Replacement Therapy

- The basic objective of replacement therapy is to restore the volume and composition of the body fluids to normal one.
- Volume contraction is a life threatening condition because it impairs the circulation, blood volume decreases, cardiac output falls and the integrity of microcirculation is compromised.

- In volume depletion of sufficient magnitude to threaten life, a prompt infusion of isotonic sodium chloride solution is indicated.
- In an extreme case, intravenous therapy at the rate of 100 ml per minute for the first 1000ml has been considered necessary for the successful treatment of cholera.

Sodium Replacement

Sodium Chloride: NaCl (MW 58.44)

- It contains no added substances.
- it occurs as colourless cubic crystals or as white crystalline powder having saline taste.
- It is freely soluble in water, and slightly more soluble in boiling water, soluble in glycerine and slightly soluble in alcohol.

- Use: Used as fluid and electrolyte replenisher, manufacture of isotonic solution, flavour enhancer.
- Isotonic solutions are used in wet dressings, for irrigating body cavities or tissues
- Hypotonic solutions are administered for maintenance therapy when patients are unable to take fluids and nutrients orally for one to three days.
- Hypertonic solution/injection are used when there is loss of sodium in excess.

Official preparations of Sodium chloride

Sodium Chloride Injection

- a sterile isotonic solution of sodium chloride in water for injection.
- It contains not less than 0.85 % and not more than 0.95 % w/v of sodium chloride.
- It contains no antimicrobial agents.
- It is a clear, colourless solution with pH between 4.5-7.0.

Sodium Chloride Hypertonic Injection

(Hypertonic saline)

- It is a sterile solution of sodium chloride in water for injection.
- It contains not less than 1.52 % and not more than 1.68 % w/v of sodium chloride.
- It contains no antimicrobial agents. It is a clear, colourless solution with pH between 5.0-7.5.

- **Compound Sodium Chloride Injection (Ringer injection)**

1. not less than 0.82 % and not more than 0.9 % w/v of sodium chloride.
2. not less than 0.0285 %, not more than 0.0315 % w/v of potassium chloride.
3. not less than 0.03 % and not more than 0.036% w/v of calcium chloride in water for injection.

It contains no antimicrobial agents. It is a clear, colourless solution with pH between 5-7.5.

Sodium Chloride and Dextrose Injection

- It is a sterile solution of sodium chloride and dextrose in water for injection.

  It is clear colourless or faintly straw colored solution with pH between 3.5-6.5.

- It contains not less than 95% and not more than 105 % w/v of the stated amount of sodium chloride and dextrose as given below:

Combinations of Sodium Chloride and Dextrose

%of Sodium Chloride	%of Dextrose	%of Sodium Chloride	%of Dextrose
0.11	5	0.45	5
0.18	5	0.45	10
0.20	5	0.90	2.5
0.225	5	0.90	5
0.3	5	0.90	10
0.33	5	0.90	25
0.45	2.5		

Potassium Replacement

- Potassium Chloride: KCl (MW 74.56).
- Potassium chloride contains not less than 99 % calculated with reference to dried substance.
- It occurs as white crystalline solid, cubic crystals. It is less soluble in water than sodium chloride, and slightly more soluble in boiling water, soluble in glycerine and insoluble in alcohol.

- Use: Electrolyte replenisher in potassium deficiency, familial periodic paralysis, myasthenia gravis.
- Contraindication: renal impairment.
- **Potassium Chloride injection**
- **Ringer injection**

Calcium Replacement

- Calcium Lactate: MW 308.30
- Calcium chloride contains not less than 97% and not less than 103% of Calcium Chloride dihydrate.

  It occurs as white odourless powder, it is soluble in water, practically insoluble in alcohol.
- Use: An excellent source of calcium in oral treatment of calcium deficiency.

