THE RESPIRATORY SYSTEM II

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I. Chemichal & physiologic events affecting diffusion of O_2 & CO_2
II. Exchange of O_2 & CO_2 during respiration
III. Transport O_2 in blood
IV. Transport CO_2 in blood
V. Respiratory regulation of acid base balance
VI. Measurement of acid base balance : pH of blood

RESPIRATION

: the interchange of O_2 & CO_2 between the body and its environment

Processes :

1. Pulmonary ventilation
2. The difusion O_2 & CO_2 between the alveoli and the blood
3. The transport of O_2 & CO_2 to and from the cells of the organism via the blood
4. The regulation of ventilation

External Respiration/pulmonary gas exchange

: the diffusion of O2 from air in the alveoli of the lungs to the blood in pulmonary capillaries and diffusion of CO2 from the blood in pulmonary capillaries to the air in the alveoli of the lungs

Internal Respiration/ systemic gas exchange

: The exchange of O2 and CO2 between systemic capillaries and tissue cells

I.Chemichal & physiologic events affecting diffusion of O_2 & CO_2

Boyle's Law

Pressure X Volume = Constant

Gay-Lussac's Law

Volume = Constant X temperature(K)

Ideal Gas Law

$PV = nRT$

- Dalton's Law
- : each gas in a mixture of gases exerts its own pressure as if no other gases were present.

The pressure of a specific gas in a mixture is called its partial pressure (P_x)

The total pressure of the mixture :

by adding all the partial pressures

Atmospheric pressure (760 mmHg)

$$P_{N2} + P_{O2} + P_{H2O} + P_{CO2} + \mathbf{P}_{other\ gases}$$

- The partial pressure determine the movement of O_2 and CO_2 between :
- - the atmospheric and lungs

  - the lungs and blood

  - the blood and body cells.

Each gas diffuses across a permeable membrane from the area where its partial pressure is greater to the area where its partial pressure is less.

The greater the difference in partial pressure, the faster the rate of diffusion

- Atmospheric air contains
- Nitrogen : 78.62%
- Oxygen : 20.84%
- Carbon dioxide : 0.04%
- Water : 0.5%

- At 37°C, the water vapor pressure is 47 mmHg -→
- The sum of the partial pressures of the other components of air must contribute
- 760 – 47 = 713 mmHg

- **Henry's Law**
- : the quantity of a gas that will dissolve in a liquid is proportional to the partial pressure and its solubility.

Much more CO_2 is dissolved in blood plasma because the solubility of CO_2 is 24 times greater than that of O_2

N_2 , has no known effect on bodily functions --→

At sea level pressure very little it dissolves in blood plasma because its solubility is very low

Solubility coefficients gases in water at 37 °C and 1 atm of pressure

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

The rate of diffusion process be influenced by

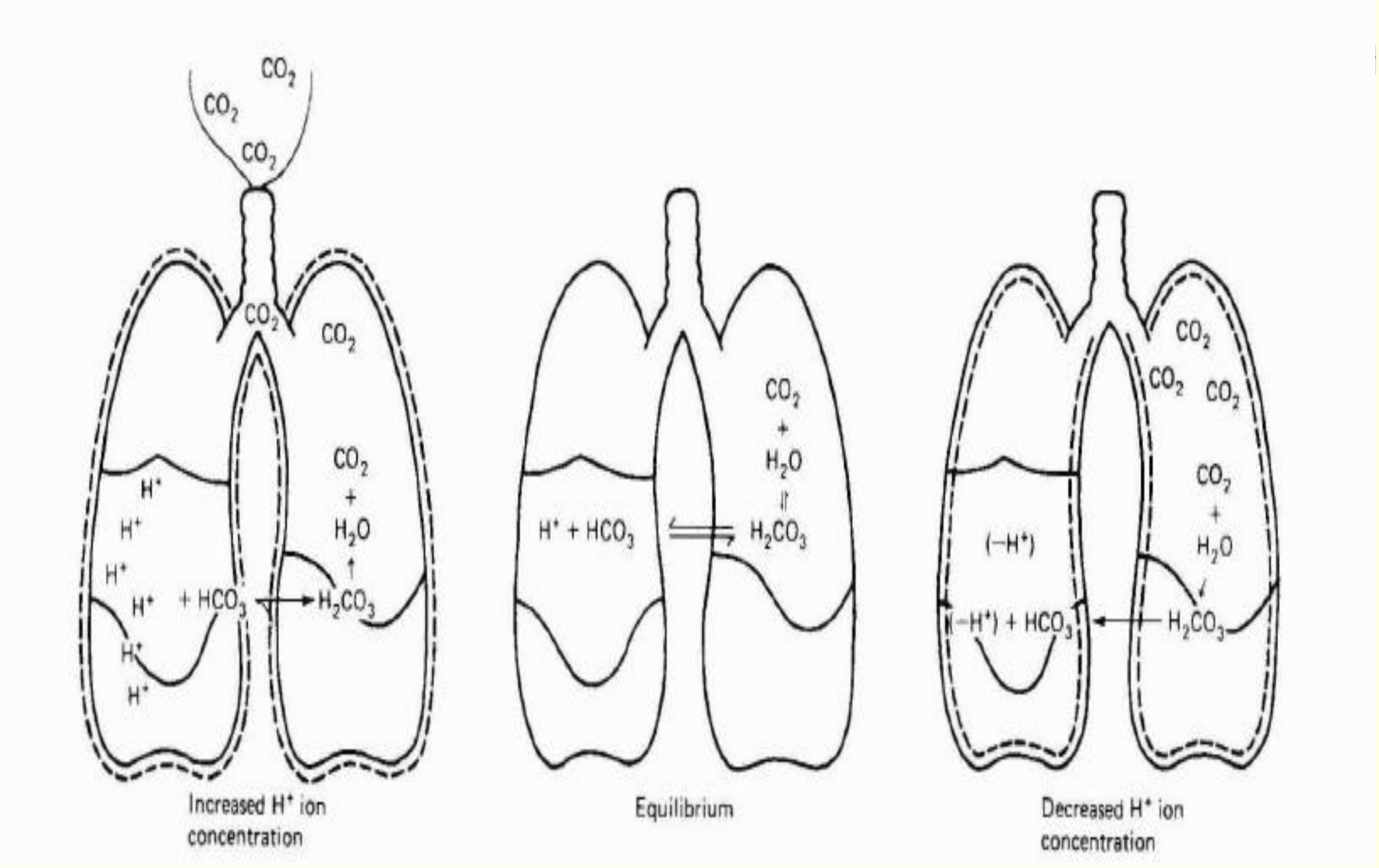
- the difference between the partial pressure of the gas above the liquid and its tension within it
- the cross-sectional area of the gas-liquid interphase
- the distance the molecules
- the solubility of the gas in the liquid
- velocity/kinetic movement of the molecules

The rate of pulmonary and systemic gas exchange depends on :

