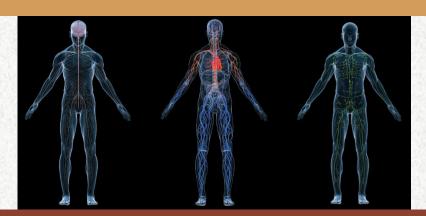
GUYTON AND HALL Textbook of Medical Physiology

TWELFTH EDITION



Chapter 40:

Transport of Oxygen and Carbon Dioxide in Blood and Tissue Fluids

Slides by Robert L. Hester, PhD

Diffusion

iffusion 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 O₂ 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 $0.25-0.6~\mu$. 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 m²..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

Basics of the Respiratory System

- Characteristics of exchange membrane
 - High volume of blood through huge capillary network results in
 - Low vascular resistance through lungs
 - Pulmonary 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

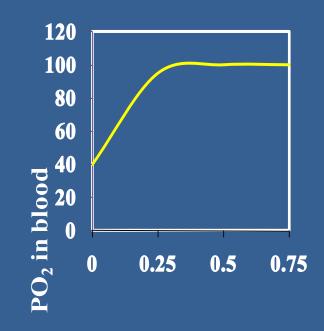
Diffusion =
$$(P_1-P_2)$$
 * Area * Solubility

Thickness * \sqrt{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

Diffusion Capacity

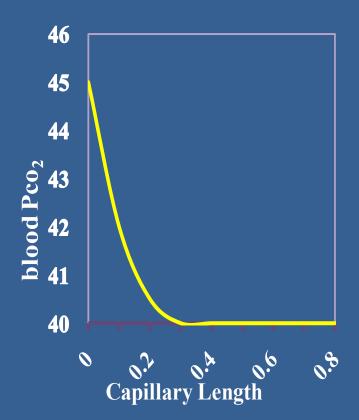
- Oxygen
 - Diff capacity 22ml/min/mmHg *gradient of 11mmHg
 - 250 ml/min diffusion of oxygen



Capillary Length

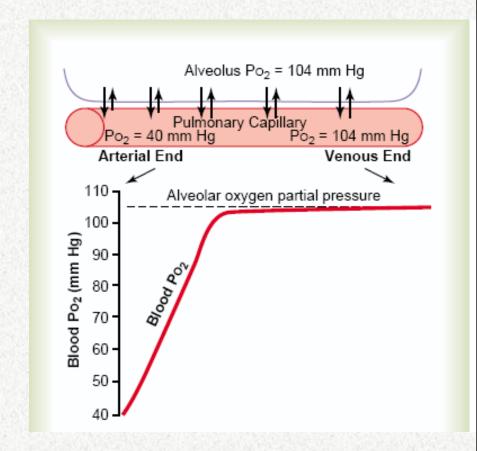
Diffusion Capacity

- Carbon Dioxide
 - Diff capacity 400ml/min/mm Hg *gradient < 1 mmHg
 - 200 ml/min diffusion of carbon dioxide

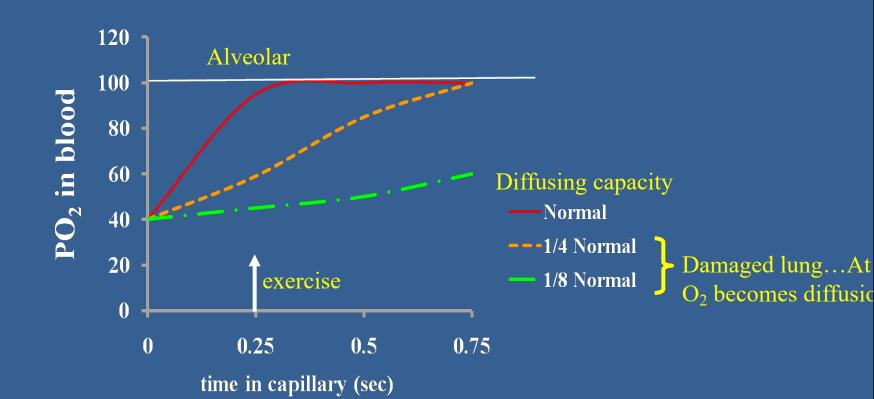


xygen Diffusion from the Alveoli to the Pulmonary circulation

- O₂ diffuses into the pulmonary capillaries because the PO₂ in the alveoli is high. Note: O₂ utilizes less than one third of the respiratory membrane...perfusionlimited
- PO₂ 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



Uptake of Oxygen in Lungs



Why PO₂ arterial < Alveolar PO₂?

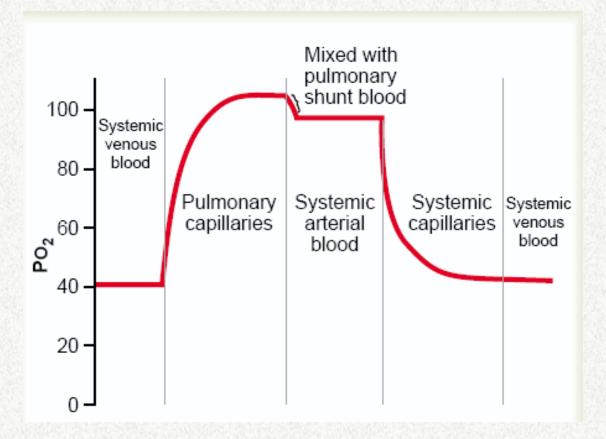
- P_AO₂ =100 while systemic P_aO₂ is only 95 mm Hg?
- 1. Venous admixture (pollution)
- A. BRONCHIAL Circulation: 50% goes back to right atrium, and 50% to left atrium.
- B. Cardiac veins
- C. Pulmonary Circulation: 2% of all venous blood doesn't pass through pulmonary capillaries (A-V anastomosis) "physiological shunted blood".
- 2. Low VA/Q in the base of the lung.



Transport in arterial blood & Pulmonary shunt flow

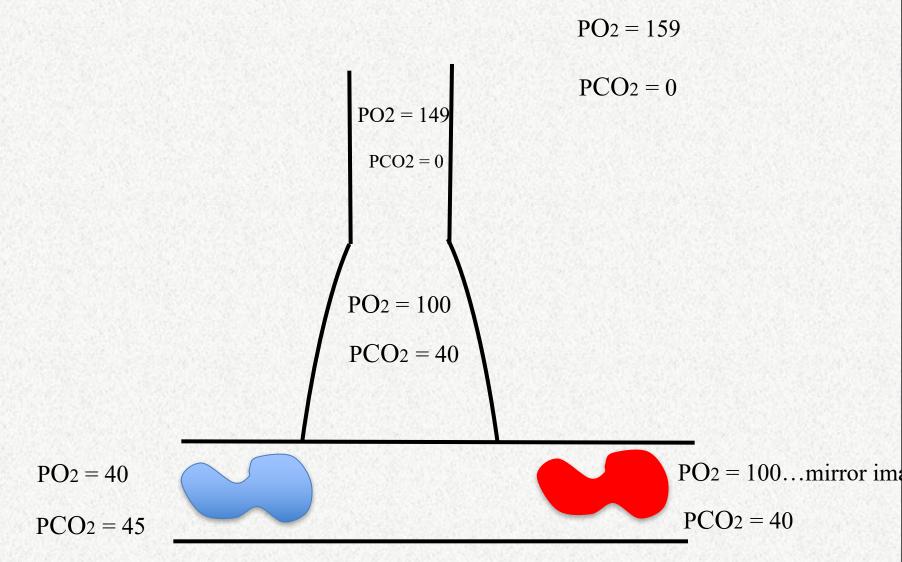
Due to the bronchial circulation the arterial PO₂ falls to 95 mm

