Chapter 11

Fluids and electrolytes

11.1 Fluid disorders

All the biochemical processes in organism, necessary for life, take place in aqueous environment. The organism gains water in three ways:

- **Receiving pure water**. Organism receives 1200–1500 ml of pure water daily. This input is easily balanced.

- **Receiving water by food intake**. The amount of water in food is variable. Organism receives 1000 ml of water daily in this way. When no food is taken, we have to substitute not only the daily intake of water but the amount of water released from food as well.

- **Gaining water from biochemical processes**. Water is released in the process of oxidation. At about 35 ml of water is released during oxidation of 100g of proteins, 60 ml of water during oxidation of 100 g of glycids and 107 ml of water is released during oxidation of 100 g of lipids. We can estimate that the daily water intake is 300–500 ml in this way and in case of destructive metabolism even more.

The total water intake is approximately 2500 ml a day, but it is very variable. The organism adapts to this variability by adaptation of the elimination processes.

Elimination of water. Water is eliminated by urine, perspiration, respiration, stools and vomiting.

1. **Urine**. The kidneys are the most important regulation mechanism for the elimination of water and in this way for maintainance of homeostasis. They excrete all superfluous substances to urine and resorb necessary solutes from primary urine. Diuresis ranges between 1200–1500 ml a day.

2. **Perspiration**. Nearly 600–800 ml of water is lost daily during perspiratio insensibilis. It might be even more in some specific situations. Appart from extreme climatic and working conditions it is the fever which increases the loss of water during perspiration. Old people with fever may even develop a dehydration.

3. **Respiration**. 400–500 ml of water is lost daily by respiration. We have to mention that it is the loss of pure water without electrolytes in this case.

4. **Stools**. 100 ml of water is lost daily by stools. The loss of water and also electrolytes might be extreme during diarrhoea.

5. **Vomiting**. The clinic result of water loss might be very serious during some patological conditions. Very important is the loss of chlorides, which dominates in the clinic symptoms, and also the loss of sodium and H^+.

Water, that represents 60 per cent of body weight in males and 50 per cent in females, doesn't exist as pure water in the organism. It contains a lot of soluble substances – solutes which are mostly osmotic active. According to the qualitative and quantitative differences in content of soluble substances we classify the total body water into several compartments (spaces) where reciprocal exchange take place.

It is common and usefull to divide the total body water in the organism into extracellular and intracellular.

11.1.1 Extracellular fluid (ECF)

The extracellular fluid represents all the fluid outside the cells. Its total amount is approximately 14 litres in a 70 kg person (1/3 of total body fluid-TBF). We divide the extracellular fluid into: interstitial fluid, plasma, cerebrospinal fluid, intraocular fluid, gastrointestinal fluid and fluid in potential space.

Interstitial fluid represents the fluid in space between cells. The small part of it is free and flows through, but the bigger part is firmly captured in the space by hydrated substances. For example, collagen fibres absorb a large amount of fluid and the polymerised hyaluronic acid absorbs even a larger part of fluid. Hyaluronic acid forms a gelly substance between cells of most body tissues. Despite these bounds, soluble substances move freely by diffusion in the fluid.

Plasma is a part of extracellular fluid which continuously communicates with the interstitial fluid through capillary pores. The total capillary surface is extremely large and reaches 5000 square metres by estimation. It is easy to imagine the large part of fluid which can move from intravascular to extravascular space and vice versa. Keeping a relatively stable volume of intravascular fluid is conditioned by presence of proteins in plasma. Protein molecules are too big for crossing the capillary wall freely. The persistance of proteins in vascular space creates an oncotic power which has the tendency to retain water. The presence of oncotic pressure, which acts against the hydrostatic pressure, forms a base of Starling's thesis concerning factors which regulate exchange of fluid between vascular and extravascular space.

