Basics of Fluid and Electrolytes

(An updated version)

...اورہم نے ہر جاندار چیز کو پانی سے بنایا کیا پھر بھی یقین نہیں کرتے

سورۃ الانبیاء، آیت نمبر 30

اور اللہ نے ہر چلنے پھرنے والے (جاندار) کی پیدائش (کی کیمیائی ابتداء) پانی سے فرمائی ...

سورۃ النور، آیت نمبر 45

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Preface

The administration of fluids and electrolytes is an integral part of patient care. Knowledge regarding physiology of intravenous fluids is essential for their appropriate routine use and during emergency situations.

Although intravenous solutions are very frequently prescribed and the electrolyte panel is one of the most frequently ordered investigations in the emergency department, very little importance is given to fluid and electrolytes in the undergraduate curriculum. Inappropriate use of intravenous fluids can be a cause of increased morbidity and mortality. This includes not only the amount of the fluid but also the type of the solution.

In choosing the suitable type of intravenous fluid, it is important to know the components of the commonly available solutions. No one solution can fit all – the modern approach to intravenous solutions has enabled an increased understanding of clinical application of the various solutions in line with the clinical condition of the patient.

The Basics of Fluids and Electrolytes is an endeavor from Otsuka Pakistan for Continuing Medical Education and is been presented in a user-friendly format for better understanding. However, it is not a substitute for standard textbooks and journals and reference should be made to them whenever required.

1 Intravenous Fluid Administration --- A Short History

The first ever known intravenous infusion was administered in 1492 in an attempt to save the life of a dying pope through administering blood by a vein-to-vein anastomosis. Dr. James Blundell carried out the first successful transfusion in 1818 in a patient during childbirth.

However, the first use of intravenous fluids can be traced back to 1830's during the cholera epidemic. In 1832 during the epidemic, William O' Shaughnessy highlighted the importance of restoring saline levels for managing cholera. This idea was picked up by Thomas Latta who then put it into practice.

Ringer's Solution was developed by Sidney Ringer as an isotonic solution of sodium, potassium and calcium chloride in 1883. The routine use of saline infusions during major surgery was initiated by Rudolph Mata in 1924.

Alexis Hartmann introduced Lactated Ringer's Solution in 1932. He described the buffering action of intercellular fluid in maintaining the composition of blood and emphasized the replacement of lost electrolytes and water to completely overcome the effects of dehydration. He described the methods for the preparation of sodium lactate solution, Lactated Ringer's Solution, Dextrose solution and Sodium Bicarbonate Solution.

In the Journal of American Medical Association Hartmann wrote in 1934:

"Lactete-Ringer's solution may be given by any of the parenteral routes. It has almost entirely replaced the use of physiologic solution of sodium chloride or Ringer's solutions in the St. Louis Children's Hospital for routine treatment of dehydration with or without the knowledge of coexisting chemical changes".

The integration of body fluid physiology and clinical practice was made possible by the pioneering work of James Gamble and Dan Darrow. Gamble was the first to describe the nature and composition of extracellular fluid. He described the ECF as closely resembling to the sea water. Darrow showed how the body fluids react to deficiencies of potassium and increased or decreased amounts of sodium. He was the

first to add potassium to parenteral fluid therapy and emphasized on the replacement of estimated deficits rather than rapidly restoring ECF. It was many years later that this deficit parenteral replacement gave way to oral rehydration therapy (ORT).

The principles governing the administration of fluids in the perioperative period have been the subject of much debate. Pringle and his colleagues were the first to observe a reduction in urine volume after surgery. However, Francis Moore recommended restricted fluid regimens in the perioperative period. By contrast, Tom Shires and colleagues ascribed the loss of extracellular fluid in surgery to internal redistribution and advocated additional fluid infusions for replacement of these losses.

Fluid management in surgical patients since then, have evolved from the initial, salt-rich solutions being replaced by dextrose-based solutions, to the current critical care regimens. Recent volume kinetic studies of infused fluids have helped in further understanding of fluid mechanics in surgical patients.

2 Introduction to Body Fluids

Intravenous therapy is almost routine now. Almost every patient in the hospital will have some sort of intravenous (IV) access. However intravenous therapy should not be routine. In many disease processes the wrong IV solution could do harm to the patient. There should be a working knowledge of all types of IV fluids, with the understanding that exceptions exist for all the rules.

BODY FLUIDS

The body fluids provide a medium in which all the chemical reactions of the cells take place. It also provides a medium of transport for different substances. These fluids are constantly losing and replacing their constituents and their composition remains remarkably constant at all times.

The body mass can broadly be divided into body fat and fat free body mass (lean body mass). A large part of body mass is made up of water. Stored fat is water free.

BODY FLUID COMPARTMENTS

The total body water (TBW) is 73.2 percent of lean body mass. This body water is distributed throughout the body and consists of several fluid ***compartments*** each filled with fluid having peculiar characteristics. Broadly speaking there are two fluid compartments:

Extracellular Fluid

All the cells of the body are surrounded by a fluid called the ***Extracellular Fluid*** (ECF). This fluid provides nutrients and oxygen to the cells. It also carries away the metabolic waste products of the cell.

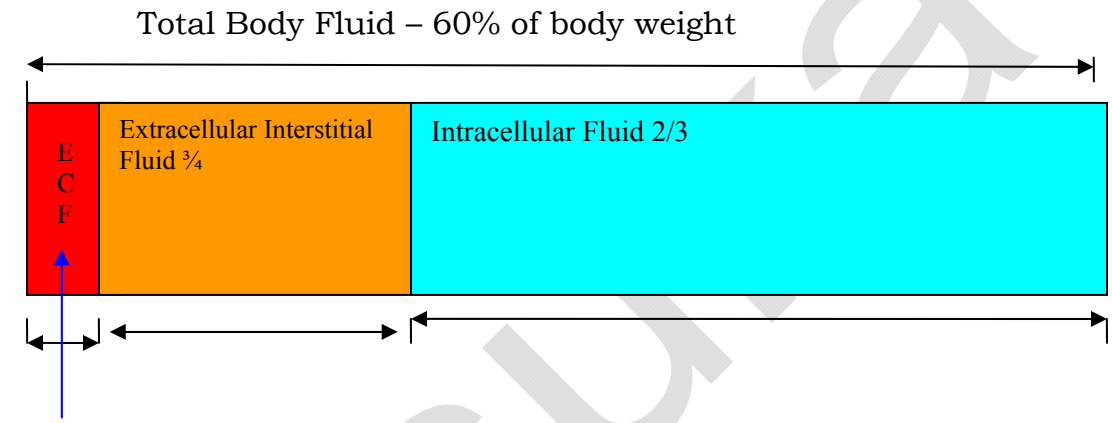
ECF comprises 1/3rd of the total body fluids, and accounts for 20% of body weight. This ECF is divided into 2 parts:

(a) Plasma: This is the part of ECF which together with other cellular components of blood occupy the vascular system (i.e. the vessels). This fluid is ***Intravascular*** and comprises about 25% of the ECF (5% of body weight).

(b) Interstitial Fluid: This is the part of ECF which lies outside the vascular compartment and bathes the cells. It comprises 75% of the ECF (15% of body weight).

Intracellular Fluid

This is the fluid found within the cells. The cells of the body contain a large amount of water which comprises 2/3rd of the total body water and accounts for 40% of the body weight.



Transcellular Fluid

Apart from the ECF and ICF, a third compartment of body fluids is also described. These are known as the ***Transcellular Fluids***. These fluids occupy specific locations as a result of transport through cells and include cerebrospinal fluid, pericardial fluid, pleural fluid, gastrointestinal fluid and intraocular fluid. These fluids comprise a very small fraction of total body water and are usually considered a part of ECF.

FUNCTIONS

Extracellular fluid serves as a conduit between cells and organs. It regulates the intracellular fluid volume and ionic distribution. Alterations in ECF are accompanied by a change in ICF as well.

Plasma is a route of rapid transit and interstitial fluid serves as a supply zone, bathing each cell and serving to allow the entire cell surface to be used as a source of exchange.

COMPOSITION

Apart from water, the various compartments also contain solutes, both electrolytes and non-electrolytes. Electrolytes are substances which dissociate (split) in aqueous solution into positively and negatively charged ions which are known as ***cations*** and ***anions*** respectively. These ions are responsible not only for conducting electrical currents but also regulating a number of other processes.

Non-electrolytes are substances which do not dissociate into solution e.g. glucose and urea.

A balance between the positive and negative charges is always maintained. An equivalent is used as the unit of measurement which denotes the weight of an element in grams that forms a bond with 1 gram of hydrogen or replaces it. As the concentrations of the ions are very low, calculations are made in milli-equivalents and expressed per liter of fluid (mEq/L). However calculations are also made using molecular weight (expressed as mmol/L). The concentrations are also sometimes expressed in mg% which can be converted to mEq/L or mmol/L according to the following equations:

$$\text{mEq/L} = \frac{\text{mg\% x 10 x valency}}{\text{Atomic or molecular weight}}$$

$$\text{mmol/L} = \frac{\text{mg\% x 10}}{\text{Atomic or molecular weight}}$$

(10 denotes the conversion of 100 ml. to 1 liter)

Extracellular Fluid

Sodium is the main cation of ECF which also contains a large amount of chloride, reasonably large amount of bicarbonate, but small quantities of potassium, calcium, magnesium, phosphate and organic acid ions.

The two compartments of ECF, the plasma and interstitial fluid have similar ionic compositions. However, the plasma contains a higher concentration of proteins. These proteins have a negative charge and

therefore, bind positively charged ions, thus increasing their concentration in the plasma.

In the interstitial fluid the anions have a slightly higher concentration. However, the concentration of the ions in the plasma and interstitial fluid are considered equal for all practical purposes.

Intracellular Fluid

A large amount of potassium and phosphate ions are present in the ICF and moderate quantities of magnesium and sulfate ions. However, only small quantities of sodium and chloride ions are present in ICF and almost no calcium. A large amount of protein is also present.

Plasma(mEq/L)		**Interstitial Fluid(mEq/L)**		**Intracellular Fluid(mEq/L)**	
Cations	Anions	Cations	Anions	Cations	Anions
Na^+ 142	Cl^- 103	Na^+ 145	Cl^- 115	K^+ 160	HPO_4^- 140
Ca^{++} 5	HCO_3^- 27	K^+ 4	HCO_3^- 30	Mg^{++} 35	Proteins 55
K^+ 4	Proteins16	Ca^{++} 3	Proteins 1	Na^+ 10	HCO_3^- 8
Mg^{++} 3	Organic acids 5	Mg^{++} 2	Organic Acids 5		Cl^- 2
	HPO_4^- 2		HPO_4^- 2		
	SO4^{--} 1		SO_4^{--}1		
154mEq/L	154mEq/L	154mEq/L	154mEq/L	205mEq/L	205mEq/L

Composition of Different Fluids

Anion Gap

The total amount of cations are always balanced by the total amount of anions. However the laboratories only report the amounts of sodium, chloride, potassium and bicarbonate. The difference between the sum of the cations (sodium and potassium) and the anions (chloride and bicarbonate) is represented by the anion gap. This is usually calculated by the following equation:

Anion Gap = (sodium + potassium) – (chloride + bicarbonate)

The normal value is 12 ± 2 mEq/L.

The calculation of the anion gap is helpful in determining the acid-base disorders. When there is a high anion gap in association with metabolic acidosis, it is usually due to a nonchloride acid i.e. lactic acid or ketoacid. In such situations, the decrease in plasma bicarbonate is due

to these acids and there is no alteration of plasma chloride. Hence, this condition is known as ***Normochloremic Acidosis*** and usually results from excess production of endogenous acids or uremia. However, when the acid added to ECF is hydrochloric acid, then each mEq. of bicarbonate is replaced by an equivalent amount of chloride, and the sum of chloride and bicarbonate remains constant, and therefore a normal anion gap. This condition is known as ***Hyperchloremic Acidosis*** and usually is a result of net loss of base from the body such as that occurring in diarrhea.

3 Osmosis

When a substance ***(solute)*** is dissolved in water ***(solvent)*** the concentration of water decreases. If this solution is separated from pure water by a semi-permeable membrane which is permeable (which allows passage) to solvent molecules but not to the solute molecules, the water (solvent) will move down its concentration gradient into the solution.

This diffusion of the solvent into a region where there is a higher concentration of solute is termed Osmosis. Therefore, whenever there is a concentration difference for water, net movement of water occurs across the membrane and this net movement of water is known as ***Osmosis***. In different conditions osmosis can lead to swelling or shrinking of the cells.

OSMOTIC PRESSURE

The tendency for the movement of solvent molecules to a region of higher solute concentration can be prevented by applying pressure to the more concentrated solution. This pressure necessary to prevent solvent migration is known as the ***Osmotic Pressure.***

The osmotic pressure is determined by the number of particles per unit volume of fluid and not by the mass or weight of the particles. In other words the osmotic pressure is the concentration of the solution in terms of number of particles and the unit for it *is* ***Osmole.***

Osmolality

An osmole is the gram molecular weight of a solute. Let us consider the example of glucose. The chemical formula for glucose is $C_6 H_{12} O_6$.

The molecular weight of a substance is calculated by multiplying the atomic weight of each constituent element by its number of atoms. For glucose this is calculated as follows:

C_6 = 12 x 6 = 72 (Atomic weight of carbon is 12 ; no. of atoms is 6)
H_{12} = 1 x 12 = 12 (Atomic weight of hydrogen is 1; no. of atoms is 12)
O_6 = 16 x 6 = 96 (Atomic weight of oxygen is 16; no. of atoms is 6)

$C_6 H_{12} O_6$ = 180

So the molecular weight of glucose is 180. This weight expressed in grams is known as the gram molecular weight and equals 1 osmole as glucose does not dissociate in solution.

However, for substances which dissociate in solution the situation is somewhat different e.g. sodium chloride (NaCl).

The molecular weight of sodium chloride is :

NaCl or [(23x1)+(35.5x1)] = (23+35.5) = 58.5
(Atomic wt. of sodium : 23
Atomic wt. of chlorine: 35.5)

This weight expressed in grams represents the gram molecular weight. But as NaCl dissociates into sodium and chloride ions, the gram molecular weight equals 2 osmoles because the number of osmotically active particles is twice as that in the undissociated state.

Therefore, Osmolality is defined as the number of osmoles of a solute dissolved/kilogram of water (solvent). This can also be expressed in terms of milliosmoles which is 1/1000 of an osmole/ kilogram of solvent.

Osmolarity

Since it is difficult to measure kilograms of water in a solution which is required to determine osmolality, the characteristics of body fluids are expressed by another term ***Osmolarity***, which is the osmolar concentration per liter of solution rather than osmoles per kilogram of water (solvent).

For dilute solutions, like body fluids, the quantitative differences between osmolarity and osmolality are less than 1%. Therefore, it is more practical to measure osmolarity.

Osmolarity is a measure of the concentration of molecular and ionic particles in a solution. If there is a change in the osmolarity of ECF compartment, water must move out of the cells or the solute must move into the cells to restore osmotic equilibrium.

When osmolarity is altered, a transient phase exists during which water flows in such a way as to re-establish equilibrium. Changes in body fluid osmolarity originate with ECF because gain or loss of solutes or water occur via the ECF. The ECF osmolarity may be altered via two mechanisms:

1. Altering solute content of fluid
2. Altering water content of fluid.

Some solutes called ***Permeant Solutes*** freely cross most cell membranes e.g. urea. Others called ***Impermeant Solutes*** do not easily move as the cell membranes are impermeable to them e.g. mannitol. Sodium ions also come under the category of impermeant solutes. An increase of ECF osmolarity due to such substances causes movement of water from the cells causing dehydration.

Glucose is a permeant solute in normal individuals as it readily enters the cells. However, it becomes an impermeant solute in diabetes mellitus as it requires insulin for its movement into the cells.

A solution is said to be ***Isosmotic*** when its osmolarity is equal to that of plasma. The normal osmolarity of plasma varies from as low as 280 mOsm/L to as high as 295 mOsm/L.

Importance of Sodium

The major cation and solutes present in the ECF are sodium ions and sodium salts. Therefore sodium is the major determinant of plasma osmolarity. Minor contributors are glucose and urea. Plasma osmolarity can therefore be estimated by the following formula:

$$\text{Plasma Osmolarity} = 2\text{Na (mEq/L)} + \frac{\text{Glucose (mg/dl)}}{18} + \frac{\text{BUN (mg/dl)}}{2.8}$$

Thus hyperglycemia and uremia cause an increase in the plasma osmolarity. The presence of other solutes that may reach high concentration (e.g. mannitol) can change the situation and in such cases the formula may not be appropriate.

Calculation of Osmolarity

Several methods are used to obtain numerical values of osmolarity. The most commonly used equations are as follows:

1. For a non-electrolyte (e.g. glucose)

$$\frac{\text{Grams/Liter}}{\text{Molecular weight}} \times 1000 = \text{mOsm/L}$$

2. *For a strong electrolyte (e.g. sodium chloride)*

$$\frac{\text{Grams/Liter}}{\text{Molecular weight}} \times \text{Number of ions formed} \times 1000 = \text{mOsm/L}$$

CALCULATING FLUID EXCHANGES

Let us suppose that 3 liters of normal saline (0.9% sodium chloride) is infused in a male patient weighing 60 kg. suffering from persistent vomiting. Assume that the original osmolarity of the ECF is 285 mOsm/L.

Now let us calculate the changes step by step for understanding purposes. We must remember that the total body water in males is 60% of the body weight.

Initial Conditions

1. Total body water — 60 x 0.6 = 36 liters
2. ICF volume — 60 x 0.4 = 24 liters
3. ECF volume — 60 x 0.2 = 12 liters
4. Total body osmoles — 36 x 285 = 10260
5. Total ICF osmoles — 24 x 285 = 6840
6. Total ECF osmoles — 12 x 285 = 3420

{60 = wt.in kg.; total body water(60%)= 0.6; ICF volume(40%)=0.4; ECF volume(20%)= 0.2}

After Infusing The Fluid

1. Total body water — 36 + 3 = 39 liters
2. ICF volume — 24 liters
3. ECF volume — 12 + 3 = 15 liters

(we have infused the fluid into the ECF)

4. Total body osmoles — 10260 + 924 = 11184

(No equilibrium. The osmolarity of 1 liter of normal saline is 308 mOsm. Therefore infusing 3 liters will provide a total of 924 osmoles.

5. Total ICF osmoles — 6840 (no change initially)
6. Total ECF osmoles — 3420 + 924 = 4344

Final Equilibrium

1. Osmotic equilibrium 11184 ÷ 39 = 286.7mOsm/L
   (total body osmoles divided by the total body water)

2. Total ICF volume 6840 ÷ 286.7 = 23.85 liters
   (total ICF osmoles divided by the final osmolarity)

3. Final ECF volume 4344 ÷ 286.7 = 15.15 liters
   (total ECF osmoles divided by the final osmolarity)

Thus it is seen that the infused fluid remains in the ECF and in fact draws out a little water from the ICF thereby decreasing ICF volume. In the final equilibrium there is a slight increase in the osmolarity while a much larger increase occurs in the ECF volume.

In order to cross check the calculations, the final volumes of the ICF and ECF can be summed up and the figure thus obtained should be equal to the volume of initial body water plus the amount infused (in this example 23.85 + 15.15 = 39 liters which is equal to 36 + 3 = 39 liters.]

REGULATION OF OSMOLARITY

The regulation of osmolarity of body fluids in the normal range is also responsible for maintaining normal cell volumes and water balance. A balance between electrolyte-free water intake and excretion is required for maintaining normal plasma osmolarity. Although various mechanisms operate to achieve this balance, two are most important and are discussed below:

Osmoreceptor - ADH System

Special cells located in the hypothalamus of brain, known as ***Osmoreceptors*** are stimulated whenever osmolarity of ECF increases. Signals from these cells pass to the posterior pituitary gland which secretes ***antidiuretic hormone (ADH).***

ADH in turn acts on the kidneys to retain water and return the osmolarity to normal. The opposite sequence of events occur when osmolarity of ECF decreases.

Thirst Mechanism

Fluid intake is necessary to counterbalance any fluid loss which occurs through different routes. This intake is regulated by thirst mechanism which also controls ECF osmolarity. Osmoreceptors for thirst are also present in the hypothalamus and are stimulated when water is deficient and the osmolarity of body fluids is high.

INCREASED EXTRACELLULAR VOLUME

This occurs in many diseases. The increase may be in the interstitial fluid, in blood volume or in both.

Causes

The most commonly encountered conditions include congestive heart failure, nephrotic syndrome and hepatic cirrhosis. Other causes include renal failure and drugs.

Clinical Features

These depend upon specific cause. However the most common finding is peripheral swelling (edema). This may be evident in the ankles, face or sacrum. A raised jugular venous pressure and cardiomegaly may be present.

Treatment

The underlying cause should be treated. Sodium restriction is beneficial in some cases. The mainstay of treatment is the use of diuretics.

DECREASED EXTRACELLULAR VOLUME

Loss of water and salt causes shrinkage of ECF volume and can have profound effects.

Causes

Common causes of decreased volume are losses from the gastrointestinal tract such as diarrhea and vomiting, hemorrhage, loss of fluid in burns and use of diuretics. These are summarized in the table below:

Inadequate dietary intake	**Skin**
Gastrointestinal	Excessive sweating
Diarrhea	Burns
Vomiting	**Renal**
Fistula	Impaired sodium reabsorption
Hemorrhage	**Diuretics**
External	**Metabolic**
Internal	Diabetes mellitus

Extracellular Volume Depletion

In all these conditions the decreased extracellular volume is accompanied by a decrease in total body sodium and in many cases a decrease in potassium as well.

In addition to these causes, clinical features of volume depletion are also seen in cases of septicemia, although the sodium and water content are normal or increased.

Clinical features

Thirst, nausea, vomiting, and postural dizziness are common features, although the symptoms may be variable. In severe cases confusion and coma may occur due to hypotension and impaired cerebral blood flow.

Treatment

The principle of management is to replace the lost fluids. The type of fluid and rate of replacement depends on the clinical setting. In cases of diarrhea, replacement of water and electrolytes is necessary while Ringer's Lactate or whole blood is the treatment of choice in cases of hemorrhage.

Rapid infusion is necessary if there is hypotension, confusion and oliguria. In such cases plasma expanders (colloids) may be used initially.

Decreased ECV And Normal Body Sodium

Hypovolemia (i.e. decreased extracellular volume) can also occur as a result of leakage of fluid from the capillaries. Injury (as may occur in trauma or surgery) induces the release of ***cytokines*** which affect the permeability of the capillaries. As a result there is leakage of proteins (albumin) into the interstitium. Sodium and water follows albumin into the interstitium or to another compartment (third space).

During surgery, as a result of injury to the tissues, potassium is released from the cells in the early post-operative period, but hyperkalemia rarely occurs if renal function is normal.

More commonly patients undergoing surgery can develop hypokalemia. This occurs with alkalosis (both respiratory and metabolic), massive isotonic sodium replacement and when there are large losses of gastrointestinal fluids. This occurs because:

1. Potassium competes with hydrogen ions for renal tubular excretion in exchange for sodium ions.
2. Potassium secretion from renal tubules is increased when sodium is infused.

3. There is loss of potassium from the kidneys secondary to sodium retention which occurs in response to loss of sodium from intestinal fluid losses.

Moreover, post-operative patients experience pain, which is a stimulus for the release of ***Antidiuretic Hormone (ADH).*** This hormone further aggravates hypovolemia and causes decreased plasma osmolarity and hypotension.

Treatment

Lost ECF in case of surgical patients should be adequately replaced along with electrolytes. As already discussed above, ***Ringolact-D*** would be a useful solution for the initial phases as it would provide the required fluid along with adequate glucose as a nutritional source which would prevent protein catabolism and ketosis. This fluid would provide a low amount of potassium as well.

However, in late post-operative period ***Plabolyte-M*** would be recommended as it contains a high amount of potassium which helps in preventing the hypokalemia that can occur during this period.

TONICITY

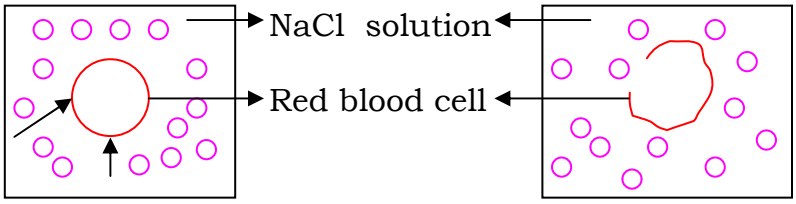
The effect of a fluid on cellular volume is known as ***Tonicity***. When there is an increased concentration of impermeant solutes, ***hypertonicity*** is the result which causes movement of water out from the cells and hence dehydration. ***Hypotonicity*** has the opposite effect and causes cell swelling and bursting. Thus a solution may be ***isotonic, hypertonic or hypotonic.***

Infusing Hypotonic / Hypertonic Solutions

Hypotonic Infusion

When red blood cells (RBC's) are placed in a hypotonic solution (e.g. 0.5% NaCl) the water passes into the RBC in order to maintain

equilibrium. As a result the cells swell, membranes burst and the contents are released.



