ACID BASE BALANCE

-- Normal Mechanism
-Cause of Imbalance
-C
ompensation

Acid base balance

- For normal functions of body and normal enzyme activity a normal Hydrogen ion concentration(normal PH) is essential.
- PH is the negative log of Hydrogen (H^{+} Ion) concentration.
- A Hydrogen ion is a single free proton released from Hydrogen atom.
- Normal [H^{+}]of arterial blood=0.00004meq/l which is equal to PH 7.4.

- PH of arterial blood = 7.4
- PH of venous blood = 7.35
- Intra cellular PH is slightly lower then plasma PH.
- PH of urine is 4.5 - 8.0
- **Acidosis** is the PH of body fluid less then normal.
- **Alkalosis** is the PH of the body fluid is more then normal.
- PH limit for human survival is 6.8 – 8.0

ACIDS

- Acids are molecules that release H^{+} Ion (proton) in solutions("proton donors“).

Strong acids dissociate rapidly and release large amount of H^{+} Ion .

$HCl \text{------}\rightarrow \quad H^{+} \quad + \quad Cl^{-}$

Weak acids have less tendency to dissociate and release less amount of H^{+}Ion

$H2CO3 \text{------}\rightarrow \quad H^{+} \quad + \quad HCO3^{-}$

Sources of $[H^+]$

- Carbonic acid formation: the major source of H^+ is from metabolically produced CO_2
- Inorganic acid produced during nutrient breakdown: dietary proteins contain a large quantity of sulfuric acid and phosphoric acid
- Organic acid resulting from intermediary metabolism: lactic acid and fatty acids

BASES

- Bases are molecules that can accept H^{+} Ion .
  ("proton acceptors“).
- **Strong bases** react strongly with H^{+} Ion .

$$H^{+} + OH^{-} \dashrightarrow H2O$$

- **Weak bases** bind weakly with H^{+} Ion .

$$H^{+} + HCO3^{-} \dashrightarrow H2CO3$$

Production of bases in the body:

- Blood alkalinity increases when the level of acid in the body decreases or when the level of base increases e.g:
- A vegeterian diet has a tendency for alkalinity because it produces salts of organic acids such as Na lactate which utilizes H+ ions making the body alkaline.
- Physiologically imp.base in the body is Bicarbonate ion & biphosphate ion of buffer systems.

Defence against change in PH

- 1.Buffer system of our body.
- 2.Respiratory system of our body.
- 3. Renal control of our body.

MECHANISMS OF REGULATION OF pH

The mechanisms of regulation of blood pH involves the following factors:

(a) "Front-line" defence: They are mainly:

- *Buffer systems* in the blood: Which restricts pH change in body fluids.
- *Respiratory mechanisms:* Regulation of excretion of CO_2 and hence, regulation of H_2CO_3 concentration in EC fluid.

(b) "Second-line" defence: This is achieved by kidneys *(Renal mechanisms).* Ultimate excretion of excess of acid or base and thus ultimate regulation of concentration of H^+ and HCO_3^- ions in EC fluid.

(c) Dilution factor: The acids introduced into and formed in the body are distributed throughout the ECF volume.

Buffer system

- resists sudden changes in pH.
- ***<u>General Components</u>***

buffer contains:

A)~ a weak acid & its salt 20:1 ($NaHCO_3$/ H_2CO_3)

Addition of strong acid

$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$

HCl = strong non volatile acid

H_2CO_3 = weak and volatile acid

Produced $H_2CO_3 \text{-----} \rightarrow H_2O + CO_2$ (exhaled out)

Addition of strong base

$NaOH + H_2CO_3 \rightarrow NaHCO_3 + H_2O$

B)~ a weak base & its salt (NH_4OH+NH_4Cl)

- Buffer system reacts within in fraction of a second
- **ONLY KEEP H+ TIED UP.**

- PLASMA BUFFERS

- $\frac{NaHCO_3}{H_2CO_3}$
- $\frac{Na_2HPO_4 \text{ (Alk } PO_4)}{NaH_2PO_4 \text{ (Acid } PO_4)}$
- $\frac{Na - Pr}{H\ Pr}$
- $\frac{\text{Na organic acid}}{\text{H organic acid}}$

Buffers of RB Cells

- $\frac{K\ HCO_3}{H_2CO_3}$
- $\frac{K_2H\ PO_4}{K\ H_2\ PO_4}$
- $\frac{K\ Hb}{H\ Hb}$
- $\frac{K\ Hb\ O_2}{H\ Hb\ O_2}$
- $\frac{\text{K organic acid}}{\text{H organic acid}}$

BUFFERS OF KIDNEYS

1. Phosphate Buffer system
2. Ammonia and Ammonium buffer systems
3. Urate and citrate also play a minor role

- **VARIOUS BUFFER SYSTEMS:**
- **$NaHCO_3$ / $H2CO_3$ = 20:1**
- Quantitatively most imp buffer system of E.C.F (extra cellular fluid).
- $NaHCO_3$ + HL(Lactic acid)
- $H^+ + HCO_3$ ---------→ H_2CO_3

H_2CO_3 -----------→ $H_2O + CO_2$ (Exhaled)

A strong fixed acid ------→ Weak volatile acid

(Lactic Acid)

Phosphate Buffer

Na_2HPO_4 / NaH_2PO_4

$Na2HPO_4$ + HCl -----→ NaCl + NaH2PO4

NaH_2PO_4 + NaOH-----→ Na_2HPO_4 +H2O

Imp Buffer of renal tubular fluid and I C F.

Phosphate are imp because , phosphate are

Concentrated due to reabsorption of water but phosphate it self are not reabsorbed.

Protein(zwitter ion)

- Imp Intra cellular(I C) Buffer system:
- High concentration with in the cell.

In acidic media:

Act as a base and NH_2 group takes up H^+ Ion

.

