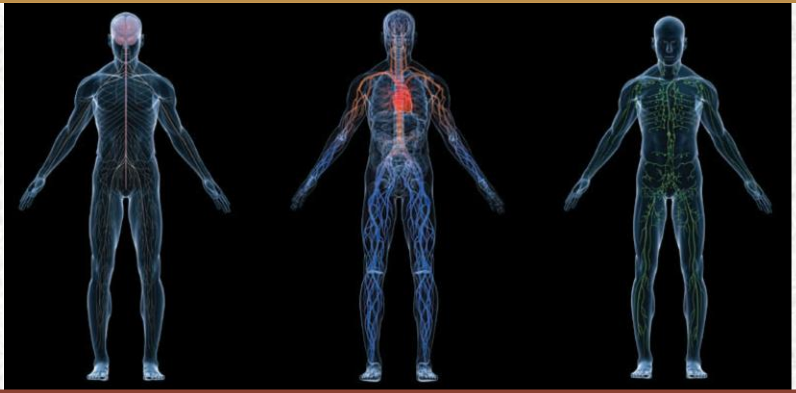
UNIT VII

GUYTON AND HALL *Textbook of*

Medical Physiology

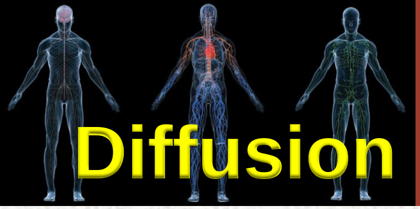
TWELFTH EDITION



Chapter 40:

Transport of Oxygen and Carbon Dioxide in Blood and Tissue Fluids

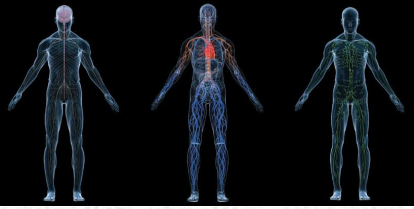
Slides by Robert L. Hester, PhD



Diffusion Capacity of The Respiratory Membrane

It is the volume of gas that diffuses through the membrane each minute for pressure difference of one mm Hg.

- Normal value for O_2 is **21** ml/min/mm Hg
- Normal value for CO_2 is about 20 times greater than O_2.
- During muscular exercise, increase 2-3 times due to
  - recruitment and distension of capillaries.
  - Improvement in ventilation/ Perfusion ratio
- Lungs receive blood from
  - Pulmonary artery - deoxygenated blood
  - Bronchial arteries – oxygenated blood to perfuse muscular walls of bronchi and bronchioles



Respiratory Membrane

1. The gases of respiratory importance are highly soluble in lipids. Therefore they can easily diffuse through tissues, including the respiratory membrane….. The respiratory membrane is composed of 6 layers: Thickness is only 0.25 – 0.6 μ. to allow rapid diffusion of gases

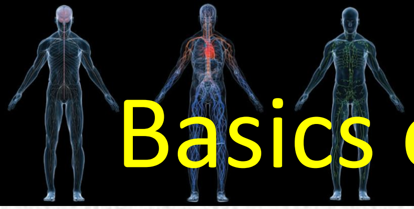
- A layer of slight fluid lining the alveolus and containing surfactant
- Alveolar epithelium
- Epithelial basement membrane
- Interstitial space
- Capillary basement membrane
- Capillary endothelial membrane.

Factors affecting the rate of gas diffusion through The respiratory membrane

- **The surface area of the membrane is 50-100 m^2..difficult to estimate**
- **The pressure difference across the respiratory membrane….this also is very difficult to estimate**
- **Diffusion coefficient:** depends on its **solubility** of the gas and square root of its **molecular weight** (makes MW least important factor)…easy to estimate

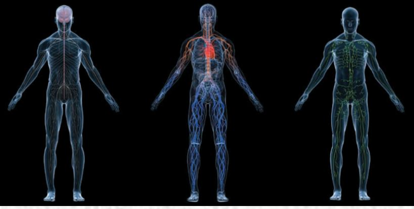
Diff.Coef= (Gas's solubility / √ MW)

$$\text{Diff.Coef} = \frac{\text{Gas's solubility}}{\sqrt{MW}}$$



Basics of the Respiratory System

- Characteristics of exchange membrane
  - High volume of blood through huge capillary network results in
    - **Low vascular resistance through lungs**
      - **P**ulmonary circulation = 5L/min through lung
      - Systemic circulation = 5L/min through entire body
    - Pulm.Capillary hydrostatic blood pressure is low (7-10 mmHg)
    - This Means
      - » Filtration is not a main theme here, we do not want a net loss of fluid into the lungs as rapidly as the systemic tissues
      - » Any excess fluid is still returned via lymphatic system



Determinants of Diffusion

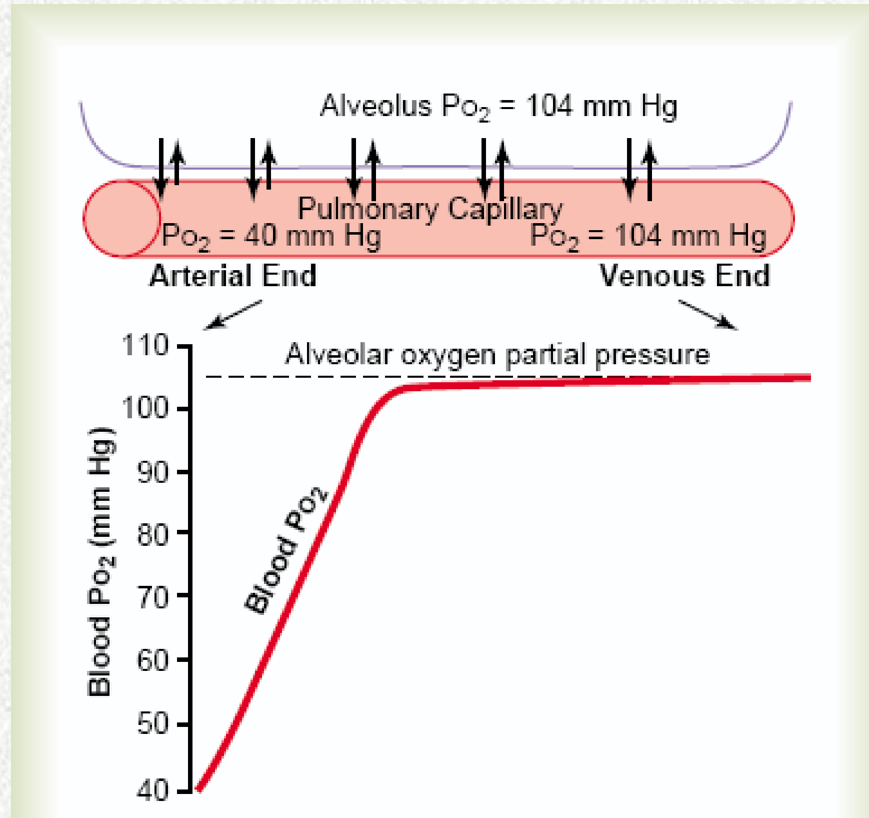
Ficks Law

$$\text{Diffusion} = \frac{(P_1 - P_2) * \text{Area} * \text{Solubility}}{\text{Thickness} * \sqrt{\text{MW}}}$$

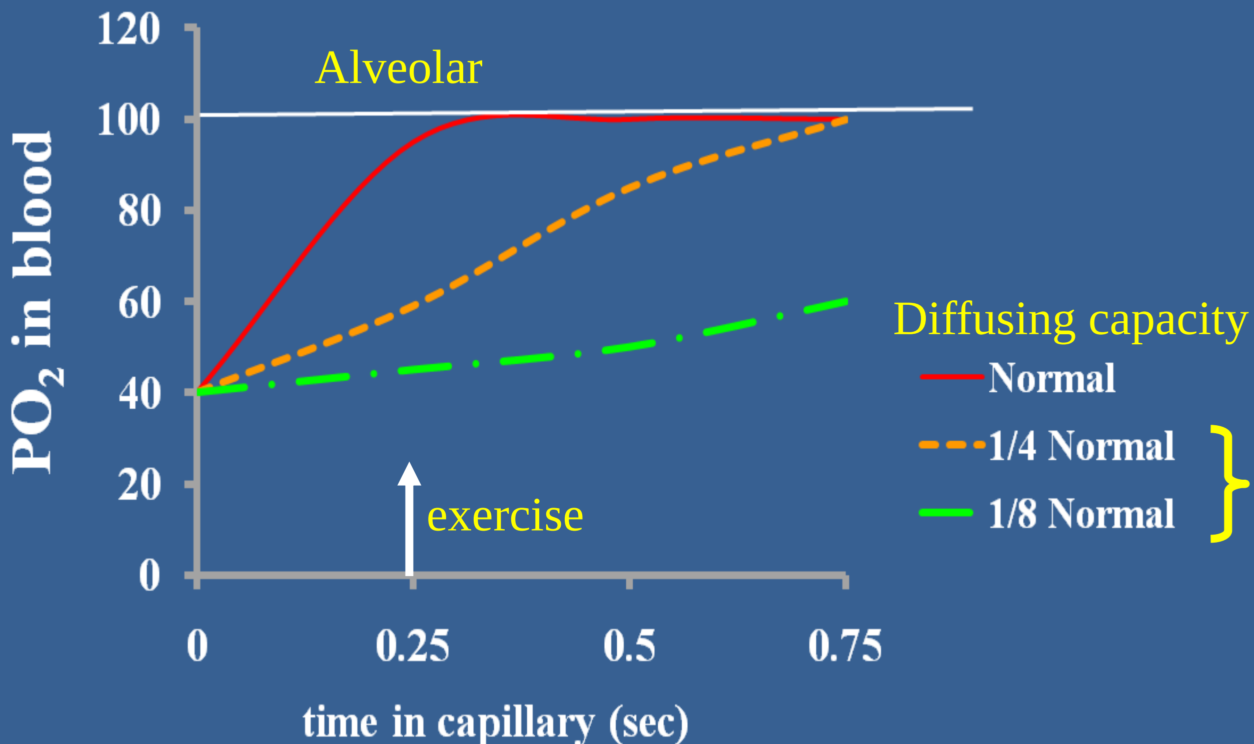
- Pressure Gradient
- Area
- Distance
- Solubility and MW are fixed
- Area and thickness are the characteristic of the membrane
- Solubility and MW are the characteristic of the gas

Oxygen Diffusion from the Alveoli to the Pulmonary circulation

- O_2 diffuses into the pulmonary capillaries because the PO_2 in the alveoli is high. Note: O_2 utilizes less than one third of the respiratory membrane…perfusion-limited
- PO_2 in the pulmonary capillaries increased very fast (1/3 distance) it takes 0.3 sec leaving the rest 0.5 sec with no more exchange. In pathophysiology look at the next slide



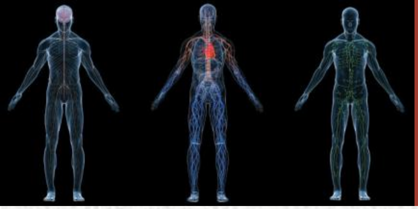
Uptake of Oxygen in Lungs



Damaged lung…At
O_2 becomes diffusio

Why PO_2 arterial <Alveolar PO_2?

- **P_AO_2 =100 while systemic P_aO_2 is only 95 mm Hg?**
- **1. Venous admixture (pollution)**
- **A. BRONCHIAL Circulation**: 50% goes back to right atrium, and 50% to left atrium.
- **B. Cardiac veins**
- **C. Pulmonary Circulation:** 2% of all venous blood doesn’t pass through pulmonary capillaries (A-V anastomosis) “physiological shunted blood”.
- **2. Low VA/Q in the base of the lung.**

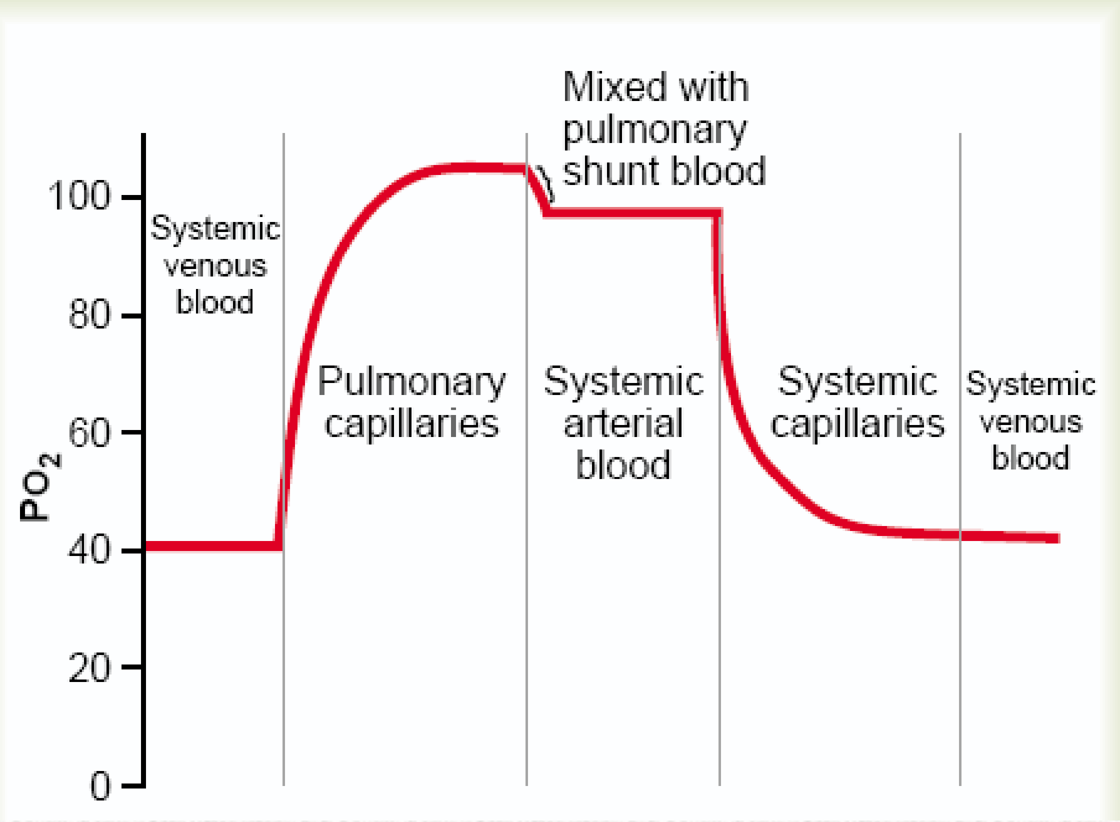


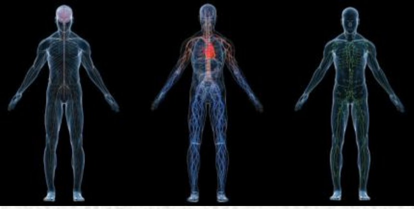
- **Venous admixture (pollution)**
- Some venous blood in the left ventricle comes from: pleural Veins, bronchial venous blood which empty into pulmonary veins (bronchial circulation) & in the heart venae chordae minimae, thebesian vessels & anterior cardiac veins. **BRONCHIAL Circulation**: 50% goes back to right atrium, and 50% to left atrium. We care about the portion which goes to Lt Atrium. Some of the capillary of the bronchial circulation anastomose with pulmonary veins making this pollution.
- **Pulmonary Circulation:**
- 2% of all venous blood doesn't pass through pulmonary capillaries (A-V anastomosis) "physiological shunted blood". The above accounts for 2% of Q.
- **2. Low VA/Q in the base of the lung.**
- P_AO_2 in the base is 90 mm Hg, while in the apex is 130 mm Hg.
- Theoretically, $[(3 \times 90 \text{ base}) + (1 \times 130 \text{ apex})] \div 4 = 100$. This equation is true for mixed alveolar air … but not for mixed arterial blood. Because hyperventilated lung does not compensate for hypoventilated lung in term of oxygen…..WHY? Because HbO_2 dissociation curve is sigmoidal and not linear.
- If ↓ V/Q ratio is decreased then increasing F_{IO2} is by 1% is normally followed by an increase in P_aO_2 by 3-5 mm Hg.. However, if P_aO_2 is increased only by 1 mm Hg then the hypoxemia is due to true anatomical shunt.
- FI_{O2}: fraction of inspired O_2

Transport in arterial blood & Pulmonary shunt flow

This slide says that arterial P_aO_2 is less than PO_2 alveolar. Again……WHY?

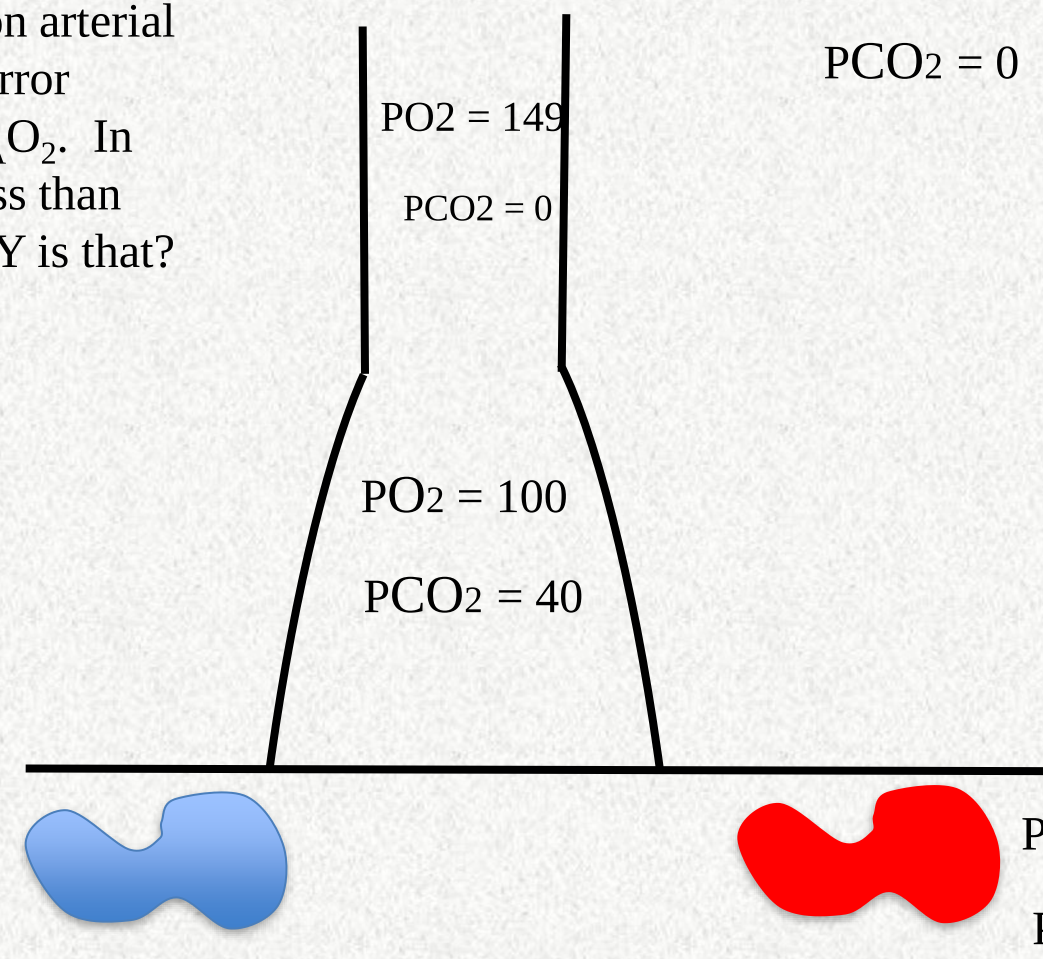
Due to the bronchial circulation the arterial PO_2 falls to 95 mm Hg





Alveolar and Blood Gases

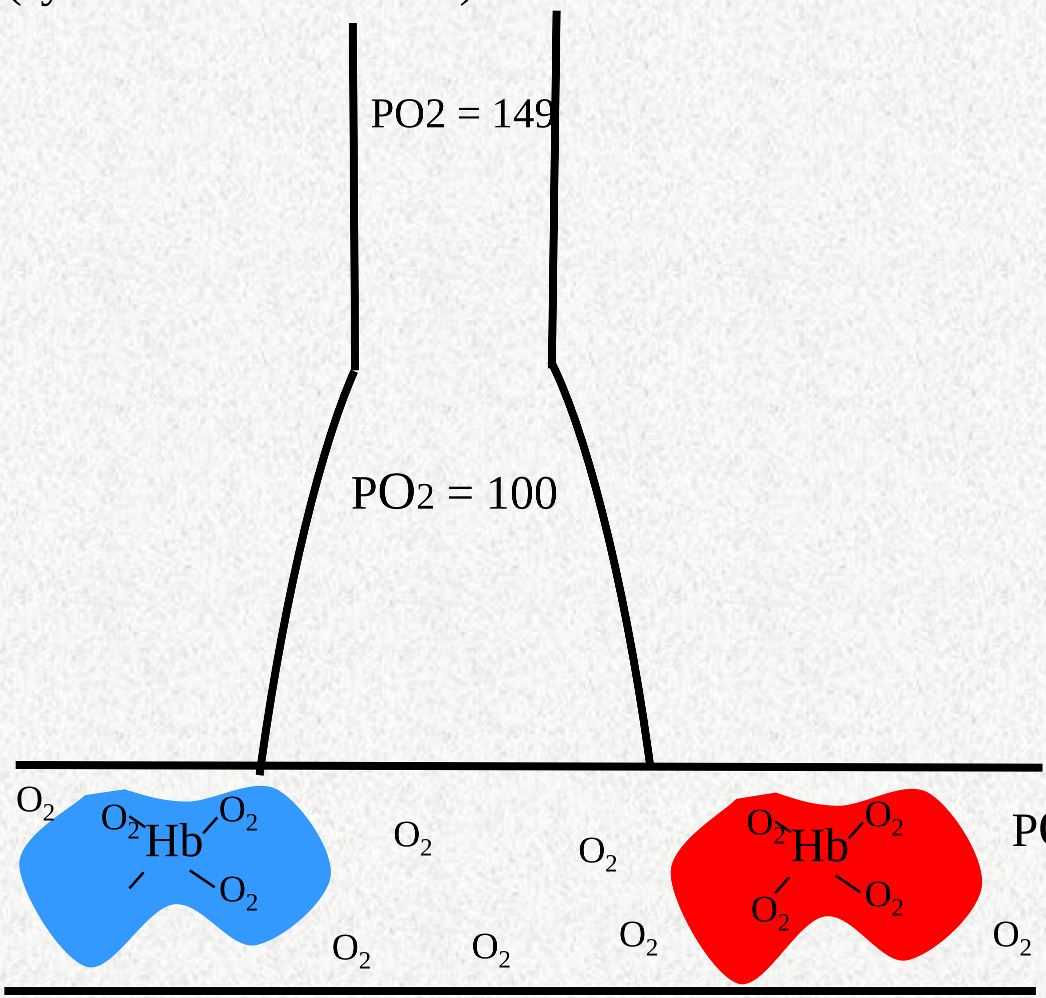
This slide says that for hypothetical situation arterial P_aO_2 should be a mirror image of alveolar P_AO_2. In actuality, P_aO2 is less than P_AO2 alveolar. WHY is that?



