GAS TRANSPORT & PH IN THE LUNG

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objectives

To learn :

1-Rate of diffusion of gases in the lung.

2- O_2 & CO_2 transport in the blood.

3-oxygen –Hb dissociation curve & the factors affecting O_2-Hb affinity.

4- Acid–Base Balance & Gas Transport.

5-Acidosis & Alkalosis & their types.

6- hypoxia : definition, causes, types& treatment.

7-Hypercapnia & Hypocapnia.

- partial pressure gradients for O_2 and $CO_2$are the key to gas movement and that O_2 "flows downhill" from the air through the alveoli and blood into the tissues, whereas CO_2 "flows downhill" from the tissues to the alveoli.

- Consider air, which has an approximate composition of 79 % N2 &21% O2.
- The total pressure of this mixture at sea level averages 760 mm Hg.
- each gas contributes to the total pressure in direct proportion to its concentration.
- Therefore, 79% of the 760 mm Hg is caused by nitrogen (600 mm Hg) and 21 % by oxygen (160 mm Hg).
- , the "partial pressure" of N2 in the mixture is 600 mm Hg, and the "partial pressure" of O2 is 160 mm Hg; the total pressure is 760 mm Hg, the sum of the individual partial pressures.
- .

Rate of diffusion

several factors affect the rate of gas diffusion in a fluid:

(1) the solubility of the gas in the fluid

(2) the cross-sectional area of the fluid

(3) the distance through which the gas must diffuse,

4) the molecular weight of the gas

(5) the temperature of the fluid.

- about 99% of the O_2 that dissolves in the blood combines with the O_2-carrying protein hemoglobin.
- about 94.5% of the CO_2 that dissolves enters into a series of reversible chemical reactions that convert it into other compounds.
- the presence of hemoglobin ↑ the O_2-carrying capacity of the blood 70-fold, and the reactions of CO_2 increase the blood CO_2 content 17-fold.

Oxygen Transport
Oxygen Delivery to the Tissues

O_2 delivery to a particular tissue depends on :

1-amount of O_2 entering the lungs,

2- adequacy of pulmonary gas exchange

3- blood flow to the tissue

A- the degree of constriction of the vascular bed in the tissue

B-cardiac output

4- the capacity of the blood to carry O_2

amount of O_2 in the blood is determined by :

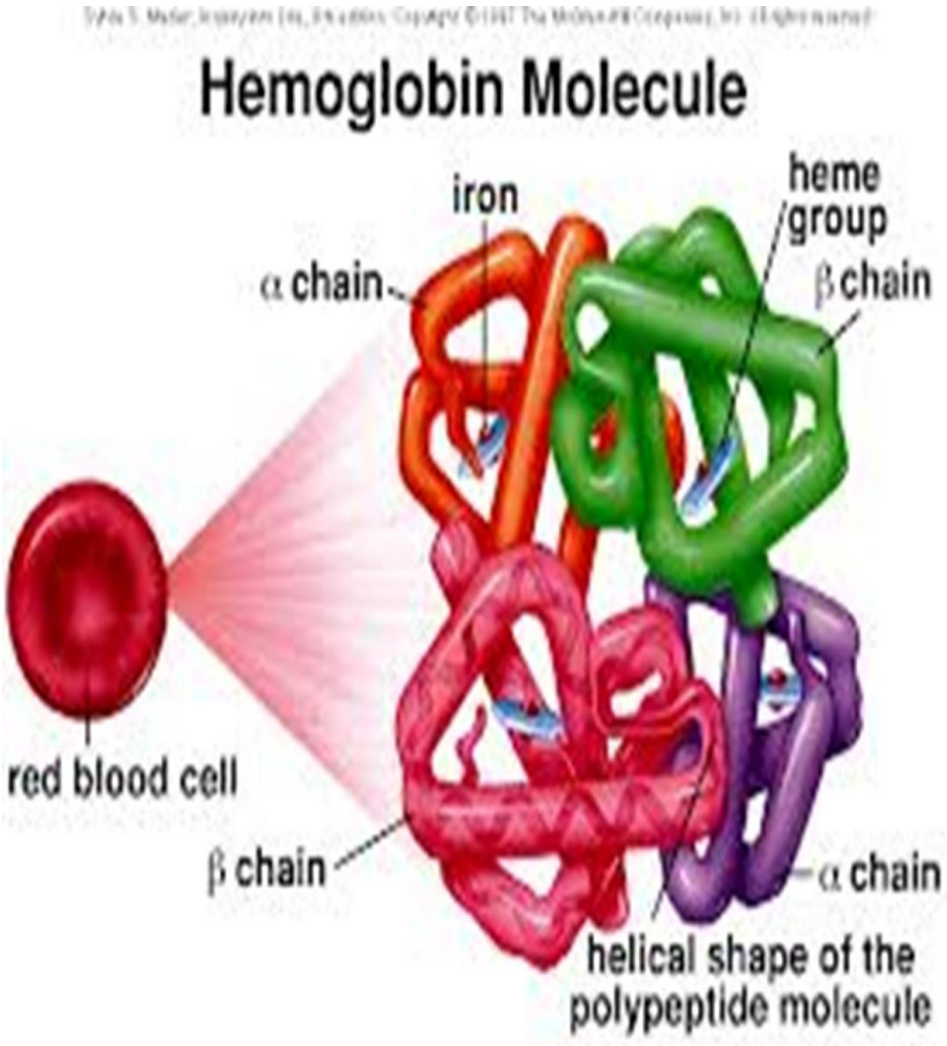
1-amount of dissolved O_2

2- amount of hemoglobin in the blood

3- affinity of the hemoglobin for O_2

Reaction of Hemoglobin & Oxygen

Combination of the1st heme in the Hb molecule with O_2 increases the affinity of the 2nd heme for O_2, and oxygenation of the second increases the affinity of the3ed , and so on, so that the affinity of Hb for the fourth O_2 molecule is many times that for the first.

