L.3 BODY FLUIDS

Type of body fluids

Water is the main fluid constituent of human body. Rough estimates suggest that water represent nearly two-thirds (60%-70%) of adult total body weight. This percentage is said to be of *LEAN body mass (LBM)*, which is a hypothetical concept that refers to a person's body weight excluding fat tissue.

In order to function properly, the human body needs to maintain *constant volume* and *balanced composition* of body fluids: i.e. optimum **homeostasis** state. This fluid component in different tissue compartments is in fact in constant exchange, along with solutes, both internally (among body compartments) and externally (with the environment).

NB: Solutes may either be:
Electrolytes (e.g. Na+, K+, Cl-, HCO3-, Mg++, Ca++)
Non-electrolyte (e.g. glucose, urea, creatinine)

Water intake is the first step in regulating this balanced state to attain stability of countless physiological processes including, but not limited to, temperature regulation, circulation, digestion, metabolism, secretion, synthesis of essentials compounds and excretion of waste products.

Water is found in all parts of the human body from cellular level, through tissues and organs, and serves as the *stable physiological medium for transport processes*. It's found in continuous exchange among cells, interstitial fluid and capillaries, and is essential in maintaining adequate vascular volume and properly functioning blood circulation.

DAILY INTAKE OF WATER

Generally, we add water to our bodies from two main sources:

1. Direct ingestion

Consuming and ingestion of water as liquids or water in drinks and food (beverages), which adds nearly **2100 ml/day** to the body fluids.

2. Body synthesis

through oxidation of carbohydrates (CHO), and this adds nearly **200 ml/day**.
These two mechanisms collectively grant nearly 2300 ml/day total water intake.

The total intake of water is highly variable among different subjects (inter-personal variation) and also over time on daily basis for the same subject (intra-personal variation), depending on climate, age, physical activity, habits, and even personal preferences.

DAILY LOSS OF BODY WATER

Our body exchanges water continuously through sensible and insensible ways.

- **Water Loss by the Kidneys**

Urine is the final product of complex, multistage and highly regulated processes in the kidneys that allow our bodies to properly adjust and regulate water versus electrolyte excretion. The rate of excretion and concentration of urine and its constituents is the end product of sophisticated steps. These process once again varies according to climate change, age, general health and physical activities.

A typical example of how these processes work is during hot weather and/or fasting when the kidneys continuously monitor and adjust the quantities of water and electrolytes through absorption, excretion and re-absorption. In general, the normal range for 24-hour urine volume output ranges from **800 to 2,000 ml/day** among healthy adults.

- **Water Loss in Sweat**

Sweating is another method of water excretion that depends largely on several factors. The amount of water lost by sweating varies highly, depending on environmental temperature, physical activity and general health. The usual volume of sweat is around **100 ml/day**, but may increase significantly during, for ex., extremely hot weather or during heavy exercise to reach between 1-2 L/hour!

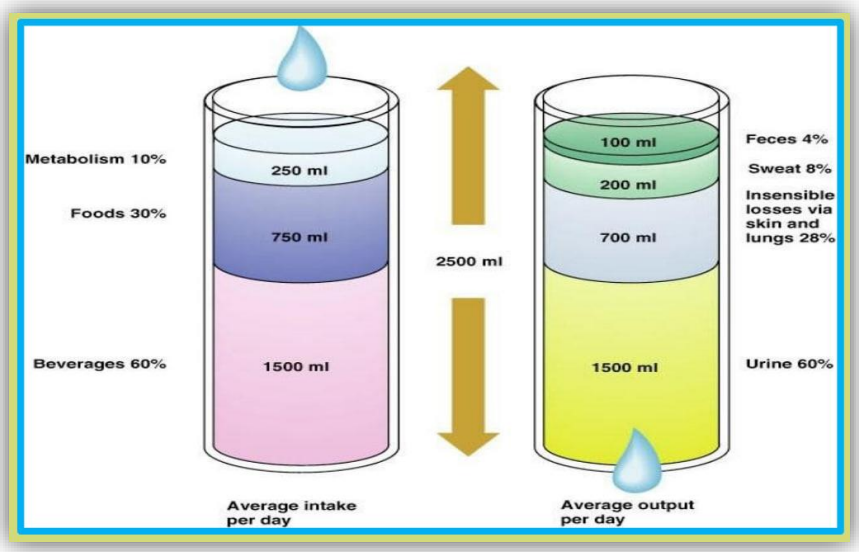
- **Water Loss in Feces**

In normal situation, only small quantities of water (~ **100 ml/day**) are usually excreted via stool. This loss also varies and may exceed few to several liters per day in case of severe watery diarrhea.