In basic media:

Act as acid and COOH group give H^+ Ion **.**

- **60%-70% of total buffering of body fluid occurs inside of cell and much of this result from the intra cellular protein.**

Haemoglobin

Haemoglobin (Hb) is not only important in the carriage of oxygen to the tissues but also in the transport of CO2 and in buffering hydrogen ions

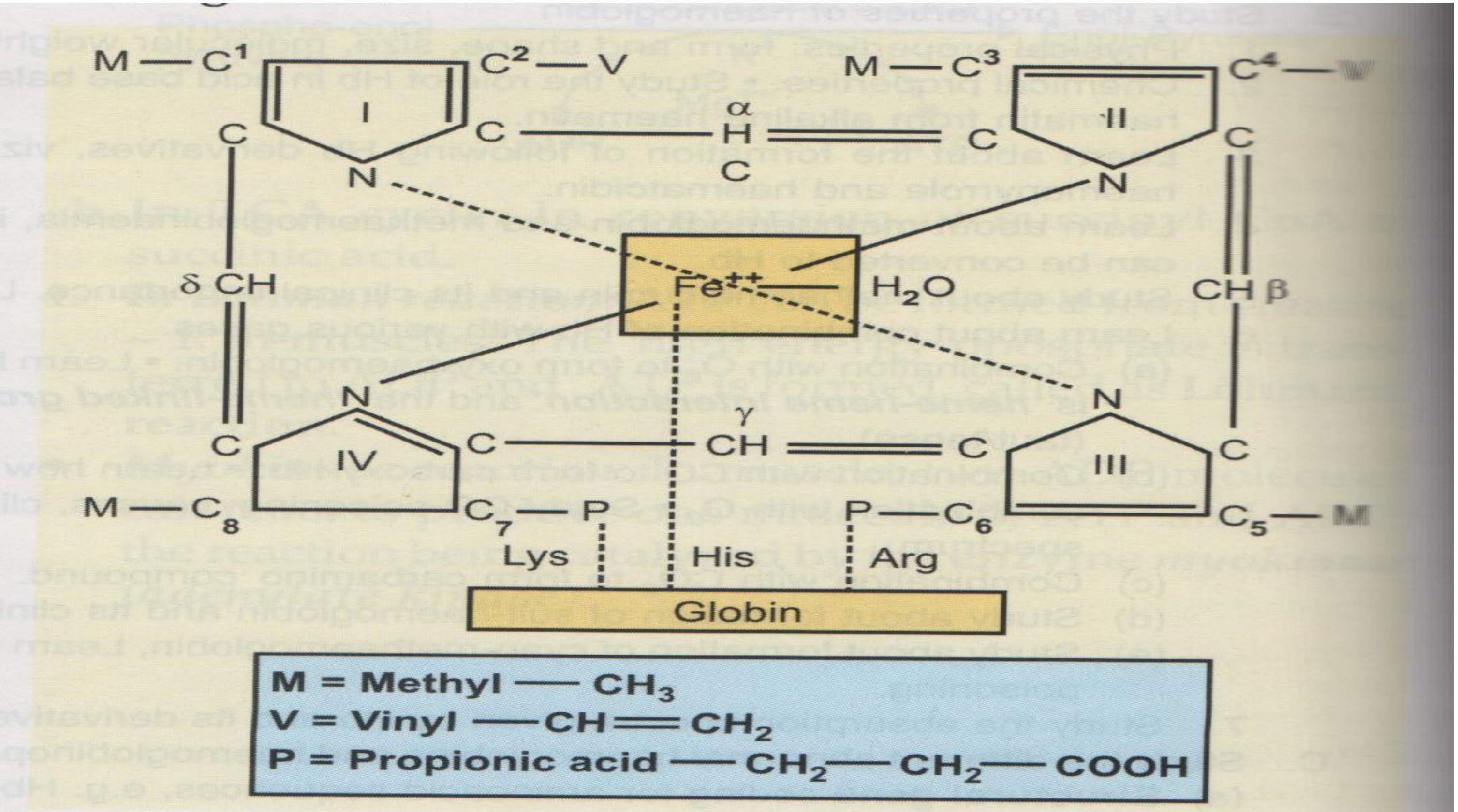
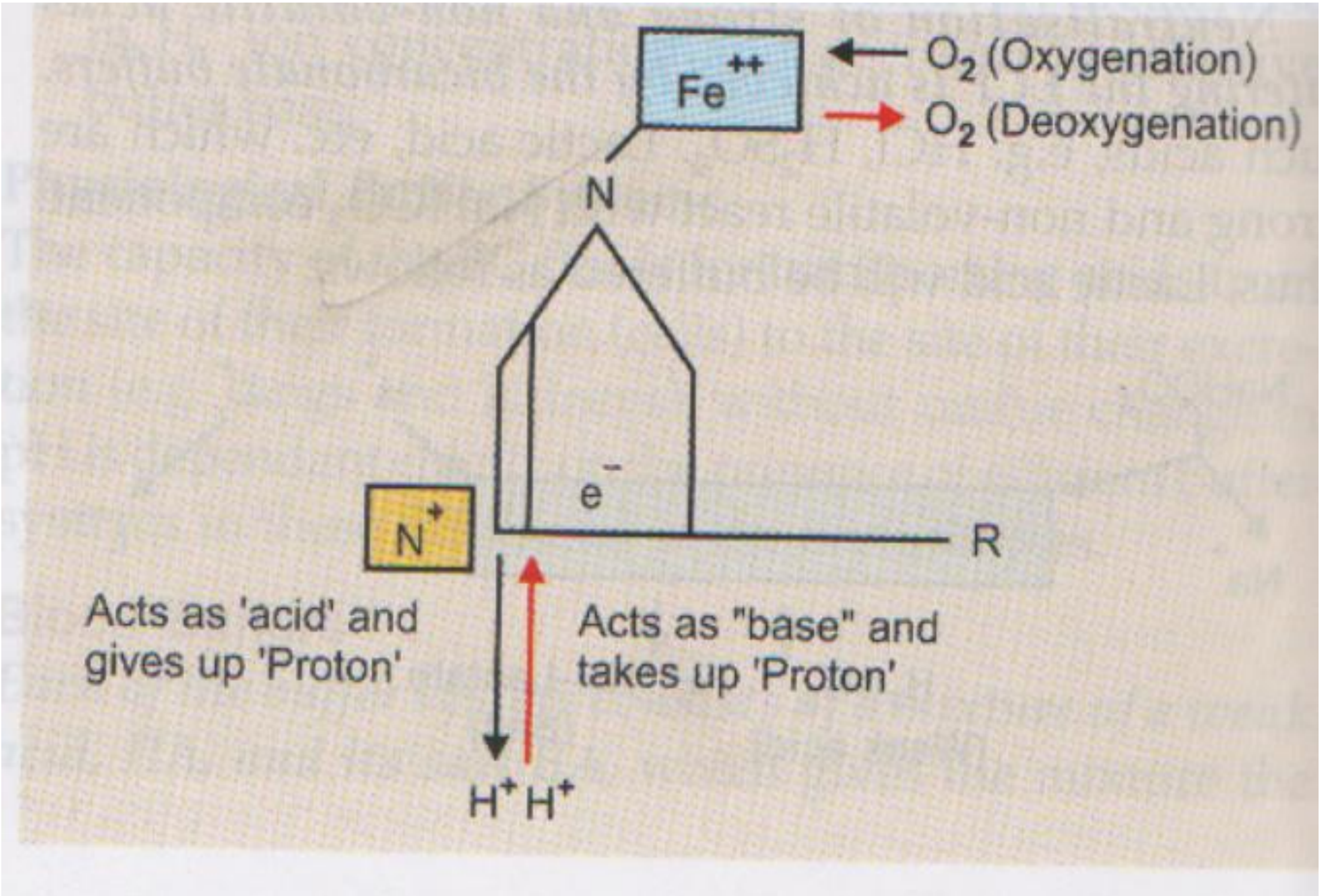


FIG. 11.1: STRUCTURE OF HEME

The buffering capacity of Hb is due to $COOH$, NH_2 , Guanidine group and imidazole group.