Hg



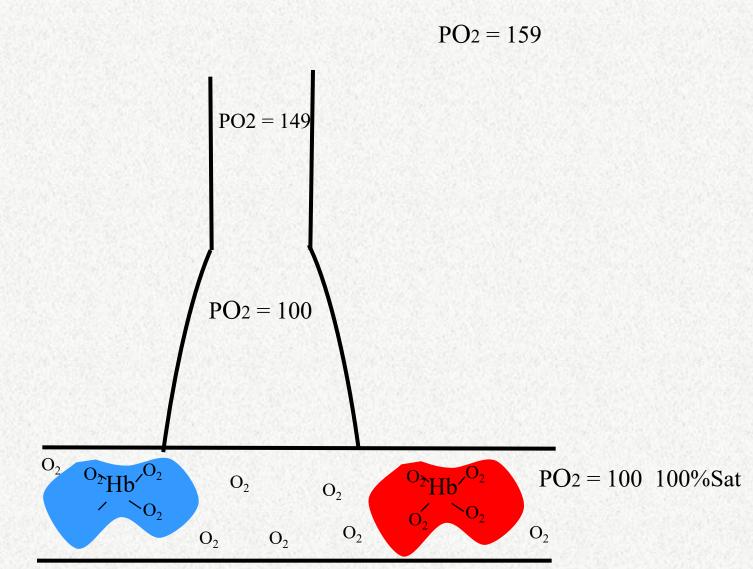


Alveolar and Blood Gases





Alveolar and Blood PO₂



 $PO_2 = 40 75\% Sat$

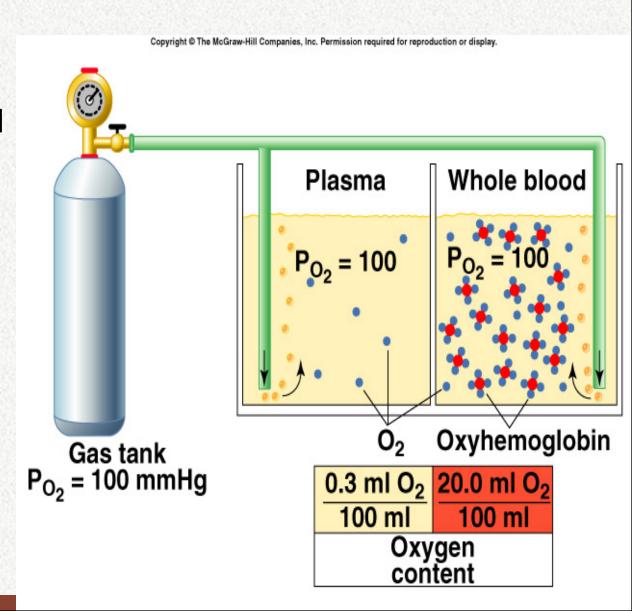


Hemoglobin and 0₂ Transport

= 5 million per μl blood million Hb/RBC.

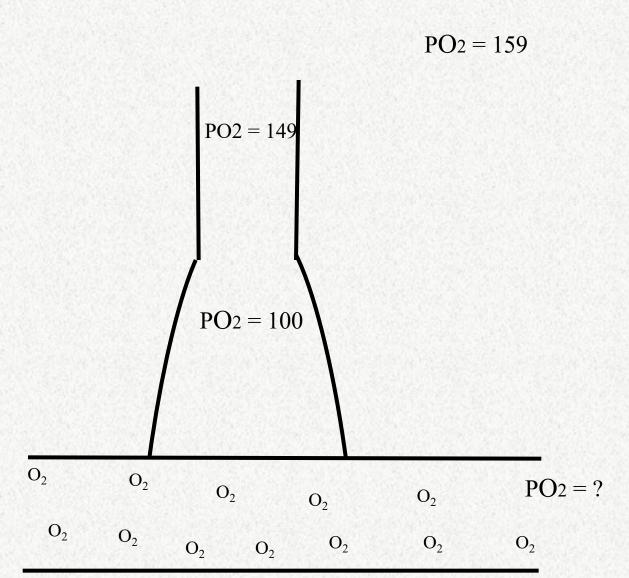
h Hb has 4 polypeptide ins and 4 hemes.

he center of each heme up is 1 atom of iron to can combine with 1 ecule 02.





Alveolar and Blood PO₂





Question....

A vasodilator is infused into a paralyzed muscle. What happens to PO₂ within that muscle?

- A. Increases
- B. Decreases
- C. No change



Question

Arterial PO₂ is 100 mmHg and content is 20 ml O₂/dl. What is arterial PO₂ if $\frac{1}{2}$ of all of the red cells are removed?

- A. $PO_2 = 0$ mmHg
- B. $PO_2 = 30 \text{ mmHg}$
- C. $PO_2 = 50 \text{ mmHg}$
- D. $PO_2 = 60 \text{ mmHg}$
- E. $PO_2 = 100 \text{ mmHg}$



Question

Systemic arterial PO₂ is 100 mmHg and hematocrit is 40%. What is systemic arterial PO₂ if blood is added to increase hematocrit to 50?

A.
$$PO_2 = 50 \text{ mmHg}$$

B.
$$PO_2 = 70 \text{ mmHg}$$

C.
$$PO_2 = 100 \text{ mmHg}$$

D.
$$PO_2 = 120 \text{ mmHg}$$

E.
$$PO_2 = 149 \text{ mmHg}$$



Hypothetical

- What happens to <u>mixed venous</u> PO₂ 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



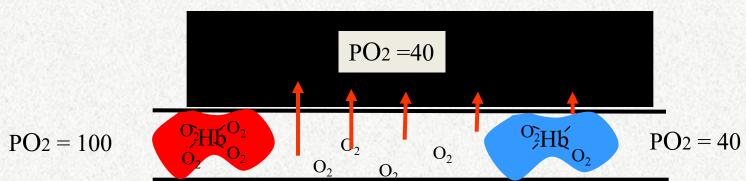


Answer

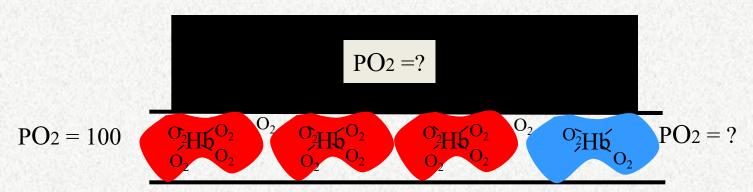
$$713*0.45 = 321 \text{ mmHg} = \text{inspired PO}_2$$