- **Insensible Water Loss**

Insensible loss of water is an important way through which the body regulate water exchange and temperature. The body uses this insensibly regulated method as we continuously loose of water by ***evaporation*** *from the respiratory system* and also by ***diffusion*** *through the skin*. Together these methods excrete nearly **700 ml of water per day** under normal conditions.

Insensible loss of water through skin happens independently and not related to sweating and occurs normally even in subjects whom congenitally lack sweat gland.

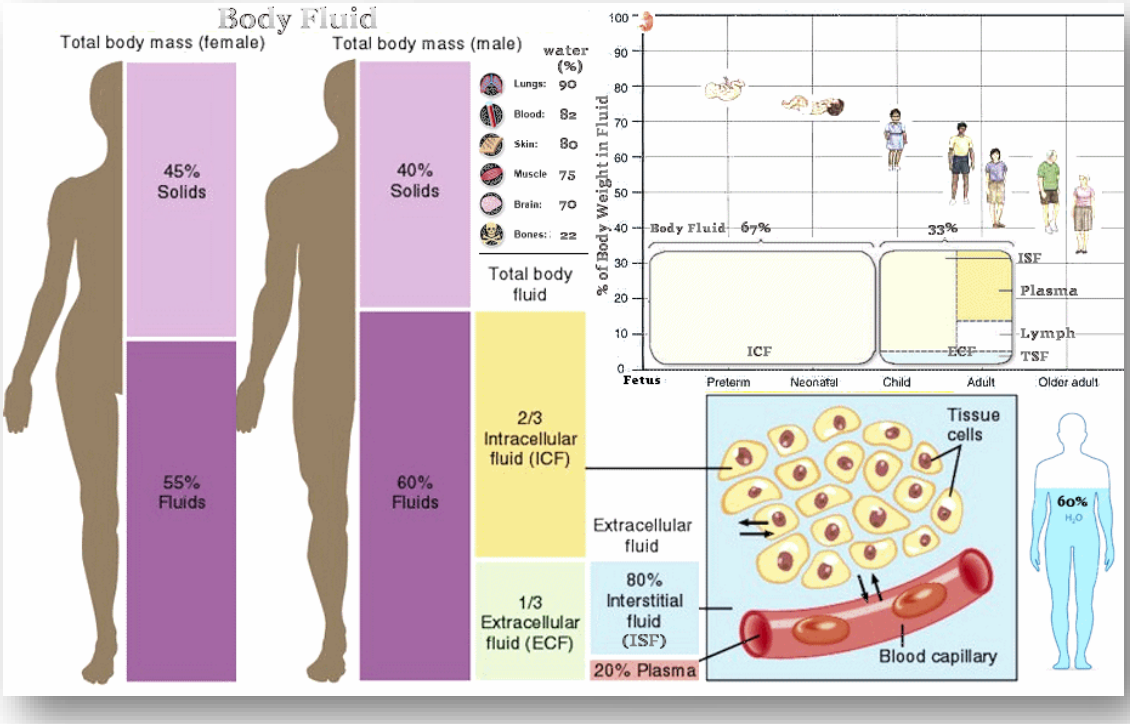


TOTAL BODY FLUID

In adult male, the total fluid volume is approximately 60% of the total body weight (varies with age: ~80% in newborn; 50-55% in elderly), compared to approximately 55% of the total body weight in adult female. This fluid is divided into two major compartments:

1) **Intracellular** ICF 2) **Extracellular** ECF compartments

The two compartments are separated by *cellular plasma membrane* (between the ICF & ECF) and *blood vessels walls* (between plasma and interstitial fluid).