Alveolar and Blood PO_2

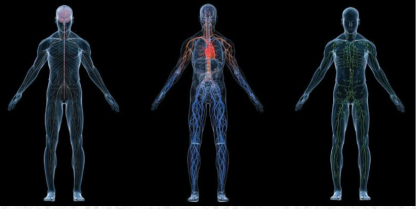
From 75% saturation (mixed venous blood) to fully saturated blood (systemic arterial blood)

$PO_2 = 159$



$PO_2 = 40$ 75% Sat

$PO_2 = 100$ 100%Sat



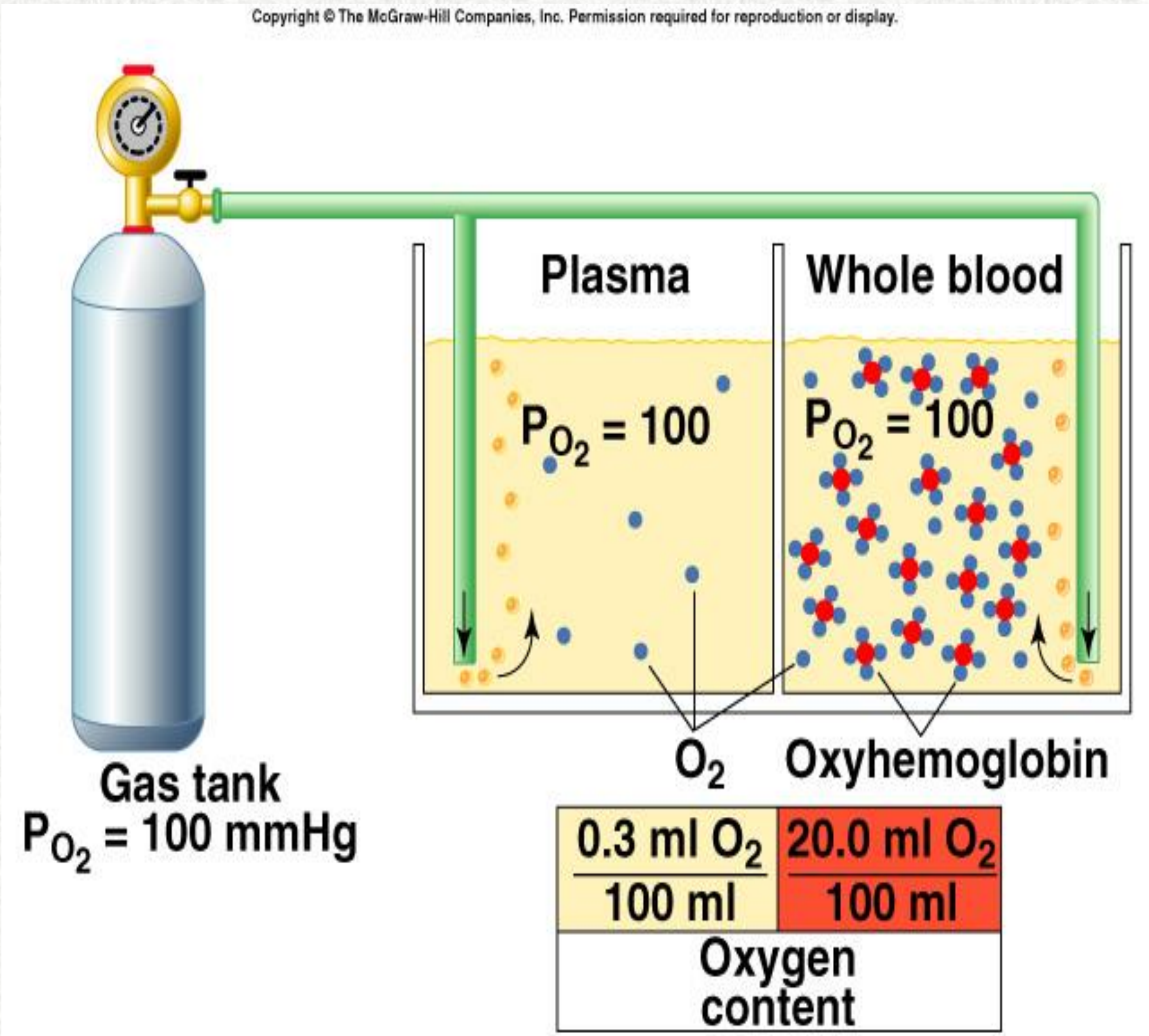
Hemoglobin and 0_2 Transport

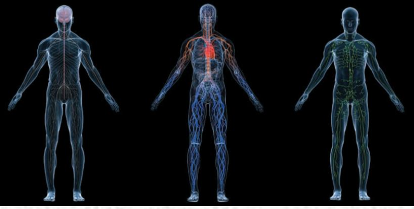
C= 5 million per μl blood

0 million Hb/RBC.

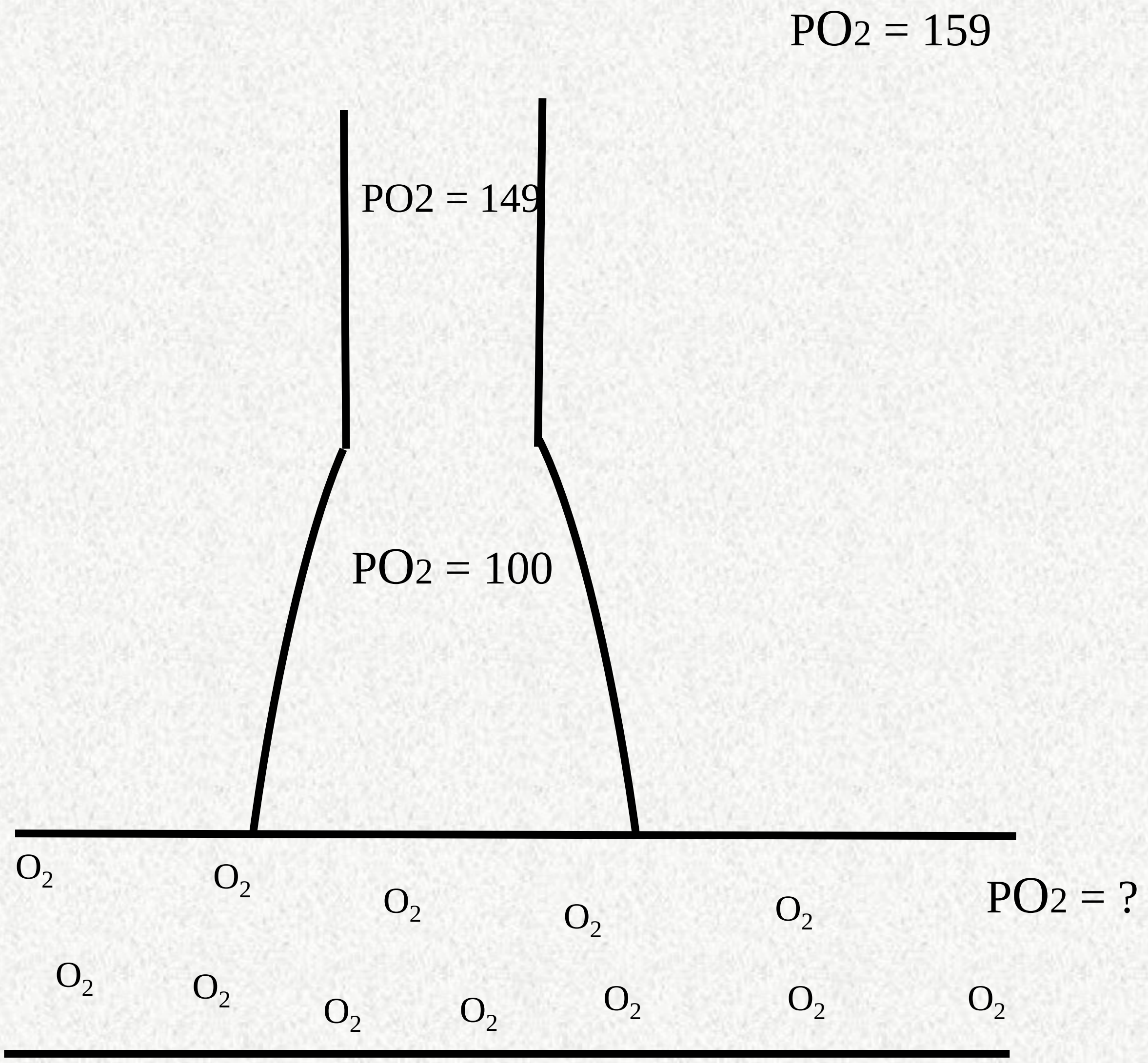
h Hb has 4 polypeptide
ins and 4 hemes.

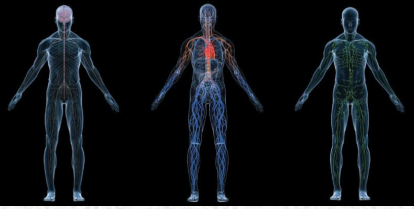
he center of each heme
up is 1 atom of iron
t can combine with 1
lecule 0_2.





Alveolar and Blood PO_2





Question….

A vasodilator is infused into a paralyzed muscle. What happens to PO_2 within that muscle?

A. Increases

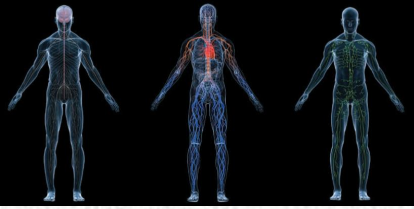
B. Decreases

C. No change

Question

Arterial PO_2 is 100 mmHg and content is 20 ml O_2/dl.
What is arterial PO_2 if ½ of all of the red cells are removed?

A. PO_2 = 0 mmHg
B. PO_2 =30 mmHg
C. PO_2 =50 mmHg
D. PO_2 =60 mmHg
E. PO_2 =100 mmHg



Question

Systemic arterial PO_2 is 100 mmHg and hematocrit is 40%. What is systemic arterial PO_2 if blood is added to increase hematocrit to 50?

A. PO_2 = 50 mmHg
B. PO_2 =70 mmHg
C. PO_2 =100 mmHg
D. PO_2 =120 mmHg
E. PO_2 =149 mmHg

Hypothetical

- What happens to ***mixed venous*** PO_2 in an anemic person?
- Normal
- Lower
- Higher

Question

A person is breathing from a gas tank containing 45% oxygen. What is the alveolar PO_2?