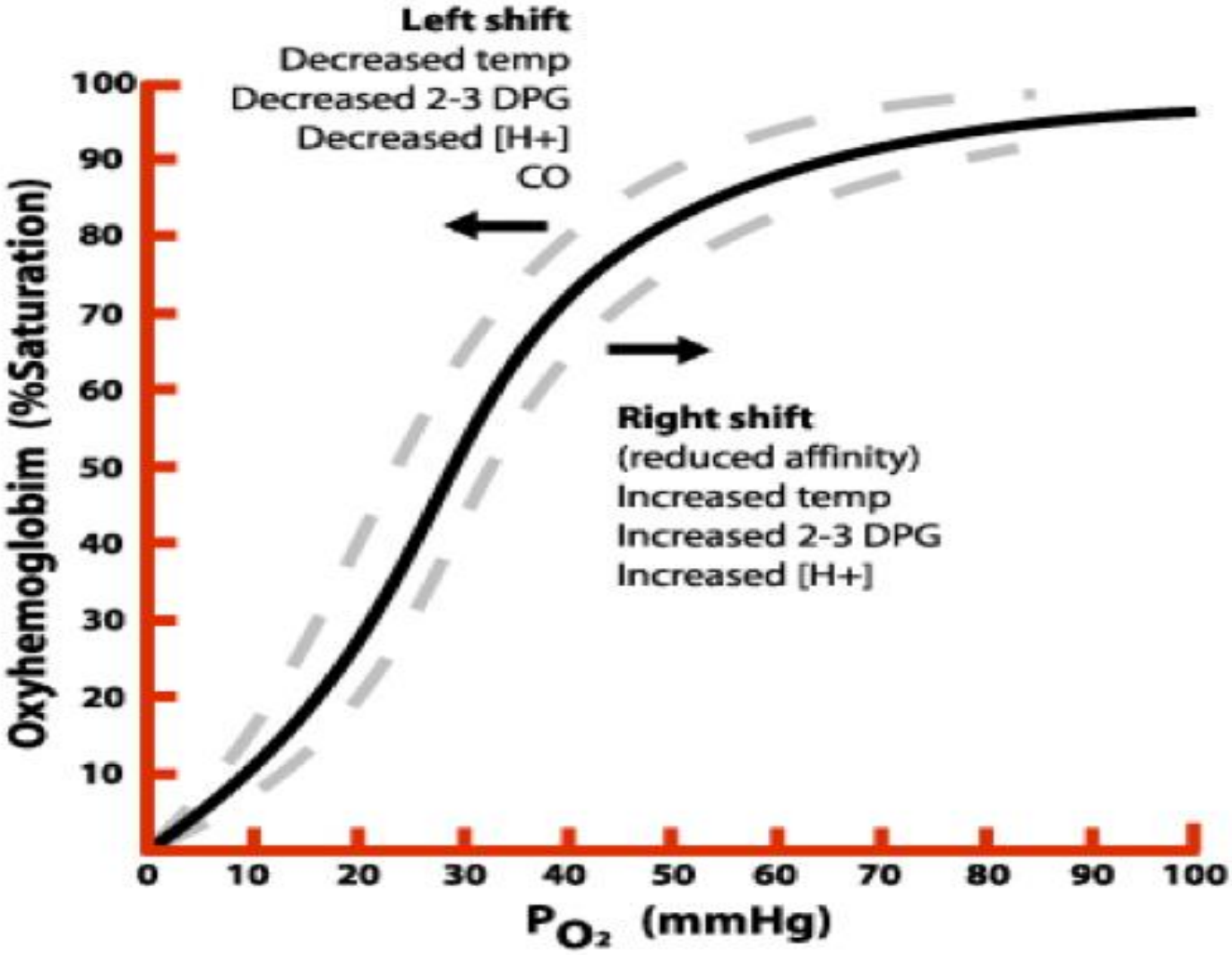


- When blood is equilibrated with 100% O_2 (PO_2 = 760 mm Hg), the normal hemoglobin becomes 100% saturated
- In vivo, the hemoglobin in the blood at the ends of the pulmonary capillaries is about 97.5% saturated with O_2 (PO_2 = 97 mm Hg).
- Because of a slight admixture with venous blood that bypasses the pulmonary capillaries (physiologic shunt), the hemoglobin in systemic arterial blood is only 97% saturated.

In venous blood at rest, the hemoglobin is 75% saturated
.
(Table 36–1); ganong

Factors Affecting the Affinity of Hemoglobin for Oxygen

- the **pH,** the **temperature,** and the concentration of **2,3-biphosphoglycerate (BPG; 2,3-BPG).**
- A ↑ in temperature or a ↓ in pH shifts the curve to the right.
- When the curve is shifted in this direction, a higher PO_2 is required for hemoglobin to bind a given amount of O_2.



AnaesthesiaUK

- a fall in temperature or a rise in pH shifts the curve to the left, and a lower PO_2 is required to bind a given amount of O_2.
- A convenient index for comparison of such shifts is the P_{50}, the PO_2 at which hemoglobin is half saturated with O_2.
- The higher the P_{50}, the lower the affinity of hemoglobin for O_2

Bohr effect

- Is decrease in O_2 affinity of hemoglobin when the pH of blood falls .
- deoxygenated Hb (deoxyhemoglobin) binds H^+ more actively than does oxygenated Hb (oxyhemoglobin).
- The pH of blood falls as its CO_2 content increases, so that when the PCO_2 rises, the curve shifts to the right and the P_{50} rises.
- Most of the unsaturation of hemoglobin that occurs in the tissues is secondary to the decline in the PO_2, but an extra 1–2% unsaturation is due to the rise in PCO_2 and consequent shift of the dissociation curve to the right.

Bohr's Effect

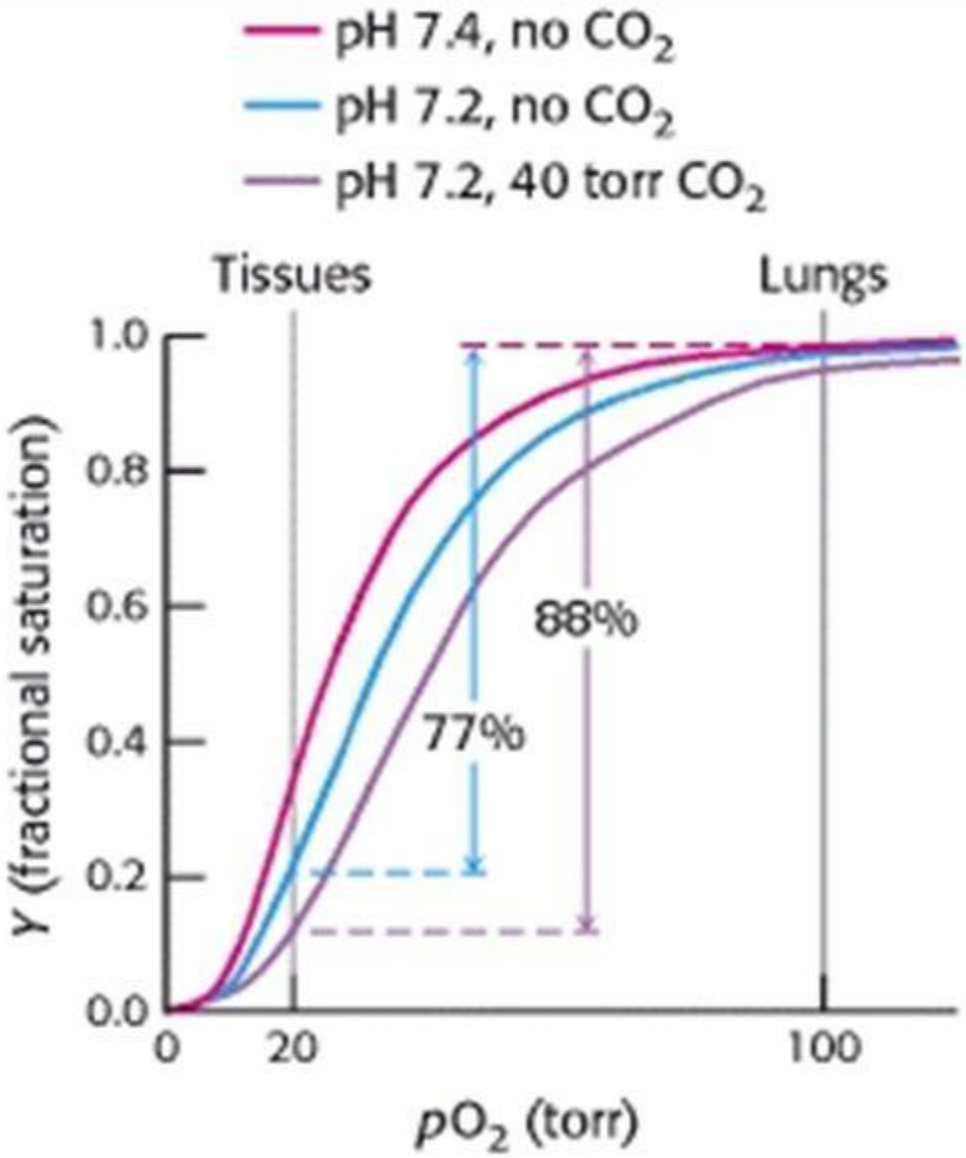
- Represents the effect of PCO_2 and H^+ (acidity) on the O_2-Hb dissociation curve.