Alveolar
$$PO_2 = 321-(40/0.8)=321-50 = 271 \text{ mmHg}$$

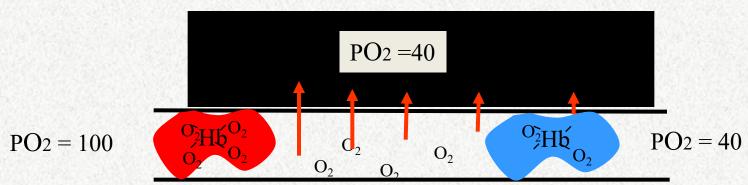




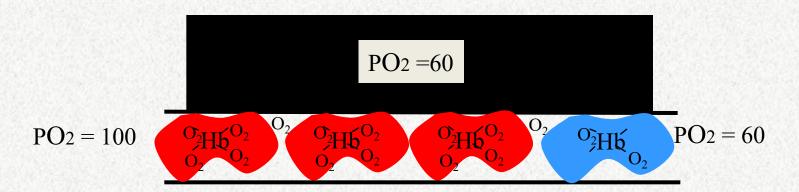
Increased Flow and normal metabolism



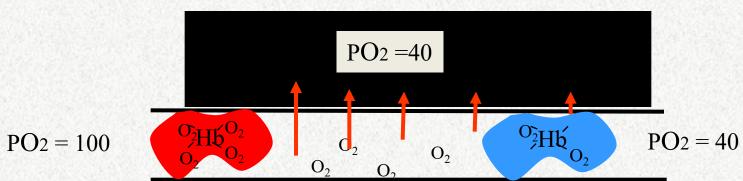




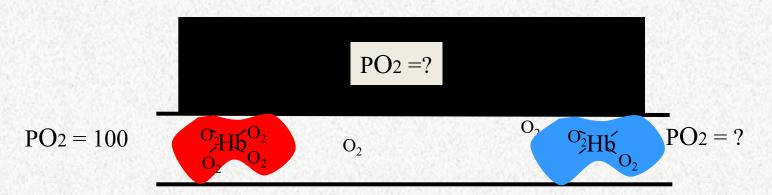
Increased Flow and normal metabolism



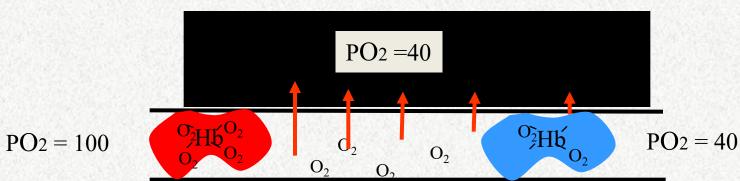




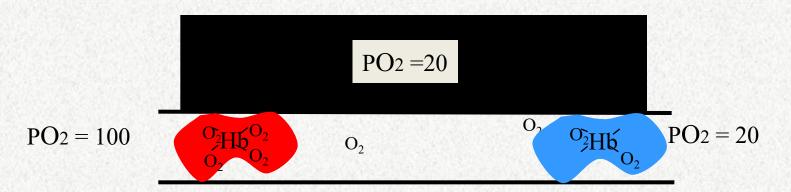
Increased Metabolism and normal blood flow







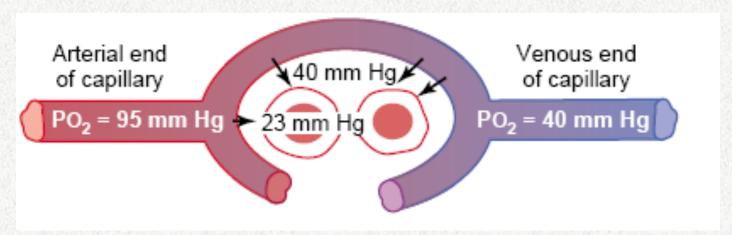
Increased Metabolism and normal blood flow





PO₂ in systemic circulation (Diffusion from peripheral capillaries)

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.





Increased Blood Flow to Tissue

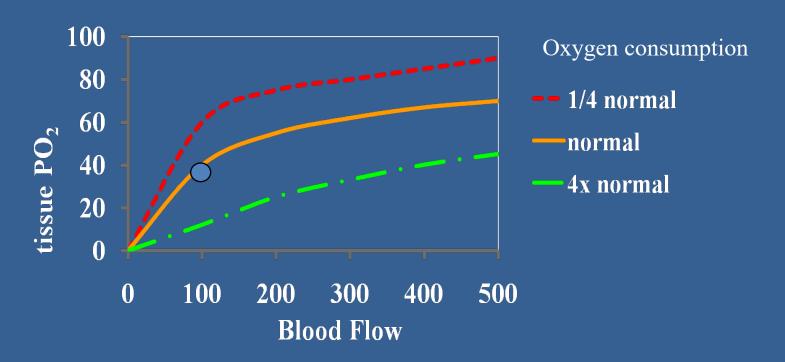
- Normal blood flow
 - 200 ml O₂/lit of arterial blood * 5 lit blood/min= 1000 ml/min
 - VO₂/min...250 ml are consumed at rest (25%)
- Utilization Coefficient or (Extraction ratio):
- Is the % of blood that gives up its O₂ as it passes through tissue capillaries. Normally is 25%. In exercise 75% 85%. In some local tissues with extremely high metabolic rate → 100%.



O2 Uptake during Exercise

- VO₂ increases during exercise until it reaches VO₂max...what limits VO₂max...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 PO₂ of 95-100 mmHg
- Tissue has a PO₂ of 30-40 mmHg
- Tissue PO₂ 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
Pother gases	=0.0006	x 760mm Hg	= 0.5 mmHg
		TOTAL	= 760.0 mmHg

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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 ₂ O	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 O₂
- Arterial Blood
 (PO₂ 95 mm Hg;
 PCO₂ 40 mm Hg;
 Hb 97% Saturated)
- Venous Blood (PO₂ 40 mm Hg; PCO₂ 45 mm Hg; Hb 75% Saturated)



Oxygen Transport

- Partial Pressure (mm Hg)
 - driving force for diffusion
- Percent Saturation (no units)
 HbO₂
 (Hb+O₂) is called oxyHb
- Content (ml O₂/100 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=PaO₂ X Solubility of O₂ Solubility 0.003 ml
 O₂/100 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 O₂/min
 - Would require 83 1/min blood flow
- Hemoglobin
 - 97% of the transported O2 is in this form

$$O_2 + Hb \longrightarrow HbO_2$$



Law of dissolved gases

0	0.034
Oxygen	0.024
Carbon dioxide Carbon monoxide	0.57 0.018
	0.018
Nitrogen Helium	0.012
Hellum	0.008

- Much more CO₂ is dissolved in blood than O₂
 because CO₂ is 20 times more soluble.
- The air we breathe is mostly N₂, very little dissolves in blood due to its low solubility.

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 O₂ 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).

