ACID BASE BALANCE

Acid = Proton donor
Base = Proton acceptor
pH = Negative logarithm of H^+ concentration
Neutral pH = 7
Acid = pH less than 7.
Alkali = pH more than 7

Regulation of Plasma pH

→ Plasma pH is maintained in a narrow range.
→ Normal plasma pH is 7.4 ± 0.02 (7.38 - 7.42)
→ Intracellular pH may be less than this.

If plasma pH decreases below normal, it is called acidosis.
If plasma pH increases above normal, it is called alkalosis.
Change in pH is dangerous. The pH range that is compatible with life is 6.8 - 7.8.

Plasma pH is regulated by 3 Mechanisms

1. Buffers
2. Respiratory regulation
3. Renal regulation

Buffers

Buffers are solutions that resist the change in pH when an acid or alkali is added.

→ A buffer is composed of a weak acid and its salt with a strong base [or weak base and its salt with a strong acid].

Eg: Bicarbonate Buffer:
$NaHCO_3 / H_2CO_3$.

Phosphate Buffer:
Na_2HPO_4 / NaH_2PO_4.

pH of a buffer obeys Henderson-Hasselbalch equation.

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

where pK is the acid dissociation constant of the buffer (pKa).

Factors affecting pH of a Buffer

From Henderson-Hasselbalch equation, it can be seen that pH of a buffer is affected by
(a) pK of buffer: the more pK, more pH
(b) Ratio of [salt] to [acid].

The buffering capacity depends on the actual concentration of the salt and acid.

→ A buffer is most effective when the pH is equal to its pKa

This occurs when the ratio of [salt] to [Acid] is 1.

Effective range of a buffer is pK-1 to pK+1.

→ Buffers act as the first line of defence against acid base disturbances.

Important Buffers of body fluids

Plasma	Intracellular	RBC
Bicarbonate	Phosphate	Hemoglobin
Phosphate	Protein	Phosphate
Protein	Bicarbonate	Bicarbonate

Bicarbonate Buffer ($NaHCO_3/H_2CO_3$)

Bicarbonate/carbonic acid buffer is the most important buffer in plasma.

→ pKa of Bicarbonate buffer is 6.1.

$[HCO_3^-]$ = 24 ± 2 mmol/L.

$[H_2CO_3]$ = 1.2 mmol/L.

(This is equal to a $paCO_2$ of 40 ± 2 mm Hg)

As per Henderson-Hasselbalch equation, a buffer is effective when pH = pK-1 to pK+1, and when Ratio of [Salt] to [Acid] is 1.

In case of bicarbonate buffer, pK is 6.1 which is different from plasma pH.

→ Ratio of [salt] to [Acid] is 20 (24/1.2)

Even then, Bicarbonate buffer is effective because of 2 reasons:

① "Open at both ends"

Bicarbonate is regulated by renal mechanisms and carbonic acid (CO_2) is regulated by respiratory mechanisms. Kidneys regulate the level of bicarbonate by increasing or decreasing the excretion of H^+ by various mechanisms.

Respiratory mechanisms regulate pCO_2 (and thereby H_2CO_3) by increasing or decreasing the rate of respiration.

② Metabolism usually produce acids. So, plasma is prone for an acid load. plasma keeps an excess of alkali to compensate for this (that is 20 times that of acid.) This is called alkali reserve.

Phosphate Buffer (Na_2HPO_4/NaH_2PO_4)

Most important intracellular buffer. Phosphate buffer has more than one pK value because of the presence of more than one ionisable groups. So it can act as an effective buffer over a wide range of pH. that is why it acts effectively as a buffer.

Protein Buffer

Proteins like Albumin, Hb etc act as good buffers.

Proteins act as buffers due to their ionizable side chains.

Among the aminoacids, the most effective one is imidazole group of Histidine. Its pK value (6.8) is close to the plasma pH.

→ Hemoglobin is 6 times more effective compared to plasma proteins because:

(a) Conc. of Hb is 2 times that of plasma proteins.

(b) Number of Histidine residues is 3 times that of plasma proteins.

Buffers act as the first line of defense against an acid base disturbance.

Respiratory Regulation.

