## UNIT VII

## GUYTON AND HALL Textbook of Medical Physiology <br> TWELFTH EDITION

Chapter 40:


## Transport of Oxygen and Carbon Dioxide in Blood and Tissue Fluids

## 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 $\mathrm{O}_{2}$ is $21 \mathrm{ml} / \mathrm{min} / \mathrm{mm} \mathrm{Hg}$
- Normal value for $\mathrm{CO}_{2}$ is about 20 times greater than $\mathrm{O}_{2}$.
- 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.
- The surface area of the membrane is $50-100 \mathrm{~m}^{2}$..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 / V 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
- Pulmonary circulation $=5 \mathrm{~L} / \mathrm{min}$ through lung
- Systemic circulation $=5 \mathrm{~L} / \mathrm{min}$ 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

$$
\text { Diffusion }=\frac{\left(\mathrm{P}_{1}-\mathrm{P}_{2}\right) * \text { Area } * \text { Solubility }}{\text { Thickness } * \sqrt{\text { MW }}}
$$

- 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


## Diffusion Capacity

Oxygen
Diff capacity 22 $\mathrm{ml} / \mathrm{min} / \mathrm{mmHg}$ * gradient of 11 mmHg
$250 \mathrm{ml} / \mathrm{min}$ diffusion of oxygen


Capillary Length

## Diffusion Capacity

Carbon Dioxide Diff capacity 400 $\mathrm{ml} / \mathrm{min} / \mathrm{mm} \mathrm{Hg}$ * gradient $<1 \mathrm{mmHg}$ $200 \mathrm{ml} / \mathrm{min}$ diffusion of carbon dioxide


## Oxygen Diffusion from the Alveoli to the Pulmonary circulation

- $\mathrm{O}_{2}$ diffuses into the pulmonary capillaries because the $\mathrm{PO}_{2}$ in the alveoli is high. Note: $\mathrm{O}_{2}$ utilizes less than one third of the respiratory membrane...perfusionlimited
- $\mathrm{PO}_{2}$ 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



## Uptake of Oxygen in Lungs



## Why $\mathrm{PO}_{2}$ arterial <Alveolar $\mathrm{PO}_{2}$ ?

- $\mathrm{P}_{\mathrm{A}} \mathrm{O}_{2}=100$ while systemic $\mathrm{P}_{\mathrm{a}} \mathrm{O}_{2}$ 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.


## Transport in arterial blood \& Pulmonary shunt flow

Due to the bronchial circulation the arterial $\mathrm{PO}_{2}$ falls to 95 mm Hg


## Alveolar and Blood Gases



## Alveolar and Blood $\mathrm{PO}_{2}$

$$
\mathrm{PO}_{2}=159
$$



## Hemoglobin and $\mathrm{O}_{2}$ Transport

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$=5$ million per $\mu \mathrm{l}$ blood million $\mathrm{Hb} / \mathrm{RBC}$.
h Hb has 4 polypeptide ins and 4 hemes.
he center of each heme up is 1 atom of iron can combine with 1 ecule $\mathrm{O}_{2}$.

> Gas tank
> $\mathrm{P}_{\mathrm{O}_{2}}=100 \mathrm{mmHg}$

## Alveolar and Blood $\mathrm{PO}_{2}$



## Question....

A vasodilator is infused into a paralyzed muscle. What happens to $\mathrm{PO}_{2}$ within that muscle?
A. Increases
B. Decreases
C. No change

## Question

Arterial $\mathrm{PO}_{2}$ is 100 mmHg and content is $20 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}$. What is arterial $\mathrm{PO}_{2}$ if $1 / 2$ of all of the red cells are removed?
A. $\mathrm{PO}_{2}=0 \mathrm{mmHg}$
B. $\mathrm{PO}_{2}=30 \mathrm{mmHg}$
C. $\mathrm{PO}_{2}=50 \mathrm{mmHg}$
D. $\mathrm{PO}_{2}=60 \mathrm{mmHg}$
E. $\mathrm{PO}_{2}=100 \mathrm{mmHg}$