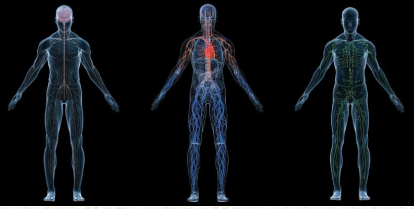
A. 149 mmHg

B. 250 mmHg

C. 270 mmHg

D. 320 mmHg

E. 340 mmHg



Answer

760-47=713

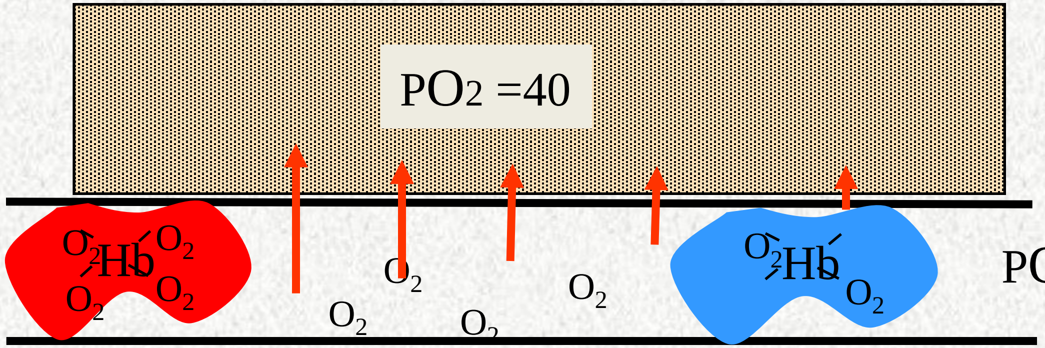
713*0.45 = 321 mmHg = inspired PO_2

Alveolar PO_2 = 321-(40/0.8)= 321-50 =

271 mmHg

Blood and Muscle PO_2

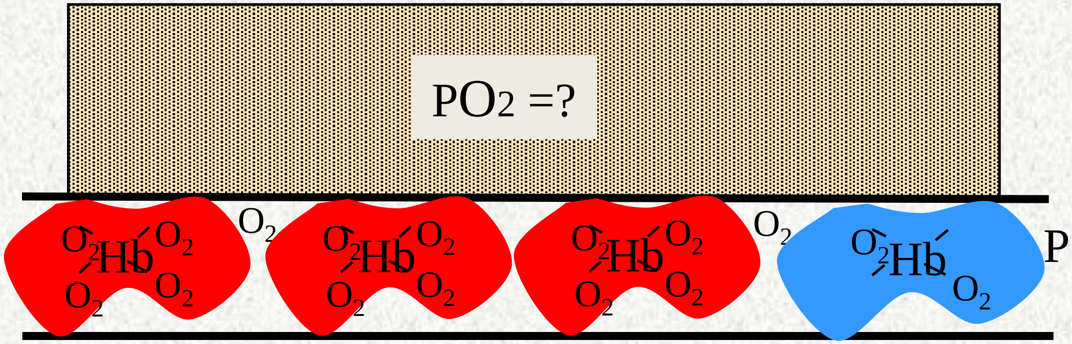
$PO_2 = 100$



$PO_2 = 40$

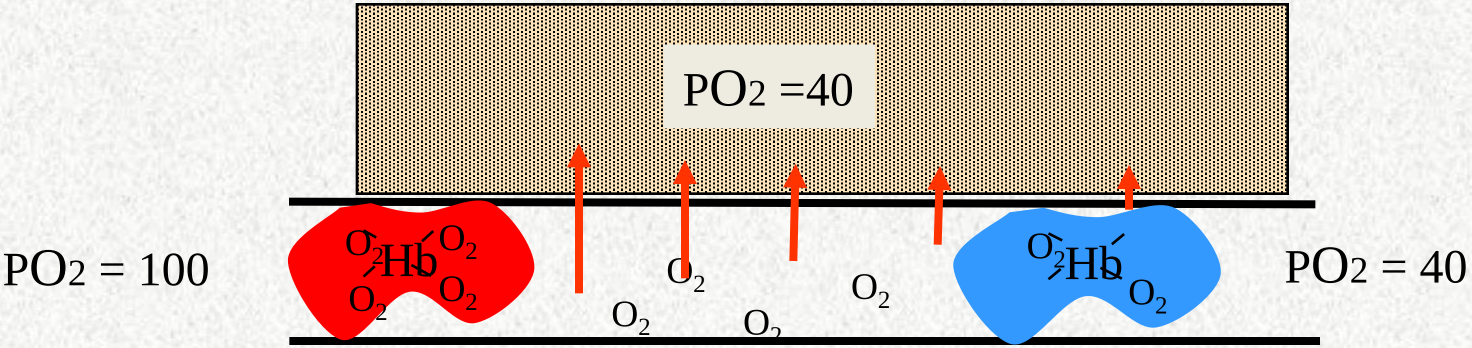
Increased Flow and normal metabolism

$PO_2 = 100$

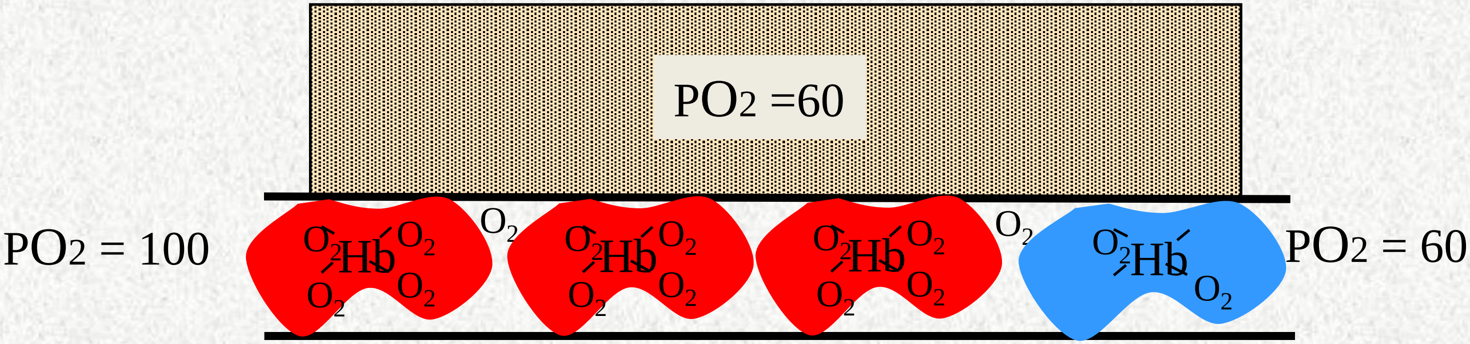


$PO_2 = ?$

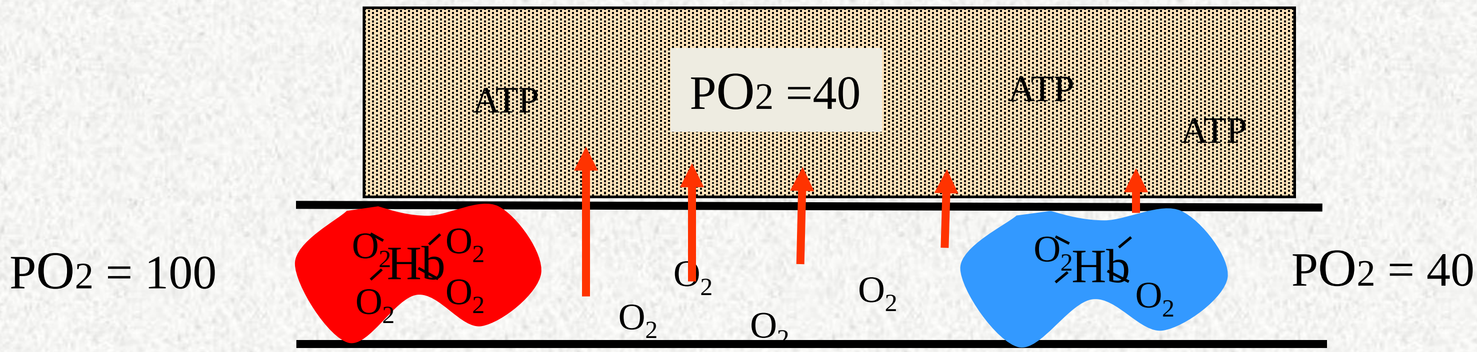
Blood and Muscle PO_2



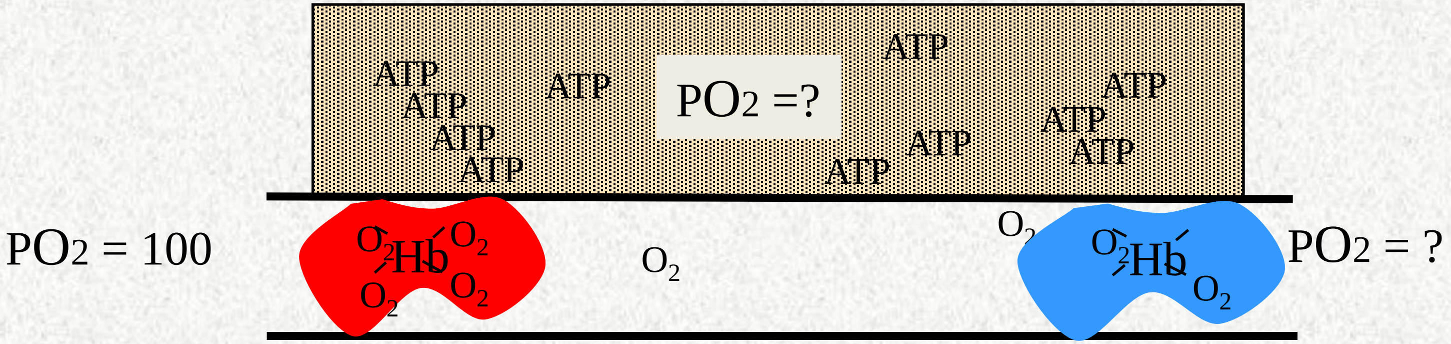
Increased Flow and normal metabolism



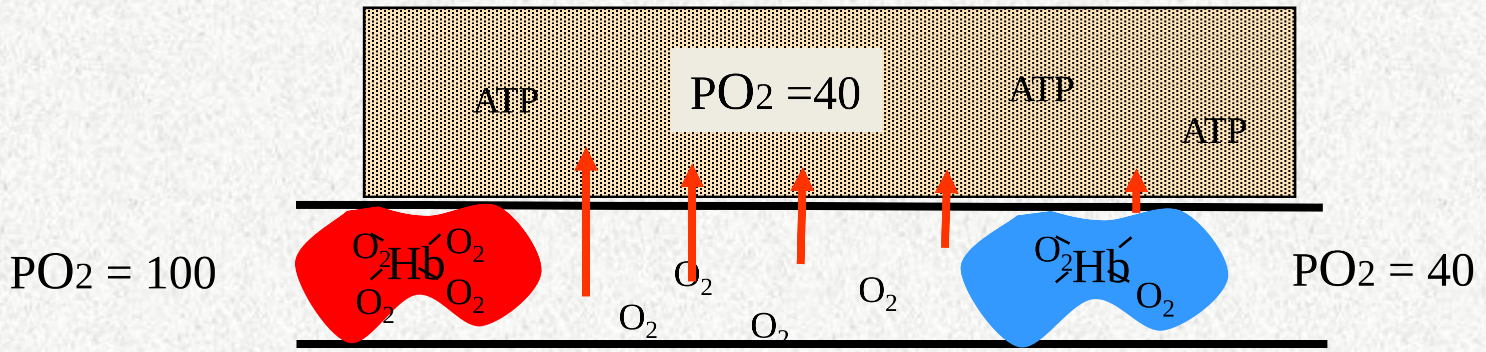
Blood and Muscle PO_2



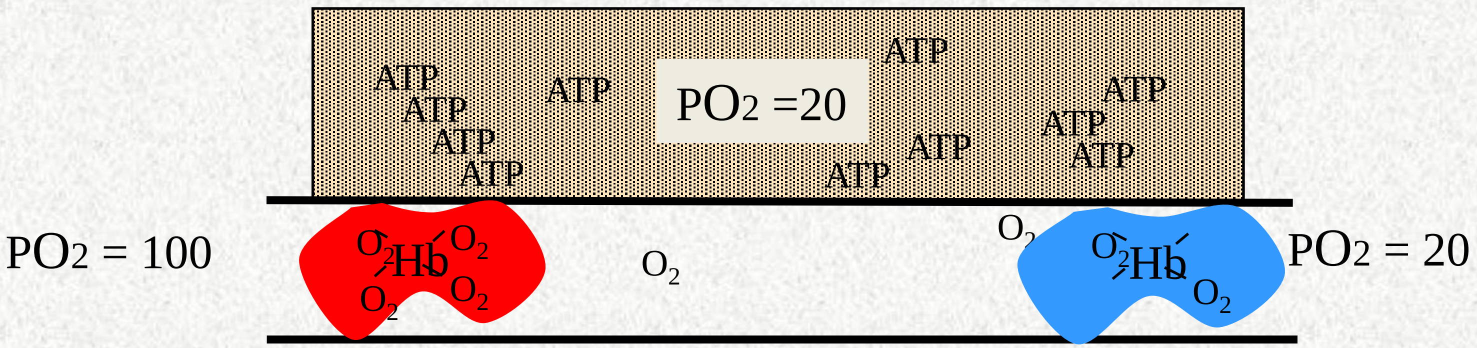
Increased Metabolism and normal blood flow



Blood and Muscle PO_2

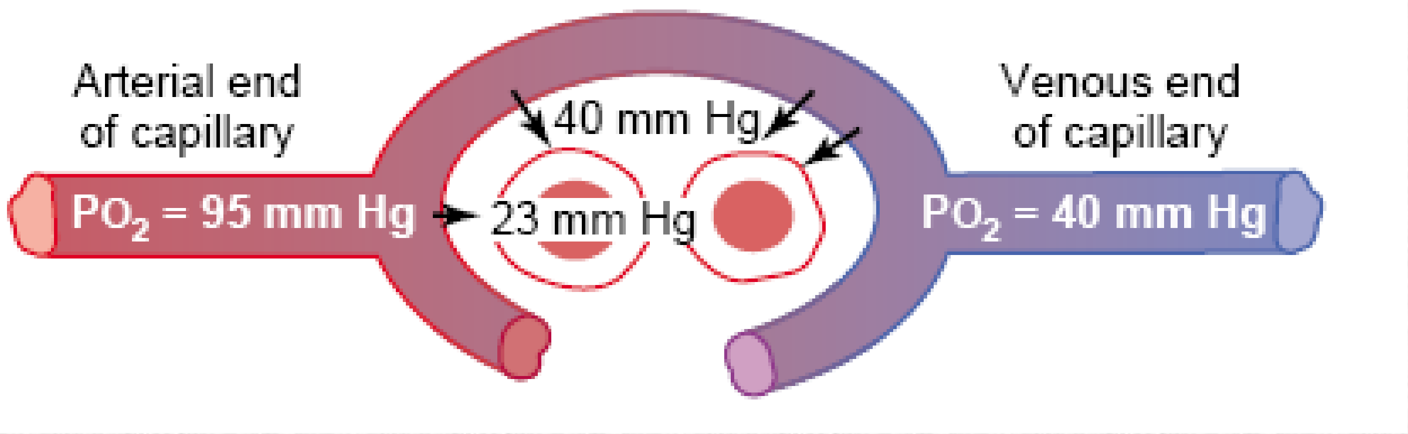


Increased Metabolism and normal blood flow



PO_2 in systemic circulation (Diffusion from peripheral capillaries)

- Oxygen is always being used by the cells. Therefore, the intracellular PO_2 in the peripheral tissue cells remains lower than the PO_2 in the peripheral capillaries.



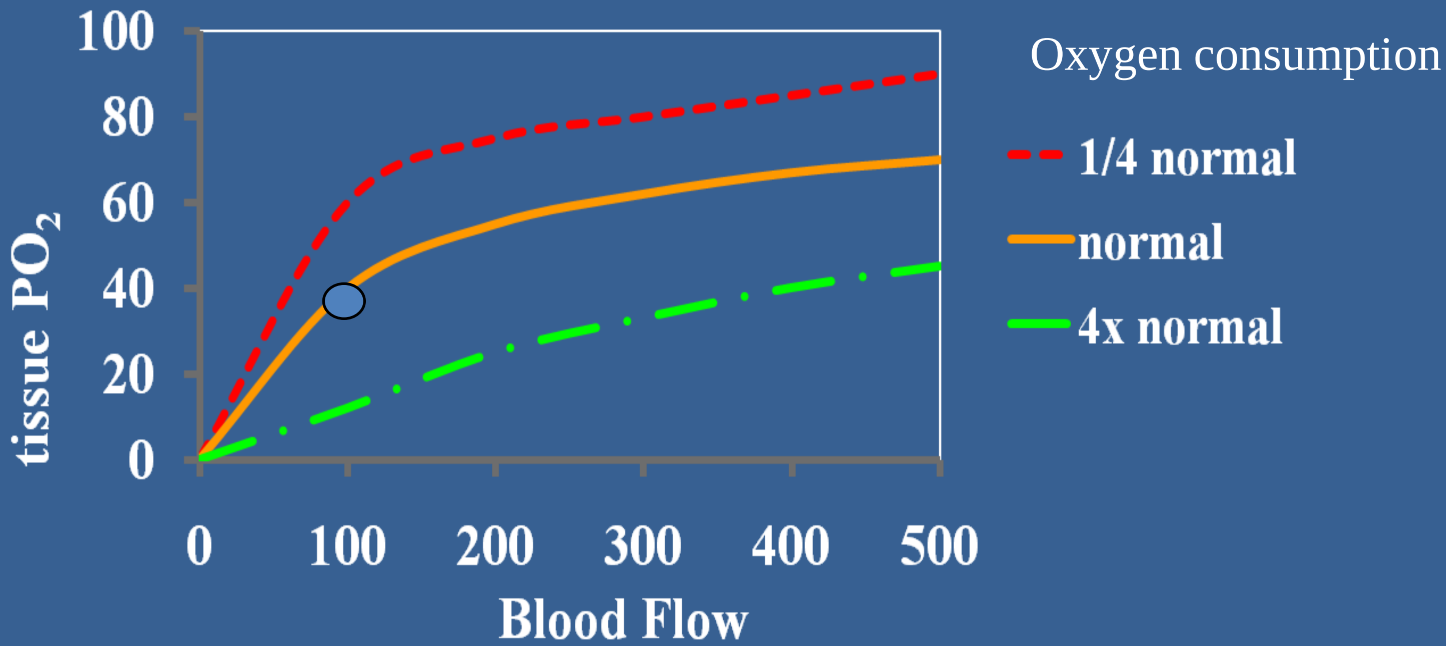
Increased Blood Flow to Tissue

- Normal blood flow
  - 200 ml O_2/lit of arterial blood * 5 lit blood/min= 1000 ml/min
  - VO_2/min…250 ml are consumed at rest (25%)
- **Utilization Coefficient or (Extraction ratio):**
- Is the % of blood that gives up its O_2 as it passes through tissue capillaries. Normally is 25%. In exercise 75% - 85%. In some local tissues with extremely high metabolic rate → 100%.

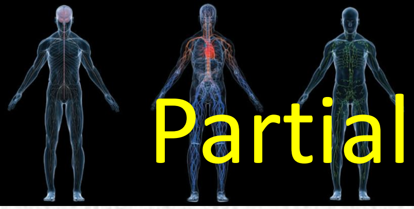
O_2 Uptake during Exercise

- VO_2 increases during exercise until it reaches VO_2max…what limits VO_2max…lung? CVS? number of mitochondria?
- Increased cardiac output and thus muscle blood flow and extraction ratio…all make more O_2 available to the exercising tissues
- Decreased transit time…Normal lung can still oxygenate blood beside this issue
- Increased diffusing capacity
  - Opening up of additional capillaries
  - Better ventilation/perfusion match
- Equilibration even with shorter time

Diffusion of Oxygen at the Tissue

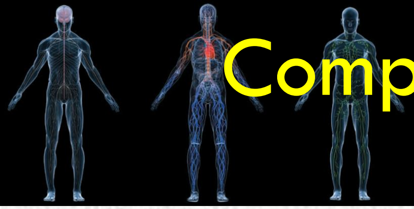


- Arterial blood has PO_2 of 95-100 mmHg
- Tissue has a PO_2 of 30-40 mmHg
- Tissue PO_2 is determined by balance of O2 delivery and O2 usage.



Partial Pressures of Gases in Inhaled Air

PN_2	=0.786	x 760mm Hg	= 597.4 mmHg
P_{O2}	=0.209	x 760mm Hg	= 158.8 mmHg
P_{H2O}	=0.004	x 760mm Hg	= 3.0 mmHg
P_{CO2}	=0.0004	x 760mm Hg	= 0.3 mmHg
$P_{other\ gases}$	=0.0006	x 760mm Hg	= 0.5 mmHg
		TOTAL	= 760.0 mmHg

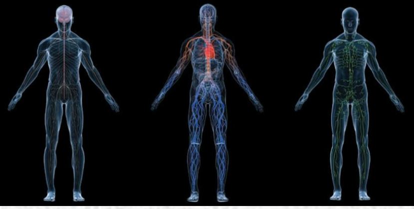


Composition of Alveolar Air—Its Relation to Atmospheric Air

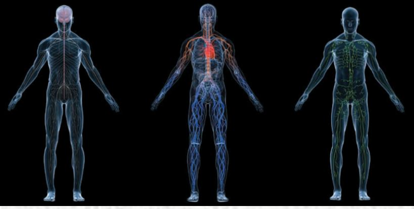
	Inhaled Atmospheric Air		Humidified Air	Alveolar Air	Expired Air
	mm Hg	%	mm Hg	mm Hg	mm Hg
PN_2	597	78.6	563	569	566
PO_2	**159**	**20.8**	**149**	**104**	**120**
PCO_2	0.3	0.04	0.3	**40**	27
PH_2O	**3.7**	**0.5**	**47**	**47**	**47**
Total	760	100	760	760	760

GAS CONTENT OF BLOOD.

- **One DL of Blood Contains 15 g of Hemoglobin**
- **One DL of arterial Blood Contains 20 ml of O_2**
- **Arterial Blood**
  (PO_2 95 mm Hg;
  PCO_2 40 mm Hg;
  Hb 97% Saturated)
- **Venous Blood**
  (PO_2 40 mm Hg;
  PCO_2 45 mm Hg;
  Hb 75% Saturated)



- Hemoglobin
  - One gm of Hb can bind reversibly 1.34 ml of O_2
  - Normally in male adult we have
    - 15 gm Hb/100 ml blood that can bind:
    - 20 ml O_2 /100 ml blood (1.34 * 15)
  - Anemic
    - 10 gm Hb/100 ml blood binds only 13 ml O_2 /100 ml blood

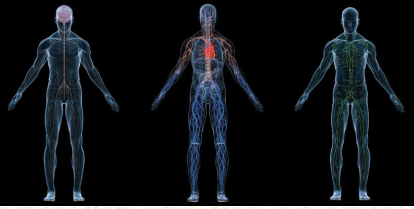


Oxygen Transport

- Partial Pressure (mm Hg)
  - driving force for diffusion
- Percent Saturation (no units)

  $\underline{HbO_2}$

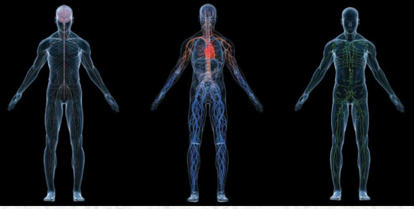
  $(Hb+O_2)$ is called oxyHb
- Content (ml O_2/100 ml blood)
  - The absolute quantity of oxygen in the blood is the most important among others



Transport of Oxygen in Blood

- Henry's law
- Dissolved oxygen=PaO_2 X Solubility of O_2 Solubility 0.003 ml O_2/100 ml blood
- - In normal blood; the [O_2] in its dissolved form is equal to= 0.3 ml O_2/100 ml blood
  - Normal oxygen consumption 250 ml O_2/min
  - Would require 83 l/min blood flow
- Hemoglobin
  - 97% of the transported O2 is in this form

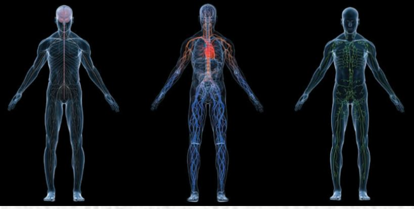
$$O_2 + Hb \rightleftharpoons HbO_2$$



Law of dissolved gases

Oxygen	0.024
Carbon dioxide	0.57
Carbon monoxide	0.018
Nitrogen	0.012
Helium	0.008

- Much more CO_2 is dissolved in blood than O_2 because CO_2 is 20 times more soluble.
- The air we breathe is mostly N_2, very little dissolves in blood due to its low solubility.



Partial pressure of gas in liquid = [gas] ÷ solubility coef "S" (this is Henry's law)

Solubility coef. O_2 0.024 L/L blood.atm

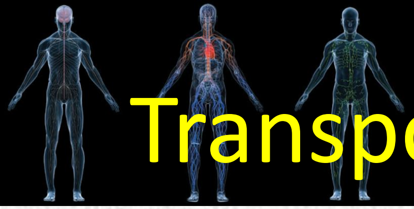
CO_2 0.57 (20 times more than O_2)

CO 0.018

N_2 0.12

Consider diffusion coef. For O_2 equals 1.

	D	**S**	
O_2	1	0.003 ml%/1 mm Hg	0.024 L O_2/L blood. atm
CO_2	20.3	→ 0.06 ml%	0.57 L CO_2/L blood. atm
CO	0.81	0.018	
N_2	0.53	0.012	

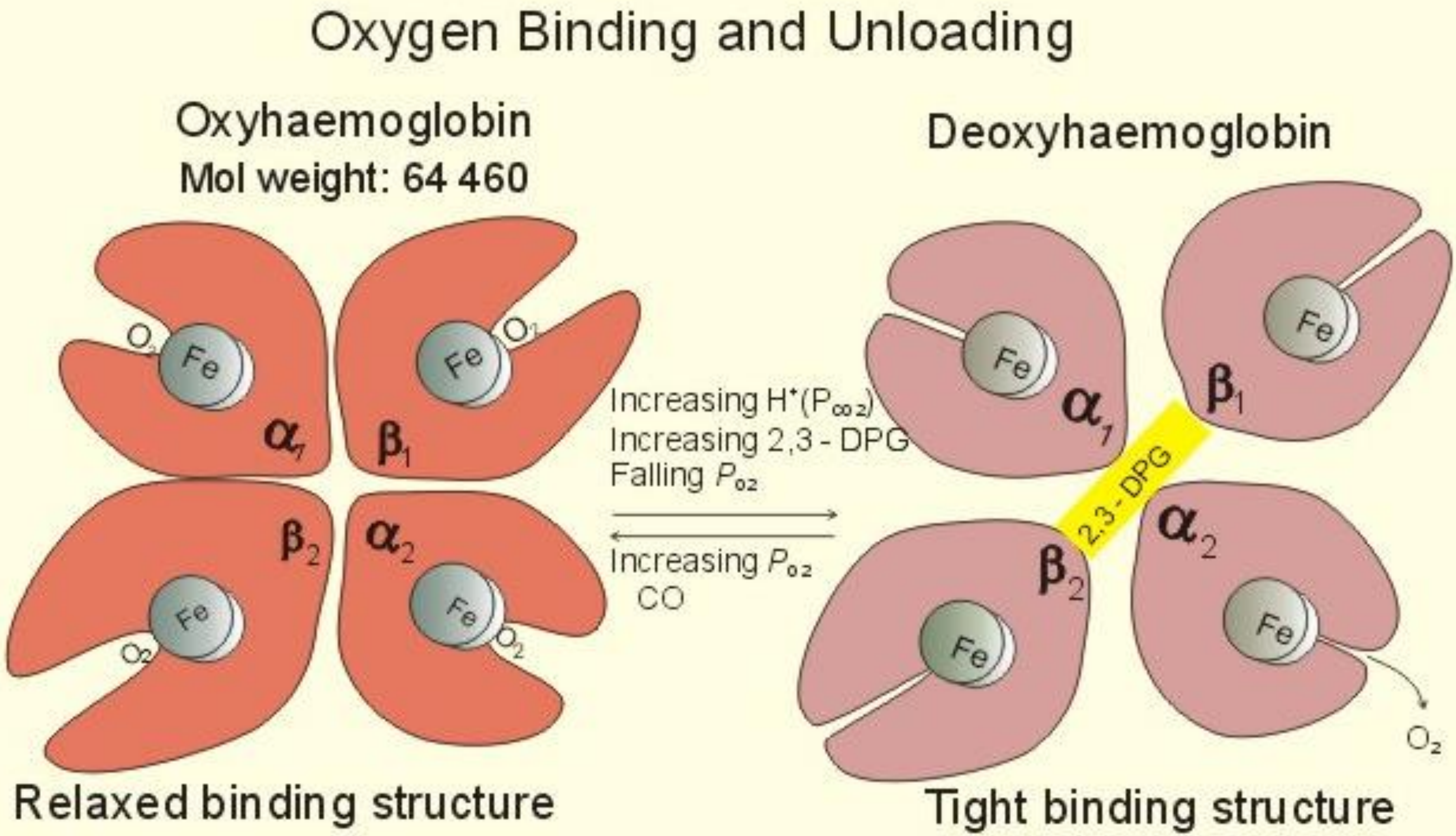


Transport of Oxygen and Carbon Dioxide

- Oxygen transport
  - Only about 1.5% is in the dissolved form (in plasma)
  - 98.5% bound to hemoglobin in red blood cells
    - Heme portion of hemoglobin contains 4 iron atoms – each can bind one O_2 molecule
    - Only dissolved portion can diffuse out of blood into cells
    - Oxygen must be able to love (bind, associate, load, increase affinity) and hate dissociate (hate, unload
    - decrease affinity).