It is the second line of defense. This is done by regulating the excretion of CO_2 and thus adjusting the H_2CO_3 levels

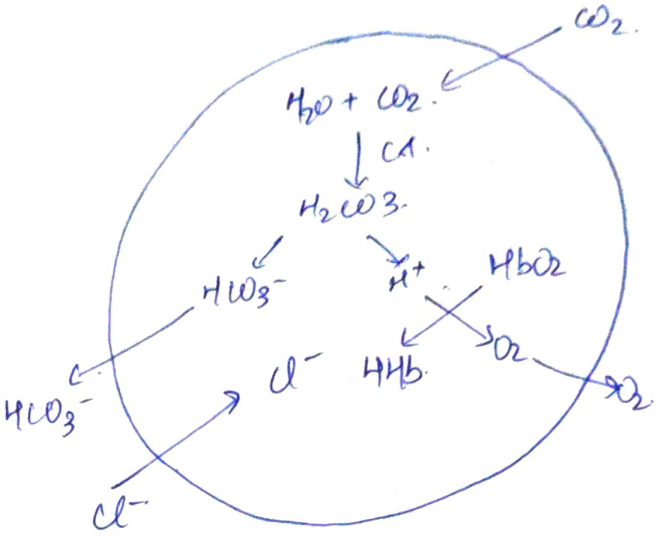
→ Chemoreceptors that regulate the respiratory centre are sensitive to H^+ concentration.

→ When pH decreases the chemoreceptors sense this and stimulate the respiratory centre. This increases the rate of respiration and increases the removal of CO_2.

→ When pH increases, the opposite happens and the rate of respiration decreases.

Role of Hb in removal of CO_2.

In cells,



→ CO_2 enters RBCs from cells & combines with water to form carbonic acid. This splits to HCO_3^- and H^+. Oxy Hb releases oxygen into cells and combines with H^+. Bicarbonate diffuses into plasma in exchange for chloride. This is called chloride shift.

Transport of CO_2 as bicarbonate helps to transport CO_2 without decreasing the plasma pH. This is called isohydric transport of CO_2.

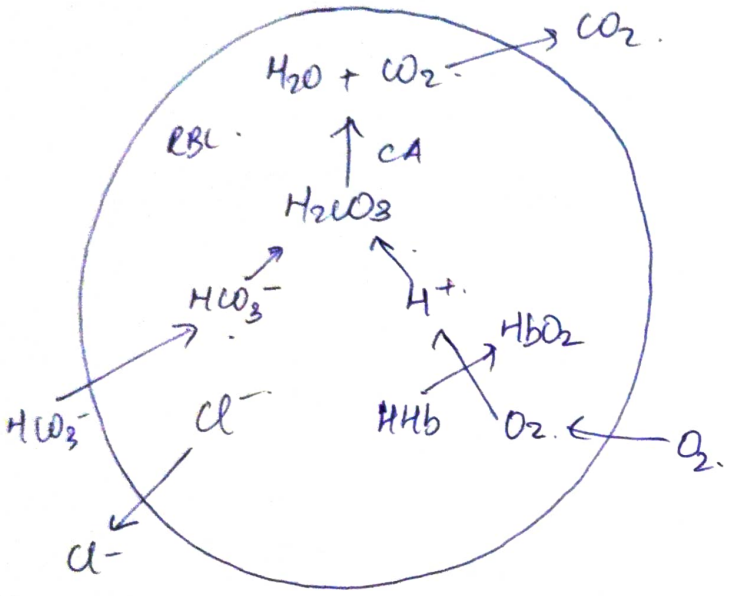
It has two advantages:

(a) Large amounts of CO_2 can be transported without decreasing pH of plasma.

(b) Bicarbonate thus generated contributes to alkali reserve.

The opposite changes happen when RBCs reach lungs. (Explain)

In lungs.



Renal Regulation

This is the final defense mechanism against an acid base disturbance.

→ pH of glomerular filtrate & same as that of plasma (7.4)

→ Average pH of urine is around 6.

→ This shows that there is net acidification of the tubular fluid.

→ Depending on the acid-base status, pH of urine can vary from 4.5 to 8.

→ Acidification of tubular fluid by the kidney occurs by 4 different mechanisms.

1. Excretion of H^+ with generation of Bicarbonate (HCO_3^-)
2. Reabsorption of filtered bicarbonate.
3. Excretion of titratable acidity
4. Excretion of ammonium (NH_4^+) ions.

Excretion of H^+ with generation of Bicarbonate (HCO_3^-).

This occurs in PCT.