## Question

Systemic arterial $\mathrm{PO}_{2}$ is 100 mmHg and hematocrit is $40 \%$. What is systemic arterial $\mathrm{PO}_{2}$ if blood is added to increase hematocrit to 50 ?
A. $\mathrm{PO}_{2}=50 \mathrm{mmHg}$
B. $\mathrm{PO}_{2}=70 \mathrm{mmHg}$
C. $\mathrm{PO}_{2}=100 \mathrm{mmHg}$
D. $\mathrm{PO}_{2}=120 \mathrm{mmHg}$
E. $\mathrm{PO}_{2}=149 \mathrm{mmHg}$

## Hypothetical

- What happens to mixed venous $\mathrm{PO}_{2}$ in an anemic person?
- Normal
- Lower
- Higher


## Question

A person is breathing from a gas tank containing $45 \%$ oxygen. What is the alveolar $\mathrm{PO}_{2}$ ?
A. 149 mmHg
B. 250 mmHg
C. 270 mmHg
D. 320 mmHg
E. 340 mmHg

## Answer

$760-47=713$
$713 * 0.45=321 \mathrm{mmHg}=$ inspired $\mathrm{PO}_{2}$

Alveolar $\mathrm{PO}_{2}=321-(40 / 0.8)=321-50=$
271 mmHg

## Blood and Muscle $\mathrm{PO}_{2}$

$\mathrm{PO}_{2}=100$
$\mathrm{PO}_{2}=40$


## Increased Flow and normal metabolism

$\mathrm{PO}_{2}=100$


## Blood and Muscle $\mathrm{PO}_{2}$

$\mathrm{PO}_{2}=100$


Increased Flow and normal metabolism
$\mathrm{PO}_{2}=100$


## Blood and Muscle $\mathrm{PO}_{2}$

$\mathrm{PO}_{2}=100$


Increased Metabolism and normal blood flow


## Blood and Muscle $\mathrm{PO}_{2}$

$\mathrm{PO}_{2}=100$


Increased Metabolism and normal blood flow


## $\mathrm{PO}_{2}$ in systemic circulation (Diffusion from peripheral capillaries)

- Oxygen is always being used by the cells. Therefore, the intracellular $\mathrm{PO}_{2}$ in the peripheral tissue cells remains lower than the $\mathrm{PO}_{2}$ in the peripheral capillaries.



## Increased Blood Flow to Tissue

- Normal blood flow
- $200 \mathrm{ml} \mathrm{O}_{2} /$ lit of arterial blood * 5 lit blood $/ \mathrm{min}=$ $1000 \mathrm{ml} / \mathrm{min}$
- $\mathrm{VO}_{2} / \mathrm{min}$... 250 ml are consumed at rest ( $25 \%$ )
- Utilization Coefficient or (Extraction ratio):
- Is the \% of blood that gives up its $\mathrm{O}_{2}$ as it passes through tissue capillaries. Normally is $25 \%$. In exercise $75 \%-85 \%$. In some local tissues with extremely high metabolic rate $\rightarrow$ $100 \%$.


## $\mathrm{O}_{2}$ Uptake during Exercise

- $\mathrm{VO}_{2}$ increases during exercise until it reaches $\mathrm{VO}_{2}$ max... what limits $\mathrm{VO}_{2}$ max...lung? CVS? number of mitochondria?
- Increased cardiac output and thus muscle blood flow and extraction ratio...all make more $\mathrm{O}_{2}$ 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 $\mathrm{PO}_{2}$ of $95-100 \mathrm{mmHg}$
Tissue has a $\mathrm{PO}_{2}$ of $30-40 \mathrm{mmHg}$
Tissue $\mathrm{PO}_{2}$ is determined by balance of O 2 delivery and O 2 usage.