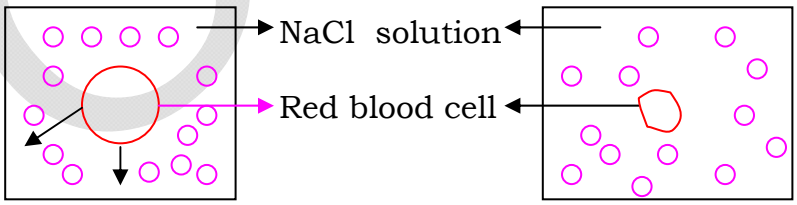
Effect of a Hypotonic Solution
(Movement of water into, and subsequent bursting of RBC's)

This bursting of cells is known as ***Haemolysis*** and the concentration which causes haemolysis is called the ***Fragility Point of RBC's***. This is less than 0.45% of NaCl.

When a small amount (upto 5 ml) of such a concentration is intravenously administered, it quickly mixes with blood and the concentration is raised above the fragility point before any damage can be done. A large volume of such a concentration when infused rapidly, can however cause haemolysis.

Hypertonic Infusion

When RBC's are placed in a hypertonic solution (e.g. 5% NaCl) the water passes out of the cells to maintain tonicity. The cells, therefore, shrink and its wall appears crenated (irregular). This is a reparable damage and the shape is regained when the pressure equalizes on both sides of the membrane.



Effect of a Hypertonic Solution
(Movement of water out of, and subsequent shrinkage of RBC's)

The tonicity of standard intravenous solutions is defined by their electrolyte concentration (cations). If the sum of sodium and potassium (and other cations) ions is more than 150 mEq/L (the approximate cation concentration of plasma) the solution is considered to be ***hypertonic***. If

this sum is less than 150 mEq/L than the solution is considered as a ***hypotonic*** solution.

The following table gives the osmolarity and tonicity of the commonly used intravenous solutions:

Solution	**Tonicity**	**Osmolarity mOsm/L**	**Sodium mEq/L**	**Chloride mEq/L**	**Glucose g/L**
5% D/W	154	252	0	0	50
0.9% NaCl	150*	308	150	150	0
D5/N.Saline	154	560	154	154	50
Ringer's Solution	155.5	309	147	156	0
Ringer's Lactate	137	272	130	108.7	0
Ringolact-D	137	550	130	108.7	50
Plabolyte-M	83	442	60	60	50

(*can vary according to pharmacopoeial standard used)

Tonicity and Osmolarity of commonly used solutions

However it must be remembered that dextrose immediately enters the cells and is metabolized. As a result many of the solutions though isotonic or hypertonic in vitro, behave as a hypotonic or isotonic solution in vivo e.g. 5% D/W, 10%D/W, Ringer's lactate with 5% Dextrose water (Ringolact-D), etc. The following table summarizes the tonicity and osmolarity of such solutions:

Solution	**Tonicity**	**Osmolarity**
5% D/W	Hypotonic	Hypo-osmolar
10% D/W	Hypotonic	Hyper-osmolar
0.9% Saline	Isotonic	Isosmolar
D5/Normal Saline	Isotonic	Hyper-osmolar
Ringer's Solution	Isotonic	Isosmolar
Ringer's lactate	Isotonic	Isosmolar
Ringolact-D	Isotonic	Hyper-osmolar
Plabolyte-M	Hypotonic	Hyper-osmolar

The optimal rate of infusion of carbohydrates is 4 mg/kg/minute. At this rate carbohydrates are metabolized and do not cause hyperglycemia and osmotic effects. Higher rates of infusion can cause an osmotic effect.

Sodium

Sodium is the most abundant cation in the body and the principal cation in the extracellular fluid. Sodium content of the body determines the volume of the extracellular fluid. Disorders of sodium regulation generally present because of abnormalities in the ***volume*** of the extracellular fluid.

INTAKE

The average dietary salt intake varies between 100-250 mEq/day. This corresponds to 2.3 - 5.7 grams of sodium or 6-15 grams of sodium chloride (NaCl). In some areas of the world salt intake is very high such as in Japan, Pakistan and India.

Dietary Sources

Sodium is present in most natural foods, in low amounts in fruits and vegetables and in moderate amounts in meat and milk. It is added to food for seasoning and preserving. Sodium chloride is the most common food additive. Processed foods have the highest sodium content while fresh fruits and vegetables have the lowest.

SODIUM LOSS

Salt loss occurs through sweat, stool, and urine. Under certain conditions urinary excretion can be as low as 1mEq/day or as high as 200 mEq/day. Hot weather and diarrhea are important causes of major salt loss.

ABSORPTION

In addition to the oral intake, 20-30 grams of sodium is secreted into the intestinal secretions each day. If this sodium is not absorbed, as occurs in diarrhea, sodium levels can decrease substantially. Under normal conditions almost all of this is absorbed and less than 0.5% of intestinal sodium is lost in the feces each day.

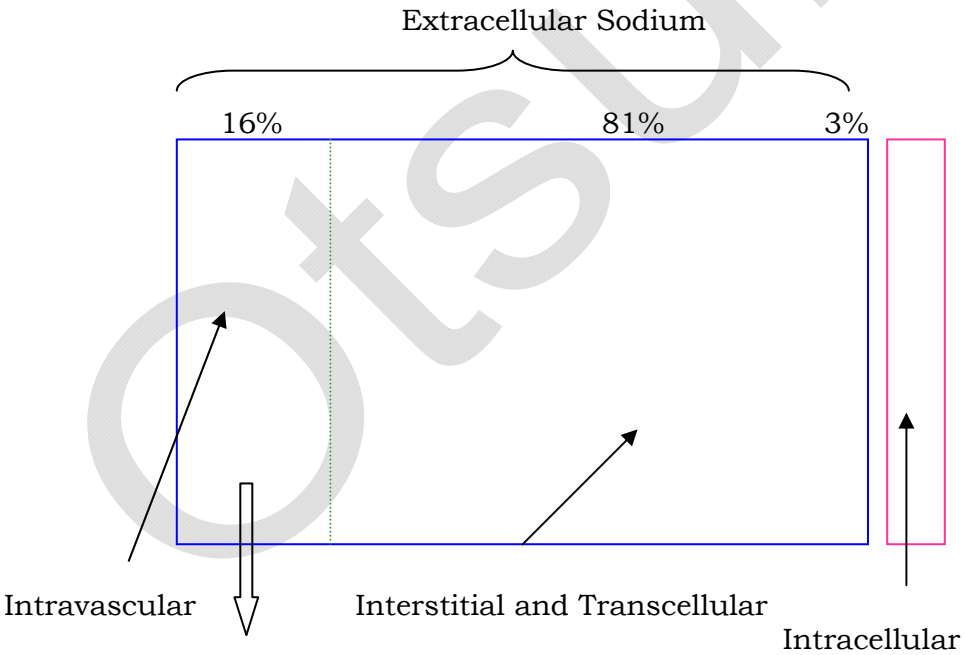
FUNCTIONS OF SODIUM

Sodium is the principal extracellular cation and the sodium content of the body determines the volume of the extracellular fluid.

A normal sodium concentration is necessary for the correct functioning of all the ***excitable tissues*** such as the nerves, skeletal muscles and cardiac muscle.

BODY SODIUM AND ITS DISTRIBUTION

Normal adult sodium content is 55-60 mEq/kg or about 4200 mEq in a 70kg person. A large portion (about 30%) of total body sodium is in a bound form in bone and other tissues and is therefore not available for ***exchange***. This is the ***non-exchangeable pool***. Rest of the 70% is the ***exchangeable pool*** and is mainly found in the extracellular fluid. Only about 3% of sodium is present within the cells.



Distribution of Exchangeable Sodium

The exchangeable sodium is distributed in the plasma, interstitial fluid and transcellular fluids. The distribution of sodium in body compartments is illustrated in the above diagram.

The concentration of sodium in the plasma (intravascular) averages 142 mEq/L and is the ***Effective Circulating Volume*** and is regulated by nervous and renal mechanisms.

SODIUM REGULATION

The sodium concentration is regulated in parallel with the ECF volume and osmolarity as they are closely linked. The sodium concentration and osmolarity of body fluids determines the distribution of fluids between the intracellular and extracellular compartments.

Different mechanisms operate in controlling the sodium concentration along with osmolarity and fluid volume. These are described in the following paragraphs.

Pressure Reflexes

Baroreceptors are nerve endings which are present in the walls of large arteries in the chest and neck regions, particularly the internal carotid artery and aortic arch. These receptors are sensitive to stretch. Baroreceptors are also present in the walls of the atria and pulmonary arteries.

Whenever there are changes in the blood volume caused by changes in ECF volume, the baroreceptors are stimulated and pass signals to the hypothalamus in the brain and to the kidneys, which affect renal salt and water excretion as follows:

Antidiuretic hormone (ADH)

This hormone is secreted from the posterior pituitary gland in response to the stimuli from the hypothalamus, whenever the osmolarity increases (i.e. increased sodium concentration or water loss).

ADH passes to the kidneys and acts on the distal tubules, collecting tubules and collecting ducts, increasing their water permeability. As a result water reabsorption increase, which causes a decrease in osmolarity and sodium concentration.

Renin-Angiotensin-Aldosterone System

Specialized cells in the initial portion of distal tubules (of kidney) known as ***Macula Densa*** are in close contact with ***Juxtaglomerular (JG) Cells*** in the walls of the afferent arterioles of the glomerulus and are sensitive to changes in sodium chloride concentration.

Dietary salt intake can cause changes in the glomerular filtration rate and the reabsorption of sodium chloride in the proximal tubules of kidney. Both of these determine the rate of flow and NaCl concentration in the loop of Henle and Macula Densa.

A low flow rate and a decreased NaCl concentration stimulates Macula Densa cells which causes the release of an enzyme ***Renin*** from the JG cells. Renin acts on another plasma protein ***Angiotensinogen*** to form ***Argiotensin- I*** which splits into ***Angiotensin- II*** by the action of ***Angiotensin Converting Enzyme.***

Angiotensin-II:

(i) Directly acts on the kidney to retain salt and water.
(ii) Causes the adrenal glands to secrete the hormone ***Aldosterone.***

One of the most important functions of aldosterone is to cause marked increase in sodium reabsorption by the kidney tubules. Aldosterone acts mainly on the collecting tubule, but also on the distal tubule and collecting duct to increase sodium reabsorption in exchange for potassium secretion.

However, sodium reabsorption also leads to water reabsorption and therefore does not affect the total concentration of sodium.

DISORDERS OF SODIUM BALANCE

Disturbances of sodium concentration are caused by disturbances of water balance. The two conditions are known as ***Hyponatremia*** and ***Hypernatremia***.

Hyponatremia

This is a common condition and is said to occur when the serum sodium is less than 135 mEq/L. The condition can result from loss of sodium or gain of water. Consequently Hyponatremia may be associated with a low ECF volume, normal ECF volume or an increased ECF volume.

Hyponatremia with Low Extracellular Volume (ECV)

In this situation there is primarily loss of salt (sodium) in excess of water resulting in decreased concentration of sodium and decreased extracellular volume (ECV). The deficit may be due to renal or extrarenal causes.

Renal Causes

1. Thiazide diuretics
2. Osmotic diuresis

Extrarenal Causes

1. Diarrhea
2. Vomiting
3. Excessive sweating
4. Nasogastric suction
5. Fistulas
6. Hemorrhage
7. Burns
8. Intestinal obstruction
9. Pleural effusion

The differentiation between renal and extrarenal loss is done by determining urinary sodium.

Urinary sodium less than 20 mEq/day : In patients with hypovolemia, the kidneys are activated to conserve sodium. In such situations the sodium excretion in urine falls to very low levels (less than 20 mEq/day) and urine sodium concentration is 15 mEq/L or less. This frequently occurs in the case of extrarenal causes of sodium loss such as diarrhea, vomiting and burns.

Urine sodium more than 150 mEq/day : The normal 24-hour sodium excretion is approximately equal to the dietary intake (around 150-200 mEq/day). Hypovolemic patients excreting more sodium than 150 mEq/day indicate loss of sodium due to renal causes (Renal salt wasting). This most commonly is due to the administration of thiazide diuretics and osmotic diuresis. Chronic renal failure also results in decreased capacity of kidneys to conserve sodium.

Values between 20-150 mEq/day : Intermediate levels in a patient with hypovolemia indicate that the salt conservation by the kidneys is defective but do not point whether renal or extrarenal cause is

responsible. In many cases the kidneys lose salt secondary to disordered sodium regulatory mechanisms. The following classification may be used as a guide:

Renal Causes:

Drugs : Diuretics
Other Drugs : Mannitol, Methylxanthines, etc.
Renal Diseases: Chronic renal failure, Renal cystic disease, etc.

Secondary Causes:
Addison's Disease
Congenital adrenal hyperplasia

Clinical Picture

The patient presents with features of salt loss and volume depletion.

The manifestations are largely related to dysfunction of the central nervous system, and they are more obvious when the decrease in the serum sodium concentration is large or rapid (i.e., occurring within a period of hours).

Most common symptoms are headache, nausea, vomiting, muscle cramps, lethargy, restlessness, disorientation, and depressed reflexes. Most patients with a serum sodium concentration exceeding 125mEq/L are asymptomatic, those with lower values may have symptoms, especially if hyponatremia has developed rapidly.

Complications of severe and rapidly evolving hyponatremia include seizures, coma, permanent brain damage, respiratory arrest, brain-stem herniation, and death.

These are summarized below:

Symptoms	**Signs**
Thirst	Dry mouth
Muscle cramps	Cold skin
Nausea	Tachycardia
Postural dizziness	Loss of skin elasticity
Confusion	Hypotension
Coma	Shock

Treatment

Salt and water both should be replenished. Although Dextrose Saline may be administered, Ringer's Lactate (***Ringolact)*** or ***Plabolyte-M*** would be advisable if the patient is vomiting.

Hyponatremia with Normal ECV

In this situation the main abnormality are causes such as:

1. Syndrome of Inappropriate ADH secretion (SIADH)
2. Addisons disease
3. Glucocorticoid deficiency
4. Hypothyroidism

Clinical Features

These will correspond to the underlying disease and will vary accordingly. In SIADH excessive amounts of ADH are released despite low plasma osmolarity and normal ECV. The presentation is vague with confusion, nausea and irritability. Later fits and coma may occur.

Patients with Addison's disease will present with weight loss, anorexia, weakness, impotence, myalgias, nausea, vomiting and diarrhea. Abdominal and joint pain may also occur.

Hypothyroidism will be manifested as anorexia, intolerance to cold, weight gain, tiredness, constipation, change in appearance, decreased libido, dry coarse skin and menstrual abnormalities.

Treatment

This is directed towards the underlying cause and hyponatremia does not require any specific treatment e.g. in case of thyroid insufficiency, thyroid hormones should be administered.

Hyponatremia with Increased ECV

In this setting hyponatremia is associated with edematous states such as congestive cardiac failure, hepatic cirrhosis and nephrotic syndrome.

There is decrease in effective circulating volume. The clinical features and treatment depend on the specific cause.

Relationship Between Sodium And Osmolarity

Without insulin, glucose cannot permeate cell membranes. Hyperglycemia causes the water to flow out of the cells, diluting the plasma sodium. When osmotic equilibrium is reestablished, the plasma sodium is still low, even though the plasma osmolarity is increased due to the presence of glucose. For each 100 mg/dL increase in plasma glucose, the plasma sodium concentration decreases by about 1.6 mEq/L.

For example if the plasma glucose rises from 100 to 500 mg/dL, an increase of 400 mg/dL, the plasma sodium would be decreased by 6.4 mEq/L { 140 – (1.6 x 4)} . Here 140 is the normal sodium concentration, 1.6 is the decrease / 100 mg increase in glucose and 4 depicts the 400 mg/dL of glucose.

Hypernatremia

This is defined as a plasma sodium concentration more than 145 mEq/L. Hypernatremia also causes increased osmolarity as it is the major cation in ECF. It may be caused due to a loss of water from ECF, which concentrates the sodium ions or due to an excess of sodium in ECF.

These include:

1. ADH deficiency.
2. Administration of hypertonic sodium solutions.
3. Total parenteral nutrition.
4. Hyperosmolar diabetic coma.

Clinical features

As a result of hypertonicity, water shifts out of the cells causing a decrease in ICF volume. The major risk is damage to the brain. Symptoms include altered mental status, weakness, and neurologic deficits. Seizures and coma may occur.

Treatment

This is directed towards treating the underlying cause and correcting the water deficit.

6 Potassium

Potassium is the most abundant cation within the cells of the body. It plays a major role in maintaining the fluid and electrolyte balance and cell integrity. It is also required for a number of other cellular processes. The kidneys are the principal regulators of potassium balance.

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INTAKE

Potassium enters the body through food, medications and potassium-containing intravenous fluids. The average daily potassium intake is about 50-100 mEq/day or about 0.75-1.25 mEq/Kg body weight, depending on the fruit and vegetable intake. However this intake may vary from as low as 10 mEq/day to 400 mEq/day.

In most natural foods, the anion accompanying potassium is usually a non-chloride which are poorly reabsorbed by the kidneys. Ingestion of these potassium salts, therefore helps the kidneys to eliminate potassium.

The normal daily enteral potassium requirements are about 500 mg (22 mEq/kg). The parenteral requirements are 1-2 mEq/Kg/day, assuming normal organ function and without abnormal losses.

Dietary Sources and Absorption

Whole foods of all kinds - fruits, vegetables, legumes, grains, meat, fish and poultry are good sources of potassium. Fresh foods contain much more potassium than sodium. Potassium ions are actively absorbed in the small intestine.

The body also ***releases*** potassium into the ECF whenever there is cell breakdown or when there is a drop in the pH.

POTASSIUM LOSS

Under normal circumstances about 90% of potassium ingested each day is excreted in the urine. Less than 15% of ingested potassium is excreted in the feces and a small amount is lost in sweat.

The amount excreted in feces during disease states such as diarrhea can increase markedly. The secretion of potassium in the gut is also influenced by ***aldosterone***.

Sweat has a mean potassium concentration of 9 mEq/L. However, this concentration can increase, particularly during physical training in a hot climate.

FUNCTIONS OF POTASSIUM

Potassium is critical for many metabolic functions of cell such as:

1. Optimal action of many enzymes.
2. Growth, division and maintenance of normal cell volume.
3. Maintaining electrical potential across cell membranes.
4. Excitation and contraction in neuromuscular cells.

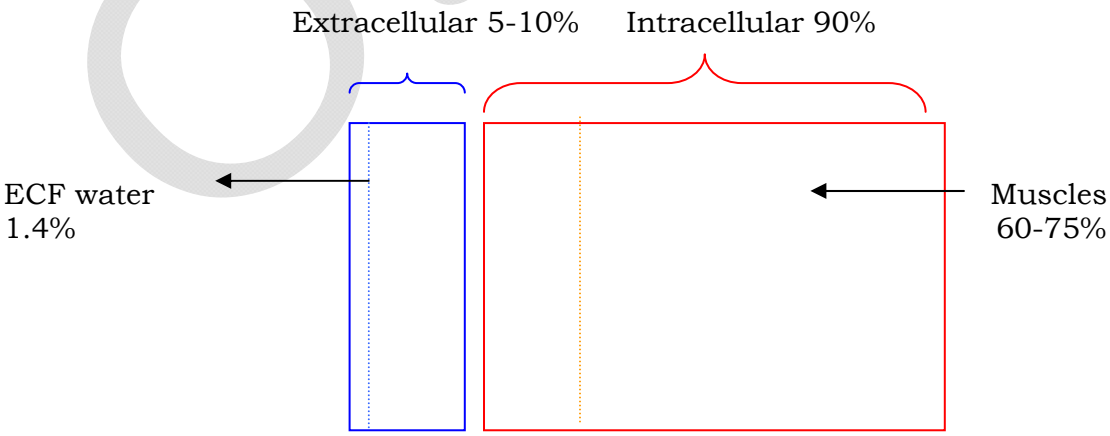
BODY POTASSIUM AND ITS DISTRIBUTION

Potassium is the second most abundant cation in the body. It is about 50 mEq/Kg in a young adult male. Therefore, a 70 Kg man contains about 3500 mEq of potassium. This value decreases with age owing to a decrease in body muscle mass and an increase in fat content. It decreases by about 2 mEq/Kg/decade.

In women total body potassium is approximately 25% lower than men in relation to weight because of the higher percentage of fat.

Distribution

About 90% of total body potassium is located within the cells and the majority of this (60-75%) is within muscles. The remainder of the potassium is in other organs and red blood cells.



Distribution of Potassium

Extracellular potassium varies from 5-10%. Only 1.4% of this is present in the ECF water; the remainder is found principally within bone.

Normal serum potassium ranges from 3.5 – 5.0 mEq/L. Serum values are approximately 0.4 mEq/L greater than plasma determinations. The higher levels in the serum are because of potassium release during clot formation.

Hypokalemia is defined as a state when the potassium concentration is below the normal range i.e. below 3.5 mEq/L.

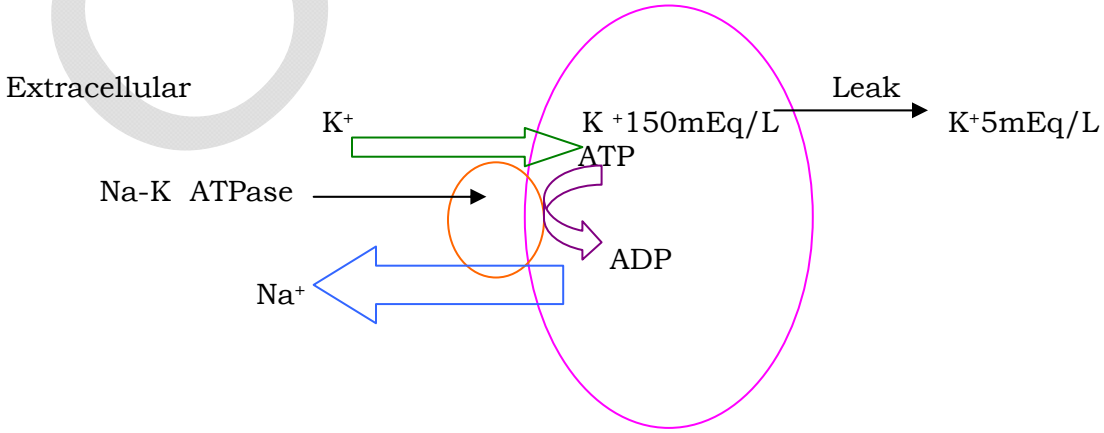
Hyperkalemia occurs when the serum levels are > 5.0 mEq/L.

The normal serum potassium varies between 3.5 - 5.0 mEq/L.

POTASSIUM REGULATION

The regulation of potassium between the cells and the ECF is regulated by the ***sodium potassium pump.*** The activity of the pump is catalyzed by the enzyme ***Na-K ATPase*** (sodium-potassium adenosine triphosphatase). The energy derived from this pump is utilized to transport potassium into the cell against a concentration gradient in exchange for sodium.

This pump is an electrogenic pump i.e. it pumps three sodium ions out of the cell in exchange for two potassium ions into the cell. As a result, the inside of the cell becomes more negative. This reduces the outward movement of potassium through membrane channels.



Potassium Regulation

Factors Affecting Na-K Pump

The activity of the pump is controlled by several factors, among them many hormones. Briefly they are described below:

Insulin

Insulin is secreted by the pancreas and causes an increased uptake of potassium by the cells. Insulin predominantly affects cells in the liver, muscles and adipose tissue. Its action is independent of its effect to increase glucose uptake into the cell.

Beta-Adrenergic Agonists

These agents promote cellular uptake of potassium by the Na-K pump. Beta-blocking agents decrease the potassium uptake.

Alpha-Adrenergics

These agents in contrast to beta-agonists, increase plasma concentration of potassium. This action occurs through hepatic potassium release. They also modify uptake of potassium by muscle cells.

Aldosterone

Apart from the kidneys, aldosterone also acts in the extrarenal tissues such as muscles, liver, adipose tissue, salivary glands, sweat glands and colon. The hormone increases the activity of Na-K pump to increase cellular uptake of potassium. Aldosterone blood levels are regulated by extracellular potassium concentration.

Acid-Base Changes

Acidosis increases the movement of potassium from the cells into ECF and therefore increases serum potassium concentration. Alkalosis has the opposite effect.

Condition	**Change in Plasma K+ (mEq/L) / 0.1 unit pH**
Metabolic acidosis	0.7
Metabolic alkalosis	-0.3
Respiratory acidosis	0.1
Respiratory alkalosis	-0.25

Effect of acid-base changes on plasma potassium

Plasma Osmolarity

An acute increase in plasma osmolarity increases the plasma potassium concentration. Serum potassium increases by about 0.6 mEq/L for each increase of 10 mOsm/kg of osmolality.

Renal Regulation of Potassium

Kidneys play a vital role in maintaining potassium homeostasis. Potassium excretion by the kidneys can vary widely under different physiological conditions.

