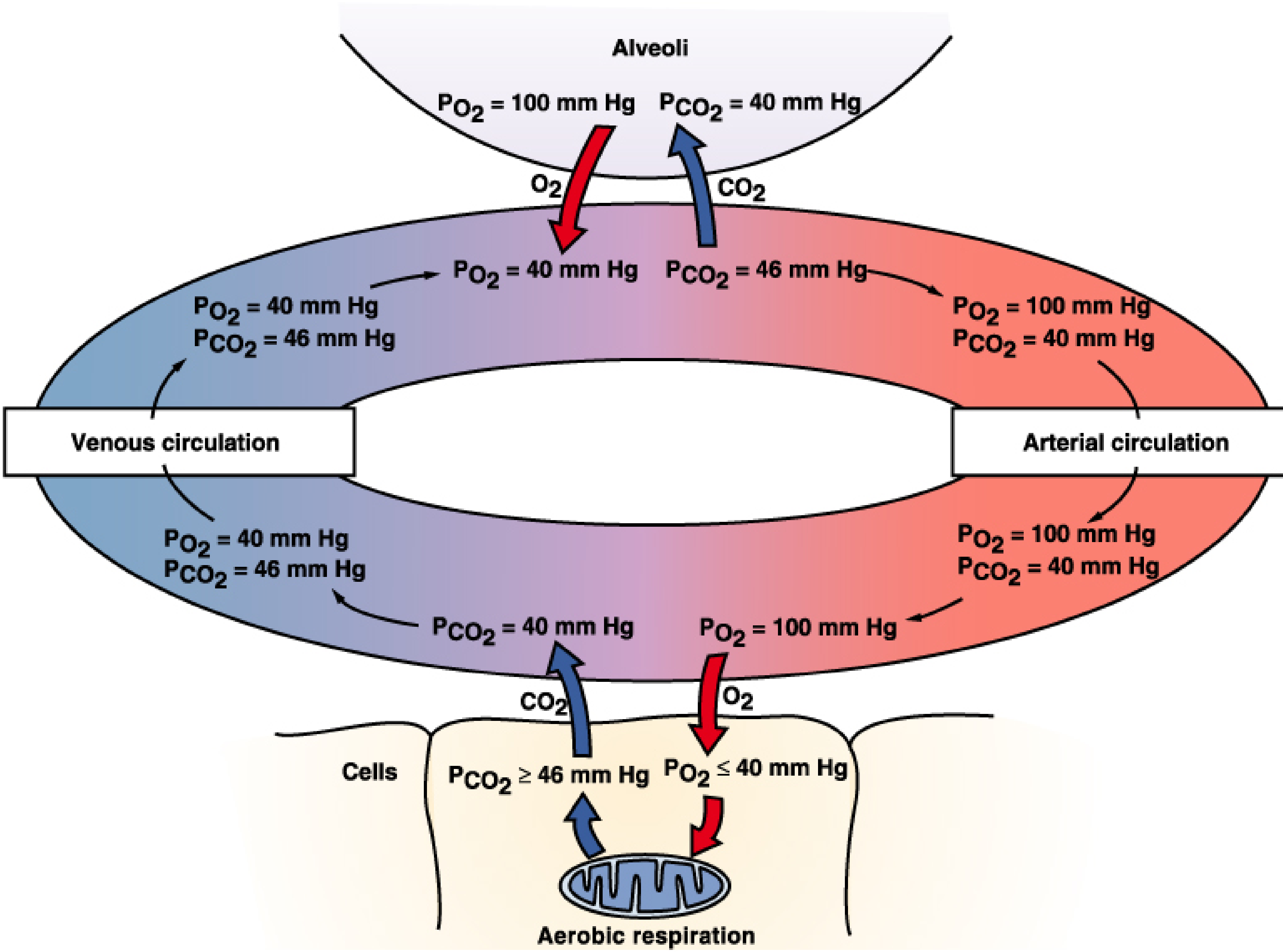
1. Dalton's Law - total pressure of a mixture of gases = sum of pressures of individual gases in the mix

   • pressure of a single gas in the mixture = **partial pressure**

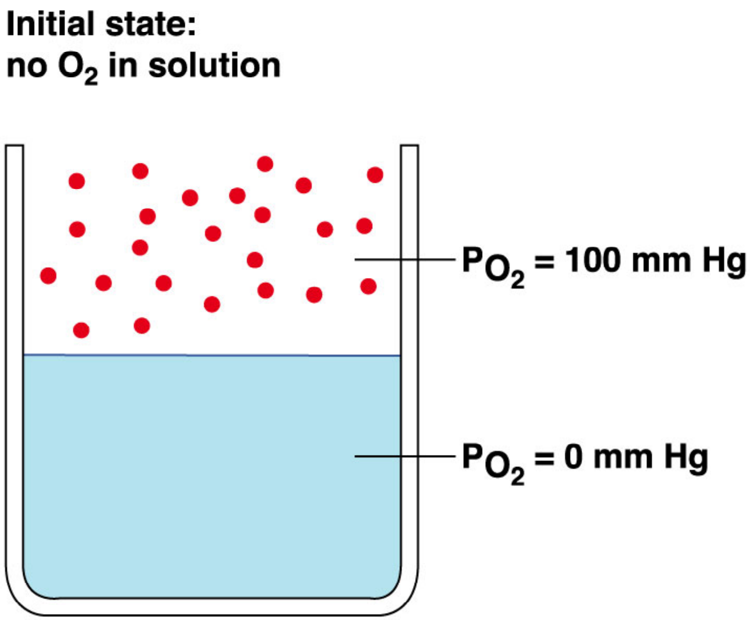
2. Boyle's Law – P = 1/V; this is what increases and decreases partial pressures as the lungs inflate and deflate with each breath

