11.2 Electrolyte balance and its disturbances

The trace elements and minerals are necessary for the maintenance of biochemical reactions inside the cells. Their most important roles are:

- to maintain the suitable osmolarity and volume of body fluids,
- to maintain the appropriate acid-base balance,
- to create the suitable physico-chemical environment for cellular functions. Excitability of nervous and muscular fibers and, generally, normal functions of glandular, muscular and nervous cells depend on the ionic composition and the balance between intracellular and extracellular compartments.
- being a part of important compounds with specific functions in organism (iron, iodine, zinc, and magnesium).

It is important to concentrate on element's intake, elimination, and concentration in ECF or ICF during investigation their turnover.

11.2.1 Sodium

Sodium represents more than 90 per cent of cations in the extracellular fluid (its concentration is 140 mmol/l in ECF and 3–35 mmol/l in ICF, depending on type of tissue). That is why sodium determines the **osmotic pressure** together with corresponding anions. As a result, the amount of sodium is responsible for **the volume of extracellular fluid**. As there exists a balance between extra and intracellular fluid, any change of Na^+ concentration causes the shift of water between cells and extracellular environment.

Sodium has an important role in the maintainance of **acid-base balance**. The concentration of sodium determines the amount of needed bases.

The presence of Na^+ is important for the maintainance of normal **membrane potentials** and normal **cardiac function**.

Sodium is found in two fractions in organism, exchangeable and non exchangeable.

The **exchangeable** fraction is represented by sodium in extracellular fluid, intracellular fluid, and 15 per cent of bone sodium (on bone surface).

The **non exchangeable** fraction is fixed inside the bones, and do not share the sodium functions mentioned above.

Under normal conditions, the amount of sodium is constant in particular body fluid compartments. The concentration gradient between ICF and ECF is maintained by sodium pump, transporting the sodium outside the cell using the ATP energy. About 10 per cent of all the sodium in organism exists intracellulary.

Sodium can be mobilized from bones, to supply the loss from extracellular fluid. In acidosis, sodium is excreted by urine together with acid radicals. As a result the shift of sodium from bones to extracellular fluid occurs. In positive sodium balance, sodium is deposited inside the bones, on contrary.

Sodium balance. The amount of sodium remains nearly constant under physiological conditions. The sodium food intake ranges between 140–260 mmol daily. As the sodium intake is regulated only a little (by the actual taste of food), the regulation depends on elimination of sodium.

The sodium loss via the skin is not significant when the temperature of outside environment is comfortable. Approximately 10 mmol Na^+ a day is lost by sweating in basal conditions. This amount rises in hot conditions, mostly in fever. Sodium loss via stool represents only 1–2 per cent (nearly 10 mmol/day) of total Na^+ loss. This way becomes more important in diarrhea, where elimination of Na^+ and other electrolytes rises extremely. Kidneys are most important in regulation of sodium elimination. Approximately 120–240 mmol Na^+ a day is excreted by kidneys.

The kidneys are able to excrete urine both with very high or very low sodium content. Many factors affect the natriuresis. For example, haemodynamic and physical factors, aldosterone, renin-angiotensin system, kallikrein-kinin system, prostaglandins, and newly discovered natriuretic substances (ANF, natriuretic hormon ?) as well.

1. Haemodynamic factors – changes of blood flow in kidneys with the resulting affection of glomerular filtration. This mechanism takes place in fast and short term changes of Na^+

excretion, but the maintainance of glomerulotubular balance prevents further continuation of these changes.

2. Physical factors – oncotic pressure, which decreases during albumin's concentration decline. This results in slower resorption of Na^+ and water in tubules.

3. Aldosterone, which increases the resorption of Na^+ from primary urine.

4. Renin-angiotensin system. The constriction of vas afferens decreases the renal blood flow. As a result, decrease of glomerular filtration and decrease of Na^+ amount in primary urine occurs. Finally sodium excretion is decreased. On the other hand, angiotensin supresses the resorption of sodium from primary urine by a direct effect on tubules and so contributes to a higher Na^+ excretion. Clinical features and conditions determines the dominating mechanism.