## Partial Pressures of Gases in Inhaled Air

| $\mathrm{PN}_{2}$ | $=0.786$ | $\times 760 \mathrm{~mm} \mathrm{Hg}$ | $=597.4 \mathrm{mmHg}$ |
| :--- | :--- | :--- | :--- |
| $\mathrm{P}_{\mathrm{O} 2}$ | $=0.209$ | $\times 760 \mathrm{~mm} \mathrm{Hg}$ | $=158.8 \mathrm{mmHg}$ |
| $\mathrm{P}_{\mathrm{H} 2 \mathrm{O}}$ | $=0.004$ | $\times 760 \mathrm{~mm} \mathrm{Hg}$ | $=3.0 \mathrm{mmHg}$ |
| $\mathrm{P}_{\mathrm{CO} 2}$ | $=0.0004$ | $\times 760 \mathrm{~mm} \mathrm{Hg}$ | $=0.3 \mathrm{mmHg}$ |
| $P_{\text {other gases }}$ | $=0.0006$ | $\times 760 \mathrm{~mm} \mathrm{Hg}$ | $=0.5 \mathrm{mmHg}$ |
|  |  | TOTAL | $=760.0 \mathrm{mmHg}$ |

## Composition of Alveolar Air—lts Relation to Atmospheric Air

|  | Inhaled <br> Atmospheric Air |  | Humidified <br> Air | Alveolar Air | Expired <br> Air |
| :--- | :---: | :---: | :---: | :---: | :---: |
|  | mm Hg | $\%$ | mm Hg | mm Hg | mm Hg |
| $\mathbf{P N}_{\mathbf{2}}$ | 597 | 78.6 | 563 | 569 | 566 |
| $\mathbf{P O}_{\mathbf{2}}$ | $\mathbf{1 5 9}$ | $\mathbf{2 0 . 8}$ | $\mathbf{1 4 9}$ | $\mathbf{1 0 4}$ | $\mathbf{1 2 0}$ |
| $\mathbf{P C O}_{\mathbf{2}}$ | 0.3 | 0.04 | 0.3 | 40 | 27 |
| $\mathbf{P H}_{\mathbf{2}} \mathbf{O}$ | $\mathbf{3 . 7}$ | $\mathbf{0 . 5}$ | $\mathbf{4 7}$ | $\mathbf{4 7}$ | $\mathbf{4 7}$ |
| $\mathbf{T o t a l}$ | 760 | 100 | 760 | 760 | 760 |

## GASICONTENT OF B L OOD.

- One DL of Blood Contains 15 g of Hemoglobin
- One DL of arterial Blood Contains $\mathbf{2 0 ~ m l}$ of $\mathbf{O}_{2}$
- Arterial Blood
( $\mathrm{PO}_{2} 95 \mathrm{~mm} \mathrm{Hg}$;
$\mathrm{PCO}_{2} 40 \mathrm{~mm} \mathrm{Hg}$;
Hb 97\% Saturated)
- Venous Blood
( $\mathrm{PO}_{2} 40 \mathrm{~mm} \mathrm{Hg}$;
$\mathrm{PCO}_{2} 45 \mathrm{~mm} \mathrm{Hg} ;$
Hb 75\% Saturated)


## Oxygen Transport

- Partial Pressure (mm Hg)
- driving force for diffusion
- Percent Saturation (no units) $\mathrm{HbO}_{2}$
$\left(\mathrm{Hb}+\mathrm{O}_{2}\right)$ is called oxyHb
- Content ( $\mathrm{ml} \mathrm{O}_{2} / 100 \mathrm{ml}$ 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 $=\mathrm{PaO}_{2}$ X Solubility of $\mathrm{O}_{2}$ Solubility 0.003 ml $\mathrm{O}_{2} / 100 \mathrm{ml}$ blood
-     - In normal blood; the $\left[\mathrm{O}_{2}\right]$ in its dissolved form is equal to $=$ $0.3 \mathrm{ml} \mathrm{O}_{2} / 100 \mathrm{ml}$ blood
- Normal oxygen consumption $250 \mathrm{ml} \mathrm{O}_{2} / \mathrm{min}$
- Would require 83 1/min blood flow
- Hemoglobin
$-97 \%$ of the transported O 2 is in this form