1. Partial pressure difference of the gases
2. Surface area available for gas exchange
3. Diffusion distance
4. Molecular weight and
5. solubility of gases

$$DR \propto \frac{PD \times A \times S}{D \sqrt{MW}}$$

Regulation of hydrogen ion concentration by the Respiratory System



II. Exchange of O_2 & CO_2 during respiration

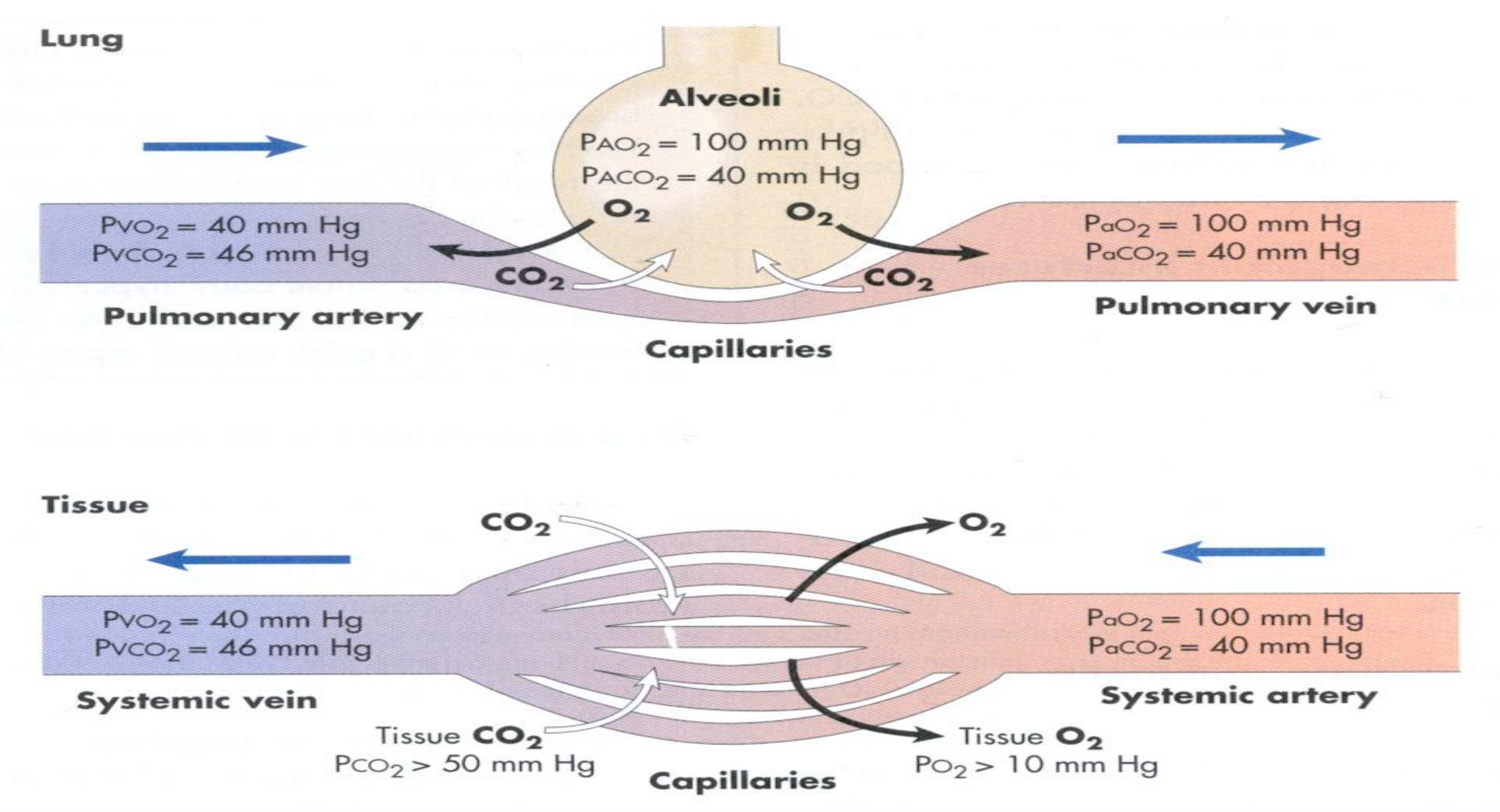
PO_2 of the blood as enters the pulmonary cap : 40 mmHg

PO_2 in alveolus : 104 mmHg

surface area of the membrane is large

membrane is extremely thin → uptake O_2 from the alveolus into the pulmonary cap blood uccurs rapidly

Gas Exchange in Lungs & Tissues



Normal Blood Gas values

Parameter	Arterial	Mixed Venous	Capillary
pH	7.35-7.45	7.31-7.41	7.35-7.45
P_{O_2}	80-100 mmHg	35-40 mmHg	Less than arterial*
O_2 saturation	95%-97%	70%-75%	Less than arterial
P_{CO_2}	35-45 mmHg	40-50 mmHg	35-45 mmHg
HCO_3	22-26 mEq/L	22-26 mEq/L	22-26 mEq/L
Total CO_2 content	20-27 mEq/L	20-27 mEq/L	20-27 mEq/L
Base excess	+2 to −2	+2 to −2	+2 to −2

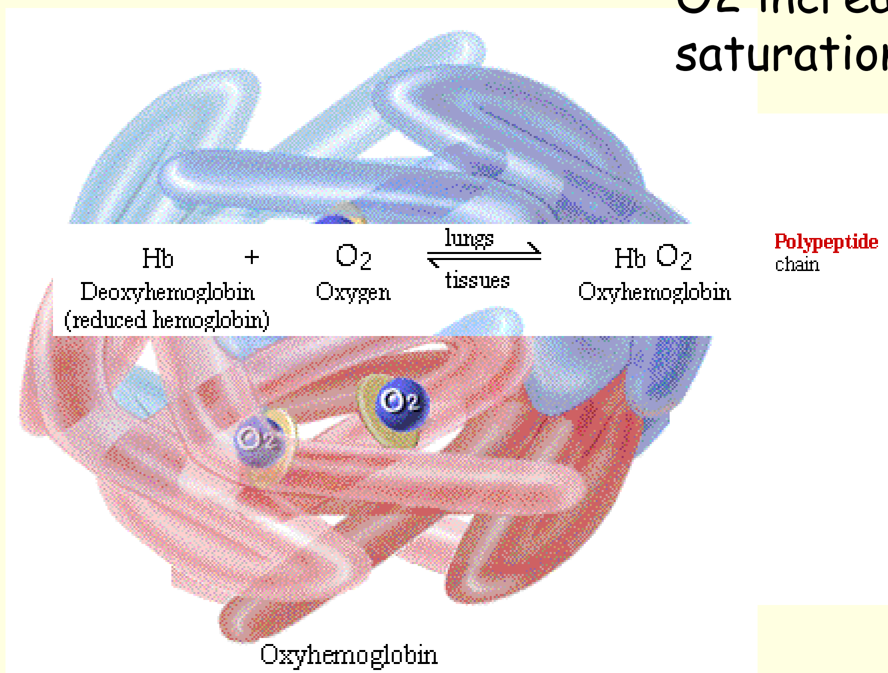
- III. Transport of O_2 in blood
- O_2 is transported by the blood either,
  - Combined with haemoglobin (Hb) in the red blood cells (>98%) or,
  - Dissolved in the blood plasma (<2%).

- Hemoglobine
- - is the principal molecule responsible for transport O_2 & CO_2 in blood
- - normally,97-98% O_2 transported from the lungs to the tissues is carried in reversible combination with the Hb molecule

Haemoglobin

Haemoglobin molecules can transport up to four O2's

Co-operative binding: haemoglobin's affinity for O2 increases as its saturation increases.



When 4 O2's are bound to haemoglobin, it is 100% saturated, with fewer O2's it is partially saturated.

Oxygen binding occurs in response to the high PO2 in the lungs

- **$Hb + O_2 \leftarrow\text{-------}\rightarrow Hb\,O_2$**

- The degree combination of O_2 with Hb or dissociation of Hb O_2 to release O_2 is determined by PO_2 in medium surrounding the Hb

At the PO_2 104 mmHg : Hb ± 97% saturated
at the PO_2 40 mmHg : Hb is 70% saturated

Haemoglobin Saturation

- Haemoglobin saturation is the amount of oxygen bound by each molecule of haemoglobin
- Each molecule of haemoglobin can carry four molecules of O2.
- When oxygen binds to haemoglobin, it forms OXYHAEMOGLOBIN;
- Haemoglobin that is not bound to oxygen is referred to as DEOXYHAEMOGLOBIN.

