**PATHOLOGY OF METABOLISM**

Different pathological processes cause increase or decrease of basal metabolic rate. Since the basal metabolism is considerably influenced by the endocrine glands, disturbances in basal metabolism occur especially in endocrine disorders.

An increase in basal metabolic rate (up to 70% and higher) is observed in hyperfunction of the thyroid gland (thyrotoxicosis). Administration of the hormone of this gland (thyroxin) produces the same effect. Hypersecretion of somatotropic hormone (gigantism, acromegaly) as well as hyperfunction of the sexual glands are accompanied by increase of basal metabolic rate. Rise of sympathetic nervous system’s activity and hypersecretion of adrenalin and epinephrine, as well as feverish reactions cause increase of basal metabolism.

Decrease of basal metabolism is observed in hypofunction of the thyroid (myxedema, cretinism), sexual and adrenal glands, destruction or atrophy of the anterior lobe of the hypophysis (hypophyseal cachexia). Starvation also is accompanied by decrease of basal metabolic rate.

In discussing the disorders of metabolism it is convenient to deal with each form of metabolism separately. But one must keep in mind that the various forms of metabolism are closely interrelated.

The following forms of disturbances in carbohydrate metabolism are distinguished:

1. disturbances in carbohydrate digestion and absorption;
2. disturbances in synthesis and breakdown of glycogen;
3. disturbances in intermediate metabolism of carbohydrates;
4. disturbances in regulation of carbohydrate metabolism.

Since the enzymes breaking down starch and glycogen exist in different digestive juices (saliva, pancreatic juice, intestinal juice), and deficiency of one of them as compensated by hypersecretion of another, pathological processes connected with the disturbance of hydrolysis of polysaccharides are rare.

Deficiency and even complete cessation of secretion of amylolytic enzymes is comparatively frequent in babies (atrophic states, pancreatitis, acute necrosis of pancreas, pancreatofibrisis) and lead to the fermentative dyspepsia.

Disturbance of absorption of carbohydrates in intestine may depend on:

1) mechanical causes (acceleration of nutrients’ movement along the digestive tract);

2) disturbance of phosphorylation(the process that is necessary for absorption of monosaccharides and goes on by the participation of enzyme hexokinase) which may be caused by the inflammatory diseases of intestine and specific inhibitors of hexokinase(phloridzin, monoiodacetate).

Hormones of the thyroid gland accelerate phosphorylation. That is why in hyperthyroidism monosaccharides are absorbed from the intestinal wall rapidly, while hypothyroidism (myxedema) is accompanied by delay of this process. Glucocorticoids also stimulate absorption of monosaccharides.

There are uncommon hereditary diseases, which are connected with the deficiency of enzymes catalysing hydrolysis of saccharose (saccharosuria), and lactose (lactosuria).

Disturbances in synthesis and breakdown of glycogen lead to increase or decrease of its content in tissues. Decrease of glycogen content of cells (especially in liver cells and muscle fibers) may be caused by:

1) reduction of synthesis of glycogen (hypoxia, inflammatory processes in liver, pseudoparalytic myasthenia, etc.);

2) rapid breakdown of glycogen (intense emotional excitement, pain, physical strain, convulsive state, hyperthermia, hypothermia, asphyxia, hyperfunction of adrenal glands, anterior lobe of pituitary body, thyroid gland, etc.).

Excessive accumulation of glycogen in tissues is characteristic of glycogenoses - the diseases caused by deficiency of enzymes which catalyse breakdown of glycogen. 12 types of glycogenoses are known of which 11 are well studied. According to the clinical course (depending on tissues where the glycogen is most accumulated) they are divided into the following groups (in brackets the missing enzyme is indicated):

1) Hepatic form:

Type I - Gierke’s disease (glucose-6-phosphatase);

Type IV - Anderson's disease (1,4 glucan, 6 and glucosyltransferase);

Type VI - Hers' disease (liver glycogen-phosphorylase);

Type IX - Hug’s disease (kinase of phosphorylase B);

TypeX - (proteinkinase);

TypeXI - (phosphohexoisomerase).

2) Myopathic form:

Type V- Mc Ardle’s disease (muscle glycogen-phosphorylase);

Type VIII-Tarui’s disease (phosphofructokinase);

3) Mixed (hepatic+myopathic) form:

Type III - Cori’s (Forbes') disease (amylo-1,6 glucosidase, glycogen-branching enzyme);

Type VII - Thomson’s disease (phosphoglucomutase);

4) Generalized form:

Type II - Pompe’s disease (acid α-glucosidase).

The most of types of glycogenoses are inherited as autosomal recessive disorders; only inheritance of the type XI is of sex-linked recessive form.

The first signs of the hepatic form of glycogenosis manifest themselves in the first year of life: fit of hypoglycemia in the morning on an empty stomach (with loss of consciousness and clinic convulsions in extremities) which passes off after intake of sugar, short stature, large belly (owing to large liver), thin extremities, round face, metabolic acidosis, ketonemia. The development of this form of glycogenosis frequently stops after 16-18 years of age, but sometimes the main signs of the disease (hepatomegaly, hypoglycemia) do not pass off.

The principal symptoms of the myopathic forms of glycogenosis manifest themselves after 7-10 years of age: the children are not mobile and tire easily, myasthenia is gradually increasing, palpitation and dyspnea appear even after the easy physical work, heart borders widen, atrophy and hypotony of muscles develop. Usually myophatic glycogenesis is not dangerous for life, but in rare cases patients die in 20-30 years of age.

The generalized form of glycogenosis is characterized by accumulation of glycogen in many tissues, most often in the heart and skeletal muscle, leading to cardiomegaly and hypotonia.

Disturbances in intermediate metabolism of carbohydrates, that is, in the intermediate phases of glucose utilisation in the tissues, consist in the disturbances connected with the mechanisms of its oxidation and conversion. Disturbances in intermediate metabolism of carbohydrates are found in the following pathological processes:

1) hypoxia-leads to acidosis in the blood and disturbances of enzymatic processes in the organism;

2)protracted strenuous muscular activity-both in physiological and pathological (epilepsy, tetanus, etc.) cases cause increase of lactic acid in tissues;

3) diseases of the liver caused by the damage of its parenchyma-cause disturbance of glycogen’s resynthesis, hyperlactacidemia, acidosis;

4) deficiency of vitamin B1-is associated with difficulties of pyruvic acid oxidation and leads to increase of blood content of pyruvic acid and lactic acid (as the product of hydrogenation of pyruvic acid).

A particularly important part in disorders of carbohydrate metabolism is played by disturbances in the processes of its regulation. One of the main signs of pathological processes connected with the disorders in regulatory mechanisms of the carbohydrate metabolism is change in blood sugar concentration, which normally ranges in human organism from 80 to 120 mg % (4.44-6.66 mmol/l).

Low sugar level in the blood is called hypoglycemia, and its access in the blood hyperglycemia.

In clinical conditions hypoglycemia occurs comparatively rare. It is caused by the following factors:

1) Hypoglycemia of new-born-is observed in all babies after the birth. This is connected with deprivation of organism of sugar, which it received through placenta. In new-borns whose mothers are diabetics beta cells of pancreatic islands function more severely and sometimes it is eliminated only after injection of glucose. Blood sugar may come down to 20mg% (1.11mmol/l).

2) Alimentary hypoglycemia-is connected with carbohydrate deficiency.

3) Hyperfunction of beta-cells of pancreatic islands-may result in hyperinsulinism (increased insulin secretion).

4)The diseases connected with severe damage of hepatic parenchyma (severe forms of cirrhosis, carcinoma)-cause hypoglycemia (especially in hungry persons) as a result of limitation of glyconeogenesis.

5) Glycogenosis-cause hypoglycemia as a result of decreased glycogen breakdown.

6) Poisoning by the substances inactivating hexokinase.

7) Disturbed carbohydrate regulation by the nervous system.

8) Hyposescretion of hormones participating in regulation of carbohydrate metabolism (thyroxin, adrenalin, glucocorticoids).

9) Induced hypoglycemia (insulin, sulfonylurea, alcohol, aknee nut poisoning).

Hypoglycemia manifests itself mainly in dysfunction of the nervous system which is particularly sensitive to decreased sugar concentration in the blood. Because energy needs of nerve cells is satisfied by the energy formed as a result of oxidation of monosaccharides (the amount of glycogen in them is insignificant). When blood sugar comes down to 50-80 mg% (4.44-2.77 mmol/l) production of adrenalin is increased which causes tachycardia and sensation of hunger.

Hypoglycemia is marked by general weakness, excessive perspiration, tremor, headache, nausea, impaired memory, sleepiness and periodic paralysis. Decrease of sugar in the blood to 40mg% (2,22 mmol/l) causes at first excitation in the central nervous system which then is replaced by the inhibition and leads to hypoglycemic coma, and even to death. The hypoglycemic coma is characterized, besides above-mentioned signs of hypoglycemia, by loss of speech, convulsions, loss of consciousness. Development of these phenomena may be prevented or eliminated by intravenous administration of glucose solution.

Experimentally hypoglycemic coma is produced by injection of large doses of insulin.

According to the etiologic factors the following types of hypoglycemia are distinguished:

1) Alimentary hyperglycemia-is connected with intake of large amounts of sugar. Usually intake of 100-150 g of glucose by healthy persons increases blood content of sugar, which reaches maximal level (7.32-9.32 mmol/l) after 30-42 minutes. Then blood sugar falls and 2 hours later approaches the normal level, 3 hours later becomes even lower than the initial level (before the intake of glucose). This is connected with production of insulin.

The result of this sugar tolerance test is represented as “sugar curve”. To appreciate the results of the sugar tolerance the following coefficient is used:

B - A . 100%

# A

A-is blood content of glucose on an empty stomach, B-the maximal level of glucose load. Normal coefficient is no mare than 50%. In severe disorders of carbohydrate metabolism (diabetes mellitus) it is more than 80%.

2) Emotional hyperglycemia –is a result of excitation of sympathetic nervous system, which leads to acceleration of glycogen’s breakdown in liver and stimulates function of thyroid and adrenal glands (whose hormones also accelerate breakdown of glycogen and glycogenesis). Pain, asphyxia and other sates causing excitation of sympathetic nervous system exert their influence by the same mechanism.

3) Hormonal hypoglycemia –is result of increased production of some hormones.Glucagon accelerates breakdown of glycogen by the way of phosphorylation in liver. Adrenalin activates both liver and muscle phosphorylase. Glucocorticoids increase blood sugar by two ways: they accelerate glyconeogenesis and activating glucose-6-phosphotase in liver, stimulate breakdown of glycogen. Thyroxin accelerates absorption of glucose in intestine. Somatotropic hormone increases production of glucagon in pancreas, stops synthesis of glycogen by the way of inactivation of hexokinase and causes rapid breakdown of insuliase by the way of activation of liver insulinase. Adrenocorticotropic and thyrotropic hormones influence the metabolism of sugar by the way of acceleration of synthesis of glucocorticoids and thyroxin.