I. Intracellular fluid (ICF)

The intracellular fluid compartment represents fluids content in all cells collectively and it constitutes nearly **40% of total body weight**. The different constituents found in the fluid of each cell contains its specific mixture, however, their concentrations are largely similar despite variations in cell structures, tissue type and functions. The composition of these fluids is similar in cells of different species of animals, humans, and even microorganisms.

II. Extracellular fluid (ECF)

Fluids that are found in the extracellular constitute collectively around **20%** of total body weight, or about **14** liters in a 70 kg adult man.

The two largest compartments of the extracellular fluid are:

1. The **interstitial fluid**

Represent more than three quarters **3/4** of ECF or approximately **11 liters**.

2. **The plasma**

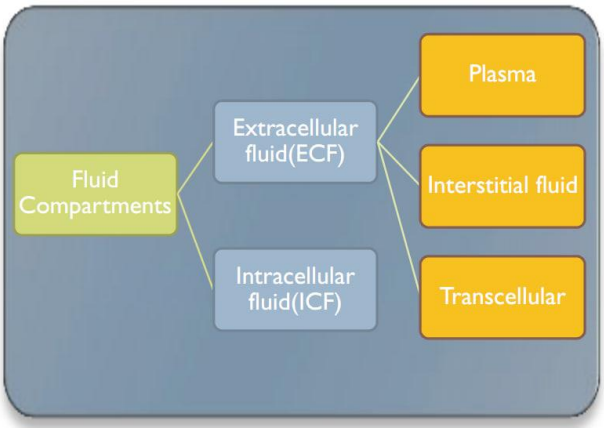
Represent almost one quarter **1/4** of the extracellular fluid, or about **3 liters.** Plasma is the non-cellular part of the blood. Substances are in constant exchanges with the interstitial fluid through the *special and highly permeable pores found in the capillary membranes* through which, proteins, solutes may be exchanged easily with the extracellular fluid compartment.

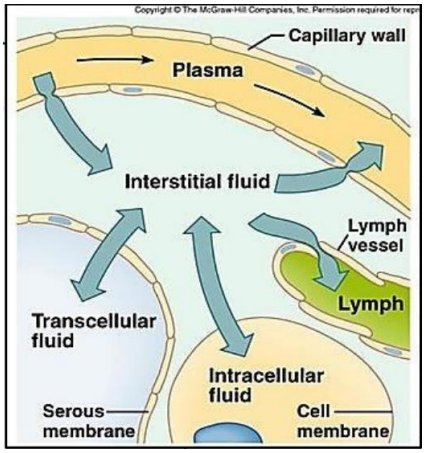
The other "smaller" compartment of the extracellular fluid is:

3. **Transcellular fluid**

Transcellular fluid is found in small amounts in specialized compartments and constitute nearly 1 to 2 liters. Fluid in this compartment is represented by the followings:

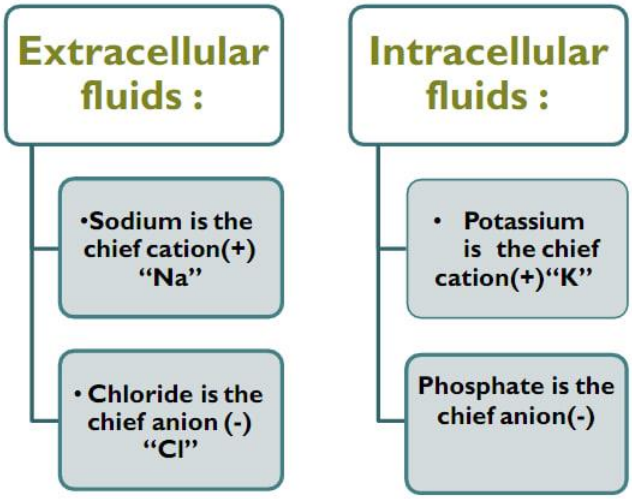
Synovial fluid;
Peritoneal fluid;
Pericardial fluid;
Intraocular (Vitreous humor) and
Cerebrospinal fluid (CSF).