Potassium is freely filtered at the glomerulus. About 40-50% of the potassium is absorbed by the proximal tubules. Potassium is secreted into the tubules during its passage through the descending limb of the loop of Henle. It is again reabsorbed in the thick ascending limb of the loop. Almost all the potassium is reabsorbed in this segment and only 10% of the filtered potassium enters the distal tubule.

Renal regulation of potassium, therefore, depends on the factors which act on the distal sites of the nephron including distal convoluted tubules, collecting tubules and collecting ducts.

The different factors which affect the distal nephron are briefly described below:

1. ***Plasma Potassium Concentration***

This has a profound effect on renal potassium excretion. High concentrations increase potassium secretion mainly in the distal convoluted tubule and the collecting tubules. Low concentration levels have an opposite effect.

2. ***Aldosterone***

Secreted by the adrenal cortex, high levels of aldosterone increase the secretion of potassium in the collecting ducts in exchange for sodium. Low levels of aldosterone inhibit potassium secretion.

3. ***Glucocorticoids***

These hormones also cause an increase in the secretion of potassium through Na-K pump. This probably is a result of increased flow to the distal parts of the nephron, secondary to an increase in glomerular filtration rate (GFR).

4. ***Sodium Concentration***

The sodium concentration and the amount delivered to the distal nephron also affect the amount of potassium secreted. If more sodium is delivered, then more potassium is secreted as sodium is reabsorbed in exchange for potassium.

5. ***Acid-Base Status***

Acute ***acidosis*** (decrease in the pH) decreases and ***alkalosis*** (increase in the pH) increases potassium secretion by the distal convoluted tubules. As changes in pH also alter other processes that influence potassium secretion, relatively little change in potassium balance is seen with more chronic acid-base disorders.

6. ***Antidiuretic Hormone (ADH)***

This hormone is secreted by the posterior pituitary gland and increases potassium secretion and sodium absorption by the collecting ducts.

DISORDERS OF POTASSIUM BALANCE

Hypokalemia

Hypokalemia is defined as a state when the potassium concentration is below the normal range i.e. below 3.5 mEq/L. The commonest causes of hypokalemia are gastrointestinal losses as occurs in vomiting and diarrhea and increased renal excretion such as occurs during treatment with diuretics. Hypokalemia can occur as a result of depletion of body potassium or due to its redistribution.

Depletion of Body Potassium

Decreased intake

A dietary deficiency of potassium is unlikely, but diets low in fresh fruits and vegetables make it possible. A reduction in potassium intake to less than 10 mEq/day results in a cumulative deficit of 250-300 mEq in 7-10 days.

A relative deficiency of potassium can occur when the potassium demand for new cell formation is high and the intake is not sufficiently high.

Extrarenal losses

Potassium loss can occur through routes other than the kidneys. Most commonly this results from the loss of lower gastrointestinal tract secretions which contain large amounts of potassium. This is depicted in the table below.

Secretion	**Amount (mEq/L)**
Gastric	10
Duodenal	15
Biliary	5
Pancreatic	5
Jejunal	6
Ileal	8
Colonic	90

Average potassium concentration in GI fluids

The different causes which can thus lead to potassium loss are described below:

1. Diarrhea
2. Vomiting
3. Nasogastric suction
4. Purgative abuse
5. Excessive sweating

Renal losses

Many different mechanisms can result in excessive loss of potassium in the urine. This might be a result of ***primary renal damage*** as occurs in renal tubular damage and renal tubular acidosis or it may be due to a ***secondary stimuli*** such as ***Mineralocorticoid (aldosterone)*** excess as occurs in liver failure, nephrotic syndrome and congestive cardiac failure.

Redistribution of Body Potassium

Hypokalemia can occur without a change in cellular potassium stores due to a number of factors which can influence potassium distribution across the cell membranes. These include the following:

1. Acid–base alterations
2. Insulin excess
4. Drugs
    a) Beta-adrenergic agonists such as procaterol and salbutamol.
    b) Theophylline
    c) Calcium channel blockers

Clinical Features

The clinical manifestations of hypokalemia may broadly be categorized into neuromuscular, that may affect the skeletal muscles or the smooth muscles of the GIT, cardiac and endocrinologic.

Patients with hypokalemia complain of Malaise, Muscular weakness, Fatigue, Cramps and myalgia. These complaints become prominent when serum potassium concentrations fall below 3.0 mEq/L. Thus it is important that the patient might be suffering from hypokalemia but the symptoms might not be severe enough to be noticed.

Severe hypokalemia can result in two major neuromuscular complications. These are paralysis and rhabdomyolysis.

Paralysis usually involves the extremities and the legs are more commonly affected than the arms. The musculature of the trunk can also be affected and can lead to life-threatening respiratory muscle paralysis. Severe paralytic complications are seen when the serum potassium levels fall below 2.6 mEq/L.

Severe potassium depletion (below 2.0 mEq/L) can lead to muscle damage and necrosis (muscle death).

Hypokalemia can result in decreased gastrointestinal tract motility. Symptoms can range from simple constipation to complete paralysis of the intestinal tract, known as paralytic ileus. Complete paralysis usually is seen with serum potassium levels below 2.5 mEq/L

The most significant effects of hypokalemia are on the heart. These include arrhythmias, ECG changes and the potentiation of digitalis intoxication.

Hypokalemia can also have other endocrine effects. These include a decrease in serum aldosterone and an increase in plasma renin. It also can lead to glucose intolerance.

Treatment

This depends on the degree of potassium depletion and the urgency of clinical situation. A deficit of about 350 mEq occurs for each mEq/L decrease in serum potassium below a level of 4.0 mEq/L.

Three basic types of potassium salts can be administered. These are potassium chloride, potassium phosphate and potassium bicarbonate or the metabolic precursors of bicarbonate such as gluconate, citrate or acetate.

In patients with metabolic acidosis, potassium bicarbonate or a bicarbonate precursor is preferred. Potassium phosphate is advisable when there is a deficiency of both potassium and phosphate. Potassium chloride should be used in patients with metabolic alkalosis or when the acid-base status is normal.

In general, potassium should be administered orally, unless a situation requires prompt replacement or if oral therapy is not feasible. Oral potassium preparations are available as liquids, enteric coated preparations and as slow-release preparations. Liquids have an unpleasant taste. Enteric coated tablets result in gastrointestinal ulcerations and slow-release preparations also cause asymptomatic lesions in the upper gastrointestinal tract.

Parenteral Potassium Administration

Intravenous potassium may be given in a peripheral vein in concentrations up to 40 mEq/L. Administration via a central vein should be avoided. A concentration up to 60mEq/L may be used in a central vein.

The risks associated with intravenous potassium chloride are well known. It is one of the most commonly implicated agents associated with medication errors leading to fatal incidents. Intravenous potassium chloride can be fatal if given inappropriately.

There have been many reports of critical incidents associated with the preparation and administration of intravenous (IV) potassium chloride indicating that patients are at risk. Patients have actually died in hospitals after being mistakenly injected with potassium chloride instead of normal saline. Thus it is recommended that:

Ampoules of potassium chloride should be removed from the ward stock and replaced with premixed potassium solutions.

Potassium chloride should be prescribed in concentrations available as ready made infusions.

Prescribing should be standardized, and premixed solutions should be encouraged.

The maximum hourly rate and daily limits that a patient may receive, in addition to infusion rates and infusion pump requirements, should be specified.

In non-urgent situations the concentration in intravenous fluids should not exceed 40 mEq/L and the rate of administration should not exceed 10 mEq/hour. In urgent conditions the rate may be increased up to 40 mEq/hour. In this circumstance cardiac monitoring is advisable.

However, regardless of the route or speed of administration, serum potassium levels should be monitored regularly as a guide to effectiveness of therapy.

Simultaneous Administration of Potassium and Dextrose

It is generally believed that intravenous potassium should not be administered along with dextrose. This belief is based on the view that as glucose is taken up by the cells, potassium will also enter the cells, as the transfer of both is mediated by insulin.

The uptake of potassium is regulated by the Na-K pump. Insulin specifically activates a specific isoform of the Na-K-ATPase. It must be remember that the uptake of potassium by insulin is independent of the uptake of glucose by insulin. Both the effects can be disassociated. Thus potassium can be added to any suitable intravenous fluid containing dextrose, saline or both.

Hyperkalemia

This is defined as a plasma potassium concentration more than 5.0 mEq/L. A value between 4.5-5.0 mEq/L falls in the gray zone but is considered as high by most clinicians.

Causes of Hyperkalemia

This usually is a result of increased load, decreased secretion or redistribution of potassium.

Increased load

This may be caused by an increase in exogenous (diet, medications, blood transfusions and intravenous fluids) or endogenous potassium load (injury, hemolysis, hemorrhage, catabolism).

Decreased excretion

This may be due to renal failure, drugs (ACE inhibitors, NSAIDS, potassium sparing diuretics and heparin), or aldosterone deficiency.

Redistribution

This may occur in acidosis, hyperosmolarity, malignant hyperthermia, digitalis intoxication and exercise.

Clinical Features

Hyperkalemia causes abnormalities in membrane polarization of excitable tissues. The most important clinical effect of hyperkalemia is on the heart and causes abnormalities in cardiac conduction, hypotension, bradycardia and asystole.

Hyperkalemia also causes tingling, paresthesias, weakness and flaccid paralysis.

Treatment

This is directed towards counteracting cardiac toxicity, moving potassium into the cells and removing excess potassium from the body.

Calcium antagonizes the effects of hyperkalemia on cardiac conduction and consequently calcium gluconate is administered as 10-30 ml of a 10% solution. Insulin is given along with glucose to drive potassium into the cells.

Cation exchange resins are used to remove potassium from the body.

7 Calcium

Calcium is one of the body's most abundant ions. Its homeostasis is especially important and complex. The calcium concentration in the blood does not reflect the calcium status.

INTAKE

The average dietary intake of calcium varies widely. However the recommended daily intake for adult men and non-pregnant adult women is 800 mg. For adolescents and pregnant and lactating women it is 1200 mg.

Dietary Sources

The main dietary sources of calcium are milk and milk products. Calcium is also found in various dark-green leafy vegetables, but the presence of certain binders such as oxalic acid in them, reduces the bioavailability of calcium.

FUNCTIONS OF CALCIUM

Calcium is important for regulating the neuromuscular transmission processes and also regulates many enzymes. It also plays a vital role in clotting of the blood.

BODY CALCIUM AND ITS DISTRIBUTION

Body of a normal 70 kg. adult contains about 1200 grams (1-2 kg) of calcium. 99% of the total calcium is present within the bones and teeth. Less than 1% is present in the ECF and is found in the ionized, bound and complexed forms.

The most important form of calcium is the ionized form and almost 45% of plasma calcium is present in this form. The bound form is about 40% (mostly bound to albumin) and the remainder (15%) is in the form of complexes with sulfate, phosphate and bicarbonate.

Calcium Concentrations

The normal plasma calcium is 8.8-10.4 mg/dl (2.2-2.6 mmol/L). However, only the free, unbound, ionized calcium is active physiologically. In males, 20 years and above, and in females 18 years

and above this value is 4.75-5.3 mg/dl, while in younger age it is 4.9-5.5 mg/dl (The average value as a whole is 4.8 mg/dl or 1.2 mmol/L).

Proteins and pH levels affect the ratio of ionized to total calcium. A decrease in pH increases the ionized calcium, while alkalosis exerts an opposite effect. There is an increase of 2 mg/dl calcium for every 0.1 unit decrease in pH and vice versa.

A change of 1 gram/dl in albumin concentration is associated with a 0.8 mg/dl change in total calcium, while a change of 1 gram/dl in globulin concentration is associated with a 0.16 mg/dl change in total calcium concentration.

CALCIUM REGULATION

Calcium concentration is controlled by three mechanisms:

1. Serum calcium levels are increased by parathyroid hormone, secreted by the chief cells of the parathyroid glands.

2. The levels are decreased by calcitonin, a substance synthesized in the thyroid gland.

3. The absorption of calcium from the gastrointestinal tract is increased by vitamin D. Increased levels of vitamin D increase the serum levels of calcium and vice versa.

DISORDERS OF CALCIUM BALANCE

Hypercalcemia

The common causes of hypercalcemia are:

1. Endocrine disorders
    - (i) primary hyperparathyroidism
    - (ii) thyrotoxicosis
    - (iii) adrenal insufficiency

2. Ingestion of
    - (i) excessive vitamin D
    - (ii) excessive calcium (as in calcium preparations)

3. Malignancy
4. Drugs e.g. thiazides
5. Granulomatous diseases e.g. sarcoidosis
6. Miscellaneous
    (i) immobilization
    (ii) hypophosphatemia

Symptomatology

Symptoms of hypercalcemia do not occur unless the serum calcium concentration is more than 11 mg/dl. Most common symptoms are nausea, vomiting, constipation, lethargy, drowsiness, irritability and depression. Renal calculi may also occur. Occasionally peptic ulceration occurs. Severe cases are associated with renal failure as a result of volume depletion and nephrocalcinosis.

Hypercalcemia should always be considered in the setting of renal failure, nephrolithiasis, psychiatric disturbances and pancreatitis.

Severe hypercalcemia (> 15 mg/dl) is a medical emergency.

Management

This should be directed towards the underlying cause. However efforts should also be made to lower the serum levels of calcium. Mild cases only require a diet that is adequate in sodium (200 mEq/day) and plenty of oral fluids (2-3 liters/day). Cases in which serum calcium is more than 12 mg/dl should be treated promptly. Many patients are dehydrated due to vomiting and the resulting decrease in glomerular filtration rate causes a decrease in calcium excretion.

Simple hydration is often sufficient to lower the serum calcium levels. Rehydration therapy in this condition is given in detail in the section on Fluid Therapy in Special Situations.

Hypocalcemia

The common causes of hypocalcemia include the following:

1. Renal failure
2. Decreased intake of vitamin D
3. Hypoparathyroidism
4. Malignancy

Symptomatology

Neuromuscular irritability occurs causing paresthesiae, circumoral numbness, cramps and anxiety which may lead to tetany. Generalized seizures can follow. Dry skin and brittle nails may be evident. Electrocardiogram reveals a prolonged QT interval.

Management

In severe cases (seizures or tetany) 10% calcium gluconate should be administered intravenously over 5-10 minutes. Oral calcium should also be started. A total of 5 grams of elemental calcium should be given over 24 hours. Further management is outlined in the section on Fluid Therapy in Special Situations.

8

Magnesium

Magnesium is the second most abundant intracellular cation and the fourth most abundant cation of the body after calcium, potassium and sodium. It is the second most abundant cation present in the intracellular fluid.

INTAKE AND SOURCES

Magnesium is part of the chlorophyll molecule and so green leafy vegetables are rich sources of magnesium. Nuts, legumes, whole grains, meats and sea food are other major sources of magnesium. The recommended daily requirement is 300-350 mg. and the average intake is about 150-350 mg/day. Therefore, magnesium deficiency may occur rather easily. Ingestion of ***hard water*** can significantly contribute to magnesium intake.

FUNCTIONS OF MAGNESIUM

Magnesium is an important cofactor for many enzymatic reactions and biologic processes and is necessary for energy metabolism. The release of energy as ATP is magnesium-dependant. Therefore magnesium is essential for glucose metabolism, for the synthesis of proteins, fats and nucleic acids and for membrane transport processes. It is important for mineralization of bone, muscular relaxation, neurotransmission and also controls secretion of parathyroid hormone.

Magnesium also serves structural functions such as maintaining fluidity and stability of phospholipid bilayers, protein tertiary or quaternary structures and DNA double helices. Magnesium is said to be the key factor in regulating the different steps of cell proliferation

Magnesium enters into the cells via an electrochemical gradient due to the relative electronegativity of the interior of the cell. As a result magnesium is actively transported out of the cell to maintain normal intracellular concentrations.

BODY MAGNESIUM AND ITS DISTRIBUTION

The total magnesium content of the body is 2000 mEq. Less than 1% of this is present in extracellular fluid and 60-65% in found in bones and serves as a reservoir for maintaining a normal serum concentration of

magnesium. Most of the rest (about 20%) is in the muscles and soft tissues.

The normal serum magnesium concentration is 1.5-1.9 mEq/L. However, this is a poor reflection of total body magnesium content. The intracellular concentrations are 5-20 mmol/L. Most of it is bound to proteins and negatively charged molecules.

MAGNESIUM REGULATION

Magnesium levels are mainly controlled by gastrointestinal absorption and excretion. It is absorbed along the entire gastrointestinal tract, but maximal absorption occurs in the ileum and distal jejunum. The absorption is inversely proportional to the amount ingested and normally only 1/3 of the dietary magnesium is absorbed.

However, kidneys play a major role in magnesium homeostasis. Approximately 2 g of Mg^{+2} is filtered daily by the human kidney and almost 100 mg appears in the urine. Thus, approximately 95% of the filtered Mg^{+2} is reabsorbed (about 10%-15% in the proximal tubule and 70% in the ascending thick limb of Loop of Henle) and 5% is excreted in the urine (less than 1 mEq/day).

The excretion of magnesium through kidneys is affected by a number of factors including sodium and calcium excretion, parathyroid hormone and extracellular fluid volume. The excretion is decreased when sodium and calcium excretion is decreased, with decreased ECF volume and with increased levels of parathyroid hormone.

DISORDERS OF MAGNESIUM BALANCE

Hypomagnesemia

This condition occurs when serum magnesium levels are less than 1.5 mEq/L. Hypomagnesemia is seen in almost 12% of hospitalized patients. And in about 60% patients in ICU. The common causes include:

1. Excessive gastrointestinal losses e.g. severe diarrhea and fistulas, intestinal malabsorption and intestinal bypass surgery.
2. Insufficient intake (protein-calorie malnutrition).
3. Increased urinary excretion e.g. diuretics, hypercalcemia.
4. Alcoholism.

5. Increased catecholamine levels such as that occurring in stress and acute illness.
6. Acute pancreatitis can also be associated with hypomagnesemia.
7. Hypomagnesemia is also common in patients with diabetes and seems to be the result of renal Mg^{+2} wasting.

However it should be remembered that the correlation between serum concentration and intracellular levels is poor. The serum levels do not necessarily reflect the total body stores.

Clinical Features

The symptomatology depends upon the rate of development and the total deficit, rather than the serum concentration. Low levels of serum magnesium lead to impaired secretion of parathyroid hormone and hypocalcemia.

The deficiency of magnesium can cause neuromuscular hyperexcitability, tetany, carpopedal spasm, muscle cramps and fasciculations, vertigo, ataxia, nystagmus, aphasia, tremors, weakness, hemiparesis, depression, delirium, cardiac arrhythmias, hypocalcemia and hypokalemia that is usually resistant to treatment until magnesium is replaced.

Management

Mild cases can be managed by the administration of oral magnesium salts in the form of chloride, lactate and gluconate. The initial daily dose of 300-600 mg. of elemental magnesium is recommended. However it must be remembered that magnesium salts act as laxatives and may cause diarrhea. To minimize this effect, the total dose may be administered in 3-4 divided doses.

In cases of severe (<1 mEq/L in the serum) and symptomatic hypomagnesemia (neuromuscular or neurologic manifestations or cardiac arrhythmias) Mg^{+2} should be replaced by intravenous administration of 2 g of Mg^{+2} sulfate in 100 ml of 5% dextrose water (Pladex-5) over 5 to 10 min and followed by a continuous infusion of 4 to 6 g/d for 3 to 5 days if renal function is relatively normal.

Hypermagnesemia

This condition occurs when serum magnesium levels are greater than 2.5 mEq/L. The most common causes are excessive intake and acute and chronic renal failure. It is also seen in severe trauma, burns and endocrine disorders such as adrenal insufficiency. Severe acidosis can also result in hypermagnesemia.

Clinical Features

Most often the condition is asymptomatic. When the serum levels rise more than 4 mEq/L, the symptomatology becomes evident and is manifested as depression of neuromuscular activity such as decreased deep tendon reflexes. It also causes a decrease in blood pressure and prolongation of PR interval and QRS duration. Complete heart block and cardiac arrest may occur. Elevated magnesium concentration also leads to hypocalcemia, nausea and vomiting.

Management

The most important aspect of management is to review the condition of the patient and discontinue any magnesium preparations (such as antacids), particularly if the patient has an impaired renal function. Excessive magnesium is excreted by the kidneys.

Severe cases can be treated by intravenous calcium. Calcium antagonizes the toxic effects of magnesium. Usually 100-200 mg. of elemental calcium is administered over 5-10 minutes. Simultaneously any existing acidosis should be corrected. In patients with renal failure, hemodialysis can effectively control magnesium.

9

Phosphorus

Phosphorus is the second most abundant mineral and the fourth most abundant element in the body. As with potassium, most of the phosphorus is within the cells.

INTAKE AND SOURCES

Milk, milk products, meat and fish are high sources of phosphorus, although vegetables and fruits also provide some phosphorus. It is an important constituent of all body tissues and a structural component of bones and teeth.

FUNCTIONS OF PHOSPHORUS

Phosphorus plays a vital role in cell metabolism and energy transfer. Many organic compounds contain high amounts of phosphorus. These include nucleic acids, high-energy compounds, co-enzymes and many others. It facilitates nerve and muscle function and plays a role in acid-base homeostasis.

BODY PHOSPHORUS AND ITS DISTRIBUTION

Normal plasma concentration of phosphates differ according to age and sex. However in adults it ranges from 2.7-4.7 mg/dl, while in children it is 3.7-5.9 mg/dl. Highest values are observed in infants (3.7-8.5 mg/dl).

Though phosphorus is present in the plasma as free or protein-bound phosphate, the laboratory measurements are often reported as elemental phosphorus. The phosphorus values in mg/dl should be multiplied by 0.32 to get the phosphate values in millimoles. Inorganic phosphate in the plasma exists as the univalent ($H_2PO_4^-$) and divalent (HPO_4^{--}) forms. As the valency of phosphate is variable, therefore milliequivalents should not be used.

PHOSPHATE REGULATION

The phosphates contained in the diet are hydrolyzed in the gastrointestinal tract to form inorganic phosphate. The amount of phosphate absorbed from the GIT is about 65%-70% of the amount ingested. The absorption is increased by vitamin-D metabolites. The

kidneys play a vital role in regulating phosphate concentrations. The mechanism consists of filtration and reabsorption. This reabsorption occurs normally in the proximal convoluted tubule only.

The normal excretion of phosphate is affected by many hormones and varies under different conditions. These are summarized in the table below:

Factor	Renal Effects
Increased intake	Decreases reabsorption
Increased parathyroid hormone	Increases excretion
Increased thyroid hormone	Increases reabsorption
Increased insulin	Increases reabsorption
Vitamin-D	Increases reabsorption
Glucocorticoids	Increases excretion
Metabolic acidosis	Increases excretion
Respiratory alkalosis	Decreases excretion
Increased ECF volume	Decreases reabsorption

Factors Affecting Renal Excretion of Phosphate

DISORDERS OF PHOSPHATE BALANCE

Hypophosphatemia

This condition occurs when the serum values are less than 2.5 mg/dl. This may occur due to a redistribution or depletion of phosphate. Redistribution is seen as a result of shift from the ECF to ICF such as in respiratory alkalosis or increased carbohydrate intake. This is usually mild if the total phosphate stores are within the normal range, but can have profound effects if the stores are already depleted.

Phosphate depletion is most often encountered in uncontrolled diabetes, malnutrition with hyperalimentation, alcoholism, use of phosphate binding-antacids and renal phosphate wasting.

Clinical Features

Clinical manifestations include rhabdomyolysis, hemolytic anemia, impaired chemotaxis, platelet dysfunction, metabolic acidosis, cardiac failure, osteomalacia and seizures. Coma may also occur.

Management

The management can be considered under mild (1.8-2.5 mg/dl), moderate (1.0-1.8mg/dl) and severe (< 1.0mg/dl) hypophosphatemia.

Mild cases require no specific treatment and a search for specific cause should be instituted. Moderate cases can be treated with oral supplements of phosphate along with correction of any underlying cause (such as diabetes, discontinuation of antacids, etc.). Milk is a good source of phosphate and provides 0.9-1.0 mg. phosphate/ml.

Serum phosphate levels can increase by 1.5 mg/dl after ingestion of 1 gram of elemental phosphate within 1-2 hours.

In severe cases phosphate 0.16 mmol/kg. IV should be administered to asymptomatic cases and 0.24 mmol/kg. to symptomatic cases. The serum levels of phosphate should be monitored regularly.

Hyperphosphatemia

This is defined as a plasma concentration of more than 5.0 mg/dl. The most common cause is renal failure. It also occurs as a result of cell destruction such as in hypercatabolism, rhabdomyolysis, hemolysis and administration of cytotoxic agents. It is also seen in states such as respiratory acidosis, lactic acidosis and diabetic ketoacidosis where redistribution into ECF occurs.

Clinical Features

The condition is usually asymptomatic but can result in hypocalcemia. This in turn causes an increase in calcium absorption from the intestines and mobilization from the bones. If severe, this can lead to hypotension, seizures, tetany and even death.

Management

This includes dietary restriction of phosphate along with the use of agents which limit the absorption of phosphate from the gastrointestinal tract such as aluminium, magnesium or calcium salts. Non-citrate calcium compounds e.g. calcium acetate are preferable, which should be administered immediately before or after the meals. However, if given during fasting, it can lead to increased calcium absorption.