4) Hyperglycemia caused by narcosis - ether and morphine set free vegetative centres of the brain from the inhibiting influence of cerebral cortex, resulting in increased adrenalin secretion. Chloroform disturbs also the glycogen forming function of liver.

5) Hyperglycemia as a result of insulin deficiency-is one of main signs of diabetes mellitus.

**Diabetes mellitus (Gr. diabetes-to pass through, Lat. mel-honey) is a result of absolute or relative insulin deficiency.** The importance of insulin deficiency in the pathophysiology of diabetes mellitus has been firmly established since the studies of Minkowsky in pancreatectomized animals and the epoch-making discovery of insulin by Banting and Best. Later it was indicated that pituitary and adrenal hormones interfere with the action of insulin and may contribute to hyperglycemia.

Absolute (pancreatic) insulin deficiency means that synthesis of this hormone in organism is ceased or sharply decreased. This is caused by insufficiency of the beta-cells of the pancreatic islets, which may be hereditary or a result of pancreatectomy, tumors or cystic degeneration of pancreas, hemochromatosis, etc. Insulin deficiency is caused also by atherosclerosis and spasm of blood vessels supplying pancreatic islets, weakness of beta-cells as a result of overstrain. Disturbance of purine metabolism also may lead to the development of diabetes mellitus. Because in this condition alloxan is formed which is the poison that selectively damages beta cells.

One of the main causes of the absolute insulin deficiency is the hereditary weakness of beta cells. Some authors connect the origination of diabetes mellitus with the hereditary predisposition: probability to fall ill for persons with both diabetic parents is 100%, with one diabetic parent –50%. But in favourable conditions the person with hereditary predisposition to diabetes may not fall ill.

Relative (extrapancreatic) insulin deficiency is caused by hormonal and non-hormonal insulin antagonists in the peripheral tissues and blood. Hormonal antagonists of insulin are: adrenocorticotropic hormone, somatotropic hormone, glucocorticoids, adrenalin, thyroxin, triiodothyronine, glucagon, etc. The non-hormonal factors causing relative insulin deficiency are: insulinase (the enzyme which is synthesized in the liver), non-specific proteases (which breakdown the insulin by the hydrolitic way), synalbumin (combination of beta-polypeptide chain of insulin molecule with protein albumin), non-esterificated fatty acids, lipoprotein inhibitor, antibodies acting against insulin, etc. It is assumed that by the age somatic mutations occur in beta-cells and they synthesize insulin molecules of antigen properties which cause formation of antibodies against insulin. At the first periods of diabetes mellitus connected with the relative insulin deficiency, beta-cells function strenuously, which leads to functional and morphological changes in the cells. These cause secondary absolute insulin deficiency.

Diabetes mellitus is generalized chronic metabolic disorder manifesting itself in its fully developed form by hyperglycemia, glucosuria, increased protein breakdown, ketosis and acidosis. If the disease is prolonged, it is usually complicated by degenerative changes of the blood vessels, the retina, the kidneys and the nervous system. About 1% of population suffers from diabetes mellitus.

Generally speaking, if not specified, diabetes mellitus means primary or idiopathic diabetes mellitus. The secondary diabetes mellitus is occurrence of hyperglycemia associated with some identifiable causes such as chronic pancreatitis, pastpancreatectomy, hormone-producing tumors, certain drugs, hemochromatosis and genetic endocrinologic disorders.

Primary or idiopathic diabetes mellitus, the common form, is currently divided into 2 major categories:

Type I diabetes, previously termed juvenile-onset diabetes, or insulin-dependent diabetes mellitus (IDDM). This is ketosis-prone state with onset generally before age 25 to 30 in individuals who are not obese.

Type II diabetes, previously called maturity-oncet diabetes or noninsulin dependent diabetes mellitus (NIDDM). In this type there is resistance to ketosis, treatmentwith insulin is generally not necessary, onset is usually after age 40, and 70 per cent or more of patients are obese.

In most circumstances type II diabetes is brought about by a failure of insulin secretion to keep pace with the augmented demands for insulin engendered by obesity. But in some patients insulin resistance may be present even in the absence of obesity and may bring about diabetes despite hypersecretion of insulin.

Severe resistance to the action of insulin may develop secondarily in diabetic patients who have been treated with insulin for months or years. This may be due to marked overproduction of antibodies to exogenous insulin. Even less commonly, severe insulin resistance may be due to a decrease in the number of insulin receptors on target tissues or to the presence of a circulating antibody to the insulin receptor.

Recently a third type of spontaneous diabetes has been described under the term maturity-onset diabetes of youth (MODY). In this group ketosis-resistant non insulin dependent, generally asymptomatic form of diabetes is present in individuals before age 25.

These classifications admit many exceptions. For instance, some older diabetics are ketosis prone and insulin-dependent.

Insulin deficiency causes disturbances in all types of metabolism, which distinctly manifest themselves in diabetes mellitus. It has been suggested that the metabolic abnormalities associated with diabetes result not from insulin lack by itself, but rather from a bihormonal disturbance of alpha cell and beta cell function. For instance, glucagon accelerates the development of ketosis in circumstances of absolute insuline lack.

According to modern concepts in diabetes mellitus, on the one hand, utilization of glucose by cell is reduced, on the other hand, glyconeogenesis and breakdown of glycogen are accelerated.

Insulin deficiency causes a number of changes in fermentative processes. Sharp decrease of hexokinase synthesis leads to decrease of glucose-6-phosphate formation in hepatic cells and therefore, synthesis of glycogen is delayed. Pentosephosphate cycle is inhibited and activity of glucose-6-phosphotase is increased. Therefore, glucose-6-phosphate is dephosphorylated and enters the blood in the form of glucose. Passing of glucose through cell membrane is decreased, it is poorly assimilated by tissues. Conversion of glucose into fat is inhibited. Glyconeogenesis (formation of glucose from lactate, pyruvate, amino acids, fatty acids and other products of non – carbohydrate metabolism) is sharply accelerated owing to absence of suppressing influence of insulin on the enzymes ensuring glyconeogenesis in the cells of liver and kidneys (pyruvate carboxylase, glucose-6-phosphatase, etc.).

Thus, in diabetes mellitus excess production of glucose and its insufficient utilization by tissues take place. This leads to hyperglycemia. In severe cases of diabetes hyperglycemia reaches 500 mg% (27.8 mmol/l) and higher. This leads to the sharp increase of the osmotic pressure of blood, dehydration of the organism’s cells, severe disorders in the functions of the central nervous system, (hyperosmotic coma).

The hyperglycemia (sugar) curve in diabetes is considerably extended in time in comparison with that of in healthy persons.

The hyperglycemia in diabetes mellitus is of double significance:

1. It is one of the main compensatory reactions of the organism and plays an adaptive role. Because in the presence of hyperglycemia, glucosa comparatively easily enters the tissues.
2. The concentration of glucoproteids and mucoproteids is increased which are easily accumulated in the connective tissue and promote formation of hyaline. Therefore, early development of atherosclerosis is characteristic of diabetes. In elderly persons it is frequently combined with hypertensive disease.

When hyperglycemia reaches renal threshold for glucose, that is, 160-200 mg% (8,88-11.10 mmol/l), it is accompanied by glucosuria because of insufficient reabsorption of glucose; the higher the hyperglycemia, the more pronounced the glucosuria. In severe cases the sugar excreted in the urine amounts to 8-10%. Since the osmotic pressure of urine is increased, a great quantity of water passes into it and diuresis is increased up to 5-10 litres and more. This is called polyuria. Dehydration of organism develops which causes violent thirst-polydipsia. Formerly in diabetes excessive appetite was also observed-polyphagia.

In insulin deficiency formation of fats from carbohydrates, as well as resynthesis of tryglycerides from the fatty acids, are decreased, lipolytic effect of somatotropic hormone (which is normally suppressed by insulin) is strengthened as a result of the increased transport of fat from the fat depots to the liver (to replace the glycogen which disappears from the liver in diabetes), fats accumulate in the blood. The liver frequently undergoes fatty degeneration. Lipocaine prevents the process, because it accelerates assimilation of methionine, which stimulates endogenous synthesis of choline that is included in lecithin.

The insulin deficiency that is combined with the insufficient lipocaine production is called total diabetes. It is accompanied by the fatty infiltration of the liver. In the mitochondria of the hepatic cells ketone bodies (acetone, acetoacetic acid and beta-hydroxybutyric acid) are intensively formed. Their normal concentration in blood is no more than 2 mg% (0.02 g/l). In diabetes mellitus hyperketonemia develops, that is, their concentration is considerably increased (up to 20-60 mg%) and they begin to exert toxic action, especially suppress the activity of the central nervous system. One of the most severe complications of the diabetes mellitus, that is, diabetic coma (Kussmaul’s coma) or hyperglycemic coma, develops. It is characterized by loss of consciousness, rapid and weak pulse, decrease of the arterial pressure, periodic breathing. Alkali reserve is exhausted, and uncompensated acidosis develops (ph-7. 1-7.0). Development of hyperglycemic coma may be prevented or eliminated by administration of insulin.

It is very important to distinguish hyperglycemic coma from hypoglycemic coma. Because the medical aid in these two states is quite opposite. Usually the hyperglycemic coma develops gradually, whereas for hypoglycemic coma the rapid occurrence of its signs is characteristic. In the hyperglycemic coma the blood sugar is more than 350 mg% (19.43 mmol/l), there are large quantities of sugar in urine and ketone bodies in blood, arterial pressure is low, breathing - periodic, muscular tension-weak, the tongue and skin-dry, elasticity of skin is decreased. In the hypoglycemic coma, quite the reverse, the blood sugar is less than 40 mg% (2.22 mmol/l), there is no sugar in urine and blood content of ketone bodies, as well as arterial pressure and breathing are normal (sometimes-superficial breathing), muscular tension is high (sometimes - fits of convulsions), the tongue is moist, the skin-moist and pale. Ketone bodies are excreted in the urine (ketonuria) in the form of sodium salts. This leads to decreased sodium concentration in the blood; osmotic pressure of urine is increased which promotes polyuria. Surplus of acetoacetic acid is used for formation of cholesterol. So, in diabetes mellitus metabolism is also disturbed and hypercholeesterinemia occurs.

In diabetes mellitus protein metabolism is also thoroughly disturbed. Synthesis of proteins is decreased. Because stimulating influence of this process is ceased or greatly weakened, and the level of energetic metabolism is decreased. In insulin deficiency glyconeogenesis (formation of carbohydrates from amino acids and fats) is intensified. As a result of formation of a large amount of metabolites (ammonia, urea, etc.) in severe forms of diabetes mellitus content of nitrogen compounds in the blood and urine is increased.