The relationship between the % saturation of the Hb in blood & PO_2 of the blood

The oxygen dissociation curve of Hb

---→ dependent upon the PCO_2 in the blood

When fully saturated :

1 g Hb combines with 1.34 ml O_2

[Hb] : 14.5 g/dl of blood -→

The total O_2 that could be carried as HbO would be :

$$14.5 \times 1.34 = 19.4 \text{ ml/dl blood}$$

- → + the amount of O_2 physically dissolved in blood 0.33 ml/dl -------→ the total
- O_2capacity of blood approximately 20 ml/dl

- ------→ it is evident that the O_2 capacity of the blood is almost entirely a function of the blood Hb concentration

- Transport of O_2
- - 1.5% dissolved in plasma
- - 98,5 % as Hb- O_2

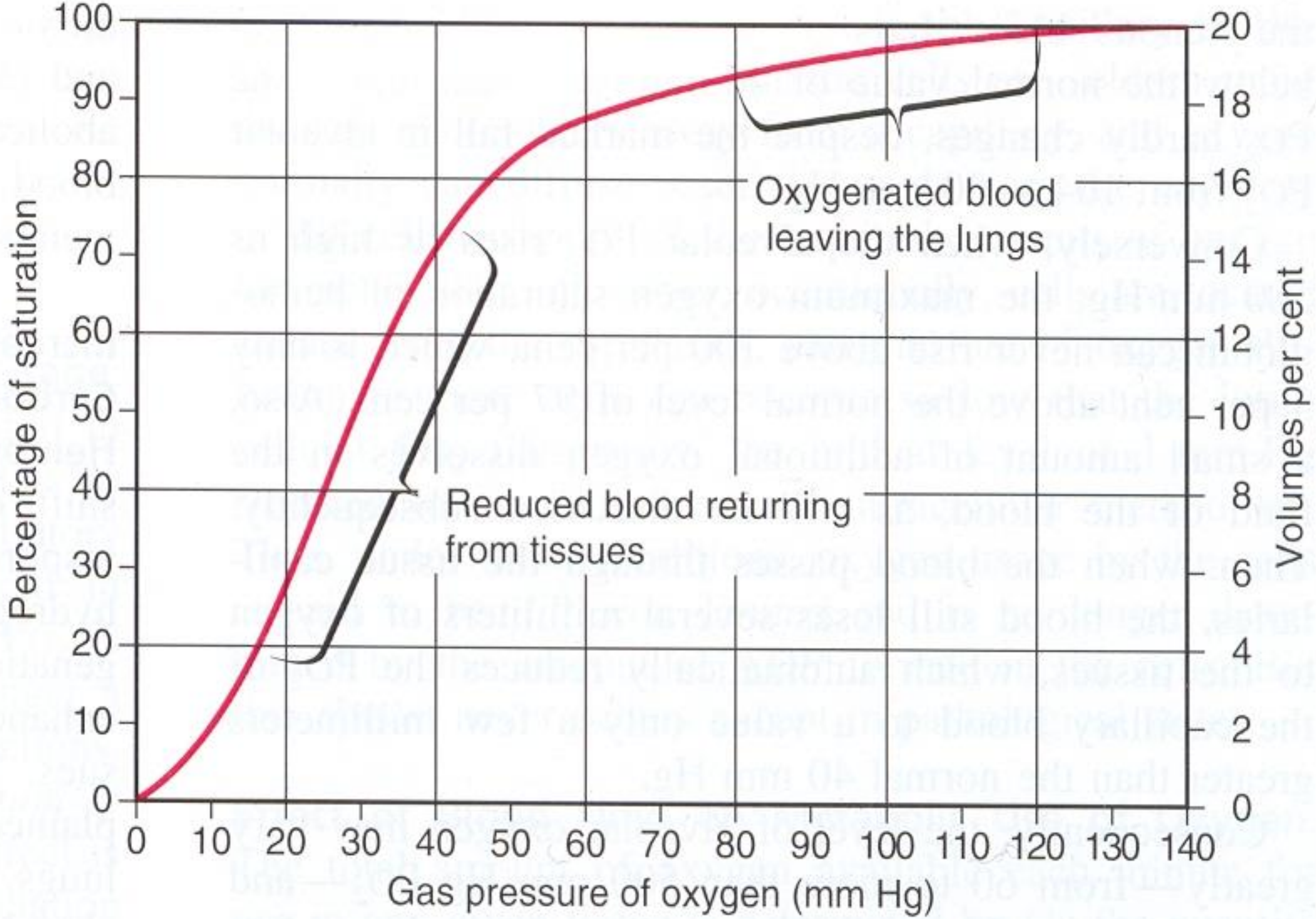
- The shape of the O_2-Hb dissociation curve is "***sigmoid***"

  Is that of normal, pH of blood 7.4 and PCO_2 40 mmHg at sea level

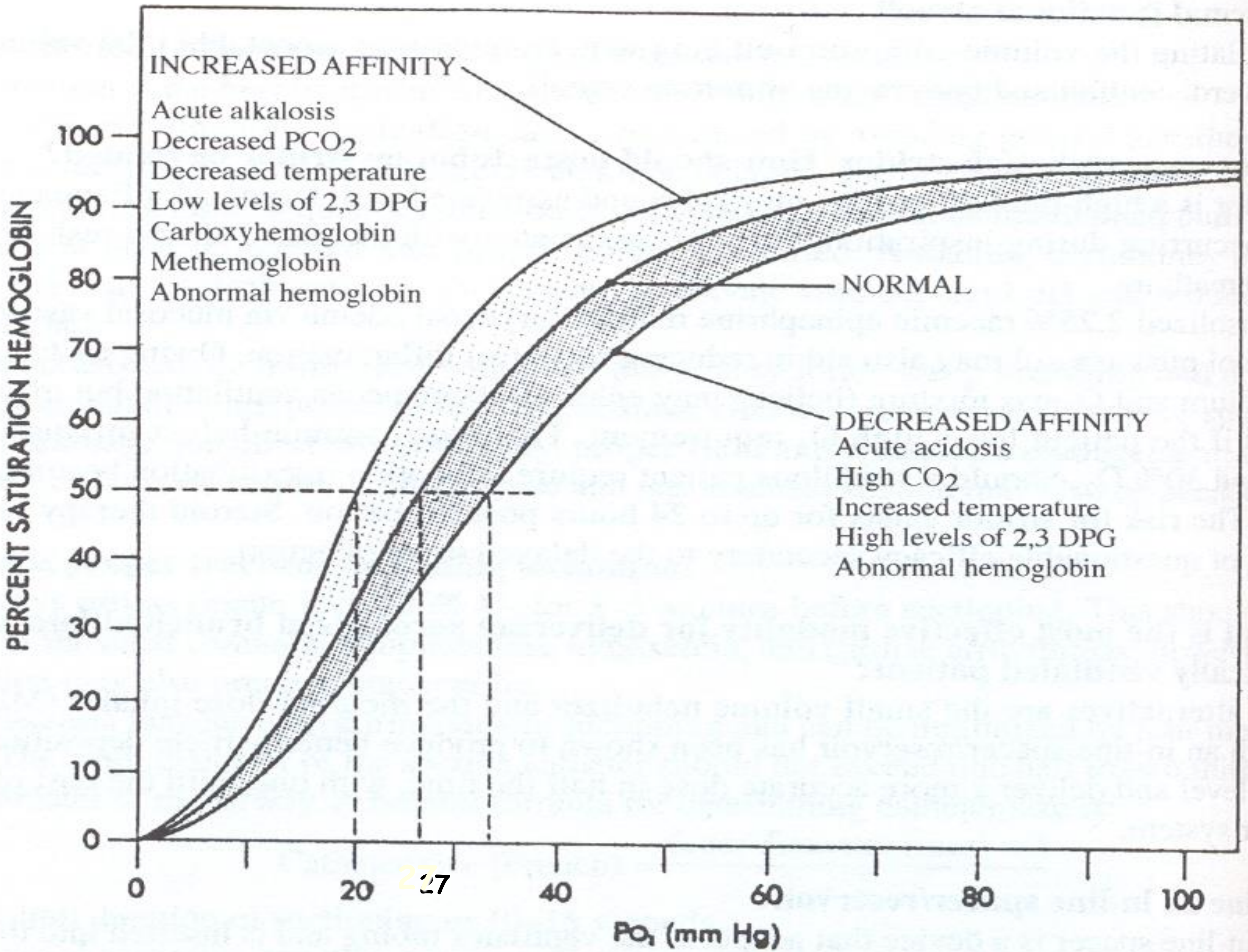
The property of Hb- O_2 interaction result from 2 properties important to the transport of O_2

