

Regulatory Mechanism against changes in $[H^+]$ of Blood

Two types of metabolic acids produced

1- Fixed acids, non-gaseous

- phosphoric and sulphuric acids produced from sulphur & phosphorus of proteins and lipoproteins, nucleoproteins
- organic acids as Pyruvic, Lactic, keto acids (e.g. acetoacetic, β -hydroxy butyric acid) and uric acid

2- Volatile acids

the physiological expt. = Carbonic acid
Amount produced daily equivalent to
36 litres of 1.0 N acid.

Buffering Capacity depends on:-

1- Conc. of buffer

2- pK_a of the buffer and the desired pH

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Various mechanisms :-

- Buffer mechanism - First
- Respiratory mechanism - second line of defence
- Renal mechanism
Third 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's, can eliminate the excess acid or base from body.

The Principal buffers of the Blood:-

Buffer System

Plasma
(extra cellular buffer)

Erythrocyte
(intra cellular buffer)

Bicarbonate

$NaHCO_3 / H_2CO_3$

$KHCO_3 / H_2CO_3$

Phosphate

Na_2HPO_4 / NaH_2PO_4

K_2HPO_4 / KH_2PO_4

Protein

$Na Protein / H. Protein$

$K Hb / H. Hb$

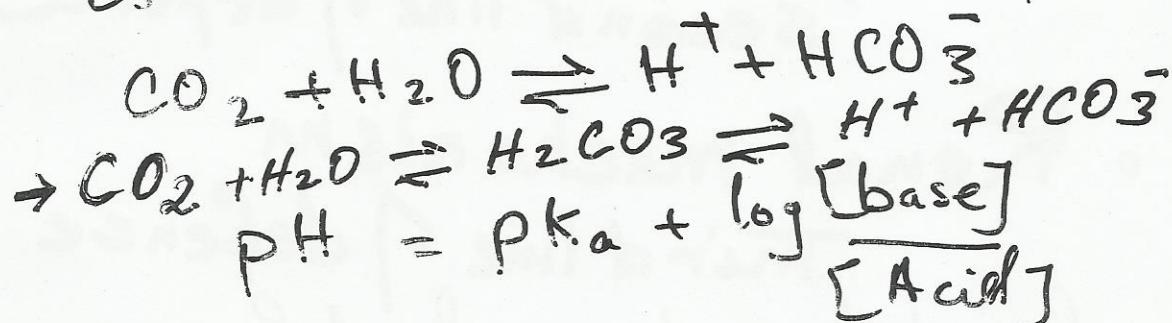
$K HbO_2 / H. HbO_2$

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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

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

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

$$\frac{[\text{HCO}_3^-]}{[\text{CO}_2]} = \frac{2.0}{1}$$

} solubility coefficient of CO_2
0.03 mM / Hg

Normal values

$$\text{pH} = 7.4$$

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

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

The Bicarbonate Buffer System

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Under physiological condition with
plasma pH = 7.4 ; pKa = 6.1
 $HCO_3^- / H_2CO_3 = 20/1$

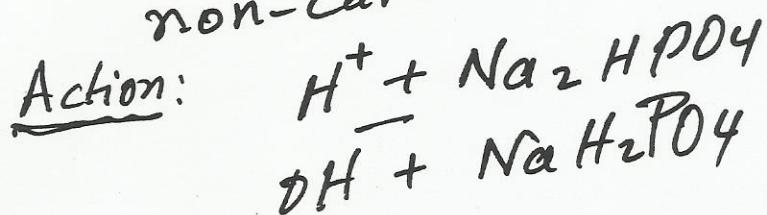
Mechanism:-

- $HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$
Excess CO_2 greatly stimulates respiration which eliminate CO_2 from extracellular fluid.
- $OH^- + H_2CO_3 \rightarrow NaHCO_3 + H_2O$
 $CO_2 + H_2O \xrightarrow{C.A.} H_2CO_3$ to replace above decrease $[CO_2]$ to decrease respiration to decrease rate of CO_2 expiration

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

Phosphate Buffer Systems:-

pKa 7.1 - 7.2 — v. good
Considerable in intracellular & tubular fluids of kidney.
in RBC, 2,3 BPG is 4.5 mmole/l is in particular considerable — 16% of non-carbonate buffer contribution



Protein Buffers

Proteins, especially Albumin, account for 95% of non-bicarbonate buffering value in the plasma.

