Oral rehydration salt/ORS

Sagar Bansal

Oral rehydration therapy (**ORT**) is a type of fluid replacement used as a treatment for dehydration. It involves drinking water mixed with sugar and salt, while continuing to eat. When dehydration is severe, the therapy also includes supplemental zinc. Caretakers are taught the signs of worsening dehydration. The World Health Organization and UNICEF specify indications, preparations and procedures for ORT.[1]

Since its introduction and development for widespread use in the latter part of the 20th century, oral rehydration therapy has decreased human deaths from dehydration in vomiting and diarrheal illnesses, especially in cholera epidemics occurring in children. It represents a major advance in global public health. It is on the World Health Organization's List of Essential Medicines, a list of the most important medication needed in a basic health system.[2]

Prior to the introduction of ORT, death from diarrhea was the leading cause of infant mortality in developing nations. Between 1980 and 2006, the introduction of ORT is estimated to have decreased the number of infant deaths, worldwide, from 5 to 3 million per year.[3][4]However, in 2008, diarrhea remained the second most common cause of death in children under five years (17 percent), (after pneumonia (19 percent)).[5] Moreover, by the same year, the use of ORT in children under five had declined.[6]

Medical uses[**Oral rehydration therapy is a treatment for the symptoms of dehydration. ORT is less invasive than the other strategies for fluid replacement, specifically intravenous (IV) fluid replacement. Mild to moderate dehydration in children seen in an emergency department is best treated with ORT.**

ORT in combination with anti-nausea drugs is indicated for vomiting patients as a strategy to be able to take fluid orally. In an emergency department setting, vomiting, dehydrated patients take these drugs as soon as possible to enable taking fluid by mouth sooner.[7]

Persons taking ORT should eat within 6 hours and return to their full diet within 24–48 hours.[8]

Contraindications

ORT is contraindicated in the case of protracted vomiting despite proper administration of ORT, worsening diarrhea in excess of fluid intake, onset of stupor or coma, or intestinal blockage (ileus). Short-term vomiting is not a contraindication to receiving oral rehydration therapy. In persons who are vomiting, drinking oral rehydration solution at a slow and continuous pace will help the person not vomit.[8]

Preparation

Examples of commercially available oral rehydration salts. On the left from Nepal. On the right from Peru.

WHO and UNICEF jointly maintain official guidelines for the manufacture of ORS and recommend various alternative preparations, depending on material availability. Commercial preparations are available as either pre-prepared fluids or packets of oral rehydration salts (ORS) ready for mixing with the fluid.[9][10]

WHO/UNICEF's formula is 2.6 grams (0.092 oz) salt (NaCl), 2.9 grams (0.10 oz) trisodium citrate dihydrate $C_6H_5Na_3O_7,2H_2O$, 1.5 grams (0.053 oz) KCl, 13.5 grams (0.48 oz) anhydrous glucose $C_6H_{12}O_6$ per litre of fluid.[11]

A basic oral rehydration therapy solution is composed of salt, sugar, and water in solution, made using a standard ratio and is appropriate for use in situations when ORS must be prepared without the standard ingredients.[12][13]

- 30 ml sugar : 2.5 ml salt : 1 litre fluid
- 6 teaspoons sugar : 0.5 teaspoon salt : 1 quart fluid (approx. 1 litre)

The Rehydration Project states, "Making the mixture a little too diluted (with more than 1 litre of clean water) is not harmful."[14]

The optimal fluid is plain, clean water. However, fluids such as rice water, coconut water, vegetable broth, yogurt, weak unsweetened tea, unsweetened fresh fruit juice or even nonpotable water are recommended when plain, clean water is unavailable. Water can be boiled or treated with chlorine. However, ORS is *not* withheld on the basis of potentially unsafe water. Rehydration takes precedence.[1]

The molar ratio of sugar to salt should be 1:1 and the solution should not be hyperosmolar.[15] The Mayo clinic suggests half a teaspoon of salt, six level teaspoons of sugar and 1 litre (34 US fl oz) water.[16] The British Columbia health service suggests sugar free fruit juice mixed with water in a ratio of 1:4.[17]

New formula oral rehydration salts By WHO

A new formula for oral rehydration salts (ORS), has been released by the World Health Organization. The new formula ORS, a sodium and glucose solution. is widely used to treat children with acute diarrhoea. Since WHO adopted ORS in 1978 as its primary tool to fight diarrhoea, the mortality rate for children suffering from acute diarrhoea has fallen from 5 million to 1.3 million deaths annually.

The new improved formula is the result of extensive research sponsored by WHO's Department of Child and Adolescent Health and Development and supported by the United States Agency for International Development (USAID). The latest study was conducted in five developing countries among children from one month to two years old with acute diarrhoea and dehydration.

The study's findings suggest that using the low-sodium, low-glucose ORS formulation reduces the need for intravenous fluids by 33 percent. The effect of this reduction could result in fewer children requiring hospitalization, fewer secondary infections, a diminished need to handle blood with its potentially dangerous consequences, and lower health care costs.

Reduced osmolarity ORS	**grams/litre**	**Reduced osmolarity ORS**	**mmol/litre**
Sodium chloride	2.6	Sodium	75
Glucose, anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Glucose, anhydrous	75
Trisodium citrate		Potassium	20
dihydrate	2.9	Citrate	10
		Total Osmolarity	**245**

IRON AND HAEMATINICS:

Definition—

Haematinics are the chemical agents or substances which are required for normal erythropoiesis. A **hematinic** is a medicine that increases the hemoglobin content of the blood. Hematinics are used to treat iron-deficiency anemia. Hematinics are usually vitamins or minerals that are essential for normal erythropoiesis. Recently, they have been used in conjunction with Folic Acids to help the body to produce and maintain new cells and prevent malignant DNA changes

These are—

Iron (Fe), Cobalt (Co), Zinc (Zn), Vit-B12, Folic acid and Erythropoietin.

Iron (Fe)

Required for Hgb production. In the absence of adequate iron a small red cell with insufficient Hgb will be formed giving rise to microcytic and hypochromic anaemia. Fe^{++} forms the nucleus of the porphyrin ring, which when combined with appropriate globin chain forms Haemoglobin.
*** Intake of Iron is 20mg/day from which 1mg/day (5%) is absorbed.

Distribution of Iron in the body—

- 70% is in the form of Hgb in RBC.
- (10-20)% is in the storage form as haemosiderine.
- 10% is in the form of myoglobin, a haem containing protein which is present in the muscle.
- Less than 1% is in the cytochrome and other Fe^{++} containing enzymes and as transport iron transferine.

Iron is required in the body for—

Synthesis of Hgb
Synthesis of myoglobin
Cytochrome P450 enzyme synthesis

Pharmacokinetics of Iron—

Iron is normally available in the diet in the form of haem or iron complex to various organic compounds.