The usual dosage is 500-1500 mg. three times a day. Hemodialysis is required in patients with high serum levels (10-12 mg/dl).

10

Acid Base Balance

Regulation of hydrogen ion concentration is similar in many ways to the regulation of other ions in the body such as sodium and potassium. There is a balance between the intake / production of hydrogen ions and the net removal of hydrogen ions from the body. As in the case of other ions, the kidneys play a major role in this homeostasis. However, other buffering mechanisms (blood, lungs) also exist to achieve this balance.

The control of hydrogen ion concentration is important because the activities of almost all enzyme systems in the body are influenced by the hydrogen ion concentration. Therefore, changes in its concentration can alter body functions.

ACIDS AND BASES

A hydrogen ion is a single free proton released from a hydrogen atom. ***Acids*** are those substances which can release hydrogen ions in solution e.g. hydrochloric acid (HCl) in water dissociates into hydrogen (H^+) and chloride (Cl^-) ions. Similarly carbonic acid (H_2CO_3) ionizes in water to form H^+ and bicarbonate ions (HCO_{3^-}).

Base is an ion or a molecule that can accept a hydrogen ion e.g. bicarbonate ion (HCO_{3^-}) is a base because it can combine with a H^+ to form carbonic acid.

Alkalosis and Acidosis

The term ***Alkali*** is often used in place of base. However an alkali is a molecule formed by a combination of one or more of alkaline metals (such as sodium or potassium) with a highly basic ion such as a hydroxyl ion (OH^-). The basic part of the molecule reacts quickly with hydrogen ion to remove them from solution. Thus alkalis are typical bases. Therefore, ***alkalosis*** means excess removal of hydrogen ions from the body.

Conversely excess addition of hydrogen ions to the body fluids is known as ***acidosis.***

pH

The hydrogen ion concentration of body fluids is normally kept at a very low level of 0.00004 mEq/L (40 nEq/L). Under normal conditions it varies only about 3.5 nEq/L but under extreme conditions it may fluctuate enormously causing death.

As the hydrogen ion concentration is very low, it is usually expressed on a logarithm scale using pH units. pH is related to hydrogen ion concentration (Eq/L) by the following formula:

$pH = \log 1/H^+ = - \log [H^+]$

pH = 7.4

Thus it can be seen that pH is inversely related to the hydrogen ion concentration. Therefore, a ***low pH (Acidosis)*** corresponds to a high hydrogen ion concentration while a ***high pH (Alkalosis)*** corresponds to a low hydrogen ion concentration.

REGULATORY PROCESSES

There are three main systems which regulate the hydrogen ion concentration in the body fluids to prevent excessive variations i.e. acidosis or alkalosis. These are:

1. Chemical buffer systems
2. Respiratory regulation
3. Renal mechanisms.

Chemical Buffer Systems

A buffer is a substance (which prevents a change or a system that tends to maintain constancy) which can reversibly bind with hydrogen ions.

$$\text{Buffer} + H^+ \rightleftharpoons \text{H buffer}$$

This is a reversible reaction. Therefore H^+ combine with the buffer to form a weak acid (H buffer). This acid can remain undissociated or can dissociate to form H^+ and buffer. Whenever the H^+ ion increases, the reaction is displaced towards right and they bind with the buffer. On the other hand when H^+ ion concentration decreases this reaction shifts towards left and the H^+ are released. Thus changes in H^+ concentration are minimal.

There are many clinical buffer systems in the body. These include the bicarbonate buffer system, phosphate buffer system and the protein (hemoglobin) in the blood. These buffer systems are the first line of defense against changes in acid - base balance. In the ECF the most important is the bicarbonate buffer system.

Bicarbonate Buffer System

This system consist of carbonic acid (H_2CO_3) which is a weak acid and bicarbonate salt (sodium bicarbonate : $NaHCO_3$)

During metabolism carbon dioxide (CO_2) is being continuously formed. This combines with water to form carbonic acid in the presence of an enzyme ***carbonic anhydrase***.

Carbonic acid dissociates weakly to form small amounts of H^+ and HCO_3^-

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$NaHCO_3$ occurs in the ECF. It dissociates completely to form sodium ions and bicarbonate ions.

$$NaHCO_3 \rightleftharpoons Na^+ + HCO_3^-$$

When a strong acid such as HCl is added to this system, the increased hydrogen ions released from the acid ($HCl \longrightarrow H^+ + Cl^-$) are buffered by HCO_3^- .

$$\uparrow H^+ + HCO_3^- \longrightarrow H_2CO_3^- \longrightarrow CO_2 + H_2O$$

As a result carbonic acid is formed which dissociates into CO_2 and water. The carbon dioxide in turn stimulates respiration and is exhaled through the lungs.

Similarly when a strong base such as sodium hydroxide (NaOH) is added to this system, the strong base (NaOH) is replaced with a weak base $NaHCO_3$.

$$NaOH + H_2CO_3 \rightarrow NaHCO_3 + H_2O$$

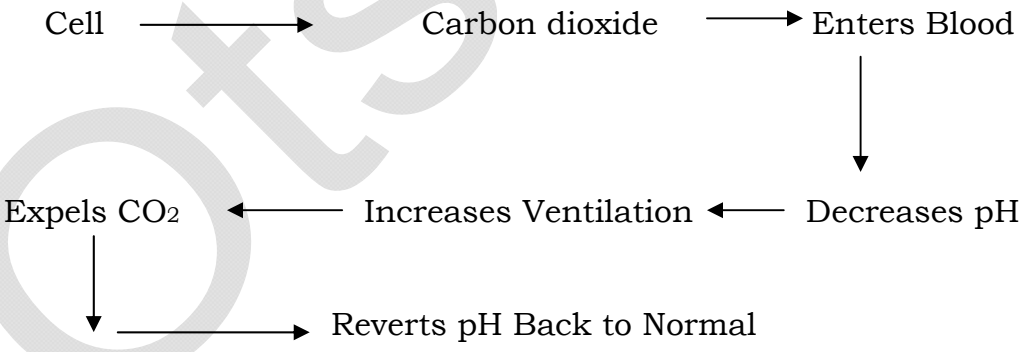
Here the hydroxyl ion (OH^-) combines with carbonic acid to form additional bicarbonate. At the same time the concentration of H_2CO_3 also decreases causing more CO_2 to combine with water.

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow \uparrow HCO_3^- + H^+$$
$$\quad\quad\quad\quad\quad\quad\quad\quad + \quad\quad\quad\quad +$$
$$\quad\quad\quad\quad\quad\quad\quad\quad NaOH \quad\quad\quad\quad Na^+$$

The net result is a decrease in CO_2 in the blood. This tends to inhibit respiration, decreasing its elimination through the lungs and returning its concentration in the blood.

Respiratory Regulation

The respiratory system controls the acid base disturbances by controlling the CO_2 concentration through the lungs. CO_2 is continuously formed as a result of metabolism in the cells. From the cells it passes into the blood. As a result, increase in the concentration of CO_2 and pCO_2 (partial pressure of carbon dioxide) occurs in the ECF which decreases the pH of blood. This blood is transported to the lungs where it goes into the alveoli and is transported into the atmosphere. This in turn decreases the CO_2 concentration in the blood i.e. the hydrogen ion concentration (pH) reverts back to its previous normal level.



The respiratory system can thus control the pH through respiratory rate (ventilation). An increase in this eliminates CO_2 from ECF which reduces the hydrogen ion concentration. Conversely decreased rate increases the CO_2 , thus increasing the hydrogen ion concentration in the ECF.

Renal Mechanisms

The kidneys are the most powerful acid base regulatory system and exert their effect by excreting an acidic or a basic urine. An acidic urine decreases the amount of acid in the ECF while a basic urine decrease the amount of base in the ECF.

Normally a large amount (4320 mEq/day) of bicarbonate ions are filtered continuously into the renal tubules through the glomerulus. If all this were to be excreted it would result in a massive loss of base from the ECF.

Simultaneously the body also secretes large amounts of hydrogen ions (acid) into the tubular fluid. These acids are non-volatile acids derived from the metabolism of proteins. These acids are nonvolatile because they are not H_2CO_3 and therefore can not be removed by the lungs. The kidneys are responsible for excretion of these acids.

The reabsorption of the bicarbonate and the secretion (excretion) of hydrogen ions are both achieved through secretion of hydrogen ions by the kidney tubules.

When there is a reduction in the ECF hydrogen ion concentration (alkalosis), the kidneys fail to reabsorb all the filtered bicarbonate, thus increasing its excretion. The bicarbonate ions are therefore not available to buffer the hydrogen ions. As a result the ECF hydrogen ion concentration increases.

In acidosis the kidneys reabsorb all the bicarbonate which is added back to the ECF. This reduces the ECF hydrogen ion concentration towards normal.

11 Acid Base Disorders

A change in the arterial blood pH may occur due to an abnormality in the plasma bicarbonate concentration or in PCO_2 (partial pressure/concentration of CO_2) or both. When the disturbance is primarily due to bicarbonate concentration (due to addition or loss of non-volatile acid or alkali to or from ECF) the resulting disorder is termed ***metabolic***. A low pH due to decreased bicarbonate concentration is known as ***metabolic acidosis*** whereas a high pH with increased bicarbonate concentration is called ***metabolic alkalosis***.

However, when the main disturbance is that of carbon dioxide which denotes a primary increase or decrease in respiration, the resulting disorder is termed ***respiratory.*** A low pH due to increased CO_2 is known as ***respiratory acidosis*** and a high pH due to reduced CO_2 is called ***respiratory alkalosis***.

These disorders are summarized in the following table:

Acid-Base Disorder	[H^+]	pH	Primary Disturbance
Respiratory Acidosis	Increased	Decreased	Increased pCO_2
Metabolic Acidosis	Increased	Decreased	Decreased [HCO_3^-]
Respiratory Alkalosis	Decreased	Increased	Decreased pCO_2
Metabolic Alkalosis	Decreased	Increased	Increased [HCO_3^-]

METABOLIC ACIDOSIS

Metabolic acidosis can result from many causes. These include:

1. Formation of excess quantities of metabolic acids
2. Ingestion or infusion of excess acids
3. Failure of kidneys to excrete acids normally formed
4. Loss of base from the body

There are two types of metabolic acidosis. Both are characterized by a decrease in the [HCO_3^-] but they differ in how that decrease occurs. Secretional metabolic acidosis is caused by a direct loss of bicarbonate-rich fluid such as diarrhea. Titrational metabolic acidosis is caused by the presence of non-CO_2 acids that titrates bicarbonate causing a decreased [HCO_3^-].

Secretional and titrational metabolic acidosis can be differentiated by their effects on the anion gap (AG).

Anion Gap (AG):

The anion gap is a calculated value based on the principle of electroneutrality which states that the total anions in the body must always be equal to the total cations. We regularly measure the most significant ions: Na^+, K^+, Cl^- and HCO_3^-. The ions we do not regularly measure are referred to as unmeasured ions. There are unmeasured cations (Ca^{+2}, Mg^{+2}, and gammaglobulins) and unmeasured anions (albumin, phosphates, sulfates, and organic acids). The unmeasured anions outnumber the unmeasured cations and the difference is the anion gap. The anion gap is easily calculated from the ions we do measure:

$$AG = (Na^+ + K^+) - (Cl^- + HCO_3^-).$$

Unmeasured cations do not undergo significant changes in health or disease and so changes in the anion gap are almost always associated with changes in the unmeasured anions.

Effect On Anion Gap In Metabolic Acidosis:

With secretion-type metabolic acidosis, the anion gap is normal. The body compensates for the increased loss of bicarbonate by a retaining Cl-. As such, as the $[HCO_3^-]$ decreases, the $[Cl^-]$ increases and the anion gap remains normal.

It is important to note here that during hemodynamic emergencies (e.g. sepsis, burns, or trauma) great volume is administered intravenously. When the given solution is devoid of buffer (e.g. HCO3-), such as normal saline, the existing HCO3- in the ECF is diluted & results in metabolic acidosis.

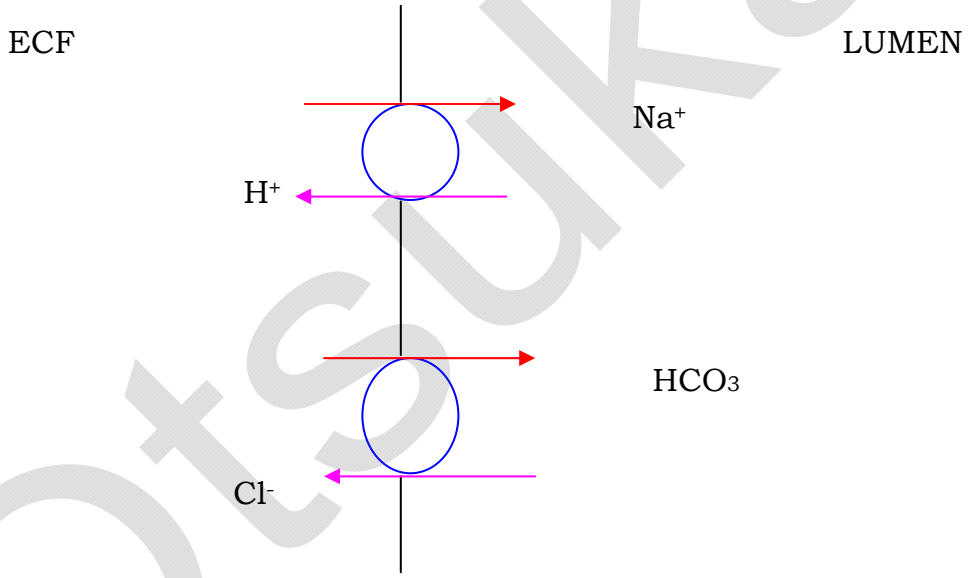
With titrational metabolic acidosis, the anion gap is increased. Remember that titration type metabolic acidosis is associated with increased levels of exogenous or endogenous acids. Since HCO_3^- is consumed to buffer these organic acids and there is no effect on the [Cl-], the anion gap increases. The anion gap is therefore very useful in determining a possible etiology for metabolic acidosis that can be confirmed based on history and clinical signs.

Clinically, loss of base and excess formation of acid are most commonly encountered. These are discussed below:

Diarrhea

Severe diarrhea is probably the most common cause of metabolic acidosis. Normally, the small intestine neutralizes the acidic contents of the stomach (due to the presence of hydrochloric acid (HCl)). Sodium bicarbonate is added to the contents of the intestinal lumen and HCl is simultaneously added to the ECF by means of Na^+/ H^+ and Cl^- / HCO_3^- exchange transport system.

However during secretory diarrhea, there is excessive transport resulting in addition of a large amount of sodium bicarbonate to the diarrhea fluid. Simultaneously an equal amount of hydrochloric acid is added to the ECF, thus causing acidosis along with hyperchloremia.



Exchange Transport System

The electrolyte and volume loss in diarrhea causes ECF depletion. This stimulates the release of renin from the kidneys (JG apparatus) and aldosterone from the adrenal glands. Potassium is lost in the diarrheal fluid as well as in the urine due to an increase in aldosterone levels.

The kidneys attempt to correct the situation and lead to a net acid excretion in the urine. There is also a negative urinary anion gap.

Vomiting

Vomiting/suction of only the stomach contents would lead to alkalosis. However, vomiting/suction of large amounts of contents from deep in the GIT would cause loss of bicarbonate and result in metabolic acidosis as occurs in diarrhea.

Diabetes Mellitus

In this condition the normal use of glucose by the tissues is inhibited. Therefore, the fats are split into acetoacetic acid (a ketone body) which is then metabolized for providing energy. In uncontrolled diabetes the levels of this acid become very high causing metabolic acidosis.

Hyperalimentation

Rapid administration of large quantities of acids may lead to metabolic acidosis as may occur during hyperalimentation. This is due to the fact that some amino acids are metabolized to acids within the body.

Renal Failure

In chronic renal failure the kidneys are unable to reabsorb the bicarbonate and therefore result in metabolic acidosis.

METABOLIC ALKALOSIS

An arterial pH more than 7.45 (normal 7.4) and serum bicarbonate concentration greater than 26 mEq/L (normal 24 mEq/L) indicates metabolic alkalosis. This condition occurs due to :

- Excess retention of bicarbonate ion
- Loss of hydrogen ions from the body

This disorder is not as common as metabolic acidosis. However, the important causes are discussed below:

Vomiting /Nasogastric Suction

Hydrochloric acid (HCl) is normally secreted by the parietal cells of the gastric glands present in the stomach. During the formation of HCl carbonic acid ($H_2CO_3^-$) is split to form H^+ and HCO_3^-. The hydrogen ions enter the gastric lumen while HCO_3 enters the blood stream.

During vomiting or nasogastric aspiration, chloride is lost along with hydrogen ion (i.e. HCl is lost) while there is a rise in plasma bicarbonate giving rise to metabolic alkalosis.

The loss of chloride ion leads to ECF depletion. As a result there is secretion of aldosterone that causes potassium secretion in the renal tubules leading to hypokalemia. The kidneys try to conserve chloride, and its excretion rapidly falls to negligible levels.

Thus metabolic alkalosis is accompanied by ECF depletion as well as hypokalemia, both of which should also be managed adequately.

Other Causes

Administration of diuretics can also lead to metabolic alkalosis. It can also be caused by increased secretion of aldosterone and exogenous bicarbonate administration.

Treatment

The best treatment is to correct the abnormality causing the disorder. However, various agents can be used to neutralize excess acid or base in the ECF.

Sodium bicarbonate can be used in cases of metabolic acidosis. But as it has dangerous physiological effects, other substances are preferred instead. Sodium salts of lactate **(Ringolact, Ringolact-D**), acetate **(Plabolyte-M)** or gluconate are therefore preferred. The lactate and acetate portions are metabolized in the body, thus leaving the sodium in the ECF in the form of sodium bicarbonate. This increases the pH of the fluids towards normal.

The common form of metabolic alkalosis caused by vomiting or nasogastric suction or due to diuretics is responsive to the administration of electrolyte solutions containing sodium and chloride such as Normal Saline **(Plasaline)**. However as hypokalemia is also a feature of these disorders, potassium should also be adequately replaced **(Ringer's Solution).**

RESPIRATORY ACIDOSIS AND ALKALOSIS

Respiratory acidosis occurs whenever there is a decreased rate of pulmonary ventilation (respiration) which increases the concentration of carbon dioxide in ECF. This occurs when there is a damage to the respiratory center in the medulla oblongata, during obstruction of respiratory passageways, pneumonia and certain neuromuscular defects.

Respiratory alkalosis is caused by overventilation by the lungs. This is commonly seen in psychoneurotic conditions. It is also seen in severe anemia and high altitude which causes hypoxia.

12 Fluid Therapy in Special Situations

DIARRHEA AND DEHYDRATION

Diarrhea is the passage of unusually loose or watery stools, usually at least three times in a 24 hour period. There is an increased loss of water and electrolytes during diarrhea causing dehydration. Concomitant vomiting may worsen the dehydration. The amount of fluid and electrolytes lost, as well as the consistency of stools vary considerably. The stools are softer and more frequent in breastfed children than those who are bottle-fed.

The degree of dehydration depends on the amount of fluid lost and is reflected in the signs and symptoms. It is important to recognize dehydration and assess its severity for proper management. The classification of dehydration according to the World Health Organization is as follows:

No Dehydration	Some Dehydration	Severe Dehydration
Not enough signs to classify as some or Severe dehydration	Two or more of the following signs: ▪ Restlessness ▪ irritability ▪ sunken eyes ▪ drinks eagerly, thirsty ▪ skin pinch goes back slowly	Two or more of the following signs: ▪ lethargy/unconsciousness ▪ sunken eyes ▪ unable to drink or drinks poorly ▪ skin pinch goes back very slowly (≥2 seconds)

Another simple approach has been advocated by the National Institute for Health and Clinical Excellence (NICE). This scheme identifies several "Red Flags" that signify worsening clinical condition of the patient. This classification also acts as a guide to fluid management of the patient according to the clinical condition. The following table outlines this classification:

Increasing Severity of Dehydration →			
	No Clinically Detectable Dehydration	Clinical Dehydration	Clinical Shock
Symptoms	Appears well	Appears to be unwell or deteriorating	---
	Alert and responsive	Altered responsiveness	Decreased level of consciousness
	Normal urine output	Decreased urine output	----
	Skin color unchanged	Skin color unchanged	Pale or mottled skin
	Warm extremities	Warm extremities	Cold extremities
Signs	Alert and responsive	Altered responsiveness	Decreased level of consciousness
	Skin color unchanged	Skin color unchanged	Pale or mottled skin
	Warm extremities	Warm extremities	Cold extremities
	Eyes not sunken	Sunken eyes	---
	Moist mucous membranes (except after a drink)	Dry mucous membranes (except for 'mouth breather')	---
	Normal heart rate	Tachycardia	Tachycardia
	Normal breathing pattern	Tachypnoea	Tachypnoea
	Normal peripheral pulses	Normal peripheral pulses	Weak peripheral pulses
	Normal capillary refill time	Normal capillary refill time	Prolonged capillary refill time
	Normal skin turgor	Reduced skin turgor	----
	Normal blood pressure	Normal blood pressure	Hypotension (decmpensated shock)

Advances in ORT

Acute diarrhea is a leading cause of child morbidity and mortality despite the increasing awareness and use of Oral Rehydration Therapy (ORT) since its advent in 1978 by World Health Organization (WHO) and United Nations Children Fund (UNICEF). Both these organizations recommended the use of Oral Rehydration Solution (ORS) that provided 90 mEq/L of sodium with a total osmolarity of 311 mOsm/L.

Numerous studies were undertaken during the last three decades to improve the composition of ORS. Based on these studies, WHO now recommends using the new improved ORS for treating children with acute non-cholera diarrhea. This new ORS has a low osmolarity of 245 mOsm/L with a sodium concentration of 75 mEq/L and glucose 75mmol/L. The composition of this new ORS is as follows:

Component	Grams/L	Component	Mmol/L
Sodium chloride	2.6	Sodium	75
Glucose, anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Potassium	20
Trisodium citrate dehydrate	2.9	Citrate	10
		Glucose, anhydrous	75
		Total Osmolarity	245

The New Low Osmolar ORS

However, WHO also have other criteria for an acceptable ORS formulation:

- The total substance concentration (including that contributed by glucose) should be within the range of 200–310 mmol/l
- The individual substance concentration:
  - Glucose — Should at least equal that of sodium but should not exceed 111 mmol/l
  - Sodium — Should be within the range of 60-90 mEq/l
  - Potassium — Should be within the range of 15-25 mEq/l
  - Citrate — Should be within the range of 8-12 mmol/l
  - Chloride — Should be within the range of 50-80 mEq/l

In mild to moderate cases, oral rehydration therapy will suffice to correct the fluid and electrolyte abnormalities. The following table provides guidelines (from World Health Organization) as an approximate guide for provision of ORS in adults and children with some dehydration.

Approximate Amount of ORS to be Given in First 4 Hours						
Age	Less than 4 months	4-11 months	12-23 months	2-4 years	5-14 years	15 years or older
Weight	Less than 5 kg	5-7.9 kg	8-10.9 kg	11-15.9 kg	16-29.9 kg	30 kg or more
In mL	200-400	400-600	600-800	800-1200	1200-2200	2200-4000

Guidelines for Managing Dehydration in Children and Adults with Some Dehydration

Following points are of importance:

- Mothers should be encouraged to continue breastfeeding
- Give more ORS, if the patient desires.
- An additional 100-200 mL clean water should be administered if the old (containing 90 mEq/L sodium) ORS solution is used
- In severe/unresponsive cases IV therapy should be started.

Management of Severe Dehydration

In patients with severe dehydration IV replacement of fluid and electrolytes is advisable. The following table provides a guideline for intravenous rehydration:

Initial Intravenous Management		
Ringer's Lactate (Ringolact) : 100 mL/kg, in divided doses Ringer's Lactate with 5% Dextrose (Ringolact-D) has the added advantage of providing glucose to help prevent hypoglycemia.		
	Infants (under 12 months)	Older children
30 mL/kg	1 hour	30 minutes
70 mL/kg	5 hours	2 ½ hours

When the patient's condition is stabilized, and the urine output is confirmed, the intravenous solution can be changed to Plabolyte-M.

The composition of these intravenous solutions are given below:

	Electrolytes (mEq/L)						
	Na^+	K^+	Cl^-	Ca^{++}	HCO_3^-	Dextrose (g/L)	Calories (kcal/L)
Ringolact	130	4	108.7	2.7	28	---	---
Ringolact-D	130	4	108.7	2.7	28	55	187
Plabolyte-M	60	20	60	3	2 (as acetate)	55	187

Another approach for intravenous rehydration involves the assessment of total fluid requirements that include the maintenance requirements, deficit and measurement of the ongoing losses. A simplified scheme is given below:

	Fluid	Sodium	Potassium
Maintenance		2-4 mEq/kg	2-4 mEq/kg
0-10 kg.	100 ml/kg		
11-20 kg.	1000 ml + 50 ml/kg for each kg above 10		
> 20 kg.	1500 ml + 20 ml/kg for each kg above 20		
Deficit	100 ml/kg	8-10 mEq/kg	8-10 mEq/kg
On-going losses	These should be measured for replacement.		