$$
\mathrm{O}_{2}+\mathrm{Hb} \quad \rightleftarrows \mathrm{HbO}_{2}
$$

## Law of dissolved gases

Oxygen
Carbon dioxide
Carbonmonoxide
0.024

Nitrogen
0.57

Helium
0.012
0.008

- Much more $\mathrm{CO}_{2}$ is dissolved in blood than $\mathrm{O}_{2}$ because $\mathrm{CO}_{2}$ is 20 times more soluble.
- The air we breathe is mostly $\mathrm{N}_{2}$, 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 $\mathrm{O}_{2}$ 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).

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$-2,3 \mathrm{BPG}$ is inside RBC. If no DPG the $\mathrm{HbO}_{2}$ 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 $\mathrm{CO}_{2}$ to HCO , otherwise by using Acetazolamide (CA inhibitor) $\mathrm{PCO}_{2}$ reaches 80 mmHg
- Prevent $\uparrow$ in blood viscosity.


## Oxygen Binding and Unloading

Oxyhaemoglobin
Deoxyhaemoglobin
Mol weight: 64460


- 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 ( $\mathrm{Fe}^{2+}$ ).
- $\mathrm{Fe}^{2+}$ 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 $\mathrm{O}_{2}$.


## Hemoglobin

- Methemoglobin:
- Has iron in the oxidized form ( $\mathrm{Fe}^{+++}$).
- Blood normally contains a small amount. but ferric $\mathrm{Fe}^{+3}$ which is useless because it does not release $\mathrm{O}_{2}$. 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 $\mathbf{2 5 0}$ times stronger than the bond with oxygen.
- Therefore, transport of $\mathrm{O}_{2}$ to tissues is impaired.


## Hemoglobin (ominesen

- 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 $\mathrm{PO}_{2}$
- Loading/unloading depends:
$-\mathrm{PO}_{2}$ of environment.
- Affinity between hemoglobin and $\mathrm{O}_{2}$.


## Oxyhemoglobin Dissociation Curve

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


## Oxyhemoglobin Dissociation Curve

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## Effect of 2,3 DPG on $\mathrm{O}_{2}$ 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
$\longrightarrow \longrightarrow$
- Fetal hemoglobin (HbF):
- Has $2 \gamma$-chains in place of the $\beta$-chains... $\gamma$ chain does not bind $2,3, \mathrm{DPG} . .$. therefore, HbF has higher affinity towards $\mathrm{O}_{2} \ldots$ make sense...mother's placenta PO2 is low ( $<40 \mathrm{mmHg}$ )


## Effects of pH and Temperature

The loading and unloading of $\mathrm{O}_{2}$ influenced by the affinity of hemoglobin for $\mathrm{O}_{2}$.
Affinity is decreased by:
$\downarrow$ blood pH
$\uparrow$ temperature
个 2,3-DPG
个 PCO2

- All Shift the curve to the right.



## Values to remember

- $\mathrm{PO}_{2}$
- 10
- 20
- 25
- 30
- 40
- 50
- 60
- 80
- 100

Remember this rule...it is close enough!
4,5, 6
$\mathrm{Po}_{2}(\mathrm{mmHg})$
\%Sat
$4050 \quad 60$
708090

## $\mathrm{O}_{2}$ Sat (\%)

2535$50 \quad P_{50}$60

75 Venous85

90 Respiratory center stimulation
96
98
Almost Fully saturated

## Dissociation Curve



## Hemoglobin Dissociation Curve



## Hemoglobin Dissociation Curve



## Hemoglobin Dissociation Curve



## Shifts of Dissociation Curve

- Right shift occurs at tissue level...Bohr's effect
$-\uparrow \mathrm{PaCO}_{2}$ or $\uparrow$ arterial $\mathrm{H}^{+} \rightarrow \downarrow$ affinity for oxygen or increase $\mathrm{O}_{2}$ 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 $\rightarrow \uparrow$ 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\%