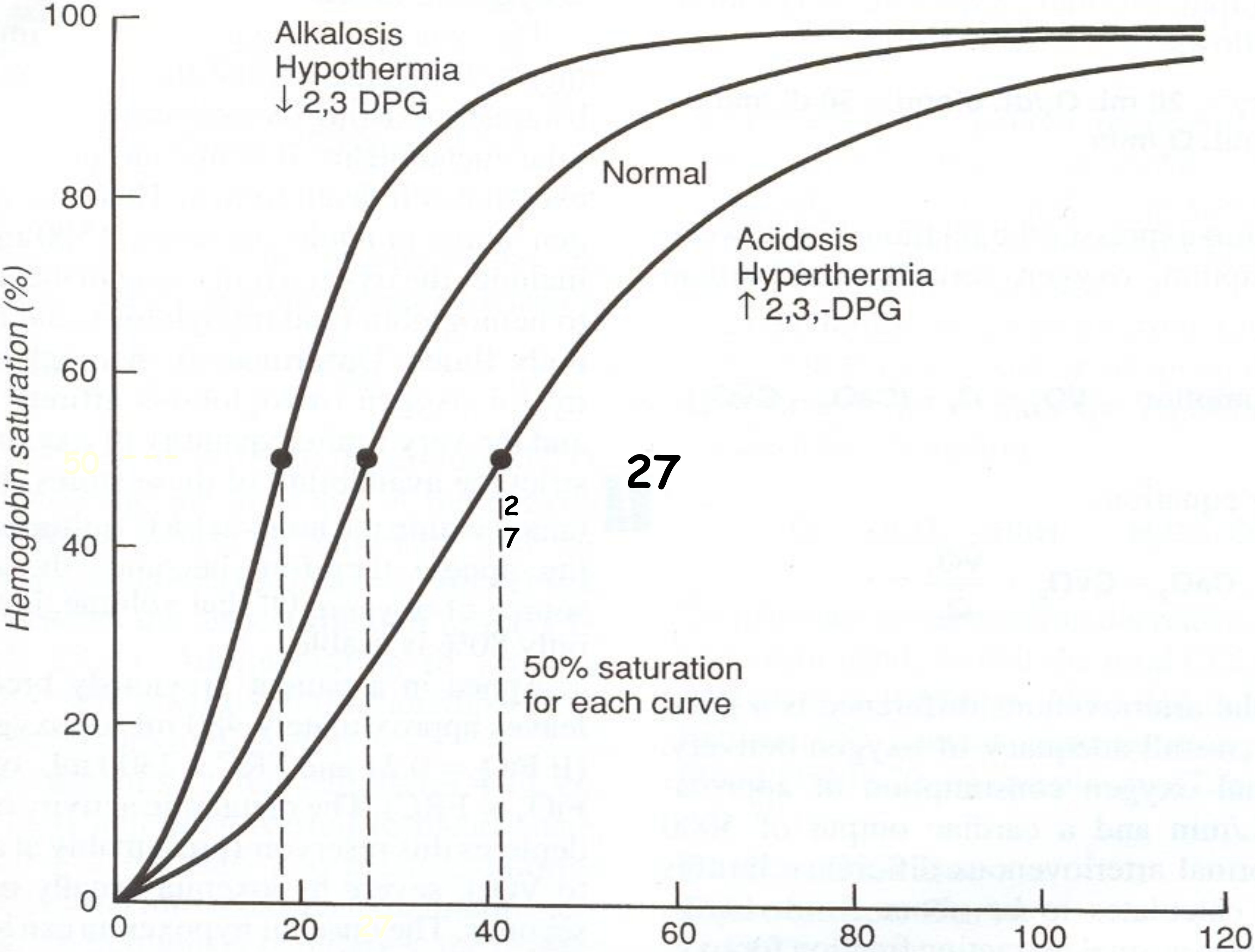
1. The relatively flat portion of the curve above an O_2 tension of 70-80 mmHg result minimal loss of O_2 from Hb

- 2. the precipitous change of the curve below a PO_2 of 40 mmHg ensures that a
- Disproportionately greater release of O_2 from Hb will occur at any given decline in PO_2
- - a shift of the dissociation curve to the right result in greater release of O_2 from the HbO2 at a given PO_2 (decreases the affinity of Hb for O_2)
- - a shift to the left increases the affinity of Hb forO_2



Percentage of saturation
Volumes per cent
Gas pressure of oxygen (mm Hg)
Oxygenated blood leaving the lungs
Reduced blood returning from tissues
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
2
4
6
8
12
14
16
18


INCREASED AFFINITY
Acute alkalosis
Decreased PCO_2
Decreased temperature
Low levels of 2,3 DPG
Carboxyhemoglobin
Methemoglobin
Abnormal hemoglobin
NORMAL
DECREASED AFFINITY
Acute acidosis
High CO_2
Increased temperature
High levels of 2,3 DPG
Abnormal hemoglobin
PERCENT SATURATION HEMOGLOBIN
100
90
80
70
60
50
40
30
20
10
0
0
20
27
40
60
80
100
PO_2 (mm Hg)



Alkalosis
Hypothermia
↓ 2,3 DPG
Normal
Acidosis
Hyperthermia
↑ 2,3,-DPG
27
2
7
50% saturation
for each curve
Hemoglobin saturation (%)
100
80
60
40
20
0
0
20
40
60
80
100
120

The factors that bring about a rightward shift of HbO2 dissociation:

1. increased H^+ or acidity (decreased blood pH)

decreases the affinity of Hb for O_2)

Lactic acid, carbonic acid (from active tissue) bring about a rightward shift of HbO2 dissociation:

Increased blood pH --- increases the affinity of Hb for O_2)

A shift of the HbO2 dissociation curve to the left

2. increased CO_2 tension = Bohr effect

3. increased temperature

in situations where there are increased demands for O_2 by the tissue

4. Increased erythrocyte concentration of 2.3 DPG under stressful situations (decreased atm press)

Association Hb + BPG ---- decreases the affinity of Hb for O_2)