As a result of disorders in biosynthesis of proteins in diabetes mellitus formation of antibodies and regenerative processes are reduced. Therefore, resistance of organism against infectious factors is decreased.

In the experiment usually alloxan diabetes is reproduced. Alloxan selectively damages the β - cells. The experimental diabetes mellitus may be reproduced also using ditison or hormones, which act against insulin. For example, administration of hormones of anterior lobe of pituitary body (somatotropic hormone, adrenocorticotropic hormone) for a long time causes diabetes (metahypophyseal diabetes) in animals.

The following forms of disturbances in lipide metabolism are distinguished:

1) disturbances in digestion and absorption of fats in intestine;

2) disturbances in passage of fats from the blood into tissues;

3) disturbances in deposition of fats (obesity);

4) disturbances in intermediate fat metabolism;

5) disturbances in phospholipide metabolism;

6) disturbances in cholesterol metabolism.

Digestion of fats is disturbed in a number of diseases of pancreas when lipase is not secreted into intestine in due amounts:

1) aplasia of pancreatic duct,

2) pancreatonecrosis,

3) fibrosis and hypoplasia of the pancreas,

4) pancreatitis.

Since a sufficient amount of the bile is needed for activation of lipase and emulsification of fats, naturally, all the diseases connected with disturbances of bile secretion cause malassimilation of fats by the organism:

1) congenital aplasia of biliary ducts;

2) dyskinesia of biliary ducts;

3) obstruction of biliary ducts by gallstones or squeezing from the outside;

4) hepatogenous jaundice;

5) biliary cirrhosis.

When lipase and bile acids are not excreted into intestine, steatorrhea develops, that is, feces contains much fats and becomes of greyish - white colour.

Absorption of lipides in intestine is disturbed in the following cases:

1) intestinal diseases which are accompanied by diarrhea (nutrients pass through digestive tract rapidly and steatorrhea develops);

2) disturbance of phosphorylation in the intestinal mucous membrane (poisoning with phloridzin and monoiodacetate);

3) vitamin A and B deficiency (decreased quantity of enzymes participating in the resynthesis of triglycerides).

The healthy human organism assimilates about 95% of lipides of nutrients. 5% is excreted in feces and certain quantity - by sebaceous and sweat glands. In some diseases (seborrhea) amount of fats excreted by sebaceous glands is increased.

In normal urine only traces of fats may be revealed. Excretion of fats in urine (lipuria) may be caused by:

1) excessive intake of fats in the food;

2) damage of the bone marrow;

3) fracture of tubular bones;

4) traumatic injury of the greater part of adipose tissue;

5) lipoid nephrosis.

Disturbances in absorption of fats may cause, besides steatorrhea and lipuria, also hypovitaminoses (A, D, E, K) chronic diseases of skin, deficiency of linolic and linolenic acids, etc.

1. Disorders in the lipide metabolism between the blood and tissues lead to the disturbances in passage of fats from the blood into tissues. The normal concentration of the neutral fats in the blood is 1-2 g/l. Increase of fat content of the blood is called hyperlipemia. The following types of hyperlipemia are distinguished:
	1. Alimentary (resorptional) hyperlipemia - occurs as a result of intake of large amounts of fats in the food. It is of temporary character (6-8 hours) but may become protracted in disorders of passage of fats from capillaries into cells.
	2. Retention hyperlipemia - is due to retarded passage of fat from the blood into tissues because of disturbed complexes of fats and plasma in hemorrhagic anemia, obstructive jaundice, diabetes mellitus, myxedema, nephrosis, etc.). This type of hyperlipemia occurs chiefly as a result of increased blood content of albumin and specific lipoprotein lipase (lucidity factor).
	3. Transport hyperlipemia - is a result of rapid mobilization of fats from the fat depots because of glycogen deficiency in the liver (in starvation, severe diabetes mellitus, nephrosis).
	4. Essential hyperlipemia - is rare hereditary disease, which is found mostly in males. In its homozygous form all the symptoms of the disease (hepatosplenomegaly, chylous plasma, fits of pain in belly, etc.) are found, whereas heterozygous organisms are predisposed to hyperlipemia and atherosclerosis.

Disturbances in deposition of fats leads to obesity (adiposis). Obesity is pathological deposition of fat in fat depots with the result that the weight of the body considerably increases (in some cases up to 190 kg and more).

Obesity may be caused by increased consumption of food with relatively low expenditure of energy, insufficient consumption of the fat reserves and their resultant increased formation in cases of normal nutrition or by combination of both factors.

An excessive appetite, especially connected with injury to the diencephalic region (which regulates the appetite) is of considerable importance (after an attack of encephalitis in tumors or trauma of hypothalamus - hypothalamic obesity).

In hyposecretion of hormones which stimulate mobilization and catabolism of lipides in the organism (thyroxin, somatotropic hormone, thyrotropic hormone) passage of fat from tissues into the blood is delayed. Adrenocorticotropic hormone, glucocorticoids and insulin stimulate synthesis of fats from carbohydrates and cause their excessive accumulation in fat depots.

When the hypofunction of sexual glands is accompanied by the functional disorders in the hypothalamic centers, accumulation of fat in adipose tissues is accelerated.

So, from etiologic standpoint cerebral, hormonal and alimentary types of obesity are distinguished. Hereditary factors also play a part in the development of obesity.

The main clinical forms of obesity are the following:

1. Lipodystrophia progressiva (Barraquer-Simons disease) - is connected with damage to metabolic centers in diencephalon, spinal cord, sympathetic ganglia. Decrease of fatty tissues in head and chest and obesity in the lower parts of the body are characteristic of this disease.
2. Adiposogenital (Babinsky - Frohlich) syndrome - is caused by damage to hypothalamus and anterior lobe of pituitary body; development of fatty tissues is accelerated in lower parts of abdomen and in thighs.
3. Icenko - Cushing disease- is connected with the hyperfunction of anterior lobe of pituitary body and adrenal glands. Obesity in upper parts of the body (face, shoulders, breast, upper part of the abdomen) is observed. The «moon face» is characteristic of this disease.
4. Hypofunction of thyroid gland - fat is accumulated equally in all surface of the body.
5. Hypofunction of sexual glands - fat is accumulated in subcutaneous tissues of thighs and abdomen.
6. Hypersecretion of insulin - synthesis of fats from carbohydrate metabolism products is accelerated and as the result of hypoglycemia appetite is increased.

Obesity exercises negative influence on vital activity of the organism:

1. Accumulation of fat in the mediastinum and pericardium mechanically makes difficult the activity of heart.

2. Large amount of fat in myocardium makes weaker its contractility.

3. Obesity decreases vital capacity.

4. As a result of obesity the organs of locomotor system are deformed.

5. Frequently obesity is accompanied by atherosclerosis and hypertension.

6. There is interrelation between diabetes mellitus and obesity. Increasing activity on the insular apparatus, initial obesity may lead to its weakening and development of diabetes.

There is inversely proportional connection between glycogen reserve and fat reserve of liver. Increase of one of them is accompanied by decrease of another one. 5% of normal liver’s dry mass consists of fats. In some diseases content of fats increases up to 50-60%. This is called fatty in -filtration of liver. According to the etiologic factors 5 types of fatty infiltration of liver are distinguished:

1) excessive intake of nutrients rich of carbohydrates and fats;

2) acceleration of synthesis of fats from carbohydrates in the organism (in vitamin B1 and B2 deficiency);

3) rapid mobilization of fats from fat depots into liver (in diabetes mellitus, starvation);

4) disturbance of transport of fats from liver to other tissues (hepatocirrhosis, deficiency of vitamin B6, methionine, lipocaine, linolic acid, excessive intake of cholesterol);

5) weakening of fatty acids catabolism in liver (influence of hepatotropic poisons-carbon tetrachloride, chloroform, phosphric compounds).

Relatively stable products of intermediate metabolism of the higher fatty acids are acetone, acetoacetic and betaoxybutyric acids, which are called ketone bodies. They are formed mainly in the liver and oxidized in other tissues to carbon dioxide and water. The normal blood consists 2-4 mg% (0.02-0.04 g/l) of ketone bodies.

Principal manifestations of disordered intermediate fat metabolism are ketonemia (increase of ketone bodies in the blood), ketonuria (increase of ketone bodies in the urine) and ketosis (accumulation of ketone bodies in the organism). They are observed in the following cases:

1) prolonged starvation;

2) diabetes mellitus;

3) renal glucosuria;

4) thyrotoxicosis;

5) hypersecretion of somatotrpic hormone and glucocorticoids;

6) poisoning by the alkaline - metals and combinations of ammonium.

Diurnal urine of the healthy person contains no more than 40 mg of ketone bodies, whereas in diabetes mellitus their content may be increased up to 50 g.

Development mechanisms of ketosis are the following:

1) carbohydrate deficiency (diabetes mellitus, starvation);

2) simultaneous deficiency of lipocaine and insulin;

3) damage to liver (leads to development of ketosis and fatty infiltration of liver).

In spite of differences in chemical and physiological properties of fats and lipoids (phos-polipides and cholesterol), a close connection between fat and lipoid metabolism exists. An excess of phospholipides (especially of lecithin) in the blood frequently accompanies lipemia. There are several hereditary diseases connected with deposition of phospholipides in the tissues:

1) Gaucher’s disease - is connected with deficiency of enzyme cerebrosidase. This results in accumulation of cerebrosides in macrophages of spleen, liver, lymph nodes, bone marrow.

2) Niemann - Pick disease - is characterized by increase of sphingomyelins in different cells. This results from deficiency of enzyme phosphorylcholinesterase.

3) Tay - Sachs disease (amaurotic idiocy) - is charactized by increase of gangliozides in different cells, atrophy of optic nerve, dementia.

4) Hunter - Pfaundler disease (gargoylism) - is characterized by increase of gangliozides in the brain and disturbance of micopolysaccharide metabolism.

Amaurotic idiocy and gargoylism are called also gangliozidoses.

The normal blood content of cholesterol is 1.8 - 2.3 g/l (180-230 mg%). This may be decreased (hypocholesteremia) or increased (hypercholesteremia).

The exogenous cholesterol does not play significant part in human pathology. Decrease of cholesterol in food causes acceleration of its endogenous synthesis.

Hypocholesteremia may be caused by:

1) hyperthyroidism,

2) cachexia,

3) acute infectious diseases,

4) pulmonary tuberculosis,

5) acute pancreatitis,

6) malignant anemia,

7) hemolytic jaundice,

8) acute diseases of liver.