Absorption of iron—

Iron is most readily absorbed in the ferrous state. But most of the dietary iron is in the ferric form. No more than a trace amount of iron is absorbed in the stomach. But the gastric secretion (HCl) dissolves the iron and permits it to form soluble complexes with ascorbic acid (vit-C). Vitamin-C and other substances aid its reduction into ferrous form. This is why the patients with partial gastrectomy usually have iron deficiency anaemia. Most of the iron is absorbed in the upper part of the small intestine that is duodenum and upper part of the jejunum. Te mucosal cell contains as intracellular iron carrier. Some iron is supplied to mitochondria by the carrier, but the remainder is partitioned between Apoferritin in the mucosal cells and Transferin which is the iron transporting polypeptide in the plasma. Apoferritin, which is also found in many other tissues combines with iron to form Ferritin.

Distribution—

Iron is transported in the plasma bound to transferin (transferin is a β-globulin that specially binds to ferric iron). Iron can thus be transported from intestinal mucosal cells or from storage form in the liver and spleen to the developing erythroid cells in the bone marrow.

Storage—

Iron can be stored in 2 forms,

Ferritin (ferric iron + apoferritin)
Haemosiderine (when there is excess ferritin)

Ferritin is the most readily available form of storage iron. Ferritin consists of core crystal of ferric hydroxide covered by a protein shell of apoferritin.
Haemosiderine consists of aggregates of ferric cone crystals partially or completely stripped of apoferritin.
Both ferritin and haemosiderine are stored in the macrophages of liver, spleen and bone marrow. Ferritin is also present in the plasma and intestinal mucosal cells.

Excretion—

There is no mechanism of excretion of iron. A small amount of iron is lost by the exfoliation of the intestinal mucosal cells into the stool and trace amount is excreted through bile, urine and sweat.

Regulation and iron absorption—

It is regulated by the amount of storage iron. Specially the amount of ferritin present in the intestinal mucosal cells. When both iron stores are depleted or when erythropoiesis is increased, the amount of transferin in the plasma is increased and its percent saturation in with iron is decreased. So, more iron is moved from the intra-cellular iron carrier to the transferin and less binds to apoferritin.
When the body iron store is sufficient, the opposite happens.

Indication or use of iron—

- Iron deficiency anaemia
- In children during rapid growth period
- In pregnant and lactating mother

Causes of iron deficiency anaemia—

1. Hook worm infestation
2. Bleeding peptic ulcer
3. After gastrectomy
4. GIT malignancy
5. Small intestinal disease leading to mal-absorption

Features of iron deficiency anaemia—

1. red cells are microcytic and hypochromic
2. serum iron is less than 40 µgm/dl
3. total iron binding capacity (TIBC) is greater than 400 µgm/dl

Treatment—

Iron can be given in oral from or parenteral form. Oral iron corrects the deficiency as rapidly and completely as parenteral iron.

Oral iron therapy—

A wide variety of preparations are available,

Ferrous Sulphate
Ferrous Glucorate
Ferrous Fumerate
Ferrous Sucinate

Ferrous Fumerate (33%) contains more iron than Ferrous Sulphate (20%). But ferrous Sulphate is cheap and easily absorbable.
Iron should be continued for 3-6 months after the Hgb level has returned to normal to replenish iron sores.

Indications of parenteral iron therapy—

Patients genuinely unable to take iron by mouth because,

1. Pain, vomiting or diarrhoea
2. Patient with post-gastrectomy
3. After small bowel resection
4. Inflammatory bowel disease
5. GIT upset, malabsorption syndrome

Iron(II) gluconate

Iron(II) gluconate, or **ferrous gluconate**,[1] is a black compound often used as an iron supplement. It is the iron(II) salt of gluconic acid. It is marketed under brand names such as *Fergon*, *Ferralet*, and *Simron*.

Uses

Ferrous gluconate is effectively used in the treatment of hypochromic anemia. The use of this compound compared with other ironpreparations results in satisfactory reticulocyte responses, a high percentage utilization of iron, and daily increase in hemoglobin that a normal level occurs in a reasonably short time.[3]

Ferrous gluconate is also used as a food additive when processing black olives. It is represented by the food labeling E number E579 in Europe. It imparts a uniform jet black color to the olives.[4]

Toxicity

Ferrous gluconate may be toxic in case of overdose. Children may show signs of toxicity with ingestions of 10–20 mg/kg of elemental iron. Serious toxicity may result from ingestions of more than 60 mg/kg. Iron exerts both local and systemic effects: it is corrosive to the GI mucosa, it can have a negative impact on the heart and blood (dehydration, low blood pressure, fast and weak pulse, shock), lungs, liver, gastrointestinal system (diarrhea, nausea, vomiting blood), nervous system (chills, dizziness, coma, convulsions, headache), and skin (flushing, loss of color, bluish-colored lips and fingernails).[5][6] The symptoms may disappear in a few hours, but then emerge again after 1 or more days.

Properties	
Molecular formula	$C_{12}H_{22}FeO_{14}$
Molar mass	446.14 g mol^{-1}
Appearance	Light yellow to brown powder
Odor	Slight caramel odor
Melting point	188 °C (370 °F; 461 K) dihydrate
Solubility in water	soluble
Solubility	soluble in glycerin negligible in alcohol

Iron(II) sulfate

Iron(II) sulfate (Br.E. **iron(II) sulphate**) or **ferrous sulfate** is the chemical compound with the formula $FeSO_4$. It is used medically to treat iron deficiency, and also for industrial applications. Known since ancient times as **copperas** and as green vitriol, the blue-green heptahydrate is the

most common form of this material. All iron sulfates dissolve in water to give the same aquo complex $[Fe(H_2O)_6]^{2+}$, which has octahedral molecular geometry and is paramagnetic.

Hydrates[edit]

Iron(II) sulfate can be found in various states of hydration, and several of these forms exist in nature.

- $FeSO_4 \cdot H_2O$ (mineral: szomolnokite,[7] relatively rare)
- $FeSO_4 \cdot 4H_2O$ (mineral: rozenite,[8] white, relatively common, may be dehydratation product of melanterite)
- $FeSO_4 \cdot 5H_2O$ (mineral: siderotil,[1] relatively rare)
- $FeSO_4 \cdot 6H_2O$ (mineral: ferrohexahydrite,[2] relatively rare)
- $FeSO_4 \cdot 7H_2O$ (mineral: melanterite,[9] blue-green, relatively common)

Iron(II) sulfate heptahydrate

The heptahydrate in solution (water as solvent) transforms to both heptahydrate and tetrahydrate when the temperature reaches 56.6 °C (133.9 °F). Then at 64.8 °C (148.6 °F) they form both tetrahydrate and monohydrate.[4]

All mentioned mineral forms are connected with oxidation zones of Fe-bearing ore beds (pyrite,marcasite, chalcopyrite, etc.) and related environments (like coal fire sites). Many undergo rapid dehydration and sometimes oxidation.