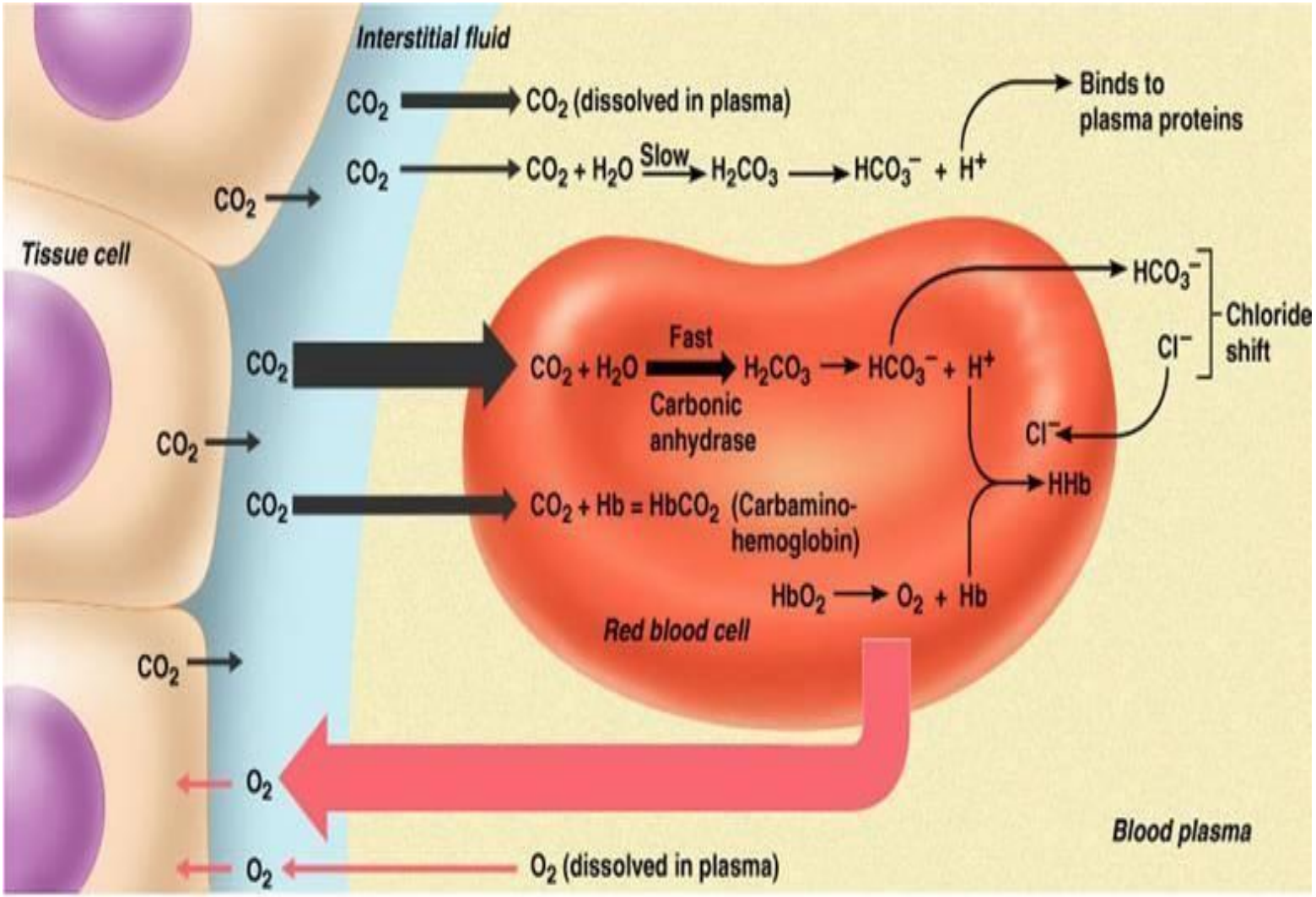
Physiological Acid Base Balance

- Abnormalities of the pH of body are frequently encounter and are of major clinical importance.
- Acedemia and alkalemia refer respectively to an abnormal decrease or increase in the pH of the blood.
- Acidosis and alkalosis refer respectively to clinical state that can lead to either acedemia or alkalemia.

- However in each condition the extent to which there is an actual change in pH depends in part on the degree of compensation which varies in most clinical disturbances.

- Acids are constantly being produced during metabolism.
- Most metabolic reactions occur only within narrow pH range of 7.38-7.42, therefore the body utilizes several buffer systems, two of them are bicarbonate and carbonic acid (HCO_3^- : H_2CO_3) present in plasma and kidney and monohydrogen phosphate/dihydrogen phosphate (HPO_4^{2-} : $H_2PO_4^-$) found in cells and kidney.

- **RBC's** have hemoglobin buffer system which is most effective single buffer system for buffering the carbonic acid produced during metabolic process.
- For each millimole of oxygen that dissociates from hemoglobin (Hb) 0.7 millimole of H+ are removed.