Imidazole contain two group

1. Fe^{++} containing group = Concerned with carriage of O_2.
2. Imidazole N_2 group: which can give up proton (H^+) and accept H^+ depending on PH of the medium.

So buffering capacity of Hb is due to the presence of imidazole nitrogen group.

Imidazole group of Histidine

Each molecule of Hb contain 38 moles of histadine. In alpha chain histadine at 8 7 position and in β chain at 92 Position is directly linked with Fe^{++} of haem.

- Guanidine is the functional group on the side chain of Arginine.
- Imadazole group is present in Histadine

Respiratory Regulation

- Act with in few min (3 – 12).
- Control PH by altering CO2 elimination from body by lungs.
- ↑ blood PCO2 and (↑ H^{+} Ion) stimulates respiratory centre so increases the rate and depth of respiration and so there is ↑CO2 removal from the body(E C F) through lungs in air.
- ↓ in blood PCO2 and (↓ H^{+} Ion) depresses R.C.
- Respiratory centre is sensitive to change in PH and PCO2.

Respiratory Regulation

- Respiratory regulation acts rapidly and keeps the Hydrogen Ion concentration from changing too much, until the much more slowly responding kidneys can eliminate the imbalance.
- **Effect of respiratory control of PH:(50-75%):**

If PH fall from 7.4 to 7, the respiratory system return the PH to the value about 7.2 – 7.3 .

Renal control of acid base balance

- By excreting acidic and basic urine.
- Relatively slow to response.
- Most powerful acid/base regulation system.
- **Mechanism:**
- 80 meq of H^+ non volatile acids excreted/day.
- 4320 meq of HCO_3^- /day.
- Each HCO_3^- require one H^+ to reabsorbed.
- So 4320+80= 4400 meq of H^+ /day must be secreted by renal tubules.

- 4400 meq of H^+ are secreted by the renal tubules.

Out of this 4400 meq of H^+,

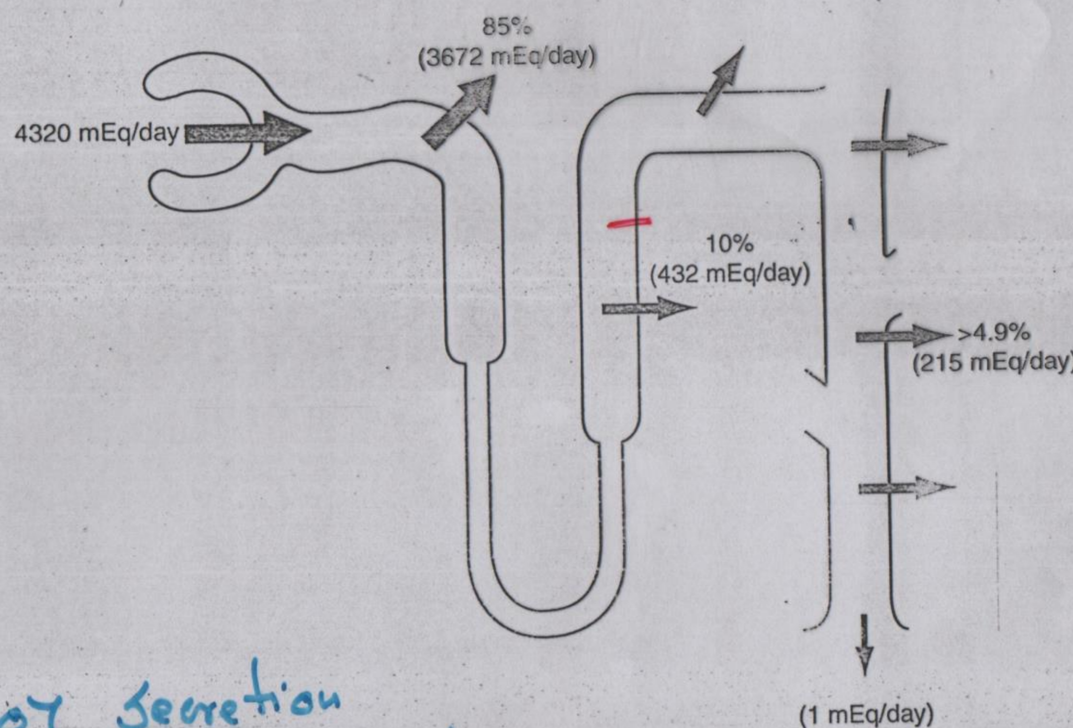
- 80 meq of H^+ are excreted to get rid of Non volatile Acids.
- 4320 meq are required to combine with 4320 meq of HCO_3 filtered in tubule,

Renal control of acid base balance

- **Kidneys regulate the PH by three basic mechanism:**
- Secretion of H^{+}Ion .
- Reabsorption of filtered $HCO3^{-}$.
- Production of new $HCO3^{-}$.

- The kidneys control the acid base balance by producing acidic or basic urine.
- **Excreting acidic urine** reduce the amount of acids in extra cellular fluids.
- **Excreting basic urine** reduce the amount of base in the extra cellular fluids.
- Large amount of HCO_3^- are filtered into the tubules i.e. 4320 meq/day
- Large number of H+ ions are also secreted in the tubular lumen by the tubular epithelial cells to remove 80meq/day of non-volatile acids and to absorb filtered HCO3-
- i.e. 4320 + 80 = 4400meq/day

Secretion of H^+ and reabsorption of HCO_3^-:

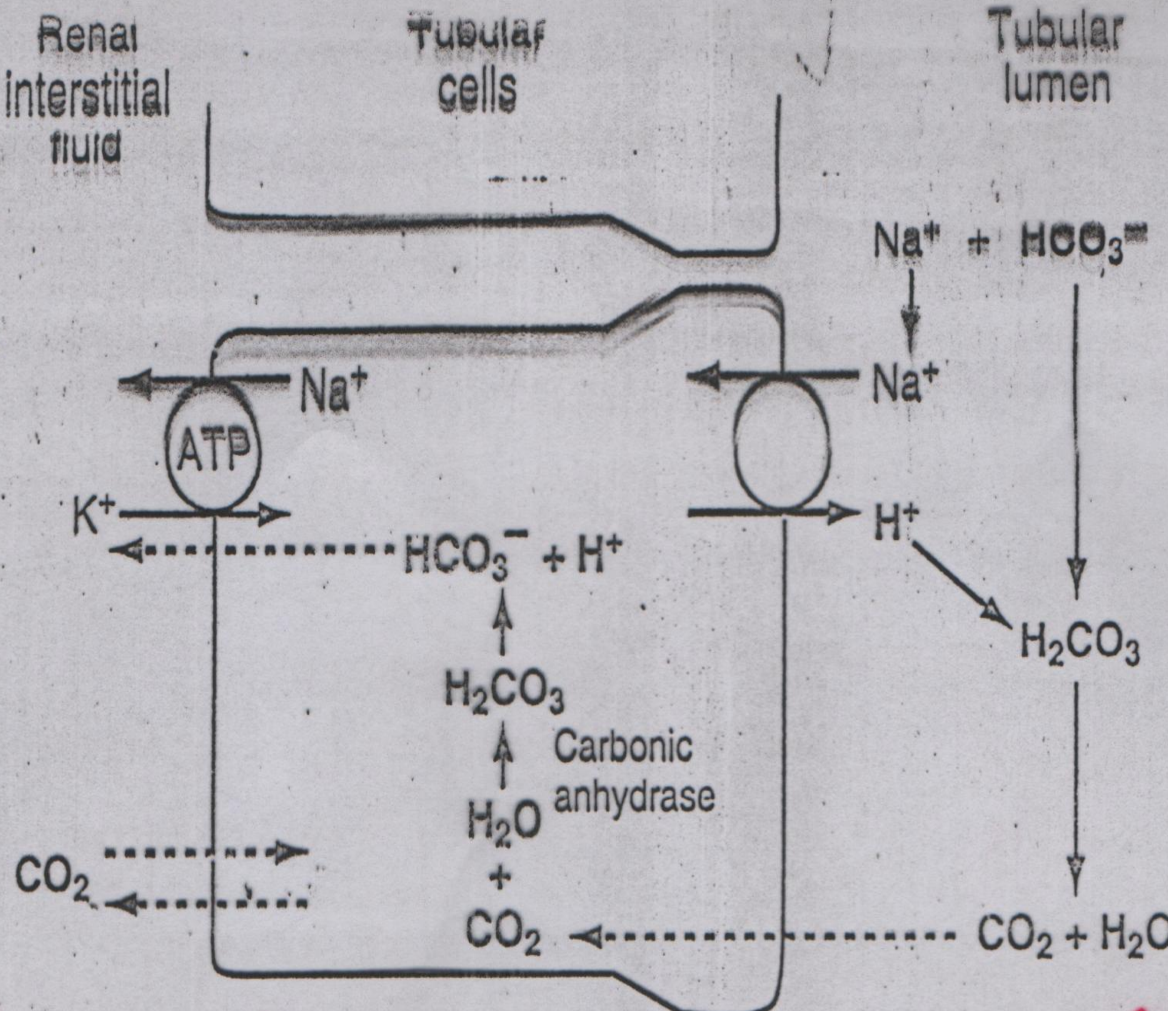


Mechanism of secretion of H^+ is different in different Tubular segments

____ In Prox tubules H^+ conc can be ↑ only about 3_4 folds, and Tubular fluid PH can be reduced to only about 6.7 although large amount of H^+ are secreted by this segment.i.e 85% .

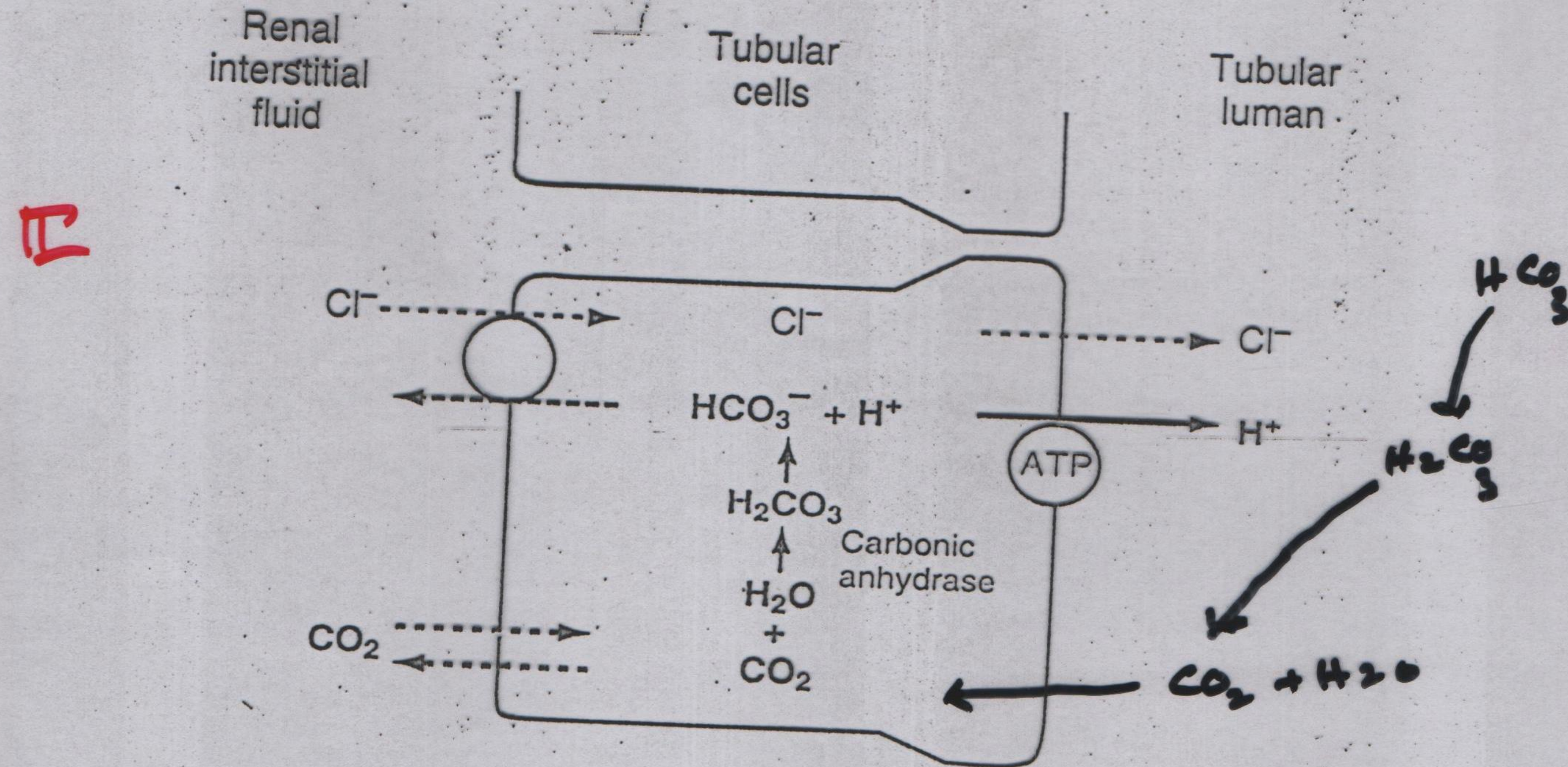
____ In collecting Tubules H^+ conc can be ↑ up to 900_ fold, decreasing the Tubular fluid PH to about 4.5. although only 5% H^+ secreted in this segment normally.