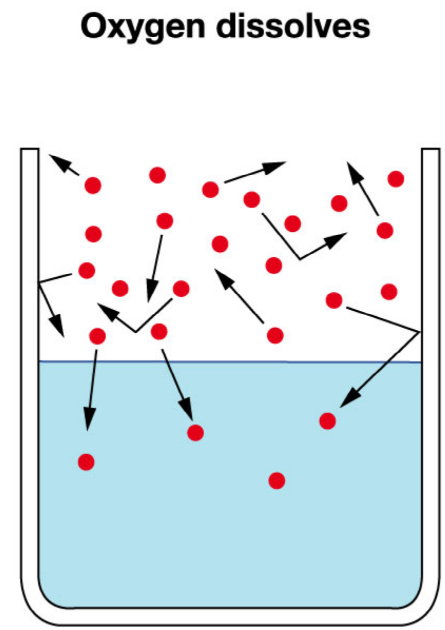


3. Gases move from an area of high pressure toward an area of low pressure



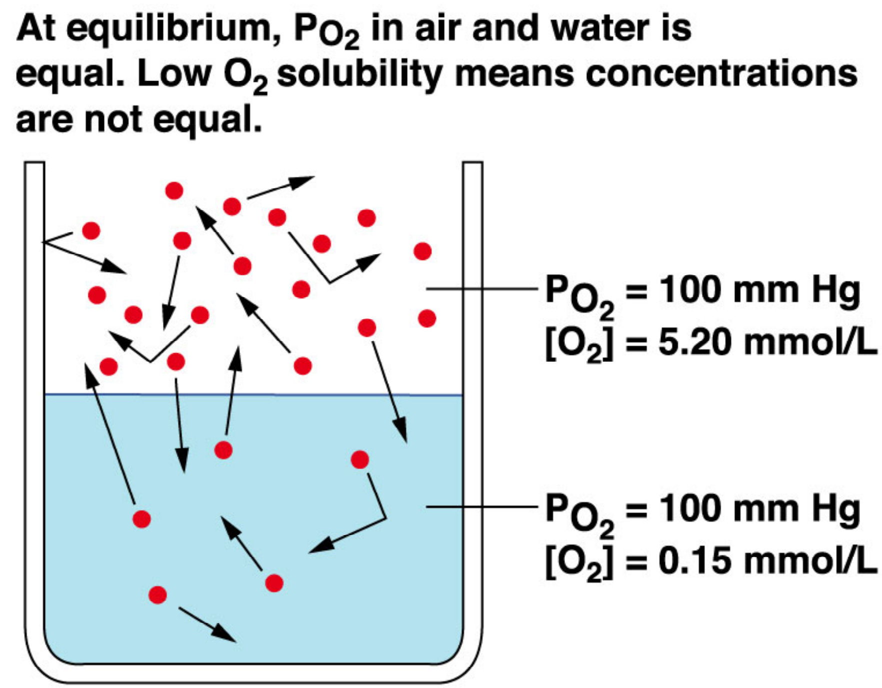
Alveoli
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
O_2
CO_2
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
Venous circulation
Arterial circulation
P_{O_2} = 40 mm Hg
P_{CO_2} = 46 mm Hg
P_{O_2} = 100 mm Hg
P_{CO_2} = 40 mm Hg
P_{CO_2} = 40 mm Hg
P_{O_2} = 100 mm Hg
CO_2
O_2
Cells
$P_{CO_2} \geq$ 46 mm Hg
$P_{O_2} \leq$ 40 mm Hg
Aerobic respiration



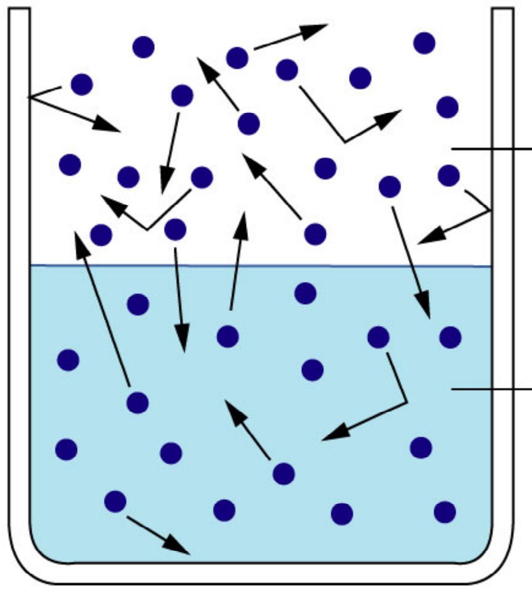


4. Henry's Law – the amount of gas that will dissolve in a liquid is determined by the partial pressure of the gas and the gas's solubility in the liquid.

O2 is not very soluble in water



When CO_2 is at equilibrium at the same partial pressure, more CO_2 dissolves.



- CO_2 has good solubility in water, therefore there will be a greater partial pressure of CO_2 in plasma than partial pressure of O_2.

Results:

- Blood must find a better mechanism for carrying O_2 to and from the tissues.
- CO_2 can be carried in the plasma, on RBCs or is converted to bicarbonate.

Composition of Alveolar Gas

- The atmosphere is mostly oxygen and nitrogen, while alveoli contain more carbon dioxide and water vapor
- These differences result from:
  - Gas exchanges in the lungs – oxygen diffuses from the alveoli and carbon dioxide diffuses into the alveoli
  - Humidification of air by conducting passages
  - The mixing of alveolar gas that occurs with each breath

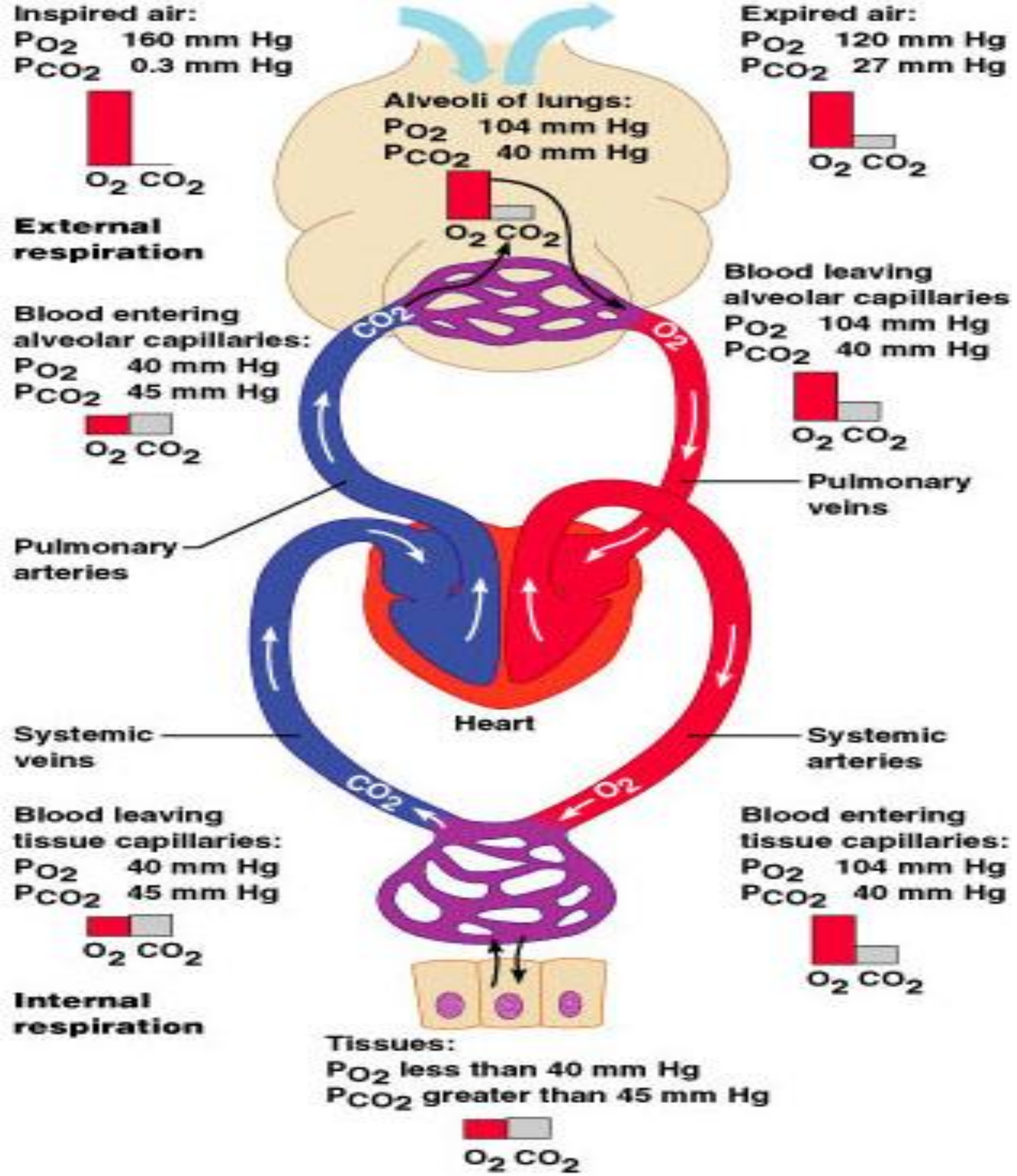
External Respiration: Pulmonary Gas Exchange