5. Kallikrein-kinin system which increases the blood flow in kidneys, the diuresis and natriuresis.

6. Prostaglandins, contributing to a higher Na^+ elimination. Vas efferens is suggested to be their target place.

7. Natriumuretically acting substances (ANF-atrial natriuretic factor and natriuretic hormone), which suppress the Na^+ resoption in tubules and so increase Na^+ excretion.

Sodium disorders. Despite the precise regulatory mechanisms of Na^+ turnover, sodium disorders are quite a common clinical problem.

The loss of sodium by excessive sweating leads to hyponatremia indirectly. Since sweat contains less sodium than plasma the water loss is greater than sodium loss with resulting hyperosmolarity of extracellular fluid. In **Addison's disease** the inability to retain sodium in kidneys occurs. As a result a negative sodium balance with hypovolemia, hyponatremia, and hyperkalemia appears. Then an intake of mineralocorticoids is required.

A number of **kidney diseases** result in inability of salt retaining (salt loosing nephritis, chronic pyelonephritis, ect.). In this conditions, the plasma sodium is maintained only by a higher salt intake. During a limited salt intake, the tubular cells do not respond to the stimuli of sodium retention. As a result a progressive hyponatremia and hypochloremia occur.

A large amount of sodium is lost during a **diuretic therapy** in normal kidneys. The saluretic's aim is to induce a negative sodium balance. If they are applied intermittently, organism compensates this loss. The application of saluretics daily for a long time might cause an electrolyte wastage.

In pathological conditions, a serious loss of Na^+ from **gastrointestinal tract** may occur. The pancreatic juice, bile and secretions from small intestine contain sodium nearly in the same concentration as plasma. Under normal conditions, sodium is resorbed from the intestine, and only a small loss of Na^+ by stool appears. In diarrhea the sodium loss reaches a considerable level.

Sodium retention is accompanied by the increase in total body sodium. The sodium surplus does not lead to hypernatremia and hyperosmolarity, because the resulting stimulation of ADH leads to retention of water. Water and sodium are retained in the proximal tubuli, too. As a result an expansion of ECF occurs, so the actual level of plasma Na^+ doesn't change. During a considerable sodium retention, edema or accumulation of fluid in body cavities may develop. The relationship between sodium retention and hypertension is a subject of an intense investigation.

The most common causes of an excessive total sodium are: high intake, low elimination, and Na^+ sequestration.

1. High Na^+ intake.
   The organism may receive a large amount of sodium per os, by a nasogastric probe or parenterally. While using a nasogastric probe, a sufficient amount of fluid must be administered as the organism can not provide the appropriate excretion of Na^+ in a small volume of urine.

2. Low Na^+ elimination.
   It is a common cause of positive Na^+ balance occuring upon heart failure, liver cirrhosis with ascites, nephrotic syndrome, renal insufficiency and delayed gestosis or endocrine disorders.

   (a) Heart failure is probably the most common cause of Na^+ retention.

(b) Liver cirrhosis. Na^+ retention results from hypoproteinemia, secondary hyperaldosteronism, decreased renal function and most probably from other tubular disorders.

(c) Nephrotic syndrome. Na^+ retention results from hypoproteinemia with resulting hypovolemia and from secondary hyperaldosteronism.

(d) Oligoanuric phase of renal insufficiency (mostly acute renal failure and terminal stage of chronic renal insufficiency).

(e) Endocrine disorders. Mainly two groups of disorders cause low sodium elimination. It is primary and secondary hyperaldosteronism and natriuretic hormone defficiency. Natriuretic hormone: The low Na^+ elimination results from inadequate production or function of natriuretic hormone. At least two natriuretic hormones are described in literature. It is suggested that a hormone retaining sodium exists as well.

3. Sequestration of Na^+.

It is caused by an unequal distribution of Na^+ (eg.: in hollow organs, in burns and bruises of soft tissues). Symptoms of hypovolemia are present.

11.2.2 Chlorides

Daily food intake of chlorides is 140–260 mmol. Their total amount in organism is around 1400 mmol. Elimination of chlorides via urine is only a bit lower than their intake, because nearly 10 mmol Cl^-/day is excreted by sweating. Nearly the same amount is excreted by stool. Chlorides are distributed in ECF, forming its main anion. Plasma Cl^- concentration is around 100 mmol/l. The shift of chlorides between ICF and ECF appears in pathological conditions, such as heart failure and disturbances of acid base balance.