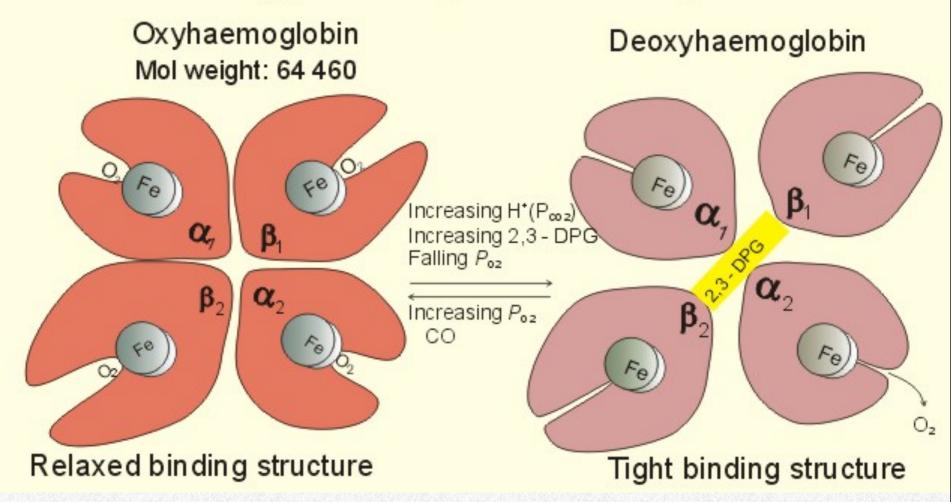
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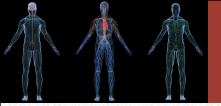
is inside the RBCs and not circulating freely in the plasma

- 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 CO₂ to HCO3, otherwise by using Acetazolamide (CA inhibitor) PCO₂ reaches 80 mmHg
- Prevent ↑ in blood viscosity.

Oxygen Binding and Unloading



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



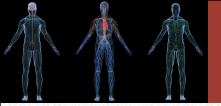
Hemoglobin

Oxyhemoglobin:

- Normal heme contains iron in the reduced form (Fe²⁺).
- Fe²⁺ 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 .



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 O₂. 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.



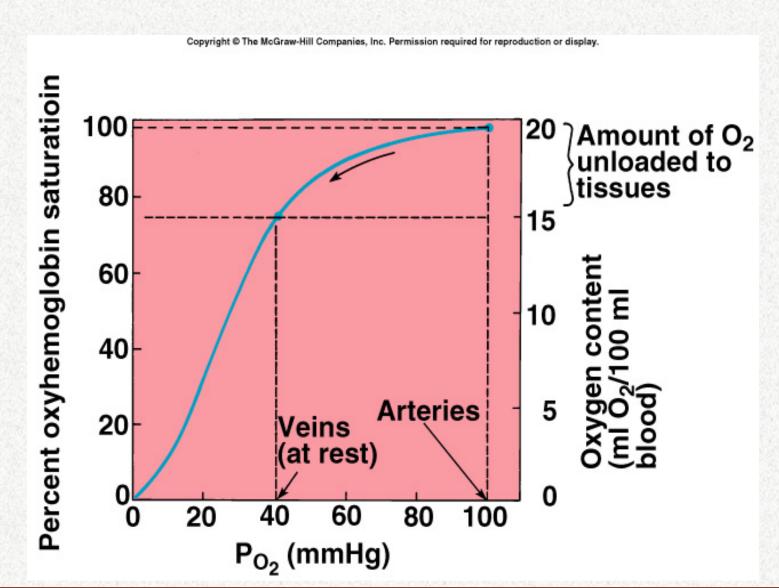
Hemoglobin (continued)

- 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 PO₂
- Loading/unloading depends:
 - PO₂ of environment.
 - Affinity between hemoglobin and O₂.



- Graphic illustration of the % oxyhemoglobin saturation at different values of PO₂.
 - Loading and unloading of O_2 .
 - Steep portion of the sigmoidal curve, small changes in PO₂ produce large differences in % saturation (unload more O₂).
- 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.







Effect of 2,3 DPG on O₂ 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 G-3-P \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)

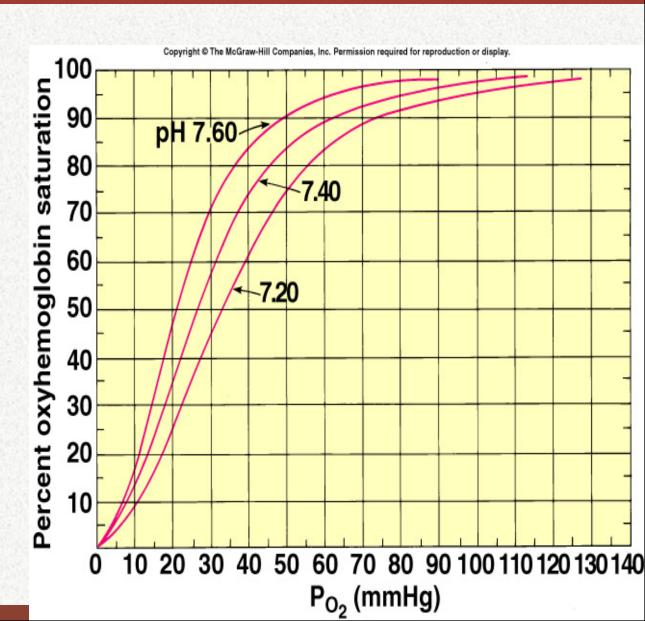


Effects of pH and Temperature

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

Affinity is decreased by:

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





Po₂ (mmHg)

%Sat

Values to remember

•	PO2	U2 Sat (<u>%)</u>
•	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 ruleit is close enough!		
	4,5,6		7-8-9

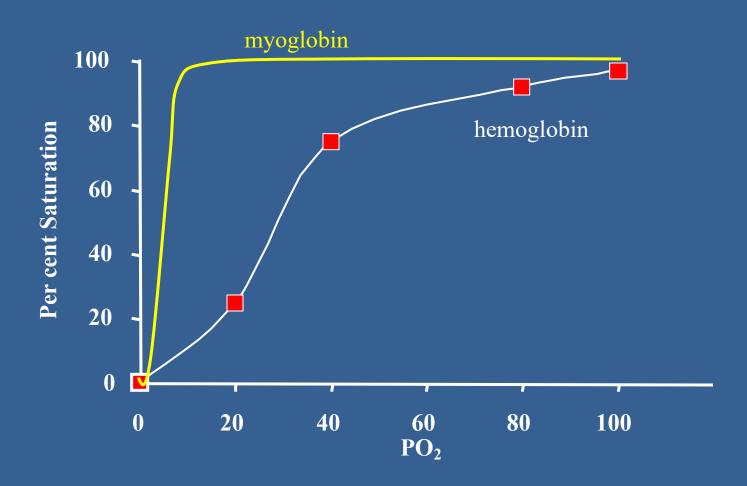
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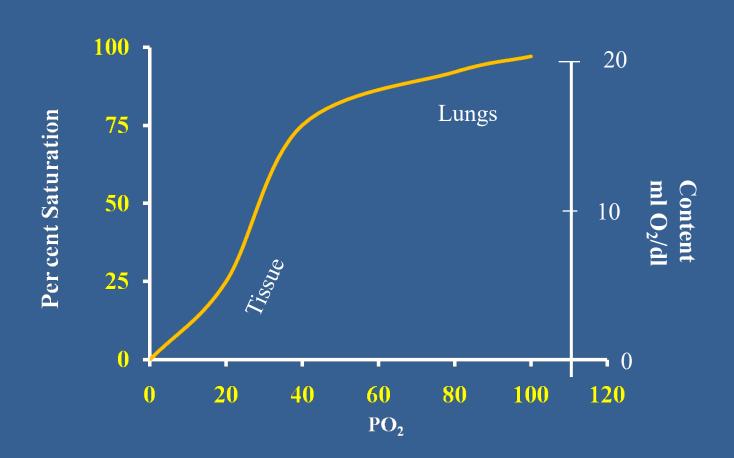
70 80 90

