

Regulatory Mechanism against¹ Changes in $[H^+]$ of Blood

Two types of metabolic acids produced

1. Volatile acids

The physiologically most important is Carbonic acid. $20,000 \text{ mEq. is produced daily from metabolism}$ [60-80 mEq. per day]

2. Fixed Acids

Organic acids as :
Pyruvic, lactic, keto acids (e.g. acetoacetic, β -hydroxybutyric acid), uric acid

Phosphoric and sulphuric acids produced from sulphur & phosphorus of proteins, lipoproteins and nucleoproteins

Buffering Capacity depends on:

Conc. of buffer

pK_a of the buffer and the desired pH

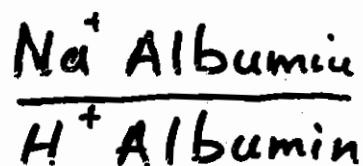
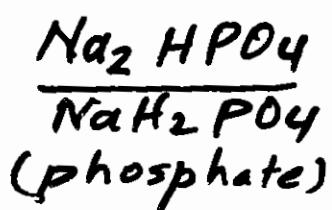
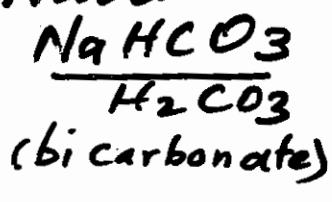
Mechanism of Regulation of pH

1. Buffer mechanism - First defence
2. Respiratory mechanism -
second line of defence
3. Renal Mechanism
3rd line of defence

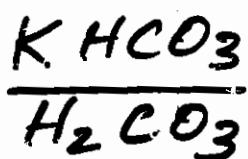
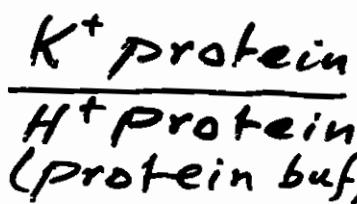
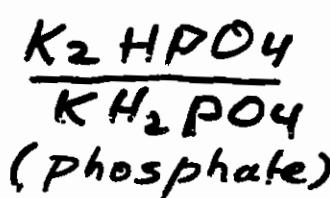
The first two lines of defence keep the $[H^+]$ from changing too much until the more slowly responding third line of defence, the kidney can eliminate the excess acid or base from the body

Buffer systems of the body

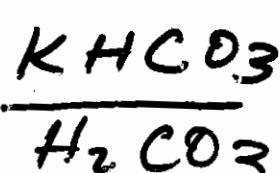
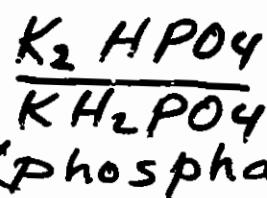
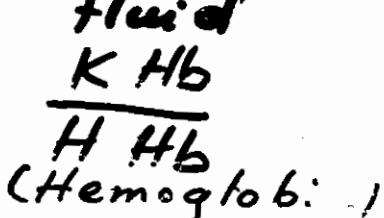
Extracellular fluid