Why Hb is inside the RBCs and not circulating freely in the plasma

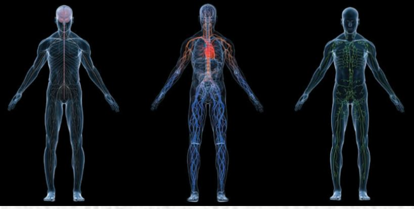
- 2,3 BPG is inside RBC. If no DPG the HbO_2 curve is no more sigmoidal, it becomes like that for myoglobin…a mutase in RBC convert 1,3 BPG to 2,3 BPG
- . NADH-met-Hb reductase inside RBC converts methHb (ferric) to reduced Hb (ferrous).
- Protection against degradation enzymes in plasma.
- Protection against filtration through the kidneys.
- Presence of C.A. which converts CO_2 to HCO3, otherwise by using Acetazolamide (CA inhibitor) PCO_2 reaches 80 mmHg
- Prevent ↑ in blood viscosity.



- **The total amount of Oxygen carried by Hb in blood depends upon:**
  - **The percentage saturation of Hb.**
  - **The amount of Hb in the blood.**

Hemoglobin

- Oxyhemoglobin:
  - Normal heme contains iron in the reduced form (Fe^{2+}).
  - Fe^{2+} shares electrons and bonds with oxygen.
- Deoxyhemoglobin:
  - When oxyhemoglobin dissociates to release oxygen, the heme iron is still in the reduced form.
  - Hemoglobin does not lose an electron when it combines with 0_2.



- Since solubility of O_2 in blood is low then the amount transported, as dissolved O_2 is also low. Our body provides a mechanism for transporting O_2. the O_2 binding protein (Hb).
-
- Adult (A) HbA $\alpha_2\beta_2$ α = 141 β 146 M.W 64.460
- Fetal (P) HbF $\alpha_2\gamma_2$ 2% of normal blood. γ chain doesn't bind 2,3,DPG….the curve is shifted to the left.
- Sickle (S) Hb^S $\alpha_2\beta_2{}^S$
- $Hb(A_2)$ $\alpha_2\delta_2$ 2% of adult Hb.

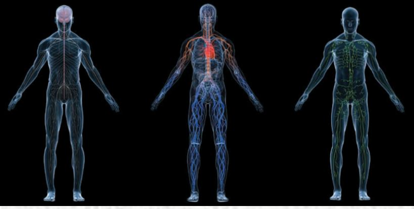
Hemoglobin (continued)

- Methemoglobin:
  - Has iron in the oxidized form (Fe^{+++}).
    - Blood normally contains a small amount. but ferric Fe^{+3} which is useless because it does not release O_2. NADH-meth-Hb reductase can convert ferric to ferrous form
- Carboxyhemoglobin:
  - The reduced heme is combined with carbon monoxide.
  - The bond with carbon monoxide is **250** times stronger than the bond with oxygen.
    - Therefore, transport of O_2 to tissues is impaired.

Hb is in its ferrous state F^{+2}, this can bind O_2 reversibly, but ferric Fe^{+3} is useless because it does not release O_2. NADH-meth-Hb reductase can convert ferric to ferrous form.

Hb: has 4 chains, each having heme group (iron – containing porphyrin rings)., which can bind one molecule of O_2.

Hb	or deoxygenated Hb or reduced Hb or ferrohemoglobin
HbO_2	oxy-Hb
Hb (ferric)	Oxidized or methHb . or ferrihemoglobin (1% of the total Hb).
HbCO	carboxy Hb.
$HbCO_2$	carbamino Hb.



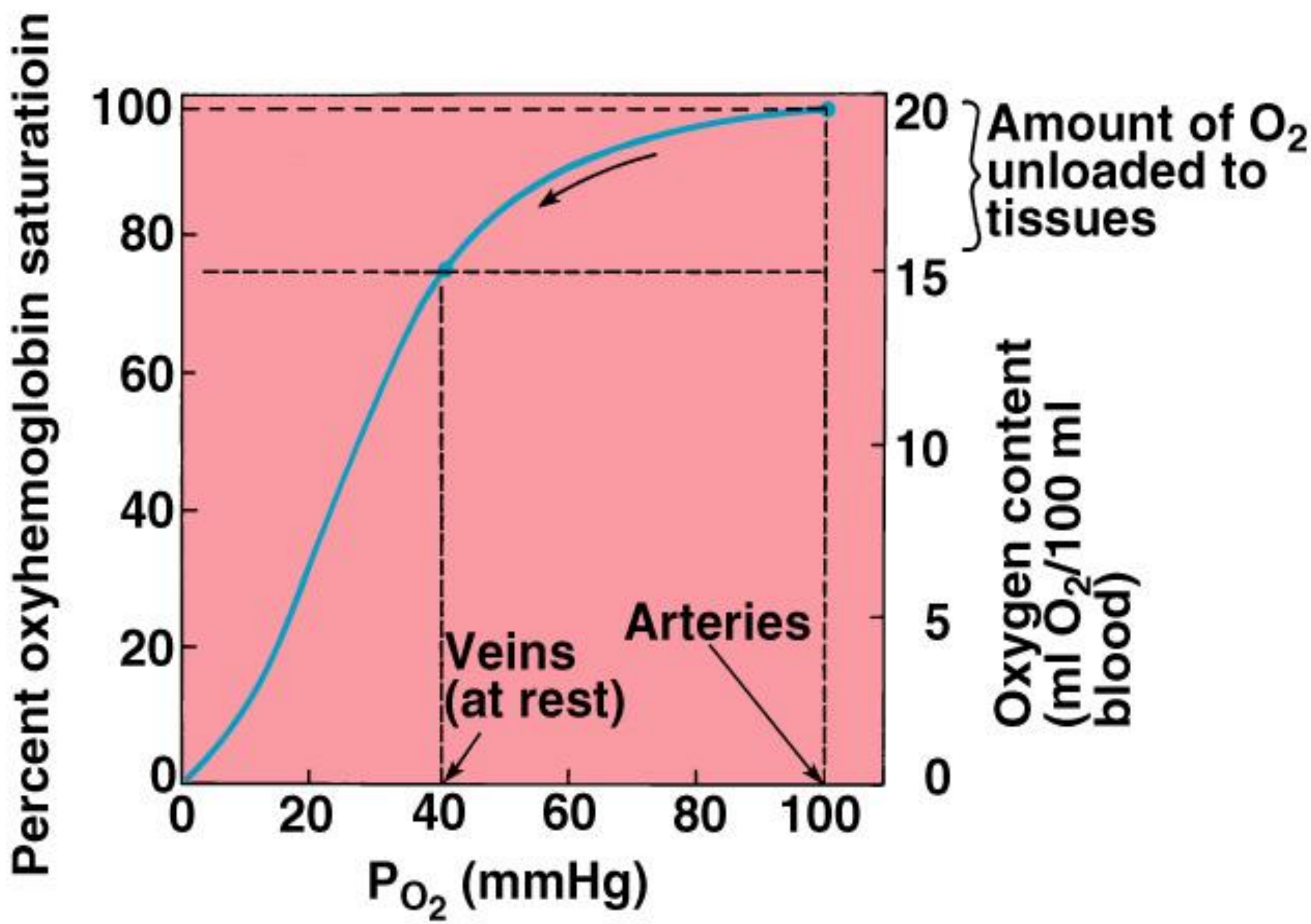
Hemoglobin (continued)

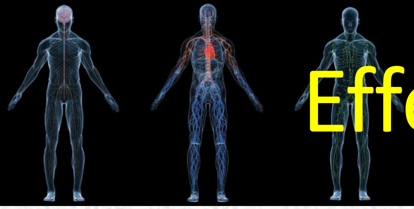
- Oxygen-carrying capacity of blood determined by its hemoglobin concentration.
  - Anemia:
    - [Hemoglobin] below normal.
  - Polycythemia:
    - [Hemoglobin] above normal.
  - Hemoglobin production controlled by erythropoietin.
    - Production is stimulated by the decrease in renal PO_2
- Loading/unloading depends:
  - PO_2 of environment.
  - Affinity between hemoglobin and O_2.

Oxyhemoglobin Dissociation Curve

- Graphic illustration of the % oxyhemoglobin saturation at different values of PO_2.
  - Loading and unloading of O_2.
    - Steep portion of the sigmoidal curve, small changes in PO_2 produce large differences in % saturation (unload more O_2).
- Decreased pH, increased temperature, increased 2,3 DPG, and increase PCO_2 all will decrease affinity of hemoglobin for $O_2 \rightarrow$ greater unloading of $O_2 \rightarrow$ Shift of the Hb-O_2 dissociation curve to the right. Hb hates O_2 or the so called decrease affinity.

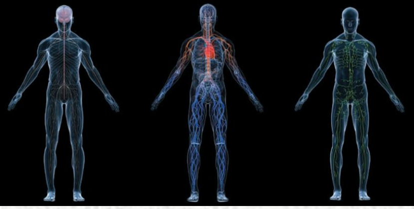
Oxyhemoglobin Dissociation Curve





Effect of 2,3 DPG on O_2 Transport

- Anemia:
  - When RBCs or blood [hemoglobin] falls, each RBC produces greater amount of 2,3 DPG.
    - Since RBC lacks both nucleus and mitochondria, it produces ATP through anaerobic metabolismm, which makes enough 2,3,DPG available
    - Glucose $\rightarrow$ G-6-P $\rightarrow$ 1,3 DPG (2,3 DPG) $\rightarrow\rightarrow$ G-3-P $\rightarrow\rightarrow$
- Fetal hemoglobin (HbF):
  - Has 2 γ-chains in place of the β-chains… γ-chain does not bind 2,3,DPG…therefore, HbF has higher affinity towards O_2…make sense…mother's placenta PO2 is low (<40 mmHg)

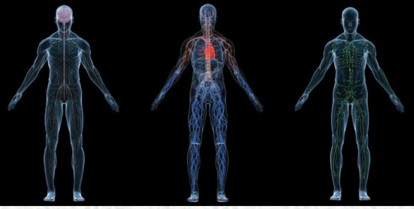


RBCs have no mitochondria and thus respire anaerobically (glycolysis) $\rightarrow$ produce 2,3BPG. For each Hb molecule there is one molecule 2,3 BPG in RBCs. 2,3 BPG binds deoxyHb much better than binding oxy-Hb. If CO_2 increases for several hours (chronic acidosis) this will shift oxy-Hb curve to the right, but BPG concentration would decrease and thus shifting the curve back to the left (back to normal). The disadvantage is the unloading of Hb becomes less.

Probably BPG act on Hb at the same site where CO_2 binds, so when PCO_2 $\downarrow$ (high altitude) DPG might $\uparrow$ to bring the curve back to normal.

HbF has lower affinity for O_2, but since it does not bind BPG so it has high affinity for O_2. PaO_2 in fetus is only 30-40, therefore shift HbF to the left is important.

$$\mathbf{HbO_2 + BPG \leftrightarrow Hb\text{-}BPG + O_2}$$

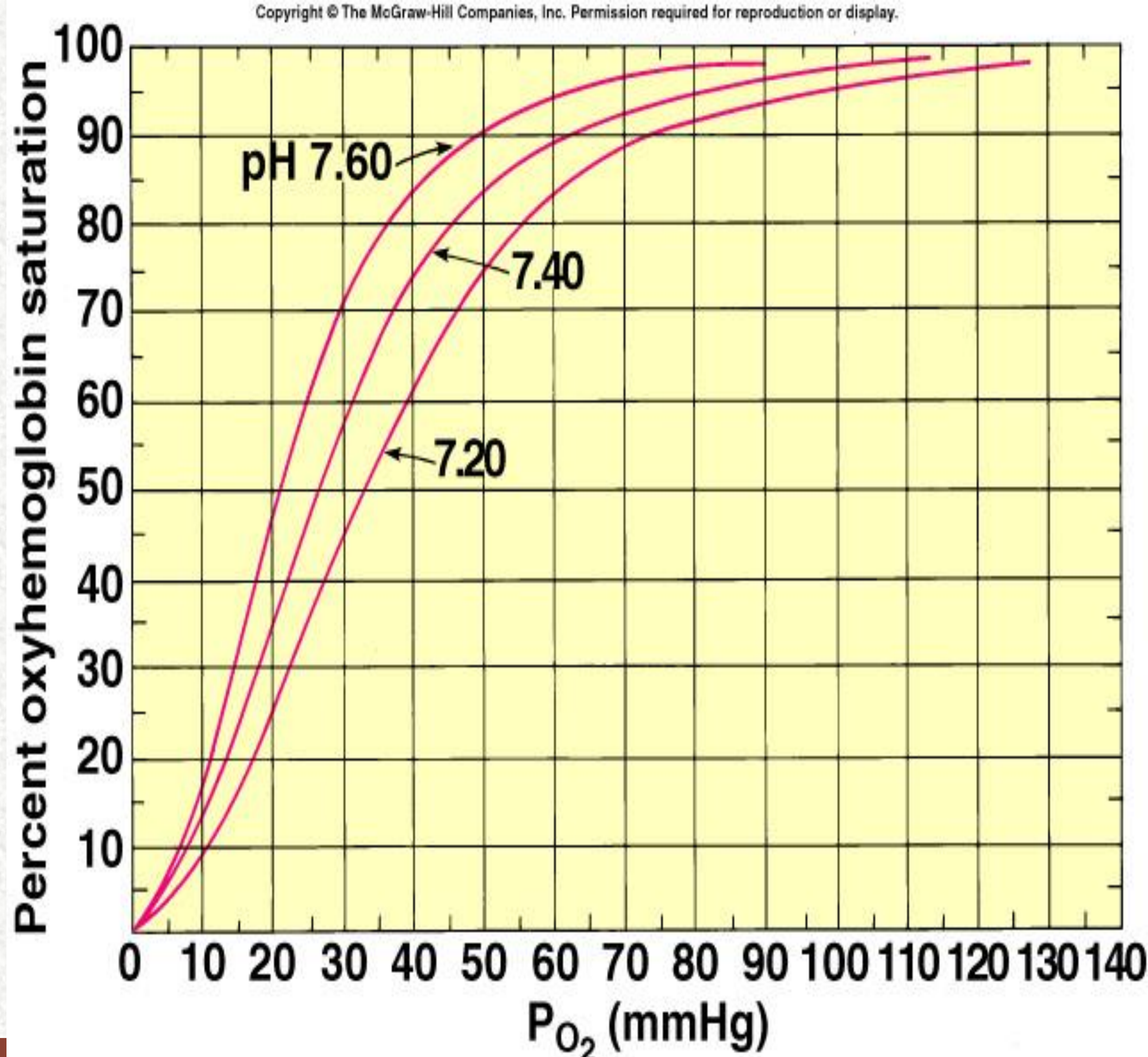


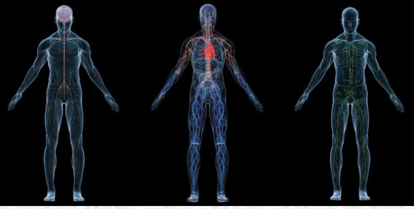
Effects of pH and Temperature

- The loading and unloading of O_2 influenced by the affinity of hemoglobin for O_2.

Affinity is decreased by:

- ↓blood pH
- ↑temperature
- ↑ 2,3-DPG
- ↑ PCO2
  - All Shift the curve to the right.





1. Allosteric interactions (cooperative interaction):

The 4 heme groups talk to each other, the first O_2 binds break some salt bridges which needs high energy input, the last O_2 needs very little energy since most salt bounds have been broken.

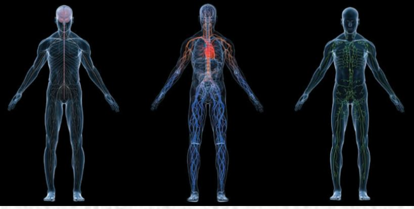
Molecular interactions among the 4 heme groups → S - shaped HbO_2

A. O_2 binding is affected by other binding in 2^{nd} heme.

B. O_2 binding is affected by H^+ binding distinct sites.

C. O_2 binding is affected by CO_2 binding distinct sites.

D. O_2 binding is affected by 2,3 DPG binding distinct sites.



Values to remember

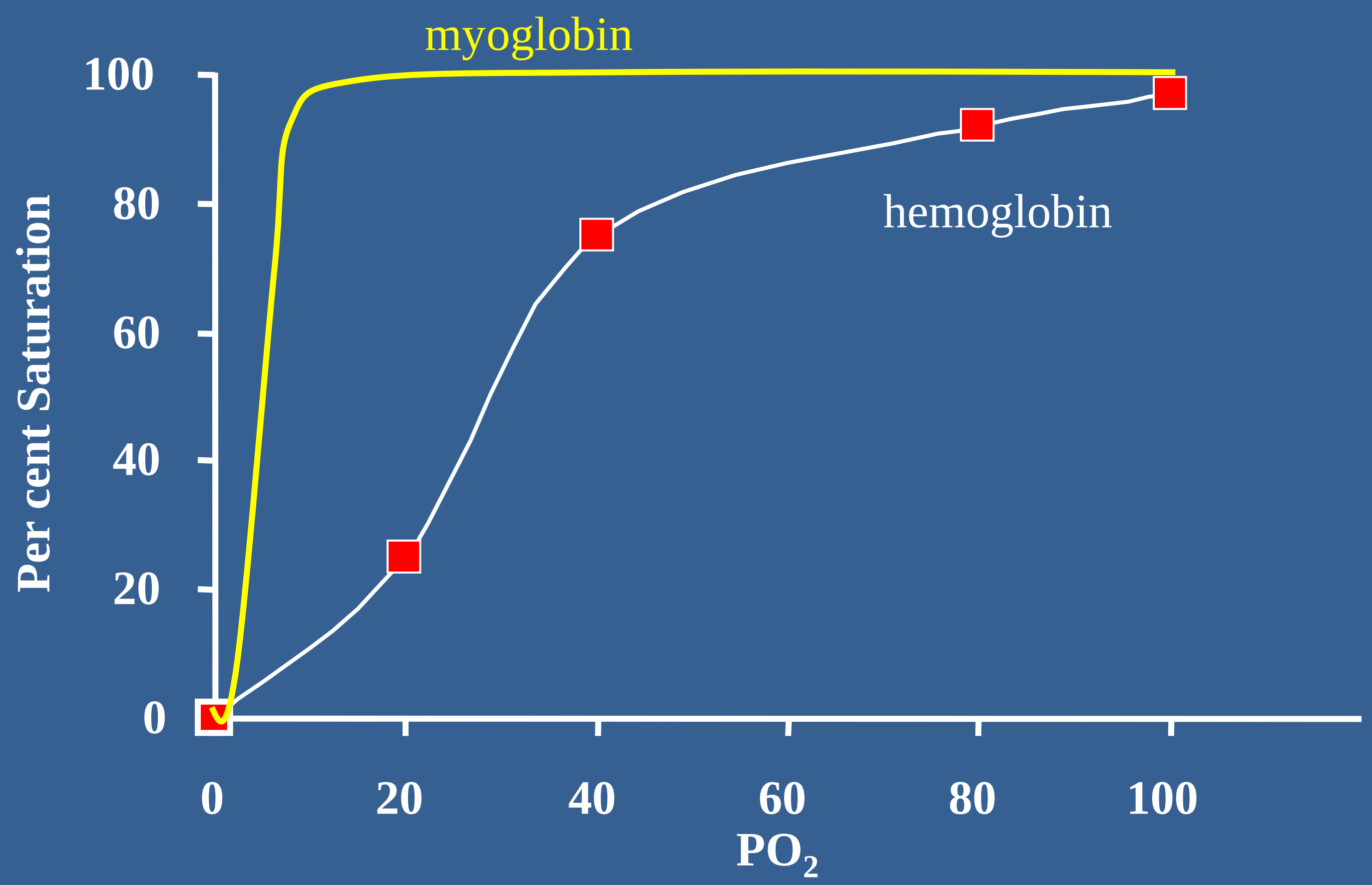
PO_2	O_2 Sat (%)	
10	25	
20	35	
25	**50**	**P_{50}**
30	60	
40	**75**	**Venous**
50	85	
60	**90**	**Respiratory center stimulation**
80	96	
100	**98**	**Almost Fully saturated**

Remember this rule…it is close enough!