Production and reactions

In the finishing of steel prior to plating or coating, the steel sheet or rod is passed through pickling baths of sulfuric acid. This treatment produces large quantities of iron(II) sulfate as a by-product.[13]

$$Fe + H_2SO_4 \rightarrow FeSO_4 + H_2$$

Another source of large amounts results from the production of titanium dioxide from ilmenite via the sulfate process.

Ferrous sulfate is also prepared commercially by oxidation of pyrite:

$$2\ FeS_2 + 7\ O_2 + 2\ H_2O \rightarrow 2\ FeSO_4 + 2\ H_2SO_4$$

Uses

Industrially, ferrous sulfate is mainly used as a precursor to other iron compounds. It is a[reducing agent](), mostly for the reduction of [chromate]() in [cement]().

Nutritional supplement

Together with other iron compounds, ferrous sulfate is used to fortify foods and to treat [iron-deficiency]() [anemia](). Constipation is a frequent and uncomfortable side effect associated with the administration of oral iron supplements. Stool softeners often are prescribed to prevent constipation.

Colorant

Ferrous sulfate was used in the manufacture of [inks](), most notably [iron gall ink](), which was used from the [middle ages]() until the end of the eighteenth century. Chemical tests made on the Lachish letters [circa 588/6 BCE] showed the possible presence ... of iron (Torczyner, *Lachish Letters*, pp. 188–95). It is thought that oak galls and copperas may have been used in making the ink on those letters.[14] It also finds use in [wool]() [dyeing]() as a [mordant]().

Other uses

It has been applied for the purification of water by [flocculation]() and for [phosphate]() removal in municipal and industrial [sewage]() treatment plants to prevent [eutrophication]() of surface water bodies

Properties	
Molecular formula	FeO_4S
Molar mass	151.91 g mol^{-1}
Appearance	White crystals (anhydrous) White-yellow crystals (monohydrate) Blue-green crystals (heptahydrate)
Odor	Odorless
Density	3.65 g/cm^3 (anhydrous) 3 g/cm^3 (monohydrate) 2.15 g/cm^3 (pentahydrate)[1] 1.934 g/cm^3 (hexahydrate)[2] 1.895 g/cm^3 (heptahydrate)[3]
Melting point	680 °C (1,256 °F; 953 K) (anhydrous) decomposes[5] 300 °C (572 °F; 573 K) (monohydrate) decomposes 60–64 °C (140–147 °F; 333–337 K)

	(heptahydrate) decomposes[3][10]
Solubility in water	Monohydrate: 44.69 g/100 mL (77 °C) 35.97 g/100 mL (90.1 °C) Heptahydrate: 15.65 g/100 mL (0 °C) 20.5 g/100 mL (10 °C) 29.51 g/100 mL (25 °C) 39.89 g/100 mL (40.1 °C) 51.35 g/100 mL (54 °C)[4]
Solubility	Negligible in alcohol

Dietary element/ Mineral Supplement

Dietary elements (commonly known as **dietary minerals** or **mineral nutrients**) are the chemical elements required by living organisms, other than the four elements carbon,hydrogen, nitrogen, and oxygen present in common organic molecules. The term "dietary mineral" is archaic, as the substances it refers to are chemical elements rather than actualminerals.

Chemical elements in order of abundance in the human body include the seven major dietary elements calcium, phosphorus, potassium, sulfur, sodium, chlorine, and magnesium. Important "trace" or minor dietary elements, necessary for mammalian life, include iron, cobalt, copper, zinc, molybdenum, iodine, bromine, and selenium (see below for detailed discussion).

Over twenty dietary elements are necessary for mammals, and several more for various other types of life. The total number of chemical elements that are absolutely needed is not known for any organism. Ultratrace amounts of some elements (e.g., boron, chromium) are known to clearly have a role but the exact biochemical nature is unknown, and others (e.g. arsenic, silicon) are suspected to have a role in health, but without proof.

Most chemical element that enter into the dietary physiology of organisms are in the form of simple compounds. Larger chemical compound of elements need to be broken down for absorption. Plants absorb dissolved elements in soils, which are subsequently picked up by the herbivores that eat them and so on, the elements move up the food chain. Larger organisms may also consume soil (geophagia) and visit salt licks to obtain limiting dietary elements they are unable to acquire through other components of their diet.

Bacteria play an essential role in the weathering of primary elements that results in the release of nutrients for their own nutrition and for the nutrition of others in the ecological food chain. One element, cobalt, is available for use by animals only after having been processed into

complicated molecules (e.g., vitamin B12), by bacteria. Scientists are only recently starting to appreciate the magnitude and role that microorganisms have in the global cycling and formation of biominerals.

Essential chemical elements for mammals

Some sources state that sixteen chemical elements are *required* to support human biochemical processes by serving structural and functional roles as well as electrolytes:[1]However, as many as 26 elements in total (including the common hydrogen, carbon, nitrogen and oxygen) are suggested to be used by mammals, as a result of studies of biochemical, special uptake, and metabolic handling studies.[2] However, many of these additional elements have no well-defined biochemical function known at present. Most of the known and suggested dietary elements are of relatively low atomic weight, and are reasonably common on land, or at least, common in the ocean (iodine, sodium):

Periodic table highlighting dietary elements

H																	He
Li	Be											B	C	N	O	F	Ne
Na	Mg											Al	Si	P	S	Cl	Ar
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba	* Lu	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra	** Lr	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Uut	Fl	Uup	Lv	Uus	Uuo

*	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb
**	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No

The four organic basic elements	Quantity elements	Essential trace elements	Possible structural or functional role in mammals

The following play important roles in biological processes:

Dietary element	RDA/ AI (mg)	Category	High nutrient density dietary sources	Insufficiency	Excess
Potassium	4700 mg	A systemic electrolyte and is essential in coregulatingATP with sodium.	Legumes, potato skin, tomatoes, bananas, papayas, lentils, dry beans, whole grains, avocados, yams, soybeans, spinach, chard, sweet potato,	hypokalemia	hyperkalemia