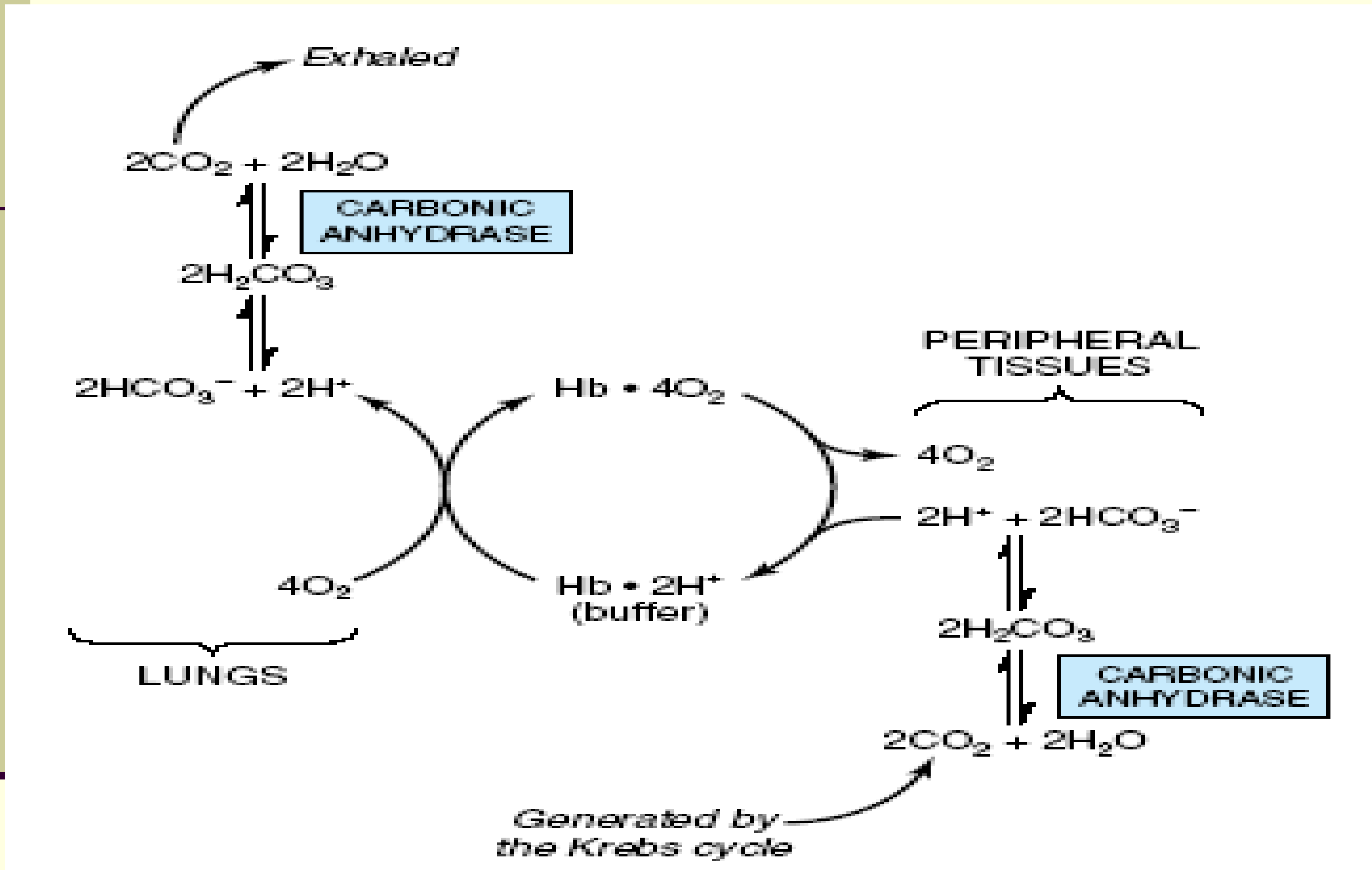
- tiroksin, GH,epinefrin, norepi &testosteron
- ---- increases formation of BPG

- BPG increase in person who lived in high altitute

- A shift of the HbO2 dissociation curve to the left
- - is an incereased content of HbF in the erythrocytes

- **- Carbon Monoxide**
- Haemoglobin binds with carbon monoxide 240 times more readily than with oxygen. The presence of carbon monoxide on one of the 4 haem sites causes the oxygen on the other haem sites to bind with greater affinity. This makes it difficult for the haemoglobin to release the oxygen to the tissues and has the effect of ***shifting the curve to the left***. With an increased level of carbon monoxide, a person can suffer from severe hypoxemia while maintaining a normal pO2.

- **- Effects of Methemoglobinema**
- Methemoglobinemia is a form of abnormal haemoglobin where ferrous (Fe^{2+}), which is normally found in haemoglobin, is converted to the ferric (Fe^{3+}) state. This causes a ***leftward shift in the curve*** and prevents oxygen from being released



- The Bohr effect.

IV. Transport CO_2 in blood

In the blood

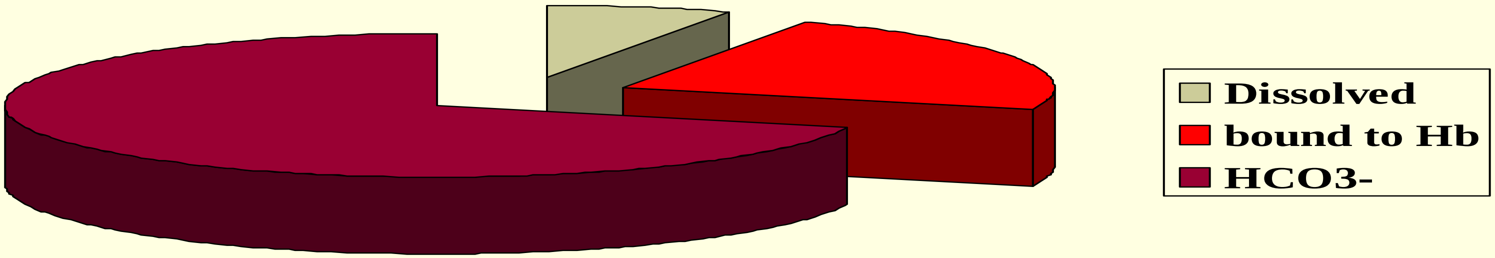
$CO_2 + H_2O \leftarrow\text{--}\rightarrow H_2CO_3 \text{----}\rightarrow H^+ + HCO_3^-$

Carbonic anhidrase enzyme (present in erythrocyte) that catalyzes the reaction, inhibited by acetazol amide

99.9% completion, only 0.1% remains in the undissociated form

Carbon Dioxide Transport

Method	Percentage
• Dissolved in Plasma	7 - 10 %
• Chemically Bound to Hemoglobin in RBC's	20 - 30 %
• As Bicarbonate Ion in Plasma	60 -70 %



- At rest, the metabolizing tissue cells consume about 250 ml of O_2 and produce about 200 ml of carbon dioxide each minute.
- $C_6H_{12}O_6 + 6O_2 > 6CO_2 + 6H_2O + ATP$
- The newly formed carbon dioxide is transported from the tissue cells to the lungs by six different mechanisms, three in plasma and three in RBC's.

In Plasma

- About 1% of the CO_2 that dissolves in the plasma chemically combines with free amino groups and forms a carbamino compound.
- About 5% of the CO_2 that dissolves in plasma ionizes as bicarbonate.
- Dissolved CO_2 in the plasma accounts for about 5% of the total CO_2 released at the lungs.