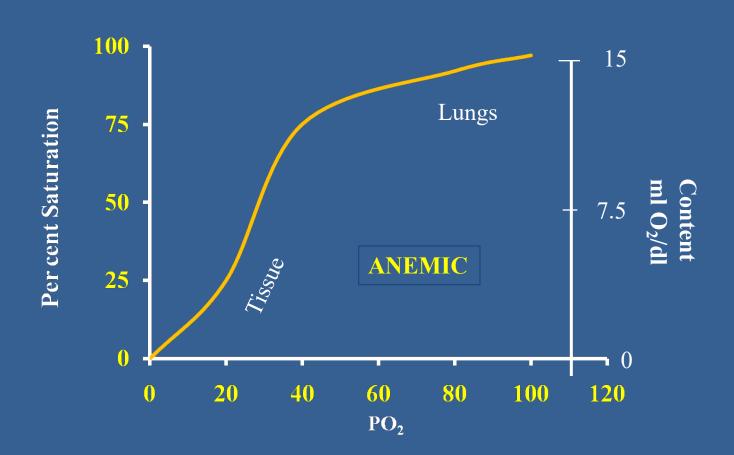
O- C-+ /0/\

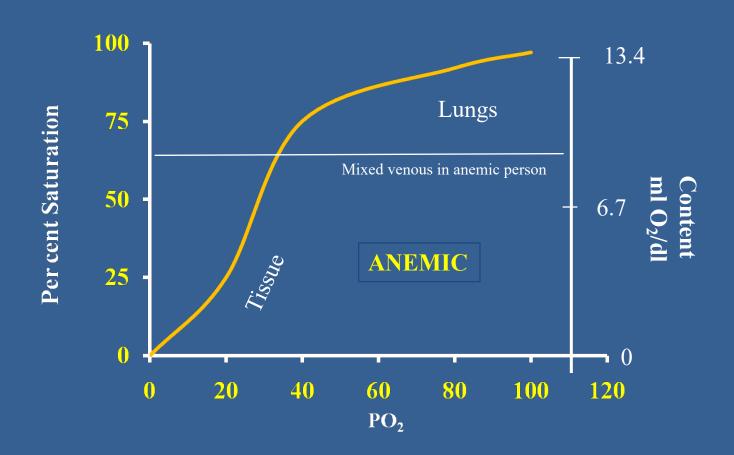
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Dissociation Curve







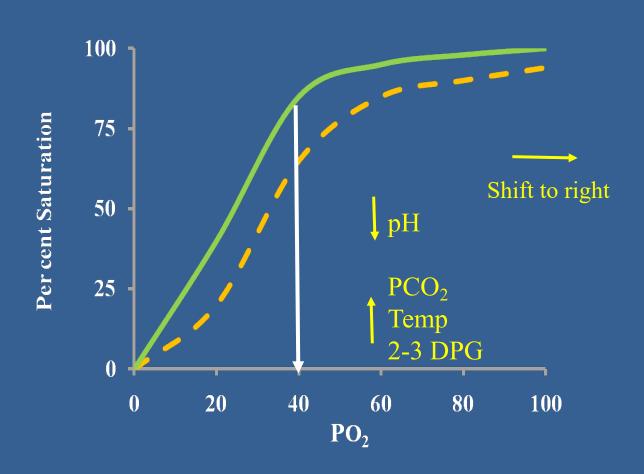




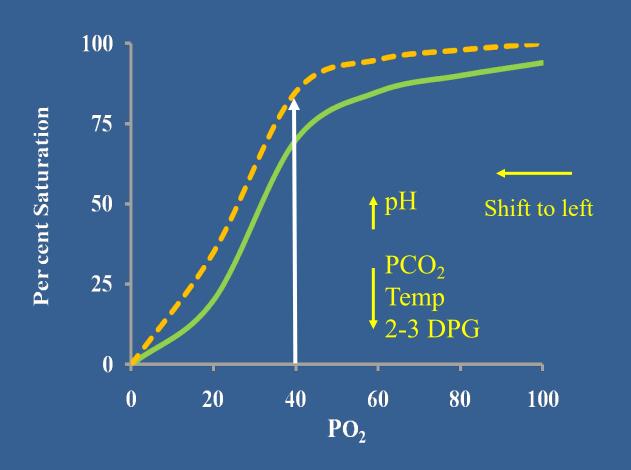
Shifts of Dissociation Curve

- Right shift occurs at tissue level...Bohr's effect
 - -↑PaCO₂ or ↑ arterial H⁺→ ↓ affinity for oxygen or increase O₂ 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

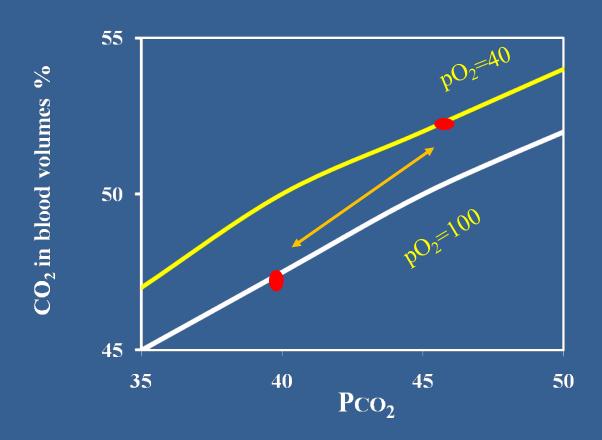


Left Shift of Dissociation Curve Bohr's effect



Haldane Effect

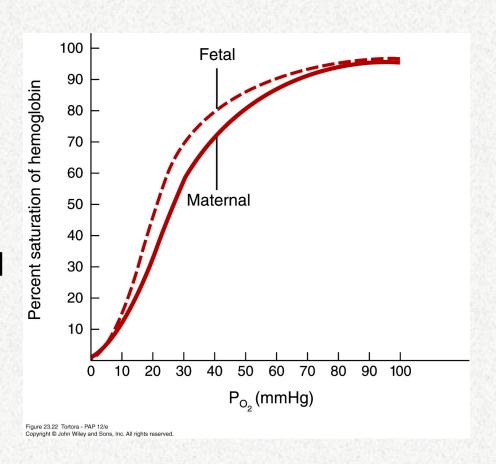
Venous 52 vol% Arterial 48 vol%





al 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



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Alveoli

- Over wide range hemoglobin will be highly saturated
- example: PO₂ of 60 mmHg correspond to 90% saturation

Tissue

- Normal: consume 5 ml O₂/100 ml blood (P_iO₂ 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 O₂/dl

- Calculate oxygen content
 - Patient has saturation of 60%
 - Patient has Hb of 15 gm/dl



Calculations

- Calculate % saturation
 - $-10 \text{ gm/dl} * 1.34 \text{ ml O}_2/\text{gm Hb} = 13.4 \text{ ml O}_2/\text{dl}$
 - This is max oxygen carrying capacity
 - $(6.5 \text{ ml O}_2/\text{dl}) / (13.4 \text{ ml O}_2/\text{dl}) = \sim 50\%$