Many factors are involved in the regulation of fluid exchange between extra- and intravascular spaces. They are discussed in pathological conditions separately. Their effect on disorders in the fluid distribution between intra and extracellular spaces is not always clearly understood. For example there is a very week correlation between venous pressure and edema when only venous pressure is changed. The relation between hypoproteinemia and edema in nephrotic syndrom is known. But this edema may subside without measurable changes in concentration of plasma proteins. These facts signalize that the change of the capillary permeability is one of the mechanisms that might lead to imbalance between extra- and intracellular space. The capillary wall may be so altered by inflammation or physical or chemical trauma that a large amount of proteins can move to the interstitial fluid.

11.1.2 Fluid in other extracellular spaces

Cerebrospinal fluid is found in the brain and subarachnoid spaces surrounding the brain and the spinal cord. Due to a limited diffusion through the blood brain barrier (bbb) and due to the active secretion of some substances from the choroidal plexus as well, this fluid is slighly different from interstitial fluid and plasma. But the difference is not very large, and the cerebrospinal fluid can be considered to be a part of interstitial fluid.

Intraocular fluid has got similar characteristics to the cerebrospinal fluid. It is a product of both diffusion and secretion.

There are many spaces in the organism, containing only a small amount of fluid normally. But in some pathological conditions the amount of fluid can be very large in these spaces. They are known as **potential spaces**. For example it is the space between the visceral and parietal pleura. Under physiological conditions this space contains only 10–15 ml of viscous fluid but during disease this amount can reach several litres. Other potential spaces are the **peritoneal** cavity, **pericardial** cavity, **joint** cavities and **bursae**. The fluid in these potential spaces communicate freely with the surrounding interstitial fluid and so we consider it to be a part of interstitial fluid.

The fluid in **gastrointestinal tract** is extracellular fluid as well.

The amount of this liquid varies according to the intake and digestion of food. So it is possible to find nearly 1 litre of fluid in GIT. In certain pathological conditions, for example ileus, the amount of fluid can reach nearly 10 liters. The gastrointestinal fluid (except secretions of some glands) is, regarding electrolytes, similar to the interstitial fluid and so it is considered as a part of it.

11.1.3 Intracellular fluid (ICF)

About 25–40 liters of fluid (2/3 of the TBF) is called the **intracellular fluid**. The fluid in each cell contains its specific mixture of different components, but the concentration of these components is very similar. Due to this fact, the intracellular fluid of all the different types of cells is considered as one big compartment of fluid, even if it is an aggregate of trillions small compartments.

11.1.4 The characteristic of the main body fluid compartments

The knowledge of the individual compartments is essential for the understanding of the physiological mechanisms of homeostasis, for estimating the dose of different drugs and diagnostic substances and for the understanding of many **pathological situations** as well. For example, the relative portion of ECF to the whole body weight in newborn is higher than in adult. That is the reason why the newborn can not regulate the volume of ECF, and is relatively more susceptible to **dehydration**.

The composition of fluids determines the presence of **osmotic forces** which are important for the maintainance of volume in the main compartments of total body fluid (TBF).

They can by devided into three groups:

1. **Low molecular organic substances**, that can cross the cellular membrane relatively fast. For example we can mention urea, glucose, or amino acids that only slightly contribute to the distribution of water in the body in physiological conditions.

2. **High molecular organic substances**, mainly plasma proteins, are very essential in the exchange of water between circulating blood and interstitial fluid due to their oncotic pressure.

3. **Inorganic substances (electrolytes)** are the most important constituents of body fluids. They considerably contribute to distribution and retention of water in separated compartments of body fluids.

The composition of intracellular fluid differs from the composition of blood plasma in many cases. It is because Na^+ is the main cation and Cl^- is the main anion of ECF, whereas the intracellular fluid contains mainly K^+ and P^- (especially its phosporylated organic forms) together with protein anions. The maintainance of transmembral gradients for Na^+ and K^+ is one of the most energy demanding processes in the cells, provided by transport mechanisms.