Hypercholesteremia may be due to:

1) excessive intake of cholesterol with the food (egg yolks, butter, liver) - alimentary hypercholesteremia;

2) decrease of lipolytic ability of aorta wall;

3) excessive mobilization of chollesterol from tissues (in diabetes mellitus);

4) insufficient excretion of cholesterol by the liver and intestine (in obstructive jaundice and chronic liver disease);

5) changes of physicochemical properties of plasma proteins (in lipoid nephrosis);

6) disturbed oxidation of cholesterol (in hypofunction of the thyroid gland);

7) hereditary hypercholesteremia (blood content of cholesterol is increased up to 5-10 g/l).

Disturbances in cholesterol metabolism and its accumulation in the blood may give rise to certain pathological processes: cholelithiasis, lipoid nephrosis, senile keratoleucoma, dermal and bony xanthomatosis. But the most important manifaestation of hypercholesteremia in the humen organism is atherosclerosis.

Atherosclerosis consists in a thickening of the intima mainly of large arteries and deposition of lipoid substances (cholesterol and its esters) in it. Many factors play a part in the occurrence of atherosclerosis: disturbances of metabolism, hormonal factors, arterial hypertension, changes in the vascular wall, hereditary and ethnic factors, hypercholesteremia; emotional stress, etc.

N.N. Anichkov ascribed atherosclerosis to accumulation in the organism (in the blood) of cholesterol and its infiltration of vascular walls (alimentary - infiltration theory). In the experiments of N.N. Anichkov and S.S. Khalatov feeding of rabbits on cholesterol - rich food or cholesterol (dissolved in oil) produced atherosclerotic changes similar to human atherosclerosis.

But at present it is considered that exogenous cholesterol does not play a significant role in the development of human atheroselerosis. It is connected with the changes in quantitative correlation between cholesterol and lecithin (cholesterol / lecithin coefficient), increase of content of β - lipoproteides.

According to immunologic theory atherosclerotic changes are connected with formation of - β - lipoproteide - antoantibody complexes which circulate in the blood and are settled on the intima of arteries. Neuro - metabolic theory attaches great importance to the hormonal factors and psyshoemotional strain in the development of atherosclerosis. Really, emotional stress, arterial hypertension, diabetes mellitus, hypothyrosis accelerate this process. In our experiments (N.J. Mikailzade, 1969) daily quintuple stimulation (during 63 day) of posterior hypothalamus and midbrain reticular formation in rabbits receiving cholesterol, intensified atherosclerotic changes the aorta wall. Thrombogenic theory is based on the connection between the state of vascular wall and development of atherosclerosis. Damage to arterial wall (arteritis, thrombosis) accelerates development of the atherosclerotic changes.

Experimental model of atherosclerosis is reproduced by the method proposed by N.N. Anichkov and S.S. Khalatov (1912) rabbit is given cholesterol (0.1-0.5 g/kg of body mass) daily during several months. This method allows to reproduce atherosclerosis also in hens, pigeons, monkeys, swines. To animals which are resistant against cholesterol (dog, rat) simultaneously methylthiouracil is given. It suppresses thyroid gland activity and in this way accelerates endogenous synthesis of cholesterol.

The following forms of disturbances in protein metabolism are distinguished:

1) disturbances in nitrogen balance;

2) disturbances in degestion and absorption of proteins;

3) disturbances in sythesis of proteins;

4) disturbances in intermediate amino acid metalbolism;

5) disturbances in final stage of protein metabolism;

6) disturbances in blood content of proteins;

7) disturbances in nucleic acid metabolism.

Since nitrogen compounds enter the orgnism mainly in the nutrients of protein origin, one of the principal indices characterizing the protein metabolism is nitrogen balance, that is, the ratio between the quanity of nitrogen entering the organisim in the food and that of excreted from the organism. The state when these are equal, is called «nitrogen equilibrium». This is observed in people of middle age that receive food of full value.

The positive nitrogen balance is the state when less nitrogen is excreted from the organism than that entering with food. This means that synthesis of protein prevails over its disintigration. The postive nitrogen balance is observed in the period of growth of the organism, pregnancy recovery after severe diseases, concentrated sports trainings that are accompanied by increase of mass of muscles. In all of these cases anabolism prevails over catabolism and retention of nitrogen occurs, that is, nitrogen is delayed in the organism. Somatotropic hormone, insulin, sex hormones accelerate synthesis of proteins and cause positive nitrogen balance. The negative nitrogen balance is the state when more nitrogen is excreted from the organism than that entering with food. It is observed in the period of starvation, protein deficiency, diseases proceeding with rapid disintegration of organism’s tissues, in old persons. The catabolic hormones (glucocorticoids, thyroxin) cause the negative nitrogen balance.

Disturbances in digestion and absorption of proteins are caused by various pathological conditions of the gastrointestinal tract: hyposecretion of gastric, pancreatic, intestinal juices, acceleration of gastric and intestinal peristalsis, inflammatory and destructive changes in the gastric and intestinal walls, etc.

Disorders of the intestinal function give rise to increased putrefaction accompanied by greater deamination and decarboxylation of amino acids, that is, formation of indole, phenol, skatole, cresol, cadaverine, putrescine, as well as products of incomplete protein conversion. These are absorbed through the intestinal wall and may lead to intoxication (especially in children). Disturbances of biosynthesis of proteins may be caused by a number of factors, in the first place by defective compostion of proteins in the food and pathological mutations, that is, genetic factors.

Deficiency of any of nonreplaceable amino acids (arginine, leucine, methionine, phenylalanine, etc.) may cause disturbances in interstitial synthesis of proteins, negative nitrogen balance, general weakness, disorders in nervous system, etc. Absence or deficiency of each nonreplaceable amino acid causes some specific changes in the organism. For instance, absence of arginine in the food leads to suppression of spermatogenesis, absence of methionine results in fatty infiltration of liver, deficiency of histidine is accompanied by decrease of concentration of hemoglobin, etc.

Most of disorders in the genetic apparatus of the organism are accompanied by the disturbances in biosynthesis of proteins. The acquired types of these disorders are connected with the somatic mutations and hereditary types-with the mutations of sex cells. So, the most of hereditary diseases are connected with the fact that certain protein molecule is not synthesized or its anomalous form is synthesized. Therefore, these diseases are called the «molecular diseases» or proteinopathies.

Proteinopathies are divided into 2 large groups:

1. Enzymopathies - are defects of protein molecules of fermental character, they cause disturbances in certain stage of metabolism.

2. Non-enzymatic proteinopathies - are defects of proteins fulfilling different functions (transport of substances through cell membrane, receptor, immune) in the organism. They are accompanied by disorders in concrete function of the protein the synthesis of which is disturbed.

Hereditary deficiency of all proteins of fermental nature may be found in the organism. For instance, acatalasemia is the hereditary disease connected with the deficiency of enzyme catalase in tissues (its severe forms are accompanied by ulcera of mucous membranes). Genetic defects of coagulation factors of proteinase nature cause disturbances in blood coagulability.

The hereditary diseases connected with disturbances in phenylalanine and thyrosine metabolism are comparatively frequent:

1. Phenylketonuria (phenylpyruvic acidic oligophrenia) - is connected with deficiency of enzyme phenylalanine - 4 - hydroxylase which converts phenylalanine into tyrosine. This disease is characterized by dementia, fits of convulsions, hypopigmentation of hairs. To diagnose phenylketonuria, on the fresh urine several drops of 5% iron trichloride acetate solution is added, and it becomes of olive - green colour.

2. Albinism - DOPA (dioxyphenylalanine - product of tyrosine’s oxidation) is not converted into DOPA quinone and synthesis of pigment melanin is disturbed. The main signs of the disease (hypopigmentation, whiteness of hairs, reddish colour of the iris of eyes) do not seriously exercise the vital acitivity of the patients, but they are sensitive to sunlight.

3. Tyrosinemia - is connected with parahydroxy - phenylpyruvate oxidase deficiency. Blood content of tyrosine and parahydroxyphenylpyruvic acid are increased, and they are excreted in urine. The physical development of these children is delayed.

4. Alkaptonuria - is caused by homogentisinate oxidase deficiency. Homogentisic acid which is converted into alkapton, is excreted in urine (the rag moistened in child’s urine becomes of black colour) and is accumulated in some tissues (ears, nose, cheeks, sclera are tinged black). In some cases joints are severely damaged and the movements are disturbed.

5. Homocysteinuria - is connected with cystathionine synthetase deficiency. A large amount of homocystein is accumulated in the blood and tissues and is excreted in the urine. This causes arrest of mental development and periodic convulsions.

6. Histridinemia - is connected with histidase deficiency. Histidine content of blood and urine is sharply increased. The central nervous system activity is disturbed (the general muscular hypotonia, convulsions, etc).

7. Disease of decarboxylase deficiency (“disease of birch sap”) - blood content of ketonic formations of valine, leucine and isoleucine is increased and they are excreted in urine. The main clinic signs of the disease are: charcateristic birch sap smell of urine, vomiting, periodic convulsions, muscular hypertension, los of sight.

Non - enzymatic proteinopathies include hemoglobinopathies (hereditary defects of hemoglobin molecule), agammaglobulinemia (hereditary defects of formation of antibodies which lead to weakness of immune reactions of the organism), transport proteinopathies (connected with hereditary pathology of proteins participating in transport of different substances through cell membranes), etc. The frequent protenopathies are:

1. Aminoaciduria - is connected with disturbance of protein system regulating transport of amino acids (their reabsorption) in tubules of the kidney excretion of which in urine is increased 3-5 times.

2. Cystinuria - is defect of specific protein molecule participating in transport of cystin whose large amounts are excreted in urine and cause formation of cystin calculi in kidneys.

3. Glucosuria, fructosuria, galactosuria, pentosuria - are connected with disturbances in synthesis of transport proteins in renal parenchyma, and corresponding monosaccharides are excreted in the urine. These proteinopathies are called «renal diabetes».

Disturbances in intermediate amino acid metabolism include disorders in processes of deamination and decarboxylation of amino acids and metabolism of separate amino acids (which form the basis of a number of hereditary enzymopathies).

Weakening of deamination occurs as a result of decrease of aminoxidases activity and disturbances of oxidation processes (hypoxia, hypovitaminoses B2, C, PP). Disturbance of deamination causes increase of amino acid content of blood (hyperaminoacidemia) and their increased excretion in urine (aminoaciduria). Formation of urea is decreased. The pathological processes causing decrease of protein synthesis (starvation, disturbances of hepatic function), as well as deficiency of vitamin B6, glucocorticoids, thyroid hormones lead to disturbances in transamination. When formation of urea is disturbed, acceleration of transamination occurs.