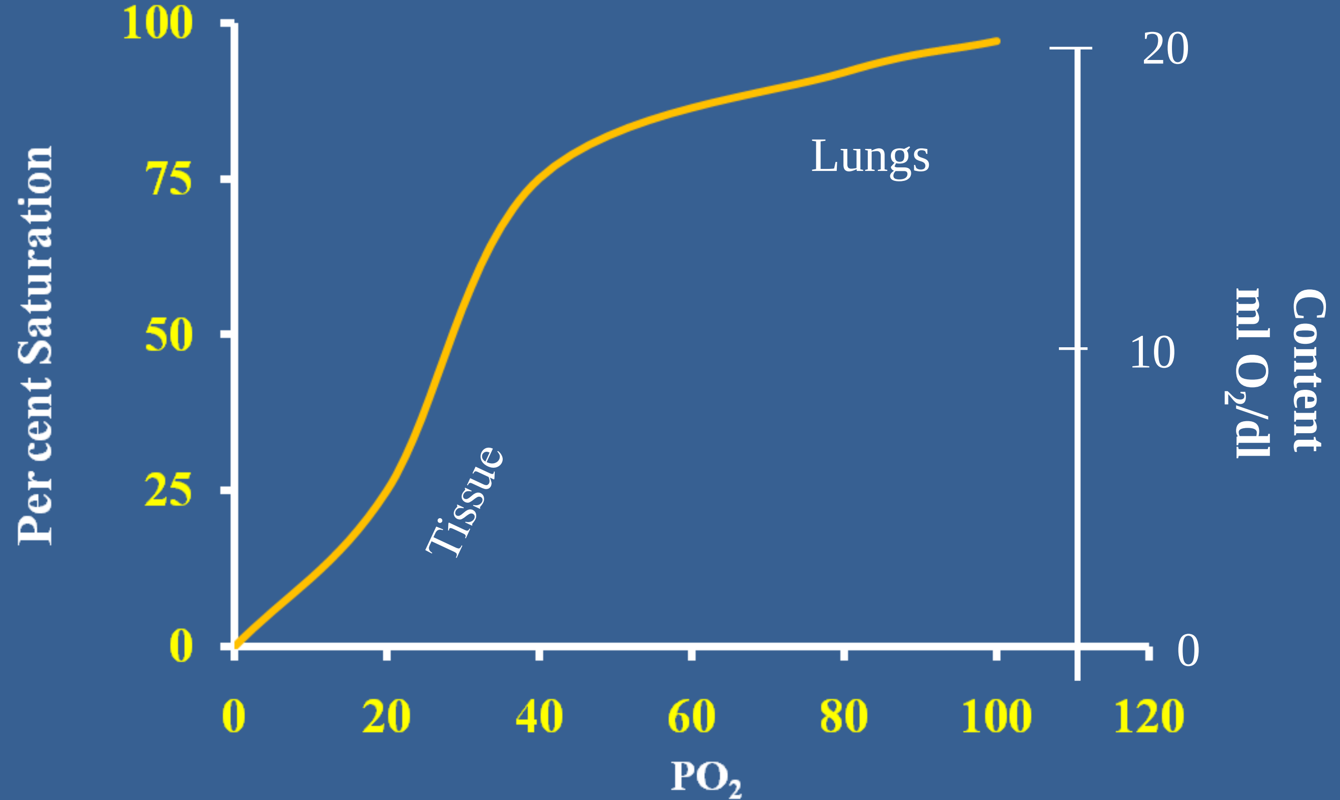
4,5, 6 7-8-9

Po_2 (mmHg)	40	50	60
%Sat	70	80	90

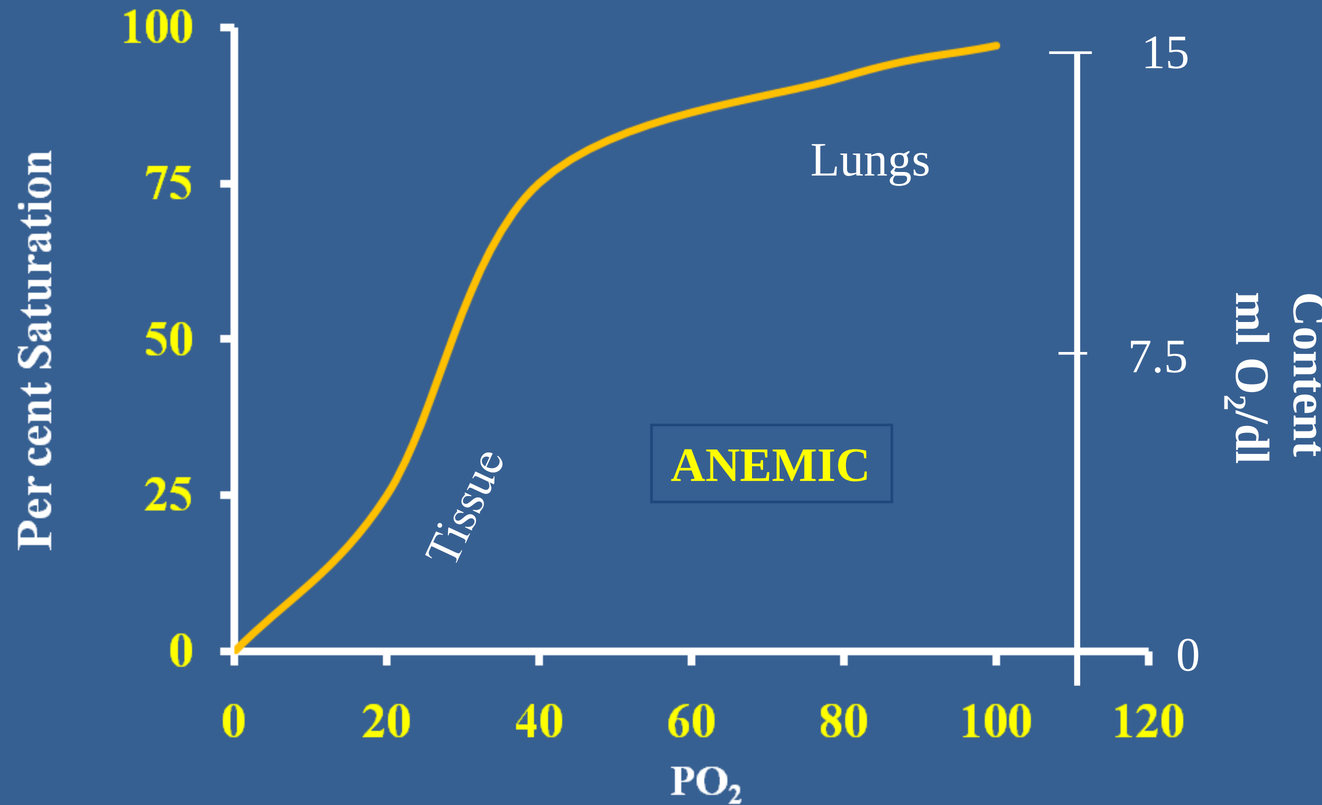
Dissociation Curve



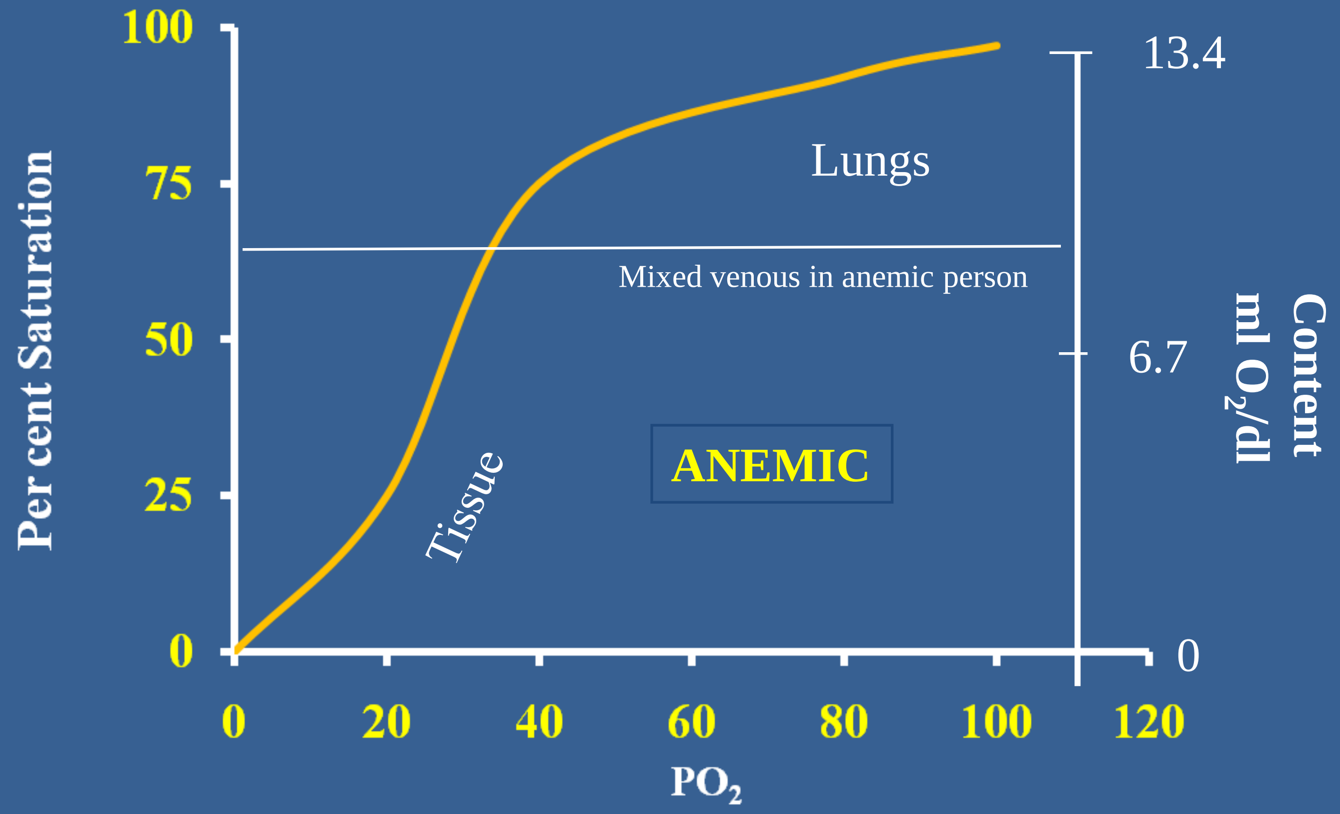
Hemoglobin Dissociation Curve



Hemoglobin Dissociation Curve



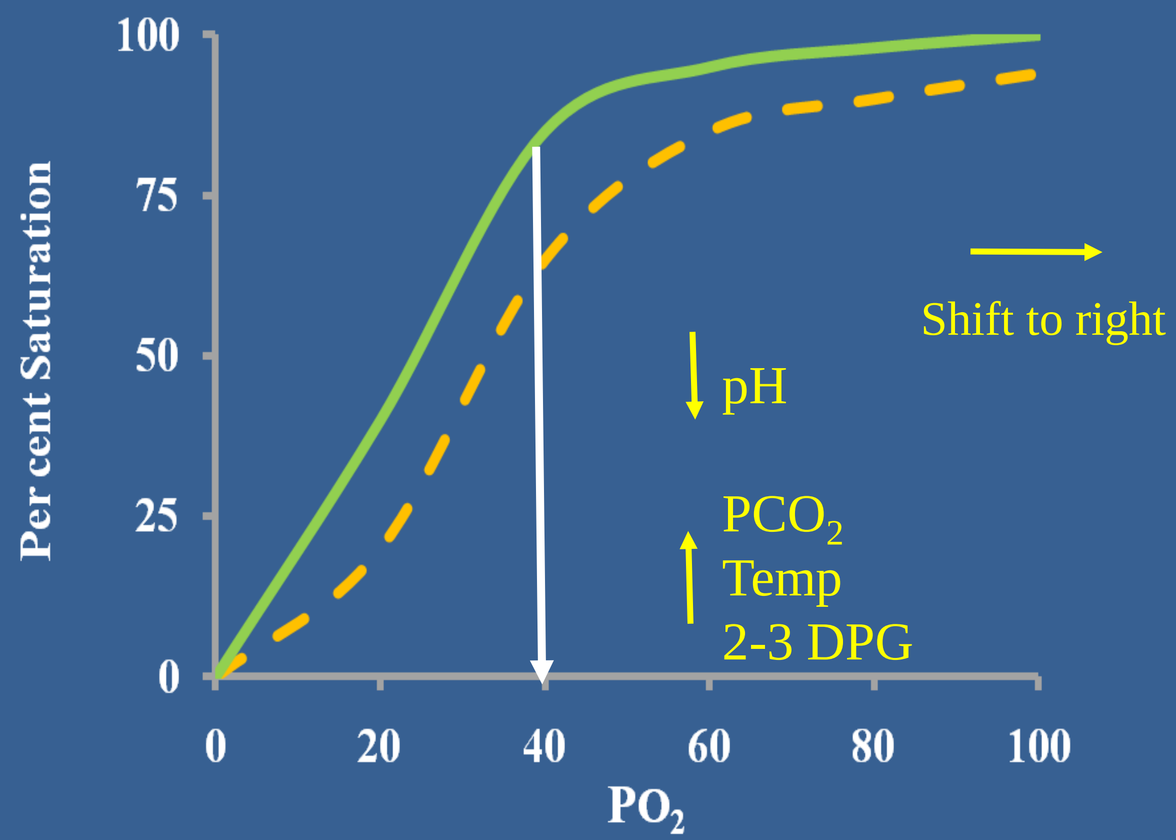
Hemoglobin Dissociation Curve



Shifts of Dissociation Curve

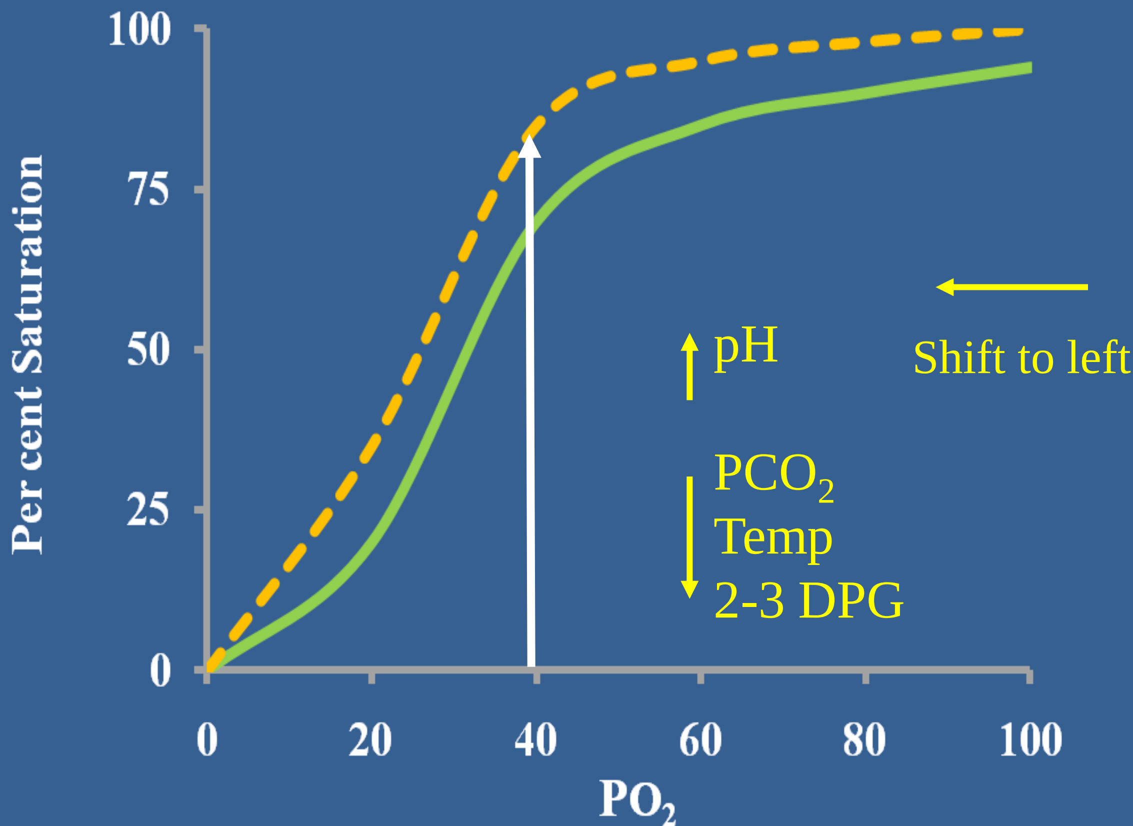
- Right shift occurs at tissue level…Bohr's effect
  - ↑$PaCO_2$ or ↑ arterial H^+→ ↓ affinity for oxygen or increase O_2 release…this occur at the tissue level
- Left shift at lungs…Haldane's effect is the reverse Bohr's effect
  - loss of carbon dioxide at lungs → ↑affinity of Hb towards oxygen

Right Shift of Dissociation Curve



- Venous Hb-O_2 curve is slightly shifted to the right (↓ pH, ↑ PCO_2).

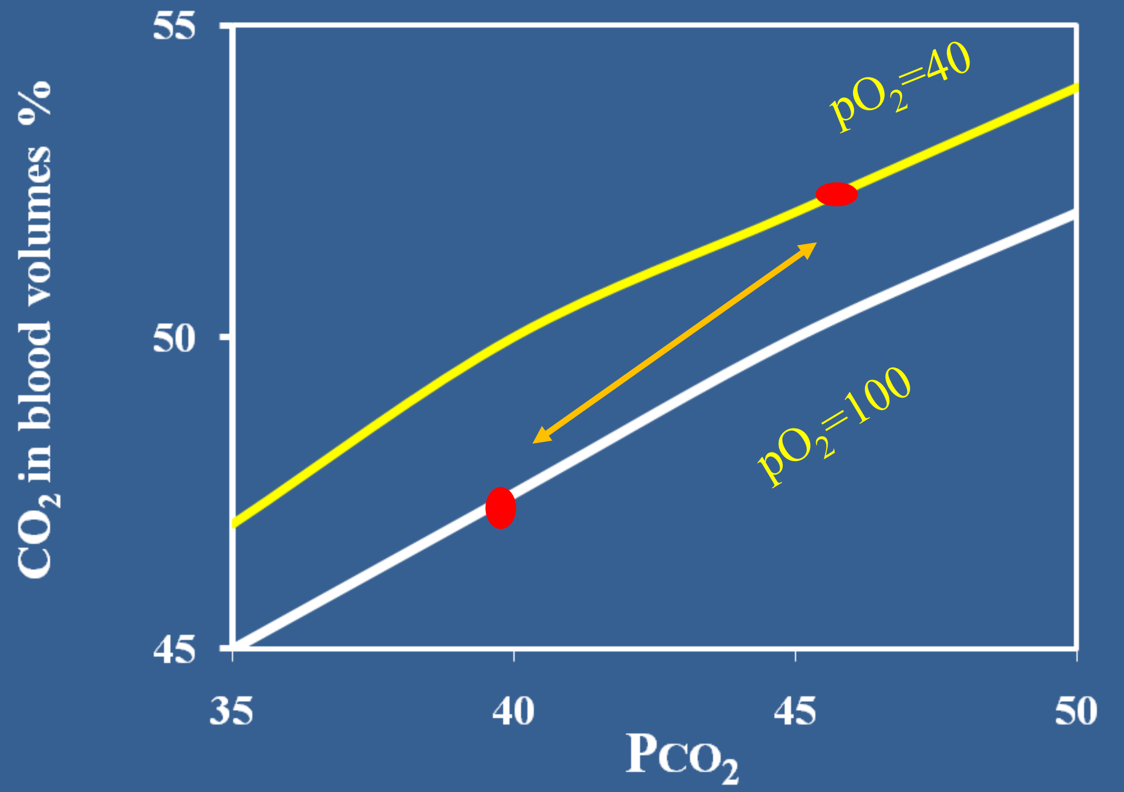
Left Shift of Dissociation Curve
Bohr's effect



Haldane Effect

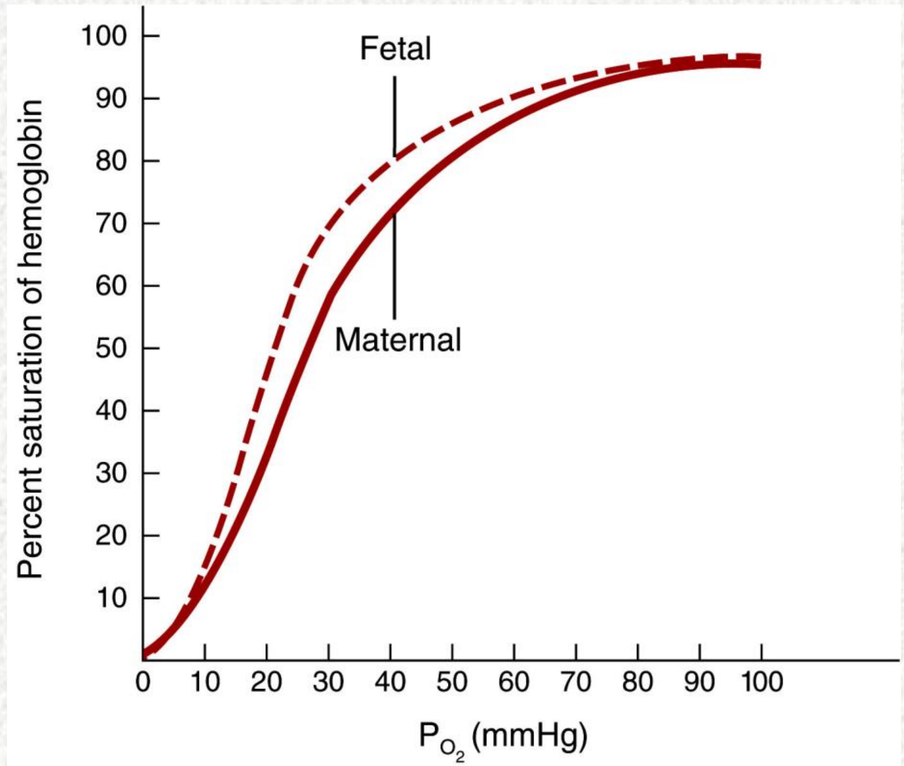
Venous 52 vol%

Arterial 48 vol%



Fetal and Maternal Hemoglobin

- Fetal hemoglobin has a higher affinity for oxygen than adult hemoglobin
- Hb-F can carry up to 30% more oxygen
- Maternal blood's oxygen readily transferred to fetal blood



Hemoglobin Dissociation Curve

- Alveoli
  - Over wide range hemoglobin will be highly saturated
  - example: PO_2 of 60 mmHg correspond to 90% saturation
- Tissue
  - Normal: consume 5 ml O_2/100 ml blood (P_iO_2 is 40 mmHg)
  - During exercise: 15 ml of O_2 /100 ml blood (P_iO_2 is only 20 mmHg)

Question

A person has a hemoglobin concentration of 10 gm/dl. The arterial oxygen content is 6.5 ml O_2/dl. What is the saturation?