- At tissues: Increased PCO_2 & H^+ concentration ⟶
  shift of O_2-Hb curve to the right.
- At lungs: Decreased PCO_2 & H^+ concentration ⟶
  shift of O_2-Hb curve to the left.

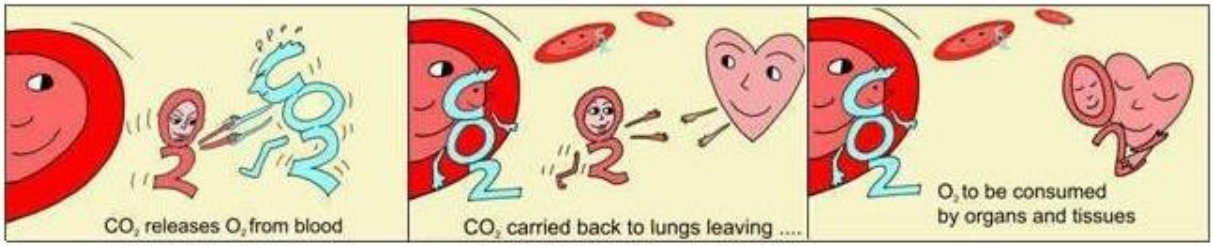
So, Bohr's effect facilitates

i) O_2 release from Hb at tissues.
ii) O_2 uptake by Hb at lungs.

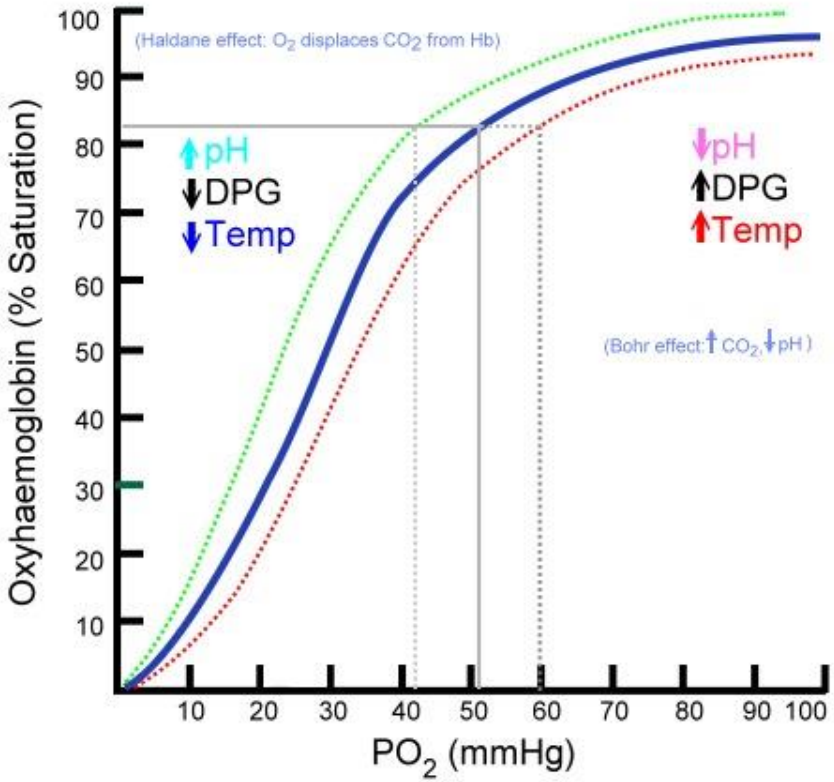
Hb binding to O_2 is affected by pH and CO_2



Bohr Effect:
Decreased pH
Increases O_2
unloading!!



What is Bohr Effect?



- 2,3-BPG is very plentiful in red cells, which is a product of glycolysis .
- an ↑ of 2,3-BPG shifts the reaction to the right, causing more O_2 to be liberated.

- Because acidosis inhibits red cell glycolysis, the 2,3-BPG concentration falls when the pH is low.
- Conversely, thyroid hormones, growth hormones, and androgens can all increase the concentration of 2,3-BPG and the P_{50}.

- Exercise produce an increase in 2,3-BPG within 60 min, although the rise may not occur in trained athletes.
- The P_{50} is also increased during exercise, because the temperature rises in active tissues and CO_2 and metabolites accumulate, lowering the pH