- Factors influencing the movement of oxygen and carbon dioxide across the respiratory membrane
  - Partial pressure gradients and gas solubilities
  - Matching of alveolar ventilation and pulmonary blood perfusion
  - Structural characteristics of the respiratory membrane

Partial Pressure Gradients and Gas Solubilities

- Although carbon dioxide has a lower partial pressure gradient:
  - It is 20 times more soluble in plasma than oxygen
  - It diffuses in equal amounts with oxygen

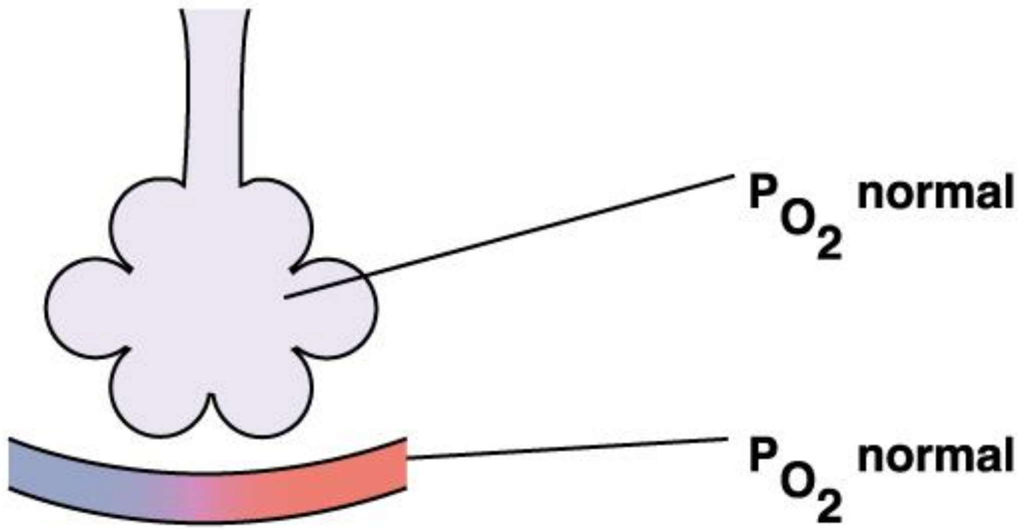
Partial Pressure Gradients



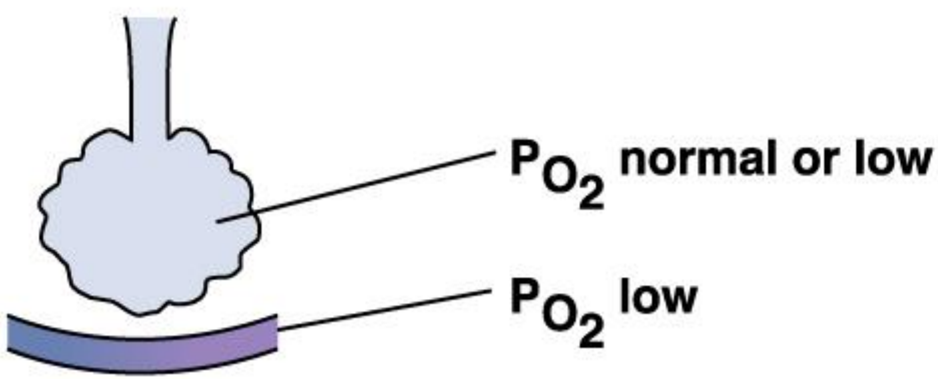
Surface Area and Thickness of the Respiratory Membrane

- Respiratory membranes:
  - Are only 0.5 to 1 μm thick, allowing for efficient gas exchange
  - Have a total surface area of about 60 m^2 (40 times that of one's skin)
  - Thicken if lungs become waterlogged and edematous, whereby gas exchange is inadequate and oxygen deprivation results
  - Decrease in surface area with emphysema, when walls of adjacent alveoli break through

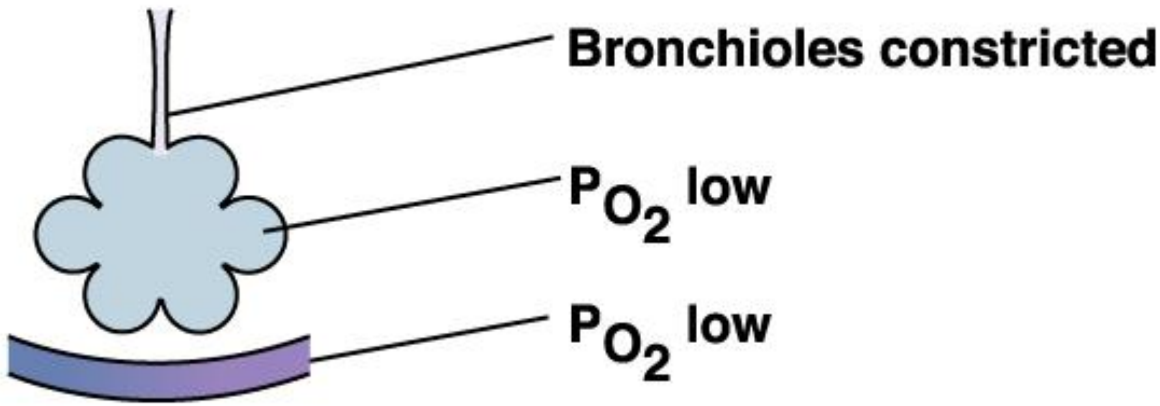
Normal lung



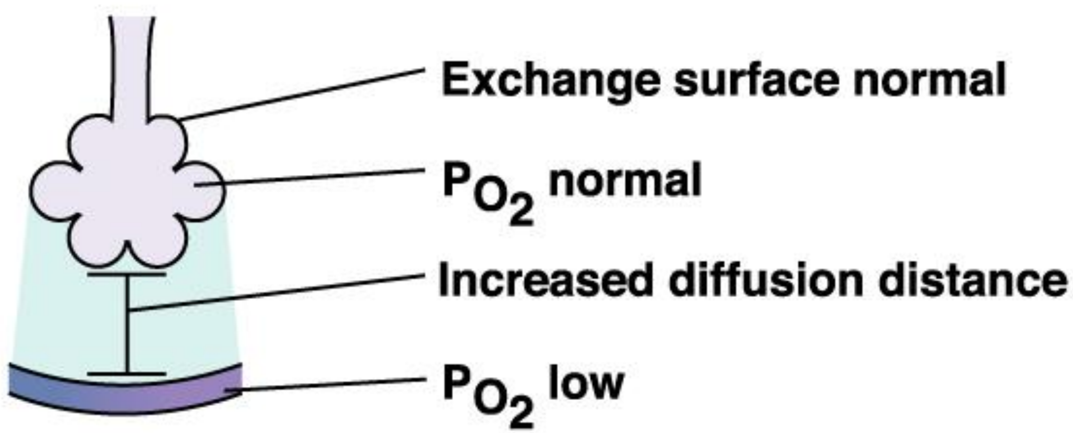
Emphysema: destruction of alveoli means less surface area for gas exchange.



Asthma: increased airway resistance decreases airway ventilation.



Pulmonary edema: fluid in interstitial space increases diffusion distance. Arterial P_{CO_2} may be normal due to higher CO_2 solubility.