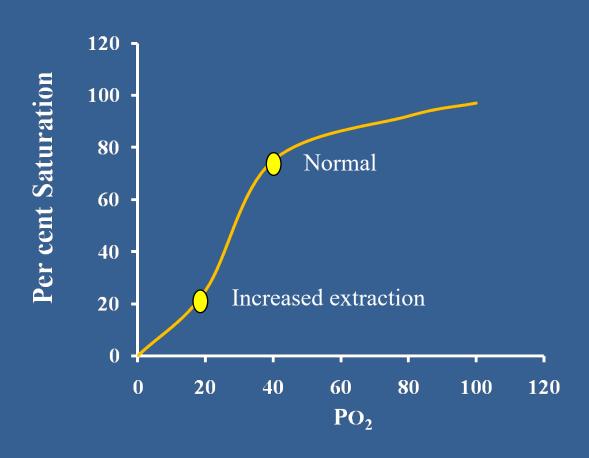
- Calculate oxygen content
 - $-15 \text{ gm/dl} * 1.34 \text{ ml O}_2/\text{dl} = 20 \text{ ml O}_2/\text{dl}$
 - This is max oxygen carrying capacity
 - $-20 \text{ ml O}_2/\text{dl} * 60\% \text{ saturation} = 12 \text{ ml O}_2/\text{dl}$



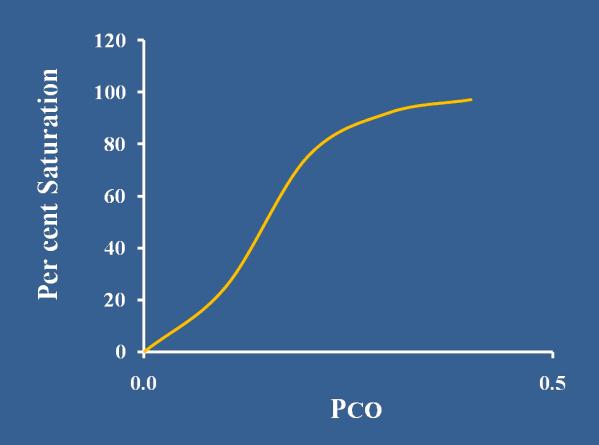
Calculations

- Assume Hb is 10 gm/dl
- 100% saturation give a content of 13.4 ml/dl blood
- At rest body uses 5 ml O₂/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. CO₂ dissolved in plasma
- d. CO₂ bound to plasma proteins



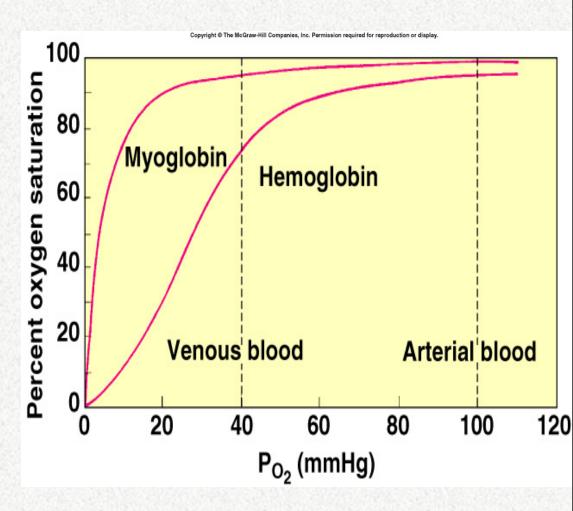
Inherited Defects in Hemoglobin Structure and Function

- 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

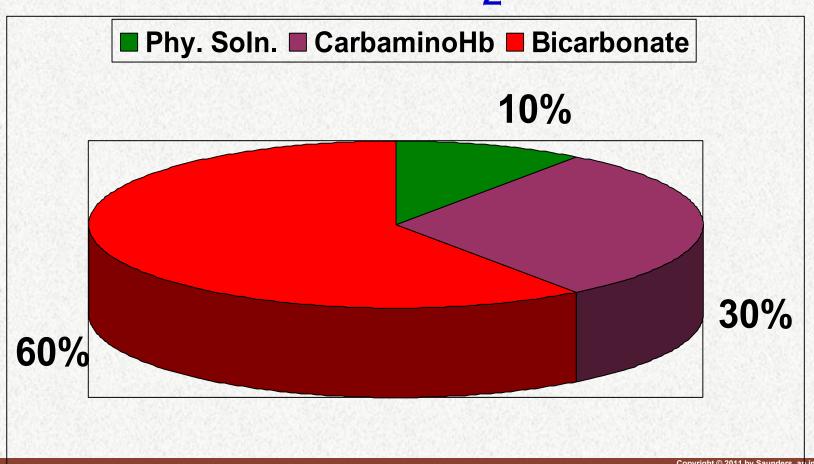
- Red pigment found exclusively in striated muscle.
 - Slow-twitch skeletal fibers and cardiac muscle cells are rich in myoglobin.
 - Have a higher affinity for 0₂ than hemoglobin.
 - May act as a "go-between" in the transfer of O_2 from blood to the mitochondria within muscle cells.



 May also have an O₂ storage function in cardiac muscles.



TRANSPORTED FROM THE BODY CELLS BACK TO THE LUNGS (TIDAL CO₂) AS (THE 4 ML):



Fate of CO₂ in blood

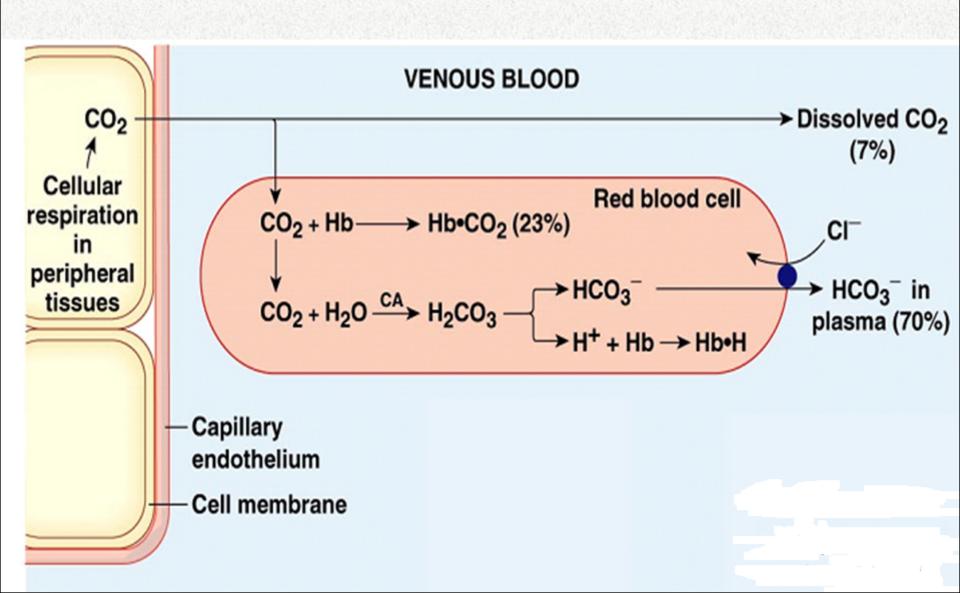
In plasma

- 1. Dissolved
- 2. Formation of carbamino compounds with plasma protein
- 3. Hydration, H⁺ buffered, HCO₃⁻ in plasma