A. 25%

B. 50%

C. 75%

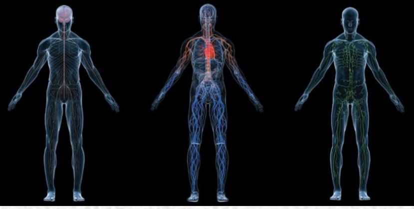
D 100%

Calculations

- Calculate % saturation
  - Patient has Hb of 10 gm/dl
  - Venous oxygen content is 6.5 ml O_2/dl
- Calculate oxygen content
  - Patient has saturation of 60%
  - Patient has Hb of 15 gm/dl

Calculations

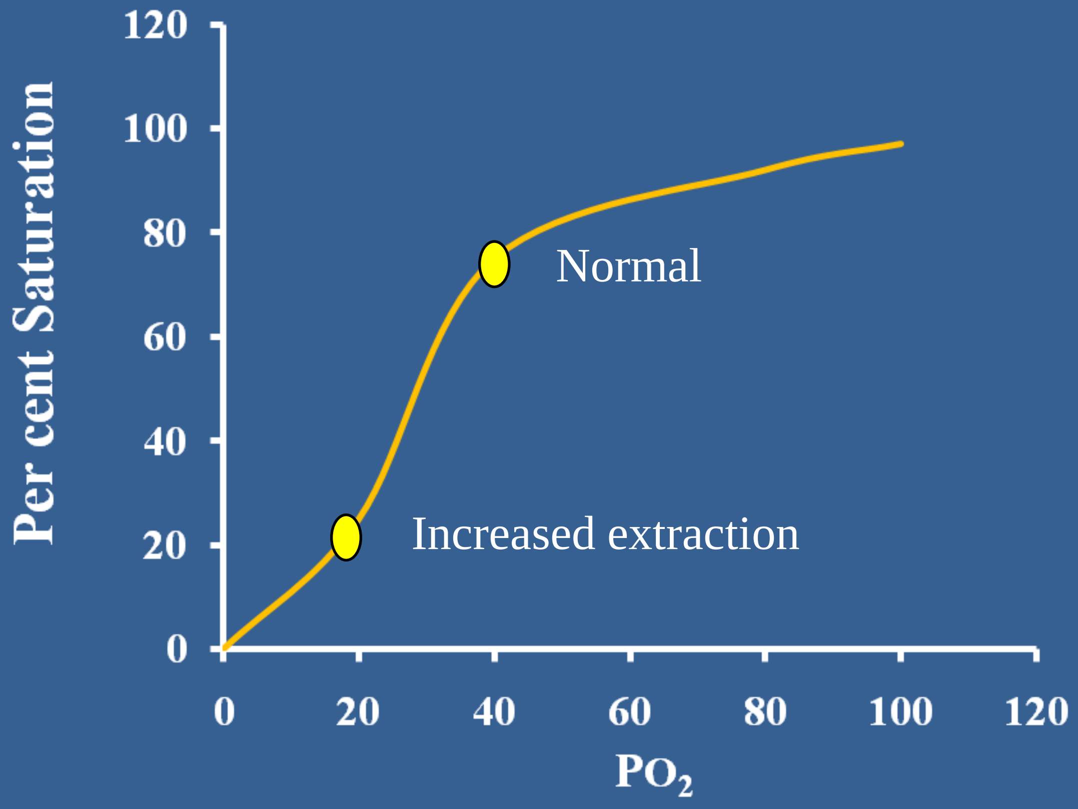
- Calculate % saturation
  - 10 gm/dl * 1.34 ml O_2/gm Hb= 13.4 ml O_2/dl
    - This is max oxygen carrying capacity
  - (6.5 ml O_2/dl) / (13.4 ml O_2/dl) = ~50%
- Calculate oxygen content
  - 15 gm/dl * 1.34 ml O_2/dl = 20 ml O_2/dl
    - This is max oxygen carrying capacity
  - 20 ml O_2/dl * 60% saturation = 12 ml O_2/dl



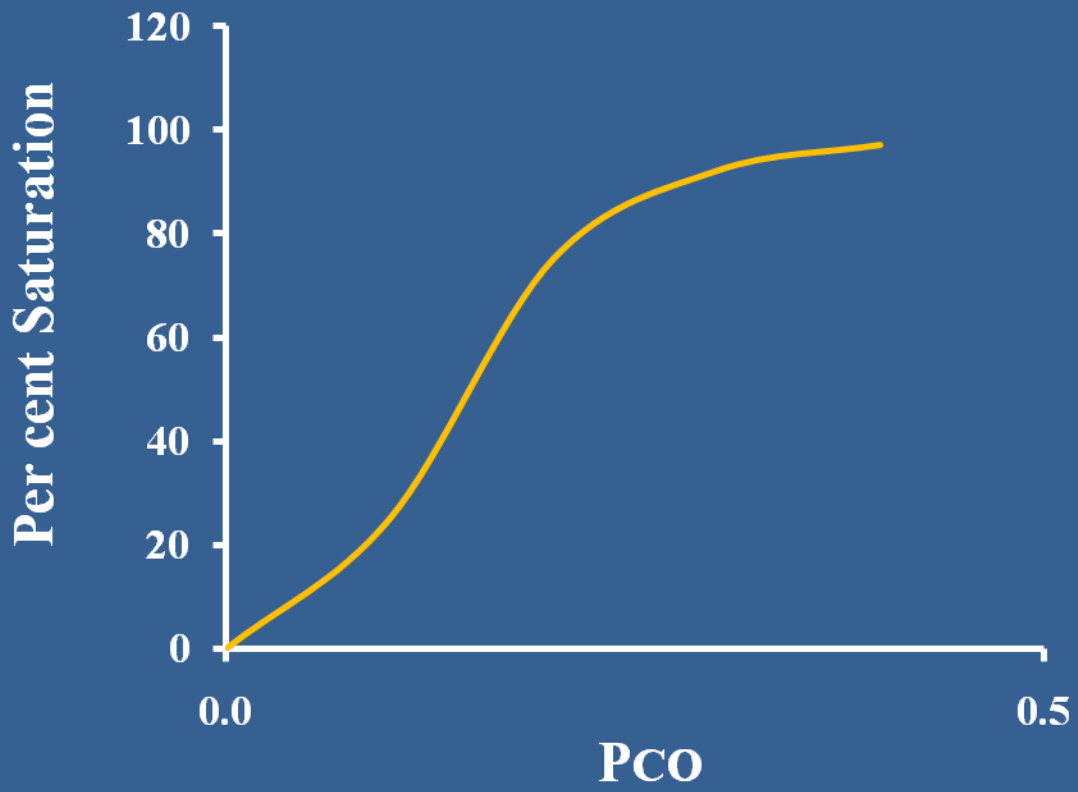
Calculations

- Assume Hb is 10 gm/dl
- 100% saturation give a content of 13.4 ml/dl blood
- At rest body uses 5 ml O_2/dl
- This leaves a mixed venous content of 8.4 ml/dl
- Saturation is now 8.4/13.4 = 63%

Increased Oxygen Extraction



Carbon Monoxide Dissociation Curve



Question

Which of the following is least important for the transport of carbon dioxide?

a. hydrogen ions bound to hemoglobin

b. carbonic anhydrase

c. CO_2 dissolved in plasma

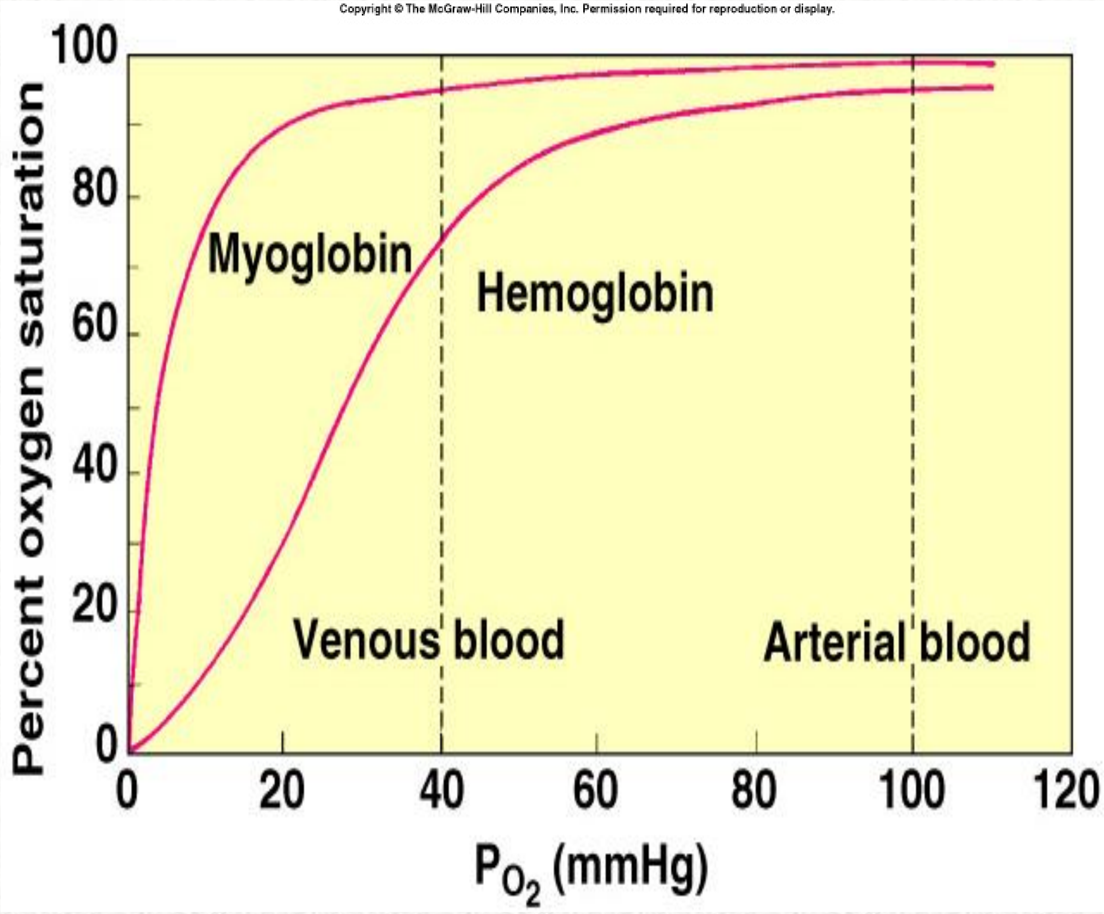
d. CO_2 bound to plasma proteins

Inherited Defects in Hemoglobin Structure and Function

- Sickle-cell anemia:
  - Hemoglobin S differs in that **valine is substituted for glutamic acid on position 6 of the β chains**.
    - Cross links form a “paracrystalline gel” within the RBCs.
      - Makes the RBCs less flexible and more fragile.
- Thalassemia:
  - Decreased synthesis of α or β chains, increased synthesis of γ chains.

Muscle Myoglobin

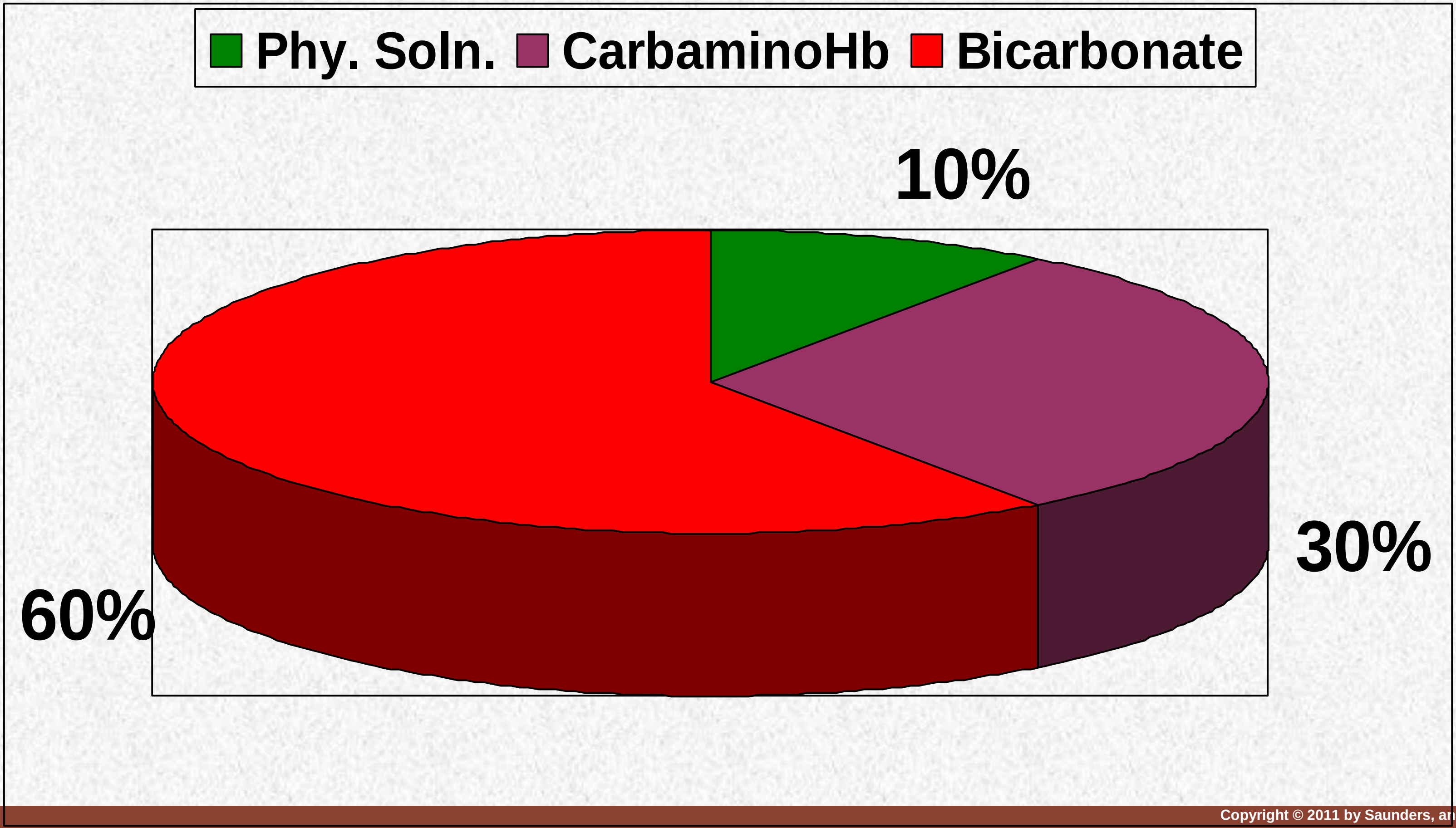
- Red pigment found exclusively in striated muscle.
  - Slow-twitch skeletal fibers and cardiac muscle cells are rich in myoglobin.
    - Have a higher affinity for 0_2 than hemoglobin.
  - May act as a “go-between” in the transfer of 0_2 from blood to the mitochondria within muscle cells.



- May also have an O_2 storage function in cardiac muscles.

Carbon dioxide in blood

transported from the body cells back to the lungs (Tidal CO_2) as (the 4 ml):



Carbon dioxide in blood

Fate of CO_2 in blood

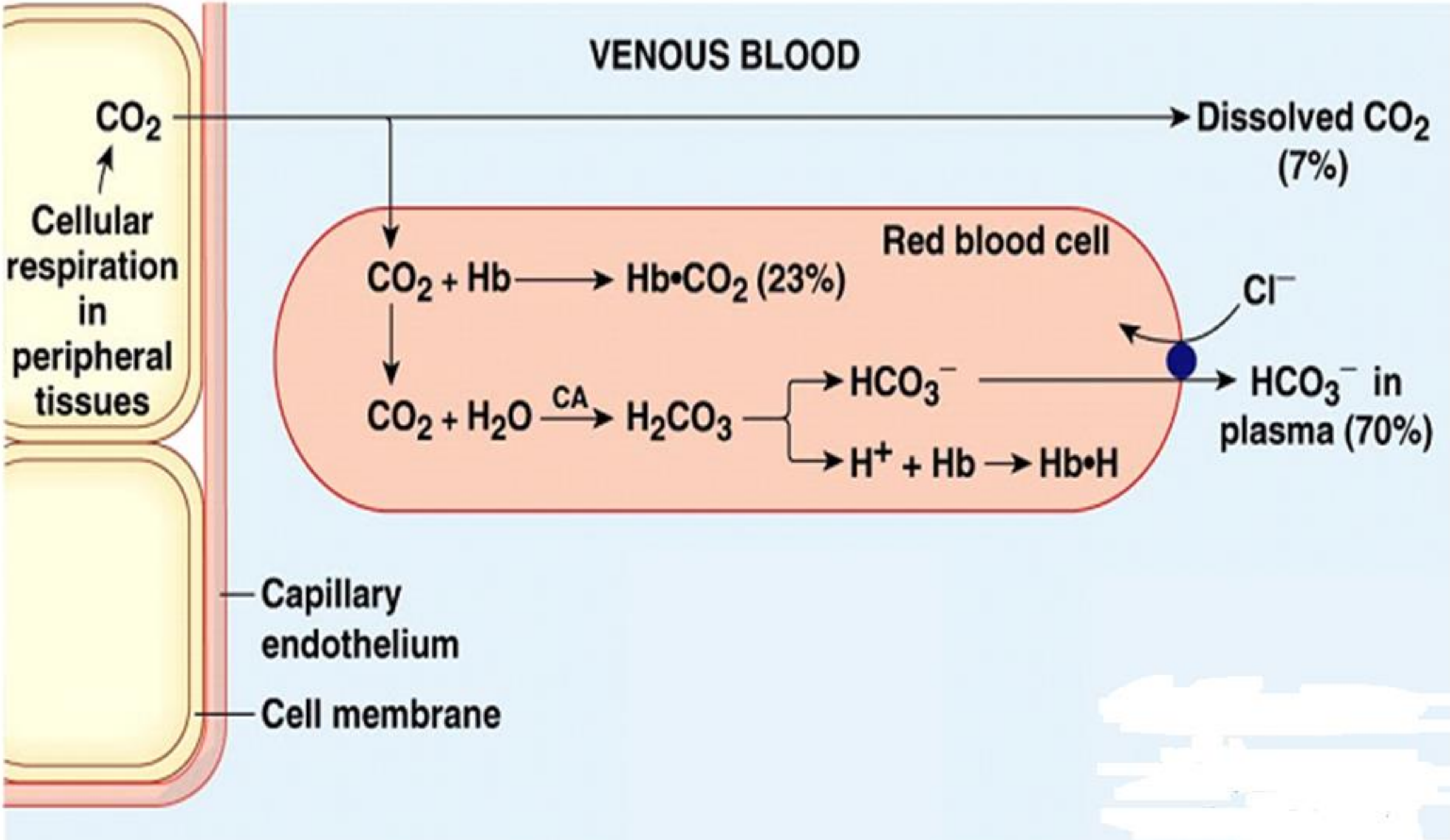
In plasma

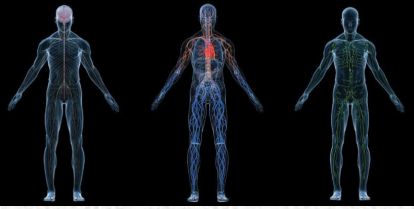
1. Dissolved
2. Formation of carbamino compounds with plasma protein
3. Hydration, H^+ buffered, HCO_3^- in plasma