- Presence of dissociable acid (COOH) and basic ($-\text{NH}_2$) groups
- In particular imidazole gr. of the side chains of histidine ($\text{pK}_a = 7.3$)
- Albumin contains 16 His / mole

Hemoglobin Buffer

- major intracellular buffer of blood
- Hb has a high conc. of His 38 molecules // mole of Hb
- It buffers H_2CO_3 and CO_2
- It works in cooperation with the bicarbonate system.
(Details in the future 3rd yr)

Relative Capacity of Buffer Systems ⁽⁶⁾

In the body :-

52% Tissue cells	6% RBC	40% $\text{HCO}_3/\text{H}_2\text{CO}_3$	0.2% 1.8% ↓ Phosph- Proteins
58% Intracellular Buffering		42% Extra-cellular Buffering	

Buffers Act Quickly but not Permanently

- They do not eliminate acids from body or replenish alkali reserve
- Respiratory & Renal Mechanism are very essential for final elimination

Normal pH range :-

7.38 — 7.42 (7.4)

Acidosis

When $\text{PH} < 7.38$

= $\text{PH} < 7.25$, life is threatened

acidosis \rightarrow CNS depression and Coma
when $\text{PH} < 7.0$ death occurs

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Metabolic Acidosis

Untreated diabetes
 Starvation diet
 high-protein diet
 low-fat diet } \rightarrow Ketone bodies
} \rightarrow Ketosis \rightarrow $\uparrow [H^+]$

Normal metabolism

Volatile acids
 H_2CO_3
 $20,000 \text{ mEq/day}$
 Excreted as CO_2 by lung

fixed acids
 e.g. lactate, keto acids, uric acid
 sulphuric & phosphoric acids. ($60-80 \text{ mEq/day}$)
 Buffered & H^+ excreted by kidney

Respiratory Acidosis

$[CO_2]$ caused by Pulmonary problems

Proteins
 lipoproteins
 Nucleoproteins } \rightarrow Sulphuric and
} + phosphoric acids

Alkalosis

$\text{PH} > 7.42$

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

induces muscular hyperexcitability
 and tetany

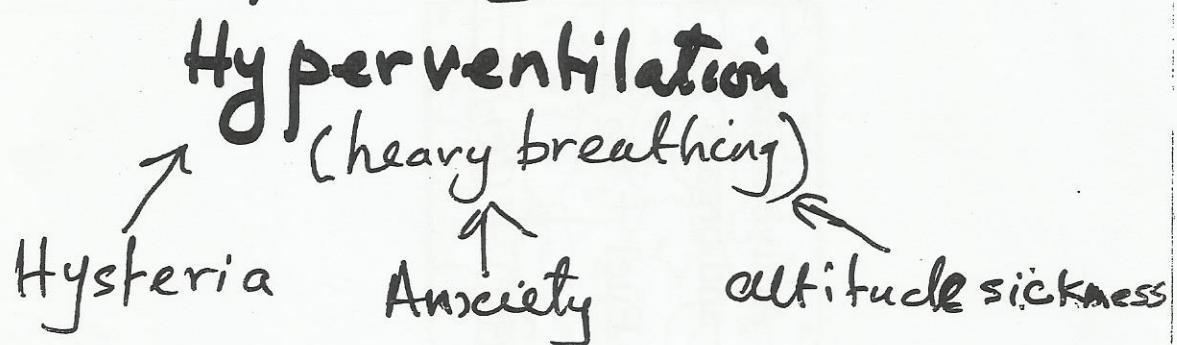
• Metabolic alkalosis

1. Results from clinical administration
 in excess of salts of metabolic acids,
 e.g. Na.lactate & NaHCO_3 and
 severe vomiting