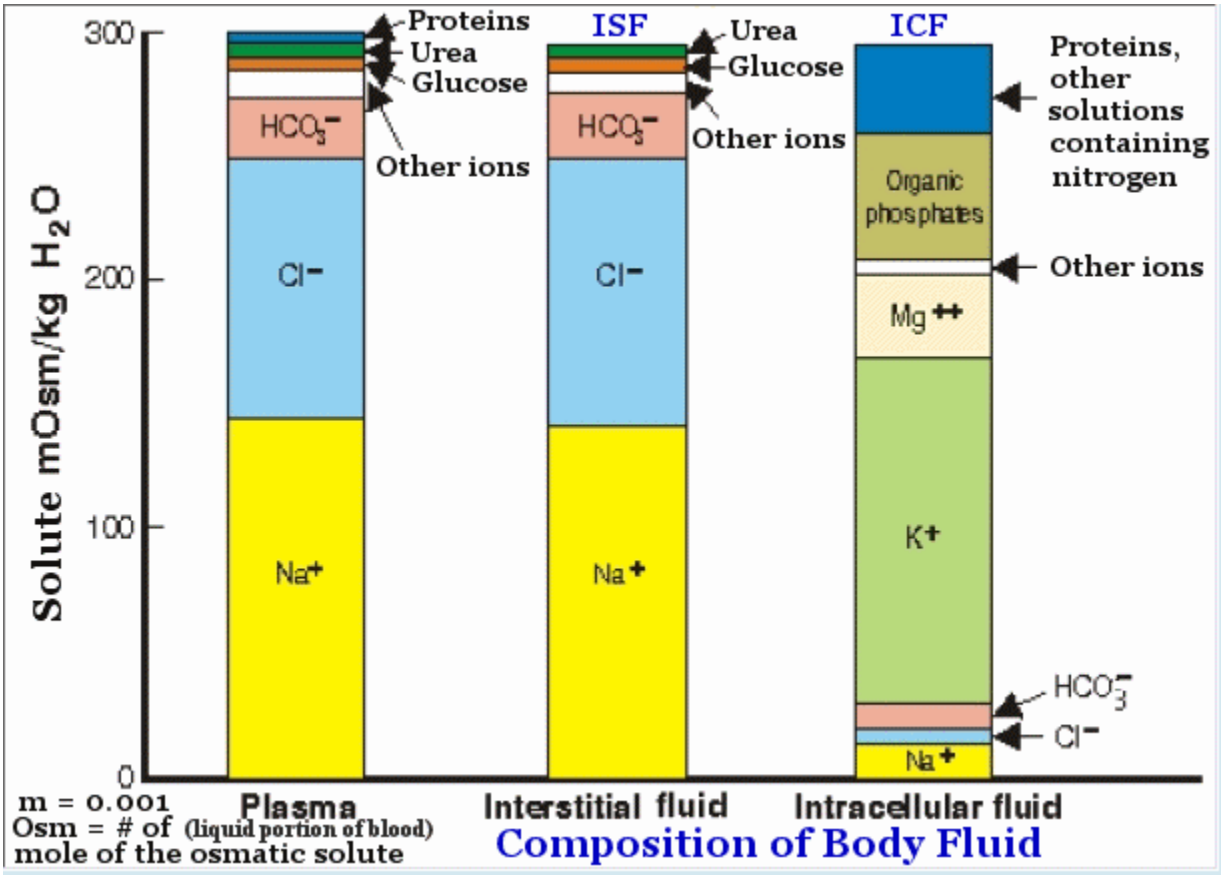




Constituents of extracellular and intracellular fluids

The **ECF** contains high amounts of sodium, chloride and bicarbonate ions, plus nutrients for cells, such as oxygen, glucose, fatty acids and amino acids … etc.
The **ICF** differs significantly from the ECF particularly, it contains large amount of potassium, magnesium and phosphate ions.