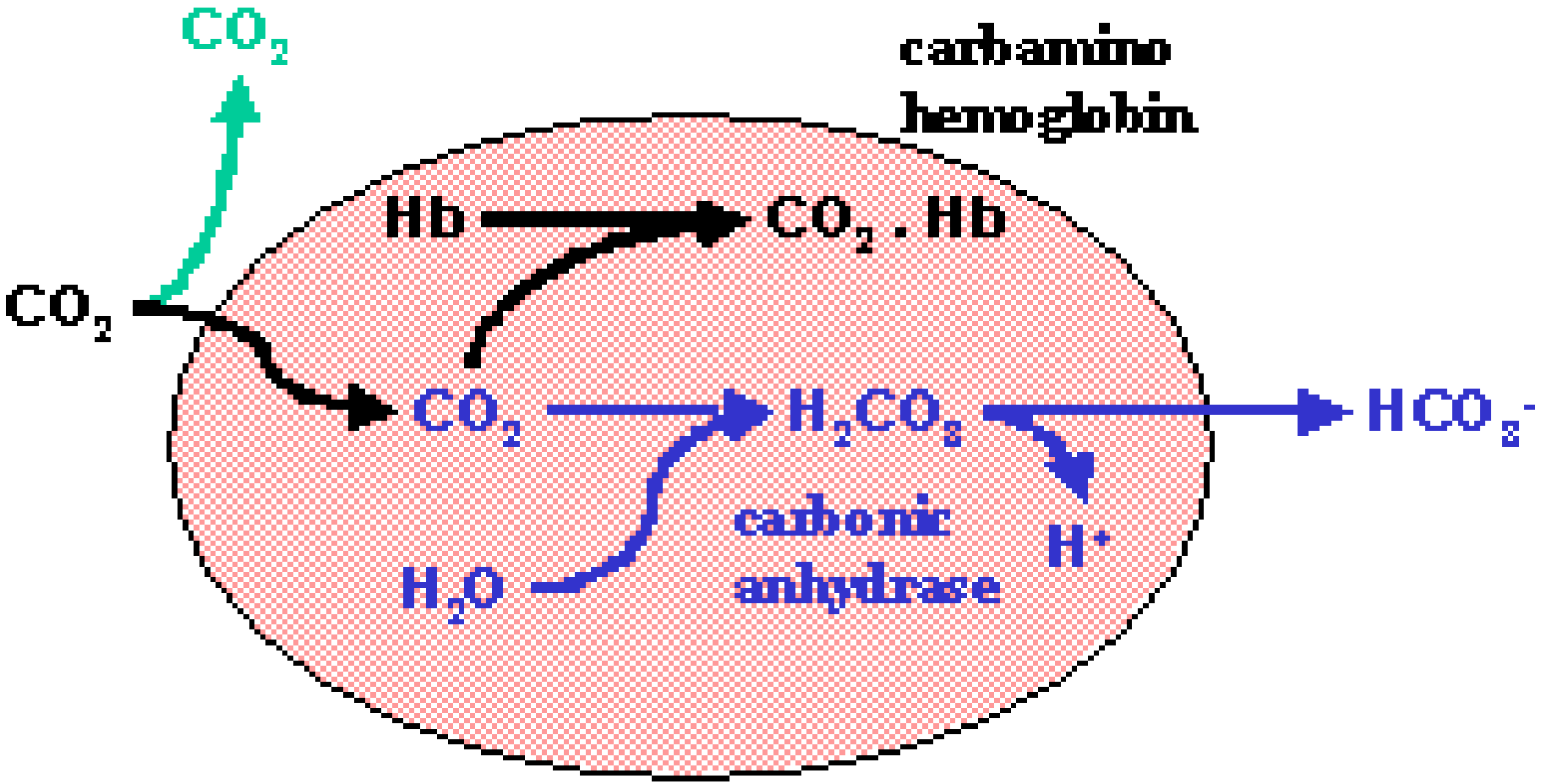
Myoglobin

- Myoglobin is an iron-containing pigment found in skeletal muscle.
- it resembles hemoglobin but binds 1 rather than 4 mol. of O_2 per mole.
- it takes up O_2 from hemoglobin in the blood.

Myoglobin

- It releases O_2 only at low PO_2 values, but the PO_2 in exercising muscle is close to zero.
- The myoglobin content is greatest in muscles specialized for sustained contraction.
- The muscle blood supply is compressed during such contractions, and myoglobin may provide O_2 when blood flow is cut off.

Carbon dioxide transport



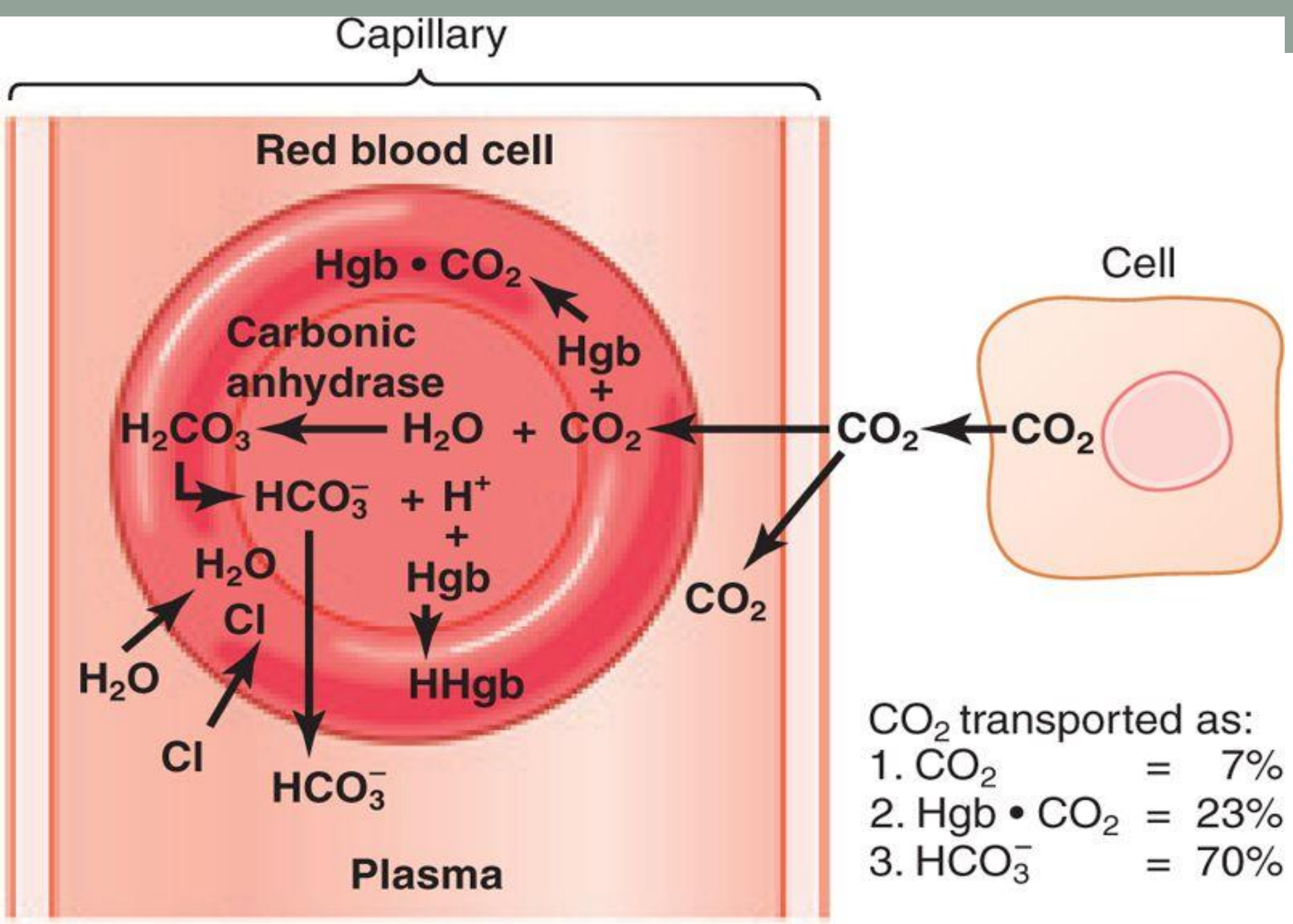
- binding of O_2 to hemoglobin reduces its affinity for CO_2.
- venous blood carries more CO_2 than arterial blood, CO_2 uptake is facilitated in the tissues, and CO_2 release is facilitated in the lungs.
- About 11% of the CO_2 added to the blood in the systemic capillaries is carried to the lungs as carbamino-CO_2.

Chloride Shift

- Because the rise in the HCO_3^- content of red cells is much greater than that in plasma as the blood passes through the capillaries, about 70% of the HCO_3^- formed in the red cells enters the plasma.
- The excess HCO_3^- leaves the red cells in exchange for Cl^-.