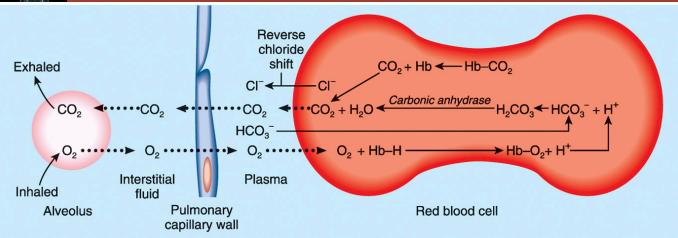
In red blood cells

- 1. Dissolved
- 2. Formation of carbamino-Hb
- 3. Hydration, H⁺ buffered, 70% of HCO₃- enters the plasma
- 4. Cl⁻ shifts into cells; mosm/L in cells increases

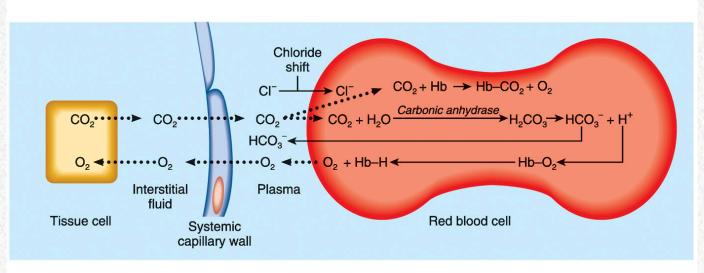
ARBON DIOXIDE IN BLOOD







(a) Exchange of O2 and CO2 in pulmonary capillaries (external respiration)



(b) Exchange of O₂ and CO₂ in systemic capillaries (internal respiration)

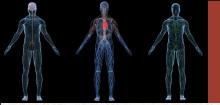
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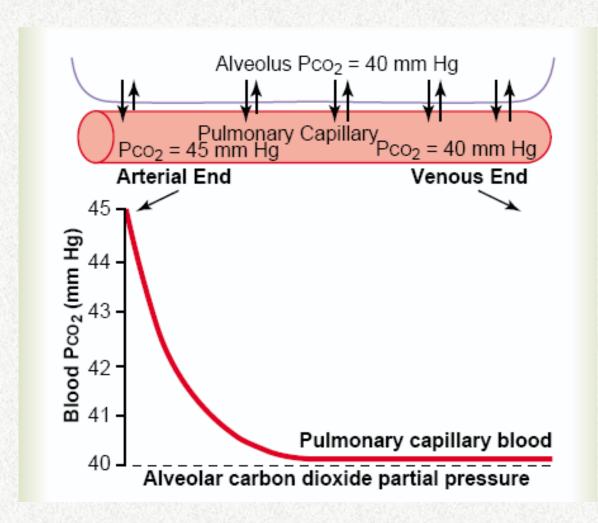


CO₂ Transport

- CO₂ transported in the blood (the 4 ml):
 - $-HCO_3^-$ (60%).
 - Dissolved $C0_2$ (10%).
 - Carbaminohemoglobin (30%).

$$H_20 + CO_2 \stackrel{CA}{\longleftrightarrow} H_2CO_3$$
High PCO₂







CO₂ TRANSPORT

B 88.				
		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

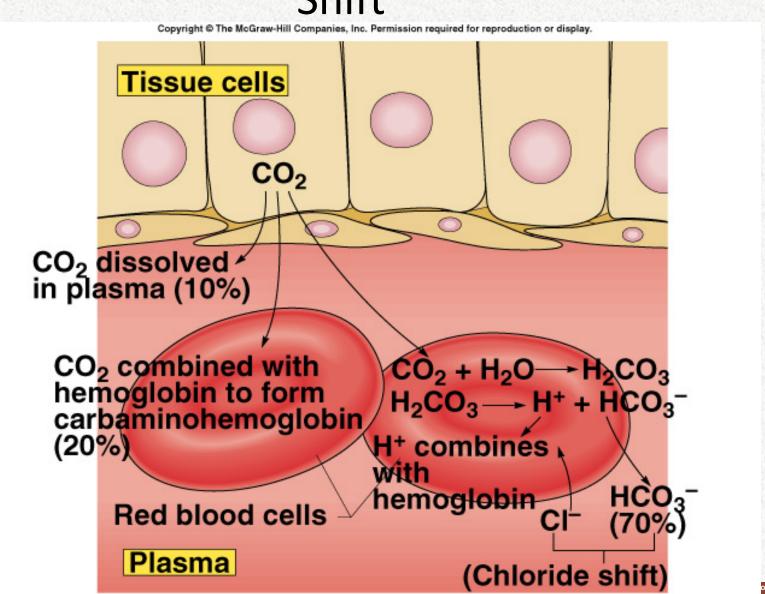
Chloride Shift at Systemic Capillaries

- $H_2O + CO_2 \iff H_2CO_3 \implies H^+ + HCO_3^-$
- At the tissues, CO₂ diffuses into the RBC; shifts the reaction to the right.
 - Increased [HCO₃-] produced in RBC:
 - HCO₃ diffuses into the blood.
 - RBC becomes more +.
 - Cl⁻ attracted in (Cl⁻ shift).
 - H⁺ released buffered by combining with deoxyhemoglobin.
- HbC0₂ formed.
 - Unloading of O_2 .



Carbon Dioxide Transport and Chloride

Shift



of Elsevier Inc



At Pulmonary Capillaries

- $H_2O + CO_2 \iff H_2CO_3 \iff H^+ + HCO_3^-$
- At the alveoli, CO₂ diffuses into the alveoli; reaction shifts to the left.
- Decreased [HCO₃⁻] in RBC, HCO₃⁻ diffuses into the RBC.
 - RBC becomes more -.
 - Cl⁻ diffuses out (reverse Cl⁻ shift).
- Deoxyhemoglobin converted to oxyhemoglobin.
 - Has weak affinity for H⁺.
- Gives off HbCO₂.