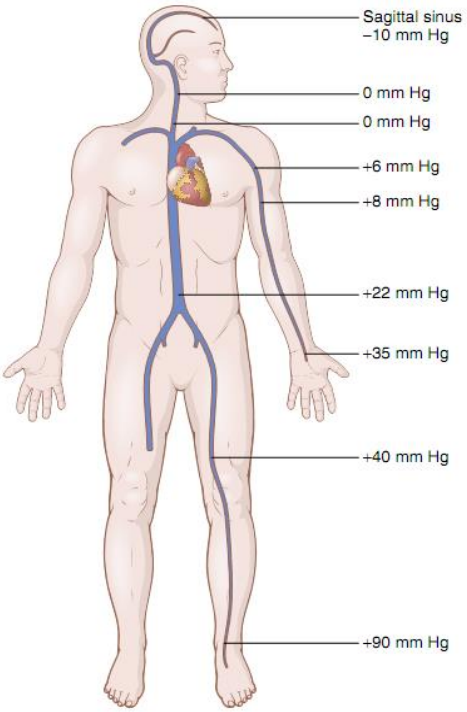


Major factors contribute to the movement of fluid

1) **Hydrostatic pressure (HP)**

HP refers to the pressure (or force) that is exerted, due to the force of gravity, by a fluid at equilibrium at any point of time (therefore is called *gravitational* or *hydrostatic* pressure). This pressure is built up by the weight of liquid and increases with the depth of the liquid above.

HP represents the ***outward*** pressure caused by fluid contained within a compartment and causes the movement of fluid between different compartments. HP is not constant and increases in proportion in relation to liquid's *density* and the local *gravity*. On the arterial end of capillaries, HP is high, because its driven by the force of cardiac contractility. Its higher in legs and feet due to gravity of blood.



Effects of HP on different veins in standing position

2) **Osmotic pressure (OP)**

The OP is the pressure caused by water at different concentrations due to the dilution of water by dissolved molecules (solutes) like salts and nutrients. It represents the minimum required pressure applied to a solution to *prevent* ***the inward flow*** of its pure solvent across a semipermeable membrane. It is proportional to the osmolality of a solution.

In blood vessels, fluids leave the plasma at the *arteriolar ends* of capillaries and enter the interstitial spaces because of the net outward force of HP (blood pressure effect).

Fluid returns to the plasma from the interstitial spaces at the *venular ends* of capillaries because of the net ***inward*** force of osmotic pressure (also known as colloid osmotic pressure) due to the role of plasma proteins.

The OP is created by osmotically active particles that are too big to cross the phospholipid barrier. This is largely determined by the concentration of albumin, which is the most available plasma protein found in blood.
As the HP is '***pushing***' fluid out and the OP is '***sucking***' fluid in, they are in effect working against each other.

Specialized Fluids of the Body

Lymph: A clear and colorless fluid 96% water and 4% solids

Milk: The complete natural food. Contain 83-87% water.

Cerebrospinal fluid (CSF): A clear, colorless liquid formed within the cavities of brain and around spinal cord. It regulates intracarnial pressure, serves as protective shock absorber and play a role in hunger sensation and eating behaviors

Amniotic fluid: A protective lliquid produced by amniotic membranes that also serves as medium of exchange of various substances.

Aqueous humor: It is a clear fluid filling the space in the front of the eyeball between the lens and cornea.

Sweat: It is secretion of sweat gland, regulates body temperature by cooling and evaporation. Water content of sweat varies from 99.2-99.7%

Tears: Tears are fluid produced by lachrymal glands. It is isotonic but becomes hypertonic due to evaporation as fluid passes over the cornea. Its main function include protecting the eye, lubricates the cornea and containing anti-microbial lysozymes.

L4. Edema

Fluid exchange occurs as bi-directional movement of soluble substances between the intravascular and the interstitial compartment.
Edema is the excess accumulation of body fluids in the extracellular (EC) or interstitial (IS) tissues resulting from an abnormal expansion in interstitial fluid volume.
This fluid excess is due to an *increased leakage from the blood* **and/or** *reduced removal by the lymph* system. Edema is commonly seen in the feet, ankles, and legs (gravity makes it apparent), but can also be found in many other location, such as the heart, lungs, liver, and kidneys.