Dietary element	RDA/ AI (mg)	Category	High nutrient density dietary sources	Insufficiency	Excess
			turmeric.[3][4]		
Chlorine	2300 mg	Needed for production of hydrochloric acid in the stomach and in cellular pump functions.	Table salt (sodium chloride) is the main dietary source.	hypochloremia	hyperchloremia
Sodium	1500 mg	A systemic electrolyte and is essential in coregulatingATP with potassium.	Table salt (sodium chloride, the main source), sea vegetables, milk, andspinach.	hyponatremia	hypernatremia
Calcium	1300 mg	Needed for muscle, heart and digestive system health, builds bone, supports synthesis and function of blood cells.	Dairy products, eggs, canned fish with bones (salmon, sardines), green leafy vegetables, nuts, seeds, tofu, thyme, oregano, dill, cinnamon.[3]	hypocalcaemia	hypercalcaemia
Phosphorus	700 mg	A component of bones (see apatite), cells, in energy processing, in DNA and ATP (as phosphate) and many other functions.	Red meat, dairy foods, fish, poultry, bread, rice, oats.[5][6] In biological contexts, usually seen as phosphate.[7]	hypophosphatemia	hyperphosphatemia
Magnesium	420 mg	Required for processing ATP and for bones.	Raw nuts, soybeans, cocoa mass, spinach, chard, sea vegetables, tomatoes, halibut, beans, ginger, cumin, cloves.[8]	hypomagnesemia, magnesium deficiency	hypermagnesemia
Zinc	11 mg	Pervasive and required for several enzymes such ascarboxypeptidase, liver alcohol dehydrogenase, andcarbonic anhydrase.	Calf liver, eggs, dry beans, mushrooms, spinach, asparagus, scallops, red meat, green peas, yogurt, oats, seeds, miso.[3][9]	zinc deficiency	zinc toxicity
Iron	18 mg	Required for many proteins and enzymes,	Red meat, fish (tuna, salmon), grains, dry beans, eggs, spinach,	anemia	iron overload disorder

Dietary element	RDA/AI (mg)	Category	High nutrient density dietary sources	Insufficiency	Excess
		notablyhemoglobin to prevent anemia.	chard, turmeric, cumin, parsley, lentils, tofu, asparagus, leafy green vegetables, soybeans, shrimp, beans, tomatoes, olives, and dried fruit.[3][10]		
Manganese	2.3 mg	A cofactor in enzyme functions.	Spelt grain, brown rice, beans, spinach, pineapple, tempeh, rye, soybeans, thyme, raspberries, strawberries, garlic, squash, eggplant, cloves, cinnamon, turmeric.[11]	manganese deficiency	manganism
Copper *Main article:Copper in health*	0.900 mg	Required component of many redox enzymes, including cytochrome c oxidase.	Mushrooms, spinach, greens, seeds, raw cashews, raw walnuts, tempeh, barley.[12]	copper deficiency	copper toxicity
Iodine	0.150 mg	Required not only for the synthesis of thyroid hormones, thyroxine and triiodothyronine and to prevent goiter, but also, probably as an antioxidant, for extrathyroidal organs as mammary and salivary glands and for gastric mucosa and immune system (thymus): • Iodine in biology	Sea vegetables, iodized salt, eggs. Alternate but inconsistent sources of iodine: strawberries, mozzarella cheese, yogurt, milk, fish, shellfish.[13]	iodine deficiency	iodism
Selenium	0.055 mg	Essential to activity of antioxidant enzymes likeglutathione peroxidase.	Brazil nuts, cold water wild fish (cod, halibut, salmon), tuna, lamb, turkey, calf liver, mustard, mushrooms, barley, cheese, garlic, tofu, seeds.[14]	selenium deficiency	selenosis

Dietary element	RDA/AI (mg)	Category	High nutrient density dietary sources	Insufficiency	Excess
Molybdenum	0.045 mg	The oxidases xanthine oxidase, aldehyde oxidase, and sulfite oxidase.[15]	Tomatoes, onions, carrots.[16]	molybdenum deficiency	molybdenum toxicity[17]
Bromine	none	Basement membrane architecture and tissue development.[18]			bromism

Chromium has been described as nonessential to mammals.[23][24] Some role in sugar metabolism in humans has been invoked, but evidence is lacking,[25][26] despite a market for the supplement chromium picolinate.

PREPARED BY: SAGAR BANSAL/Asst.Prof./SIP

Introduction

About 56% of the adult human body is fluid. Although most of this fluid is inside the cells and is called intracellular fluid, about one third is in the space outside the cells and is called extracellular fluid. The extracellular fluid is in constant motion throughout the body. In the extracellular fluid are the ions and nutrients needed by the cells for the maintenance of cellular life. Therefore, all the cells live in essentially the same environment, the extracellular fluid, for which reason the extracellular fluid is called internal environment of the body.

The body fluids are solutions of inorganic and organic solutes. The concentration balance of the various components is maintained in order for the cell and tissue to have a constant environment. In order for the body to maintain this internal homeostatis, (homeostasis means maintanace of static or constant conditions in the internal environment) there are regulatory mechanisms which control pH, ionic balance, osmotic pressure etc. The volume and composition of the body fluids vary tremendously from one compartment to another, and are maintained remarkably constant despite the vicissitude of daily life and the stress imposed by disease. Disturbance of fluid and electrolyte metabolism involve four properties of the body fluid-volume, osmolarity, hydrogen ion concentration (pH) and the concentration of other specific ions. The total body water is divided into three compartments 1) the intercellular compartment 2) the extracellular compartment, which consists of the plasma and the interstitial fluid and 3) the transcellular compartment, which includes the fluid within the gastrointestinal tract, humor of the eye and the excretory system of the kidneys and glands, pericardial, peritoneal, synovial, cerebrospinal fluid.

All the body fluids intracellular, extracellular (interstitial, plasma or vascular) contains electrolytes. The electrolyte concentration varies in these fluids, it is 45-50% of body weight in intercellular fluid, interstitial fluid makes 12-15 % and plasma makes 4-5% of body weight. About 40% of intracellular fluid (4lts) is dense connective tissue i.e. bone and cartilage and does not take part in quick exchange of electrolytes with the remaining body. The rest of the interstitial fluid IF (6.6lts) and plasma (3.5lts) comprise the active part of the extracellular fluids. These fluid compartments are separated from each other by membranes which are permeable to water and many organic and inorganic solutes. They are nearly impermeable to macromolecules e.g. proteins and selectively permeable to certain ions e.g. Na^+, K^+ and Mg^+ as a result, each of these fluid compartments has distinct solute pattern and the solution in each compartment is ionically balanced. For electro neutrality to exist in extracellular fluid, the sum of the concentration of cations must be equal to the sum of the concentration of anions.

The extracellular fluid contains large amounts of sodium, chloride and bicarbonate ions, plus nutrients for the cell such as oxygen, glucose, fatty acids and amino acids. The intracellular fluid contains large amounts of potassium, magnesium and phosphate ions. Measurement of electrolyte concentrations (plasma) is usually limited to Na^+, K^+, Cl^-, and HCO_3^-. The sum of the concentration of sodium and unmeasured cations (Ca^{2+}, Mg^{2+}, K^+) equals the sum of the concentration of Cl^- and HCO_3^- and unmeasured anions (phospahates, proteins, sulphates, derivatives of organic acids). The difference between the concentration of unmeasured cations and anion is known as anionic gap. Variation in this gap is a useful diagnostic indication to disorders of acid base balance.