I



H+ Secretion in Prox tub, Thick Ascending & Early distal tubules.
By Na—H- Counter Transport

The net effect of these reaction is reabsorption of HCo_3^- from Tubules, although the HCo_3^- that has actually entered the extracellular fluid is not the same, as that filtered in to tubules.



H^+ secretion in late Tubular segment

- is by Primary active H^+ secretion
- Energy is provided by ATP.

- Once all the HCO_3^- ions has been reabsorbed and is no longer available to combine with H^+, then any excess of H^+ can combine with HPO_4 and other tubular buffers e.g. Ammonium buffer system
- Whenever a H^+ is secreted into the tubular lumen and combines with a buffer other than bicarbonate, the net effect is addition/regeneration of a new bicarbonate ion into the blood.

Carbonic Anhydrase

Zinc containing metallo enzyme.

Sources: R.B cells. (Never found in plasma)

--- Most of the tissues.

---Parietal cells of the stomach.

---Renal Tubular Epithelial cells.

Also present in small quantity in

---Muscle tissues.

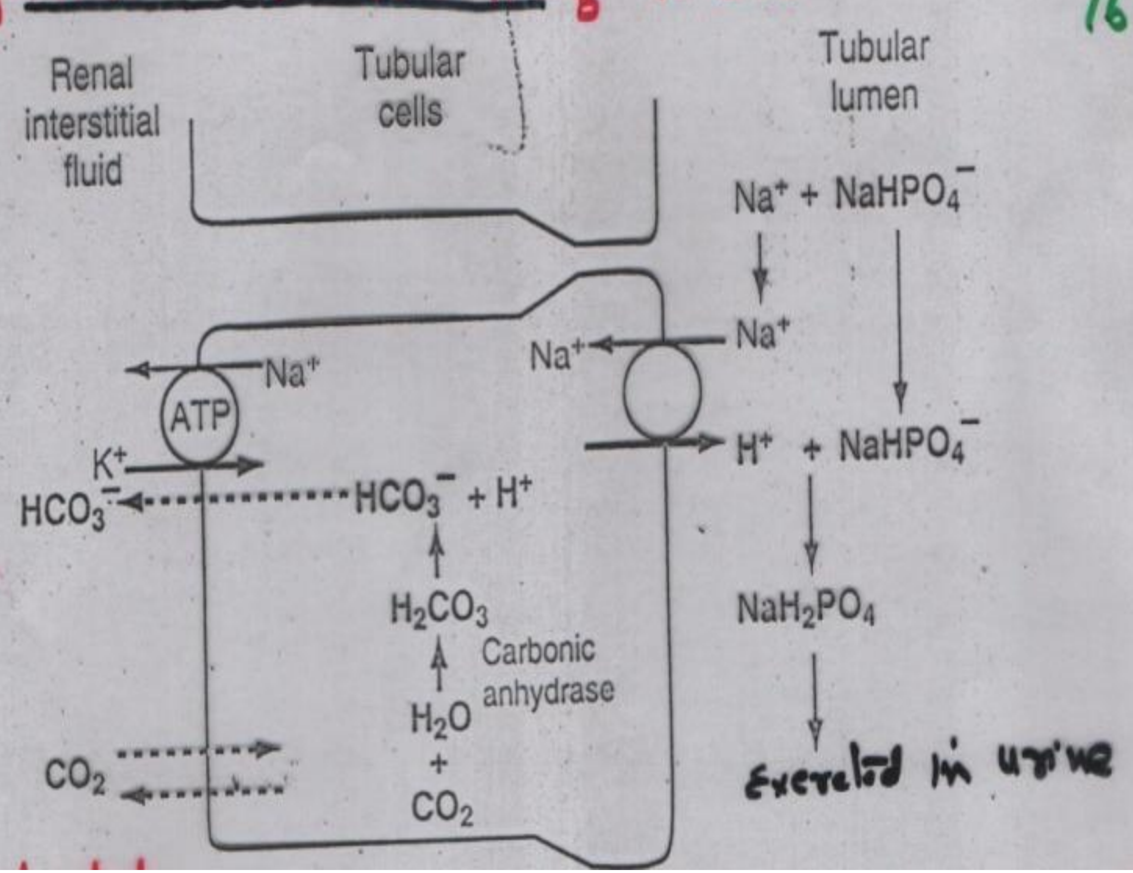
---Pancreas.

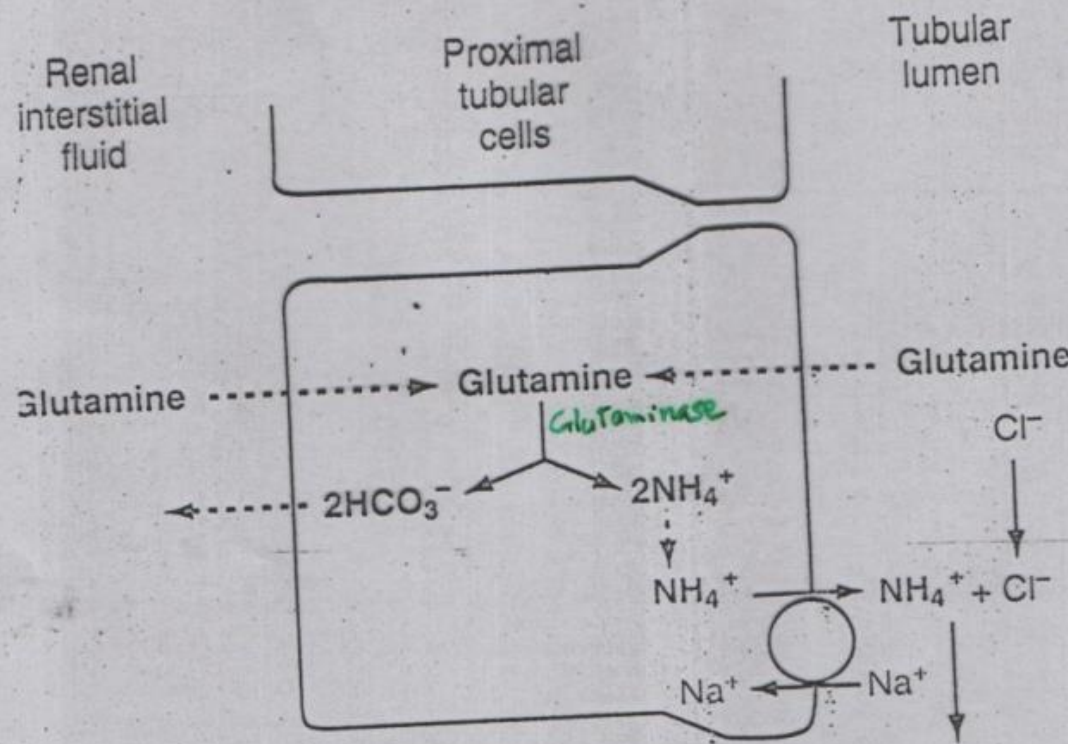
---Spermatozoa.