Chloride Shift

- Because of this **chloride shift,** the Cl^- content of the red cells in venous blood is significantly greater than that in arterial blood.
- The chloride shift occurs rapidly and is essentially complete within 1 s.



Chloride shift

- HCO_3^- content of red cells is much greater than that in plasma
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Carbon Dioxide Transport
Fate of Carbon Dioxide in Blood

- The solubility of CO_2 in blood is about 20 times that of O_2; therefore, considerably more CO_2 than O_2 is present in simple solution at equal partial pressures.
- The CO_2 that diffuses into red blood cells is rapidly hydrated to H_2CO_3 because of the presence of carbonic anhydrase.
- The H_2CO_3 dissociates to H^+ and HCO_3^-, and the H^+ is buffered, primarily by hemoglobin, while the HCO_3^- enters the plasma.
- Some of the CO_2 in the red cells reacts with the amino groups of hemoglobin and other proteins (R), forming **carbamino compounds:**

Summary of Carbon Dioxide Transport

Table 36–2 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 in cells increases

Acid–Base Balance & Gas Transport

- The major source of acids in the blood under normal conditions is through cellular metabolism.
- CO_2 formed by metabolism in the tissues is in large part hydrated to H_2CO_3,
- most of the CO_2 is excreted in the lungs, and the small quantities of the remaining H^+ are excreted by the kidneys

- Fruits are the main dietary source of alkali.
- They contain Na^+ and K^+ ,salts of weak organic acids, and the anions of these salts are metabolized to CO_2, leaving NaHCO3 and $KHCO_3$ in the body.
- Such ingestion contributes little to changes in pH and a more common cause of alkalosis is loss of acid from the body as a result of vomiting of gastric juice rich in HCl.
- This is, of course, equivalent to adding alkali to the body.

Buffering in the Blood

Acid and base shifts in the blood are largely controlled by three main buffers in blood:

(1) proteins,

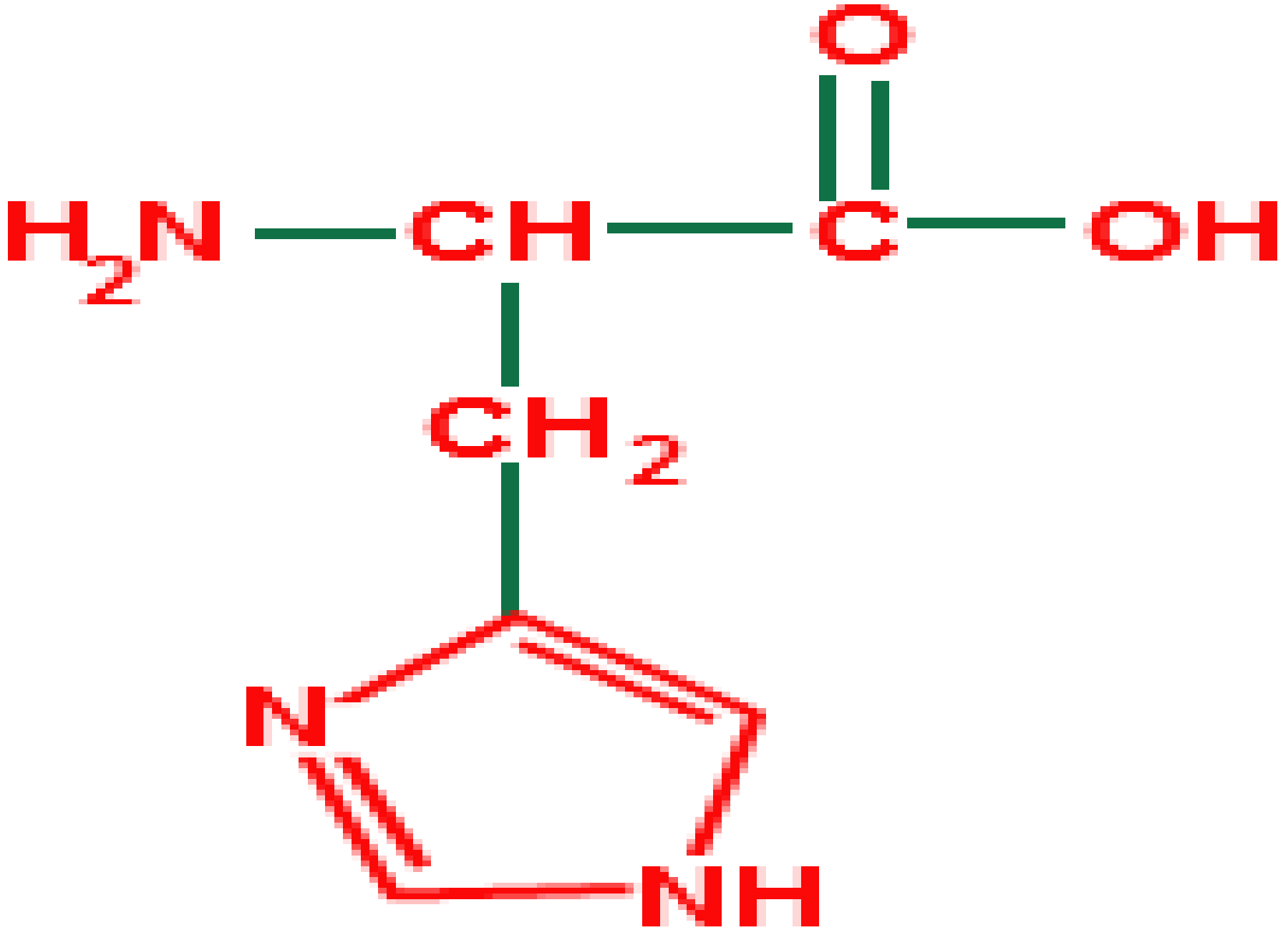
(2) hemoglobin,

(3) the carbonic acid–bicarbonate system.

Buffering in the Blood

1-Plasma **proteins** are effective buffers because both their free carboxyl and their free amino groups dissociate.