(a) Oxygen release and carbon dioxide pickup at the tissues

- Carbon dioxide, the acid anhydride of carbonic acid is continuously produced in the cells. It diffuses into the plasma and reacts with water to form carbonic acid. The increased carbonic acid is buffered by plasma proteins. Most CO2 enters the erythrocytes where it either rapidly forms H2CO3by the action of carbonic anhydrase or combines with Hb.

- The tendency to lower the pH of the erythrocytes due to increased concentration of H_2CO_3 is compensated by Hb. $CO_2 + H_2O$ Carbonic anhydrase H_2CO_3
- The bicarbonate anion then diffuses out of erythrocytes and chloride anion diffuses in. This has been named as chloride shift. The bicarbonate in plasma, along with the plasma carbonic acid now acts as efficient buffer system

- The normal HCO_3^-/ H_2CO_3 ratio is 27/1.35 meq/lt (20:1) corresponding to pH 7.4. In lungs there is reversal of the above process due to the large amount of O_2 present. Oxygen combines with the protonated deoxyhemoglobin releasing proton. These combine with HCO_3^- forming H_2CO_3 which then dissociates to CO_2 and water. The carbon dioxide is exhaled by the lungs. Thus by regulating breathing it is possible for the body to exert a partial control on the HCO_3^-/H_2CO_3 ratio.

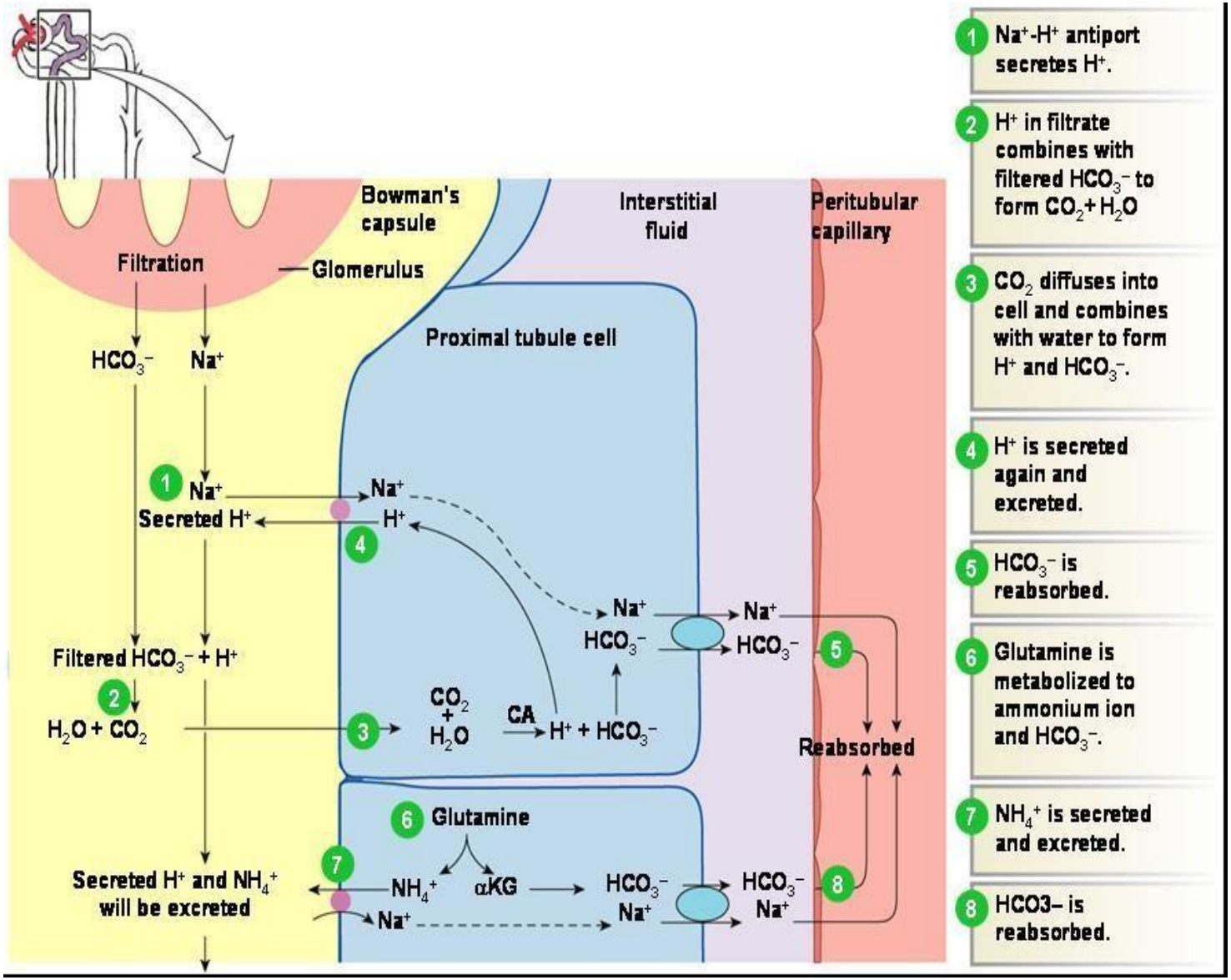
- The phosphate buffer system is also effective in maintaining physiological pH. At pH 7.4 the HPO4-2/H2PO4- ratio is approximately 4:1.
- In kidney, the pH of urine can drop to 4.5-4.8 corresponding to HPO4-2/H2PO4- ratio of 1:99- 1:100.