In the pathological processes which are accompanied by suppression of oxidative deamination (hypoxia, ischemia, destruction of tissues) conversion of amino acids occurs mostly by the way of decarboxylation with accumulation of biogenic amines. These cause disturbances in local blood circulation, increase of capillary permeability, damage of nerve ceptors.

The final products of protein metabolism are ammonia, urea, carbon dioxide and water. Ammonia is poisonous and when accumulated, injures cell protoplasm. There are several diseases connected with hereditary disturbances of detoxication of ammonia (defects of enzymes participating in formation of urea):

1. Argininosuccinaturia – is connected with defect of argininosuccinatelyase; consists in hyperacidaminuria and oligophrenia.

2. Ammoniemia – is connected with blocking of enzymes catalizing binding of ammonia and formation of ornithine in the cycle of formation of urea; blood content of ammonia and excretion of glutamine in urine are increased.

3. Citrullinuria – is caused by defect of argininosuccinate synthetaze; concentration of citrulline may be increased 50 times, in urine 15 g of citrulline is excreted daily.

Disturbances in activity of enzymes participating in synthesis of urea occur also in diseases of liver (hepatitis, congestive cirrhosis) hypoproteinemia, suppression of oxidative phosphorylation. Ammonia is accumulated in the blood and tissues, this leads to intoxication: ketogenesis is accelerated, consumtion of oxygen is decreased; comatose condition develops.

Disturbances in blood content of proteins may be of 3 types:

1) hyperproteinemia - increase of total amount of proteins in blood;

2) paraproteinemia - availability of abnormal proteins in the blood;

3) hypoproteinemia - decrease of total amount of protein in the blood;

4) dysproteinemia - changes in percentage of different protein fractions (the total content of plasma proteins being normal).

Hyperproteinemia is mostly of relative character, that is, as a result of losts of large amounts of water by the organism the general quantity of the blood is decreased, and the blood concentration of proteins becomes higher (diarrhea, vomiting connected with obstruction of small intestine, vast burns).

Absolute hyperproteinemia often is resulted from increase of globulins. In infectious and toxis processes content of globulins is increased more than that of albumins, and therefore, albumen-globulin ratio is decreased.

Hypergammaglobulinemia may occur as a compensatory state in the period of decrease of albumins in the organism (chronic diseases of liver).

Paraproteinemia is frequently accompanied by hyperproteinemia. It is observed in the followind cases:

1.In blood serum of persons with myeloma specific “myelogenic protein” (functionally inert protein of abnormal structure belonging to group of immunoglobulins) is found. Often these proteins pass the renal barrier and are excreted in the urine.

2.Macroglobulins are characteristic of Waldenstrom macroglobulinemia.

3.In the blood of persons with myeloma, nephrosis, hepatocirrhosis, leukosis, etc, cryoglobulin is found. This is very dangerous, because in the cold cryoglobulin falls out, causing thrombosis and necrosis of tissues.

Hypoproteinemia occurs mostly as a result of decrease of albumins in the blood. Disturbances in synthesis of proteins, the factors accelerating passage of serum proteins into tissues, the diseases causing loss of proteins are accompanied by hypoproteinemia. It is one of constant and frequent signs of the nephrotic syndrome. Hypoproteinemia is found also in severe damages of the hepatic parenchyma protein, deficiency (starvation, digestive disorders, carcinoma), sharp increase of capillary permeability.

Dysproteinemia is observed in the following cases:

1. Acute hepatitis , hepatocirrhosis , mechanical jaundice are accompanied by decrease of alpha –lipoproteins in blood serum.

2.In nephrotic syndrome, myxedema mononucleosis, xanthomatosis, atherosclerosis, sometimes in chronic hepatitis content of alpha-lipoproteins is above normal.

3. In pneumonia, pleuritis, tuberculosis, acute rheumatism, myocardial infarction, nephrotic syndrome ,diabetes mellitus, gout, leukosis, myeloma, etc., plasma content of glycoproteids is increased.

Pathology of nucleoprotein metabolism implies disturbances in assimilation of nucleoproteins, that is, complex protein bodies consisting of protein and nucleic acid and forming part mainly of the nuclear substance of the tissues.

Nucleoproteins are the source of formation of uric acid. Normal blood content of uric acid is 30-40mg/ l.

Increased formation of uric acid and its accumulation in the blood (hyperuricemia) occurs not only as a result of intake of more exogenous nucleic substances (meat diet, etc.) but also because of pathological destruction of cells (in pneumonia, leukemia, malignant neoplasia, fever). Disturbances in the excretory ability of the kidneys may be the cause of uric acid accumulation in the blood.

Disorders in the purine balance and excessive formation of uric acid in organism underlie gout (podagra). In some persons hereditary predisposition to gout (in the form of hyperuricemia)is observed.

Gout is characterized by attacks of inflammation of the joint. It is marked by considerable accumulation of sodium urate and its precipitation in crystals mainly in mesenchymal tissues (cartilage, joint capsules, tendons, fasciae), as well as muscles, skin and kidneys. Frequently concretions are formed. Blood content of uric acid (especially before attacks) is increased (10-15% and higher). The attacks are characterized by acute pain in the affected joint (mainly the great toe).

Along with a high concentration of uric acid in the blood gout is characterized by its low concentration in the urine. The amount of uric acid excreted in the urine sharply increases during attacks and in the period immediately following them. In the pathogenesis of gout hereditary disturbances of mucopolysaccharide and mucoprotein metabolism also play a certain part. They are deposited in tissues and become the centers of crystallization of uric acid. Allergic component also participates in the pathogenesis of gout. Diseases of kidneys, decompensation of cardiac activity, diabetic coma, leukosis, hemolytic anemia, myeloma cause rapid disintegration of nucleoproteins and increase of blood content of uric acid. These are called “the secondary gout”. Owing to activity of buffer systems of the blood as well as activity of a number of organs and systems of the organism (especially that of lungs and kidneys) the active reaction of the blood is maintained on the relatively constant level (PH of arterial blood is 7.4 , that of venous blood- 7.35). The condition characterized by reduction of alkali reserve of blood (especially bicarbonate reserve) or by an excess of acid – reacting substances is called acidosis. Relatively high alkali reserve leads to alkalosis.

If not accompanied by an appreciable shift of the blood PH they are called compensated acidosis (decrease of PH down to 7.35) or alkalosis (increase of PH up to 7.45). Uncompensated acidosis or alkalosis are observed in deep pathological disorders.PH<6.8 or >7.8 leads to death.

Gaseous (respiratory) and non-gaseous acidosis and alkalosis are distinguished. Accumulation of carbon dioxide in the fluids and tissues leads to gaseous acidosis, its accelerated elimination - to gaseous alkalosis.

 Non –gaseous acidosis is observed in excessive concentration or insufficient oxidation of acid reacting substances, non-gaseous alkalosis - in cases of administration of alkalis or loss of a large amount of acid products (for instance, gastric juice).

The following types of non –gaseous acidosis are distinguished:

1.Metabolic:

1. ketoacidosis: in diabetes mellitus, starvation, fever , hypoxia, disturbances of hepatic functions;
2. lactate acidosis: in hypoxia, disturbances of hepatic functions, infections;
3. acidosis connected with other organic and inorganic acids: in vast inflammatory processes, burns, traumata.

2. Excretory:

1. delay of acids in renal insufficiency (diffuse nephritis, uremia);
2. loss of alkalies (renal or gastroenteric).

3. Exogenous:

1. long –term use of sour food;
2. taking of some medicines (NH4CL, etc.);
3. (rarely) taking of acids.

4.Combined:

a) ketoacidosis + lactate –acidosis;

b) metabolic +excretory;

c) other combinations.

Mixed (gaseous+non- gaseous) forms of acidosis occur in asphyxia, cardiovascular insufficiency, etc.

It must be noted that in gaseous acidosis (hypercapnia) the ability of hemoglobin to be connected with O2 is decreased, less oxygen is given to tissues (hypoxia), oxidation processes do not come to the end, and conditions are created for the development of the metabolic acidosis.

Gaseous acidosis may be observed in the following cases:

1. disturbances in the external respiration (weakness of the respiratory center, asphyxia, chronic diseases of lungs);
2. disturbances in blood circulation;
3. increase of carbon dioxide in the inspired air.

Hypercapnia leads to the development of a number of compensatory reactions in the organism (increase of plasma bicarbonates, excretion of acids by kidneys and increase of reabsorption of bicarbonates). Respiration rate is increased. It is necessary to recover pulmonary ventilation.

One of the frequent complications of the non- gaseous acidosis is Kussmaul respiration (as a result of hypocapnia the respiratory center is not sufficiently stimulated). As a result of loss of sodium, potassium, calcium ions water-salt metabolism and cardiac rhythm are disturbed, disorders in neuromuscular activity, decalcification of bones occur.

To treat this type of acidosis sodium hydrocarbionate is administered and naturally the basic disease (that has caused acidosis) must be cured.

Gaseous alkalosis is observed in the following cases as a result of hyperventilation of lungs;

1. protracted artificial respiration with pure oxygen;
2. hyperthermia;
3. hysteria;
4. tumors of the brain.

In gaseous alkalosis compensatory mechanisms are directed to lowering of content of bicarbonates: reabsorption of bicarbonate ions and excretion of hydrogen ions in kidneys are reduced by the reflex way. So, acids are kept in the organism and alkalies are excreted. Together with sodium hydrocarbonate much water is excreted in urine which leads to dehydration of the organism.

In the treatment and prophylaxis of the gaseous alkalosis breathing with the gaseous mixture is important.

The following types of non – gaseous alkalosis are distinguished:

Excretory:

1. delay of alkalies (intensified reabsorption of alkaline anions in kidneys);
2. loss of acids (vomiting in pylorostenosis, ileus, toxicosis of pregnancy, gastric hypersecretion);
3. hypochloremic –“metabolic”.

Exogenous:

1. long – term use of alkaline food;
2. administration of some medicines (bicarbonate and other alkaline substances).

Compensatory reactions of the organism are directed to increase of acids and decrease of alkalies. Together with sodium compounds much water is lost. In severe cases content of calcium ions is sharply decreased and convulsions occur.

To treat the metabolic alkalosis the factor that caused it must be eliminated and weak acids, potassium salts and inhibitors of the carbonic anhydrase must be administered into organism.

Some mixed forms of acidoses and alkaloses also occur:

1. Gaseous alkalosis + metabolic acidosis (high altitude sickness, loss of blood).
2. Gaseous alkalosis + renal tubular acidosis (heart failure and treatment by carboanhydrase inhibitors).

Water balance of the organism may be changed in two directions:

1. Negative water balance (loss of water by the organism)- causes dehydration of the organism.

2. Positive water balance (retention of water in the organism)- causes hyperhydration.

Both dehydration and hyperhydration may be of 3 types:

1. isoosmotic- when the water and electrolytes are lost or delayed in the organism in the proportional amounts, and the osmotic pressure does not change;
2. hypoosmotic –as a result of dehydration or hyperhydration the osmotic pressure is decreased;
3. hyperosmotic – dehydration or hyperhydration result in increase of osmotic pressure.