2-The second buffer system is provided by the dissociation of the imidazole groups of the histidine residues in **hemoglobin**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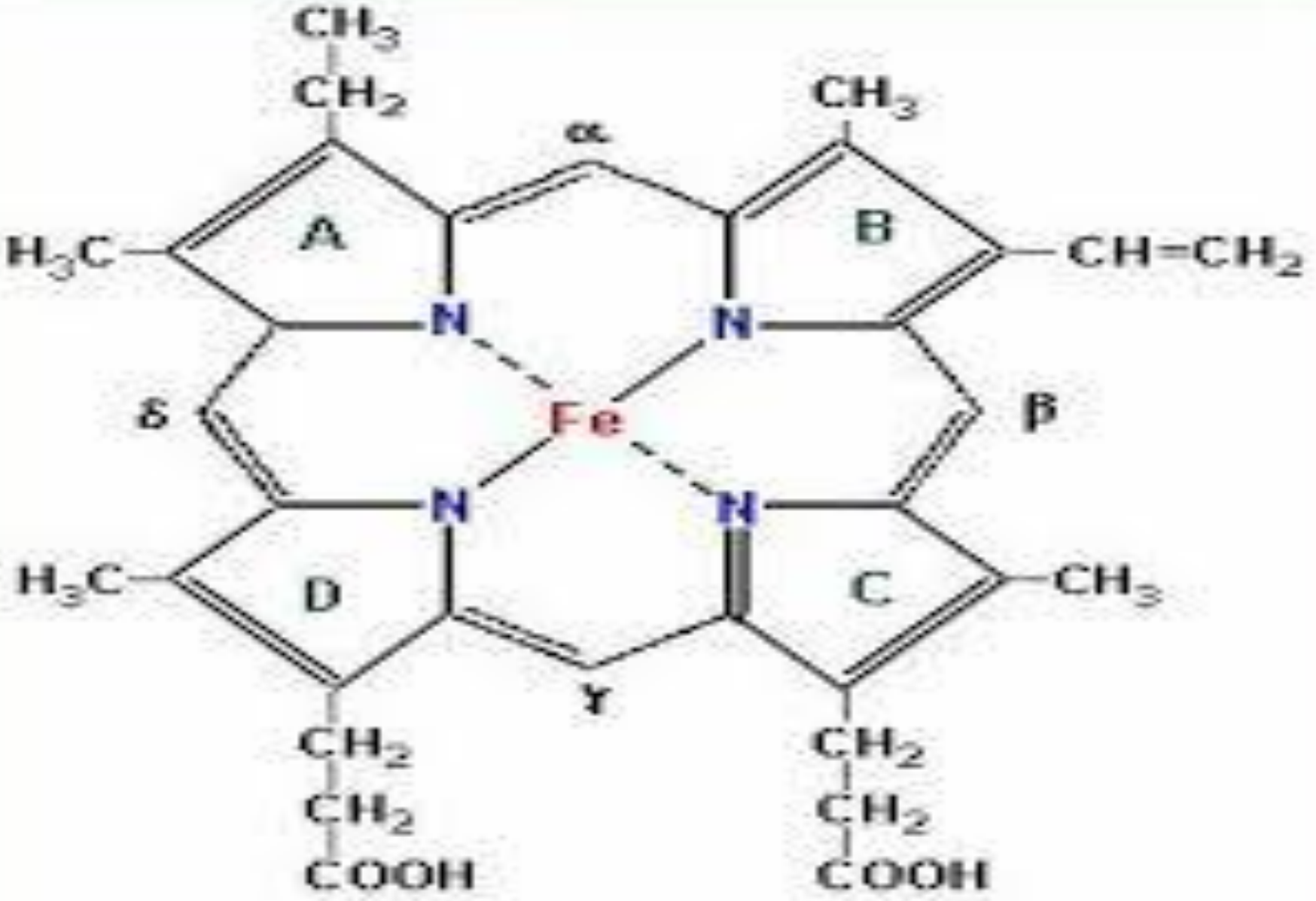

Heme Molecule

Buffering in the Blood

- In the pH 7.0–7.7 range, the free carboxyl and amino groups of hemoglobin contribute relatively little to its buffering capacity.
- However, the hemoglobin molecule contains 38 histidine residues, and on this basis—plus the fact that hemoglobin is present in large amounts—the Hb in blood has 6 times the buffering capacity of the plasma proteins.
- In addition, the action of hemoglobin is unique because the imidazole groups of deoxyhemoglobin (Hb) dissociate less than those of oxyhemoglobin (HbO_2), making Hb a weaker acid and therefore a better buffer than HbO_2.

Buffering in the Blood

- 3-The third and major buffer system in blood is the **carbonic acid–bicarbonate system:**
- H2CO3↔ $H2O + CO2$
- the system is one of the most effective buffer systems in the body because the amount of dissolved CO_2 is controlled by respiration.
- Additional control of the plasma concentration of HCO_3^- is provided by the kidneys.

- When H^+ is added to the blood, HCO_3^- declines as more H_2CO_3 is formed.
- If the extra H_2CO_3 were not converted to CO_2 and H_2O and the CO_2 excreted in the lungs, the H_2CO_3 concentration would rise.
- When enough H^+ has been added to halve the plasma HCO_3^-, the pH would have dropped from 7.4 to 6.0. However, not only is all the extra H_2CO_3 that is formed removed, but also the H^+ rise stimulates respiration and therefore produces a drop in PCO_2, so that some additional H_2CO_3 is removed.
- The pH thus falls only to 7.2 or 7.3

- There are two factors that make the carbonic-acid-bicarbonate system such a good biological buffer.
- First, the reaction $CO_2 + H_2O \rightleftarrows H_2CO_3$ proceeds slowly in either direction unless the enzyme **carbonic anhydrase** is present.
- There is no carbonic anhydrase in plasma, but there is an abundant supply in red blood cells.
- Second, the presence of hemoglobin in the blood increases the buffering of the system by binding free H^+ produced by the hydration of CO_2 and allowing for movement of the HCO_3^- into the plasma.

Acidosis & Alkalosis

- The pH of the arterial plasma is normally 7.40 and that of venous plasma slightly lower.
- acidosis→ pH less than 7.40
- Alkalosis → pH more than 7.40

Acidosis & Alkalosis

- Acid–base disorders are split into four categories:
- respiratory acidosis, → Breathing 7% CO_2
  Emphysema
- respiratory alkalosis, → Voluntary hyperventilation or
  Three-week residence at 4000-m altitude

Acidosis & Alkalosis

metabolic acidosis,→ NH_4 Cl ingestion •
Diabetic acidosis

metabolic alkalosis→ NaHCO3 ingestion •
Prolonged vomiting

Respiratory Acidosis

- Any short-term rise in arterial PCO_2 (ie, above 40 mm Hg) due to decreased ventilation results in **respiratory acidosis.**
- CO_2 that is retained is in equilibrium with H_2CO_3, which in turn is in equilibrium with HCO_3^-, so that the plasma HCO_3^- rises and a new equilibrium is reached at a lower pH.

Respiratory Acidosis

- The pH change observed at any increase in PCO_2 during respiratory acidosis is dependent on the buffering capacity of the blood.

Respiratory Alkalosis

- Any short-term increase in ventilation that lowers PCO_2 below what is needed for proper CO_2 exchange (ie, below 35 mm Hg) results in **respiratory alkalosis.**
- The decreased CO_2 shifts the equilibrium of the carbonic acid–bicarbonate system to effectively lower the $[H^+]$ and increase the pH.
- As in respiratory acidosis, initial pH changes corresponding to respiratory alkalosis

Metabolic Acidosis & Alkalosis

- **Metabolic acidosis** (or non respiratory acidosis) occurs when strong acids are added to blood.
- If, for example, a large amount of acid is ingested (eg, aspirin overdose), acids in the blood are quickly increased, lowering the available Hb^-, $Prot^-$, and HCO_3^- buffers.
- The H_2CO_3 that is formed is converted to H_2O and CO_2, and the CO_2 is rapidly excreted via the lungs.

Metabolic Acidosis & Alkalosis

- Note that in contrast to respiratory acidosis, PCO_2 is unchanged and the shift toward metabolic acidosis occurs,
- When the free $[H^+]$ level falls as a result of addition of alkali, or more commonly, the removal of large amounts of acid (eg, following vomiting), **metabolic alkalosis** results.