In Red Blood Cells

- Dissolved CO2 in the intracellular fluid of the RBC's accounts for about 5% of the total CO2 released at the lungs.
- About 21% of the CO2 combines with the RBC hemoglobin to form carbamino-Hb.
- Most of the CO2 (about 63%) is transported from the tissue cells to the lungs in the form of bicarbonate.

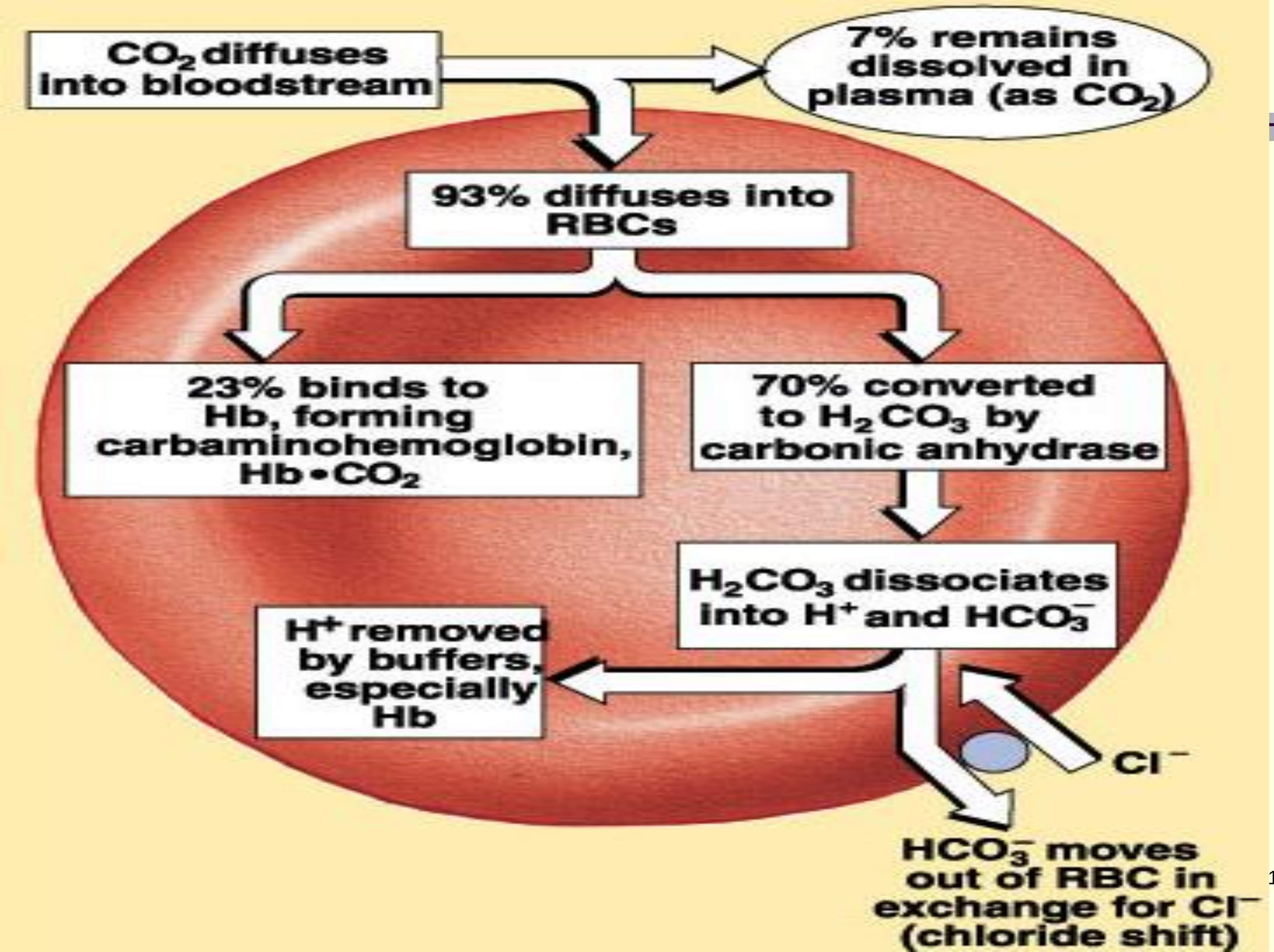
- Hb is the major buffer in the blood
- That removes the free hidrogen ion from blood to form a protonated Hb

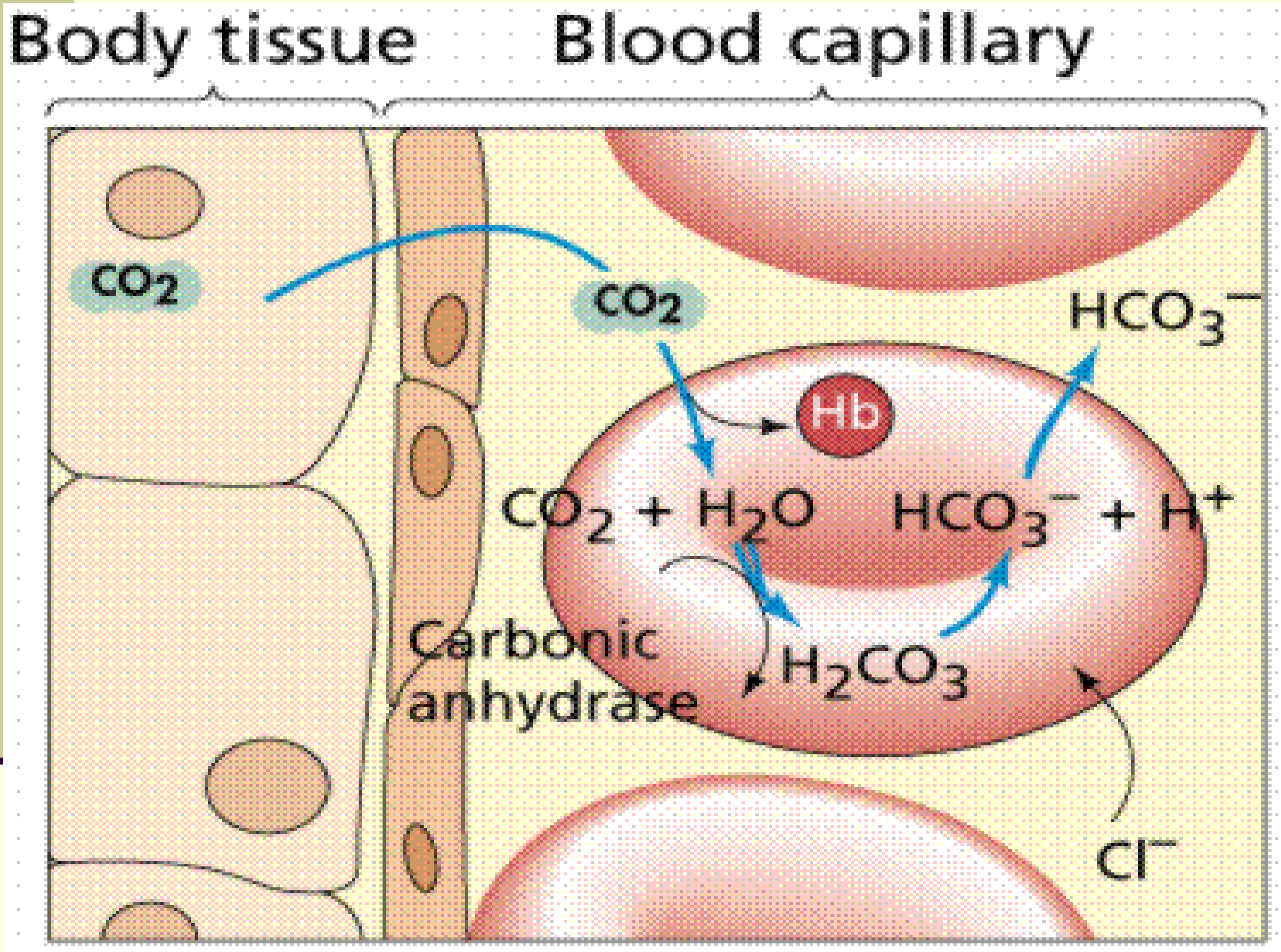
- $H^{+} + HCO_3^{-} + KHb$ ‹ ---→ $HHb + K^{+} + HCO_3^{-}$