Substance	Plasma (mmol/l)	Interstitial fluid (mmol/l)	Intracellular fluid (mmol/l)
Na^+	142	142	±10
K^+	4,5	4,75	160
Ca^{2+}	2,5	1,25	
Mg^{2+}	1	0,5	20 (+Ca)
Cations	150,0	148,5	(180)
Cl^-	103	114	±2
HCO_3^-	25	27,5	±8
PO_4^{3-}	1,0	1,5	120 (+SO_4)
SO_4^{2-}	0,5	0,5	
Proteins	16	0	50
Organic acids	4,5	5	
Anions	150,0	148,5	180

Table 11.1: Substantial components of blood plasma, interstitial fluid, and intracellular fluid

The osmolarity of each compartment always ranges between 290±10 mmol/l. This value is a little lower than theoretically calculated osmotic concentration of ions. This difference is due to the fact that the dissociation of electrolytes in biological fluids is not perfect and a part of the ions is in a nondifusible (bound) form. Because of the high permeability of the biological membranes, the deviations in the osmolarity of one compartment will quickly be reflected in other compartments. Increase in the concentration of solutes is hyperosmolarity, and a decrease in the concentration of solutes is hypoosmolarity.

For the constant osmotic pressure in body fluids, volume of water and amount of solutes must equilibrate. Though the concentration of particular ions in body fluids is variable, the resulting molar concentration, determining osmotic pressure, is almost similar. Under normal conditions, the intracellular and the interstitial fluids are **isoosomotic** with the plasma. As seen in the table above 11.1, Na^+ dominates the extracellular fluid (plasma, interstitial fluid). Other cations are present in small amounts. For the practical purpose we might consider Na^+ to the sole cation in extracellular fluid. As Na^+ is the most important cation in ECF, any change of its amount is accompanied with the change of anions amount. That is the principle of electroneutrality. At the same time, every change of Na^+ amount results in the change of ECF osmolarity. As the organism tries to maintain the osmolarity, all changes of Na^+ amount result in changes of water amount. So we can say that **the amount of ECF depends on the amount of Na^+ mainly**.

Changes of osmolarity on one side of membrane appear immediately on the other side of membrane. So the dilution of ECF (by intake of a large amount of water or by infusion containing hypoosmolar fluid) will transfer water from ECF, where osmotic pressure has dropped, into the cells, where osmotic pressure is greater. When ECF osmolarity increases, water will move from the cells to ECF according to the osmotic gradient. For example, this shift can occur upon intake of hyperosmolar solution, or upon an inadequate water intake. The stability of ECT osmotic pressure is an important factor for normal cell functions. Any change of ECF osmolarity will lead to the disturbance of water balance both in ECF and inside the cells.

The pH value of arterial blood is 7.40 ± 0.04. The pH value of interstitial fluid is similar to blood pH. The ECF pH is maintained by the buffer systems, pulmonary ventilation and kidney and this provides the required stability of pH in body fluids.

These mechanisms take place in appearance, development and culmination of many serious pathological states, because each cell can normally exist only in optimal physical and chemical conditions. To maintain normal course of enzymatic and metabolic reactions it is necessary to have a constant acid-base balance as well.

The composition of internal environment is strictly maintained by the regulatory and compensatory mechanisms of organism, even if the composition of the external environment varies considerably. These regulation mechanisms work mainly on the feedback effect (e.g. increase of ECT osmolarity $\longrightarrow$ osmoreceptors $\longrightarrow$ hypothalamus $\longrightarrow$ hypophysis $\longrightarrow$ ADH $\longrightarrow$ H_2O retention $\longrightarrow$ normalization of osmotic pressure in body fluids). **Cannon** called the maintainance of stable internal environment in higher organisms homeostasis. The extrarenal hormones, participating in electrolyte and volume homeostasis, are mainly antidiuretic hormone (ADH – adiuretin or vasopresin), aldosteron, and atrial natriuretic factor (ANF).

The renal hormones, regulating homeostasis, are mostly renin-angiotensin-aldosteron system, kallikrein-kinin system and prostaglandins.

11.1.5 Changes in the volume of body fluids

Changes in the volume of body fluid are typical of all serious diseases. During the etiopathogenic analysis we have to keep in mind following:

- The close relation between ECF and ICF, which means, that changes in the volume and chemical composition of one compartment will usually cause identical changes in the other one.
- The dependence of ECF volume on composition of ions of internal environment (this condition concerns other body fluids as well).
- The volume of total body fluid and division of fluid into particular compartments.
- The close relationship between water metabolism, electrolyte composition and acid-base balance of body fluids as well.