The electrolyte balance of the body is maintained by a regulation between the intake and output of water. The intake of water includes the fluid taken orally and the release of water during the oxidation and other metabolic process in body.

Water is eliminated from body by urine, expiration (lungs), perspiration and feces. Excessive loss of water results in concentration of body fluids which causes rise in osmotic pressure, as a result water moves out from intracellular compartment to maintain the osmotic pressure in extracellular fluid. This results in dehydration of cells. Loss of water above 20% may prove to be fatal.

Calcium

About 99% of body calcium is found in bones and the remaining is present in extracellular fluid compartment. Only 10% of the ingested calcium is absorbed from the intestinal tract and the remainder is excreted with feces. The concentration of calcium in plasma averages about 9.4mg/dl, (9-10mg/dl). The calcium level in plasma is regulated within narrow limits by parathyroid hormone. The calcium in plasma is present in three forms 1. About 40% is combined with plasma proteins and is non diffusible through the capillary membrane. 2. About 10% is combined with other substances of plasma and interstitial fluid (citrate, phosphate for instance) and is diffusible through the capillary membrane in such a manner that it is not ionized. 3. The remaining 50% calcium present in plasma is diffusible through the capillary membrane and ionized. The plasma and interstitial fluid have a normal calcium ion concentration of about 1.2mmole/lt (or 2.4mEq/lt because it is a divalent ion), a level only half of the total plasma calcium concentration.

Calcium is important for blood clotting and contraction of various smooth muscles. In cardiovascular system (CVS) Calcium is essential for contraction coupling in cardiac muscles as well as for the conduction of electric impulse in certain regions of heart. Calcium also plays role in maintaining the integrity of mucosal membrane, cell adhesion and function of the individual cell membrane as well.

Hypercalcemia: When the level of Calcium rises above normal, the nervous system is depressed, and the reflux action of CNS can become sluggish. It also decreases the QT interval of the heart which can lead to cardiac arrhythmia. It causes constipation and lack of appetite and depresses contractility of the muscle walls of the GIT. The depressive effect begins to appear when blood Calcium level rises above 12mg/dl and beyond 17 mg/dl calcium phosphate crystals are likely to precipitate throughout the body. This situation occurs due to hypoparathyroidism, vitamin D deficiency, Osteoblastic metastasis, steatorrhea (fatty stools), Cushing syndrome (hyper active adrenal cortex), acute pancreatitis and acute hypophosphatemia.

Hypocalcemia: Change in blood pH can influence the degree of calcium biding to plasma proteins. With acidosis less calcium is bound to plasma proteins. When calcium ion concentration falls below normal, the excitability of the nerve and muscle cells increases markedly.

Sodium

The sodium and its associated anions, mainly chloride, account for more than 90% of the solute in extracellular fluid compartment. The concentration of sodium is 142mEq/l in extracellular fluid, and 10 mEq/l in intracellular fluid. Plasma sodium is a reasonable indictor of plasma osmolarity under many conditions. When plasma sodium is reduced below normal level a person is said to have hyponatremia. When plasma sodium is elevated above normal level a person is said to have hypernatremia.

Hyponatremia: Decreased plasma sodium concentration can result from loss of sodium chloride from the extracellular fluid. Conditions that cause hyponatremia owing to loss of sodium chloride include excessive sweating, diarrhea and vomiting and over use of diuretics that inhibit kidney to conserve sodium. Addison's disease, which results from decreased secretion of hormone aldosterone (impairs the ability of kidneys to reabsorb sodium) can be one of the causes of hyponatremia .

Hypernatremia: Hypernatremia is increased plasma sodium level which also increases osmolarity, can be due to excessive water loss from extracellular fluid, secretion of sodium-retaining hormone aldosterone (cushing syndrome) excessive treatment with sodium salts.

Potassium

Potassium is major intracellular cation present in a concentration approximately 23 times higher than the concentration of potassium present in Extracellular fluid compartment. Extracellular fluid potassium concentration is normally precisely regulated at 4.2mEq/l. This is because many of the cell functions are sensitive to change in the extracellular fluid potassium concentration. Increase in potassium concentration can cause cardiac arrhythmias and higher concentrations can lead to cardiac arrest by fibrillation. About 95% of body potassium is contained in the cells and only 2% in extracellular fluid. Maintenance of potassium balance depends primarily on its excretion by kidney because only 5-10 percent is excreted in feces. Both, elevated and low levels of potassium, can be fatal,

Hypokalemia occurs due to high intake of potassium or in kidney damage while **Hyperkalemia** due to vomiting, diarrhea, burns, diabetic coma, over use of thiazide diuretics, alkalosis etc.

Chloride

Chloride major extracellular anion is principally responsible for maintaining proper hydration, osmotic pressure, and normal cation anion balance in vascular and interstitial compartment. The concentration of chloride is 103mEq/l in extracellular fluid, and 4 mEq/l in intracellular fluid.

Decreased chloride concentration can be the result of salt losing nephritis, leading to lack of tubular reabsorption of chloride, metabolic acidosis such as found in diabetes mellitus, in renal failure and prolonged vomiting. Increased concentration of chloride may be due to dehydration, decreased renal blood flow found with congestive heart failure (CHF) or excessive chloride uptake.

Phosphate

Phosphate is the principal anion of intracellular fluid compartment. Inorganic phosphate in the plasma is mainly in two forms HPO_4^{--} and $H_2PO_4^{-}$. The concentration of HPO_4^{--} is 1.05 mmole/L and the concentration of $H_2PO_4^{-}$ 0.26 mmole/L. When the total quantity of the phosphate in extracellular fluid rises so does the concentration of each of these ions. When pH of the extracellular fluid becomes more acidic there is relative increase in $H_2PO_4^{-}$ and decrease in $HPO_4^{- -}$ and vice versa. Phosphorous is essential for proper metabolism of calcium, normal bone and tooth development. HPO_4^{--} and $H_2PO_4^{-}$ makes an important buffer system of body.

Bicarbonate

Bicarbonate is the second most prevalent anion in extracellular fluid compartment. Along with carbonic acid it acts as body's most important buffer system. Each day kidney filters about 4320 milliequivalents of bicarbonate and under normal conditions all of this is reabsorbed from the tubules, thereby conserving the primary buffer system of the extracellular fluid. When there is reduction in the extracellular fluid hydrogen ion concentration (alkalosis) the kidneys fail to reabsorb all the filtered bicarbonate thereby increasing the excretion of bicarbonate. Because bicarbonate ions normally buffer hydrogen in the extracellular fluid, this loss of bicarbonate is as good as adding a hydrogen ion to the extracellular fluid. Therefore, in alkalosis, the removal of bicarbonate ions raises the extracellular fluid hydrogen ion concentration back towards normal. In acidosis the kidneys do not excrete the bicarbonate in the urine but reabsorb all the filtered bicarbonate and produces new bicarbonate which is added back to the extracellular fluid. This reduces the extracellular fluid hydrogen ion concentration back towards normal.