Sometimes the amounts of intracellular and extracellular fluids change disproportionately, and therefore, intracellular and extracellular types of dehydration and hyperhydration are distinguished.

Dehydration occurs in the following cases:

1. Isoosmotic dehydration – is observed immediately after acute loss of blood, in some types of polyuria, intestinal toxicoses.

2. Hypoosmotic dehydration – is resulted from loss of large amounts of electrolytes: rapid loss of intestinal juices (recurring vomiting, diarrhea), intake of large amounts of water during increased sweating, etc. Decrease of osmotic pressure leads to compensatory hypersecretion of aldosterone. Loss of water and electrolytes results in also disturbances in the acid –base equilibrium: loss of gastric juice leads to alkalosis; loss of pancreatic and intestinal juices- to acidosis.

3. Hyperosmotic dehydration –is caused by loss of water when electrolytes (especially sodium) are kept in the organism : hyperventilation, increased sweating, loss of saliva, vomiting, diarrhea, polyuria (diabetes insipidus, psychogenic polydipsia).

The main compensatory reaction in this state is hypersecretion of antidiuretic hormone.

Dehydration of cells causes unquenchable thirst, rapid breakdown of proteins, increase of body temperature, loss of conciousness in severe cases. Disturbances in blood circulation result in fall of arterial pressure, disorders in the activity of kidneys, gastrointestinal system, etc. The severe cases of dehydration lead to decrease of excretion of urine, azotemia, uremia, renal insufficiency. Accumulation of acid metabolic products results in development of the metabolic acidosis.

Loss of 2/3 of extracellular liquid leads to the death as a result of disorders in the central nervous system (convulsions, comatous condition). In such cases oxygen and glucose supply of nerve cells and the enzymatic processes in them are disturbed.

Hyperhydration is observed in the following cases:

1. Isoosmotic hyperhydration- occurs in rare cases when a great amounts of physiological solution is introduced into the organism, and soon is eliminated owing to activity of the regulating mechanisms.

2. Hypoosmotic hyperhydration (water poisoning) occurs when a great amount of the water is introduced into the organism.

Water poisoning may develop as a result of severe disturbances in renal function, for instance, reflexogenic anuria in postoperative period. The patients complain of headache, nausea, vomiting; convulsions and comatose condition are observed. The severe forms of the water poisoning result in death.

To produce water poisoning in experiment during 5-6 hours 10-12 times (once every 30 minutes) 50 mg/kg of body mass water is introduced into stomach of dog.

3. Hyperosmotic hyperhydration – may develop when one drinks a large amount of salt water (or sea-water). Some part of the intracellular fluid passes into interstitial space and blood. This causes excruciating thirst and severe changes connected with dehydration of cells.

In the following cases hyperhydration connected with disturbances in the regulatory mechanisms of the water- salt metabolism, develops:

1. hypersecretion of vasopressin and inulin;
2. primary and secondary hyperaldosteronism;
3. myxedema;
4. abstinence from intake of table salt.

Usually surplus of water in the organism easily passes from the blood into tissues, especially into intercellular spaces. But in pathological states a large amount of fluid may accumulate in intercellular spaces even under conditions of limited intake of water. Pathological accumulation of fluid in tissues (mainly in intracellular space) due to disturbed water and salt metabolism between the blood and tissues is called edema. Edema is one of the typical pathological processes.

Accumulation of fluid in serous cavities is known as dropsy. Accumulation of serum in the subcutaneous connective tissue is referred to as anasarca, accumulation of serous fluid in the peritoneal cavity- ascites, collection of serous effusion in the pericardial cavity- hydropericardium, collection of serous fluid in the pleural space- hydrathorax, an increase in the volume of cerebrospinal fluid within the skull- hydrocephalus, accumulation of fluid in the sac of the tunica vaginalis of the testis – hydrocele.

The signs of edema are an increased tissue volume, changes in the form and tension of the tissue which are evident especially in edema of the skin. The skin becomes pale and cold, its surface can be indented by pressure; such indentation is temporary and disappears soon after the pressure is released.

Noninflammatory fluid that is accumulated in the cavities is called transudate. It differs from inflammatory fluid (exudate). The transudate is characterized by low specific gravity and negligible (about 0.3% ) protein content, which varies depending on the character of the edema and its pathogenesis.

Hydrodynamic or mechanical capillary pressure and rate of the blood flow , osmotic , oncotic factors, increased capillary permeability, disturbances in the neurohumoral regulation of the lymph flow and water metabolism, etc., play an important part in the pathogenesis of edema.

According to the mechanism of development (pathogenesis) the following types of edema are distinguished:

1. mechanical (congestive) edema;
2. oncotic edema;
3. osmotic edema;
4. toxic edema (hyperpermeability of the capillary wall).

Normally, the hydrodynamic (hydrostatic) pressure in the arterial part of capillaries (35-40Hg) is higher and in the venous part (15-16 mm Hg)-lower than the oncotic pressure (25-30 mm Hg). Therofore, in the arterial part of capillaries filtration (passage of fluied from the blood into the tissue), and in the venous part – reabsorption (passage of fluid from the tissues into the blood) occur.

Increased hydrostatic pressure (especially in venous system) causes increase of filtration and decrease of reabsorption. This leads to mechanical (congestive) edema. Edemas connected with thrombophlebitis and in the legs of the pregnant women develop by this way; the mechanical factor is of great importance also in the pathogenesis of edemas connected with the heart failure.

Proteins keep water, and therefore, decrease of oncotic pressure of the blood leads to development of the oncotic edema. Oncotic factor is significant in the mechanism of development of the renal (especially in nephrosis), hepatic, cachectic edemas. Excess of sodium (in the form of chloride) changing the osmotic pressure leads to the development of the osmotic edema.

Increased capillary permeability leads to passage of plasma proteins into intercellular spaces; filtration predominates over reabsorption. Acceleration of lymph flow from tissues is important compensatory mechanism preventing development of edema whereas impeded lymph flow promotes this process. Besides, the fluid accumulated in the tissues squezees lymph vessels, and vicious circle comes into being which causes development of edema.

As a result of disorders in neurogen regulation of the tissue trophicity and water metabolism vascular wall permeability is increased, and this leads to the development of neurogen edema.

The hormonal factors participate in the mechanism of development of edemas in close connection with the neural factors. Some widespread forms of edema (of cardiac, renal, hepatic origin) develop as a result of active delay of water and electrolytes in the organism. Increased secretion of mineralocorticoids (especially of aldosterone) causes retention of hydrophilic sodium in the organism. Secretion of the antidiuretic hormone is also increased.

Although hypersecretion of aldosterone and antidiuretic hormone under these conditions is the reaction serving preservation of circulating blood volume , but it loses its defence – adaptability significance. Therefore, the diseases which are accompanied by edema, are attributed to the group of “adaptation diseases” (Selye).

Different chemical substances, bacterial toxins, poisons of animal origin increase capillary permeability and at the same time, changing metabolism in tissues, lead to the formation of substances increasing osmotic pressure of the intercellular fluid. So, toxic edema develops.

In clinics the etiologic classification of edemas is widely used. Edemas are distinguished according to their etiology as congestive, cardiac (circulatory), lymphogen, renal, cachectic (marantic), inflammatory, toxic, neurogen (neurotrophic), endocrine, allergic. The edemas of congestive origin include those which result from obstruction of veins (thrombi, emboli) and their constriction by tumors.

In the mechanism of the cardiac edema active delay of salts and water in the organism plays an important part. Weakened contractile function of the heart leads to hypovolemia (decrease of blood volume in arteries) which causes reflexogenic hypersecretion of aldosterone. At the same time renal ischemia leads to hypersecretion of renin which (by the help of angiotensin) stimultes synthesis of aldosterone. Besides, under the conditions of arterial hypovolemia production of enzyme steroid dehydrogenase (which inactivates surplus of aldosterone in blood) is decreased.

So, secondary hyperaldosteronism develops and causes hypernatremia which, stimulating osmoreceptors, leads to the increased production of antidiuretic hormone-excretion of urine is decreased. Delay of water in the organism leads to hypervolemia, ascites, edema. In cardiac insufficiency increased venous pressure and congestion as well as lymph drainage failure and increased capillary permeability (blood proteins pass into interstitial fluid) redouble the edema. The lymphogen edema is connected with the impeded lymph drainage.

Depending on the type of pathological processes in kidneys several forms of the renal edema are distinguished. In nephritis glomerular filtration is decreased, hypernatremia occurs. Owing to activation of renin – angiotensin system hypersecretion of aldosterone occurs. This intensifies hypernatremia which increases production of antidiuretic hormone. Capillary permeability for electrolytes and proteins is increased. The transudate contains 2-3 % of proteins. So, nephritic edema is characterized by increased protein content of the interstital fluid and increased hydrophilic property of tissues. In the nephrotic syndrome the water is accumulated in the intercellular space, in the first place, as a result of decreased oncotic pressure of plasma, owing to which in the arterial part of capillaries effectiveness of the hydrostatic pressure (filtration pressure) is increased, and in the venous part resorption of fluids is decreased. In the nephrotic syndrome permeability of the renal glomeruli is increased, albuminuria and hypoproteinemia occur. Hypoproteinemia is accompanied by hypovolemia which results in hypersecretion of aldosterone and antidiuretic hormone- salts and water are delayed in the organism. The nephrotic transudate contains insignificant amount of proteins. In acute renal insufficiency which develops as a result of infectious- toxic injuries, excretion of surplus of salts and water from the organism is decreased - oliguria or anuria and edema develops.

Since delay of sodium in the organism plays an important part in the origination of cardiac and renal edemas, to eliminate them it is necessary to limit intake of table salt and accelerate its excretion from the organism.

Hepatic edema is characterized by accumulation of transudate in the abdominal cavity (ascites) and increase of general volume of the extracellular fluid (edema). Ascites is caused by impeded intrahepatic circulation and subsequent increase of hydrostatic pressure in the portal vein system. Disturbance of the excretory (water and electrolytes) function of kidneys also leads to increase of fluid in abdominal cavity and intercellular space.

In hepatocirrhosis secretion of aldosterone is increased and its inactivation is decreased.

Decreased synthesis of albumins leads to hypoalbuminemia and decrease of oncotic pressure of the blood. All of these factors participate in the mechanism of hepatic edema and ascites.

Cachectic edema is observed in alimentary dystrophy (as a result of starvation), wasting disease of newborns, malignant tumors and other diseases which are accompanied by cachexia. The principal pathogenetic factors are hypoproteinemia (synthesis of proteins is disturbed) and increased capillary permeability (trophic disorders).