Diffusion of Gases

- Fick's law of diffusion

$$V_{gas} = \frac{A}{T} \times D \times (P_1 - P_2)$$

V gas = rate of diffusion
A = tissue area
T = tissue thickness
D = diffusion coefficient of gas
P_1-P_2 = difference in partial pressure

Diffusing Capacity of the Lung

- Diffusing Capacity (D_L) lumps together:
  - Diffusivity
  - Area
  - Thickness

From Fick Equation:

$$D_L = \frac{A \cdot D}{T} = \frac{\dot{V}_{gas}}{P_1 - P_2}$$

Carbon Monoxide Diffusing Capacity (D_LCO)

- Advantage: virtually no back pressure.
  - Hb binding
  - low solubility

$$D_{L_{CO}} = \frac{\dot{V}_{CO}}{P_{A_{CO}} - P_{c_{CO}}} = \frac{\dot{V}_{CO}}{P_{A_{CO}} - 0} = \frac{\dot{V}_{CO}}{P_{A_{CO}}}$$

Single Breath D_LCO

- Single inspiration of a dilute CO mixture
- 10 second breath-hold
- Measure CO uptake using infrared detector to compare inspiratory and expiratory concentrations
- **Normal Value:** 25 ml / min / mmHg (increase w/ exercise)

Diffusing Capacity for Oxygen

- Calculating D_LO_2 from D_LCO:

$$\frac{\mathbf{D}_{\mathbf{L}_{\mathbf{O_2}}}}{\mathbf{D}_{\mathbf{L}_{\mathbf{CO}}}} = \frac{\sqrt{\mathbf{28}}}{\sqrt{\mathbf{32}}} \bullet \frac{\mathbf{0.0244}}{\mathbf{0.01836}} = \mathbf{1.23}$$

$$D_{L_{O_2}} = 1.23 \bullet D_{L_{CO}}$$

Diffusing Capacity of the Lung

Decreases with loss of surface area.
Decreases with increasing membrane thickness
Decreases with ventilation/perfusion mismatching

Internal Respiration

- The factors promoting gas exchange between systemic capillaries and tissue cells are the same as those acting in the lungs
  - The partial pressures and diffusion gradients are reversed
  - P_{O2} in tissue is always lower than in systemic arterial blood
  - P_{O2} of venous blood draining tissues is 40 mm Hg and P_{CO2} is 45 mm Hg

Oxygen Transport

- Molecular oxygen is carried in the blood:
  - Bound to hemoglobin (Hb) within red blood cells
  - Dissolved in plasma

O_2 Transport

- Molecular oxygen in the blood is either dissolved in the plasma (1.5%) or bound to hemoglobin w/i the RBCs (98.5%).
- Each Hb can bind 4 molecules of O_2 and this binding is quite <u>reversible</u>.
- Hb containing bound O_2 is oxyhemoglobin and Hb w/o O_2 is deoxyhemoglobin.
- Carbon monoxide has an extremely high affinity for hemoglobin's oxygen binding site

O_2 Transport

- Loading and unloading of O_2 is given by a simple reversible equation:

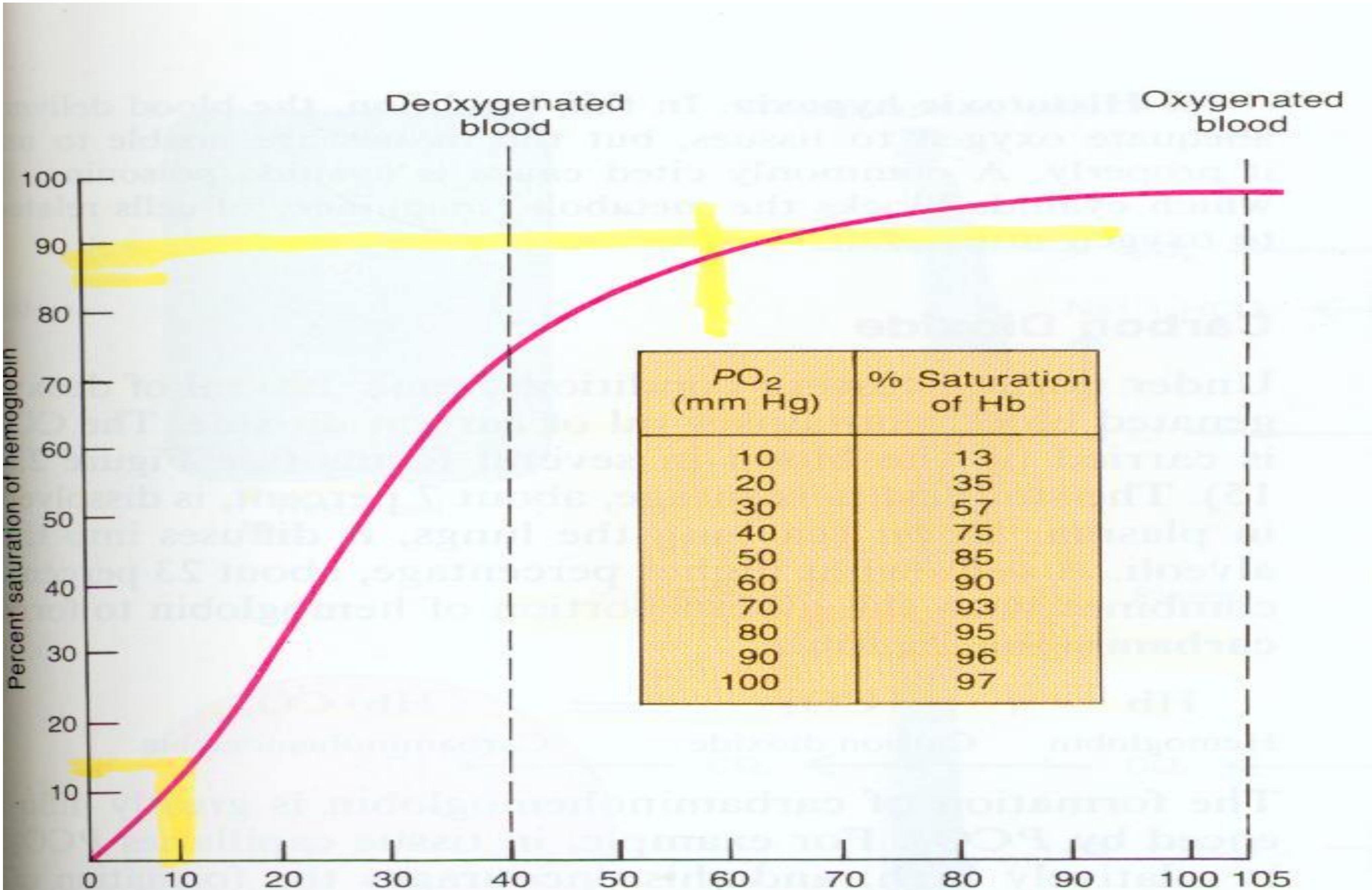
  $HHb + O_2 \leftrightarrow HbO_2 + H^+$

- O_2 binding is "cooperative"
  - The binding of the 1st O_2 molecule causes the Hb to change shape which makes it easier for the 2nd O_2 to bind. Binding of the 2nd O_2 makes it easier for the 3rd and binding of the 3rd makes it easier for the 4th.