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. A general rule is to replace one half of the estimated volume loss in the first 12-24 hours of treatment.

Sodium Replacement

Sodium Chloride: NaCl (MW 58.44)

I.P. Limit. Sodium chloride contains not less than 99.5 % and not more than 100.5 % calculated with reference to dried substance. It contains no added substances.It occurs as colorless 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 glycerin and slightly soluble in alcohol.

Test for identification:

For Sodium: To sample solution add 15 % w/v potassium carbonate heat, no precipitate. Add potassium antimonite solution, heat to boiling, cool and if necessary scratch the inside of test tube with a glass rod, a dense white precipitate is produced.

For Chloride: Dissolve sample in water, acidify with dilute nitric acid and add silver nitrate solution shake, and allow to stand, a curdy white precipitate is formed which is insoluble in nitric acid but, soluble after being well washed with water, in dilute ammonium hydroxide solution from which it is reprecipitated by the addition of dilute nitric acid.

Preparation: On commercial scale it is prepared by evaporation of sea water in shallow pans. It contains impurities of sodium carbonate, sodium sulphate, magnesium chloride, magnesium sulphate, calcium chloride etc. these impurities are removed by dissolving the salt in water in a cemented tank; some alum and lime are added. The suspended impurities are allowed to settle down. The clear solution is decanted into iron pans and concentrated. The crystals of sodium chloride settle down which are then collected and dried.

Assay: The assay of sodium chloride is dependent on the modified Volhard's method in which indirect volumetric precipitation titration is involved. An acidified solution of sodium

chloride with nitric acid is treated with a measured excess amount of standard solution of silver nitrate in the presence of nitrobenzene. Some of the silver nitrate is consumed in the reaction with sodium chloride. The remaining unreacted $AgNO_3$ is determined by titration with standard solution of ammonium thiocyanate using ferric alum (ferric ammonium sulphate) as indicator. The end point is obtained as a permanent brick red color due to formation of ferric thiocyanate.

Procedure: Accurately weigh the substance (0.1 gm) and dissolve in 50 ml water. Add 50 ml of 0.1N $AgNO_3$, 3 ml HNO_3, 5 ml nitro benzene, 2 ml ferric ammonium sulphate and mix thoroughly. The solution is titrated with ammonium thiocyanate until the color becomes brick red.

1ml of 0.1N $AgNO_3 \equiv 0.005844$ gm NaCl

Use:

Used as fluid and electrolyte replenisher, manufacture of isotonic solution, flavor 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 I.P.

Sodium chloride injection is 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, colorless solution with pH between 4.5-7.0.

Sodium Chloride Hypertonic Injection I.P. (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, colorless solution with pH between 5-7.5.

It complies with the test for pyrogens.

Compound Sodium Chloride Injection I.P. (Ringer injection)

It contains not less than 0.82 % and not more than 0.9 % w/v of sodium chloride, not less than 0.0285 %, not more than 0.0315 % w/v of potassium chloride and 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, colorless 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 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		

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

Potassium Replacement
Potassium Chloride: KCl (MW 74.56)
I.P. Limit. Potassium chloride contains not less than 99 % calculated with reference to dried substance. It occurs as sylvine (KCl) and Carnallite (KCl, $MgCl_2$)$6H_2O$ contaminated with magnesium sulphate and chlorides. 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 glycerin and insoluble in alcohol.

Test for Identification:
For potassium: To 1ml of solution add 1ml dilute acetic acid and 1ml of 10 % w/v sodium cobalt nitrite, a yellow color is produced.
For Chloride: Substance in water is added with dilute solution of silver nitrate, shake the solution and allow to stand , on standing white precipitate is obtained which is insoluble in nitric acid but soluble after being washed with water; in dilute ammonium hydroxide, from which it is reprecipitated by the addition of dilute nitric acid.

Preparation:
1. It is prepared by fusing carnallite whereby liquefied magnesium chloride hexahydrate is separated from the solid potassium chloride.
2. The crushed carnallite is dissolved by boiling with liquor leaving other impurities undissolved. These are filtered off and the filtrate is crystallizes to get cubic crystals of potassium chloride.
3. It is also prepared in laboratory by reacting HCl with potassium carbonate or bicarbonate

$$K_2CO_3 + 2HCl \longrightarrow KCl + H_2O + CO_2$$
$$KHCO_3 + HCl \longrightarrow KCl + H_2O + CO_2$$

Assay: The assay is based on Mohr's method of direct volumetric precipitation titration. An aqueous solution of the substance is titrated against a standard solution of silver nitrate using solution of potassium chromate as indicator.

$$KCl + AgNO_3 \longrightarrow AgCl + KNO_3$$

When whole of potassium chloride has been precipitated as AgCl, further addition of silver nitrate solution gives brick red color with the indicator. The end point is change of color from yellow to red.

Procedure: Accurately weigh the specified (0.25g) amount of potassium chloride and dissolve in 50 ml of water. Titrate the solution with 0.1N silver nitrate solution using potassium chromate solution as indicator.

$$2AgNO_3 + K_2CrO_4 \longrightarrow Ag_2CrO_4 + 2KNO_3$$

1ml of 0.1N silver nitrate ≡ 0.007455g of KCl

Use: Electrolyte replenisher in potassium deficiency, familial periodic paralysis, Meniere's syndrome (disease of inner ear), antidote in digitalis intoxication, myasthenia gravis.
Contraindication: renal impairment with oligouria, acute dehydration.

Potassium Chloride injection: Ringer injection

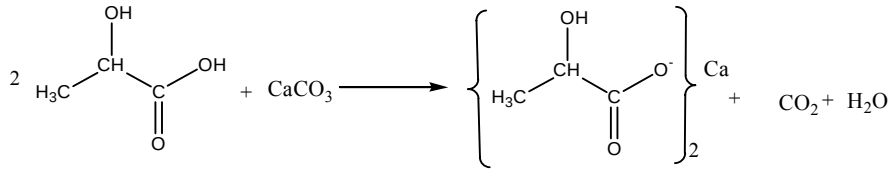
Calcium Replacement
Calcium Lactate: $C_6H_{10}CaO_6\ xH_2O$ MW 308.30 (Pentahydrate)

I.P. Limit. Potassium chloride contains not less than 97% and not less than 103% of Calcium Chloride dihydrate. It occurs as white odorless powder. The pentahydrate effloresces and becomes anhydrous at 120°. Aqueous solutions are prone to become moldy. It is soluble in water, practically insoluble in alcohol.