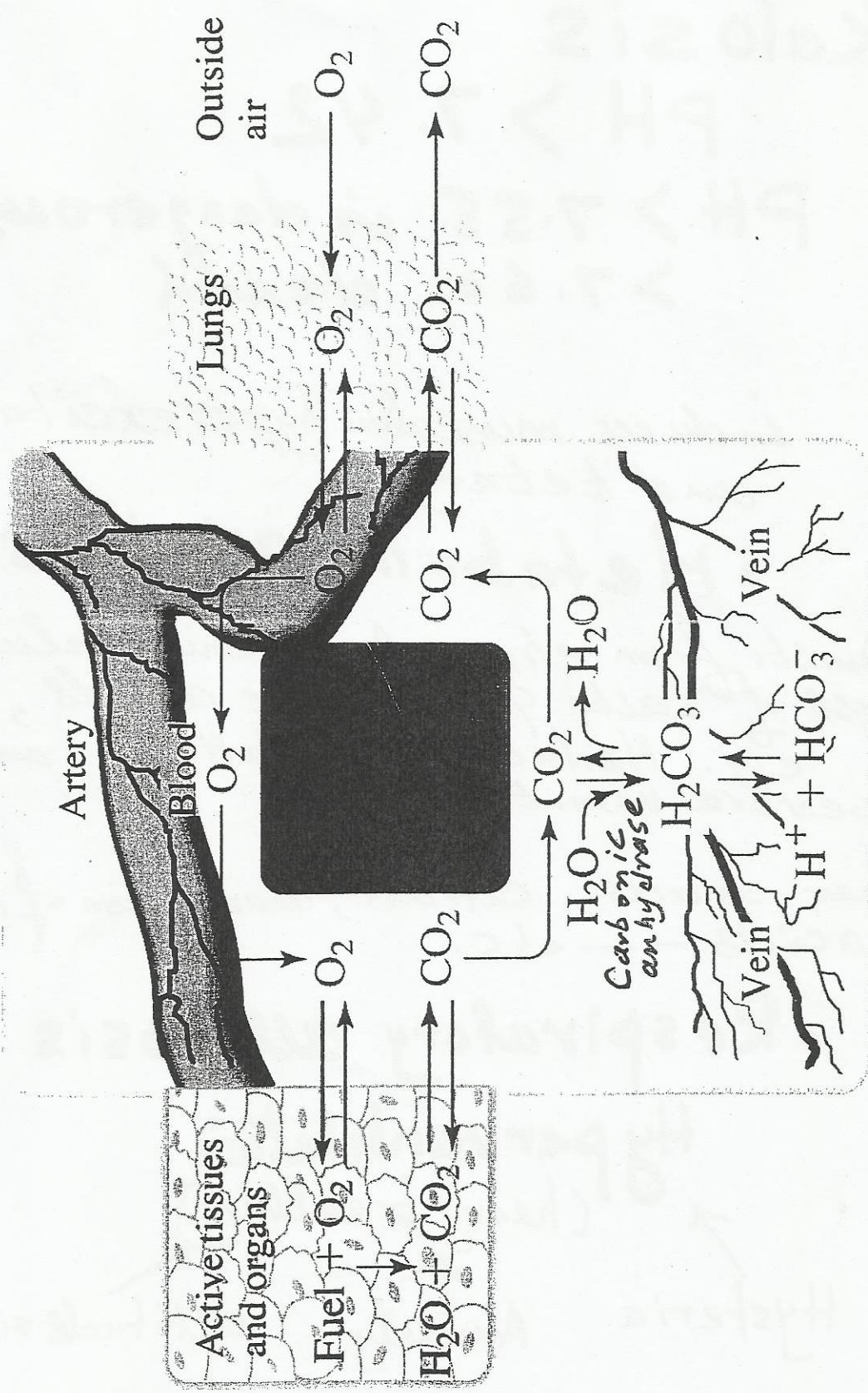
Other sources: citrate, deamination of amino
 acids — etc.