Plasma	PCT cells	Tubular lumen
Na^+ ←	Na^+ ←	Na^+
HCO_3^- ←	$HCO_3^- + H^+$	→ H^+
	↑ H_2CO_3 ↕ CA $H_2O + CO_2$	

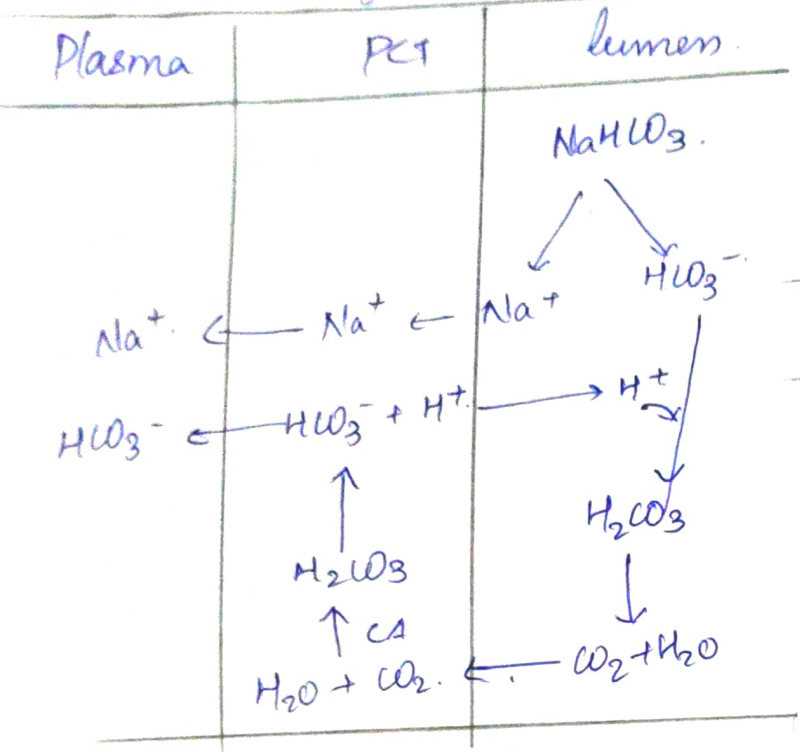
1) CO_2 and H_2O combine to form H_2CO_3 by carbonic anhydrase in tubular cells. This splits to H^+ and HCO_3^-.

3 H^+ is secreted into the tubular lumen in exchange for Na^+

Na^+ and HCO_3^- are reabsorbed into plasma.

This converts H^+ and generates HCO_3^-

Reabsorption of filtered bicarbonate



This also occurs in PCT.

→ Filtered $NaHCO_3$ splits into Na^+ and Bicarbonate.

→ Bicarbonate combine with the H^+ secreted in exchange for Na^+

→ This forms carbonic acid which splits into water and CO_2.

→ CO_2 is reabsorbed.

→ In tubular cells, this forms bicarbonate which gets absorbed with Na^+

By this mechanism, the filtered bicarbonate is reabsorbed

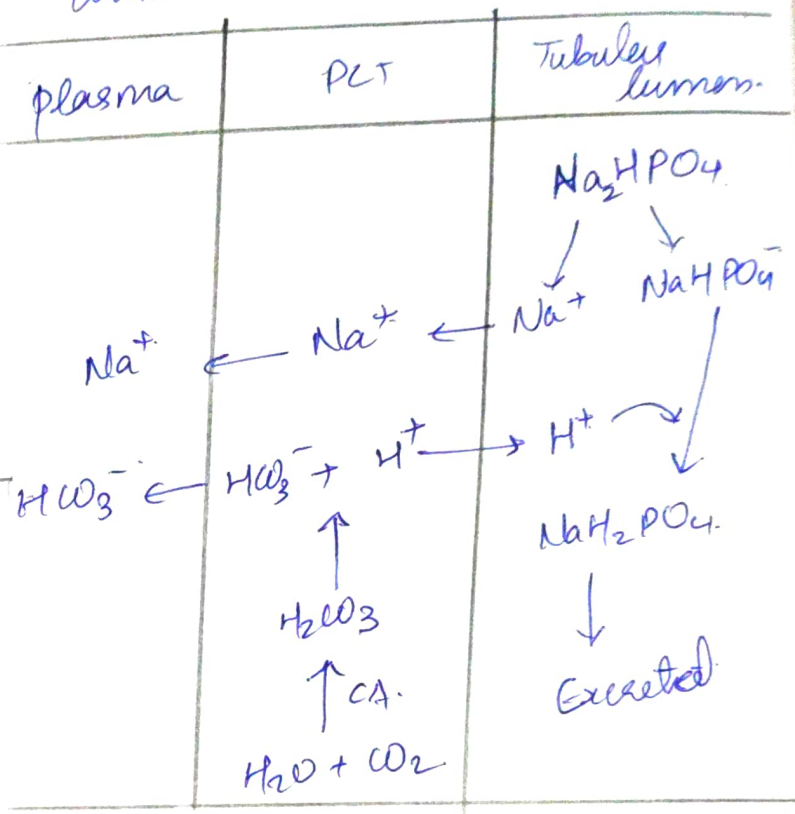
There is no net generation of bicarbonate or net excretion of H^+

Excretion of titratable acidity (phosphate mechanism)

→ ~~titratable~~ Titratable acidity is defined as the number of ml of 0.1N NaOH required to titrate 1L of urine to pH 7.4

→ Major titratable acid is sodium acid phosphate (NaH_2PO_4)

→ The process starts in PCT and continues till DCT.