Test for Identification:
For Calcium: Dissolve substance in 5 M acetic acid and add 0.5 ml of potassium ferrocyanide solution. The solution remains clear. Add ammonium chloride white crystalline precipitate is formed.
For Lactate: To sample solution add bromine water, 1 M H_2SO_4 and heat on water bath stirring occasionally until the color is discharged. Add ammonium sulphate mixture of 10% solution of sodium nitroprusside in ammonia solution. Allow to stand for 10 mins, a dark ring appears at the interface of two liquids.

Preparation:

1. It is obtained by neutralizing a hot solution of lactic acid with calcium carbonate in slight excess. The hot liquid is filtered and filtrate is evaporated to crystalline product.



2. It is also obtained by fermenting hydrolyzed starch with a suitable mold in the presence of calcium carbonate

3. Or by fermentation of mother liquor resulting from the production of milk sugar and chalk. The mixture is digested for a week at about 30°. The product is purified by crystallization.

Assay: The assay is based on complexometric method of titration wherein disodium EDTA as titrant and calcon mixture as indication. The end point is change of color from pink to blue.

Procedure: Accurately weigh specified amount of sample and dissolve in water (50 ml), titrate the solution with 0.05 M disodium EDTA to within few ml of the expected end point. Add sodium hydroxide solution and calcon mixture and continue titration till end point is observed. The color of solution changes from pink to blue.
1ml of 0.05 M disodium EDTA ≡ 0.005004 gm of calcium

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. It is most convenient to evaluate clinical disturbances of pH by reference to HCO_3^- – H_2CO_3 System

Because it is in buffer system of extracellular fluid, this results from a number of factors:

1. There is considerably more bicarbonate present in extracellular fluid than any other buffer component.
2. There is a limitless supply of carbon dioxide
3. Physiological mechanisms operate to maintain the extracellular pH function by controlling fluid
4. The bicarbonate –carbonic acid buffer system operates in conjunction with haemoglobin.

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.

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 CO_2 enters the erythrocytes where it either rapidly forms $H_2CO_3$by the action of carbonic anhydrase or combines with Hb.

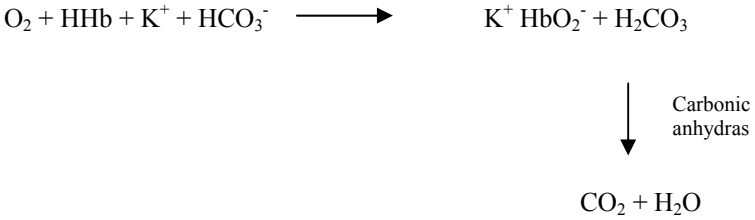
The tendency to lower the pH of the erythrocytes due to increased concentration of H_2CO_3 is compensated by Hb.

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3$$

The bicarbonate anion then diffuses out of erythrocytes and chloride anion diffuses in. This has been named as chloride shift. Te bicarbonate in plasma, along with the plasma carbonic acid now acts as efficient buffer system

$$H_2CO_3 + K^+ + HbO_2^- \longrightarrow K^+ + HCO_3^- + HHb + O_2$$

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 CO2 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 $HPO4^{-2}/H_2PO_4^-$ ratio is approximately 4:1. In kidney, the pH of urine can drop to 4.5-4.8 corresponding to $HPO4^{-2}/H_2PO_4^-$ 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 in the tubular cells. The process known as sodium hydrogen exchange.
3. The sodium bicarbonate returns to plasma (eventually being removed in the lungs as CO_2) and protons enter tubular fluid, forming acids of the anions that originally were sodium salts.

Factors altering the pH of Extra Cellular Fluid

1. Acidosis: Acidosis is defined as increase in either potential and/or nonvolatile hydrogen ion (H^+) content of body. Increase in the H^+ concentration of plasma is known as acedemia and is manifested by fall in the pH of blood. In case there is no rise in H^+ concentration of plasma, such state of acidosis (without acedemia) is known as **compensated acidosis.**

Types and Causes of Acidosis:

Metabolic acidosis: it occurs due to excess production of proton in the body which may be because of

i) Acceleration of normal metabolic process i.e. excessive catabolism e.g. in fever
ii) Administration of drugs which are proton donors e.g. salicylates, chlorides
iii) Excessive loss of alkaline fluid from the intestine, as in diarrhea
iv) Administration of large quantity of saline.

Metabolic acidosis is treated with sodium salts of bicarbonate, lactate, acetate and occasionally citrate. When there is bicarbonate deficit, administration of bicarbonate increases the HCO_3^-/H_2CO_3 ratio. Lactate, acetate and citrate ions are normal components of metabolism and are degraded to carbon dioxide and water by TCA cycle (Citric acid cycle or Krebs cycle).

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.

2. Alkalosis: Alkalosis is reduction in the total hydrogen ion content of the body. Alkalemia is reduction of hydrogen ion content in plasma and is manifested by increase in the pH of

blood. In case there is no decrease in H^+ concentration of plasma, such state of alkalosis (without alkalemia) is known as **compensated alkalosis.**

Metabolic alkalosis: Due to renal damage that cannot excrete an appreciable amount of alkali. Occurs due to alkali ingestion in presence of renal damage, 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.

Contraction alkalosis: seen following administration of mercurial diuretics which cause excessive loss of Cl^- and sodium.

Respiratory alkalosis: Respiratory alkalosis is caused by hyperventilation which washes away large amount of carbon dioxide formed in metabolism causes lowering of arterial pCO_2 and reduction in ratio of bicarbonate ion and carbonic acid with fall in hydrogen ion concentration. It Occurs due to high altitude, fever, encephalitis, hypothalamic tumor, drugs like salicylate, hot bath