Respiratory & Renal Compensation

- The two main compensatory systems are **respiratory compensation** and **renal compensation.**
- The respiratory system compensates for metabolic acidosis or alkalosis by altering ventilation, and consequently, the PCO_2, which can directly change blood pH.
- Respiratory mechanisms tend to be fast.

- In response to metabolic acidosis, ventilation is increased, resulting in a ↓of PCO_2 (eg, from 40 mm Hg to 20 mm Hg) and a subsequent ↑ pH toward normal.

- In response to metabolic alkalosis, ventilation is decreased, PCO_2 is↑, and a ↓ in pH occurs.

- For complete compensation from respiratory or metabolic acidosis/alkalosis, renal compensatory mechanisms are invoked.
- The kidney responds to acidosis by actively secreting fixed acids while retaining filtered HCO_3^-.
- In contrast, the kidney responds to alkalosis by decreasing H^+ secretion and by decreasing the retention of filtered HCO_3^-.

- Renal tubule cells in the kidney have active carbonic anhydrase and thus can produce H^+ and HCO_3^- from CO_2.
- In response to acidosis, these cells secrete H^+ into the tubular fluid in exchange for Na^+ while the HCO_3^- is actively reabsorbed into the peritubular capillary;
- for each H^+ secreted, one Na^+ and one HCO_3^- are added to the blood.

- Conversely, in response to alkalosis, the kidney decreases H^+ secretion and ↓HCO_3^- reabsorption.
- The kidney tends to reabsorb HCO_3^- until the level in plasma exceeds 26–28 mEq/L (normal is 24 mEq/L). Above this threshold, HCO_3^- appears in the urine.

Hypoxia

Hypoxia is O_2 deficiency at the tissue level.

four categories are :

(1) **hypoxic hypoxia,** in which the PO_2 of the arterial blood is reduced;

(2) **anemic hypoxia,** in which the arterial PO_2 is normal but the amount of Hb available to carry O_2 is reduced

Hypoxia

(3) **stagnant** or **ischemic hypoxia,** in which the blood flow to a tissue is so low that adequate O_2 is not delivered to it despite a normal PO_2 and hemoglobin concentration;

(4) **histotoxic hypoxia,** in which the amount of O_2 delivered to a tissue is adequate but, because of the action of a toxic agent, the tissue cells cannot make use of the O_2 supplied to them.

descriptive classification of the causes of hypoxia:

1- Inadequate oxygenation of the blood in the lungs because of extrinsic reasons

A-Deficiency of oxygen in the atmosphere

B-Hypoventilation (neuromuscular disorders)

2- Pulmonary disease

A-Hypoventilation caused by increased airway resistance or decreased pulmonary compliance

B-Abnormal alveolar ventilation-perfusion ratio (including either increased physiologic dead space or increased physiologic shunt)

C-Diminished respiratory membrane diffusion

descriptive classification of the causes of hypoxia

3- Venous-to-arterial shunts ("right-to-left" cardiac shunts)

4- Inadequate oxygen transport to the tissues by the blood

A-Anemia or abnormal hemoglobin

B-General circulatory deficiency

C-Localized circulatory deficiency (peripheral, cerebral, coronary vessels)

D-Tissue edema

descriptive classification of the causes of hypoxia

5- Inadequate tissue capability of using oxygen

A-Poisoning of cellular oxidation enzymes

b-Diminished cellular metabolic capacity for using oxygen, - because of toxicity, vitamin deficiency, or other factors

Hypoxic Hypoxia

- is a condition of reduced arterial PO_2.
- Hypoxic hypoxia is a problem in normal individuals at high altitudes and is a complication of pneumonia and a variety of other diseases of the respiratory system.

Effects of Decreased Barometric Pressure

- composition of air stays the same, but the total barometric pressure falls with increasing altitude .
- Therefore, the PO_2 also falls.
- 3000 m above sea level:
- alveolar PO_2 =60 mm Hg and there is enough hypoxic stimulation of chemoreceptors to ↑ventilation

- At higher altitude, the alveolar PO_2 falls less rapidly and the alveolar PCO_2 declines somewhat because of the hyperventilation.
- The resulting fall in arterial PCO_2 produces respiratory alkalosis.

Effects of Hypoxia on the Body

- can cause death of cells throughout the body.
- Less sever effects:
- (1) depressed mental activity, sometimes culminating in coma,
- (2) reduced work capacity of the muscles.

Oxygen Therapy in Different Types of Hypoxia

- (1) placing the patient's head in a "tent" that contains air fortified with oxygen,
- (2) allowing the patient to breathe either pure oxygen or high concentrations of oxygen from a mask,
- (3) administering oxygen through an intranasal tube.

- In *atmospheric hypoxia*, oxygen therapy can completely correct the depressed oxygen level in the inspired gases and, therefore, provide 100 % effective therapy.

- *hypoventilation hypoxia*, a person breathing 100 %oxygen can move five times as much oxygen into the alveoli with each breath as when breathing normal air.
- Therefore, oxygen therapy can be extremely beneficial.
- (However, this provides no benefit for the excess blood carbon dioxide also caused by the hypoventilation.)

- In *hypoxia caused by impaired alveolar membrane diffusion*, essentially the same result occurs as in hypoventilation hypoxia because oxygen therapy can increase the P_{O_2} in the lung alveoli from the normal value of about 100 mm Hg to as high as 600 mm Hg.
- This raises the oxygen pressure gradient for diffusion of oxygen from the alveoli to the blood from the normal value of 60 mm Hg to as high as 560 mm Hg, an increase of more than 800%.
- This highly beneficial effect of oxygen therapy in diffusion hypoxia,
- the pulmonary blood in this patient with pulmonary edema picks up oxygen 3-4 as rapidly as would occur with no therapy.

Acclimatization

- is due to the operation of a variety of compensatory mechanisms.
- The respiratory alkalosis produced by the hyperventilation shifts the oxygen–hemoglobin dissociation curve to the left, but a concomitant ↑in red blood cell 2,3-BPG tends to decrease the O_2 affinity of hemoglobin.
- The net effect is a small increase in P_{50}.

Acclimatization

- The initial ventilatory response to increased altitude is relatively small, because the alkalosis tends to counteract the stimulating effect of hypoxia.
- ventilation steadily increases over the next 4 d because the active transport of H^+ into (CSF), or possibly a developing lactic acidosis in the brain, causes a fall in CSF pH that ↑ the response to hypoxia.

Acclimatization

- After 4 d, the ventilatory response begins to decline slowly, but it takes years of residence at higher altitudes for it to decline to the initial level.
- Associated with this decline is a gradual desensitization to the stimulatory effects of hypoxia.

Acclimatization

- Erythropoietin secretion increases promptly on ascent to high altitude and then falls somewhat over the following 4 d as the ventilatory response increases and the arterial PO_2 rises.
- The increase in circulating red blood cells triggered by the erythropoietin begins in 2 to 3 d and is sustained as long as the individual remains at high altitude.