Combination of Excess of H^+ with urinary buffers and generation of new HCO_3^- ions:-

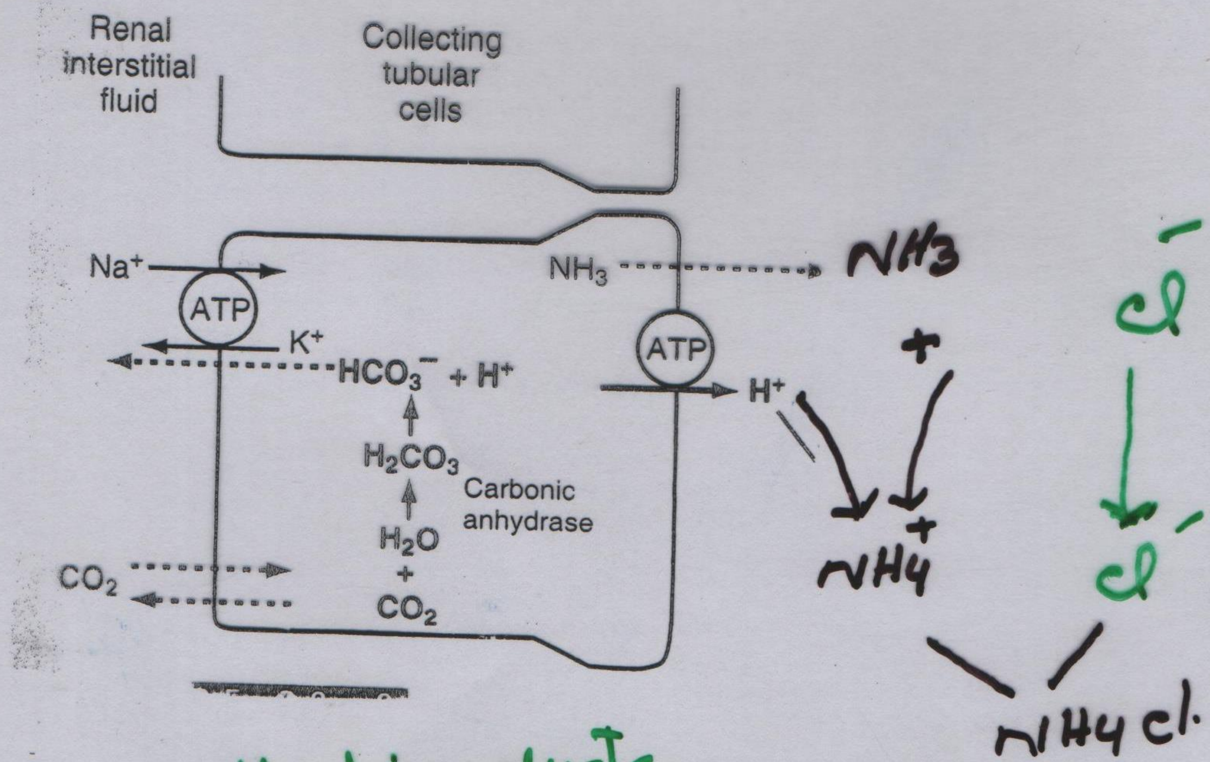
(10

16





Renal interstitial fluid
Proximal tubular cells
Tubular lumen
Glutamine
Glutamine
Glutamine
Glutaminase
2HCO3⁻
2NH4⁺
NH4⁺
NH4⁺ + Cl⁻
Cl⁻
Na⁺
Na⁺



Collecting ducts

- Permeable to NH_3
- Not Permeable to NH_4^+.

Thus when there is excess of H^+, the kidney not only reabsorb all the filtered HCo_3, but also regenerate new HCo_3.

- Under normal condition the amount of H+ ions eliminated by ammonia buffer system accounts for about 50% of acid excreted and 50% of new bicarbonates generated by the kidneys.
- However in chronic acidosis, the amount of ammonia excreted can increase to as much as 500meq/day.
- Therefore in chronic acidosis, the dominant mechanism by which acid is eliminated is excretion of ammonia.
- This also provides the most important mechanism for generating new bicarbonate during chronic acidosis.

Normal Values

pH	H^+	Pco_2	HCO_3^-
7.4	**40 mEq/L**	**40 mm Hg**	**24 mEq/L**

ACID BASE IMBALANCE

Acid base imbalance can manifest as Acidosis and alkalosis

Acidosis : Which can be

1. Metabolic acidosis
2. Respiratory acidosis

Alkalosis :

Which can be

1. Metabolic alkalosis
2. Respiratory Alkalosis

Metabolic

↑

$$\frac{HCO_3}{H_2\,CO_3} = \frac{20}{1}$$

↓

Respiratory

Metabolic Acidosis (Primary alkali deficit)

Any type of acidosis except those caused by excessive Co_2

- Fall in pH due to :

A :abnormal accumulation of non-volatile acids in body fluid.

Plasma Hco^-_3 is utilized in buffering these acids, so plasma Hco^-_3 decrease

B: Increased loss of base :

.

Causes of Metablic Acidosis

1. Formation of excessive Quantity of Metabolic acids e.g.

- Diab-Mellitus
- Starvation
- High fever
- violent exercise (L.A)

2. ingestion of acids e.g aspirin and methyl alcohol in large doses.