TYPES OF EDEMA

1. Intracellular Edema

There are three conditions are likely to cause ICF swelling:

- Low Na+ concentration (Hyponatremia).
- Inadequate nutrient delivery to the cells.
- Reduction in activities of tissues metabolic systems.

Fluid components in different tissue compartment are in fact in constant exchange of fluid and solutes both internally (among body compartments) and externally with the surrounding environment. Reduction in blood flow to a tissue, decreases the levels oxygen and nutrients.
When blood flow is lower than the need to maintain normal tissue metabolism; the ionic pumps of the cell membrane are suppressed. The leaking Na+ accumulates *intracellularly* and is no longer be pumped out, leading to excess intracellular Na+ and subsequently *osmosis of water into the cells*.

This process may increase intracellular volume area of a tissue by 2-3 times than normal, which may lead to cellular swelling and eventually cell death.
Inflammation may cause intracellular edema when cell membrane permeability increases, allowing Na+ and other ions to diffuse inside, with subsequent osmosis and influx of water into the cells.

2. Extracellular Edema

Two causes may lead to accumulation of fluid in XCF compartment

A. *Excessive capillary fluid filtration* causes accumulation of interstitial fluid and an abnormal leakage of fluid from the plasma to the interstitial spaces across the capillaries.
B. *Inability of the lymph vessels to return fluid* and protein from the interstitial space back into the circulation, often called **lymphedema**.

If clearance of plasma proteins, which leak into the interstitial space is not effective; this leads to a rise in protein concentration. Higher plasma protein concentration increases the colloid osmotic pressure of the interstitial fluid, which *drags* extra fluid out of the capillaries leading to interstitial edema.

TYPES OF EXTRACELLULAR EDEMA

Peripheral edema

A type of edema that commonly affects soft tissues of lower limbs (primarily feet and ankles or even the legs), although it may be seen in upper limbs or even the face. The area looks swollen with tight or stretched skin. It's often reflects problems in kidneys, cardiovascular system or lymph drainage faults.

Pedal edema

Accumulation of fluid in soft tissues in the feet and legs. Commonly seen in elderly due to circulatory insufficiency and in pregnant women due to compression of pregnant uterus on major vessels in pelvis.

Lymphedema

Swelling in the arms or legs may be caused by diseased lymph tissues or lymph nodes. Cancer and Cancer treatment interventions like surgery and radiation. When the cancer cells invade the lymph tissue leading to blockage of normal lymph drainage.
This may also result from severe infections of the lymph nodes, such as parasitic infection caused by filaria nematodes (Wuchereria bancrofti), also called Elephantiasis.





Pulmonary edema

Accumulation of fluids in the chest cavity and inside the lung interstitial tissues. At early stages it only affects breathing when the patient lies down as fluids spread by gravity, however, with increased volume especially in acute pulmonary edema, it affects breathing even in sitting position. This type of edema is commonly associated with cardiac and renal failures as well as infections or cancers.

Cerebral edema

When fluids accumulate in intracranial space as a result of head injury, tumor, infections or with rupture of vessels in cerebrovascular accidents (stroke). It may reflect serious life-threatening state especially in presence of signs of increased intra-cranial pressure as in brain tumors.

Macular edema

Edema may involve the eye, when fluid accumulate in the *macula*, which represents photo-sensitive tissue center back of the retinal tissue of the of the eye. This type of edema may result from damage to blood vessels of the retina. Through ophthalmoscopy, the area looks congested and swollen.

CAUSES OF EDEMA

Causes of increased extracellular (EC)/ interstitial (IS) fluid volume and edema:

1. **Increase in capillary filtration hydrostatic pressure** (either at arterial side or venous side).
   - In acute or chronic kidney failure.
   - High venous pressure (as in heart failure, venous obstruction, gravity effect)
   - Excessive vasodilation due to rise in body temperature or by effect of drugs.
   - Venule constriction
2. **Increased capillary permeability**

This increased permeability may be due to:

   - Prolonged ischemia
   - Infections (Bacterial or parasitic infections)
   - Immune reactions: release of histamine & kinin and related substances.
   - Toxins
   - Burns.