In the pathogenesis of inflammatory and toxic edemas microcirculatory disorders in the focus of damage and increased capillary permeability play a main part. These changes are connected with the influence of vasoactive substances (mediators of inflammation): histamine, serotonin, kinins, adenosine triphosphate, adenosine diphosphate, etc. As a result of local disorders in tissue metabolism, osmotic and oncotic pressures are increased in the intercellular space.

Neurogen edema develops as a result of disturbance in nervous regulation of tissue and vascular trophicity (edema of limbs in syringomyelia, edema of the face in neuralgia of the trigeminal nerve). Development of these edemas is connected with increased vascular permeability and metabolic disoders in damaged tissues.

Endocrine edemas are due to dysfunction of endocrine glands. For example, in hypothyroid edemas tissue nutrition and properties of the tissue colloids are greatly disturbed.

Allergic edema occurs as a result of sensibilization of the organism and allergic reactions (urticaria, allergic rash, arthrites, etc.). Its developmental mechanism is similar to that of inflammatory and neurogen edemas. But in the mechanisms of the microcirculatory disorders and increased capillary permeability both biologically active substances and immune complexes take part.

The outcome of edema depends on the course of the pathological process responsible for the retention of water in the tissues. After elimination of the cause, the fluid accumulated in the tissues is resorbed. But protracted edemas are sometimes characterized by loss of elasticity by the tissues with the result that the tissues do not tract and the fluid remains in them for a long time after elimination of the cause.

Edema originates as defence- adaptative reaction of the organism:

1) passage of fluid from vessels into intercellular space promotes decrease of concentration of different chemical and toxic substances and clearance of blood from poisonous substances;

2) as a result of passage of fluid into intercellular space constancy of osmotic pressure of organism's fluids is maintained;

3) toxic, inflammatory, allergic and other edemas squeeze blood and lymph vessels in the focus of damage and decrease the rate of spreading of different toxic factors (bacteria, toxins, allergens) in the organism.

But like all typic pathological processes, edemas also being defence- adaptative reactions of the organism, at the same time exert injuring action on it:

1. exercising mechanical influence(squeeze) on the tissues, edema causes disorders in blood circulation, their trophicity is disturbed , organism’s resistance against infectious agents is reduced (for instance, pulmonary edema may give rise to pneumonia);
2. protracted severe edemas cause the state of chronic hypoxia in the tissues; the parenchymal elements gradually perish and in their place those of connective tissue develop;
3. under the conditions of high osmotic pressure of transudate part of the intracellular fluid passes into intercellular space ; as a result of dehydration of cells unquenchable thirst occurs and body temperature rises;
4. under the conditions of low osmotic pressure of transudate part of it enters the cells, intracellular edema and water poisoning occur;
5. dysfunction of brain, heart , lungs and other organs when the fluid is accumulated in the ventricles of the brain, pericardiac cavity, pleural cavity, etc.

Disturbances in the mineral metabolism are partly determined by insufficient entering and assimilation of these substances in the organism, but they may also result from dysfunction of endocrine system (pituitary body, adrenal, thyroid and parathyroid glands) or insufficient entering of some vitamins (of D group) by food.

Daily need of organism in sodium is 4-5 g (10-12.5g of NaCL). Sodium is the main cation of extracellular fluid (in blood plasma –141mmol/l, in erythrocytes-17-20mmol/l). But in pathological states (cell injury, burns) content of intracellular sodium is increased.

Sodium plays an important part in the regulation of osmotic pressure.

Disturbances in sodium metabolism are closely connected with disturbances in water metabolism. The more sodium is retained in the organism, the more pronounced is the retention of water. In all processes causing dehydration sodium balance is negative.

Hyponatremia (decrease of blood sodium concentration lower than 140-135mmol/l) occurs in insufficient receiving or increased loss of sodium by the organism, increased sweating, vomiting, diarrhea, etc.

Disturbance of aldosterone secretion (Addision’s disease) leads to disorders in reabsorption of sodium in tubules of the kidney, and organism loses a great amount of sodium. The same is observed in renal insufficiency.

Sodium deficiency leads to decrease of osmotic pressure of the extracellular fluid. Water enters the cells; as a result of hyperhydration of the cells of brain, kidneys, erythrocytes, etc, their function is disturbed. Hyperhydration of erythrocytes results in hemolysis.

Decrease of blood concentration of sodium leads to myasthenia, weakness of pulse, decrease of arterial pressure (up to collapse). This is explained by decrease of potentiating influence of sodium on the action of adrenalin.

As a result of considerable loss of sodium potassium ions go out of cells into intercellular fluid and blood causing disturbances in heart activity, skeletal and smooth muscles. Muscular adynamia develops, appetite is decreased.

Sodium deficiency causes exhaustion of organism’s alkaline reserves and acidosis.

Hypernatremia (increase of blood sodium concentration above 150-200 mmol/l) and positive sodium balance occur as a result of surplus receipt of table salt, disturbed elimination of sodium from the organism (glomerulonephritis, primary and secondary hyperaldosteronism, excessive intake of glucocorticoids), etc.

General disturbances in metabolism ( protein deprivation, fever) are also accompanied by delay of sodium in the organism.

Hypernatremia leads to increase of osmotic pressure of the blood and extracellular fluid, intracellular fluid passes into extracellular space. Dehydration of cells occurs, they are wrinkled, and their functions are disturbed.

Surplus of sodium in extracellular fluid promotes delay of water in the organism and development of edema. Hypertension also develops. Because sodium potentiates action of adrenalin on the smooth muscle of arterioles and promotes their constriction. Besides, sodium ions enter the endothelial cells of muscular walls, this causes passage of water into these cells; they swell and narrow lumen of vessels.

Hypernatremia accompanied by hypersecretion of steroid hormones may cause necrosis of cardiac muscle and hyalinosis (Selye).

Potassium is the main intracellular cation of organism (in cells-110-150 mmol/l , in extracellular fluid-4-5mmol/l). In the intracellular fluids Na:K=1:20 , and in the extracellular fluids-28:1. Disturbances in sodium and potassium balances are closely connected. Increase of potassium in the organism leads to rapid excretion of sodium and water , whereas potassium dificiency causes accumulation of sodium. Aldosterone mobilizes potassium and causes its increased excretion in the urine by inhibiting its reabsorption in the kidneys, 65 % of total amount (158-180g )of potassium in the organism is in muscles. Daily potassium intake for healthy adult of average body mass is about 4g.

Hypokalemia (decrease of blood content of potassium lower than 4 mmol/l ) occurs in causes of insufficient intake of potassium in the food ,its loss in digestive juices (vomiting , diarrhea ) or increased excretion in urine (hyperaldosteronism , protracted treatment by large doses of adrenocorticotropic hormone and glucocorticoids).

Hypokalemia is accompanied by changes in potentials of nerve and muscle cells and decrease of their excitability. This leads to hyporeflexia , myasthenia , decreased vascular tension and motility of stomach and intestine. Excitability, conduction and processes of repolarization in myacardium are disturbed. In severe cases cardiac arrest may occur. The severe hypokalemia causes disorders in processes of reabsorption and secretion of different substances in tubules of kidney.

Hyperkalemia (increase of potassium concentration in blood plasma above 6 mmol/l ) occurs as a result of excessive intake of food products rich in potassium, treatment by high doses of drugs containing potassium, disturbance of excretion of potassium from the organism, etc. Hyperkalemia is one of main signs of Addison’s disease. Hyperkalemia is more dangerous than hypokalemia. Plasma concentration of potassium equal to 8-13 mmol/l may cause death as a result of “potassium intoxication”. This state may develop even after rapid transfusion of large amount of blood (potassium goes out of erythrocytes ).

Clinically potassium intoxication manifests itself in paresthesia, myasthenia, arrhythmia, bradycardia, collapse, darkened consciousness.

Death occurs as a result of diastolic cardiac arrest.

Calcium and phosphorus are part of oxyapatite type combinations that form the main mineral substance of bones and teeth. Therefore, the metabolism of phosphorus in the organism is closely connected with calcium metabolism, and calcium metabolism is disturbed in all pathological states that are accompanied by changes in phosphorus metabolism.

The human organism contains about 1-1.5kg calcium. Blood content of calcium is 9-11mg % (2.25-2.75mmol/l ).

Disturbances in calcium and phosphorus are the following:

1) disturbances in absorption of calcium and phosphorus in intestine;

2) demineralization of bones and teeth;

3) excessive accumulation of calcium and phosphorus in bones and tissues.

Absorption of calcium and phosphorus in intestine is disturbed in cases of changes in the normal Ca/P proportion (1.2:1) in food, intake of nutritive matters rich of oxalic and inosite phosphate acids, protracted vomiting, rickets, etc.

One of important factors limiting absorption of calcium in small intestine is vitamin D deficiency which leads to rickets. In rickets osteomalacia develops that results in various deformities. Disturbances in calcium and phosphorus metabolism also underlie osteomalacia, a disease of adults, which is a result of dysfunction of gonads.

Disorders in formation of the bile and its excretion into intestine causes disturbance in absorption of fats as well as fat – soluble vitamins (including vitamin D which facilitates absorption of calcium from intestinal wall ). This has a bad effect on passage of calcium from the intestinal wall into the blood.

Calcium forms almost insoluble combination with fatty acids and therefore , its absorption is disturbed also when excessive amount of fat enters digestive system in the food.

Decrease of calcium and phosphorus compounds in bones leads to osteoporosis, that is, rarefaction of osseous tissue. This is observed in cases of protracted hypodynamia (bed rest, weightlessness ), disorders in innervation and trophicity of bones, hyposecretion of somatotropic and sex hormones, dysfunction of parathyroid, thyroid, salivary glands.

Hypocalcemia (decrease of calcium level lower than 2 mmol/l.) as a result of hypoparathyrosis is accompanied by increased blood content of inorganic phosphorus; excretion of calcium and phosphorus in urine is decreased.

Action of calcium ions is antagonistic to that of potassium ions. Therefore, calcium deficiency causes relative hyperkalemia: excitability of nerves and muscles , and contrability of muscles is changed. Cell membrane permeability is increased, ions move according to concentration gradient, membrane potential is decreased, and in muscle cells spontaneous contractions occur. Free calcium that enters the cells promotes these processes.

This is the mechanism of tetany in hypofunction of parathyroid glands or when they are removed in experiment. Convulsions set in when blood content of calcium is decreased down to 5-7mg % (1.25-1.75 mmol/l.). In severe cases fits of tetany cause death as a result of respiratory standstill. In the mild cases of disease (chronic forms) the trophic disorders develop (hypoplasia of enamel, cataract, shedding of hairs).