In red blood cells

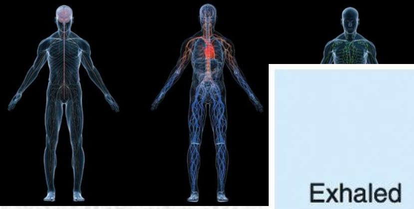
1. Dissolved
2. Formation of carbamino-Hb
3. Hydration, H^+ buffered, 70% of HCO_3^- enters the plasma
4. Cl^- shifts into cells; mosm/L in cells increases

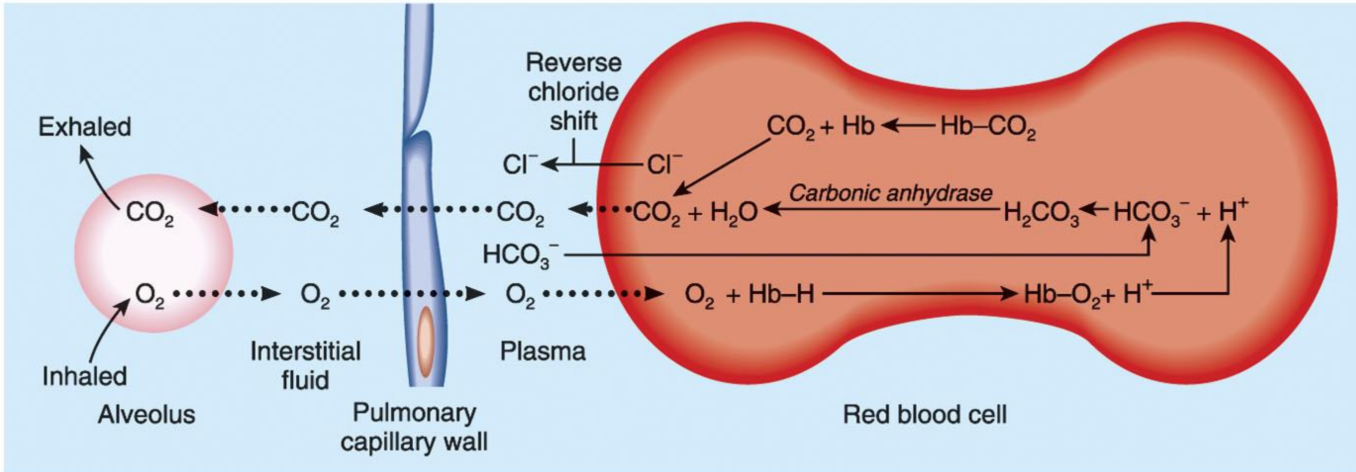
Carbon dioxide in blood



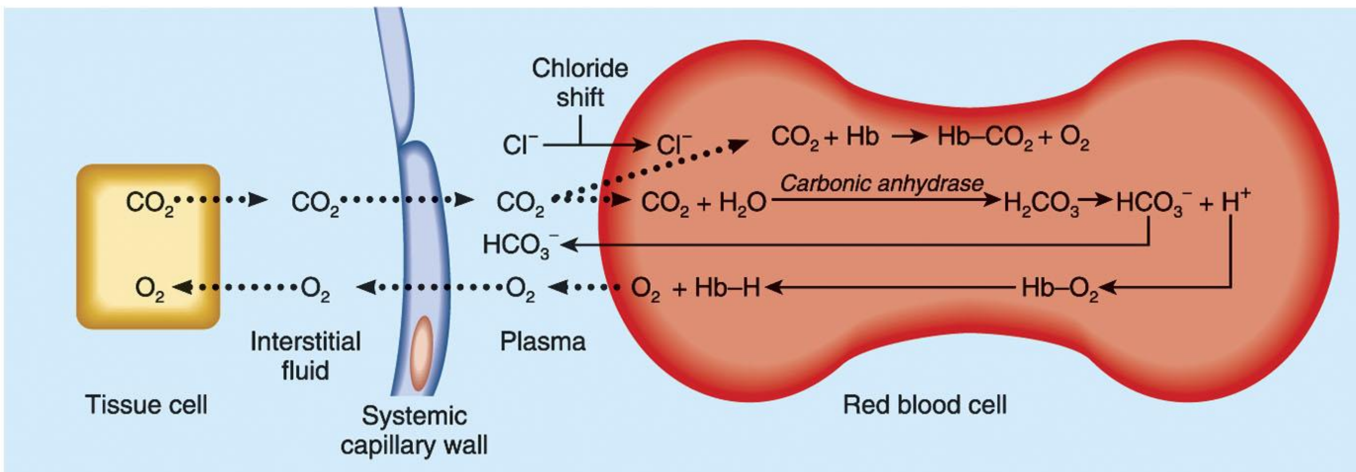


- C.A allows a tremendous amount of CO_2 to react in RBC before the blood leaves the tissue capillaries. RBCs don’t have enough time to spend in the systemic capillary in order to pick up the required amount of CO2 from the interstitial space.
- Therefore CA convers this CO2 to other compound very fast to give more good chance to absorb more CO2 from the cell. If we don’t have C.A then the CO2 diffuses into blood will not be converted to HCO3 quickly. This will interfere with more CO2 being diffused from interstitial space to capillary.





(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)



(b) Exchange of O_2 and CO_2 in systemic capillaries (internal respiration)

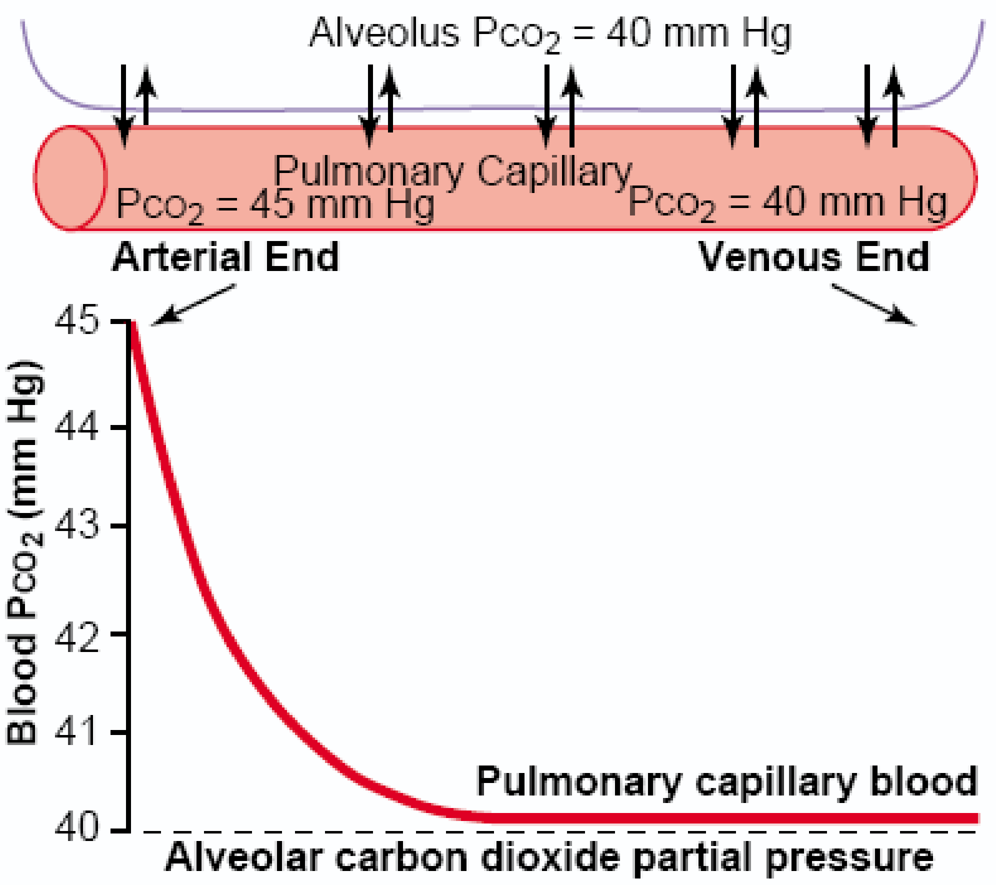
Figure 23.23 Tortora - PAP 12/e

$C0_2$ Transport

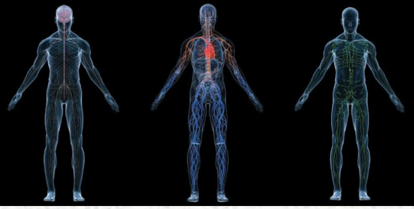
- CO_2 transported in the blood (the 4 ml):
  - $HC0_3^-$ (60%).
  - Dissolved $C0_2$ (10%).
  - Carbaminohemoglobin (30%).

$$H_20 + CO_2 \overset{CA}{\longleftrightarrow} H_2CO_3$$

High $PC0_2$



Alveolus P_{CO_2} = 40 mm Hg
Pulmonary Capillary
P_{CO_2} = 45 mm Hg
P_{CO_2} = 40 mm Hg
Arterial End
Venous End
45
44
43
42
41
40
Blood P_{CO_2} (mm Hg)
Pulmonary capillary blood
Alveolar carbon dioxide partial pressure

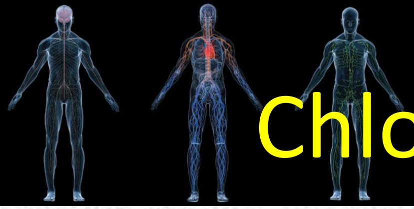


CO_2 TRANSPORT

	Arterial	Venous	A-V difference
Bicarbonate	43.2 (90%) 22.73 mM/l	45.6 (88%) 24 mM/l	2.4 (60 %)
$HbCO_2$	2.4(5%)	3.6 (7 %)	1.2 (30%)
Dissolved CO_2	2.4 (5%)	2.8 (5%)	0.4 (10%)
Total	48 (100%)	52 (100%)	4 (100%)

Transport of Carbon Dioxide

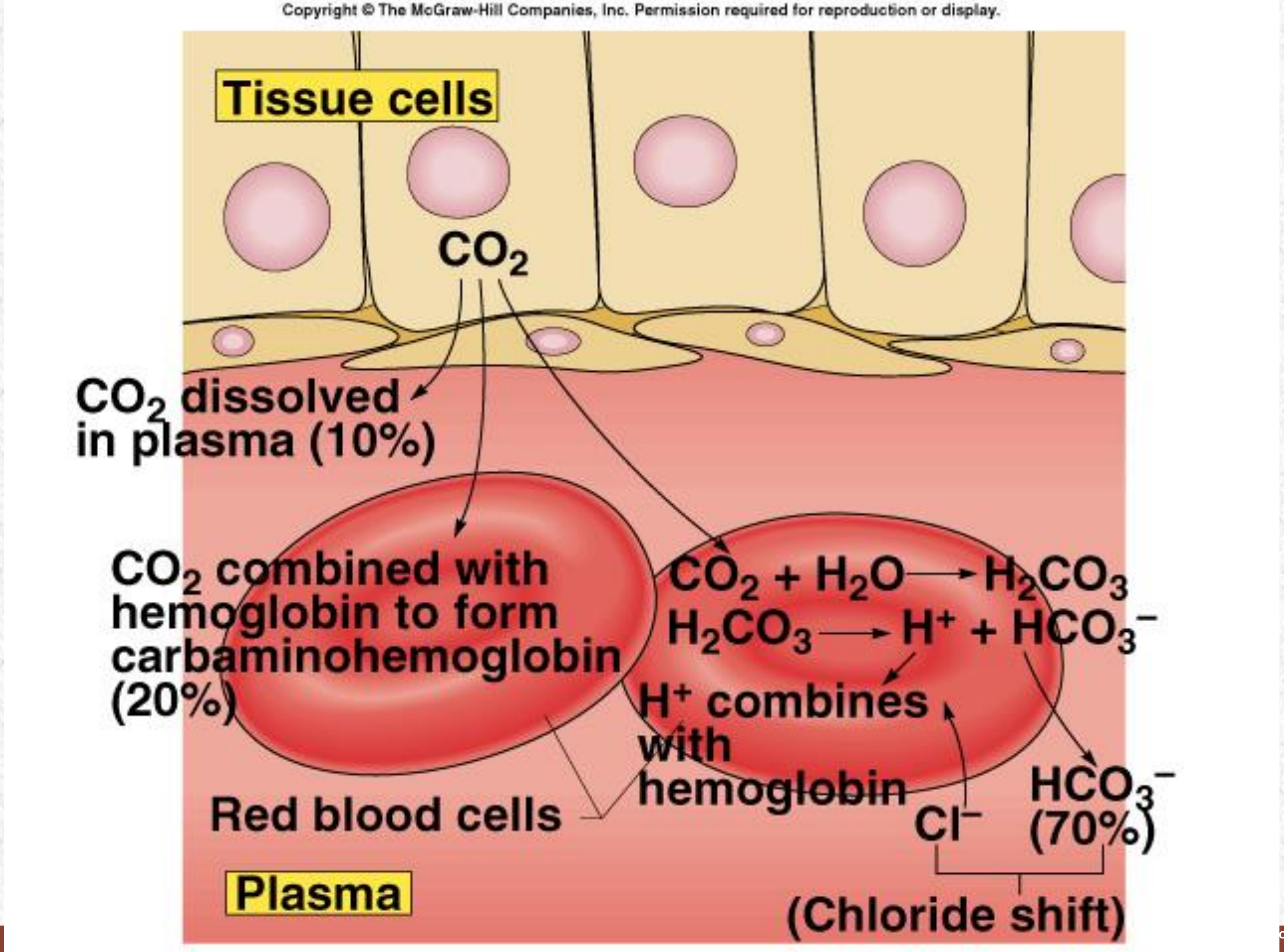
- Dissolved
  - solubility is 20-times of oxygen
  - venous blood: 2.7 ml/100 ml blood
  - arterial blood: 2.4 ml/100 ml blood
  - transported :   0.3 ml/100 ml blood
  - 7% total



Chloride Shift at Systemic Capillaries

- **$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$**
- At the tissues, CO_2 diffuses into the RBC; shifts the reaction to the right.
  - Increased $[HCO_3^-]$ produced in RBC:
    - $HC0_3^-$ diffuses into the blood.
  - RBC becomes more +.
    - Cl^- attracted in (Cl^- shift).
  - H^+ released buffered by combining with deoxyhemoglobin.
- $HbC0_2$ formed.
  - Unloading of O_2.

Carbon Dioxide Transport and Chloride Shift



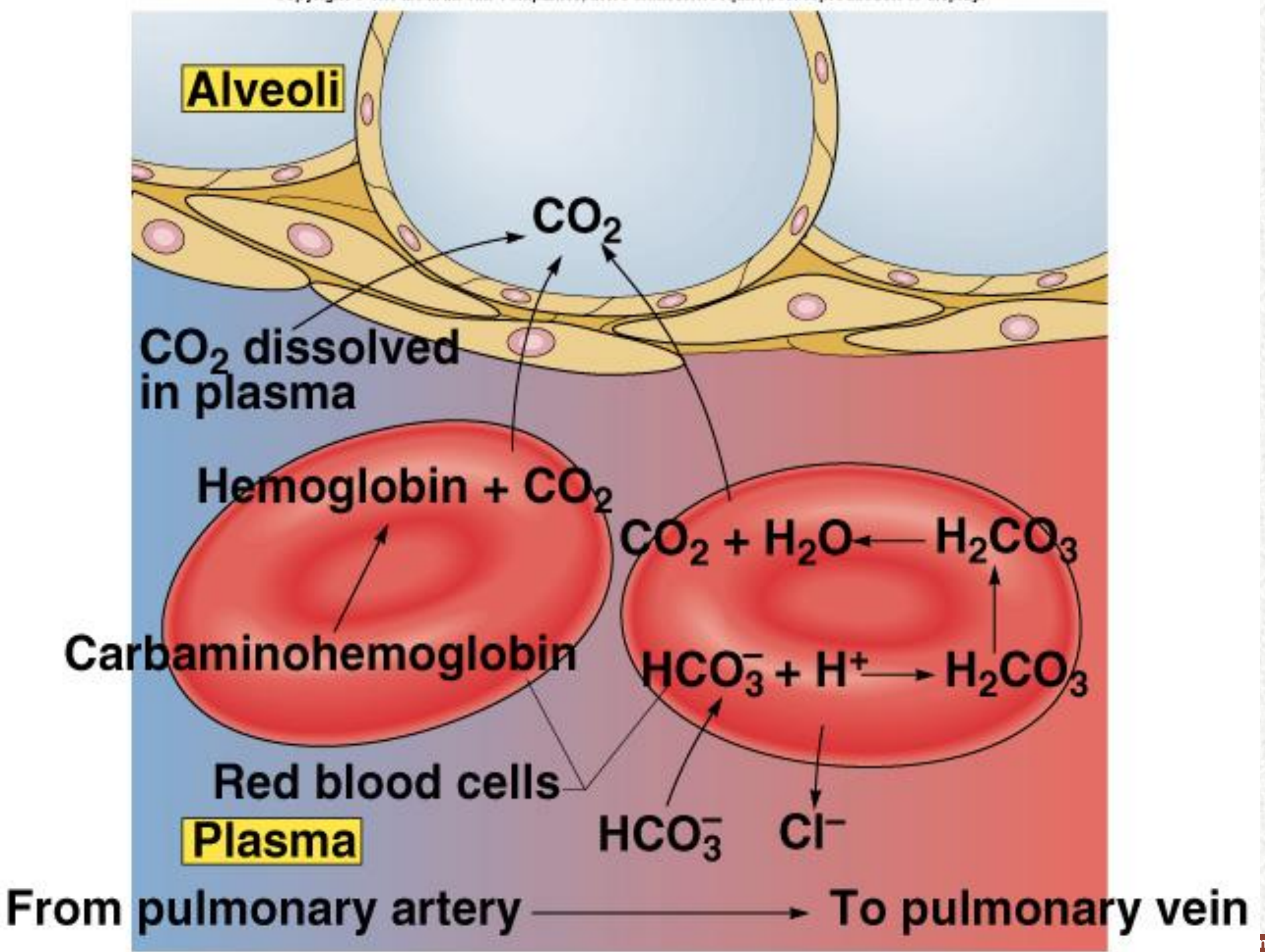
At Pulmonary Capillaries

- **$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$**
- At the alveoli, CO_2 diffuses into the alveoli; reaction shifts to the left.
- Decreased [$HC0_3^-$] in RBC, $HC0_3^-$ diffuses into the RBC.
  - RBC becomes more -.
    - Cl^- diffuses out (reverse Cl^- shift).
- Deoxyhemoglobin converted to oxyhemoglobin.
  - Has weak affinity for H^+.
- Gives off $HbC0_2$.