So it is very difficult to talk about isolated changes of ECF, not only according to pure water, but chemical composition as well. Even though we practically distinguish many states with accumulation or loss of body fluids, basically it is hyperhydration or hypohydration (respectively dehydration).

11.1.6 Dehydration

Under physiological conditions, the fluid intake and output is in equilibrium. If a disorder occurs, leading to decreased body fluid volume (respectively negative water balance), dehydration develops. Dehydration can be devided into **isoosmotic** (isotonic), **hypoosmotic** (hypotonic) and **hyperosmotic** (hypertonic).

11.1.6.1 Isoosmotic dehydration (isotonic)

This kind of dehydration occurs as a result of water loss directly related to salt loss, so there is a loss of isoosmotic fluid. The most common causes of isoosmolar fluid loss are: diseases of gastrointestinal tract accompanied by diarrhea and vomiting (pylorostenosis, gastroenteritis, colitis), accumulation of fluid in the abdominal cavity (peritonitis) or in intestine (ileus), fistulae. It can be caused by draining the gastric or intestinal content as well. From renal causes there are kidney diseases associated with isostenuria and polyuria and administration of diuretics, too. From the causes of blood circulation it is a blood loss. Burns and excessive transsudation from wounds can also cause the loss of isoosmolar fluid.

The loss of body fluids is limited to extracellular space. So haemodynamics is affected mostly and the clinical features of circulation disorder dominates. The cardiac output is decreased and as a result some changes of blood distribution in particular organs appear. The blood flow in kidneys and skin decreases. Skin turgor and intraocular pressure decreases as well. The failure of peripheral circulation – hypovolemic shock – is mostly dangerous in isoosmotic dehydration. The circulation reacts to low cardiac output by vasoconstriction. So diastolic blood pressure might increase a little and systolic blood pressure decreases due to low cardiac output. The pulse is fast and weak (so called thready pulse). Mucus membranes are dry and tongue is coated. Subjectively patient feels exhausted and weak.

The osmotic pressure of plasma is not changed and so there is no stimulation for releasing ADH from hypophysis at first. Diuresis will not decrease a much till there isn't a marked decline of ECF volume. The decline of ECF volume leads to low renal perfusion and to increase of aldosteron secretion with resulting reabsorption of sodium and water. In the beginning, even thirst is not a dominating symptom. So the loss of isoosmolar ECF can reach a considerable level without appearance of dehydration signs (marked thirst, oliguria, ect.). Later occurs thirst, probably as a result of high aldosteron release. Low renal perfusion can be associated with decreased catabolite excretion and with accumulation of urea nitrogen, that means with extrarenal azotemia. The diagnosis might be assisted with evaluation of haematocrit. The haematocrit increases as loss of fluids is limited to ECF (except from posthaemorrhagic states).

Newborns are most susceptible to this form of dehydration. The total volume of ECF is small in newborns, and then common gastrointestinal problems associated with diarrhea can lead to a relatively large loss of fluids.

According to the loss of Na^+ and other ECF solutes, intake of pure water can lead to decrease in internal environment's osmolarity, accompanied by water inflow into the cells. Decrease of ECF osmotic pressure leads to decrease of ADH secretion, resulting in water diuresis what means excretion of taken water. Simultaneously with loss of water a small amount of sodium is lost, too. That's why receiving pure water or glucose solutions not only doesn't improve, but even might worsen patient's condition. Optimal therapy requires isoosmolar solutions. It is very important to estimate the ions loss. Vomiting or gastric lavage will cause isoosmolar loss of fluid and metabolic alkalosis as well. Diarrhea on the other hand causes metabolic acidosis and potassium deficiency.