Step I :
All the three components (maintenance, deficit and on-going) should be added to give the total requirements.

Step II :
A bolus dose of 20-30 ml/kg of Ringers lactate **(Ringolact)** should be administered.

Step III :
The remaining fluid should be divided in three parts and administered over 24 hours.

Step III a :
The first aliquot should be administered as Ringers lactate **(Ringolact)** over an 8 hour period.

Step III b :

The second and third aliquots should be administered as ½,1/3 or 1/5 D/Saline (**Plabolyte-M** has a concentration between ½ and 1/3 D/Saline with added potassium and may be administered) during the remaining 16 hours.

(Ringolact and Plabolyte-M would also provide bicarbonate to help in the correction of acidosis.)

The urine volume after correction of dehydration should be 20 ml/hour or 1 ml/kg/hour.

Role of Zinc in Diarrhea

Zinc deficiency is present in 30-50% children in developing countries. Zinc deficiency predisposes to frequent diarrhoeal episodes, increasing their duration and severity and creating a vicious circle. Zinc is involved in epithelial barrier integrity, tissue repair, and immune function. Zinc deficiency reduces brush border enzymes, disrupts intestinal mucosa and increases mucosal permeability and intestinal secretion, thus making the diarrheal episode more severe and prolonged.

Zinc supplementation helps in early regeneration of intestinal mucosa causing reduction in intestinal secretion and regulation of water and electrolyte transport. Zinc by maintaining the integrity of the gut mucosa reduces and prevents the fluid losses. These responses begin to occur within 48 hours of starting zinc supplementation. Studies have shown that zinc supplementation results in a 25% reduction in duration of acute diarrhea and 40% reduction in treatment failure or death in persistent diarrhea.

In May 2004, WHO/UNICEF issued a joint statement recommending the use of zinc supplementation along with the use of new low osmolarity formulation of oral rehydration salt (ORS) as a two-pronged approach to improved case management of acute diarrhea in children.

A uniform dose of 20 mg of elemental zinc should be given during the period of diarrhea and for at least seven days after cessation of diarrhoea to children older than six months (10 mg/day for infants less than six months). Various zinc salts can be used for the management such as sulphate, gluconate or acetate.

VOMITING

Most commonly vomitus consists of the gastric contents, though it may be composed of fluid from any part of the GI tract. Common causes of vomiting include the following:

Infections
Acute cholecystitis
Nasogastric suction
Intestinal obstruction
Pregnancy
Drugs

Vomiting, particularly if prolonged, leads to fluid and electrolyte imbalances. The abnormalities include:

Volume depletion

Fluid losses occurring during vomiting are variable. Fortunately, vomiting frequently precludes any free water intake, which, if occurs, can further aggravate the situation, and severe degrees of volume depletion may occur. The condition of the patient may be further deteriorated if the ongoing processes are not given due consideration and 5% dextrose water is administered. This would lead to hyponatremia and worsening of the patient condition.

Loss of Chloride

This occurs as a direct result of the loss of gastric contents. The loss depends on the amount of the fluid lost and also on the capacity of the gastric glands to secrete HCl, which can be modified by drugs, such as H_2 - receptor antagonists.

Potassium Loss

Gastric fluid contains about 10 mEq/L of potassium. Therefore prolonged vomiting can lead to considerable loss of potassium ions from the body. Moreover the volume depletion caused by the vomiting causes an increase in the secretion of aldosterone. This leads to increased secretion of potassium in the distal parts of the nephron, thus aggravating hypokalemia. Therefore, potentially severe hypokalemia can develop, if untreated.

Metabolic Alkalosis

During vomiting, as the body loses hydrogen ions, metabolic alkalosis develops and the glomerular filtration rate decreases. The process can be reversed upon administration of adequate amounts of sodium chloride and potassium. This not only corrects the volume depletion, but also restores the potassium stores and causes the GFR to return to normal.

Therapy

Appropriate therapy includes administration of adequate amounts of fluids along with electrolytes. A suitable fluid to be administered is **Ringers Solution.** If this is not available, 0.9% sodium chloride **(Plasaline)** solution can also be administered. The total amount of the fluid administered should equal the amount lost plus the usual daily requirements.

If vomiting occurs along with diarrhea, Ringer's Lactate **(Ringolact)** may be administered.

HEAT ILLNESS

Heat illness comprises a group of disorders ranging from minor heat illnesses to heat exhaustion and heat stroke. These include ***Heat Edema***, which is a self-limited swelling of hands and feet, ***Heat cramps***, which are painful contractions that follow exertion of skeletal muscles in individuals who sweat profusely, and release more electrolytes, ***Heat tetany,*** manifested as carpopedal spasm and precipitated by rapid pH and body temperature changes and ***Heat Exhaustion***, a common problem characterized by volume depletion due to sweating in which fluid and electrolytes that are lost are not adequately replaced. ***Heat Stroke*** is a medical emergency characterized by deranged cerebral function and a body temperature usually greater than 104° F, resulting from a loss of temperature control that can rapidly lead to death.

Therapy

Appropriate therapy includes removal of the patient to a cool place, rest and administration of fluids to replace lost fluid and electrolytes. Ringer's Lactate **(Ringolact**) is a suitable fluid to be administered in cases requiring intravenous replacement. Alternatively Ringer's Lactate with 5% Dextrose **(Ringolact-D**) can also be infused as it also provides energy in the form of dextrose along with fluid and electrolytes.

FLUID THERAPY IN CALCIUM DISORDERS

Hypercalcemia

Simple hydration is often sufficient to lower the serum calcium levels. The following is a simple guideline for rehydration:

Isotonic Saline (Plasaline)

Depending on the condition of the patient 1-2 liters should be administered within 4-8 hours. This helps to increase calcium excretion in the urine. Another 2-3 liters should be administered during the next 24 hours and continued for 2-3 days. In severe cases as much as 6 liters of isotonic saline **(Plasaline)** may be given daily.

Hypocalcemia

10% calcium gluconate (10-20 ml) in severe cases of hypocalcemia, should be administered intravenously over a period of 5-10 minutes. Further calcium may be administered if symptoms persist. 10% calcium gluconate (50 ml) should be administered in 450 ml. of normal saline **(Plasaline)** or 5% Dextrose **(Pladex 5)** over 4-6 hours.

FLUID THERAPY IN SURGICAL PATIENTS

Administration of intravenous crystalloid fluids is a cornerstone of perioperative care. Goal-directed fluid therapy improves outcome in major surgery and results in a shorter hospital stay. Surgery imposes a stress on the patients. Hypovolemia is one of the stimuli leading to a neurohormonal response, which causes the release of a number of hormones that include adrenocorticotrophic hormone, catecholamines, glucagon, renin, aldosterone, angiotensin II and antidiuretic hormone.

Fluid Loss

Volume depletion can be pre-operative, intra-operative or post-operative. Mandatory preoperative fasting, for various diagnostic procedures and in preparation for surgery, incurs a fluid deficit in the patients. Use of contrast agents can cause significant loss of ECF during the pre-operative period.

During surgery, fluid loss occurs not only due to external losses (such as blood loss) but also insensible losses and internal shifts such as sequestration of fluids in an area of injury (third space effect). The sequestered fluid is again mobilized into the vascular compartment after

surgery. While it is outside the vascular compartment, adequate circulating volume must be maintained by i.v. fluids. There might also be pooling of secretions in the gastrointestinal tract.

Many anesthetic agents cause a peripheral vasodilation and a decrease in organ perfusion. The glomerular filtration pressure, which is under the control of Angiotensin II, is also decreased, leading to a decrease in urine output. Administration of narcotic agents can cause an increase in the secretion of antidiuretic hormone, and this can be exaggerated as a result of fluid loss secondary to overnight fasting. This phenomenon adds up to the already decreased urine output.

Postoperative renal dysfunction is a major cause of postoperative morbidity and mortality. Administration of intravenous crystalline fluids and maintenance of normovolaemia appears to be the most effective preventive strategy.

Activation of the neuroendocrine response as a result of surgical process leads to an increase in catabolic hormones, particularly cortisol, which along with an increased aldosterone, causes retention of sodium and water and increased excretion of potassium. Increase in ADH causes water retention.

Postoperative nausea and vomiting (PONV) is one of the most common postoperative complications, experienced by up to 70% of patients. PONV has also been found to be one of the major concerns of the patients with respect to postoperative recovery. Post-operative fluid loss can also occur through different tubes, drains, effusions and fistulas.

Administration of crystalline intravenous fluids is a simple, inexpensive therapy that can reduce postoperative nausea and vomiting and simultaneously avoiding drug-related adverse effects.

Perioperative Fluid Balance

During the perioperative period there is a need to manage the effects of preoperative fluid depletion, as discussed above, and intraoperative factors such as blood and fluid losses and the neuroendocrine response to anesthetic agents administered and the surgical process.

Fluid deficit in the pre-operative period can be calculated by the 4:2:1 formula. This takes into account the body weight in kilograms and the duration of fluid restriction in hours. For the first 10 kg. of body weight, a figure of 4 ml/kg is used, for the next 10 kg., 2 ml/kg, while 1 ml/kg for the remainder of the body weight.

Consider a patient weighing 50 kg. who has been NPO for the last 7 hours. This patient would need:

10 x 4 x 7 = 280 ml. (for first 10 kg.)
10 x 2 x 7 = 140 ml. (for the next 10 kg.)
30 x 1 x 7 = 210 ml. (for the rest of 30 kg.)

Thus this patient would have a total pre-operative deficit of 630 ml. (280 + 140 + 210).

There is also an insensible loss of fluid through the skin and respiratory tract. This loss amounts to 0.5 ml/kg/hour. The amount lost is related to the temperature, with a 10% increase for each degree rise in temperature above 99°F. Thus a patient weighing 60 kg and a temperature of 102°F, will have an insensible loss of 936 ml/24 hours.

0.5 x 60 = 30
30 + 9 = 39 (30% increase as a result 3° rise in temperature)
39 x 24 = 936ml.

The amount of fluid sequestered is dependent on the amount of surgical trauma and the surface area of the damaged tissues. Highest amount of sequestration occurs during intra-abdominal procedures where large surface area of the bowel and peritoneum are involved.

In addition, fluid is also lost through urine and stools. The loss of fluid through sweating, particularly in warm climates, such as that occurring in various regions of Pakistan can also be substantial. Under such circumstances the sweat contains about 9mEq/L of potassium and 30-60 mEq/L sodium. Thus patient requires about 2.5-3 liters of fluid/day.

A rough guide to intraoperative fluid requirement is as follows:

Minimal trauma surgery:	4 mL/kg/hour
Moderate trauma surgery:	6-8 mL/kg/hour
Severe trauma surgery:	10-15 mL/kg/hour

Electrolyte Changes

As a result of release of various hormones, free water clearance is decreased, and there is hyponatremia and hypokalemia.

During the early post-operative period there is no need of potassium as potassium is released as a result of tissue injury. However, in the later post-operative period the potassium needs to be administered.

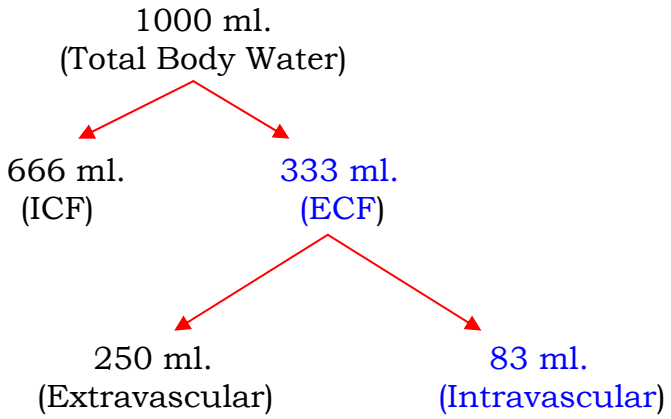
Hyponatremia occurs during the early post-operative period as free water clearance is decreased and the third space fluid is mobilized, causing increased requirements of sodium during this period. However, in the later stages, as the body starts retaining sodium, the effect of aldosterone decreases, causing decreased requirements of sodium.

Thus it is apparent that in the early stages large amount of sodium and less amounts of potassium are required, while in the later stages the situation is reversed. The patient also requires glucose to fulfill his energy requirements.

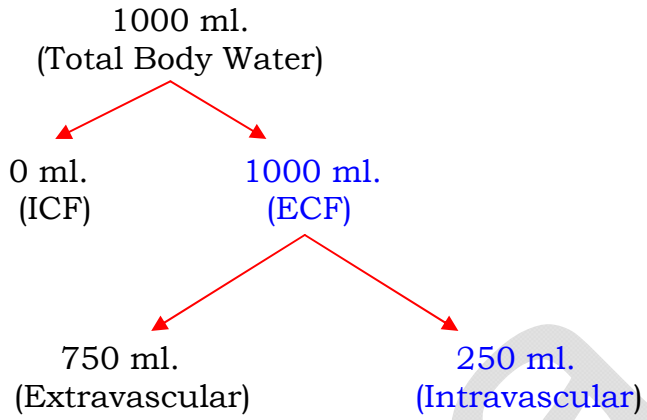
Recommended Solutions

Correction of the volume deficit requires administration of a ***Balanced Salt Solution.*** This also eliminates the post-operative salt intolerance. Administration of a balanced salt solution (such as lactated Ringer's) causes distribution of the administered fluid throughout the ECF, with about 25% (about 250 ml. when 1000 ml. is infused) of the infused solution being retained in the intravascular space. In contrast, only 10% (about 83 ml. when 1000 ml. is infused) of a hypotonic solution, such as 5% D/W is retained in the intravascular compartment as it is distributed throughout total body water.

Ringolact-D, (a balanced salt solution with dextrose) containing small amounts of potassium and large amounts of sodium, along with dextrose may be administered to the surgical patients in the early stages. Care should be taken that the patient does not become hyperglycemic. During the maintenance phase **Plabolyte-M**, containing small amounts of sodium but greater amounts of potassium, along with dextrose, can be administered to the patients.



Distribution of 1000 ml. of 5% D/W



Distribution of 1000 ml. of a Balanced Salt Solution

FLUID THERAPY IN BURNS

Injury due to burns causes necrosis of the skin and underlying tissues. Fires, steam, scalding liquids and flammable liquids are the major causes of burns. The severity of the injury is classified by the degree of the burns (first, second or third degree) and by the total surface area burned. This is usually calculated by the **Rule of 9.** This method divides the body into sections that represent 9% or a multiple of 9% of the total surface area. The different areas of the body occupy the following percentages:

Head & Neck	9%
Right Upper Limb	9%
Left Upper Limb	9%
Right Lower Limb	18%
Left Lower Limb	18%
Front of Trunk	18%
Back of Trunk	18%
Genital Area	01%
Total Surface Area	**100%**

It must be remembered that in infants and small children, the head represents a greater portion of body mass (19%) than adults. The surface area of thighs and legs change with growth. As age increases, the surface area of head decreases while that of thighs and legs increase.

Estimating the size of burn area is useful because it directly relates to the severity of the injury. It is a good prognostic index and also helps in replacing the lost fluids.

Immediately after the burn injury, changes in the cardiovascular system predominate causing loss of fluids and protein. This is mostly caused by changes in the capillary permeability and activation of the immune system.

Fluid Replacement

This should be initiated in all patients who have sustained burns of 15% or more of total body surface area. As ileus is almost always present in these patients, the fluids should be replaced intravenously. The following is a simplified approach that can be used in the majority of patients:

Step I

Calculate the total surface area burned by the Rule of 9.

Step II

Administer Ringer's Lactate **(Ringolact**), 2 ml/kg/percent burn, during the first 24 hours. The amount may be increased up to 4ml/kg/percent burn if necessary (depending upon urine output). 50% of the total fluid should be administered during the first 8 hours and the remaining over the next 16 hours.

Children younger than 15 years should be administered fluids **(Ringolact**) at the rate of 3 ml/kg/percent burn. As in adults, half of this amount should be administered during the first 8 hours and the remaining during the next 16 hours.

In children, additional water (electrolyte free) may also be required. 5% Dextrose in one-half normal saline **(Pladexsal ½)** may be used to meet the fluid requirements and also prevent hypoglycemia as children have lower glycogen stores.

Alternative formulas for calculation of fluid requirements in the burned pediatric patients have also been advocated, but these are complicated and more cumbersome.

Step III

During the next 24 hours, colloids should be administered at a rate of 0.3-0.5ml/kg/percent burn or 20%-60% of calculated plasma volume. Damage to the skin causes loss of water through evaporation also. This should be replaced by 5% Dextrose in water **(Pladex-5)** in amounts sufficient to maintain urine output. Insufficient replacement may lead to

hypernatremia. In small children 1/3 Dextrose saline **(Pladexsal 1/3)** or 1/5 Dextrose saline **(Pladexsal 1/5)** may be used.

During the replacement of fluids it should be remembered that the amounts administered should be sufficient to maintain a urine output of 30-50ml/hour in adults and 1ml/kg/hour in children who weigh less than 30 kg.

The timing refers to the time from the burn injury and not from the time of the arrival of the patient in the hospital or the clinic.

Injury due to burns also causes significant amount of proteins to be lost from the body. This can be aggravated as a result of vigorous fluid replacement. Albumin or amino acids **(Pan-Amin SG)** may be administered to maintain serum albumin concentration at about 3 grams/dl and a hematocrit above 30%.

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Otsuka People Creating New Products for Better Health Worldwide.

Plabottle is a special type of plastic bottle used for administering various intravenous solutions to the patients. It was developed by Otsuka Pharmaceutical Company, Japan.

There are many kinds of plastics, but only some of them such as polyethylene, polypropylene, polyvinyl chloride, silicones, etc. are used in pharmaceutical practice. Polyethylene and polyvinyl chloride (P.V.C.) are the common plastic containers available in the market.

ADVANTAGES OF PLABOTTLE

It is very important for the medical professionals to know whether these plastic containers conform to various standards. Different tests on the plastics have shown that the polyethylene containers (Plabottle) have the following three advantages:

Stable pH

Acid substances are more stable in polyethylene. Experiments have shown that in P.V.C. containers filled with 5% Dextrose Injection, the pH value decreases more after sterilization as compared with Polyethylene containers (Plabottle).

Low Water Vapor Permeability

The water vapor permeability of polyethylene (Plabottle) is low while that of P.V.C. is extremely high like polycarbonate. 5% Dextrose Injection stored at 42°C in an incubator shows 5.5% change of concentration after one month.

Stability of Polyethylene

Polyethylene is called ***pure plastic*** as any substances are not added to increase its stability. Plasticizers are added to PVC to increase its flexibility and softness. Furthermore P.V.C. is also added with stabilizer, because it is apt to release and decompose hydrogen chloride. 120 times

as many oxidizable substances are detected in P.V.C. as compared to polyethylene. These plasticizers and stabilizers can be a decisive factor in evaluation of plastic containers according to the biological tests prescribed in United States Pharmacopoeia (U.S.P.)

OTHER ADVANTAGES OF PLABOTTLE

In addition to the above mentioned benefits, Plabottle offers the following additional advantages:

High Quality

All products of Otsuka are manufactured under strict ***Good Manufacturing Practices*** (GMP) guidelines to ensure high quality products. Special techniques are applied to avoid pyrogens and particulate matter contamination during the process.

Pin Hole Testing

To avoid any chances of minute holes in the plastic material during the manufacturing process, a sophisticated electric device tests each and every bottle (Plabottle) for any microscopic holes undetected by the human eye. This further reduces chances of contamination.

Alcohol Spray

After filling, the nozzle is sprayed with ethyl alcohol spray to ensure a decontaminated nozzle and then capped.

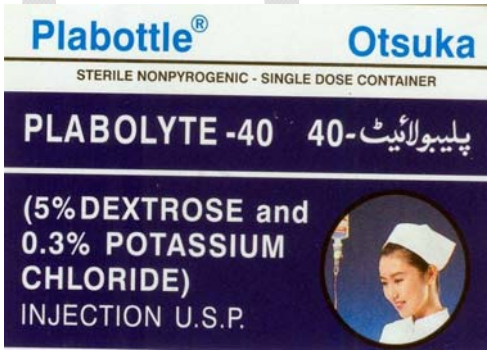
Poly Bags

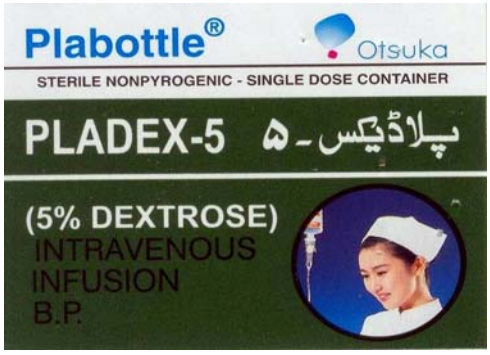
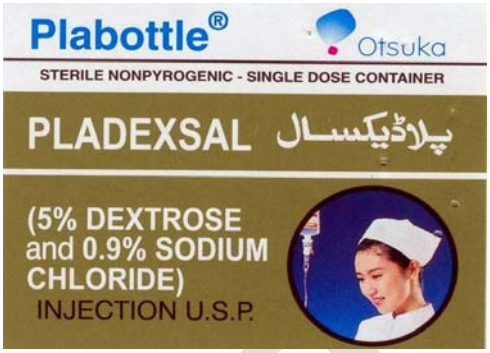
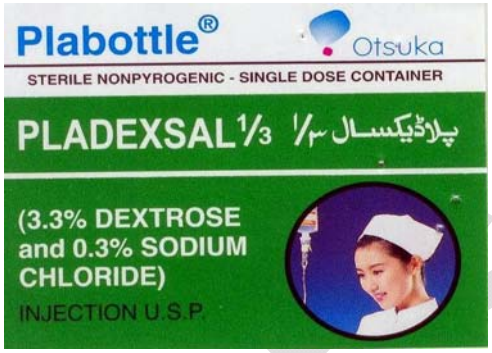
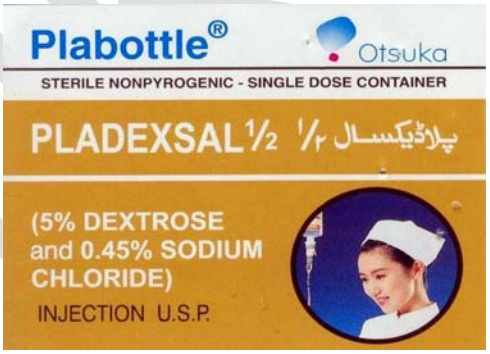
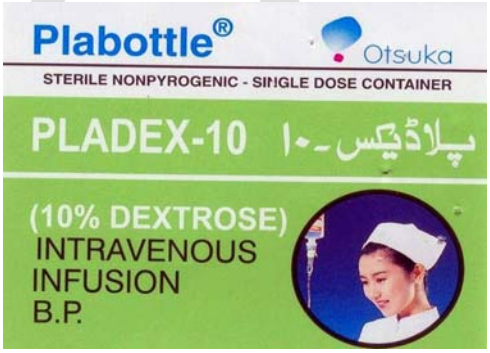
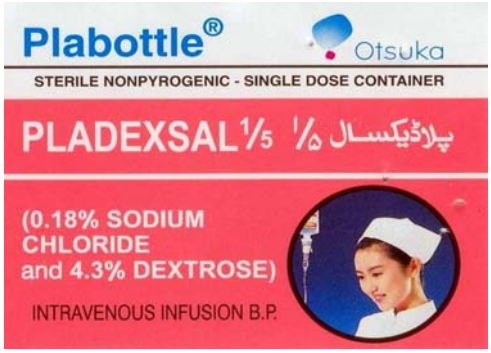
The Plabottle is provided with further protection from dust and dirt by being sealed in an outer poly bag.

Uninterrupted Flow

Plabottle provides a large sterile space. This helps in an uninterrupted flow of the solution during infusion. ***There is no need to PRICK for smooth flow.*** Such holes make the system an OPEN SYSTEM that is liable to contamination.

Product Identification



 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEX-5 پلاڈیکس ۔ ۵ (5% DEXTROSE) INTRAVENOUS INFUSION B.P.	 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEXSAL پلاڈیکسال (5% DEXTROSE and 0.9% SODIUM CHLORIDE) INJECTION U.S.P.
 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEXSAL⅓ ⅓ پلاڈیکسال (3.3% DEXTROSE and 0.3% SODIUM CHLORIDE) INJECTION U.S.P.	 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEXSAL½ ½ پلاڈیکسال (5% DEXTROSE and 0.45% SODIUM CHLORIDE) INJECTION U.S.P.
 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEX-10 پلاڈیکس ۔ ۱۰ (10% DEXTROSE) INTRAVENOUS INFUSION B.P.	 Plabottle® Otsuka STERILE NONPYROGENIC - SINGLE DOSE CONTAINER PLADEXSAL⅕ ⅕ پلاڈیکسال (0.18% SODIUM CHLORIDE and 4.3% DEXTROSE) INTRAVENOUS INFUSION B.P.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STERILE NONPYROGENIC - SINGLE DOSE CONTAINER
Ringer's Solution
رنگرز سلوشن
(COMPOUND SODIUM CHLORIDE)
INJECTION
B.P.C.