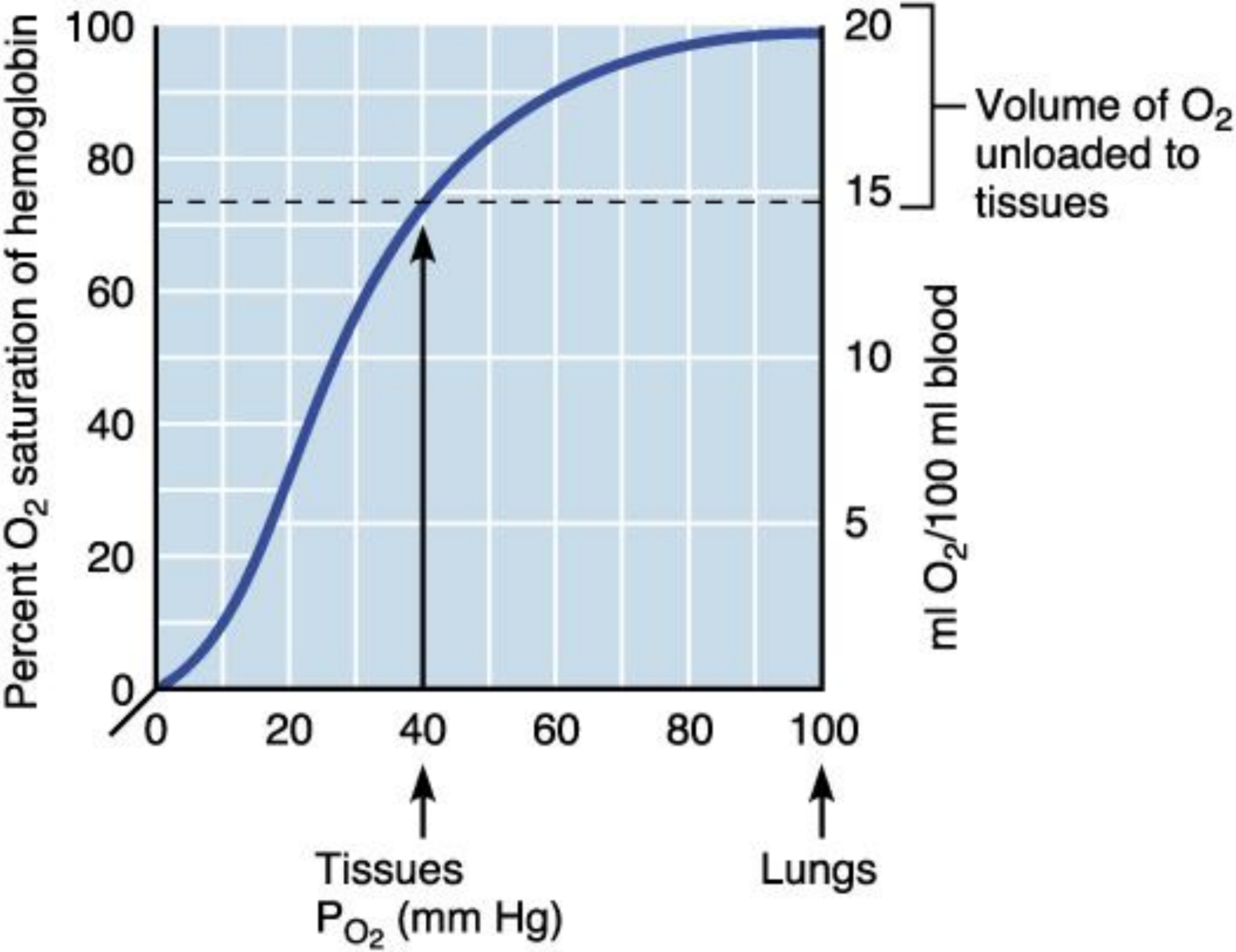
O_2 Transport

- As O_2 loading proceeds, the affinity of Hb for O_2 $\uparrow$
- When Hb has 4 bound O_2 molecules it is *saturated*. When it has 1,2, or 3 it's *unsaturated*
- When the saturation of Hb is plotted against the Po_2, we get the oxygen-hemoglobin dissociation curve.

Oxygen hemoglobin dissociation curve

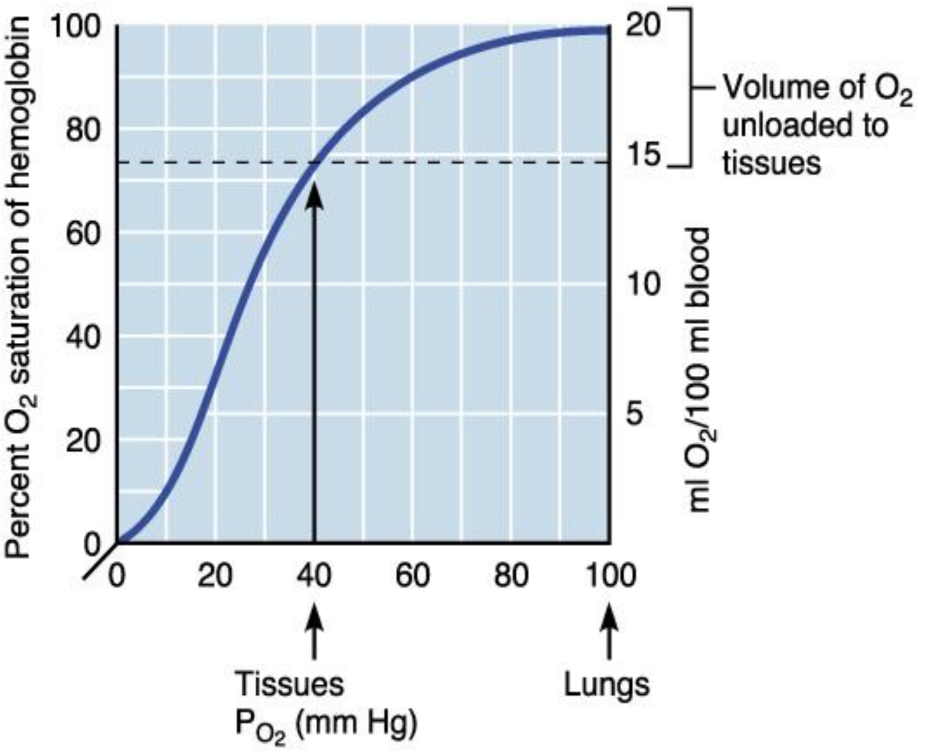


PO_2 (mm Hg)	% Saturation of Hb
10	13
20	35
30	57
40	75
50	85
60	90
70	93
80	95
90	96
100	97



Percent O_2 saturation of hemoglobin
100
80
60
40
20
0
0
20
40
60
80
100
20
15
10
5
Volume of O_2 unloaded to tissues
ml O_2/100 ml blood
Tissues
Lungs
P_{O_2} (mm Hg)

- Hb-O_2 dissociation curve is sigmoidal.
- Hb is almost completely saturated at a Po_2 of 70mmHg.
- At pulmonary Po_2 of 104mmHg, Hb is completely saturated.
- Even at the tissue Po_2 of 40mmHg, Hb is still 75% saturated



UNDERSTANDING THE HB/O DISSOCIATION CURVE

- The plateau: Provides a margin of safety in the oxygen carrying capacity of the blood
- The steep portion: Small changes in Oxygen levels can cause significant changes in binding. This promotes release to the tissues.

HB/O DISSOCIATION CURVE

- Arterial blood with 15 gm/dl Hb contains 19.8 ml O2/dl, venous blood (75 % saturated) contains 15.2 O2 ml/dl.
- 4,6 ml O2 is delivered to tissues from each 100 ml blood, 250 ml delivered to the tissues / min.
- Amount of Oxygen delivered depend on Hb level.

HB/O DISSOCIATION CURVE

- Oxygen dissociation curve is the relation of the % saturation of Hb to the level of PO2 in mm Hg.
- At PO2 100 sat. is 97.5%, at PO2 40 sat. is 75%.