The concentration of chlorides in organism is regulated similarly as sodium concentration. In opposite, chlorides are not resorbed actively in kidneys, but along the electrochemical gradient of Na^+. Chlorides are resorbed actively only in ascendent arm of Henley's loop.

Changes of chlorides intake are immediatly reflected in changes of their excretion by kidneys. During acid base disturbances, the concentration of chloride changes more then concentration of Na^+. It results from the fact that total amount of cations should be equal to total amount of anions to maintain electroneutrality. Anions have only two main variable constituents: HCO_3^- and Cl^-.

Changes in acid base balance caused by a primary change of the amount of bicarbonate are accompanied with the opposite change of chlorides. Secondary changes of the amount of bicarbonate occur during hypo- or hyperventilation. In these conditions plasma chloride concentration changes independently on plasma sodium concentration.

Disorders of chlorides turnover occur simultaneously with disorders of Na^+ turnover. The most common cause of chloride disturbances is the loss of gastric juice, occuring mainly upon an excessive vomiting or a permanent suction of gastric juice. The loss of chlorides is much bigger than the loss of Na^+ and K^+. Resulting decrease in plasma chloride concentration and simultaneous increase in plasma bicarbonate concentration occurs. Hypochloremia leads to alkalosis with resulting decrease in the ionized calcium in plasma. Tetany may develop. H^+ and Na^+ enter the cells and push the K^+ outside. It is necessary to apply chlorides, potassium, sodium and water to correct this disorder.

11.2.3 Potassium

The daily food intake of potassium ranges between 30–80 mmol. The resorbed K^+ is distributed in ECF in a low concentration (4.5 mmol/l). Despite this fact, the concentration of K^+ in ICF is high and variable in different tissues. Potassium concentration in ICF ranges between 100–160 mmol/l.

About 90 per cent of potassium in organism is excreted by urine and 10 per cent is excreted by stool. These values can be variable, for example the amount of K^+ in stool considerably increases in diarrhea. To maintain the K^+ balance in the organism intact kidneys are necessary.

Potassium is the main intracellular cation. Nearly all processes in cells are depended on gradients of potassium and natrium on both sides of the cellular membrane.

Many metabolic processes are responsible for the

shift of potassium between intra- a extracellular fluid.

The **glucose** enters the cells accompanied with potassium. Investigations performed on human erythrocytes show that during the entrance of 0,5–1,0 mmol glucose 1 mmol of potassium enters the RBC at the same time.

Glycogenolysis leads to the release of intracellular potassium on the contrary.

Tissue growth and regeneration also require potassium. The building of a new protein in cells makes potassium entering the cell. On the other side, protein degradation leads to the release of potassium from intracellular space. Cellular injury or cellular hypoxia results in leak of potassium from cells.

In alkalosis, H^+ leaves the cells and enters the extracellular fluid, while potassium enters the cells. Alkalosis becomes mitigated but hypokalemia develops. Even the primary hypokalemia can stimulate the H^+ entering the cells (the result is hypokalemic alkalosis, too).

Short term shift of potassium occurs during **depolarization and repolarization** of cellular membranes in excitable structures, related to the spread of impuls.

Kidneys have the most important role in the regulation of potassium turnover in organism, too. However, kidneys are not as perfect in sparing potassium, as in sparing sodium and chlorides. So, disorders of potassium balance occur more often.

In pathological conditions an accumulation or wastage of potassium with resulting serious disturbances of cell metabolism develope. The symptoms of potassium disorders depend mainly on the concentration of plasma sodium. Having a certain concentration of plasma potassium and different concentrations of plasma sodium, clinical symptoms are usually different. The symptoms of hypokalemia are more prominent, if the concentration of sodium is normal or increased. Similarly, symptoms of hyperkalemia are intensified by low sodium concentration, and supressed by hypernatremia. Calcium also antagonizes some physiological effects of potassium, mainly those concerning the neuromuscular excitability and heart function.