→ H^+ generated by carbonic anhydrase is secreted by in exchange for Na^+.

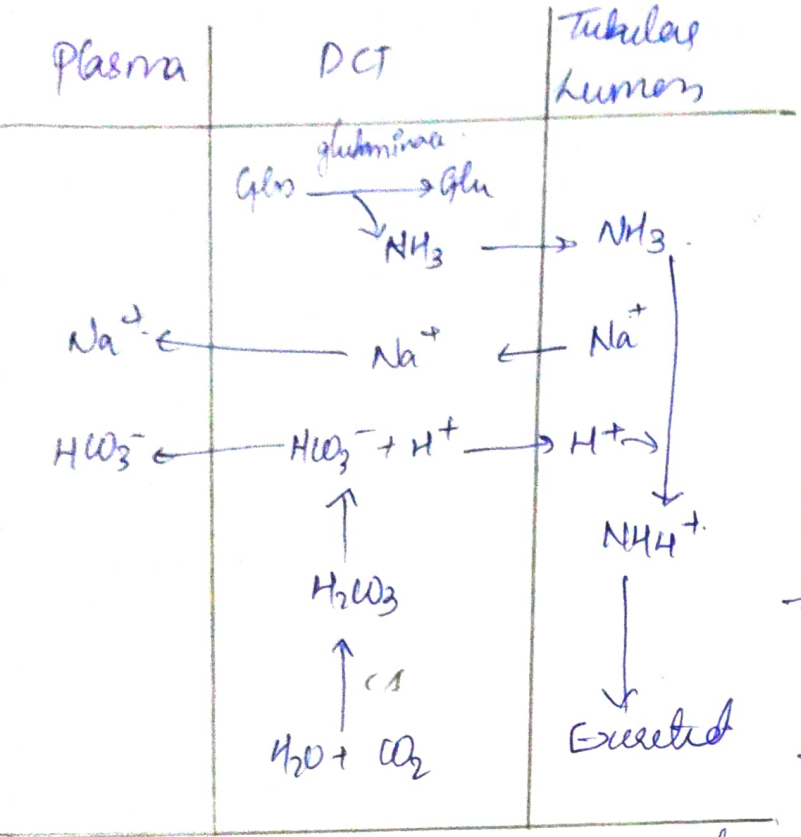
→ By addition of this H^+, basic phosphate (Na_2HPO_4) is converted to acid phosphate (NaH_2PO_4)

→ Phosphate buffer is highly effective in urine.

→ The acid / base phosphate pair is also known as "Urinary buffer"

Excretion of ammonium ions

This occurs in DCT.



Glutaminase splits glutamine to glutamate and ammonia.

- This ammonia diffuses into tubular fluid, and combines with H^+ to form NH_4^+ ions
- This helps to excrete large quantities of H^+ ions without much change in pH of urine.

→ In summary, kidney excretes acids with the help of carbonic anhydrase and glutaminase.

→ Activity of both these enzymes increases during acidosis. This helps excretion of more acids during acidosis.

ABG → Arterial Blood gas analysis.

Step 1 : look at pH (↓ → acidosis, ↑ → alkalosis) N → normal, fully compensated

Step 2 : find out the cause of pH change (find out primary disturbance)

If acidosis, look for ↑ pCO_2 (H_2CO_3) or ↓ HCO_3^-

If alkalosis, ↓ pCO_2 or ↑ HCO_3^-

Step 3 : Look for compensation.

→ If compensatory component is within normal range → uncompensated

→ If compensatory component had changed in the same direction, ⇒ compensation has started

→ If pH has come back to within 7.35 — 7.45, fully compensated.

→ If compensation has started, but pH has not come back to normal, partially compensated.

Step 4 : Calculate Anion Gap

$(Na^+ + K^+) - (Cl^- + HCO_3^-)$

Normal value

pCO_2 = 40 ± mm Hg

HCO_3^- = 24 ± 2 m mol/L

H_2CO_3 = 1.2 m mol/L

HCO_3^-/H_2CO_3 = 20 (alkali reserve)

pH = 7.38 – 7.42

Na^+ = 136 – 145 m mol/L

K^+ = 3.5 – 5.5 m mol/L

Cl^- = 96 – 105 m mol/L

Anion gap = 12 – 16 m mol/L