- The acid is excreted from kidney as follows:

  1. sodium salt of mineral or organic acids are removed from the plasma by glomerular filtration

  2. Sodium is preferentially removed from the renal filtrate or tubular fluid and in the tubular cells reacts with carbonic acid formed by the carbonic anhydrase catalyzed reaction of carbonic dioxide and water . The process known as sodium hydrogen exchange.

3. The sodium bicarbonate returns to plasma (eventually being removed in the lungs as CO2) and protons enter tubular fluid, forming acids of the anions that originally were sodium salts.


Bowman's capsule
Interstitial fluid
Peritubular capillary
Filtration
Glomerulus
Proximal tubule cell
HCO_3^-
Na^+
1 Na^+
Secreted H^+
Na^+
H^+
4
Na^+
HCO_3^-
Na^+
HCO_3^-
5
Filtered $HCO_3^- + H^+$
2
$H_2O + CO_2$
3
$CO_2 + H_2O$
CA
$H^+ + HCO_3^-$
Reabsorbed
6 Glutamine
7
Secreted H^+ and NH_4^+ will be excreted
NH_4^+
αKG
HCO_3^-
Na^+
HCO_3^-
Na^+
8
1 Na^+-H^+ antiport secretes H^+.
2 H^+ in filtrate combines with filtered HCO_3^- to form $CO_2 + H_2O$
3 CO_2 diffuses into cell and combines with water to form H^+ and HCO_3^-.
4 H^+ is secreted again and excreted.
5 HCO_3^- is reabsorbed.
6 Glutamine is metabolized to ammonium ion and HCO_3^-.
7 NH_4^+ is secreted and excreted.
8 HCO3– is reabsorbed.

Types and Causes of Acidosis:

- **Metabolic acidosis**: it occurs due to excess production of proton in the body or bicarbonate deficiency as in diabetic acidosis, renal failure and diarrhea.
- Metabolic acidosis is treated with sodium salts of bicarbonate, lactate, acetate and occasionally citrate.

- **Renal Acidosis**: where increase in H+ is due to defective renal excretion of H+. Seen in Tubular disorders, Addisons disease, drugs which interfere with tubular secretion of H+ e.g. carbonic anhydrase inhibitors

- **Respiratory Acidosis**: is due to increase in retention of carbon dioxide leading to rise in plasma carbonic acid content.
- It occurs due to chronic lung disease, respiratory muscle paralysis, by drugs that depress respiratory center.

Alkalosis

- **Metabolic alkalosis**: may be due to excessive vomiting which causes loss of H+ and Cl- ions.
- Metabolic alkalosis has been treated with ammonium salts. Its action is in kidney where it retards the Na+- H+ exchange.

- **Respiratory alkalosis**: Respiratory alkalosis is caused by hyperventilation which washes away large amount of carbon dioxide formed in metabolism causes lowering of arterial pCO2 and reduction in ratio of bicarbonate ion and carbonic acid with fall in hydrogen ion concentration.