Potassium defficiency. Potassium defficiency leads to serious alteration of striated muscles (adynamia, hyporeflexia, and paralysis of skeletal muscles), of smooth muscles (stomach atonia, urinary bladder atonia, and paralytic ileus) and also to some serious cardiac disorders. Hypokalemic alkalosis might develop. In experiments performed on rats, the potassium defficiency leads to myocardial necrosis with resulting fibrotic changes. The ECG reveals flattening or even inversion of T wave, depression of ST segment, and prolongation of QT interval, as well.

Potassium defficiency is closely related to the **hypokalemic familiar periodic paralysis**. In this hereditary disturbance the paroxysmal hypotonic paralysis of skeletal muscles and the affection of cardiac function occur. The paralytic paroxysms are closely related to the decrease in potassium concentration and to the decrease in creatinin and phosphate plasma concentration as well. Intravenous or peroral administration of KCl improves the muscular functions. The paroxysms occur spontaneously and mainly following a tiring muscle work. They occur namely during the supply of consumpted glycogen, which is accompanied by the decrease in anorganic phosphate and potassium. The application of insulin or glucose leads to development of paralytic paroxysm in predisposed individuals. A certain relation between paroxysmal muscular paralysis and primary hyperaldosteronism (Conn's syndrome) is assumed. Patients with familiar paroxysmal muscular paralysis were noticed to have a little higher aldosterone level in urine.

The symptomatology of hypokalemic familiar periodic paralysis is similar to hypokalemic states, which are clinically marked as states of potassium defficiency. Adynamia, hyporeflexia or areflexia, paresis, disturbances of heart rate, polyuria due to kaliopenic nephropathy and rarely mild edema occur. Kaliopenic nephropathy is granular, hydropic and vacuolar degeneration of tubular cells, which can be caused by long lasting hypokalemia.

Upon **chronic diarrhea** not only sodium but also a considerable amount of potassium is lost. It is due to the fact, that potassium is found in higher concentration in intestinal juice than in plasma. Defficiency of potassium is not substituted by the supplementation of water and salt only. On the contrary, the infusion of large amount of sodium chloride solution can decrease the plasma potassium concentration even more. The decrease of potassium can be manifested by muscle weakness and by paralysis of diaphragm in certain conditions.

The most common cause of potassium defficiency is **insulin therapy** of diabetic ketoacidosis. Several gramms of cellular potassium are excreted daily by urine during diabetic ketoacidosis. Since the diabetic coma develops slowly, large amount of potassium can be lost. Starting with insulin therapy, glucose enters the cells accompanied by potassium, with resulting considerable decline of plasma potassium.

Less common is potassium defficiency caused by **chronic** or **acute renal diseases** *(Potassium-losing nephropathy)*. This condition is noticed in the polyuric stage of tubular necrosis. Due to severe injury of tubular apparatus, the coordination between potassium elimination and potassium resorption is altered.

The **iatrogenic** states of potassium deficiency (caused by the medical staff) are very important. Long lasting administration of **ACTH, cortisol, prednisolon, prednison**, etc. leads to hypokalemia due to higher potassium excretion.

The administration of **saluretics** can lead to hypokalemia after few days even in therapeutic doses.

The long lasting use of laxatives can lead to hypokalemia due to a relatively high level of potassium in intestinal juice (especially if the food is not rich of potassium).

Hypercorticism is another cause of potassium deficiency in organism. Mineralocorticoids stimulate both sodium resorption and potassium excretion in renal tubules.

Hyperkalemia. Experimentally, a higher concentration of potassium in washing solution can result in disappearance of neuromuscular excitability. Upon doubling the plasma K^+ concentration, signs and symptoms of paralysis can occur. The clinical signs of hyperkalemia are similar to signs of hypokalemia: adynamia, paresthesia and even paralysis. ECG is very good differential diagnostic method. We can notice the following in hyperkalemia:

- Raising of T wave with steep edges and narrow base.
- Widening of QRS complex, mainly the S wave, so the picture of right sided bundle branch block (Wilson's block) occur.
- The disappearance of P wave, and finally
- cardiac arrest

Hyperkalemia occurs mainly in situations with **massive cellular degeneration**, for example **hemolytic crisis, crush syndrome** ect.