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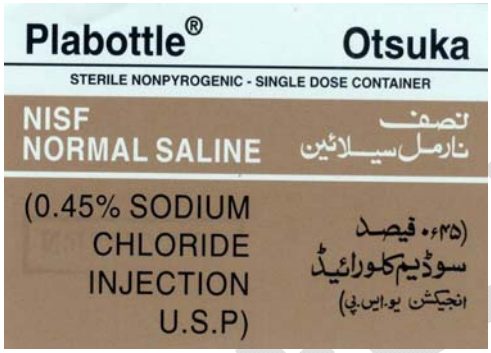
PERI SOLUTION
پیری سلوشن
(PERITONEAL DIALYSIS SOLUTION)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NISF
NORMAL SALINE
نصف نارمل سیلائین
(0.45% SODIUM CHLORIDE INJECTION U.S.P)
(۰٫۴۵ فیصد سوڈیم کلورائیڈ انجیکشن یو.ایس.پی)


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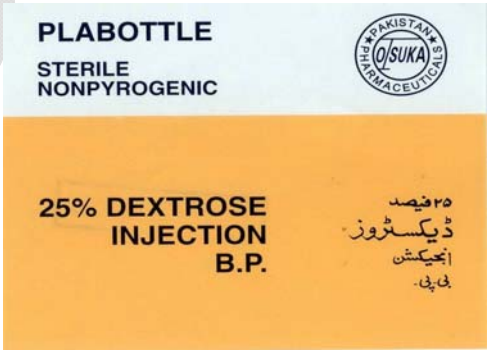
STERILE NONPYROGENIC - SINGLE DOSE CONTAINER
NEODEXSAL
نیوڈیکسال
(10% DEXTROSE and 0.18% SODIUM CHLORIDE)
INJECTION U.S.P.


PLABOTTLE
STERILE
NONPYROGENIC
PAKISTAN OTSUKA PHARMACEUTICALS
25% DEXTROSE
INJECTION
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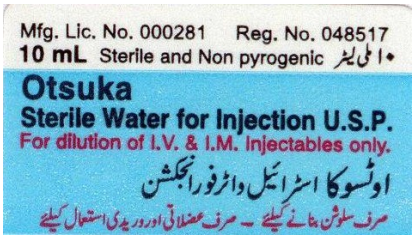
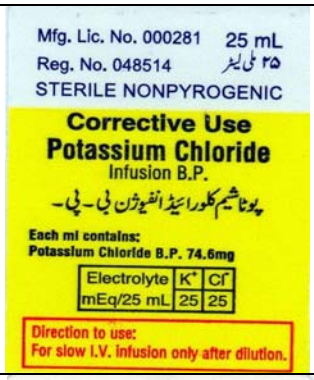
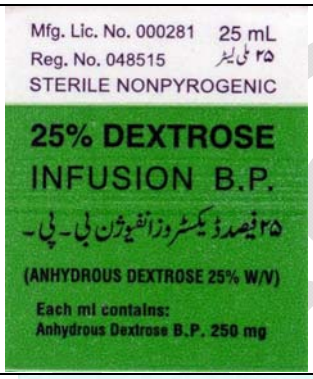
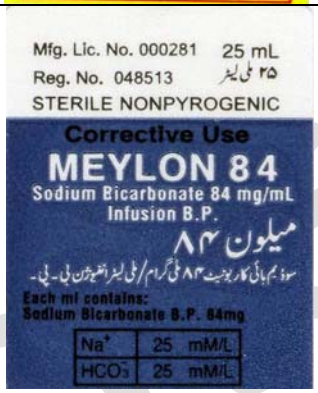
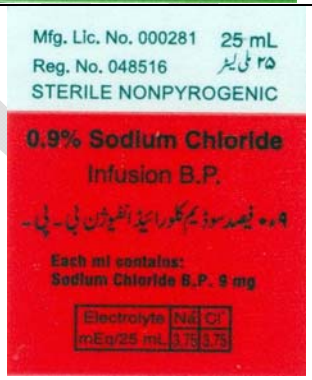
انجیکشن
بی.پی.


Mfg. Lic. No. 000281 Reg. No. 048517
10 mL Sterile and Non pyrogenic ۱۰ ملی لیٹر
Otsuka
Sterile Water for Injection U.S.P.
For dilution of I.V. & I.M. Injectables only.
اوٹسوکا اسٹرائیل واٹر فور انجکشن
صرف سلوشن بنانے کیلئے ۔ صرف عضلاتی اور وریدی استعمال کیلئے


Mfg. Lic. No. 000281 25 mL
Reg. No. 048514 ۲۵ ملی لیٹر
STERILE NONPYROGENIC
Corrective Use
Potassium Chloride
Infusion B.P.
پوٹاشیم کلورائیڈ انفیوژن بی۔پی۔
Each ml contains:
Potassium Chloride B.P. 74.6mg
Electrolyte K+ Cl-
mEq/25 mL 25 25
Direction to use:
For slow I.V. infusion only after dilution.


Mfg. Lic. No. 000281 25 mL
Reg. No. 048515 ۲۵ ملی لیٹر
STERILE NONPYROGENIC
25% DEXTROSE
INFUSION B.P.
۲۵ فیصد ڈیکسٹروز انفیوژن بی۔پی۔
(ANHYDROUS DEXTROSE 25% W/V)
Each ml contains:
Anhydrous Dextrose B.P. 250 mg


Mfg. Lic. No. 000281 25 mL
Reg. No. 048513 ۲۵ ملی لیٹر
STERILE NONPYROGENIC
Corrective Use
MEYLON 84
Sodium Bicarbonate 84 mg/mL
Infusion B.P.
میلون ۸۴
سوڈیم بائی کاربونیٹ ۸۴ ملی گرام/ملی لیٹر انفیوژن بی۔پی۔
Each ml contains:
Sodium Bicarbonate B.P. 84mg
Na+ 25 mM/L
HCO3 25 mM/L


Mfg. Lic. No. 000281 25 mL
Reg. No. 048516 ۲۵ ملی لیٹر
STERILE NONPYROGENIC
0.9% Sodium Chloride
Infusion B.P.
۰.۹ فیصد سوڈیم کلورائیڈ انفیوژن بی۔پی۔
Each ml contains:
Sodium Chloride B.P. 9 mg
Electrolyte Na+ Cl-
mEq/25 mL 3.75 3.75

PLADEX-5

(5% Dextrose Intravenous Infusion B.P.)

Therapeutic Class

Hypotonic water and carbohydrate source

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Dextrose Monohydrate equivalent or Anhydrous Dextrose B.P.	50grams
Water for Injections	q.s.

Pharmacological Effects

- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Supplies body water for hydration.
- Spares body protein by providing carbohydrate for metabolism.
- Osmolarity of D_5W is 278 mOsm/L. The fluid is isotonic when in the container. After administration, the dextrose is quickly metabolized in the body, leaving only water - a hypotonic fluid.
- The pH range is 3.5 - 6.5.
- Capable of producing diuresis depending on clinical state of the patient.

Indications

- Adult I.V. solution to keep vein open.
- Vehicle for mixing medications for I.V. delivery for all age groups.
- In children use only for medication mixtures/administration.
- Indicated for use in patients with burns on the second post-burn day.
- Can be used to supply small amounts of energy.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient. However, for non-diabetics, the maximum infusion rate should be 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Hyperglycemia.
- Fluid overload.
- Hyponatremia.
- Hypokalemia
- Water intoxication

Contraindications

- Patients at risk for increased intracranial pressure.
- Patients who have an acute neurological dysfunction.
- Hypovolemic states.
- Patients at risk for third-space fluid shifts**.**
- Elevated blood glucose concentrations.

Precautions

- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Do not administer quantity in excess of that required to keep vein open or administer appropriate dose of medication.
- Do not use solution if outdated, cloudy or the seal is not intact.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.

Osmolarity and Tonicity

Hypotonic solution as it does not contain any cations.
Iso-osmolar solution (278 mOsm/L)

Caloric Value

187 kCal/Liter

Pharmaceutical Precautions

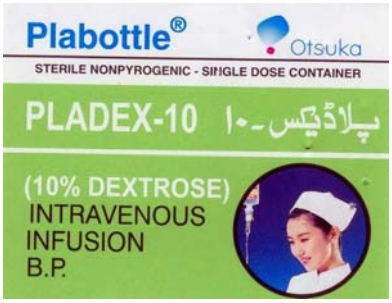
- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 100ml. in polyolefin plastic bottle (Plabottle) to minimize drug-plastic interactions and with ***Specific Pilfer Proof Filter*** (SPPF) ***Cap*** to facilitate addition of medications without compromising sterility of the product.
- 500ml and 1000ml in Plabottle.

PLADEX-10

(10% Dextrose Intravenous Infusion B.P.)



Therapeutic Class

Hypotonic water and carbohydrate source

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Dextrose Monohydrate equivalent or Anhydrous Dextrose B.P.	100grams
Water for Injections	q.s.

Pharmacological Effects

- Provides calories for some metabolic needs. Each 100mL provides 10 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Supplies body water for hydration.
- Spares body protein by providing carbohydrate for metabolism.
- Osmolarity of $D_{10}W$ is 556 mOsm/L. The fluid is isotonic when in the container. After administration, the dextrose is quickly metabolized in the body, leaving only water - a hypotonic fluid.
- The pH range is 3.5 - 6.5.
- Capable of producing diuresis depending on clinical state of the patient.

Indications

- Can be used as a source of energy.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient. However, for non-diabetics, the maximum infusion rate should be 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Hyperglycemia.
- Fluid overload.
- Hyponatremia.
- Hypokalemia
- Water intoxication
- Prolonged administration through peripheral veins may cause phlebitis.

Contraindications

- Patients at risk for increased intracranial pressure.
- Patients who have an acute neurological dysfunction.
- Hypovolemic states.
- Patients at risk for third-space fluid shifts**.**
- Elevated blood glucose concentrations.

Precautions

- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Do not use solution if outdated, cloudy or the seal is not intact.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.

Osmolarity and Tonicity

Hypotonic solution as it does not contain any cations.
Hyper-osmolar solution (556 mOsm/L)

Caloric Value

374 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.

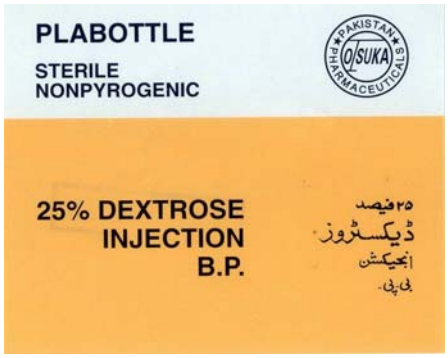
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 500ml and 1000ml in Plabottle.

25% DEXTROSE INJECTION B.P.

(Dextrose 25% in Water)



Therapeutic Class

Hypotonic water and carbohydrate source

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Anhydrous Dextrose	250grams
Water for Injections	q.s.

Pharmacological Effects

- Provides calories for some metabolic needs. Each 100mL provides 25 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen,it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Supplies body water for hydration.
- Spares body protein by providing carbohydrate for metabolism.
- Osmolarity of $D_{25}W$ is 1389 mOsm/L. The fluid is isotonic when in the container. After administration, the dextrose is quickly metabolized in the body, leaving only water - a hypotonic fluid.
- The pH range is 3.5 - 6.5.
- Capable of producing diuresis depending on clinical state of the patient.

Indications

- Used as a source of energy particularly in total parenteral nutrition.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient. However, for non-diabetics, the maximum infusion rate should be 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized. Should be administered through central vein as it can be irritating to the peripheral veins causing phlebitis.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Hyperglycemia.
- Fluid overload.
- Hyponatremia.
- Hypokalemia
- Water intoxication
- Phlebitis

Contraindications

- Patients at risk for increased intracranial pressure.
- Patients who have an acute neurological dysfunction.
- Hypovolemic states.
- Patients at risk for third-space fluid shifts**.**
- Elevated blood glucose concentrations.

Precautions

- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Do not use solution if outdated, cloudy or the seal is not intact.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.
- Monitoring of blood glucose is advisable.

Osmolarity and Tonicity

Hypotonic solution as it does not contain any cations.
Hyper-osmolar solution (1389 mOsm/L)

Caloric Value

935 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.

- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 1000ml in Plabottle.

PLASALINE

(0.9% Sodium Chloride Intravenous Infusion B.P.) (Normal Saline)

Therapeutic Class

Isotonic crystalloid salt solution

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Sodium Chloride B.P.	9.0 grams
Water for Injections	q.s.

Pharmacological Effects

- Expands circulating volume by approximating sodium content of the blood.
- Each liter provides 150 mEq of sodium and 150 mEq of chloride.
- The pH range is 3.5 - 7.5.

Indications

- Trauma
- Hypovolemic states such as prolonged vomiting.
- Environmental emergencies
- Diabetic ketoacidosis.
- H.H.N.C.
- Also useful for dilution of medications, as flushing agent for rapid I.V. medication administration and irrigation solution for eyes and wounds and bladder wash after prostate surgery.
- Can be used in children to keep vein open.
- Management of hypercalcemia. Depending on the condition of the patient, initially 1-2 liters may be administered within 4-8 hours. This helps to increase calcium excretion in the urine. Further therapy with lesser amounts may be continued for 2-3 days with monitoring of serum calcium and vital signs.

Dosage and Administration

Plasaline should be administered according to the clinical condition of the patient, age and body weight.

Diabetic ketoacidosis (DKA) and hyperglycemic, hyperosmolar, non-ketotic coma (H.H.N.C.) may require 500 – 1000mL/hour if blood glucose is greatly elevated and patients are hypotensive and/or dehydrated.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload and congestive heart failure.
- Edema.
- Electrolyte imbalance.
- Hyperchloremic acidosis.
- Hypertension.

Contraindications

- Congestive heart failure.

Precautions

- The sodium chloride content of Plasaline is 9.0 grams/L. Care is therefore required in those cases where salt intake is restricted, such as in hypertensive patients.
- In patients where sodium losses exceed chloride losses, it can cause hyperchloremia and hyperchloremic acidosis.
- Infusion of large volumes may cause dilutional acidosis due to the dilution of the bicarbonate concentration in the plasma (as the preparation does not contain bicarbonate).
- Care is required in conditions where hypokalemia and/or hypocalcemia exists or may arise as the infusion of the product can decrease the concentration of these electrolytes.
- Caution should be exercised in patients with renal failure and in those with reduced urinary output due to obstructive urinary tract diseases.
- Continuous infusion of Plasaline may cause hypernatremia, unless free water is supplied along with it.
- Monitor E.C.G. continuously.
- Frequently monitor vital signs.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 150.
Isosmotic solution (308 mOsm/L)

Caloric Value

Nil

Pharmaceutical Precautions

- Normal Saline is compatible with almost all drugs. Therefore it can be safely mixed and used with other injectable medicines. However data sheet of the medication should be referred to, before admixture.
- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 100ml. in polyolefin plastic bottles to minimize drug-plastic interactions and with ***Specific Pilfer Proof Filter*** (SPPF) ***Cap*** to facilitate addition of medications without compromising sterility of the product.
- 500ml and 1000ml in Plabottle.

PLADEXSAL

(5% Dextrose and 0.9% Sodium Chloride Injection U.S.P.)

Therapeutic Class

Isotonic crystalloid salt solution and carbohydrate source.

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Dextrose Monohydrate U.S.P.	50.0 grams
Sodium Chloride U.S.P.	9.0 grams
Water for Injections	q.s.

Pharmacological Effects

- Expands circulating volume by approximating sodium content of the blood.
- Each liter provides 154 mEq of sodium and 154 mEq of chloride.
- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Supplies body water for hydration.
- Spares body protein by providing carbohydrate for metabolism.
- The pH range is 3.5 - 6.5.

Indications

- Hypovolemic states such as prolonged vomiting.
- To replenish extracellular fluid volume when other solutions are not available.
- Trauma
- Environmental emergencies

Dosage and Administration

Pladexsal should be administered according to the clinical condition of the patient, age and body weight.

Adverse Effects

- Fluid overload and congestive heart failure.
- Edema.
- Electrolyte imbalance.
- Hyperchloremic acidosis.
- Hypertension.
- Hyperglycemia

Contraindications

- Congestive heart failure.
- Elevated blood glucose levels.

Precautions

- The sodium chloride content of Pladexsal is 9.0 grams/L. Care is therefore required in those cases where salt intake is restricted, such as in hypertensive patients.
- In patients where sodium losses exceed chloride losses, it can cause hyperchloremia and hyperchloremic acidosis.
- Infusion of large volumes may cause dilutional acidosis due to the dilution of the bicarbonate concentration in the plasma (as the preparation does not contain bicarbonate).
- Care is required in conditions where hypokalemia and/or hypocalcemia exists or may arise as the infusion of the product can decrease the concentration of these electrolytes.
- Caution should be exercised in patients with renal failure and in those with reduced urinary output due to obstructive urinary tract diseases.
- Continuous infusion of Pladexsal may cause hypernatremia, unless free water is supplied along with it.
- Monitor E.C.G. continuously.
- Frequently monitor vital signs.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 154.
Hyperosmolar solution (560 mOsm/L)

Caloric Value

170 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 500ml and 1000ml in Plabottle.

PLADEXSAL 1/2

(5% Dextrose and 0.45% Sodium Chloride Injection U.S.P.)

Therapeutic Class

- Crystalloid solution with carbohydrate source.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Dextrose Monohydrate U.S.P.	50.0 grams
Sodium Chloride U.S.P.	4.5 grams
Water for Injections	q.s.

Pharmacological Effects

- Pladexsal 1/2 has an electrolyte composition of sodium and chloride approximately ½ and ¾ of plasma respectively.
- Supplies body water for hydration.
- Provides 500 ml. of Free Water/Liter of solution.
- Provides the following electrolytes in each liter of fluid:

Sodium	77 mEq.
Chloride	77 mEq.

- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- The pH range is 3.5 - 6.5.

Indications

- Hypovolemic states including dehydration.
- Recommended as an initial solution for rehydration, for the supply of water and electrolytes in children and adults.
- Used to supply or replenish water and electrolytes before, during and after surgery.

- Indicated for the supply or replenishment of water and electrolytes in cases of possible potassium retention such as anuria, oliguria, hyperkalemia, and increased BUN.
- Used for the replenishment of chloride in hypochloremic acidosis.

Dosage and Administration

The dose is dependent upon the age, weight and clinical condition of the patient. The infusion rate should be adjusted to provide 300-500 ml./hour (about 75-125 drops/minute) for adults and 50-100 ml/hour (about 12-25 drops/minute) for children.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload.
- Congestive heart failure.
- Hyperglycemia

Contraindications

- Congestive heart failure.
- Renal failure.
- Elevated blood glucose concentration.

Precautions

- Care is required in patients with cardiac failure, renal failure and in cases where salt intake is restricted as the solution contains sodium chloride 4.5 grams/Liter.
- Care is required in diabetics.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Hypotonic solution having a tonicity of 77.
Hyperosmolar solution (406 mOsm/L)

Caloric Value

170 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

500ml in Plabottle.

PLADEXSAL 1/3

(3.3% Dextrose and 0.3% Sodium Chloride Injection U.S.P.)

Therapeutic Class

- Crystalloid solution with carbohydrate source.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Dextrose Monohydrate U.S.P.	33.0 grams
Sodium Chloride U.S.P.	3.0 grams
Water for Injections	q.s.

Pharmacological Effects

- Pladexsal 1/3 has an electrolyte composition of sodium and chloride approximately 1/3 and 1/2 of plasma respectively.
- Supplies body water for hydration.
- Provides 670 ml. of Free Water/Liter of solution.
- Provides the following electrolytes in each liter of fluid:

Sodium	51 mEq.
Chloride	51 mEq.

- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- The pH range is 3.5 - 6.5.

Indications

- Hypovolemic states including dehydration.
- Recommended as an initial solution for rehydration, for the supply of water and electrolytes in children and adults.
- Used to supply or replenish water and electrolytes before, during and after surgery.

- Indicated for the supply or replenishment of water and electrolytes in cases of possible potassium retention such as anuria, oliguria, hyperkalemia, and increased BUN.

Dosage and Administration

The dose is dependent upon the age, weight and clinical condition of the patient. The infusion rate should be adjusted to provide 300-500 ml./hour (about 75-125 drops/minute) for adults and 50-100 ml/hour (about 12-25 drops/minute) for children.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload.
- Congestive heart failure.
- Hyperglycemia

Contraindications

- Congestive heart failure.
- Renal failure.
- Elevated blood glucose concentration.

Precautions

- Care is required in patients with cardiac failure, renal failure and in cases where salt intake is restricted as the solution contains sodium chloride 3.0 grams/Liter.
- Care is required in diabetics.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Hypotonic solution having a tonicity of 51.
Hypo-osmolar solution (269 mOsm/L)

Caloric Value

112 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

500ml in Plabottle.

PLADEXSAL 1/5

(4.3% Dextrose and 0.18% Sodium Chloride Intravenous Infusion B.P.)

Therapeutic Class

- Crystalloid solution with carbohydrate source.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Dextrose Monohydrate equivalent or Anhydrous Dextrose B.P.	43.0 grams
Sodium Chloride B.P.	1.80 grams
Water for Injections	q.s.

Pharmacological Effects

- Pladexsal 1/5 has an electrolyte composition of sodium and chloride approximately 1/5 and 1/3 of plasma respectively.
- Supplies body water for hydration.
- Provides 810 ml. of Free Water/Liter of solution.
- Provides the following electrolytes in each liter of fluid:

Sodium	30 mEq.
Chloride	30 mEq.

- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- The pH range is 3.5 - 6.5.

Indications

- Hypovolemic states including dehydration.
- Recommended as an initial solution for rehydration, for the supply of water and electrolytes in neonates and infants.
- Used to supply or replenish water and electrolytes before, during and after surgery particularly in neonates and infants.

- Indicated for the supply or replenishment of water and electrolytes in cases of possible potassium retention such as anuria, oliguria, hyperkalemia, and increased BUN, particularly in neonates and infants.

Dosage and Administration

The dose is dependent upon the age, weight and clinical condition of the patient. The infusion rate should be adjusted to provide 300-500 ml./hour (about 75-125 drops/minute) for adults and 50-100 ml/hour (about 12-25 drops/minute) for children.

In neonates and pre-term babies infusion of more than 100 ml/hour should be avoided.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload.
- Water intoxication may occur if infused rapidly or in large amounts.
- Congestive heart failure.
- Hyperglycemia

Contraindications

- Congestive heart failure.
- Renal failure.
- Elevated blood glucose concentration.

Precautions

- Care is required in patients with cardiac failure, renal failure and in cases where salt intake is restricted as the solution contains sodium chloride 1.8 grams/Liter.
- Care is required in diabetics.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Hypotonic solution having a tonicity of 30.
Isosmotic solution (300 mOsm/L)

Caloric Value

160 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

500ml in Plabottle.

NISF NORMAL SALINE

(0.45% Sodium Chloride Injection U.S.P.)

Therapeutic Class

Hypotonic crystalloid salt solution

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Sodium Chloride	4.5 grams
Water for Injections	q.s.

Pharmacological Effects

- Expands circulating volume by approximating sodium content of the blood
- Each liter provides 77 mEq of sodium and 77 mEq of chloride.
- The pH range is 3.5 - 7.5.

Indications

- Management of diabetic ketoacidosis particularly in infants and children.
- Prevention and management of contrast-induced nephropathy.
- Management of acute renal failure secondary to rhabdomyolysis.
- Environmental emergencies such as heat stroke.
- Used as a vehicle for medications such as sodium bicarbonate in severe metabolic acidosis and magnesium sulphate in the management of preterm labor.

Dosage and Administration

Nisf Normal Saline should be administered according to the clinical condition of the patient, age and body weight.

For management of contrast-induced nephropathy, 0.45% saline is infused at a rate of 1 ml/kg/hour. Infusion is started 1-2 hours before contrast and continued for up to 24 hours, depending upon the duration of diuresis attained.

In the management of acute renal failure secondary to rhabdomyolysis, in adults, 1000 ml. of 0.45% saline is used to dilute 44 mEq. of sodium bicarbonate and infused at the rate of 100 ml/hour.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload, congestive heart failure and hypertension.
- Edema and electrolyte imbalance.

Contraindications

- Congestive heart failure and hypernatremia.