Electrolytes
used in acid base balance

Sodium bicarbonate

- Sodium bicarbonate contains not less than 99.0 % and not more than 101 % of sodium bicarbonate.
- Sodium bicarbonate occurs as a white odourless crystalline powder or granules. It is soluble in water (1 in 12); partially soluble in alcohol.
- Alkalinity increases on standing, agitation or heating. It is stored in well closed containers.

- Sodium bicarbonate when mixed with calcium or magnesium salts, cisplatin, dobutamine hydrochloride or oxytetracyclin forms insoluble precipitates.
- The following drugs are susceptible to inactivation on mixing with sodium bicarbonate; adrenaline hydrochloride, isoprenaline hydrochloride and suxamethonium chloride.

- Uses :1. used in the treatment of metabolic acidosis

  2.diarrohoea,

  3.acute poisoning from acidic drugs (phenobarbitone and salicylates) ,
  4.an antacid to relieve dyspepsia.

  5.Solutions of sodium bicarbonate are used as eye lotions, to aid the removal of crusts in blepharitis, as eardrops to soften and remove ear wax, and as lubricating fluid for contact lenses.

Sodium acetate

- Sodium acetate contains not less than 99.0 % .
- it occurs as colourless, transparent crystals or a white granular powder or white flakes: odourless or with a slight odour of acetic acid; m.p. 58°; decomposes at higher temperature, soluble in water (1 in 0.8), and alcohol (1 in 19). A 5 % solution in water has a pH of 7.5 to 9.2. **It is kept in airtight containers.**

- **Uses of sodium acetate:**

An effective buffer in metabolic acidosis. It is used as pharmaceutical aid (for peritoneal dialysis fluid).

Potassium acetate

- Potassium acetate contains from 99 to 101.0% of CH3COOK.
- It occurs as colourless crystals or a white crystalline powder; odourless with a faint acetic acid like odour.
- It is soluble in water and alcohol. A 5 % solution in water has a pH of 7.5 to 9.5.
- **Potassium acetate should be kept in a well-closed container**.

Sodium citrate

- Sodium citrate contains about 99% of $C_6H_5Na_3O_7$.
- it occurs as white, granular crystals or a white crystalline powder; slightly deliquescent in moist air. It is freely soluble in water; practically insoluble in ethanol.

- Uses: It is used as

1.systemic alkalizing substance,

2. has anticlotting properties.

3. It is also used for dentifrices as desensitizing agent.

4. It also has a diuretic effect due to increased body salt concentration.

Potassium Citrate

- Potassium citrate contains about 99% of $K_3C_6H_5O_7$.
- Potassium citrate occurs as transparent, odourless, hygroscopic crystals or a white granular powder, taste is saline. It is soluble in water (1 in 1) and glycerol (1 in 25), practically insoluble in alcohol.
- Aqueous solutions are slightly alkaline and may be incompatible with acidifying agents.

- **Uses of potassium citrate:**

it is used as systemic alkalizer and gastric antacid . it is used to relieve painful irritation caused by cystitis (inflammation of gall bladder)

Ammonium Chloride

- Ammonium chloride is a sterile solution of ammonium chloride in water for injection
- It contains not less than 99.5 % and not more than 105 % with reference to dried substance. HCl may be added to adjust pH.
- The NH4+ cation possess certain pharmacological activities 1. acid base equilibrium of the body
- 2. diuretic effect
- 3. expectorant effect

- Ammonium chloride is contraindicated in patients with impaired renal and hepatic functions.
- Uses: It is used in acid base therapy, and as a diuretic.

Electrolyte Combination Therapy

- Combinations of glucose and saline solutions are usually sufficient in short term therapy for restoring electrolyte loss. But in severe deficit of electrolytes due to heavy blood loss or chronic diarrhoea, solutions containing additional electrolytes are usually required.
- The combination products are of two types :
  1. fluid maintenance therapy
  2. electrolyte replacement therapy

- **Maintenance therapy** with iv fluids is required to supply normal necessity of water and electrolyte to patient who cannot take them orally.
- All maintenance therapies should contain at least 5% dextrose.
- **Replacement therapy** is required when there is excess loss of water and electrolytes caused by fever, severe vomiting and diarrhoea.

- General electrolyte composition of maintenance therapy includes:

Electrolyte	Concentrations (mEq/l)
Sodium	25-30
Potassium	15-20
Chloride	22
Bicarbonate	20-23
Magnesium	3
Phosphorous	3