Hyperkalemia appears also in **Addison's disease**, where it is accompanied by low plasma sodium concentration resulting from defficiency of mineralocorticoids.

Hyperkalemia in renal diseases associated with **oliguria** or **anuria** is caused by altered K^+ excretion. This condition can be even life threatening. The disease is usually manifested by the loss of appetite, nausea and vomiting. The inadequate intake of food and the toxic effect of waste products (due to renal retention) result in higher glycogen and protein degradation leading to increase of potassium in extracellular fluid.

The untreated diabetes mellitus with acidosis is another cause of hyperkalemia with shift of potassium from the cells to the extracellular fluid. In this condition potassium is leaving the cells due to glycogenolysis and proteolysis and due to loss of bases from extracellular fluid as well. Dehydration, associated with acidosis, increases the stage of hyperkalemia even more.

Iatrogenic hyperkalemia occurs mainly upon the administration of **potassium drugs** for stimulation of diuresis in progressive renal insufficiency with edema.

11.2.4 Calcium and Magnesium

These two elements do not exceed 5 per cent of the total cation amount in extracellular fluid. So they participate only a little on the maintainance of body fluids osmolarity and volume. They are also not very important in the regulation of acid-base balance. But calcium and magnesium ions are important for their specific effect.

The calcium concentration in the internal environment is regulated by parathyroid hormon and thyreocalcitonin. Calcium metabolism is markedly affected by vitamin D and other substances which either increase or decrease its resorption in the upper part of small intestine. The factors enhancing vitamin D resorption are: HCl in stomach, aminoacids and products of milk fermentation. The factors decreasing vitamin D resorption are: surplus of phosphates and oxalates, disturbances of fatty acids resorption and diarrhea.

11.2.4.1 Calcium

Calcium is a component of all body fluids and tissues. It has an important role in different processes such as:

- blood coagulation
- teeth and bones formation
- enzymatic activity (myosine ATPase)
- cardiac rhythm
- neuromuscular excitability
- muscle cell excitation-contraction coupling
- cell membranes permeability
- milk secretion

Calcium is provided in food in organic or inorganic form, but most probably it is resorbed only in inorganic form. The resorption of calcium takes place mainly in the upper part of small intestine. The pH of intestinal juice is very important in this process, as calcium ions are well dissolved in acid medium but they are not dissolved in alkalic medium. Sugars, mainly lactose, which raises the amount of organic acids during digestion, helps in calcium resorption. Fats (without vitamin D) decrease calcium resorption, most probably due to the formation of nonsoluble calcium soaps. Vitamin D markedly enhances the calcium resorption from intestine.

The best source of calcium is milk, but a considerable amount of calcium can be obtained by intake of *hard* water. Some vegetables such as spinach and oxalis contain oxalacetic or benzoic acid which form nonsoluble substances with calcium. In this way they worsen calcium resorption. Cereals also contain a substance (inositol hexaphosphatic acid) forming nonsoluble salts with calcium and magnesium. This explains the decalcifying effect of some cereals.

Calcium balance means the difference between calcium food intake and calcium elimination by urine and stool. The balance is positive in growth, pregnancy, acromegaly or in a period following calcium defficiency. A negative calcium balance is noticed in rachitis, coeliac disease, renal rachitis, osteomalacia, hyperparathyroidism, hyperthyroidism, starvation or calcium defficiency in food and usually during lactation.

Nearly 99 per cent of total calcium amount is deposited in bones. Calcium blood level is relatively stable and ranges between 2.25–2.75 mmol/l. Practically all the blood calcium is present in plasma, existing in 3 forms:

- bound to plasma proteins (nearly 50 per cent). Calcium binds mainly to albumin and less to globulin fraction. The binding makes it nondiffusible through the capillary membrane.
- combined with other substances in plasma and interstitial fluid (eg. citrate), diffusible through capillary membranes, but non ionized (about 5 per cent),
- diffusible and ionized calcium (45 per cent). Particularly this form is needed for most of the functions mentioned previously.