Factors affecting Hb affinity to O2

- Decreased affinity: shift of O2 dissociation curve to the right:

1. Increased temperature
2. Fall in pH (increased PCO2 – Bohr effect).
3. Increased 2,3,diphosphoglycerate in red cells.

Increased affinity: Shift to the left:

1. Low temp.
2. High pH.
3. Decreased 2,3,diphosphoglycerate.

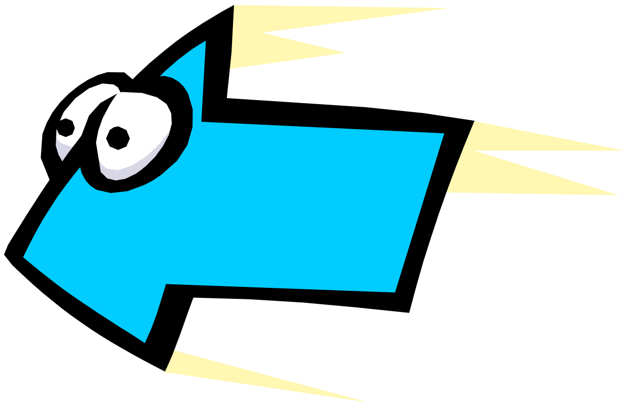
PO_2 above 100 will not increase saturation.

At PO2 60 Hb is 89% saturated.

A steep drop of saturation below PO2 60.

Left Shift-clinical situations

- Alkalosis, hypocapnia, hypothermia
- Decreased DPG,
- CO poisoning
- Blood transfusion, fetal Hgb



Factors affecting 2,3 DPG:

- 1. Low pH (acidosis) decreases 2,3 DPG.
- 2. Thyroid hormone, growth hormone, androgen leads to increased 2,3 DPG concentration.
- 3. Exercise increases 2,3 DPG after 60 min.
- 4. High altitude increases 2,3 DPG releasing O2.

Cont.

- 5. Hb F (alpha2 gama2) poor binding to 2,3 DPG leading to increased affinity to O2 and more O2 moves from mother to fetus.
- 6. Anemia can increase 2,3 DPG.

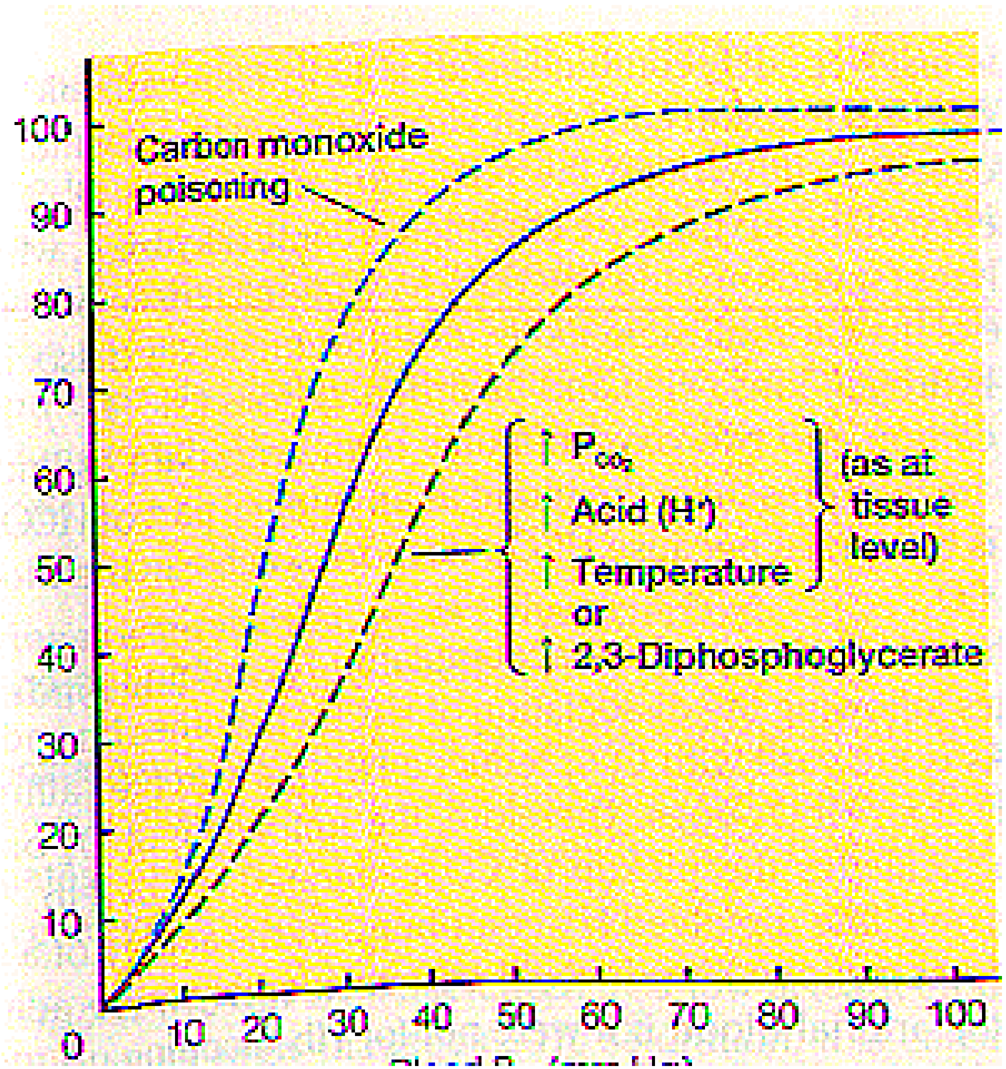
Myoglobin

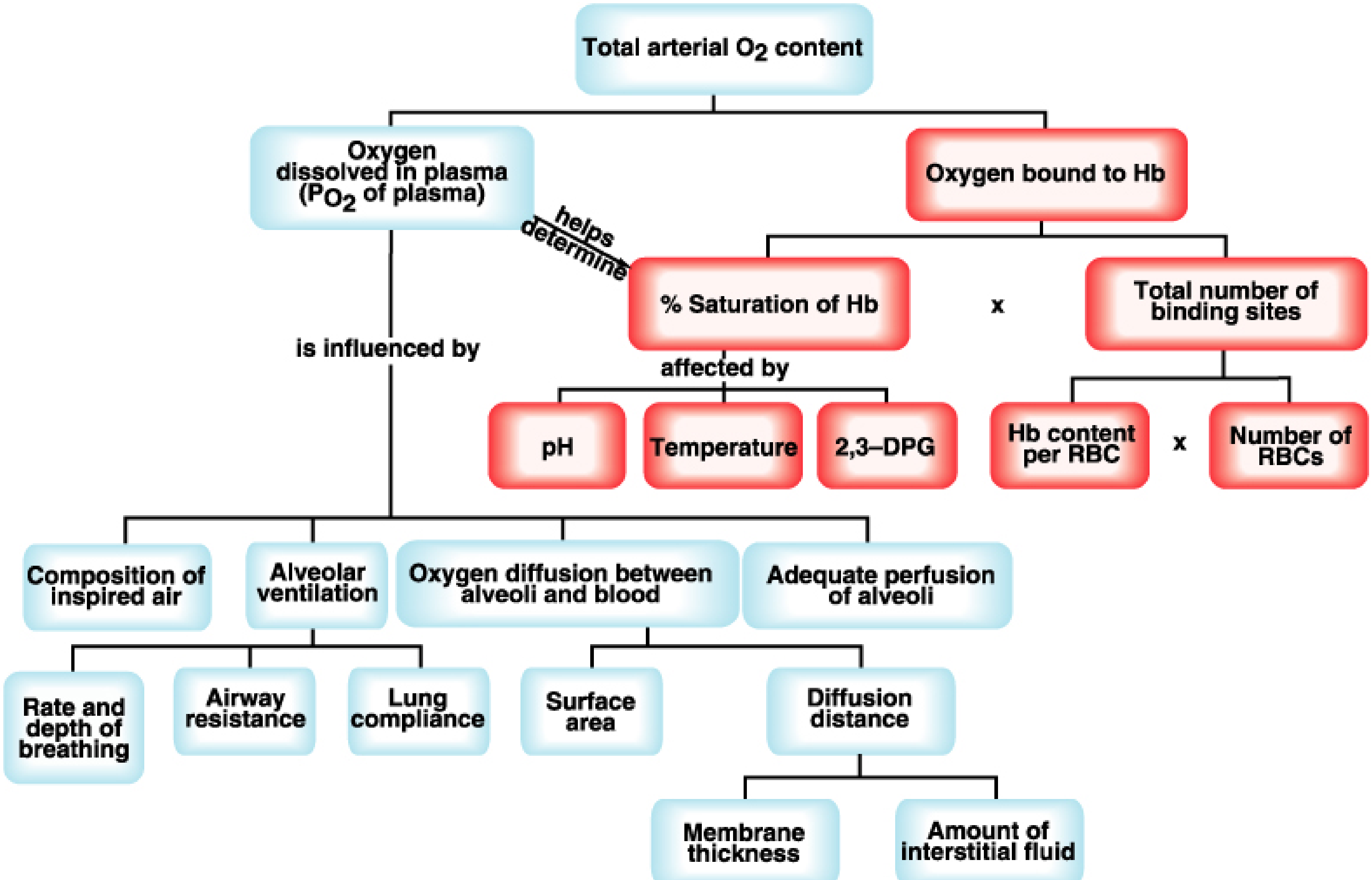
- It is an iron containing pigment in skeletal muscles.
- Binds one molecule of O2.
- Its curve to the left of Hb so it takes O2 from Hb.