Intracellular fluid



Erythrocyte fluid

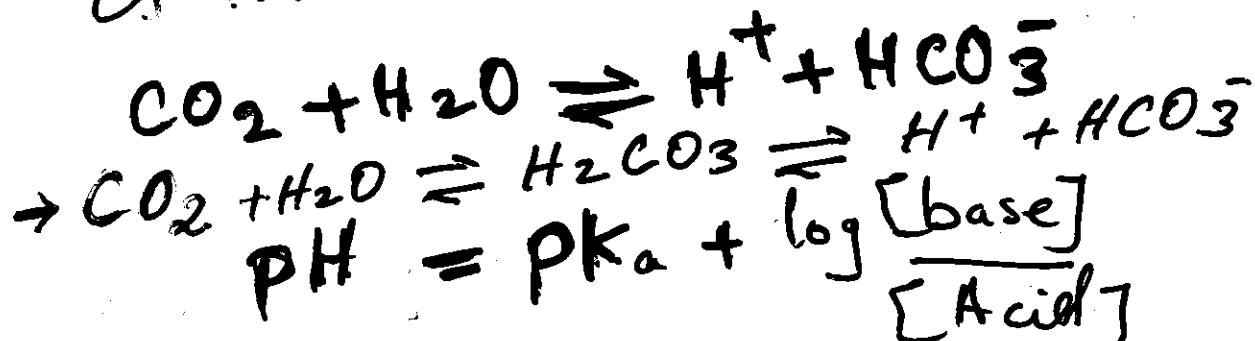


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Regulation of Blood pH

Bicarbonate Buffer

When CO_2 is dissolved in H_2O , there is little H_2CO_3



Under physiological conditions

$$7.4 = 6.1 + \log \frac{[\text{HCO}_3^-]}{[\text{CO}_2]}$$

$$1.3 = \log \frac{[\text{HCO}_3^-]}{\text{CO}_2}$$

$$\frac{[\text{HCO}_3^-]}{[\text{CO}_2]} = \frac{20}{1}$$

} solubility coefficient of CO_2
 0.03 mM/mm Hg

Normal values

$$\text{pH} = 7.4$$

$$\text{PCO}_2 = 40 \text{ mm Hg} \quad (\sim 1.2 \text{ mM})$$

$$[\text{HCO}_3^-] = 24 \text{ mM}$$

The Bicarbonate Buffer System

(4a)

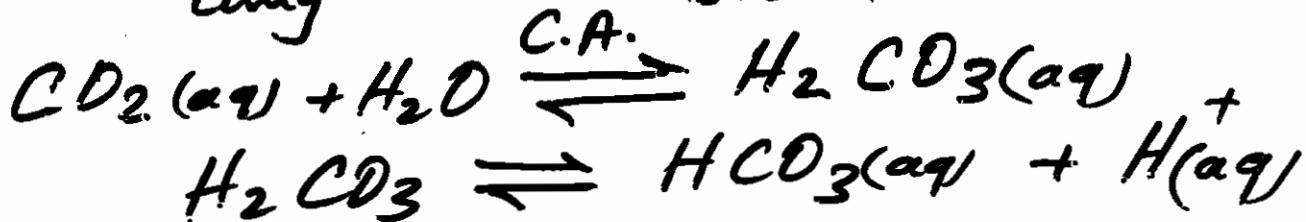
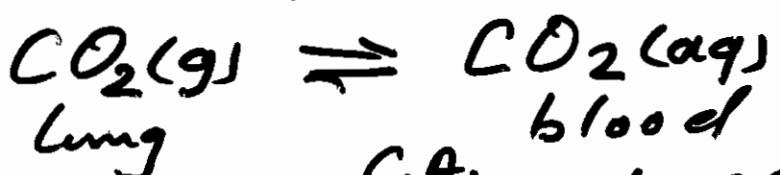
Under physiological conditions with plasma pH = 7.4 ; pKa = 6.1

$$\frac{HCO_3}{H_2CO_3} = 20/1$$

Actual pH of blood is at the upper limit of buffering range of carbonic-bicarbonate buffer