The ratio between ionized and non ionized calcium depends on the plasma pH. The lower is the plasma pH, the higher is the ionization and vice versa. This relationship can be expressed by the following equation by **Ron–Takahashi**:

$$[\,Ca^{2+}\,] = K \cdot \frac{[\,H^{+}\,]}{[\,HCO_3^{-}\,]}$$

Changes of ionized calcium level are more important than changes of its total amount. Changes in ionized calcium level lead to the signs and symptoms of hyper- or hypocalcemia. On the other hand, changes of total plasma calcium (regardless the cause), usually lead to corresponding changes of its ionized fraction.

The fraction of the diffusible nonionized calcium increases in renal insufficiency. It is important to keep in mind that massive transfusion of stored blood, containing citrate to prevent coagulation, can markedly decrease the level of ionized calcium. Mainly patients with liver disorders who can not metabolise citrate fast enough are at risk.

Hypercalcemia. The signs and symptoms of hypercalcemia are variable and many of them result from decreased muscle excitability. Elevated ionized calcium level increases the electrical resistance of cell membranes and the potential of myoneural junction. Patients complain of tiredness, backache, weakness due to muscular hypotonia and walking problems as well. Headache, confusion, depression and

sleeplessnes often mislead to the diagnosis of psychosis. Keratopathies and sight disorders are common. Hypercalcemia leads to polyuria and polydipsia. Polyuria results from inadequate calcium resorption in tubular apparatus. Osmotic diuresis with sodium, potassium, chloride and bicarbonate wastage occur. The loss of potassium might lead to hypokalemia. Hypercalciuria predispose to the development of nephrolithiasis.

Hyperparathyroidism is usually the most common cause of hypercalcemia. But it is not the only one. Hypercalcemia can be caused by osteolytic bone tumors, myelomas, malignant bronchial tumors secreting substances identical to parathyroid hormone, overdose of vitamin D, hypersensitivity to vitamin D (e.g. in sarcoidosis) and long lasting immobilization during bone diseases (such as Paget's disease). Hypercalcemia can also be found in patients with peptic ulcer, receiving a large amount of milk and sodium bicarbonate as well.

The effect of hypercalcemia can be observed when calcium plasma level exceeds 3,75 mmol/l. If the increase continues, a life-threatening hypercalcemic crisis with dehydration may develope. Such crisis appears in patients with hyperparathyroidism or in women with a disseminated mastocarcinoma. Vomiting, tachycardia, fever and finally coma can appear. Oliguria is responsible for the raise of plasma phosphate and urea.

Hypocalcemia occur mostly in **hypoparathyroidism**, **rachitis**, **chronic acidosis** and **steatorrhoe**. It is manifested by latent or symptomatic tetany. The neuromuscular tetany appears when ionized calcium decreases to half of its normal level or when total calcium level reaches 1.75 mmol/l.

The latent tetany is manifested by the following trias: positive **Trousseau's sign** (so called obstetric hand formed upon compressing the arm by manometer – flexed forearm in wrist joint, extended fingers in the metacarpophalangeal joints and thumb opposition); positive **Chvostek's sign** (a slight muscle clonus on the homolateral side upon hitting the angle of mandible by a neurological hammer); **Erb's sign** (increased neuromuscular excitability upon galvanic current).

A symptomatic tetany is manifested by spasms of both striated and smooth muscles. Spasms of the skeletal muscles are: muscle twitch up to generalized convulsions common in children and rare in adults, carpopedal spasms, spasm of the glottis leading to inspiratory stridor and spasm of mimic and masticatory muscles – trismus.

As mentioned previously, spasms might also involve smooth musculature. For example, spasms of the smooth vessel muscles can be manifested as ischemic pain in digits. The spasm might affect the coronary vessels with resulting myocardial ischemia as well.

Tetany also occurs when the total plasma calcium is normal but its ionized fraction is decreased due to the shift of pH into the **alkaline side** (vomiting, hyperventilation). Hypocalcemia and tetany might occur in renal insufficiency as well, because calcium is bound to acid organic radicals and then excreted by urine.