## 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: $\mathrm{PO}_{2}$ of 60 mmHg correspond to $90 \%$ saturation
- Tissue
- Normal: consume $5 \mathrm{ml} \mathrm{O}_{2} / 100 \mathrm{ml}$ blood $\left(\mathrm{P}_{\mathrm{i}} \mathrm{O}_{2}\right.$ is 40 mmHg )
- During exercise: 15 ml of $\mathrm{O}_{2} / 100 \mathrm{ml}$ blood $\left(\mathrm{P}_{\mathrm{i}} \mathrm{O}_{2}\right.$ is only 20 mmHg )


## Question

A person has a hemoglobin concentration of 10 $\mathrm{gm} / \mathrm{dl}$. The arterial oxygen content is 6.5 ml $\mathrm{O}_{2} / \mathrm{dl}$. What is the saturation?
A. $25 \%$
B. $50 \%$
C. $75 \%$

D 100\%

## Calculations

- Calculate \% saturation
- Patient has Hb of $10 \mathrm{gm} / \mathrm{dl}$
- Venous oxygen content is $6.5 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}$
- Calculate oxygen content
- Patient has saturation of $60 \%$
- Patient has Hb of $15 \mathrm{gm} / \mathrm{dl}$


## Calculations

- Calculate \% saturation
$-10 \mathrm{gm} / \mathrm{dl} * 1.34 \mathrm{ml} \mathrm{O}_{2} / \mathrm{gm} \mathrm{Hb}=13.4 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}$
- This is max oxygen carrying capacity
$-\left(6.5 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}\right) /\left(13.4 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}\right)=\sim 50 \%$
- Calculate oxygen content
$-15 \mathrm{gm} / \mathrm{dl} * 1.34 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}=20 \mathrm{ml} \mathrm{O} / \mathrm{dl}$
- This is max oxygen carrying capacity
$-20 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl} * 60 \%$ saturation $=12 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}$


## Calculations

- Assume Hb is $10 \mathrm{gm} / \mathrm{dl}$
- $100 \%$ saturation give a content of $13.4 \mathrm{ml} / \mathrm{dl}$ blood
- At rest body uses $5 \mathrm{ml} \mathrm{O}_{2} / \mathrm{dl}$
- This leaves a mixed venous content of 8.4 $\mathrm{ml} / \mathrm{dl}$
- 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. $\mathrm{CO}_{2}$ dissolved in plasma
d. $\mathrm{CO}_{2}$ 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 $\boldsymbol{\beta}$ chains.
- Cross links form a "paracrystalline gel" within the RBCs.
- Makes the RBCs less flexible and more fragile.
- Thalassemia:
- Decreased synthesis of $\alpha$ or $\beta$ chains, increased synthesis of $\gamma$ 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 $\mathrm{O}_{2}$ than hemoglobin.
- May act as a "go-between" in the transfer of $\mathrm{O}_{2}$ from blood to the mitochondria within muscle cells.

- May also have an $\mathrm{O}_{2}$ storage function in cardiac muscles.

TRANSPORTED FROM THE BODY CELLS BACK TO THE LUNGS (TIDAL $\mathrm{CO}_{2}$ ) AS (THE 4 ML ):
$\square$ Phy. Soln. ■ CarbaminoHb ■ Bicarbonate
10\%


## CARBON DIOXIDE IN BLOOD

## Fate of $\mathrm{CO}_{2}$ in blood

## In plasma

1. Dissolved
2. Formation of carbamino compounds with plasma protein
3. Hydration, $\mathrm{H}^{+}$buffered, $\mathrm{HCO}_{3}^{-}$in plasma

## In red blood cells

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

## CARBON DIOXIDE IN BLOOD



(a) Exchange of $\mathrm{O}_{2}$ and $\mathrm{CO}_{2}$ in pulmonary capillaries (external respiration)