P50:

- It is the partial pressure of O_2 at which Hb is 50 % saturated. It is increased by:
- 1. Thyroid hormones, growth H. & androgens.
- 2. Exercise.
- 3. High altitude.
- 4. Increased temp.
- 5. Decreased pH.
- The higher the P50, the lower is the Hb affinity for O_2.

Agents which shift the Hb/O Dissociation curve: The Bohr Effect





Total arterial O_2 content
Oxygen dissolved in plasma (P_{O_2} of plasma)
Oxygen bound to Hb
helps determine
% Saturation of Hb
x
Total number of binding sites
is influenced by
affected by
pH
Temperature
2,3–DPG
Hb content per RBC
x
Number of RBCs
Composition of inspired air
Alveolar ventilation
Oxygen diffusion between alveoli and blood
Adequate perfusion of alveoli
Rate and depth of breathing
Airway resistance
Lung compliance
Surface area
Diffusion distance
Membrane thickness
Amount of interstitial fluid

Carbon Dioxide Transport

- Carbon dioxide is transported in the blood in three forms
  - Dissolved in plasma – 7 to 10%
  - Chemically bound to hemoglobin – 20% is carried in RBCs as carbaminohemoglobin
  - Bicarbonate ion in plasma – 70% is transported as bicarbonate (HCO_3^-)

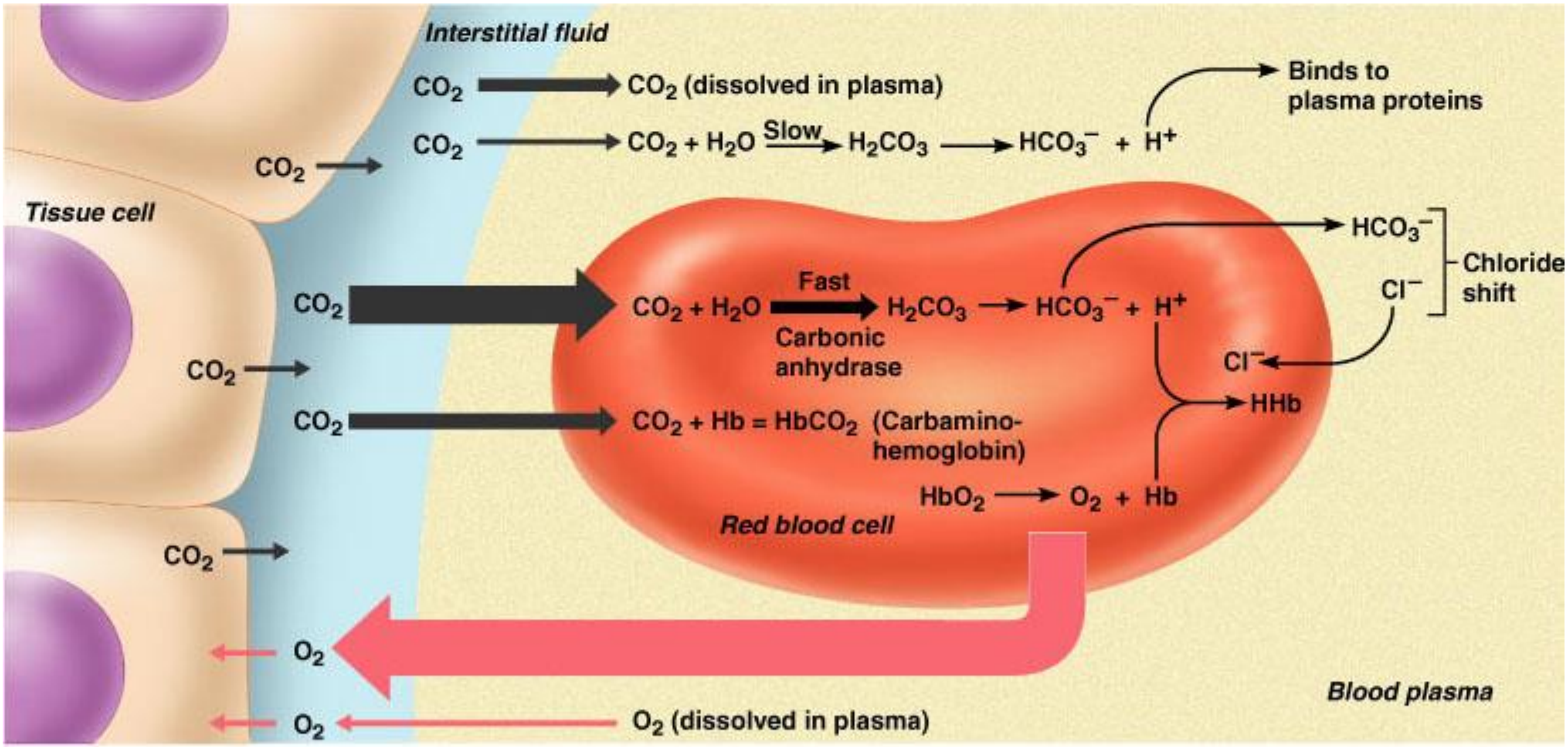
Transport and Exchange of Carbon Dioxide

- Carbon dioxide diffuses into RBCs and combines with water to form carbonic acid (H_2CO_3), which quickly dissociates into hydrogen ions and bicarbonate ions

CO_2	+	H_2O	$\leftrightarrow$	H_2CO_3	$\leftrightarrow$	H^+	+	HCO_3^-
Carbon dioxide		Water		Carbonic acid		Hydrogen ion		Bicarbonate ion

- In RBCs, carbonic anhydrase reversibly catalyzes the conversion of carbon dioxide and water to carbonic acid