11.1.6.2 Hypoosmotic (hypotonic) dehydration

This condition occurs when electrolyte loss (mainly sodium) exceeds water loss. The extracellular space shrinks and osmolarity of ECF decreases. As a consequence, water will enter cells. This process continues till osmotic pressure becomes equal on both sides of the cellular membrane. The cells become swallen. This type of dehydration can occur upon chronic pyelonephritis (the risk increases by salt free diet), polyuric phase of chronic renal insufficiency, chronic adrenal insufficiency (Addison's disease), in upon CNS diseases (encephalitis, damage in the region of paraventricular and supraoptic nuclei). Hypotonic dehydration might occur while using large doses of diuretics and laxatives, too. Salt loss occurs upon rectal tumors and long lasting salt free diet. Substitution of fluid loss by pure water (for example after long lasting vomiting and diarrhea and in states accompanied by enormous sweating) can cause this kind of dehydration as well.

Symptoms of hypoosmotic dehydration are resulting from the decrease of ECF and from the loss of Na^+ (possibly K^+), and resulting water flow into the cells. The symptoms are: general weakness, sunken eyes, low skin turgor, low blood pressure and thready pulse. The developing clinical picture is similar to shock accompanied with spasms of particular muscles, mainly of legs. The patient might fall into delirium or coma when the loss of electrolytes is continuous and very high.

The laboratory tests reveals decrease of Na^+ be-low 130 mmol/l in serum. Erythrocytes, haematocrit, and proteins are relatively increased. The therapy consists of restoration of body fluids with hyperosmolar solution (according to hypoosmolarity) and correction of possible acid base disorders.

11.1.6.3 Hyperosmotic (hypertonic) dehydration

Hyperosmotic dehydration, so called hypersalemia (water defficiency in organism), occurs when water loss exceeds electrolytes loss. The consequence of hyperosmotic dehydration affects all body compartments. First of all ECF hyperosmolarity causes transfer of fluid from relatively hypoosmolar cells to interstitium and plasma. So the osmotic pressure is equilibrated in all body compartments. Nevertheless the osmotic pressure is still higher than in normal conditions.

This type of dehydration results from low water intake (unconsciousness, abscence of thirst in case of CNS anomalies and in old people, hydrophobia or cases of drink and swallow disabilities). It occurs in conditions associated with high water loss (hyperventilation, profuse sweating, polyuria in diabetes mellitus and diabetes insipidus) as well.

The shift of water from cells into ECF maintains the necessary volume of intravascular fluid. That's why the viscosity of blood, hematocrit value and concentration of plasma proteins is normal initially. On the other hand, due to the shift of water from intracellular to extracellular spaces, intracellular dehydration results. The increase of osmolarity stimulates osmoreceptors. As a result more ADH is released and consequently more water in kidneys is reabsorbed. The amount of urine decreases and its specific gravity is increased. Although the transfer of water from cells into circulating blood maintains the blood volume, metabolic processes inside the cells are disturbed. If water loss is considerably high, clinical status becomes serious. The patient experiences severe thirst. His salivary glands secretion is decreased, mucous membranes are dry, voice is harsh, tongue is dry, skin turgor is low, and his temperature increases (due to low evaporation from skin). Later some psychological disturbances (desorientation, hallucination and eventually convulsions and coma) occur. Laboratory tests reveal high serum Na^+, high urea nitrogen (due to decreased glomerular filtration) and high serum chlorides as well. Tests reveal surplus of erythrocytes, Hb, total poteins, but a diminution of erythrocyte's size (due to intracellular dehydration). Haematocrit is normal or a bit higher. Hypovolemic shock is the most dangerous consequence of plasma volume decline and high plasma density. Therapy consists of water substitution in form of glucose solution without electrolytes.

11.1.7 Hyperhydration

Hyperhydration is a general increase of body fluids volume. It appears as a result of an excessive intake of salt and fluids, failure of excretory mechanisms and increase of their retention.

Depending on changes of electrolyte composition, hyperhydration is divided into:

- **isoosmotic** (isotonic) hyperhydration,
- **hypoosmotic** (hypotonic) hyperhydration,
- **hyperosmotic** (hypertonic) hyperhydration.

11.1.7.1 Isoosmotic (isotonic) hyperhydration

Isoosmotic hyperhydration is characterized by an excessive blood plasma volume and interstitial volume as well. As ECF osmolarity is unchanged, ICF volume remains unchanged, too.