Precautions

- The sodium chloride content of Nisf Normal Saline is 4.5 grams/L. Care is therefore required in those cases where salt intake is restricted, such as in hypertensive patients.
- Care is required in conditions where hypokalemia and/or hypocalcemia exists or may arise as the infusion of the product can decrease the concentration of these electrolytes.
- Monitor E.C.G. continuously.
- Frequently monitor vital signs.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Hypotonic solution having a tonicity of 77.
Hypo-osmotic solution (154 mOsm/L)

Caloric Value

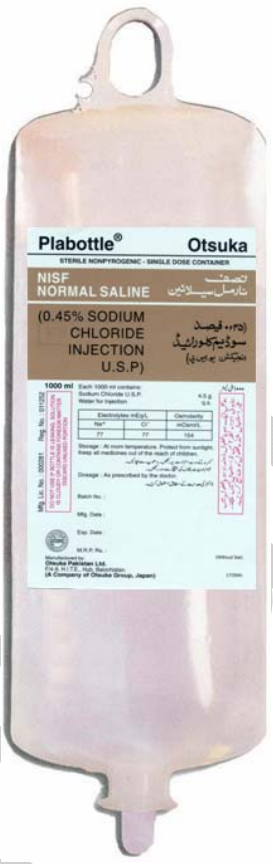
Nil

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 1000ml in Plabottle.



RINGER'S SOLUTION FOR INJECTION

(Compound Sodium Chloride Injection B.P.C.)

Therapeutic Class

- Isotonic crystalloid solution.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Calcium Chloride $2H_2O$	0.32 grams
Potassium Chloride	0.30 grams
Sodium Chloride	8.60 grams
Water for Injections	q.s.

Pharmacological Effects

- Ringer's Solution for Injection has an electrolyte composition closer to that of plasma as compared to normal saline.
- The chloride concentration of this solution is unphysiological and can cause hyperchloremia and hyperchloremic acidosis.
- It expands circulating blood volume by approximating the fluid and electrolyte composition of the blood.
- The solution does not contain bicarbonate ions and infusion of large quantities may cause dilutional acidosis.
- Provides the following electrolytes in each liter of fluid:

Sodium	147 mEq.
Chloride	156 mEq.
Potassium	4 mEq.
Calcium	2.2 mEq.

- The pH range is 5.0 - 7.5.

Indications

- Hypovolemic states including dehydration and hemorrhage.
- Supply or replenishment of chloride.
- Trauma.
- Burns
- Environmental emergencies such as severe perspiration leading to dehydration and heat stroke.
- The use of Ringer's Solution is now limited to those cases only, in which Lactated Ringer's Injection (Ringolact) is not suitable such as alkalosis and disturbances of lactic acid metabolism.

Dosage and Administration

The dose is dependent upon the age, weight and clinical condition of the patient. The infusion rate should be adjusted to provide 300-500 ml./hour (about 75-125 drops/minute) for adults.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- Fluid overload.
- Congestive heart failure.
- Hyperchloremic and dilutional acidosis.

Contraindications

- Congestive heart failure.
- Renal failure.

Precautions

- Care is required in patients with cardiac failure, renal failure and in cases where salt intake is restricted as the solution contains sodium chloride 8.6 grams/Liter.
- Caution should be exercised in patients with hypertonic dehydration.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 153.
Isosmotic solution (309 mOsm/L)

Caloric Value

Nil

Pharmaceutical Precautions

- Ringer's Solution for Injection should not be mixed with citric acid added blood, and preparations containing phosphoric acid or carbonic

acid, as the calcium content of this solution may form precipitates with these acids.

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

500ml in Plabottle.

RINGOLACT

(Lactated Ringer's Injection U.S.P)

Therapeutic Class

- Isotonic crystalloid solution.
- Physiologic electrolyte solution.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Calcium Chloride $2H_2O$	0.2 grams
Potassium Chloride	0.3 grams
Sodium Chloride	6.0 grams
Sodium Lactate	3.1 grams
Water for Injections	q.s.

Pharmacological Effects

- Lactated Ringer's Injection has an electrolyte composition and concentration quite similar to that of the extracellular fluid.
- Even large volumes of infusion of Ringer's Lactate do not easily cause sodium excess and hyperchloremic acidosis.
- It expands circulating blood volume by approximating the fluid and electrolyte composition of the blood.
- Provides the following electrolytes in each liter of fluid:

Sodium	130 mEq.
Chloride	108.7 mEq.
Potassium	4 mEq.
Calcium	2.7 mEq.
Bicarbonate(as Lactate)	28 mEq.

- Lactate is metabolized by the liver and converted to bicarbonate. One mole of lactate is metabolized in the body to produce one mole of bicarbonate. Therefore its administration has the same effect as that of bicarbonate.
- The presence of lactate not only eliminates any chances of dilutional acidosis, but also aids in the correction of mild acidosis.
- The infusion of Ringer's Lactate does not induce hypokalemia and hypocalcemia as compared to normal saline.
- The pH range is 6.0 - 7.5.

Indications

- Hypovolemic states including dehydration and hemorrhage. Indicated as the initial therapy for rehydration in severe diarrhea and vomiting. Also recommended by the World Health Organization for rehydration in severe dehydration due to diarrhea in patients of all age groups.
- Trauma.
- Burns
- Also indicated for the prevention and replenishment of extracellular fluid before, during and after surgery.
- Environmental emergencies such as severe perspiration leading to dehydration and heat illness.
- As a vehicle for Oxytocin injection, for the induction of labor or abortion.
- Can be used in children and neonates for keeping the vein open.

Dosage and Administration

The dose is dependent upon the age, weight and clinical condition of the patient.

Rehydration Therapy: In severe cases of diarrhea and vomiting, Ringer's Lactate **(Ringolact)** is indicated for the initial therapy and should be administered in a bolus dose of 20-30 ml/Kg.

Burns: When treating burned patients, the Parkland burn formula can be used.

Parkland Formula: 4ml x %Burn x Weight (kg)

50% of this amount should be given over the 1st 8 hours post burn and the rest over the next 16 hours.

Hemorrhage: Fluid resuscitation with Lactated Ringer's Injection for blood loss requires 3ml. of Lactated Ringer's Injection for every 1ml. of blood loss.

Duration of Action and Excretion

Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present. It is a balanced salt solution and when infused about 25% is retained in the ECF.

Adverse Effects

- Fluid overload.
- Congestive heart failure.

Contraindications

- Congestive heart failure.
- Renal failure.

Precautions

- Care is required in patients with cardiac failure and severe liver damage and in cases where salt intake is restricted as the solution contains sodium chloride 6.0 grams/Liter and sodium lactate 3.1 grams/Liter.
- Caution should be exercised in patients with hypertonic dehydration, alkalosis and those having disturbances of lactic acid metabolism.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 137.
Isosmotic solution (272 mOsm/L)
(Although the tonicity and osmolarity are slightly less, nevertheless Ringer's Lactate is considered to be isotonic and isosmotic).

Caloric Value

Nil

Pharmaceutical Precautions

- Lactated Ringer's Injection should not be mixed with citric acid added blood, and preparations containing phosphoric acid or carbonic acid, as the calcium content of this solution may form precipitates with these acids.
- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.5

Packaging

500ml and 1000ml in Plabottle.

RINGOLACT-D

(5% Dextrose and Lactated Ringer's Injection)

Therapeutic Class

Isotonic crystalloid solution and carbohydrate source.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Calcium Chloride $2H_2O$	0.2 grams
Potassium Chloride	0.3 grams
Sodium Chloride	6.0 grams
Sodium Lactate	3.1 grams
Anhydrous Dextrose	50.0 grams
Water for Injections	q.s.

Pharmacological Effects

- 5% Dextrose and Lactated Ringer's Injection has an electrolyte composition and concentration similar to that of the extracellular fluid along with added dextrose which acts as a caloric source.
- In stressful situations, e.g. surgery, provision of dextrose prevents gluconeogenesis, which otherwise occurs due to catabolism of fats and proteins.
- Provides calories for some metabolic needs. Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Even large volumes of infusion of the solution do not easily cause sodium excess and hyperchloremic acidosis.
- It expands circulating blood volume by approximating the fluid and electrolyte composition of the blood along with providing energy.
- Provides the following electrolytes in each liter of fluid:

Sodium	130 mEq.
Chloride	108.7 mEq.
Potassium	4 mEq.
Calcium	2.7 mEq.
Bicarbonate(as Lactate)	28 mEq.

- Lactate is metabolized by the liver and converted to bicarbonate. One mole of lactate is metabolized in the body to produce one mole of bicarbonate. Therefore its administration has the same effect as that of bicarbonate.
- The presence of lactate not only eliminates any chances of dilutional acidosis, but also aids in the correction of mild acidosis.
- The infusion of 5% Dextrose and Ringer's Lactate, does not induce hypokalemia and hypocalcemia as compared to normal saline.
- The pH range is 3.5 - 6.5.

Indications

- Hypovolemic states such as those induced by severe diarrhea and vomiting.
- Trauma and burns.
- Environmental emergencies such as severe perspiration leading to dehydration and heat illness.
- Also indicated for the prevention and replenishment of extracellular fluid before, during and after surgery.

Dosage and Administration

The usual infusion rate is 300-500 ml/hour (about 75-125 drops/minute) for adults and 50-100ml/hour (about 12-25 drops/minute) for children.

The dosage should be adjusted according to the age, weight and clinical condition of the patient. However, for non-diabetics, the maximum infusion rate of dextrose should be 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized.

Duration of Action and Excretion

- Passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.

Adverse Effects

- Fluid overload.
- Congestive heart failure.
- Phlebitis may occur.

Contraindications

- Congestive heart failure.
- Renal failure.
- Elevated blood glucose concentration.

Precautions

- Care is required in patients with cardiac failure and severe liver damage and in cases where salt intake is restricted as the solution contains sodium chloride 6.0 grams/Liter and sodium lactate 3.1 grams/Liter.
- Caution should be exercised in patients with hypertonic dehydration, alkalosis and those having disturbances of lactic acid metabolism.
- Monitor blood sugar levels.
- Monitor E.C.G. continuously.
- Frequently monitor blood pressure, pulse rate and respiratory rate.
- Frequently auscultate breath sounds for rales.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 137.
Hyperosmolar solution (550 mOsm/L)

Caloric Value

187 kCal/Liter

Pharmaceutical Precautions

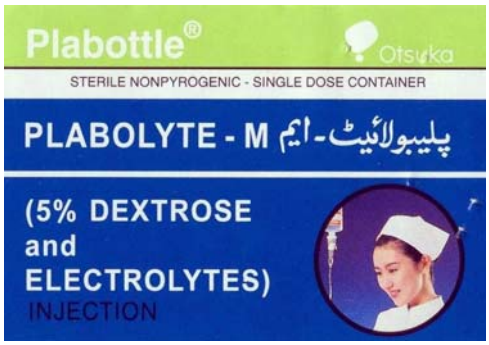
- 5% Dextrose and Lactated Ringer's Injection should not be mixed with citric acid added blood, and preparations containing phosphoric acid or carbonic acid, as the calcium content of this solution may form precipitates with these acids.
- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

500ml and 1000ml in Plabottle.

PLABOLYTE-M

(5% Dextrose and Electrolytes Injection)



Therapeutic Class

Hypotonic solution with electrolytes and carbohydrate source.

Description and Composition

A clear, colorless or slightly yellowish solution each 1000 ml. of which contains:

Calcium Chloride $2H_2O$	0.22 grams
Potassium Chloride	1.50 grams
Sodium Chloride	2.16 grams
Sodium Acetate $3H_2O$	3.13 grams
Anhydrous Dextrose	50.00 grams
Water for Injections	q.s.

Pharmacological Effects

- Plabolyte-M is a maintenance solution with high amounts of potassium in a homogenized form.
- It provides electrolytes along with calories for some metabolic needs and supplies daily requirements of water and electrolytes. Composition of this solution is based on the calculations made from daily water and electrolyte requirements of children suffering from hyponatremic dehydration and from average daily water and electrolyte requirements of normal adults.
- Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Spares body protein by providing carbohydrate for metabolism.
- Provides the following electrolytes in each liter of fluid:

Sodium	60 mEq.
Chloride	60 mEq.
Potassium	20 mEq.
Calcium	3 mEq.
Bicarbonate(as Acetate)	23 mEq.

- Osmolarity of Plabolyte-M is 442 mOsm/L. The fluid is hypotonic but hyperosmolar.
- The pH range is 5.1 – 5.3.

Indications

- Recommended as a maintenance solution for children with hyponatremic dehydration, such as due to severe diarrhea.
- Indicated in adults whose oral intake of water and electrolytes are insufficient due to various conditions.
- Recommended as a maintenance solution in adults during the late post-operative period as it also supplies some amount of energy.
- Especially useful in conditions requiring high amounts of potassium, such as maintenance phase of diarrhea and late post-operative period.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient and the quantity of water and electrolytes lost from the body. However, the usual adult dosage is 500-1000 ml. at one time by intravenous drip infusion. The infusion rate should be adjusted to provide 300-500 ml./hour (about 75-125 drops/minute) for adults, and 50-100 ml/hour (about 12-25 drops/minute) for children.

For non-diabetics, the infusion rate of dextrose should not exceed 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Hyperglycemia.
- Fluid overload.
- Hyperkalemia.

Contraindications

- Patients with hyperkalemia.
- Elevated blood glucose concentrations.

Precautions

- To avoid hyperkalemia, it is advisable to use the solution only when the urine output is more than 500 ml/24 hours or more than 20 ml/hour.
- In non-urgent situations the rate of potassium administration should not exceed 10 mEq/hour. In urgent conditions the rate may be increased up to 40 mEq/hour. In this circumstance cardiac monitoring is advisable.
- The solution should be used with care in patients with renal failure, oliguria, or azotemia.
- Care is required in patients with Addisons Disease without hyperkalemia.
- Caution should be exercised in severe burns without hyperkalemia, in cardiac failure and in diabetics.
- Monitoring of serum electrolytes and blood sugar levels is recommended during therapy.
- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.

Osmolarity and Tonicity

Hypotonic solution, having a tonicity of 83.
Hyper-osmolar solution (442 mOsm/L)

Caloric Value

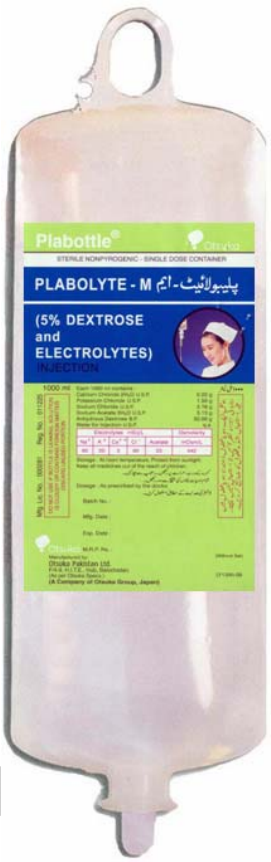
187 kCal/Liter

Pharmaceutical Precautions

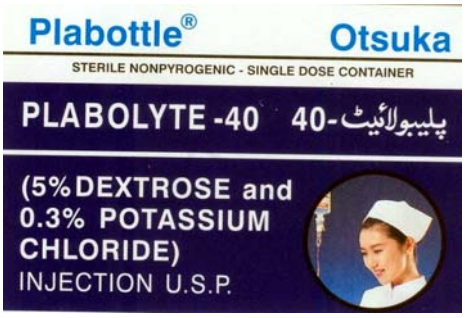
- Plabolyte-M should not be mixed with citric acid added blood, and preparations containing phosphoric acid or carbonic acid, as the calcium content of this solution may form precipitates with these acids.
- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 500ml and 1000ml in Plabottle.



PLABOLYTE-40



(5% Dextrose and 3% Potassium Chloride Injection U.S.P.)

Therapeutic Class

Crystalloid solution with a carbohydrate source.

Description and Composition

A clear, colorless solution each 1000 ml. of which contains:

Dextrose Monohydrate U.S.P.	50.0 grams
Potassium Chloride U.S.P.	3.0 grams
Water for Injections	q.s.

Pharmacological Effects

- Plabolyte-40 is a maintenance solution with a high amount of potassium in a homogenized form.
- Supplies water and potassium to fulfill daily requirements.
- Each 100mL provides 5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen, it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O. The brain does not require insulin for glucose metabolism.
- Spares body protein by providing carbohydrate for metabolism.
- Provides the following electrolytes in each liter of fluid:

Potassium	40 mEq.
Chloride	40 mEq.

- Osmolarity of Plabolyte-40 is 333 mOsm/L. The fluid is hypotonic but hyperosmolar.
- The pH range is 3.5 – 6.5.

Indications

- Recommended in conditions that require administration of high amounts of potassium along with dextrose as an energy source.

- Especially useful in late post-operative period to supplement the daily requirements of water, potassium and energy.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient. The rate of infusion should be adjusted to provide 10 mEq/hour of potassium. In urgent situations the rate may be increased to 40 mEq/hour, under cardiac monitoring.

For non-diabetics, the infusion rate of dextrose should not exceed 4mg/kg/minute. At this rate the hepatic glucose production is minimized and peripheral glucose uptake maximized.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Fluid overload.
- Water intoxication may occur if infused rapidly or in large amounts.
- Hyperglycemia.
- Hyperkalemia.

Contraindications

- Patients with hyperkalemia.
- Renal failure
- Elevated blood glucose concentrations.

Precautions

- To avoid hyperkalemia, it is advisable to use the solution only when the urine output is more than 500 ml/24 hours or more than 20 ml/hour.
- In non-urgent situations the rate of potassium administration should not exceed 10 mEq/hour. In urgent conditions the rate may be increased up to 40 mEq/hour. In this circumstance cardiac monitoring is advisable.
- The solution should be used with care in patients with renal failure, oliguria, or azotemia.

- Care is required in patients with Addisons Disease without hyperkalemia.
- Caution should be exercised in severe burns without hyperkalemia, in cardiac failure and in diabetics.
- Monitoring of serum electrolytes and blood sugar levels is recommended during therapy.
- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.

Osmolarity and Tonicity

Hypotonic solution, having a tonicity of 40.
Slightly hyper-osmolar solution (333 mOsm/L)

Caloric Value

170 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

- 1000ml in Plabottle.

OSMOTOL

(20% mannitol Intravenous Infusion B.P.)

Therapeutic Class

Osmotic diuretic

Description and Composition

A clear, colorless fluid, each 1000 ml. of which contains:

Mannitol B.P.	200.0 grams
Water for Injections B.P.	q.s.

Pharmacological Effects

- Large molecular size of this medication prevents its movement out of the vascular space. As such, an osmotic gradient is created which moves fluid from the tissues into the intravascular system.
- In the kidney, it moves into the glomerular filtrate which raises the osmotic pressure and induces diuresis.
- The pH range is 4.5 - 7.5.

Indications

- Treatment and prevention of cerebral edema.
- Reduction of intracranial pressure in neurosurgery.
- To reduce raised intraocular pressure prior to ophthalmic procedures.
- To increase urine flow in patients with acute renal failure.
- Promotion of excretion of toxic materials.
- Prophylaxis of acute renal failure.

Dosage and Administration

- The dosage and the rate of administration depends on the fluid requirements, urinary output and the condition being treated. The usual adult dose ranges from 50-200 grams/24 hours.
- Reduction of intracranial pressure:
  In adults usually 250-300 ml. of the solution infused rapidly over 15-30 minutes.
- Diuresis:
  50-200 grams over 24 hours in adults, preceded by a test dose of 200 mg/kg (about 60 ml. in a 50 kg. person) given over 3-5 minutes produces a diuresis of 30-50 ml/hour.

- Reduction of intraocular pressure:
  1.5-2.0 grams/kg. (about 10-13ml/kg) over a period of 30 minutes to obtain a prompt and maximal result. The dose should be given 1-1½ hours prior to surgery to achieve maximal effect.
- Excretion of toxic materials:
  While using as an adjunctive therapy for excretion of toxic materials the dosage depends on the fluid requirements and the urine output of the patient.
- The recommended dose for children is 200-500 mg/kg. I.V. over 30-60 minutes.
- Measurement of glomerular filtration rate:
  When mannitol is used for diagnostic purpose of measuring glomerular filtration rate, 100 ml. mannitol (20%) should be mixed with 180 ml. of normal saline and infused at a rate of 20 ml/minute.

Suggested Formula for Dose Calculation

In patients with intracerebral hemorrhage (ICH) and raised intracranial pressure (ICP), the total dose of mannitol can be calculated by considering the site of hemorrhage, volume of hematoma and the pretreated intracranial pressure reading.

Total dose of mannitol (mL of 20% mannitol) =

$$\frac{\{(X + 31.17900] \times Y - 3.39853 \times Z - 244.47590}{0.00752}$$

where:

X = pretreated ICP (mmH2O
Y = hemorrhage location; supratentorial ICH: Y = 0
Infratentorial ICH: Y = 1
Z = volume of hematoma (mL)

Duration of Action And Excretion

Mannitol is an obligatory osmotic diuretic. On intravenous administration it is confined to the extracellular space and only slightly metabolized. It acts within about 20 minutes and is rapidly excreted by the kidneys.

Adverse Effects

- Chest pain, chills, thrombophlebitis and visual disturbances.
- Hypertension.
- Congestive heart failure and pulmonary edema.
- Hypotension due to rapid volume depletion from large diuresis
- Blurred vision and convulsions may occur.
- Nausea and vomiting may occur.
- Electrolyte depletion, especially sodium.
- Irritation, pain and/or swelling at the injection site.

Contraindications

- Hypersensitivity to any component of the preparation
- Dehydration.
- Electrolyte depletion and hypovolemia.
- Suspected intracranial hemorrhage.
- Congestive heart failure.
- Acute pulmonary edema.
- Renal failure, unless a test dose has produced a diuretic response.

Precautions

- Avoid use in pregnant women. Safe use of mannitol has not been established with respect to adverse effects upon fetal development. It should not be used unless the potential benefits outweigh the possible hazards.
- Monitor ECG continuously.
- Monitor vital signs, level of consciousness, breath sounds and urine output closely during administration.
- The patient should have Foley's catheter in place.

Osmolarity and Tonicity

Hypotonic solution as it does not contain any cations.
Hyper-osmolar solution (1098 mOsm/L)

Caloric Value

Nil.

Pharmaceutical precautions

- The solution is incompatible with any medication in syringe or solution, and whole blood .
- Crystallizes at any temperature but room temperature.

- If crystals are observed, the preparation should be warmed to room temperature before administration.
- Administration through a filter is preferable.

Packaging

500ml.in plabottle.

References

Tan, Ge; Zhou, Jiyang; Yuan, Dongli; Sun, Shanquan. Formula for use of mannitol in patients with intracerebral hemorrhage and high intracranial pressure. Clinical Drug Investigation 2008; 28 (2): 81-87.

PERI SOLUTION
(Peritoneal Dialysis Solution)

Therapeutic Class

Dialysis solution.

Description and Composition

A clear, colorless solution, each 1000 ml. of which contains:

Calcium Chloride $2H_2O$	:	0.294 grams
Magnesium Chloride $6H_2O$	:	0.153 grams
Sodium Chloride	:	5.650 grams
Sodium Lactate	:	4.880 grams
Anhydrous Dextrose	:	15.0 grams
Water for Injections	:	q.s.

Pharmacological Effects

- The process of dialysis allows the selective removal of waste substances and excessive fluids from the blood.
- In peritoneal dialysis, the exchange of substances between the patients blood and the dialysis solution is made across the peritoneal membranes.
- The removal of fluid from the patients blood into the peritoneal cavity is facilitated by the high osmolarity of the solution, due to the presence of glucose in the dialysis solution.
- Provides calories for some metabolic needs. Each 100mL provides 1.5 grams of Dextrose and each gram of Dextrose Monohydrate provides 3.4kCal.
- The pH range is 5.1 – 5.3.

Indications

- For peritoneal dialysis whenever hemodialysis is difficult or impossible.

Dosage and Administration

This solution is intended for intraperitoneal administration only.

A careful assessment should be made regarding the mode of therapy (Intermittent Peritoneal Dialysis or Continuous Ambulatory Peritoneal

Dialysis), the frequency of treatment, exchange volume and the length of dialysis according to individual patient needs.

Intermittent Peritoneal Dialysis (IPD)

For dialysis of acute renal failure patients and maintenance dialysis of chronic renal failure patients the cycle of instillation and removal of dialysis fluid is repeated sequentially over a period of hours (8 to 36 hours) as many times as indicated by the condition of the patient. For chronic renal failure patients, maintenance dialysis often uses periodic dialysis (3 to 5 times weekly) for shorter time periods (8 to 14 hours per session).

Continuous Ambulatory Peritoneal Dialysis (CAPD)

For maintenance dialysis of chronic renal failure patients the solution should be used according to individual patient needs as assessed by the attending physician.

Adverse Effects

- Adverse reactions to peritoneal dialysis may be due to mechanical or solution related problems, contamination of equipment or improper technique in catheter placement.
- Complications of the procedure include abdominal pain, bleeding, peritonitis, subcutaneous infection around a chronic peritoneal catheter, catheter blockage, difficulty in fluid removal and ileus.
- Solution related adverse reactions may include fluid and electrolyte imbalances, hypovolemia, hypervolemia, hypotension or hypertension.
- The possible risk of infection should be minimized by the use of aseptic techniques throughout the procedure and its termination.
- Significant amounts of protein, amino acids and water soluble vitamins may be lost during peritoneal dialysis and replacement therapy should be provided as necessary.
- Safety in pregnancy and lactation have not been established.

Contraindications

- To be avoided in pregnancy, excessive obesity and behavioral disturbances rendering co-operation of the patient impossible in a procedure requiring relative but prolonged restriction of movement.