3. **Decreased osmotic pressure gradient across capillary wall**
   - Low plasma protein (in urine: nephrotic syndrome or from skin in burns & wounds)
   - Reduced proteins production; as in liver disease
   - Accumulation of osmotically active substances in interstitial space
4. **Reduced lymph flow and drainage or blockage of lymph return**
   - Infections (e.g., filaria nematodes)
   - Cancer or during cancer treatment e.g. radiotherapy
   - During surgery
   - Congenital absence or abnormal of lymphatic vessels.

Figure 1. Left: Pitting edema. Right: edema caused by deep vein thrombosis (DVT)





MEASUREMENT OF BODY FLUID VOLUME

In order to estimate and measure the amount of fluid in the body, scientists use an indicator substance that diffuses uniformly in different compartment.
This may be done to estimate ECF and TBW (Total Body Water) using:

- Indicator dilution method
- Dye dilution method

Measurement of ECF

To measure ECF, we need substances that diffuses uniformly in the plasma and interstitial fluid **but do not permeate** through the cell membrane into the cell (intracellular). This may be done using: Radioactive sodium, Radioactive chloride, Radioactive iothalamate, thiosulfate ion or Inulin

Measurement of Total Body Water (TBW)

To measure the TBW, we need certain forms of water, which when infused into the blood, can mix with body water and then TBW may be calculated calculate using the dilution principle:
Radioactive water (tritium, $3H_2O$) or Heavy water (deuterium, $2H_2O$)

In order to measure the Intracellular volume,

Intracellular (ICF) volume = TBW – ECF volume

Plasma Volume (PV): measured using substances that remain in vascular spaces and **don't cross the capillary wall**. Plasma volume can be measured by using Evans blue dye, which binds to plasma proteins, or by injecting serum albumin labeled with radioactive iodine. The average PV in a normal 70 kg adult is approximately 3.5 L (50–55 mL/kg)

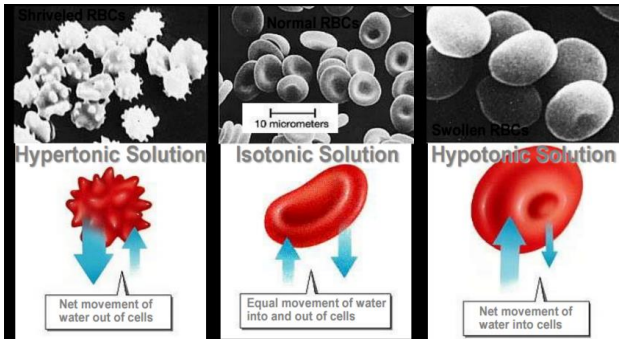
Interstitial fluid (ISF) volume = ECF volume - PV

DEHYDRATION

Dehydration means significant decrease in total body water content due to *pathologic* fluid loss, *reduced* fluid intake, or a *combination* of both.

Types of dehydration

1. Hypertonic (hypernatremic) dehydration: hypernatremia in ECF compartment, pool water from ICF
2. Hypotonic (hyponatremic) dehydration of ECF
3. Isotonic or (isonatremic) dehydration



Classification of dehydration

- Mild dehydration: when fluid loss is less than 5% of total body fluids.
- Moderate dehydration: when fluid loss is 5-9%.
- Severe dehydration: when fluid loss is 10 up to 15%.

Causes of dehydration

- Excess water loss: diarrhea and/or vomiting, urination or excessive sweating, burns.
- Reduced fluid intake due debilitating disease, terminal illness, and psychogenic causes.
- Diabetes Mellitus.

Signs and Symptoms of Dehydrations

Mild to moderate

- Excess thirst
- Dry mouth, headaches, tiredness and lack of energy
- Reduced sweating
- Reduced urine volume output with concentrated darker color
- Pale and dry skin
- Decreased tears

Severe dehydration
In addition to previous signs, intensity increases:

- Decrease in blood volume and cardiac output.
- Cardiac shock.
- Deep breath with rapid breathing and pulse.
- Highly reduced urine volume
- Confusion or disorientation and irritability

Very severe dehydration

- Organs damage e.g. kidneys, liver and brain.
- Mental depression and confusion
- Renal failure
- Coma.