Acclimatization

- The mitochondria, which are the site of oxidative reactions, increase in number, and myoglobin increases, which facilitates the movement of O_2 into the tissues.]
- The tissue content of cytochrome oxidase also increases.

Conclusion for acclimization

1- ↑ventilation for 4 days

2- after 2-3 day Erythropoietin secretion increases

3- mitochondria, increase in number, and myoglobin increases, cytochrome oxidase also increases

Diseases Causing Hypoxic Hypoxia

1- those in which the gas exchange apparatus fails, → congenital heart disease.

2- those in which the respiratory pump fails→ due to fatigue of the respiratory muscles, due to ↑breathing work or mechanical defects such as pneumothorax or bronchial obstruction.

3- abnormalities of the neural mechanisms that control ventilation,→ depression of the respiratory neurons in the medulla by morphine and other drugs.

Diseases Causing Hypoxic Hypoxia

4- Ventilation–Perfusion Imbalance •

Anemic Hypoxia

- *hypoxia caused by anemia, abnormal hemoglobin transport of oxygen*, *circulatory deficiency*, *or physiologic shunt*, oxygen therapy is of much less value because normal oxygen is already available in the alveoli.
- The problem is that one or more of the mechanisms for transporting oxygen from the lungs to the tissues are deficient.
- Even so, a small amount of extra oxygen, between 7 and 30%, can be *transported in the dissolved state* in the blood when alveolar oxygen is increased to maximum even though the amount transported by the hemoglobin is hardly altered.
- This small amount of extra oxygen may be the difference between life and death.

Anemic Hypoxia

- Hypoxia due to anemia is not severe at rest unless the hemoglobin deficiency is marked, because red blood cell 2,3-BPG increases.
- However, anemic patients may have considerable difficulty during exercise because of limited ability to increase O_2 delivery to the active tissues

Carbon Monoxide Poisoning

- CO is toxic because it reacts with hemoglobin to form **carbon monoxyhemoglobin (carboxyhemoglobin, COHb),** and COHb cannot take up O_2.
- The affinity of hemoglobin for CO is 210 times its affinity for O_2, and COHb liberates CO very slowly.
- An additional difficulty is that when COHb is present the dissociation curve of the remaining HbO_2 shifts to the left, decreasing the amount of O_2 released.

Carbon Monoxide Poisoning

- amount of COHb formed depends on
- 1- the duration of exposure to CO
- 2-the concentration of CO in the inspired air and the alveolar ventilation.
- CO is also toxic to the cytochromes in the tissues.

Carbon Monoxide Poisoning

- The symptoms of CO poisoning are those of any type of hypoxia, especially headache and nausea, but there is little stimulation of respiration, since in the arterial blood, PO_2 remains normal and the carotid and aortic chemoreceptors are not stimulated.
- The cherry-red color of COHb is visible in the skin, nail beds, and mucous membranes.
- Death results when about 70–80% of the circulating hemoglobin is converted to COHb.
- The symptoms produced by chronic exposure to sublethal concentrations of CO are those of progressive brain damage, including mental changes and, sometimes, a parkinsonism-like state.

Carbon Monoxide Poisoning

- Treatment of CO poisoning consists of immediate termination of the exposure and adequate ventilation, by artificial respiration if necessary.
- Ventilation with O_2 is preferable to ventilation with fresh air, since O_2 hastens the dissociation of COHb.
- Hyperbaric oxygenation is useful in this condition.

Hypoperfusion Hypoxia

- is due to slow circulation and is a problem in organs such as the kidneys and heart during shock.
- The liver and possibly the brain are damaged by hypoperfusion hypoxia in congestive heart failure.
- The blood flow to the lung is normally very large, and it takes prolonged hypotension to produce significant damage.

Histotoxic Hypoxia

- The cause of inability of the tissues to use oxygen is *cyanide poisoning*, in which the action of the enzyme *cytochrome oxidase* is completely blocked by the cyanide- to such an extent that the tissues cannot use oxygen even when plenty is available.

Histotoxic Hypoxia

- Hypoxia due to inhibition of tissue oxidative processes is most commonly the result of cyanide poisoning.
- Methylene blue or nitrites are used to treat cyanide poisoning.
- They act by forming **methemoglobin,** which then reacts with cyanide to form **cyanmethemoglobin,** a nontoxic compound.

Histotoxic Hypoxia

- deficiencies of some of the *tissue cellular oxidative enzymes* or of other elements in the tissue oxidative system can lead to histotoxic hypoxia.
- example occurs in the disease *beriberi*, in which several important steps in tissue utilization of oxygen and formation of carbon dioxide are compromised because of *vitamin B deficiency*.

- In the different types of *hypoxia caused by inadequate tissue use of oxygen*, there is abnormality neither of oxygen pickup by the lungs nor of transport to the tissues.
- Instead, the tissue metabolic enzyme system is simply incapable of using the oxygen that is delivered.
- Therefore, oxygen therapy provides no measurable benefit.

Hypercapnia & Hypocapnia
Hypercapnia

- Retention of CO_2 in the body **(hypercapnia)** initially stimulates respiration.
- Retention of larger amounts produces symptoms due to depression of the central nervous system: confusion, diminished sensory acuity, and, coma with respiratory depression and death.

Hypercapnia

- the PCO_2 is markedly elevated, severe respiratory acidosis is present, and the plasma HCO_3^- may exceed 40 mEq/L.
- Large amounts of HCO_3^- are excreted, but more HCO_3^- is reabsorbed, raising the plasma HCO_3^- and partially compensating for the acidosis.
- occur in :
- 1-ventilation–perfusion inequality and when alveolar ventilation is inadequate in the various forms of pump failure.

Hypercapnia

- 2-when CO_2 production is increased, in febrile patients there is a 13% increase in CO_2 production for each 1°C rise in temperature,
- 3-a high carbohydrate intake increases CO_2 production because of the increase in the respiratory quotient.
- Normally, alveolar ventilation increases and the extra CO_2 is expired, but it accumulates when ventilation is compromised.

Hypocapnia

- is the result of hyperventilation.
- During voluntary hyperventilation, the arterial PCO_2 falls from 40 to as low as 15 mm Hg while the alveolar PO_2 rises to 120 - 140 mm Hg.
- chronic effects of hypocapnia are seen in neurotic patients who chronically hyperventilate.

Hypocapnia

- 1-Cerebral blood flow may be ↓ 30% or more because of the direct constrictor effect of hypocapnia on the cerebral vessels→ light-headedness, dizziness, and paresthesias.
- 2- Hypocapnia also ↑cardiac output, has a direct constrictor effect on many peripheral vessels, but it depresses the vasomotor center, so that the blood pressure is usually unchanged or only slightly elevated.

Hypocapnia

- 3- hypocapnia are due to the associated respiratory alkalosis, the blood pH being ↑ to 7.5 or 7.6.
- The plasma HCO_3^- level is low, but HCO_3^- reabsorption is decreased because of the inhibition of renal acid secretion by the low PCO_2.
- The plasma total calcium level does not change, but the plasma Ca^{2+} level falls and hypocapnic individuals develop carpopedal spasm, a positive Chvostek sign, and other signs of tetany.