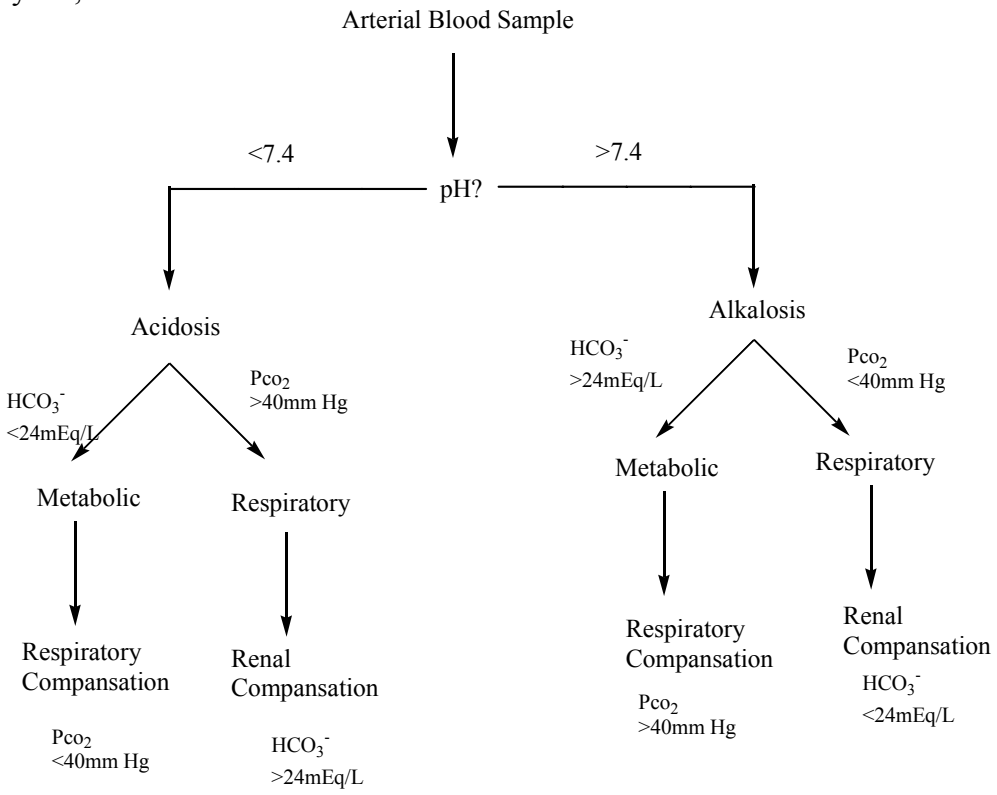


Figure: Analysis of acid base disorder.

If the compensatory responses are markedly different than those shown at the bottom of the figure, one should expect a mixed acid base disorder

Sodium bicarbonate (Sodabicarb): $NaHCO_3$: (M.W. 84.01)
I.P. limit: 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 begins to lose carbon dioxide at 50° and at 100° it is converted into sodium carbonate. It is soluble in

water (1 in 12); partially soluble in alcohol. The aqueous solution is alkaline to litmus; 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, benzyl penicillin potassium, carmustine, glycopyrronium bromide; isoprenaline hydrochloride and suxamethonium chloride.

It is stable in dry air, but slowly decomposes in moist air.

Preparation:

1. It is prepared by passing strong brine containing high concentration of ammonia trough a carbonating tower where it is saturated with carbon dioxide under pressure. The ammonia and CO_2 reacts to form ammonium bicarbonate which is allowed to react with sodium chloride to precipitate sodium bicarbonate. It is then separated by filtration
2. By passing carbon dioxide through a saturated solution of sodium carbonate.

$$Na_2CO_3 + H_2O + CO_2 \longrightarrow 2NaHCO_3$$

Chemical Properties:

1. When sodium bicarbonate is heated, it is decomposed into the normal carbonate, carbon dioxide and water.

$$2NaHCO_3 \longrightarrow Na_2CO_3 + H_2O + CO_2$$

2. A solution of sodium bicarbonate is alkaline due to hydrolysis (pH 8.2)

$$2NaHCO_3 \longrightarrow Na^+ + H_2CO_3 + OH^-$$

Sodium bicarbonate is slightly alkaline and fails to turn pehnolphthalein red. On the other hand, in sodium carbonate the carbonate ion is so extensively hydrolyzed that the solution is quite alkaline (pH is 11.6)

$$CO_3^{2-} + H_2O \longrightarrow HCO_3^- + OH^-$$

3. When a mercuric chloride solution is added to a solution of sodium bicarbonate there is no immediate formation of precipitate. After some time a reddish precipitate of HgO is formed.

$$2NaHCO_3 + HgCl_2 \longrightarrow 2NaCl + Hg(HCO_3)_2$$

$$Hg(HCO_3)_2 \longrightarrow HgO + H_2O + 2CO_2$$

4. When the bicarbonate is treated with an acid, carbon dioxide is liberated;

$$NaHCO_3 + HCl \longrightarrow NaCl + H_2O + CO_2$$

Test for purity : Tests for alkalinity; aluminum; calcium; insoluble matter; arsenic; iron; lead; chloride; sulphate; ammonium compounds.

- For detecting the presence of aluminum, calcium and insoluble matter an aqueous solution is boiled with ammonia solution and filtered. The residue is ignited and weighed.
- An aqueous solution after addition of nitric acid complies wit the limit test for chloride.

- An aqueous solution after addition of hydrochloric acid complies with the limit test for sulphates.
- Evolution of ammonia on heating the substance with sodium hydroxide indicates the presence of ammonium compound.
- An aqueous solution after addition of hydrochloric acid complies with the limit test for iron.
- Heavy metals are determined by comparing the colour produced with the substance and with standard lead solution after treatment with hydrogen sulphide solution.
- Simultaneous administration of sodium bicarbonate with other drugs inhibits the activity of the drug. Such a therapeutic incompatibility is found when sodium bicarbonate and sodium salicylate are used in equivalent amounts.

Test for identification: It gives the reactions of sodium, and of bicarbonates.
For Sodium: To sample solution add 15 % w/v potassium carbonate, heat, no precipitate, add potassium antimonite solution, heat to boiling, cool and if necessary scratch the inside of test tube with a glass rod, a dense white precipitate is produced.
For bicarbonate: to sample add magnesium sulphate no precipitate is produced. On boiling a white colored precipitate is formed.

Assay: A solution of weighed amount of sample dissolved in water is titrated with 0.5 N hydrochloric or sulphuric acid, using methyl orange as indicator.

Each ml of 0.5 N hydrochloric acid is equivalent to 0.042 g of $NaHCO_3$.

It is a direct titration method, the end point is yellow to pink. The equivalence point of this titration is at about ph 3.6 which corresponds to the colour change of methyl orange (pH 2.8 - 4.0, red-yellow). The reaction at the equivalence point is acidic because of the presence of carbonic acid.

Uses : Sodium bicarbonate is an electrolyte replenisher, and systemic alkalinizing agent used in the treatment of metabolic acidosis (increase in acidity) , diarrohoea, acute poisoning from acidic drugs (phenobarbitone and salicylates) , and as an antacid to relieve dyspepsia. 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.

Administration of sodium bicarbonate by mouth can cause stomach cramps and flatulence. Its large quantities may cause systemic alkalosis, vertigo (loss of power of balancing) and jerky muscular movement.

Sodium bicarbonate is available as mint-flavored soda-mint tablets. Ti is self-medicated, inexpensive and easily available drug. It is absorbed from the intestine which produces effects all over the body. It produces carbon dioxide gas in stomach and may cause perforation of a deep ulcer. Its onset of action is quick but the duration of action is short. It may cause rebound acidity due to short duration of action and systemic effects. When taken with milk it may cause milk alkali syndrome, characterized by deposition of calcium of milk on the kidney and increased blood urea.