(b) Exchange of $\mathrm{O}_{2}$ and $\mathrm{CO}_{2}$ in systemic capillaries (internal respiration)

Figure 23.23 Tortora - PAP 12/e
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## $\mathrm{CO}_{2}$ Transport

- $\mathrm{CO}_{2}$ transported in the blood (the 4 ml ):
$-\mathrm{HCO}_{3}{ }^{-}$(60\%).
- Dissolved $\mathrm{CO}_{2}$ (10\%).
-Carbaminohemoglobin (30\%).

$$
\mathrm{H}_{2} \mathrm{O}+\mathrm{CO}_{2} \stackrel{\text { cA }}{\leftrightharpoons} \mathrm{H}_{2} \mathrm{CO}_{3}
$$

High $\mathrm{PCO}_{2}$


## $\mathrm{CO}_{2}$ TRANSPORT

## Arterial

Venous
43.2 (90\%)
$22.73 \mathrm{mM} / 1$
45.6 (88\%)
$24 \mathrm{mM} / 1$
$\mathrm{HbCO}_{2}$
2.4(5\%)
3.6 (7 \%)
1.2 (30\%)

Dissolved $\mathrm{CO}_{2}$
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: $2.7 \mathrm{ml} / 100 \mathrm{ml}$ blood
- arterial blood: $2.4 \mathrm{ml} / 100 \mathrm{ml}$ blood
- transported : $0.3 \mathrm{ml} / 100 \mathrm{ml}$ blood
$-7 \%$ total


## Chlöride Shift at Systemic Capillaries

- $\mathrm{H}_{2} \mathrm{O}+\mathrm{CO}_{2} \Leftrightarrow \mathrm{H}_{2} \mathrm{CO}_{3} \Longleftrightarrow \mathrm{H}^{+}+\mathrm{HCO}_{3}^{-}$
- At the tissues, $\mathrm{CO}_{2}$ diffuses into the RBC; shifts the reaction to the right.
- Increased $\left[\mathrm{HCO}_{3}^{-}\right]$produced in RBC:
- $\mathrm{HCO}_{3}$ - diffuses into the blood.
- RBC becomes more +.
- $\mathrm{Cl}^{-}$attracted in ( $\mathrm{Cl}^{-}$shift).
$-\mathrm{H}^{+}$released buffered by combining with deoxyhemoglobin.
- $\mathrm{HbCO}_{2}$ formed.
- Unloading of $\mathrm{O}_{2}$.


## Carbon Dioxide Transport and Chloride

## Shift



## At Pulmonary Capillaries

- $\mathrm{H}_{2} \mathrm{O}+\mathrm{CO}_{2} \Longleftrightarrow \mathrm{H}_{2} \mathrm{CO}_{3} \Longleftrightarrow \mathrm{H}^{+}+\mathrm{HCO}_{3}^{-}$
- At the alveoli, $\mathrm{CO}_{2}$ diffuses into the alveoli; reaction shifts to the left.
- Decreased $\left[\mathrm{HCO}_{3}^{-}\right]$in $\mathrm{RBC}, \mathrm{HCO}_{3}^{-}$diffuses into the RBC.
- RBC becomes more -.
- Cl - diffuses out (reverse Cl - shift).
- Deoxyhemoglobin converted to oxyhemoglobin.
- Has weak affinity for $\mathrm{H}^{+}$.
- Gives off $\mathrm{HbCO}_{2}$.


## 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 



From pulmonary artery $\longrightarrow$ To pulmonary vein

## Blood and Muscle $\mathrm{PCO}_{2}$

$\mathrm{PCO}_{2}=40$

$$
\mathrm{PCO}_{2}=45
$$



Increased Metabolism and normal blood flow


## Blood and Muscle $\mathrm{PCO}_{2}$

$\mathrm{PCO}_{2}=40$

$$
\mathrm{PCO}_{2}=45
$$

## 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