Precautions

- Care is required if peritoneal dialysis is undertaken for patients with certain abdominal conditions such as generalized peritonitis,

localized infectious processes of the abdomen, traumatic abdominal lesions, recent abdominal surgery, extensive adhesions, the presence of intra-abdominal masses greatly restricting the volume of the cavity e.g. tumors, polycystic kidneys, bowel distention, undiagnosed abdominal disease, abdominal wall infection, fecal fistula or colostomy.

- Care should also be taken if patients suffer from severe pulmonary disease or have recently undergone aortic graft replacement.
- It is advisable to carefully monitor the weight of the patient in order to avoid fluid overloading or underhydration, which can result in severe complications including congestive heart failure, volume depletion or shock.
- Plasma electrolyte concentration of patients must also be monitored regularly during the dialysis procedure.
- This dialysis solution is potassium-free, because dialysis may be performed to correct hyperkalemia. The addition of potassium chloride (up to 4 meq/L) may therefore be indicated to prevent severe hypokalemia in patients with normal potassium levels or hypokalemia. This should be undertaken only after careful evaluation of serum potassium.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 145.
Hyperosmolar solution (372 mOsm/L)

Caloric Value

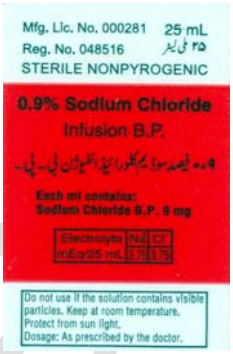
54 kCal/Liter

Pharmaceutical Precautions

- Store at room temperature.
- Do not administer unless the dialysis solution is clear and seal is intact.
- Do not use if bottle is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

Packaging

1000ml. in Plabottle.



0.9% Sodium Chloride Injection B.P.

(Sodium Chloride 0.9% w/v] (Normal Saline)

Therapeutic Class

Isotonic crystalloid salt solution

Description and Composition

A clear, colorless, sterile solution each 25 ml. of which contains:

Sodium Chloride B.P.	0.225 grams
Water for Injections	q.s.

Pharmacological Effects

- 0.9% Sodium Chloride Injection is considered to be a physiological solution as it is isotonic and isoosmotic.
- Infusion of large amounts can expands circulating volume by approximating sodium content of the blood.
- Provides the following electrolytes in each liter of fluid:

Sodium:	150 mEq
Chloride:	150 mEq

- Each ampoule of 25 mL provides 3.75 mEq of sodium and 3.75 mEq of chloride.
- The pH range is 3.5 - 7.5.

Indications

- Used as a diluting agent for I.V. medication
- Used for reconstitution of various I.V. injections
- Flushing of I.V. ports and cannula.
- As nasal drops for relieving congestion in children and adults.
- Used to dilute various bronchodilator solutions (such as procaterol, salbutamol, etc) for nebulization.
- Used for cleaning of small wounds
- Used as irrigation solution for eyes.

- Compresses (moistened gauze) of normal saline may also be used to reduce discomfort due to inflammation or skin irritation and to soften necrotic tissues.
- (Data sheet of specific medication should be referred to, before dilution, reconstitution or nebulization).

Dosage and Administration

0.9% Sodium Chloride Injection should be used in accordance with the age and clinical condition of the patient.

Duration of Action and Excretion

When infused, passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- If administered in large amounts can cause fluid overload, edema, electrolyte imbalance, hypertension and congestive heart failure.

Contraindications

- Congestive heart failure.

Precautions

- The sodium chloride content of 0.9% Sodium Chloride Injection is 0.225 grams/ampoule. Care is therefore required in those cases where salt intake is restricted, such as in hypertensive patients.
- Infusion of large volumes may cause dilutional acidosis due to the dilution of the bicarbonate concentration in the plasma (as the preparation does not contain bicarbonate).
- Care is required in conditions where hypokalemia and/or hypocalcemia exists or may arise as the infusion of the product can decrease the concentration of these electrolytes.
- Caution should be exercised in patients with renal failure and in those with reduced urinary output due to obstructive urinary tract diseases.
- Continuous infusion of 0.9% Sodium Chloride Injection may cause hypernatremia, unless free water is supplied along with it.

Tonicity and Osmolarity

Isotonic solution having a tonicity of 150.
Isosmotic solution (308 mOsm/L)

Caloric Value

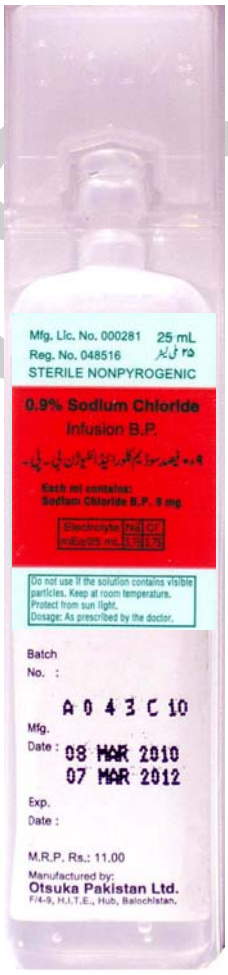
Nil

Pharmaceutical Precautions

- Normal Saline is compatible with almost all drugs. Therefore it can usually be mixed and used with other injectable medicines. However data sheet of the medication should be referred to, before admixture.
- Store at room temperature. Protect from sunlight.
- Do not use if ampoule is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.
- Shelf life is 5 years from the date of manufacturing.

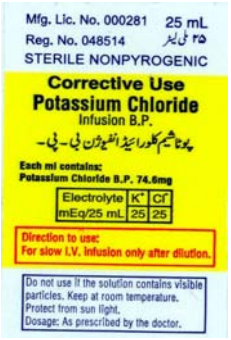
Packaging

- 25 mL. in polyolefin, twist-off, plastic ampoules.



Potassium Chloride Injection

(Potassium Chloride 7.46% w/v)



Therapeutic Class

Hypertonic crystalloid salt solution

Description and Composition

A clear, colorless, sterile solution each 25 ml. of which contains:

Potassium Chloride B.P.	1.865 grams
Water for Injections	q.s.

Pharmacological Effects

- When potassium depletion is severe and/or life-threatening cardiovascular or neuromuscular complications, are imminent, potassium should be replaced through intravenous administration, as the chloride salt.
- Potassium is better retained in the extracellular space if given along with chloride.
- Provides the following electrolytes in each liter of fluid:

Potassium:	1000 mEq
Chloride:	1000 mEq

- Each ampoule of 25 mL provides 25 mEq of sodium and 25 mEq of chloride.
- The pH range is 3.5 - 7.5

Indications

- Management of hypokalemia

Dosage and Administration

The product should be used in accordance with the clinical condition of the patient and age.

Duration of Action and Excretion

When infused, passes out of the blood stream quite rapidly, especially when normal renal function and renal blood flow are present.

Adverse Effects

- If administered in large amounts can cause fluid overload.
- Electrolyte imbalance may occur.
- Arrhythmias
- Hyperkalemia
- Phlebitis may occur, particularly if potassium is administered at a concentration more than 40 mEq/L and rate exceeding 10 mEq/hour, through peripheral veins.

Contraindications

- Patients with hyperkalemia.
- Oliguria and anuria

Warnings

- Should NEVER be infused directly into the circulation. Should always be diluted with appropriate fluid before administration.

Precautions

- In non-urgent situations the rate of potassium administration should not exceed 10 mEq/hour. In urgent conditions the rate may be increased upto 40 mEq/hour. In this circumstance cardiac monitoring is advisable.
- The solution should be used with care in patients with renal failure, oliguria, or azotemia.
- Care is required in patients with Addison's Disease without hyperkalemia.
- Monitoring of urine output is advisable (20 ml/hour or 1 ml/kg/hour).
- Care is required to avoid volume overload.
- Caution should be exercised in severe burns without hyperkalemia, in cardiac failure and in diabetics.
- Monitoring of serum electrolytes is recommended during therapy.
- Use sterile technique in venipuncture and equipment assembly.
- Monitor E.C.G. continuously.
- Monitor blood pressure, pulse rate and respiratory rate frequently.

Osmolarity and Tonicity

Hypotonic solution, having a tonicity of 1000.
Hyper-osmolar solution (2000 mOsm/L)

Caloric Value

Nil

Pharmaceutical Precautions

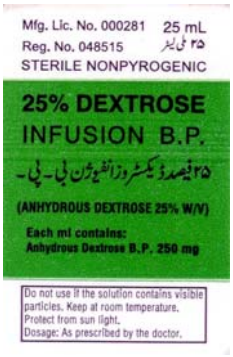
- Store at room temperature. Protect from sunlight.
- Do not use if ampoule is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.
- Shelf life is 5 years from the date of manufacturing.

Packaging

- 25 mL in polyethylene, twist-off, plastic ampoules..

25% DEXTROSE INJECTION B.P.

(Anhydrous Dextrose 25% w/v)



Therapeutic Class

Hypotonic water and carbohydrate source

Description and Composition

A clear, colorless, sterile solution each 25 ml. of which contains:

Anhydrous Dextrose	6.25grams
Water for Injections	q.s.

Pharmacological Effects

- Provides calories for some metabolic needs. Each 25mL provides 6.25 grams of Dextrose and each gram of AnhydrousDextrose provides 3.7kCal. Depending on the presence of insulin, glucose enters cells and is broken down to pyruvate. With adequate oxygen,it enters the Kreb's cycle in the mitochondria and is converted into energy (A.T.P.), CO_2 and H_2O.
- Supplies body water for hydration.
- Spares body protein by providing carbohydrate for metabolism.
- Osmolarity of 25% Dextrose is 1389 mOsm/L.
- The fluid is isotonic when in the container. After administration, the dextrose is quickly metabolized in the body, leaving only water - a hypotonic fluid.
- The pH range is 3.5 - 6.5.

Indications

- Hypoglycemia
- Used as a source of energy particularly in total parenteral nutrition.

Dosage and Administration

The dose is dependent upon the age, weight, and clinical condition of the patient. For non-diabetics, the maximum infusion rate should be 4 mg/kg/minute.

Slow administration is recommended. Administration through central veins is preferable due to high osmolarity.

Duration of Action and Excretion

- Glucose use depends on metabolic rate. It is stored in the liver and muscle as glycogen.
- Water use depends on clinical state of patient, body temperature and renal function. Excreted through the skin, lungs, and kidneys.

Adverse Effects

- Hyperglycemia.
- Fluid overload, hyponatremia, hypokalemia and water intoxication may result if infused in large amounts.
- Administration through peripheral veins can be irritating and can cause phlebitis.

Contraindications

- Elevated blood glucose concentrations.
- Patients at risk for increased intracranial pressure.
- Patients who have an acute neurological dysfunction.
- Hypovolemic states.
- Patients at risk for third-space fluid shifts**.**

Precautions

- Since the tonicity is low, avoid using in head injury patients.
- Use sterile technique in venipuncture and equipment assembly.
- Do not use solution if outdated, cloudy or the seal is not intact.
- Monitoring of blood glucose is advisable.

Osmolarity and Tonicity

Hypotonic solution as it does not contain any cations.
Hyper-osmolar solution (1389 mOsm/L)

Caloric Value

Approximately 23 kCal/ampoule

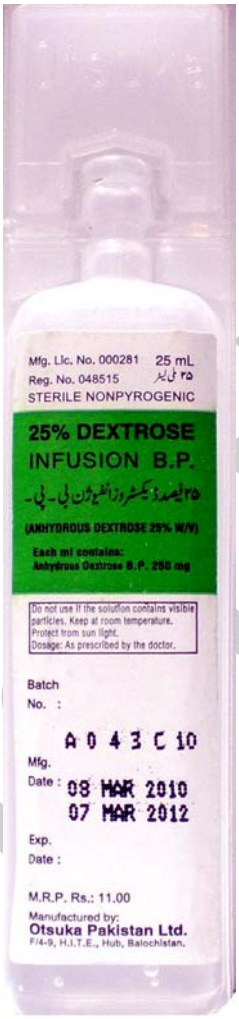
Pharmaceutical Precautions

- Store at room temperature. Protect from sunlight.
- Do not use if ampoule is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.

- Shelf life is 4 years from the date of manufacturing.

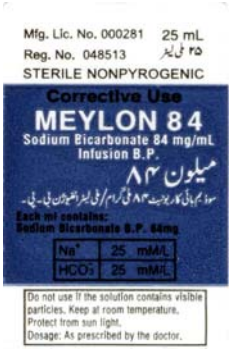
Packaging

- 25 mL in polyethylene, twist-off, plastic ampoules.



MEYLON 84

(8.4% Sodium Bicarbonate Intravenous Infusion B.P.)



Therapeutic Class

Systemic Alkalinisation Electrolyte Solution

Description and Composition

A clear, colorless, sterile solution each 25 ml. of which contains:

Sodium Bicarbonate B.P.	2.1 grams
Water for Injections	q.s.

Pharmacological Effects

- Bicarbonate is an alkalinizing agent and intravenous bicarbonate containing salts are often used to manage severe metabolic acidosis.
- Systemic alkali therapy acting as a buffer, helps in correction of acidosis and improves hemodynamic status.
- Intravenous infusion of sodium bicarbonate can enhance the excretion of salicylate by elevating intraluminal pH. This helps in secretion and trapping of salicylate in the tubular lumen.
- Provides the following electrolytes in each liter of fluid:

Sodium:	1000 mEq
Bicarbonate:	1000 mEq

- Each ampoule of 25 mL provides 25 mEq of sodium and 25 mEq of bicarbonate.
- The pH range is 7.5 – 9.5

Indications

- In management of metabolic acidosis such as ketoacidosis, hyperchloremic acidosis and lactic acidosis.
- Bicarbonate therapy is also indicated for severe metabolic acidosis after cardiac arrest.
- Management of overdosage or poisoning with toxins such as salicylate, methanol and ethylene glycol in conjunction with other measures.

Dosage and Administration

Bicarbonate solution should be used in accordance with the weight and clinical condition of the patient. Generally, sufficient bicarbonate should be administered to achieve pH levels above 7.1. The amount of bicarbonate required varies and also depends upon the rate of ongoing acid production.

As a general guideline, the amount of bicarbonate administered is determined as follows:

- Desired increase in bicarbonate concentration x 0.5 x body weight (kg)

No more than half of bicarbonate concentration deficit should be corrected over a 3-4 hour period without monitoring arterial blood gases. The response to bicarbonate administration should be closely monitored to avoid volume overload and induction of alkalosis. In severe cases, dialysis with bicarbonate dialysate should be considered.

Adverse Effects

- Hypernatremia and hyperosmolarity may occur.
- Hypokalemia. Correction of acidosis leads to movement of potassium inside the cells causing hypokalemia.
- Hypercapnia amy occur. Bicarbonate administration can result in a rapid increase in PCO2 that can diffuse across cell membranes worsening intracellular acidosis.
- Alkalosis, tetany and carpopedal spasm may occur. Rapid correction of metabolic acidosis can lead to tetany as a result of a decrease in ionized calcium concentrations.

Contraindications

- Alkalosis.
- Renal insufficiency

Precautions

- The sodium bicarbonate content of Meylon 84 is 84 mg/mL. Care is therefore required in those cases where salt intake is restricted, such as in hypertensive patients, congestive heart failure or pre-eclampsia. Care is required to avoid volume overload.
- Care is required in patients with preexisting potassium deficiency as it can promote movement of extracellular potassium into the cells and thus worsen hypokalemia. Cardiac monitoring for arrhythmias is essential in such patients.

- Overcorrection of acidosis can lead to alkalosis with the risk of tetany.
- Care is required in administration as extravasation of the solution may result in tissue necrosis at the site of administration.

Overdosage

Excessive administration may lead to metabolic alkalosis, hypokalemia and tetany. Symptoms may include tiredness, muscular weakness, shortness of breath and muscle twitching.

Management consists mainly of appropriate correction of electrolyte balance. Replacement of potassium, calcium and chloride are of particular importance.

Tonicity and Osmolarity

Hypertonic solution having a tonicity of 1000.
Hyperosmotic solution (~ 2000 mOsm/L)

Caloric Value

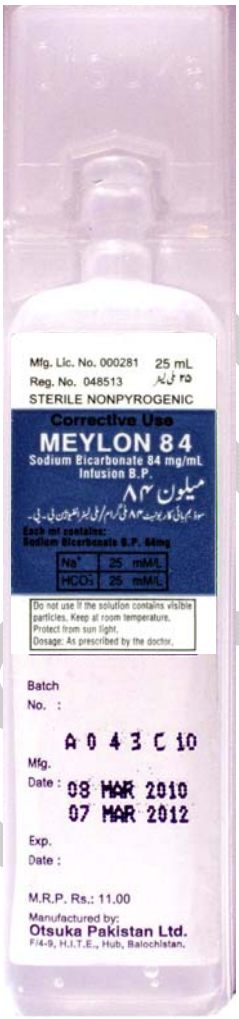
Nil

Pharmaceutical Precautions

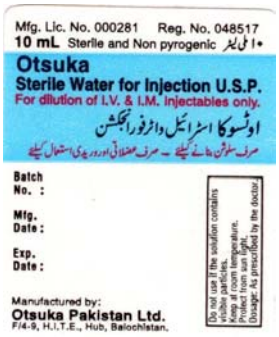
- Store at room temperature. Protect from sunlight.
- Do not use if ampoule is leaking, solution is cloudy or contains foreign matter.
- Discard unused portion.
- Keep all medicines out of the reach of children.
- Shelf life is three years from the date of manufacturing

Packaging

- 25 mL. in polyethylene, twist-off, plastic ampoules.



Water for Injections B.P.
(Sterile Water)



Therapeutic Class

Water for Injections is a non-isotonic solution.

Description and Composition

A clear, colorless, sterile, non-isotonic solution, ready-to-use, each ampoule of which contains:

Water for Injections B.P.	10 mL

It does not contain any preservatives.

Pharmacological Effects

- Water for Injections is considered to be a non-isotonic solution.
- Water for Injection is water for the preparation of medicines for parenteral administration in which water is used as a vehicle and for dissolving or diluting substances or preparation for parenteral administration.
- The chemical name is hydrogen oxide and its molecular formula is H_2O.
- The molecular weight is 18.02.

Indications

- Water for Injections is used for the reconstitution and preparation of medicines for parenteral administration and for dissolving or diluting substances or preparation for parenteral administration.

Dosage and Administration

The dosage for Water for Injections is the amount required to reconstitute or prepare other medicines for parenteral administration. Ensure that all solutions prepared with Water for Injections are isotonic before use (see **Precautions**).

Appropriate solubility, dilution and compatability with other additives must be ensured. The product information of relevant product should be referred to for ascertaining the maximum time between aseptic preparation and administration.

Solutions prepared with Water for Injections may be administered intravenously, intramuscularly or subcutaneously.

Adverse Effects

- No adverse reactions are known to be associated with Water for Injections. There should be no adverse reaction to Water for Injections if used as indicated to dissolve compatible substances to form an isotonic solution prior to injection.

- Injection of Water for Injections without the addition of solute may result in cell damage due to hypotonic effects (see **Precautions** and **Overdosage**).

Contraindications

- Incompatability or inappropriate solubility with the substance / drug being reconstituted / prepared.

Precautions

- The product information of the substance / drug being prepared / reconstituted should be referred to before dissolving or diluting, to ensure that Water for Injections is the recommended solvent or diluent.

- Ensure that the solution prepared with Water for Injections is isotonic with blood before intravenous administration.

- Water for Injections has been administered to a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

- The Product Information of the medicine to be dissolved or diluted should be checked to ensure that it is appropriate for use during pregnancy.

- Water for Injections can be administered to women who are breast-feeding.

- The Product Information of the medicine to be dissolved or diluted should be checked to ensure that it is appropriate for use during lactation.

Overdosage

- Overdose with small volume presentations of Water for Injections is unlikely. If larger volumes of Water for Injections are inadvertently injected without first ensuring isotonicity, the hypotonic effects may include local cell damage or haemolysis.

- Electrolyte abnormalities are possible. The patient should be assessed and treated appropriately.

Tonicity and Osmolarity

Non-isotonic solution.

Hypo-osmolar solution

Caloric Value

Nil.

Pharmaceutical Precautions

- Aseptic technique must be used when preparing and administering solutions for parenteral use.
- Usually solutions are prepared immediately before use.
- Store below 25°C.
- Water for Injections is for use in one patient on one occasion only.
- Discard any unused portion.

Packaging

- 10 mL plastic ampoules.

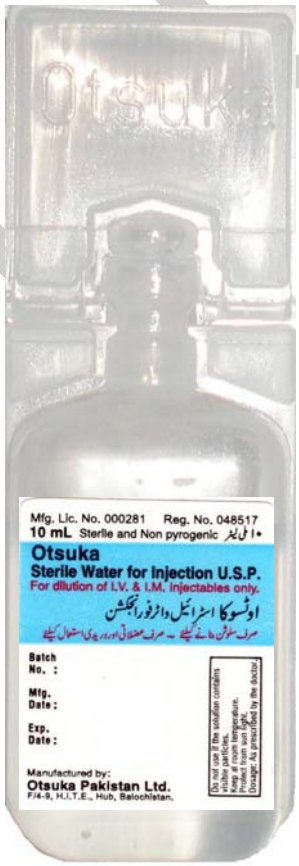


Table of Otsuka IV Solution Characteristics

Large Volume Parenterals

Brand Name	Generic Name	Electrolytes (mEq/L)							Dextrose (as monohydrate) (gms/L)	Calories (kCal/L)	Tonicity (as total cations)	Osmolarity (mOsm/L)	Packing (mL)
		Standard	Na+	K+	Ca++	Mg+	Cl-	Lactate					
Pladex-5	5% Dextrose Intravenous Infusion	B.P.	-	-	-	-	-	-	55	187	-	278	100, 500, 1000
Pladex-10	10% Dextrose Intravenous Infusion	B.P.	-	-	-	-	-	-	110	374	-	556	500, 1000
25% Dextrose Injection	25% Dextrose Injection	B.P.	-	-	-	-	-	-	275	935	-	1389	1000
Plasaline	0.9% Sodium Chloride Intravenous Infusion (Normal Saline)	B.P.	150	-	-	-	150	-	-	-	150	308	100, 500, 1000
Pladexsal	5% Dextrose and 0.9% Sodium Chloride Injection	U.S.P.	154	-	-	-	154	-	50	170	154	560	500, 1000
Pladexsal ½	5% Dextrose and 0.45% Sodium Chloride Injection	U.S.P.	77	-	-	-	77	-	50	170	77	406	500
Pladexsal 1/3	3.3% Dextrose and 0.3% Sodium Chloride Injection	U.S.P.	51	-	-	-	51	-	33	112	51	269	500
Pladexsal 1/5	0.18% Sodium Chloride and 4.3% Dextrose Intravenous Infusion	B.P.	30	-	-	-	30	-	47	160	30	300	500
Nisf Normal Saline	0.45% Sodium Chloride Injection	U.S.P.	77	-	-	-	77	-	-	-	77	154	1000
Ringer's Solution	Compound Sodium Chloride Injection	B.P.C.	147	4	2.2	-	156	-	-	-	153	309	500
Ringolact	Lactated Ringer's Injection	U.S.P.	130	4	2.7	-	108.7	28	-	-	137	272	500, 1000
Ringolact-D	5% Dextrose and Lactated Ringer's Injection	U.S.P.	130	4	2.7	-	108.7	28	50	170	137	525	500, 1000
Plabolyte-M	5% Dextrose and Electrolytes Injection	U.S.P.	60	20	3	-	60	23 (acetate)	55	187	83	442	500, 1000
Plabolyte-40	5% Dextrose and 0.3% Potassium Chloride inection	U.S.P.	-	40	-		40	-	50	170	40	333	1000
Osmotol	20% Mannitol Intravenous Infusion	B.P.	-	-	-	-	-	-	-	-	-	1098	500
Peri Solution	Peritoneal Dialysis Solution	-	140	-	4	1.5	102	43.5	16	54	145	372	1000

Small Volume Parenterals

Brand Name	Generic Name	Electrolytes (mEq/25 mL)							Dextrose (as anhydrous) (gms/25 mL)	Calories (kCal/25 mL)	Tonicity (as total cations)	Osmolarity (mOsm/L)	Packing (mL)
		Standard	Na+	K+	Ca++	Mg+	Cl-	Bicarbonate					
0.9% Sodium Chloride Injection B.P.	Sodium Chloride 0.9% w/v (Normal Saline)	B.P.	3.75	-	-	-	3.75	-	-	-	3.75	308	25
Potassium Chloride Injection	Potassium Chloride 7.46% w/v	B.P.	-	25	-	-	25	-	-	-	25	2000	25
25% Dextrose Injection B.P.	Anhydrous Dextrose 25% w/v	B.P.	-	-	-	-	-	-	6.25	~23	-	1389	25
Meylon 84	8.4% Sodium Bicarbonate Intravenous Infusion B.P.	B.P.	25	-	-	-	-	25	-	-	25	~2000	25
Water for Injections B.P.	Sterile Water	B.P.	-	-	-	-	-	-	-	-	-	0	10