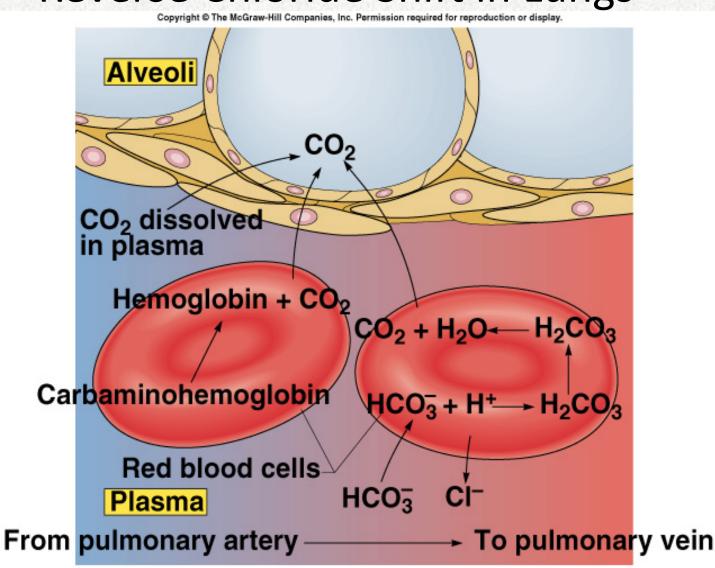


Increased Oxygen Delivery to Tissue

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

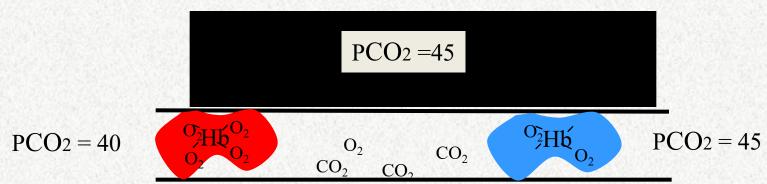


Reverse Chloride Shift in Lungs

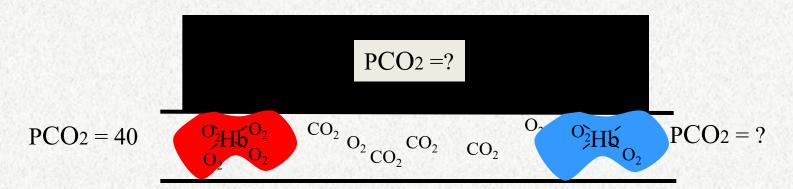




Blood and Muscle PCO₂

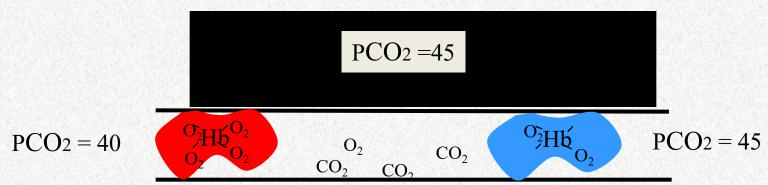


Increased Metabolism and normal blood flow

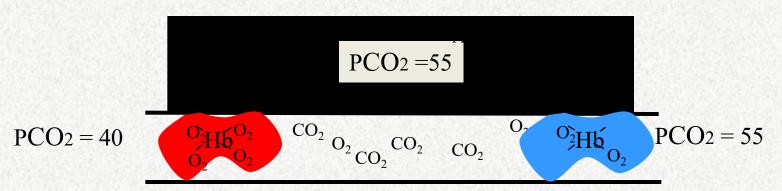




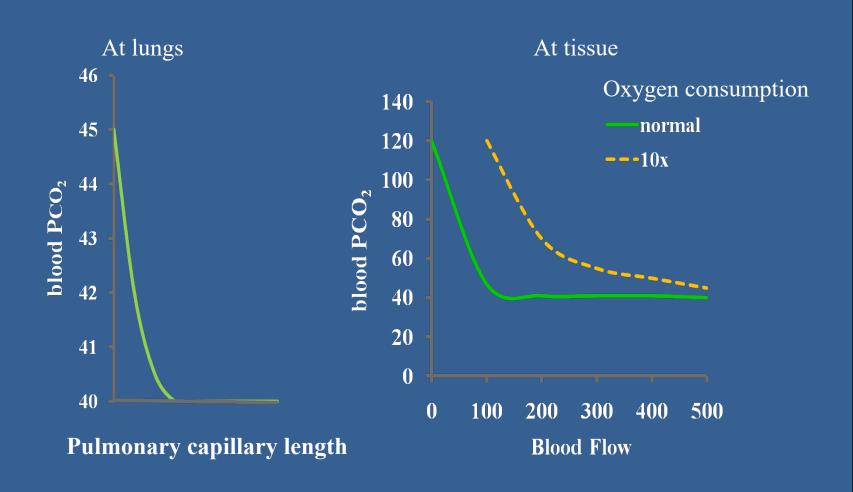
Blood and Muscle PCO₂



Increased Metabolism and normal blood flow

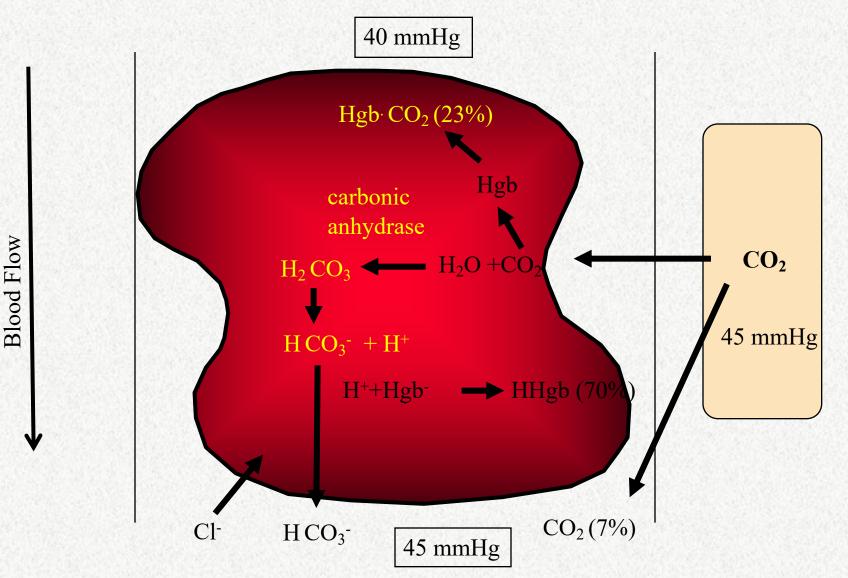


Diffusion of Carbon Dioxide



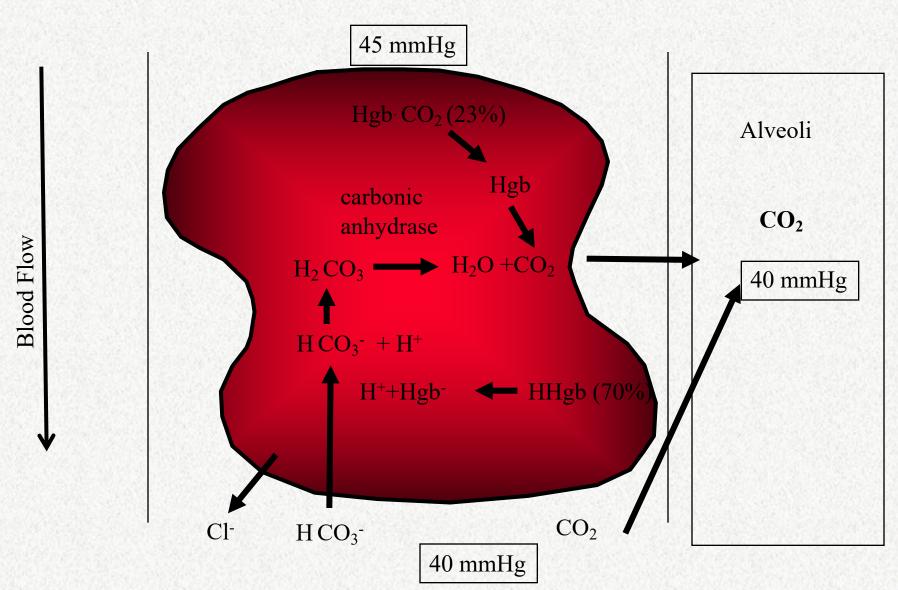


Transport of Carbon Dioxide at Tissue





Transport of Carbon Dioxide at Lung



Carbon Dioxide Dissociation Curve