- - occurs only within the red cell→ impermeable to K^{+} ----→permeable to
- HCO_3^{-} -→ diffuse out of erythrocyte in to the plasma----→ another anion must enter the erythrocyte --- Cl^{-}

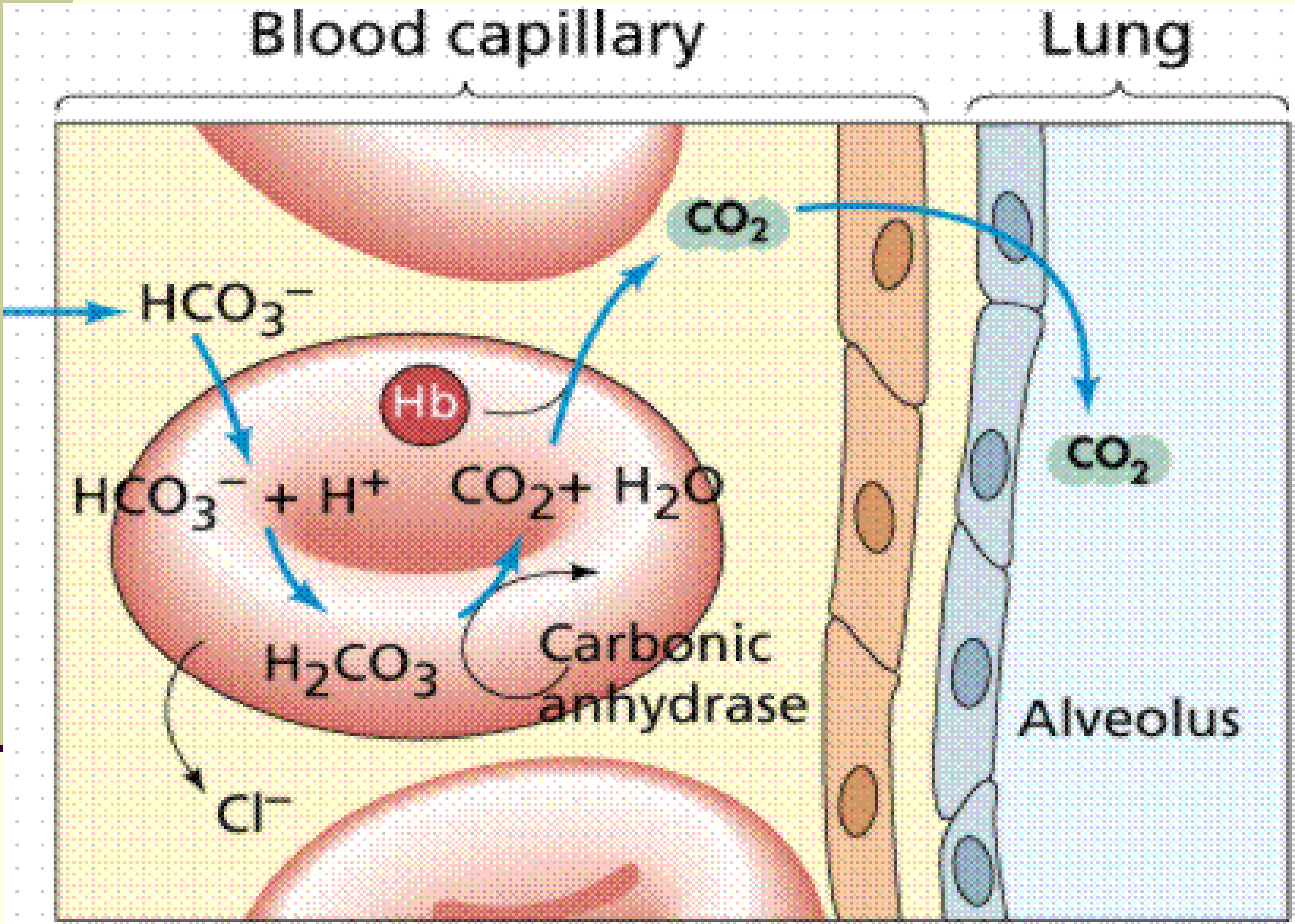
- The exchange between bic and Cl ion across the erythrocyte membrane :
- **the chloride shift**
- The phenomena the binding of O_2 to Hb displaces CO_2
- **Haldane effect**

CO_2 Transport and Cl^- Movement





Body tissue
Blood capillary
CO_2
CO_2
HCO_3^-
Hb
$CO_2 + H_2O$
$HCO_3^- + H^+$
Carbonic anhydrase
H_2CO_3
Cl^-


Blood capillary
Lung
CO_2
HCO_3^-
Hb
$HCO_3^- + H^+$
$CO_2 + H_2O$
CO_2
H_2CO_3
Carbonic anhydrase
Alveolus
Cl^-

- V.Respiratory regulation of acid base balance

- The buffering power of a buffer system is greatest at a pH = to its pKa

The pH extracellular body fluids is 7.4

pKa of the bicarbonate-CO_2 buffer system is 6.1

Handerson – Hasselbalch equation

$$pH = pKa + \log \frac{[salt]}{[acid]}$$

$$7.4 = 6.1 + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

$$1.3 = \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

Anti log 1.3 = 20 -→ $\frac{[HCO_3^-]}{[H_2CO_3]} = \frac{20}{1}$

ACID-BASE REGULATION

- Maintenance of an acceptable pH range in the extracellular fluids is accomplished by **three** mechanisms:
  - **1) Chemical Buffers**
    - React very rapidly (less than a second)
  - **2) Respiratory Regulation**
    - Reacts rapidly (seconds to minutes)
  - **3) Renal Regulation**
    - Reacts slowly (minutes to hours)

Chemical Buffers

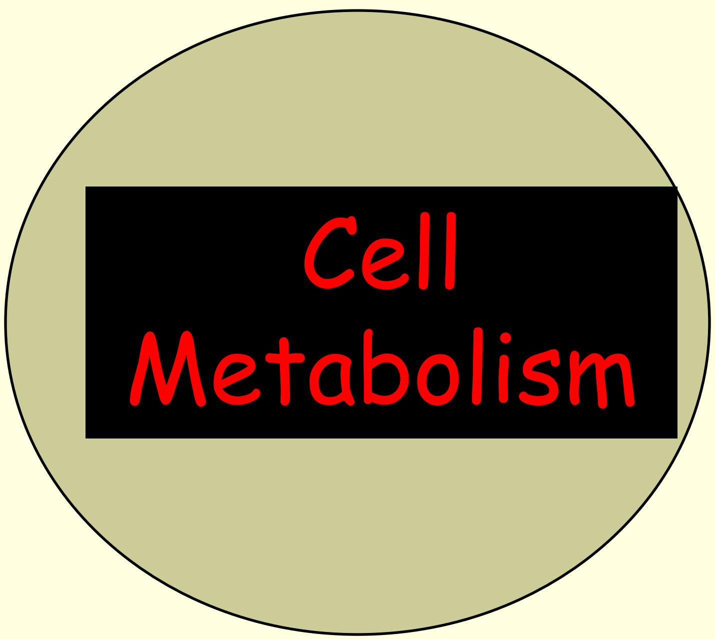
- The body uses pH buffers in the blood to guard against sudden changes in acidity
- A pH buffer works chemically to minimize changes in the pH of a solution