Increased Oxygen Delivery to Tissue

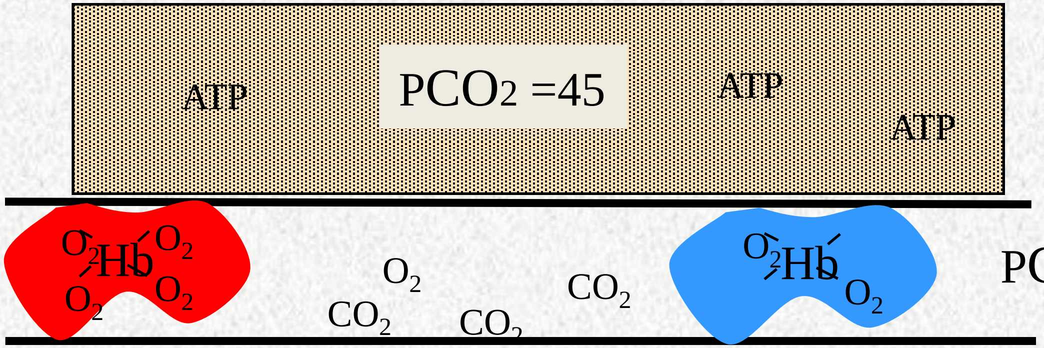
- Two means by which oxygen delivery to tissue can be increased. Name them….
  - 1:
  - 2:

Reverse Chloride Shift in Lungs



Blood and Muscle PCO_2

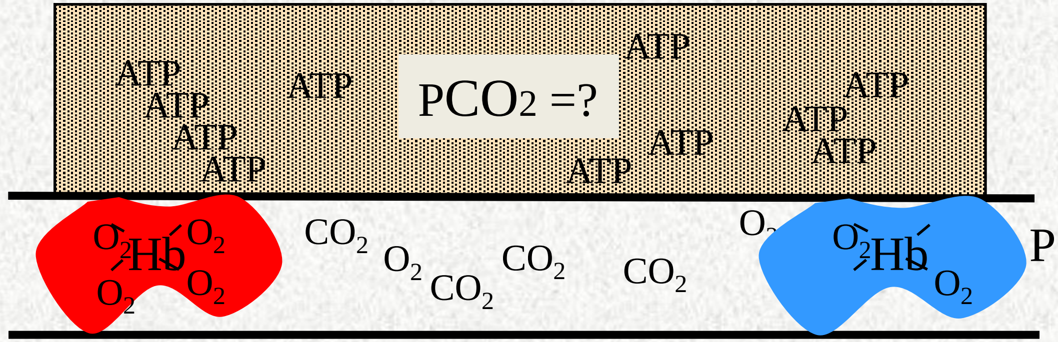
$PCO_2 = 40$



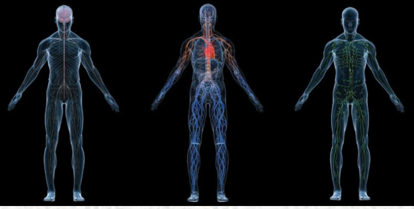
$PCO_2 = 45$

Increased Metabolism and **normal** blood flow

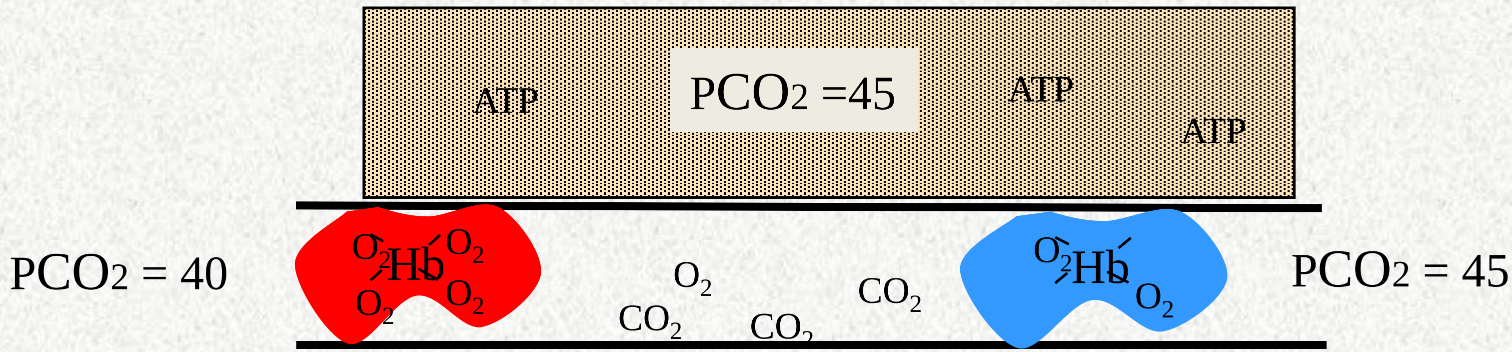
$PCO_2 = 40$



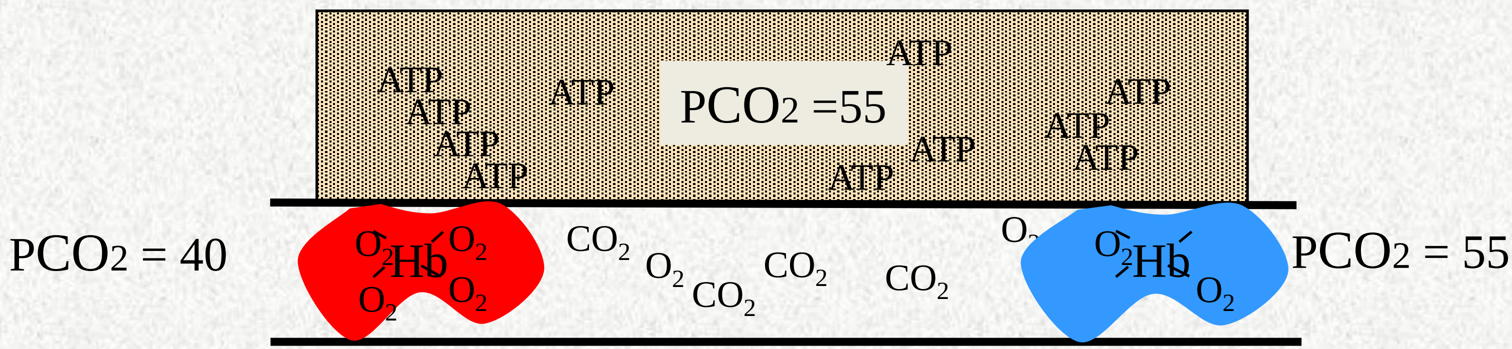
PCO_2 = ?



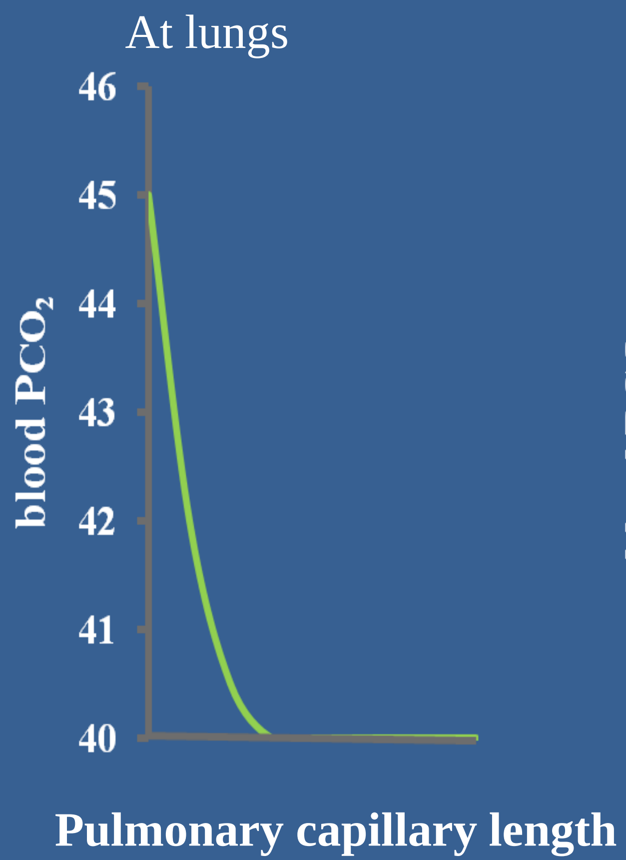
Blood and Muscle PCO_2

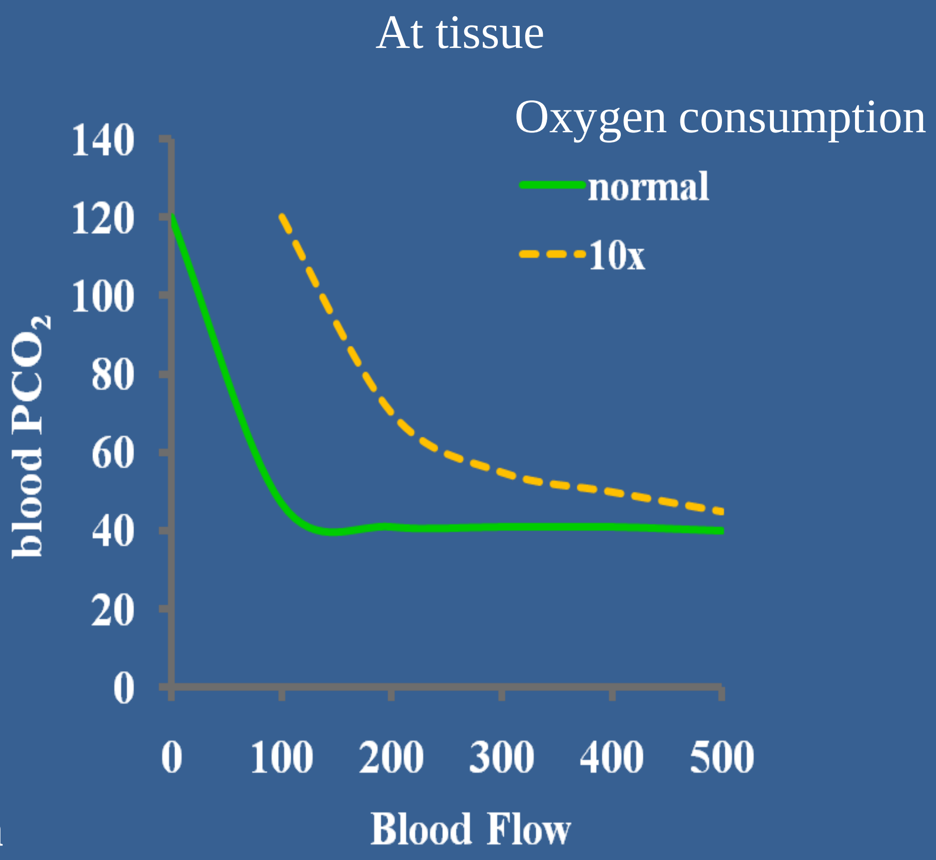


Increased Metabolism and normal blood flow

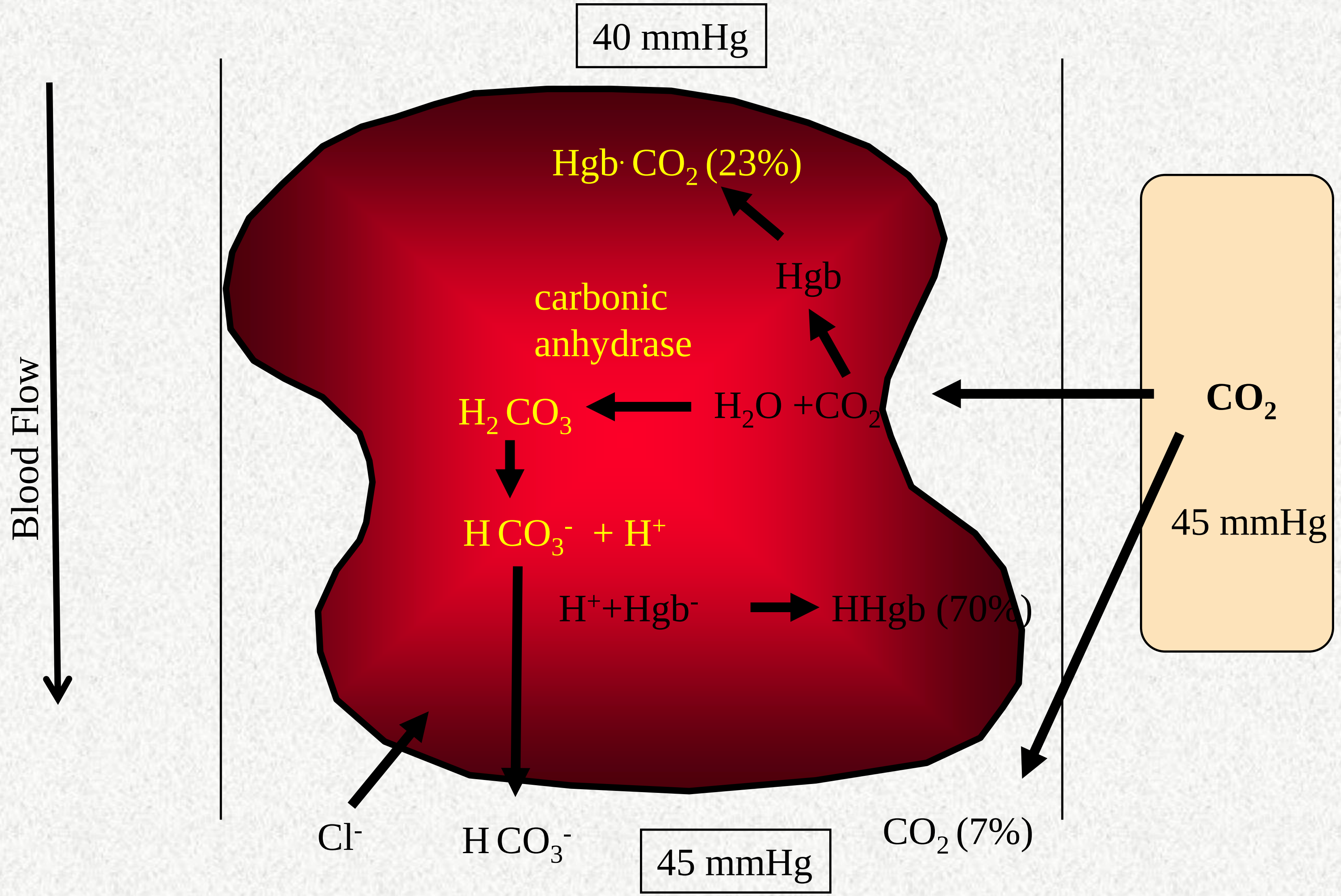


Diffusion of Carbon Dioxide

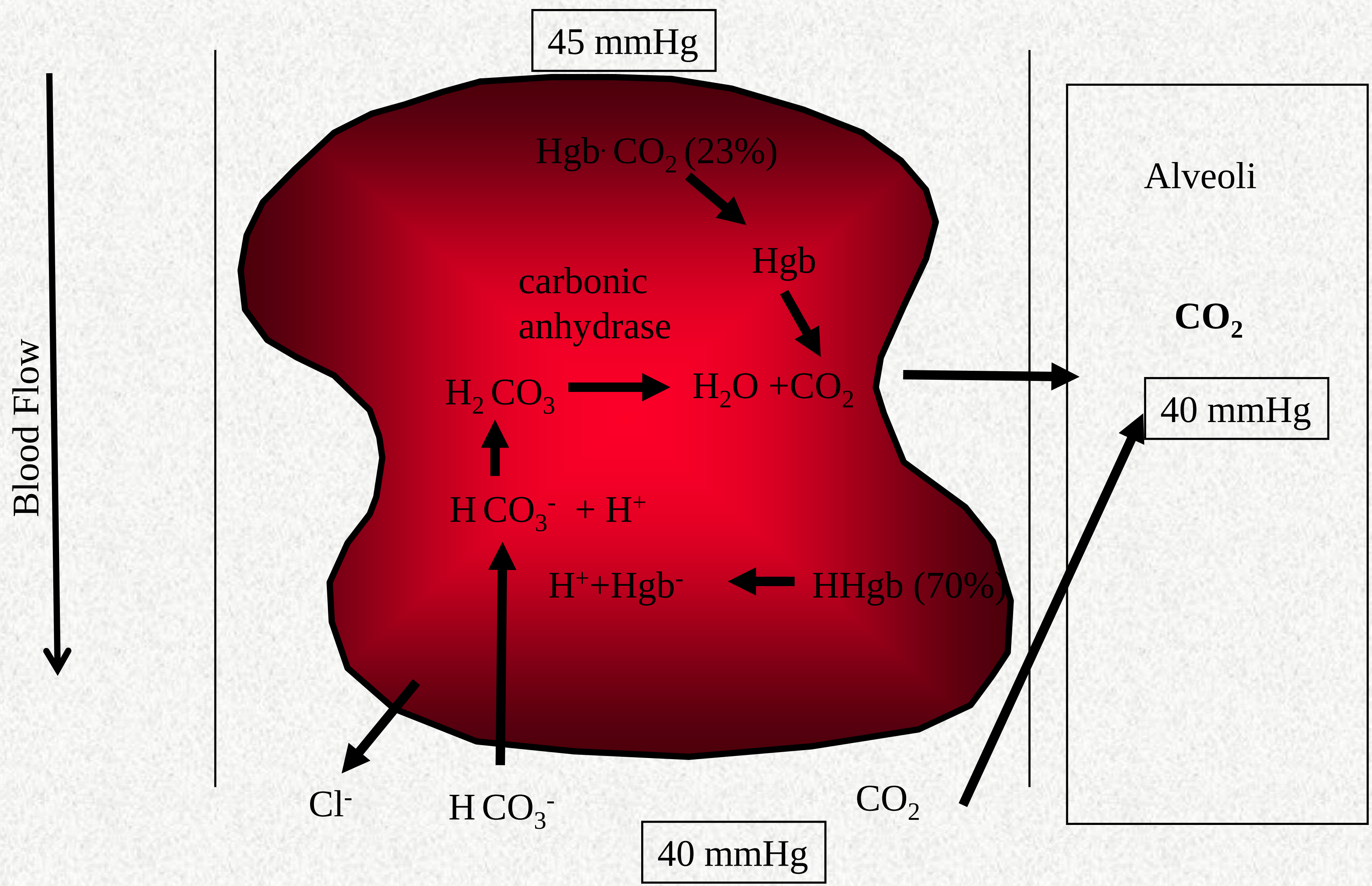




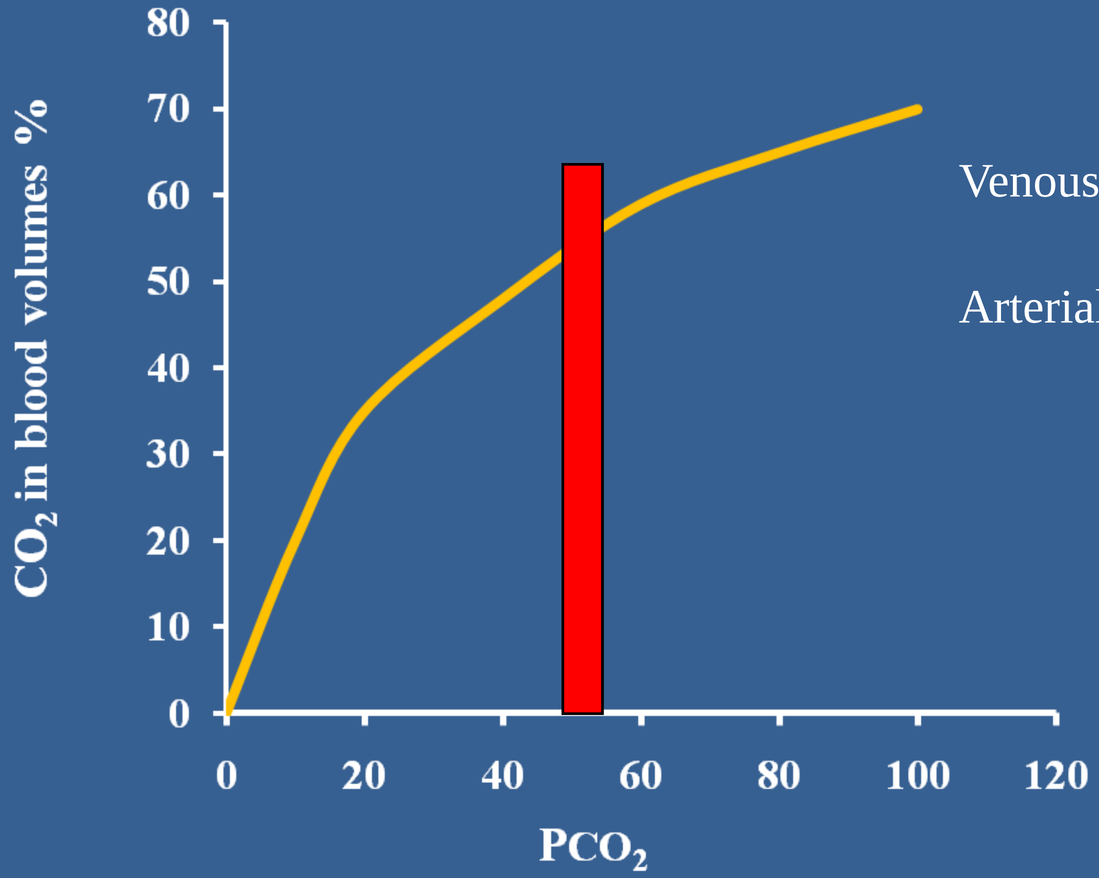
Transport of Carbon Dioxide at Tissue



Transport of Carbon Dioxide at Lung

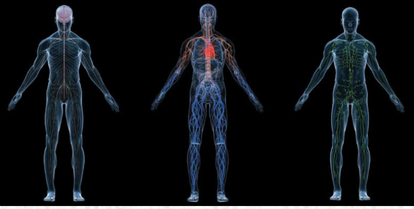


Carbon Dioxide Dissociation Curve



Venous 52 vol%

Arterial 48 vol%



At the physiological PaCO2 levels, PCO_2 dissociation curve is linear