3. Failure of kidneys to excrete metabolic acids normally formed in the body.

4.Failure of kidneys to reabsorb Hco^{-}_{3} resulting in loss of base

5.Severe diarrhea and vomiting of intestinal contents .Large quantity of Hco^{-}_{3} are lost .

- Metabolic Acidosis is the commonest disturbance of Acid base balance observed clinically.

(3) (a) Compensation of Metabolic Acidosis.

(A) chemical Buffers (immedietly)

(B) Respir Compensation (in minutes)

Acidosis ⟶ Stimulation of Resp centre
↓
↑ Rate and depth of Respiration
↓
↑ loss of CO_2
↓
↓ Formation of H_2CO_3

$\frac{HCO_3^-}{H_2CO_3} = \frac{20}{1} = \frac{10}{1} = \frac{10}{0.5}$

pH ↓ H^+ ↑ HCO_3 ↓↓ CO_2 ↓

As a result, the normal ratio of HCO_3^- / H_2CO_3 (20:1) is restored Toward normal, as level of both is ↓ in the blood

(k). Renal (ii) Compensation of Metabolic Acidosis

(Hours to days)

(If kidneys are normal)

(1) ↑ Secretion of H^+ (in acidosis) in Tubular lumen have Two effects

(i) Complete reabsorption of HCO_3^-

(ii) H^+ in excess of HCO_3^- are lost in combination with urinary buffers e.g $\frac{HPO_4}{H_2PO_4}$, NH_3 etc.

So there is ↑ Regeneration of HCO_3^- ions by

(i) HPO_4/H_2PO_4

(ii) NH_3 buffer system

(iii) Glutamine Metab → $2NH_4^+$; $2HCO_3^-$

Acidosis stimulate Glutaminase

Respiration Acidosis (Primary H_2Co_3 access)

The underlying abnormality is increase in H_2Co_3 in blood, which follows decreased elimination of Co_2 .

<u>Causes:</u>

Any factor that decrease rate and depth of pulmonary ventilation.

1. Damage to resp centre (Hypoventilation) by trauma , inflammation e.t.c
2. Loss of ventilatory functions due to diseases of plura or lung disease e.g pneumothorax, tumors, emphysema e.t.c
3. Morphine's poisoning
4. Paralysis of diaphragn
5. Certain congenital Heart diseases

6.Condition causing impairment of diffusion of CO_2 across alveolar membrane e.g emphysema , pulmonary oedema , pneumonia

7.Abnormally high conc of Co_2 in atmosphere

- It is an emergency state.
- O_2 should be adminstered
- Artificial respiration by respirator
- Drugs which stimulate Resp Centre.

(17b). Compensation of Respiratory Acidosis: ②

① Chemical Buffers

2 Resp Mechanism

↑ CO_2 ⟶ ↑ stimulation of R.C ⟶

↑ depth and rate of Resp ⟶ ↑ Loss of CO_2 → ↓ H_2CO_3

Provided the R.C and lungs are normal!

In this Resp acidosis, the Renal Compensation is of Prime importance.

③ Renal Mechanism:

(i) :. ↑ H^+ in ECF & Cells so ↑ secr of H^+

(ii) ↑ H^+ in Tubular lumen ⟶ ↑ HCO_3^- reabsorption

(iii) ↑ regeneration of HCO_3^-

(By glutamine, phosphate buffers & NH_3)

So Ratio of HCO_3 / H_2CO_3 is restored toward 20:1, as level of both is ↑ in blood. so lowering PH.

$$\frac{HCO_3}{H_2CO_3} = \frac{20}{1} = \frac{20}{2} = \frac{40}{2}$$

PH ↓ H^+ ↑ CO_2 ↑↑ HCO_3 ↑

Metabolic Alkalosis

① $\frac{HCO_3 \uparrow}{H_2CO_3}$ (15)

(Also called Primary alkali Excess)

↑ PH of blood <
- ↑ Loss of H^+ so ↓ H^+ in blood (By kidneys & stomach)
- OR
- ↑ HCO_3 in blood

Causes:

1). Vomiting of gastric contents OR Suction through N. G. Tube.

2) Administration of Diuretics → chlorThiazide

8+ Causes.

— ↑ HCO_3 reabsorption associated with ↑ Loss of H^+ so causes alkalosis.

3) Excessive aldosteroid secretion e.g Cushing's syndrome or steroid therapy

- steroids causes ↑ Loss of H^+ (and K^+) in Exchange for Na^+, which is reabsorbed, causing Hypernatremia and Hypokalemia.

4). Ingestion of alkaline drugs e.g. Sodium Bicarbonate

Compensation of Metabolic Alkalosis

Usually not much helpful and is very difficult to compensate

A. Chemical Buffers

B. Respiratory Compensation

Alkalosis → Inhibition of Resp.Centre

↓

Increased Pco_2 ← Decreased Respiratory Rate ← Decreased ventilation

↓

Increased H2Co3

So $\frac{HCo3}{H2\ Co3} = \frac{20}{1} = \frac{40}{1} = \frac{40}{2}$

So HCo3/H2 Co3 Will be restore to 20:1 as level of both is increased

PH↑ H↓ HCO_3↑↑ Co_2 ↑

Renal Compensation

- Increased HCo3 in plasma

so

- Increased Renal filtration

So

- Increased loss of HCo3

Why metabolic alkolosis is difficult to compensable

Respiratory Compensation: As soon as the depression of respiratory centre by alkalosis causes retention of PCo2 and increased H2Co3 , the increase PCo2 stimulates the respiratory centre, so the compensation is not of great significance.

Renal compensation: Due to slight respiratory compensation, increased Hydrogen ions will lead again to increased reabsorbtion of filtered HCo3. So again compensation is not very effactive.

Respiratory Alkalosis $\frac{HCO_3}{H_2CO_3 \downarrow}$

(Primary H_2CO_3 deficient)

- It is a rise in pH due to primary decrease in blood PCO_2 and H_2CO_3 .

Causes:

Hyper ventilation (Any cause) e.g

- Psychological causes – e.g Hysteria
- CNS Diseases: Meningitis, Encephalitis
- Patient on respirator
- Hyper pyrexia

<u>Pulmonary causes:</u>

- Pneumonia
- Asthma
- C.C.F
- Pulmonary embolism
- Salicylete poisoning By large dsoes e.g in ryeumatic fever.

↑Loss of Co_2 due to hyper ventilation result in decreased H_2Co_3 .

So ratio of $\frac{H\,Co_3}{H_2\,Co_3}$ ↑ i.e pH is ↑

$\frac{HCO_3}{H_2CO_3 \downarrow}$

Compensation of Respiratory Alkalosis:-

(1) Chemical Buffers

(2) Renal Compensation:- (Main Compen)

(i) ↑ Filtration of HCO_3^-, but as less H^+ secretion due to alkalosis, there is less HCO_3^- reabsorption and more loss of HCO_3.