Hyperfunction of thyroid gland also is accompanied by hypocalcemia , because calcitonin promotes passage of calcium from blood plasma into bone tissue.

Hypercalcemia (increase of calcium level above 2.5-3 mmol/l.) is caused mainly by hyperparathyroidism. Under the influence of surplus of parathormone bones lose calcium and bone tissue is replaced by fibrous tissue, bones become soft , osteodystrophia fibrosa (Recklinghausen’s disease) develops. Blood content of phosphorus, on the contrary, is decreased (as a result of hyperphosphaturia). Sometimes these changes lead to formation of urinary calculi.

Certain connection exists between physiological actions of parathormone and vitamin D. There is vitamin D in parathyroid gland cells. Increase of vitamin D in organism strengthens the action of parathormone.

Protracted hypercalcemia may lead to decreased neuromuscular excitability, paresis, paralysis.

Local depositions of calcium salts (calcinosis) is observed in inflammatory foci, mainly in connective tissue elements (necrotized parts of tissue in tuberculosis, in kidneys in mercury bichloride poisoning, at sites of hyalin degeneration , in vascular walls in atheromatosis, etc).

Since in hypoacidity calcium salts become less soluble, the changes in the tissue reaction are apparently one of the essential pathogenic factors of deposition of calcium salts.

Calcinosis is one of main complications of hypervitaminosis D, hyperparathyroidism, phenomenon of calciphylaxis. Sensibilization of tissues against parathyroid gland extraction forms the basis of calciphylaxis phenomenon. In this case calcinosis may occur in the area of injection when the substances which usually do not cause calcinosis , are induced into the organism.

Rickets, osteomalacia , osteoporosis are accompanied by hypophosphatemia. Decrease of phosphates in organism leads to weakness of synthesis of macroergic compounds (ATP, creatine phosphate) and nucleic acids in tissues, decrease of inorganic substances in bones.

Magnesium is the second cation of the intracellular fluid (13-15 mmol/l in intracellular fluid and 1-1.5 mmol/l in blood plasma). The main part of magnesium is deposited in bone tissue and muscles. As coenzyme of many fermental systems (adenosine triphosphate of muscles, cholinesterase, phosphatase, etc.) magnesium plays an important part in intermediate metabolism. Deficiency and excess of magnesium cause disturbances in the reactions of phosphorylation and dephosphorylization in tissues.

Magnesium is to a certain extent antagonist of calcium.

Protracted receiving of large amounts of magnesium in food leads to increase of excretion of calcium from the organism. In rickets magnesium enters the bones and forces out calcium.

Magnesium deficiency leads to sedimentation of calcium in arterial walls and kidneys, increase of its blood content. Neuromuscular excitability is increased.

Increase in magnesium’s blood content is observed as a result of excessive intake of food products rich of magnesium (green vegetables, peas, beans, wheat, etc.) or disturbances in excretion of magnesium from the organism (in uremia), in cases of acidosis, etc. This causes depression, and in severe cases-narcotic sleep.

 Sometimes in pancreatitis blood content of magnesium is decreased, because absorption of fatty acids is disturbed and they form insoluble combinations with magnesium. Such state, as well as hypocalcemia, causes tetany.

In human organism there is 4-5g of iron more than 70% of which is in hemoglobin, about 16% in enzymes (cytochromes, peroxidases, etc), 0.1% in plasma, the rest-in muscles (in myoglobin) and natural depots of iron (bone marrow, spleen, liver). The daily need of adult organism in iron is 12-15mg. Iron deficiency is resulted from its insufficient receiving by the organism or disorders in absorption in intestine. Insufficient receiving has a practical significance only in children whose need in iron is 2-3 times more than that of adults. Besides, the iron that is liberated in the process of disintegration of own erythrocytes is enough for adults to provide the normal hemopoiesis. Disturbances in absorption of iron are observed in deficiency of hydrochloric acid and vitamin C, existence of substances binding iron (phosphates, etc.) surplus of mucin, inflammatory process in intestine.

Iron deficiency leads to development of hypochromic iron deficiency anemia, decrease of activity of respiratory enzymes and hypoxia.

Increase in blood content of iron leads to deposition of its compounds in different tissues. Frequently endogen iron is accumulated in the form of coloured albuminous substance-hemosiderin that is liberated during massive destruction of erythrocytes. This leads to hemosiderosis and hemochromatosis; sometimes process of ossification is disturbed.

Hemosiderosis is observed in cases of hemorrhage and hemolysis in tissues, accumulation of iron- ore in lungs of mine workers. In hemochromatosis, besides hemosiderin, also pigmental substance hemofuscin is accumulated in tissues. Skin is tinged bronze, and internal organs become of brown colour. Often hepatocirrhosis and diabetes mellitus develop (“bronze diabetes”). Compounds of iron are accumulated in the foci of ossification together with calcium and phosphorus and cause Kashin-Beck chondrodystrophia type of changes. One of the main causes of disturbance of iron metabolism is decrease of quantity of cobalt and copper in the organism.

In the organism of healthy persons there is 0.5% of methemoglobin (containing trivalent iron which cannot participate in transport of oxygen). Methemoglobin is reduced under the influence of enzyme methemoglobin reductase and iron is converted into bivalent form. The disease connected with hereditary deficiency of this enzyme is called idiopathic methemoglobinemia.

Chlorine is the main anion of extracellular fluid. Its concentration in plasma is 100mmol/l. Bicarbonates take the second place (plasma concentration - 25-30mmol/l). Disturbances in chlorine metabolism develop simultaneously with those of sodium and water balance. But disturbances in chlorine and sodium metabolism result in different pathological processes. For instance, in the state of stress hypernatremia may cause necrosis in cardiac muscle, whereas chlorides are of protective significance. Hypochloremia leads to gastric juice hypacidity.

Changes in amount of bicarbonates cause disturbances in acid-base balance.

All of above -mentioned chemical elements are macroelements whose content in organism is more than 0.001%. The elements which form less than 0.001%of living organism’s total mass are called microelements or trace elements (zinc, copper, manganese, molybdenum, cobalt, etc.). At present it is considered that the living organism contains all the elements that exist in the earth’s crust. There are more than 50 trace elements in the organism. In the organism the trace elements are in enzymes, hormones, vitamins, and take part in a number of vital functions.

Zinc is in numerous enzymes (carboxypeptidase, carbonic anhydrase, cytochrome oxidase, etc.) and hormones (insulin, sex hormones, hormones of pituitary body). So, it exercises a great influence on development and growth of organism, reproduction, hemopoiesis, metabolism of carbohydrates, proteins, fats. Zinc deficiency causes inactivation of insulinase. Synthesis of insulin is decreased, its disintegration is accelerated. This may lead to development of diabetes mellitus.

Copper takes part in the hemopoiesis (synthesis of hemoglobin). It inactivates insulinase. Copper deficiency may lead to diabetes mellitus, caries, some forms of hypochromic anemia, etc. Disturbances of copper metabolism cause changes in secretion of insulin, adrenalin, thyroxin, hormones of pituitary body. Hepatolenticular degeneration (Wilson’s disease) is accompanied by increase of copper in organism. Complex of copper with amino acids is accumulated in liver, brain, kidneys, spleen, cornea, iris, and lens of the eye and causes degenerative changes in these organs.

Manganese increases activity of some enzymes (phosphatase , arginase, cholinesterase, phosphoglucomutase),its optimal doses regulate accumulation of calcium combinations in bones. In manganese deficiency process of ossification is disturbed, osteoporosis develops, activity of sexual glands is decreased, functions of the central nervous system are disturbed, pathological processes of parkinsonism type develop.

Molybdenum is in xanthine oxidase and sulfite-oxidase. Xanthine oxidase converts xanthine (product of intermediate metabolism of purines) into hypoxanthine and uric acid. Sulfite-oxidase catalyzes oxidation of sulfite to sulfate and in this way prevents accumulation of the toxic metabolic sulfite.

Excessive quantity of molybdenum in food promotes development of gout. In metabolic processes molybdenum is antagonist of copper, and therefore, its surplus causes copper deficiency; development of bones is delayed.

Cobalt is in vitamin B12. In animals that graze in territories with low content of cobalt in soil, lactation is weak, anemia and sharp emaciation are observed.

Selenium is an integral part of the erythrocyte enzyme glutathione peroxidase. Its deficiency in animals produces a wide range of symptoms, including liver necrosis, growth retardation, muscular dystrophy, hemorrhages, infertility, nonmotile sperm, pancreatic lesions, cataracts, alopecia, muscle calcification, sudden death. In children Keshan disease is observed which is cardiomyopathy attributable to selenium deficiency (Keshan is province in China that has low selenium level in its soil).

Silicon has an important role in connective tissue metabolism. Human umbilical cords and cartilage contain high levels of bound silicon as hyaluronic acid and chondroitin sulfate.

Vanadium may act in oxidation- reduction reactions, cholesterol metabolism, hard tissue metabolism or formation.

Tin is necessary for the growth of rats. It may contribute to the tertiary structure of proteins.

Fluorine is in the bones and enamel. Its excessive amount in food and water causes hyperplasia in enamel and damages it (fluorosis), bone tissue loses its hardness (much calcium and phosphorus pass from bones into the blood). Fluorine deficiency causes caries. Because it inhibits biosynthesis of saccharides, the main factor of reproduction of bacteria causing the caries.

Iodine is mainly in thyroid, salivary, gastric and other glands, hormones of thyroid gland. Iodine deficiency causes hypothyrosis, its surplus - hyperthyrosis.

Two types of disturbances of vitamin balance in the organism are distinguished:

1. Negative balance- hypovitaminosis (partial vitamin deficiency) and avitaminosis (vitamin starvation).

2. Positive balance (excessive accumulation of vitamin in the organism)- hypervitaminosis (vitamin intoxication).

Delay of growth in young animals is characteristic of all hypovitaminoses. Each concrete type of hypovitaminoses causes also specitic changes in metabolism and function of organism.

Exogenous and endogenous causes of hypovitaminoses and avitaminoses are distinguished. Exogenous causes consist of feeding by inferior (poor in vitamins) food products and dysbacteriosis as a result of protracted intake of antibiotics and sulfanilamides in high doses, etc. Endogenous causes include disturbances in absorption of vitamins in intestine and transport to tissues, genetic defects of fermental systems participating in synthesis of coferments, acceleration of vitamins disintegration, increase of physiological needs in vitamins (in the growing organisms, pregnant women), etc.

Hypervitaminoses are considerably rare than hypovitaminoses, and were studied mainly in experiment. They are manifested by a number of general symptoms (disturbances in appetite, weakening of motility of stomach and intestines, headache, nervous excitability , loss of hairs, peeling of skin, etc.), but there are also specitic symptoms characteristic of every hypervitaminosis.