Buffer

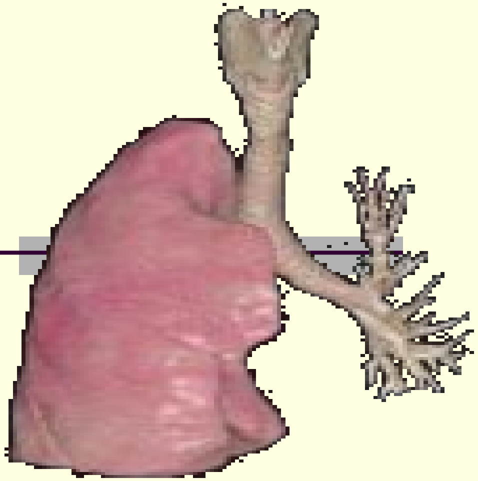
Buffer System Pairs

Weak Acid	Weak Base	% Total Buffer Action
Carbonic Acid	Sodium Bicarbonate	53
Hemoglobin	Potasisum Hemoglobinate	35
Oxyhemoglobin	Potassium Oxyhemoglobin	35
Plasma Protein	Proteinate	7
Acid Organic phosphate	Alkaline Organic phosphate	3
Acid Inorganic	Alkaline Inorganic	2

- **Respiratory Regulation**
  - Carbon dioxide is an important by-product of metabolism and is constantly produced by cells
  - The blood carries carbon dioxide to the lungs where it is exhaled



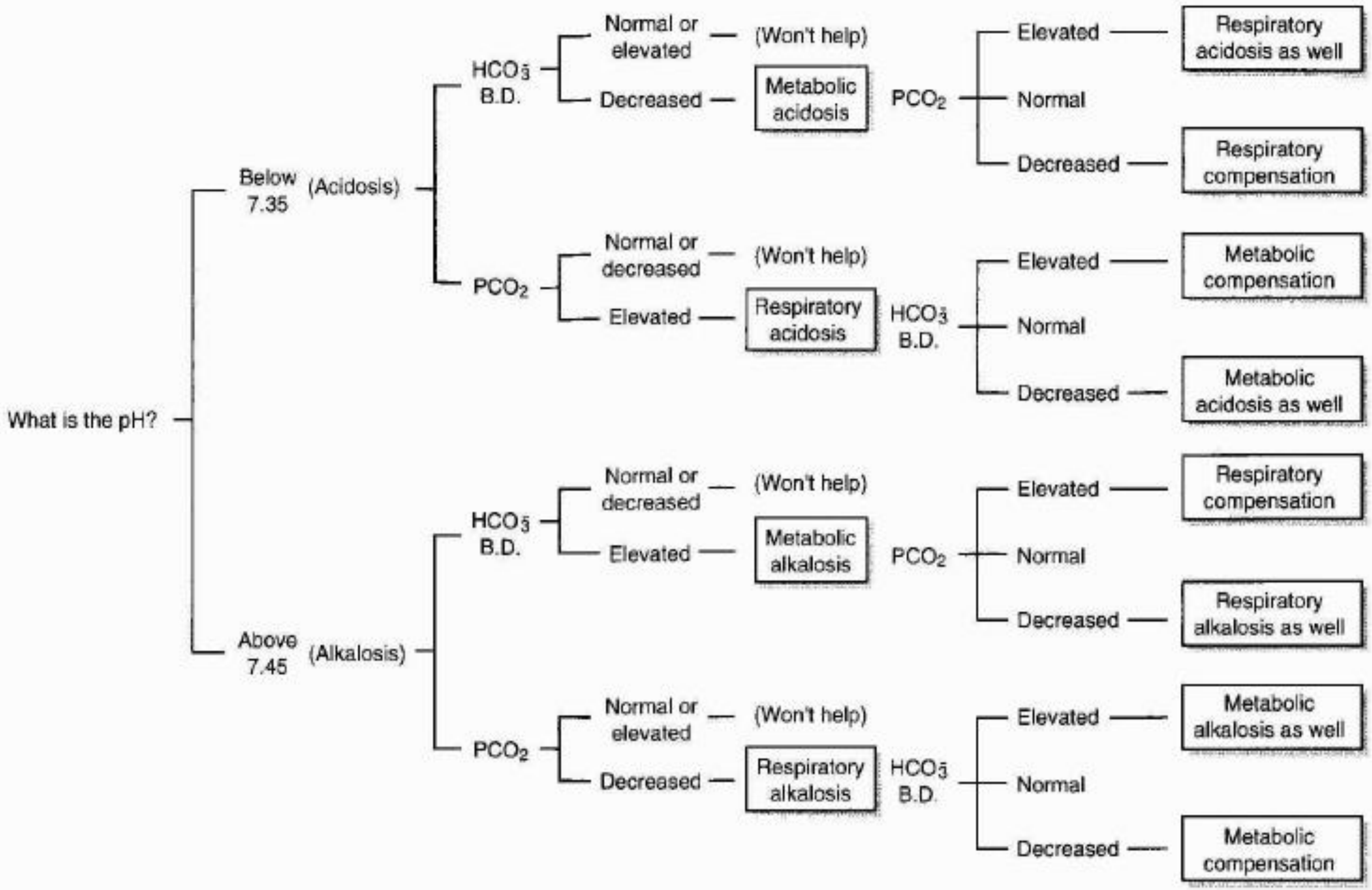
Respiratory Regulation



- When breathing is increased, the blood carbon dioxide level decreases and the blood becomes more **Base**
- When breathing is decreased, the blood carbon dioxide level increases and the blood becomes more **Acidic**
- By adjusting the speed and depth of breathing, the respiratory control centers and lungs are able to regulate the blood pH minute by minute

- **Kidney Regulation**
  - Excess acid is excreted by the kidneys, largely in the form of ammonia
  - The kidneys have some ability to alter the amount of acid or base that is excreted, but this generally takes several days

Acid Base imbalance



Acid-base disturbance

I. Respiratory acidosis

Common Cause :

- Respiratory depression (drugs, central nervous system trauma)
- Pulmonary disease (pneumonia, chronic obstructive pulmonary disease, respiratory underventilation)

Mode of compensation

- Kidneys will retain increased amounts of $HCO_{3/sub>}$ to increase pH

II. Respiratory alkalosis

Common Cause :

- Hyperventilation (emotions, pain, respirator overventilation)

Mode of compensation

- Kidneys will excrete increased amounts of HCO_3/sub> to lower pH
-

III. Metabolic acidosis

Common Cause :

- Diabetes, shock, renal failure, intestinal fistula

Mode of compensation

- Lungs "blow off" CO_2 to raise pH

IV. Metabolic alkalosis

Common Cause :

- Sodium bicarbonate overdose, prolonged vomiting, nasogastric drainage
- Hypokalemia- K & H change
- Hypochloremia- HCO3 cation Balance
- Excessive streoids- Increases Renal clearance

Mode of compensation

- Lungs retain CO_2 to lower Ph

- **SOURCE:** Pagana, K.D. and T.J. Pagana. *Mosby's Diagnostic and Laboratory Test Reference*. 3rd ed. St. Louis: Mosby, 1997.