(ii) ↓ HCO_3 regeneration.

$$\frac{HCO_3}{H_2CO_3} = \frac{20}{1} = \frac{20}{0.5} = \frac{10}{0.5}$$

pH ↑, H^+ ↓, CO_2 ↓↓ HCO_3 ↓

Respiratory Compensation:

Alkalosis and Low PCO_2 depresses Resp Centre.

So ↓ rate and depth of resp.

So ↓ Expiration of CO_2, so ↑ Blood PCO_2.

21 ③

Metabolic Acidosis :- (Primary Alkali Deficit)

$$\frac{HCO_3^-}{H_2CO_3} = \frac{20}{1} = \frac{10}{1} = \frac{10}{0.5}$$ R

pH ↓ H ↑ HCO_3 ↓↓ CO_2 ↓

Metabolic Alkalosis :- (Primary Alkali Excess)

$$\frac{HCO_3^-}{H_2CO_3} = \frac{20}{1} = \frac{40}{1} = \frac{40}{2}$$ R

pH ↑ H ↓ HCO_3 ↑↑ CO_2 ↑

Respiratory Acidosis :- (Primary H_2CO_3 Excess)

$$\frac{HCO_3^-}{H_2CO_3} = \frac{20}{1} = \frac{20}{2} = \frac{40}{2}$$ K

pH ↓ H ↑ CO_2 ↑↑ HCO_3 ↑

Resp Alkalosis :- (Primary H_2CO_3 deficit)

$$\frac{HCO_3}{H_2CO_3} = \frac{20}{1} = \frac{20}{0.5} = \frac{10}{0.5}$$ K

pH ↑ H ↓ CO_2 ↓↓ HCO_3 ↓

Table 30–3

Characteristics of Primary Acid-Base Disturbances

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

The primary event is indicated by the double arrows (↑↑ or ↓↓). Note that respiratory acid-base disorders are initiated by an increase or decrease in P_{CO_2}, whereas metabolic disorders are initiated by an increase or decrease in HCO_3^-.

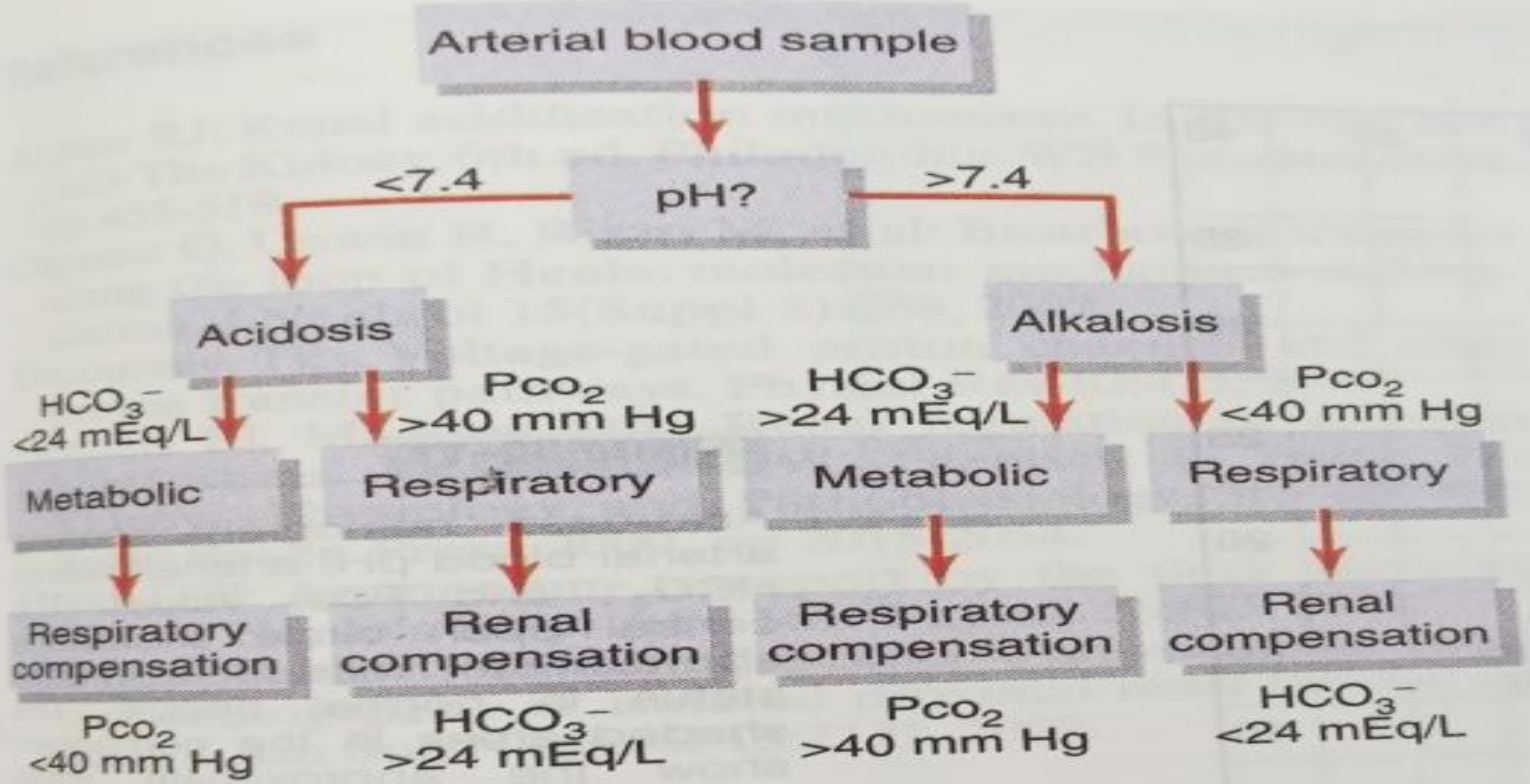


Figure 30–10

Analysis of simple acid-base disorders. If the compensatory responses are markedly different from those shown at the bottom of the figure, one should suspect a mixed acid-base disorder.

- **1. The normal ratio between the alkaline phosphate and acid phosphate in plasma is 4 : 1**
- **2. At pH 7.4, the ratio of bicarbonate : dissolved CO_2 is 20 : 1**
- **3. Quantitatively, the most significant buffer system in plasma is** Carbonic acid-bicarbonate buffer system

4. Buffering action of haemoglobin is mainly due to its Histidine

- **5. Respiratory acidosis results from** Retention of carbon dioxide

- Anion Gap
- Alkali Reserve