• Respiratory alkalosis

Hyperventilation

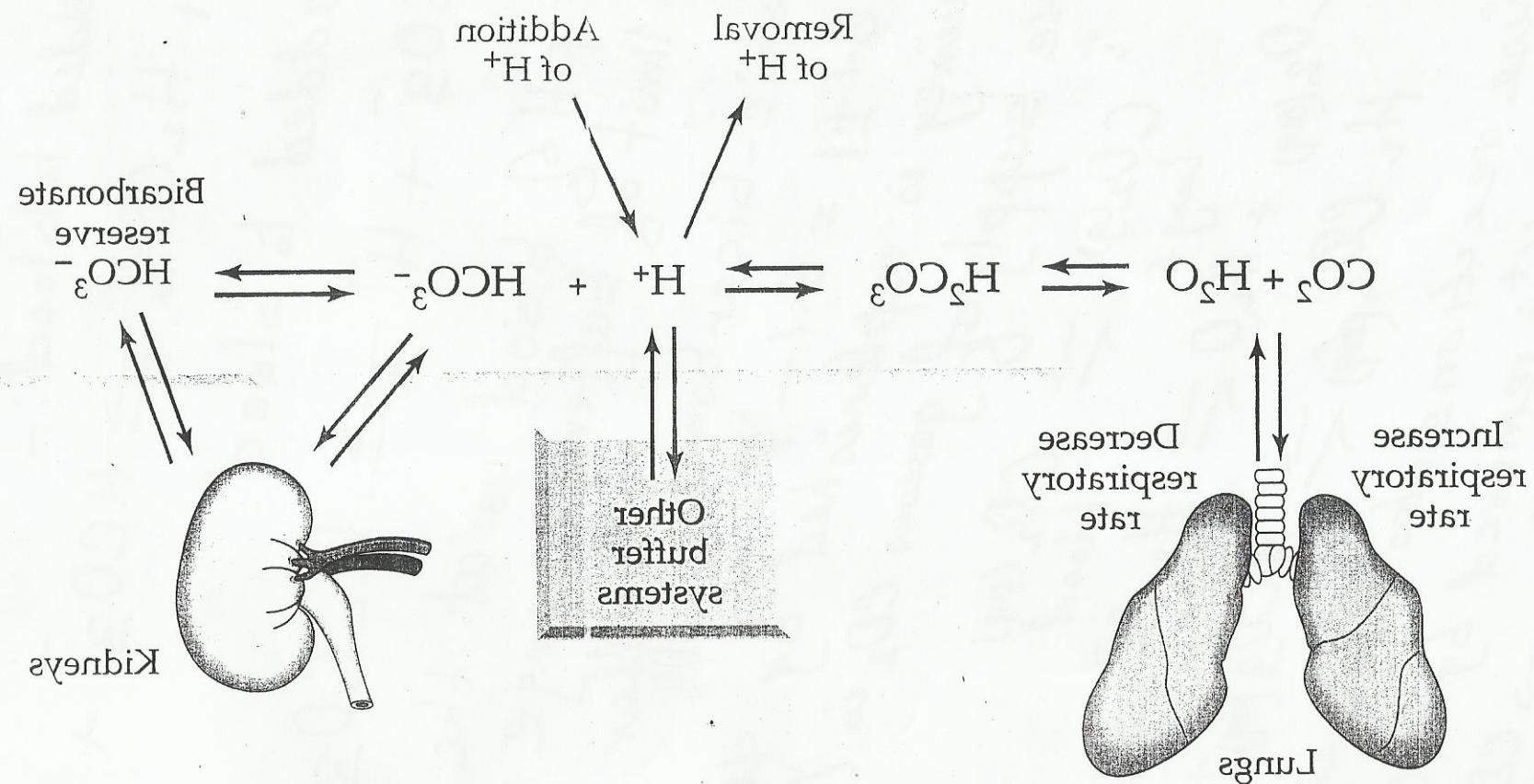


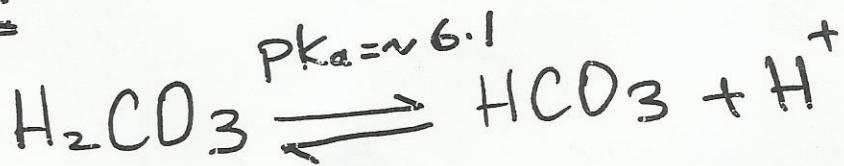
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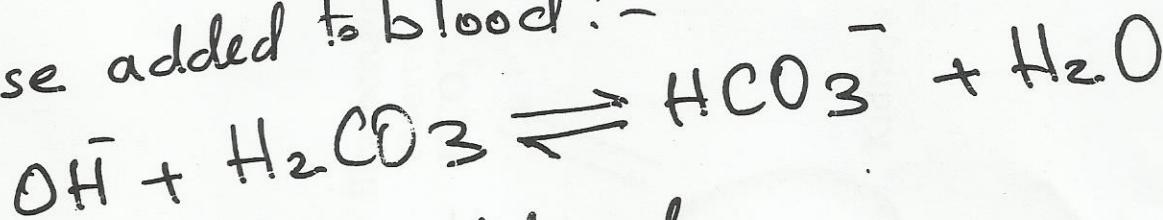
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Figure 10.6 Breathing and the bicarbonate buffer system