$$6.1 \pm 1 = 5.1 - 7.1$$

Inefficiency is replenished by the reserve supply of gaseous CO₂ in lungs



These reactions also work in reverse

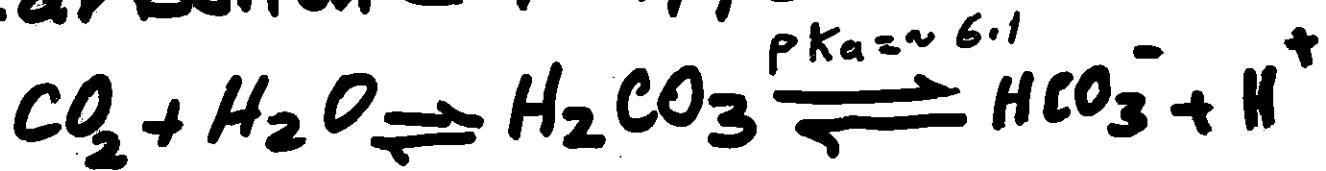
Excess H⁺ is removed by HCO₃⁻



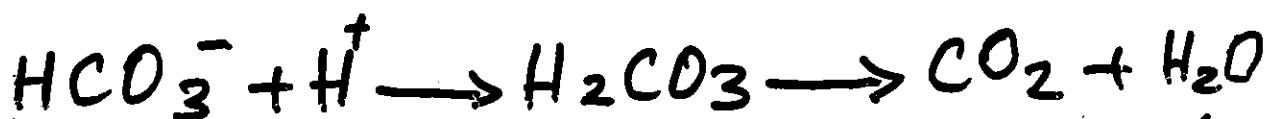
expired by
lung

Mechanism of Action of Carbonate Buffer

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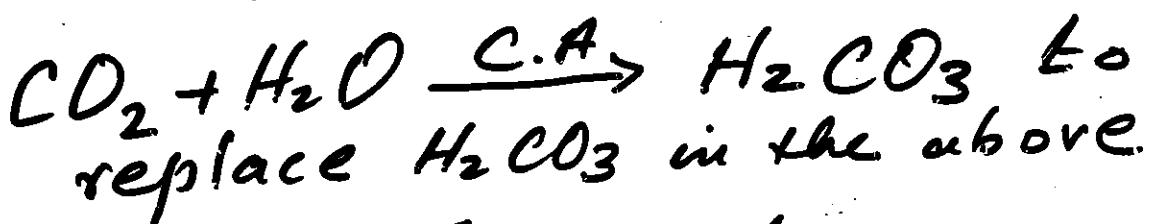
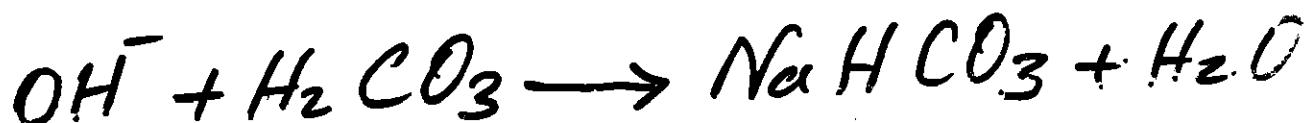


- Acid added to blood



Excess CO_2 greatly stimulate respiration which eliminate CO_2 from extracellular fluid

- Base added to the blood



Decrease $[CO_2]$ decreases respiration rate to decrease rate of CO_2 expiration

HCO_3^+ alkali reserve

$$HCO_3^- / CO_2 = \frac{25 \text{ mmole/l}}{1.25 \text{ mmole}} = \frac{20}{1}$$

Phosphate Buffer Systems:-

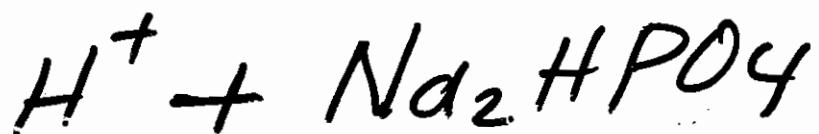
(4c)

$$pK_a = 7.1 - 7.2 \quad \underline{\text{very good}}$$

Considerable concentration in intracellular fluids and Tubular fluids of kidneys

In RBC, conc. of 2,3-BPG is 4–5 mmole/l is considerable conc \rightarrow 16% of non-carbonate buffer contribution

Action:



Protein Buffers

Proteins, especially ALBUMIN, accounts for 95% of non-carbonate buffering value in the Plasma

- Presence of dissociable acidic ($-COOH$) and basic ($-NH_2$) groups
- In particular the side chain of histidine (imidazole gr) having $pK_a = 7.3$
- Albumin contains 16 his/mole