Transport and Exchange of Carbon Dioxide



(a) Oxygen release and carbon dioxide pickup at the tissues

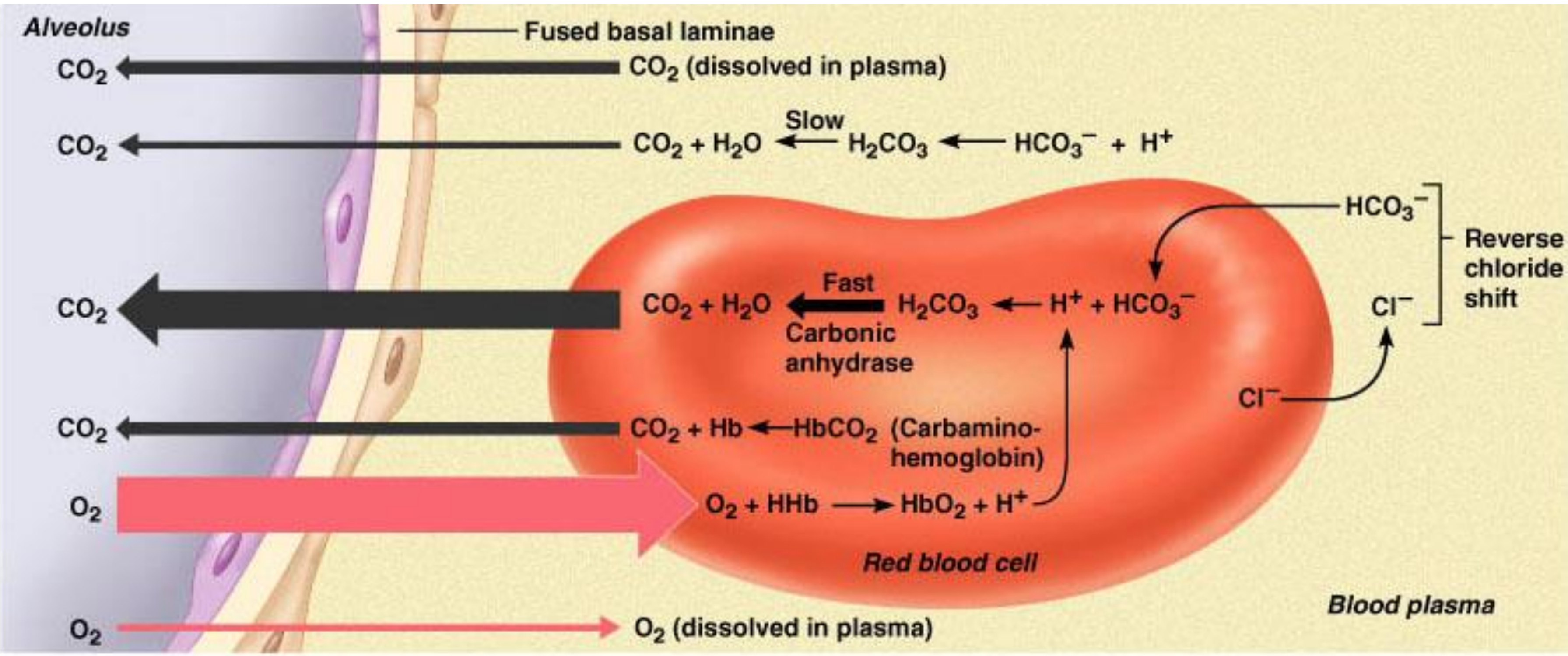
Transport and Exchange of Carbon Dioxide

- At the tissues:
  - Bicarbonate quickly diffuses from RBCs into the plasma
  - The chloride shift – to counterbalance the outrush of negative bicarbonate ions from the RBCs, chloride ions (Cl^-) move from the plasma into the erythrocytes

Transport and Exchange of Carbon Dioxide

- At the lungs, these processes are reversed
  - Bicarbonate ions move into the RBCs and bind with hydrogen ions to form carbonic acid
  - Carbonic acid is then split by carbonic anhydrase to release carbon dioxide and water
  - Carbon dioxide then diffuses from the blood into the alveoli

Transport and Exchange of Carbon Dioxide



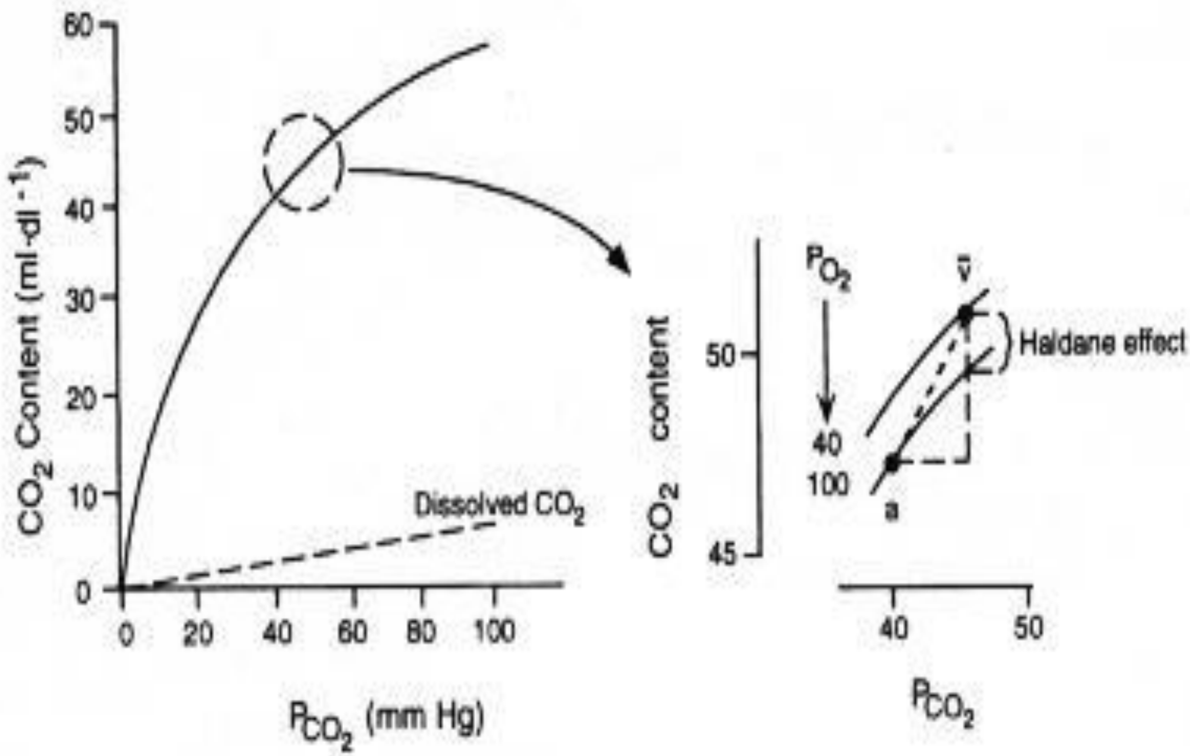
(b) Oxygen pickup and carbon dioxide release in the lungs

Figure 22.22b

Haldane Effect

- The amount of carbon dioxide transported is markedly affected by the P_{O2}
- Haldane Effect: Increasing O_2-saturation reduces CO_2 content and shifts the CO_2 dissociation curve to right. This is because, increasing P_{O2} leads to
  - Decrease in the formation of carbamino compound.
  - Release of H^+ ions from the hemoglobin and resulting in dehydration of HCO_3^-.
    These changes take place in the lungs .

Carbon Dioxide Dissociation Curve



Over the normal physiological range (P_{CO2} = 30 to 55 mmHg and P_{O2} = 40 to 100 mmHg), the CO_2 equilibrium curve is nearly linear. But, O_2 equilibrium curve is highly nonlinear.