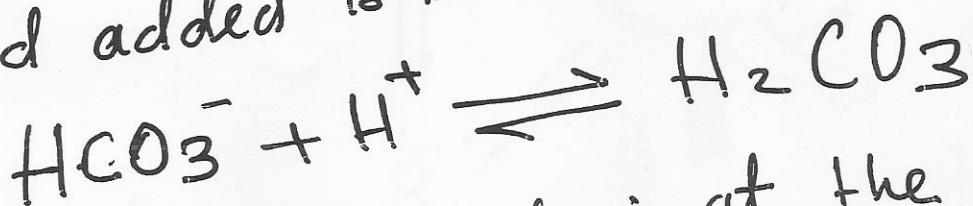


Action

base added to blood :-

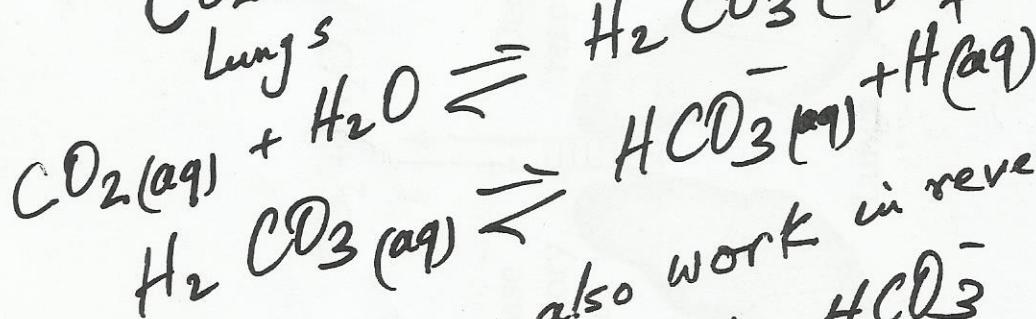
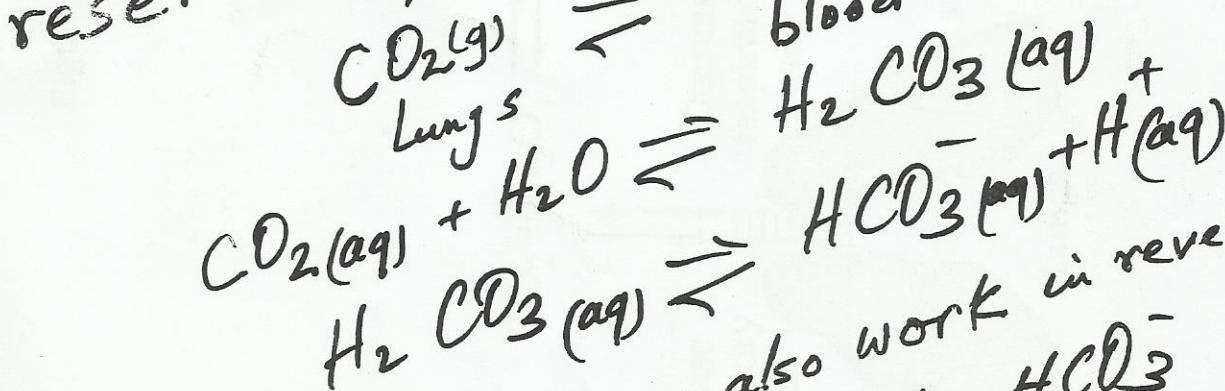
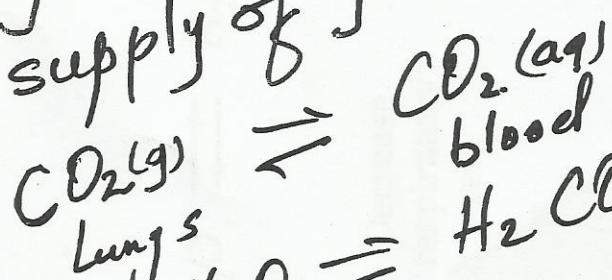


Acid added to blood



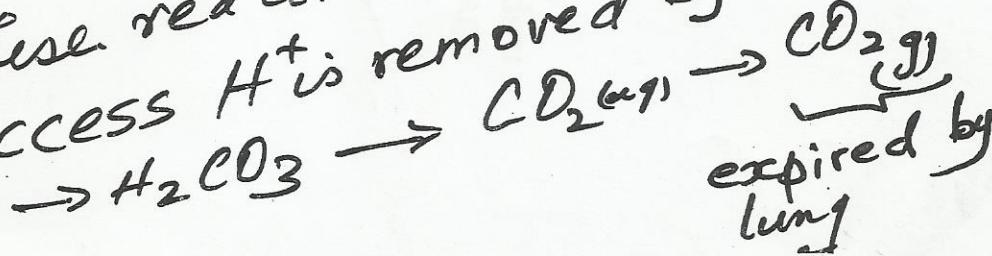
Actual pH of blood is at the upper limit of buffering range of carbonic-bicarbonate buffer

$6.1 \pm 1 = 5.1 - 7.1$
Inefficiency is replenished by the reserve supply of gaseous CO_2 in lungs



These reactions also work in reverse

excess H^+ is removed by HCO_3^-



expired by lung