In conditions, associated with long lasting negative calcium balance and resulting release of calcium from bones, **osteoporosis** and **osteomalacia** develop. The bones become soften and deformed and spontaneous fractures might result.

11.2.4.2 Magnesium

Chlorophyll is the most important source of daily magnesium requirement. Magnesium is resorbed in the upper part of intestine, and is excreted via bile and large intestine, and to a less extent via urine. The same carrier assists in resorption of both magnesium and calcium from intestine. So a low calcium intake stimulates the resorption of magnesium and vice versa. The parathyroid hormon increases magnesium resorption from intestine, whereas calcitonin has an opposite effect.

Magnesium is an important cofactor for many enzyme systems participating in the metabolism of glycides and in muscle contraction. It activates plasma and bone alkaline phosphatase, inhibits calcification and modulates the neuromuscular excitability.

Magnesium defficiency increases neuromuscular excitability. Tetany due to **magnesium defficiency** might develop. Developed tetany can not be clinically distinguished from tetany caused by calcium defficiency. Experimentally, this kind of tetany was introduced in rats, dogs and cattle. Calves, mainly feeded with milk containing a low magnesium level, often develope a severe tetany and can even perish due to convulsions. On the other hand, in human, hypomagnesemia without hypocalcemia doesn't usually lead to tetany. Several cases are described

where administration of magnesium improves clinical symptoms of tetany, but administration of calcium doesn't. In human, hypomagnesemia occurs in severe steatorrhoe, after the resection of a large part of small intestine, in chronic malnutrition, chronic alkoholism, diabetic acidosis and in chronic renal insufficiency, when glomerular filtration exceeds tubular reabsorption. Sometimes, low plasma magnesium occurs in hyperparathyroidism, and especially after surgical extirpation of parathyroid adenoma. After extirpation, salts are fastly deposited to the bone tissue, magnesium resorption is decreased and magnesium elimination by kidneys increases. Chronic magnesium defficiency leads to degenerative changes in myocard, kidneys and skin.

Neuromuscular excitability is decreased and muscle weakness appears upon raised magnesium plasma level. When magnesium plasma level exceeds 2.5 mmol/l, hypotonic status, paralysis of striated muscles, and even deep coma might develope. The depressive effect of magnesium can be removed by administration of calcium. During hypermagnesemia hyperglycemia and glycosuria might develop, probably due to magnesium effect on the enzymes of glucose metabolism.

11.2.5 Phosphorus

The total amount of phosphorus is about 1 per cent of total body weight. Phosphorus is distributed mostly in bones and teeth (80–85 per cent). A small part is distributed in cells and ECF in form of organic and inorganic compounds.

The most important functions of phosphorus are:

- participation in bone ossification as calcium phosphate and magnesium phosphate
- buffer system of ECF as primary and secondary sodium phosphate
- regulation of the intermediary metabolism of carbohydrates, fats and proteins.

The phosphorus metabolism is closely related to the calcium metabolism. This relationship appears during absorption of phospohorus from intestine. The calcium surplus in food inhibits the phosphorus resorption by creating a low soluble calcium phosphates.

The inorganic phosphorus level in adults is lower than in children. This level is regulated similarly as calcium level; by parathyroid hormone, calcitonin, vitamin D, and by calcium plasma level. A relationship exists between calcemia and phosphatemia: the product of total plasma calcium in mmol/l and inorganic plasma phosphorus in mmol/l is constant. This **solubility product** ranges between 30–40 in adults and 40–55 in children. So, the increase in calcium concentration results in the decrease of phosphorus concentration and vice versa. It was proved that children develop rachitis when the solubility product is below 35 and clinical improvement appears when it is above 40.

Some pathological conditions lead to changes in phosphorus plasma level.

Hypophosphatemia occurs in:

- Hyperparathyroidis
- Hypovitaminosis D
- Inadequate phosphorus food intake
- Steatorrhoe

Hyperphosphatemia occurs in:

- Hypoparathyroidism
- Hypervitaminosis D
- Renal insufficiency
- Severe diabetes mellitus
- Bone fractures

Phosphatases, enhancing the hydrolysis of phosphoric acid esters, play an important role in metabolism of phosphorus. They can be found in all body cells and tissues.