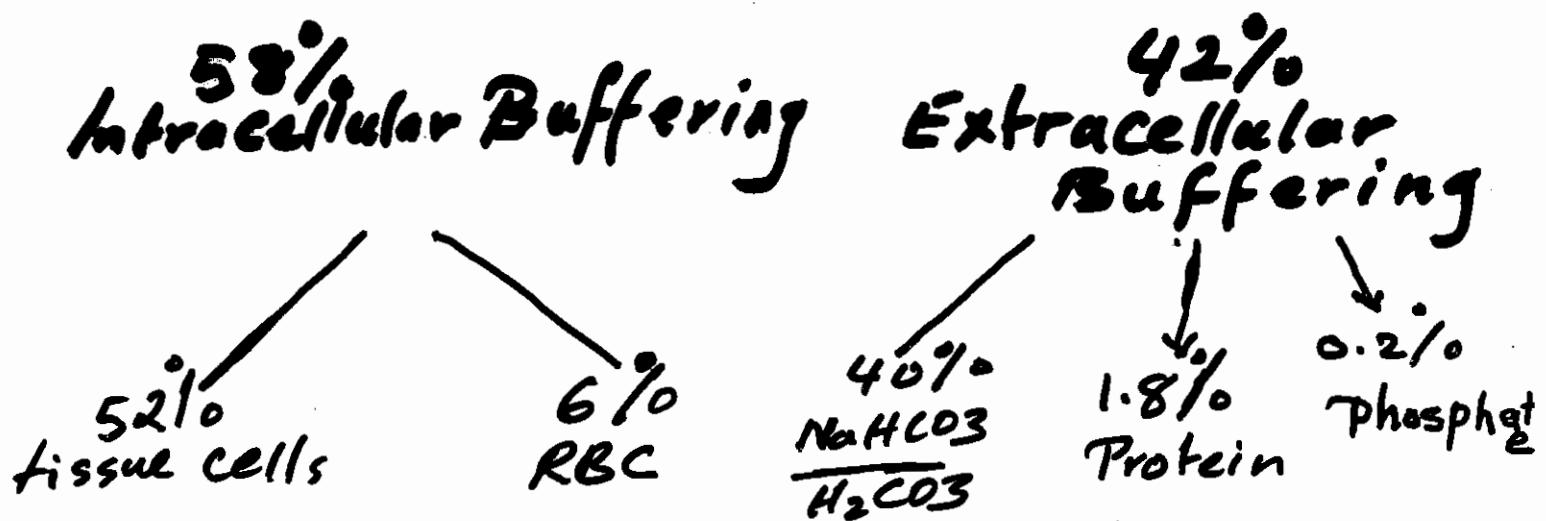
Hemoglobin Buffer

- major intracellular buffer of blood rbc
- Hb has a high conc of His (38 moles/1 mole of Hb.)
- It buffers H_2CO_3 and CO_2
- It works in cooperation with the bicarbonate system

(more details in Blood & lymph system - 3rd yr)

(6)

Relative Capacity of the Buffer Systems in the body



- Buffers act quickly but not permanently
 - They don't eliminate acids from body or replenish alkali reserve
 - Respiratory and Renal mechanisms are very essential for final elimination
- Normal pH range: $7.38 \text{---} 7.42$
 (7.4)
- Acidosis
 - when $\text{pH} < 7.38$
 - but when $\text{pH} < 7.25 \rightarrow \text{life is threatened}$
 - Acidosis $\rightarrow \text{CNS depression and coma}$
 - when $\text{pH} < 7.0$ death occurs

Metabolic Acidosis: $\downarrow [\text{HCO}_3^-]$

Untreated diabetes
Starvation diet
High protein diet
Low-fat diet

\uparrow ketone bodies
(Ketosis) $\rightarrow \uparrow [\text{H}^+]$

Lactic acidosis, therapeutic administration of HCl
kidney disorder

Normal Metabolism

Volatile acids



$\sim 20,000 \text{ mEq/day}$

excreted as CO_2 by lung

Fixed Acids

e.g. lactic acid,
ketoacids, uric acid, phosphoric and sulphuric acids

$60-80 \text{ mEq/day}$

Buffered and H^+ excreted by kidney

Compensation:-

Increased excretion of acid in urine H_2PO_4^-
Increased respiration to eliminate CO_2 NH_4^+

Respiratory Acidosis: $\uparrow [\text{CO}_2]$

Increased in $[\text{CO}_2]$ caused by

Pulmonary problems

e.g. chronic obstructive airway disease, asthma, emphysema & pneumonia; cardiac arrest, severe hypoxia — etc.

Compensation:-

Increased renal reabsorption of HCO_3^-
Increased urinary excretion of acid, rise in respiratory

Alkalosis

$\text{PH} > 7.42$

$\text{PH} > 7.55$ is dangerous
 > 7.60 death

induces muscular hyperexcitability
 and tetany

• Metabolic alkalosis

• Results from clinical administration
 in excess of alkali (e.g. NaHCO_3)

severe vomiting (loss of gastric juice)

Hypokalaemia (low cellular K^+)

$\rightarrow \uparrow [\text{HCO}_3^-]$

Compensation :- Increased excretion of HCO_3^- , respiration is depressed

• Respiratory alkalosis

Hyperventilation $\downarrow \text{PCO}_2$

(heavy breathing)

Hysteria

Anxiety

altitude sickness

hot baths, working at high temp.

Compensation :

Increased excretion of HCO_3^-
 reduction in urinary HCO_3^- excretion

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Figure 10.6 Breathing and the bicarbonate buffer system