The surplus of plasma volume, manifested by decrease of haematocrit, hemoglobin and plasma proteins (so called hemodilution), overloads the heart.

The total raise of ECF volume can be the result of administration of an excessive amount of isoosmolar solutions. This occurs usually upon a fast parenteral application of a large amount of solutions (blood transfusion, plasma transfusion and blood substituents). The consequences are mostly haemodynamic. Their range and seriousness depends on the given amount of fluid, speed of administration and ability of heart to increase cardiac output. Cardiac failure may develope.

General edema is the most common condition of isoosmolar fluid's retention and increase in ECF volume. General edema occurs together with cardiac failure, nephrotic syndrome and liver cirrhosis. The ECF volume can be several times larger than normal ECF volume. The optimal therapy is elimination of the underlying disease (heart, liver, kidneys). It is important to decrease water and Na^+ intake. Osmotic diuretics are very helpfull.

11.1.7.2 Hypoosmotic (hypotonic) hyperhydration

The surplus of water in organism causes hypoosmotic hyperhydration. Hypoosmolarity of the extracellular space (due to surplus of water) results in water shift to a relatively hyperosmolar cells. In this condition the volume of all body fluids (ICF and ECF) increases equally, but the solute concentration in fluids decreases.

Hypoosmotic hyperhydration can result from:

1. Excessive infusions of glucose solutions (gaining water from glycid metabolism).

2. Excessive water intake or infusion therapy in patients with oliguria and anuria.

3. Covering water and electrolyte loss by an excessive amount of pure water, resp. 5 per cent glucose. The most common cause of hypoosmotic hyperhydration is substitution of pure water in case of an excessive sweating.

4. The increase of ADH, due to an overproduction (Schwartz-Bartter syndrome) or due to deficient degradation in altered liver.

5. The overproduction of ADH resulting from pain during postoperation stress. Another cause of ADH overproduction might be bronchial tumor and brain lesion.

The consequences of water overproduction depend on the speed of its development. When the development is rapid, pulmonary edema might occur.

Other symptoms of so called water intoxication, probably due to brain edema, are headache, inadequate behaviour with disorientation resulting in unconsciousness (coma). Intracranial hypertension leads to nauzea and vomiting. The plasmatic Na^+ concentration is low, and the Na^+ and Cl^- content in urine is low.

The therapy consists of limiting the water intake, treating the underlying disease, and administrating osmotic diuretics. Application of hyperosmolar solutions, always recommended in the past, comes to consideration only when brain edema might develop. In anuria, water retention is the second most important indication for haemodialysis (first being potassium retention).

11.1.7.3 Hyperosmotic (hypertonic) hyperhydration

Hyperosomotic hyperhydration is defined as a condition where both the volume and the osmolarity of the ECF are increased. This leads to a shift of water from the intracellular space into the ECF. It will continue till a new osmotic balance between ECF and ICF is established. Intracellular dehydration results.

There are two possible causes for hyperosmotic hyperhydration: increased intravenous administration of NaCl (in case of renal insufficiency) and an excessive introduction of infusions (such as hyperosmolar salts or hyperosmolar sugar solutions). In the former case, the plasma Na^+ is increased and might reach 147 mmol/l, in the latter case this value is normal or decreased (the hyperosmolarity is caused by the osmotic activity of the sugars). Laboratory parameters show decreased number of RBC, low Hb and haematocrit, and a decreased RBC volume.

Water defficiency	Water surplus
loss of weihgt	weight increase
thirst	cephalalgia
oliguria	disorientation
concentrated urine	nauzea
acidosis	vomiting
fever	edema
muscle clones	muscle spasms
cardiorespiratory failure	unconsciousness

Table 11.2: Consequences of both hypohydration and hyperhydration

Etiological factors of hyperosmotic hyperhydration are e.g. adrenal tumors, acute renal failure, acute glomerulonephritis, as well as high doses of steroid hormones.

The clinical symptomatology of hyperosmotic hyperhydration is similar to the hypoosmotic hyperhydration.

During the therapy it is very important to find out the etiology of the disorder. The correction of the fluid volume should be accompanied with the correction of the osmolarity, the ionic concentrations and the pH.