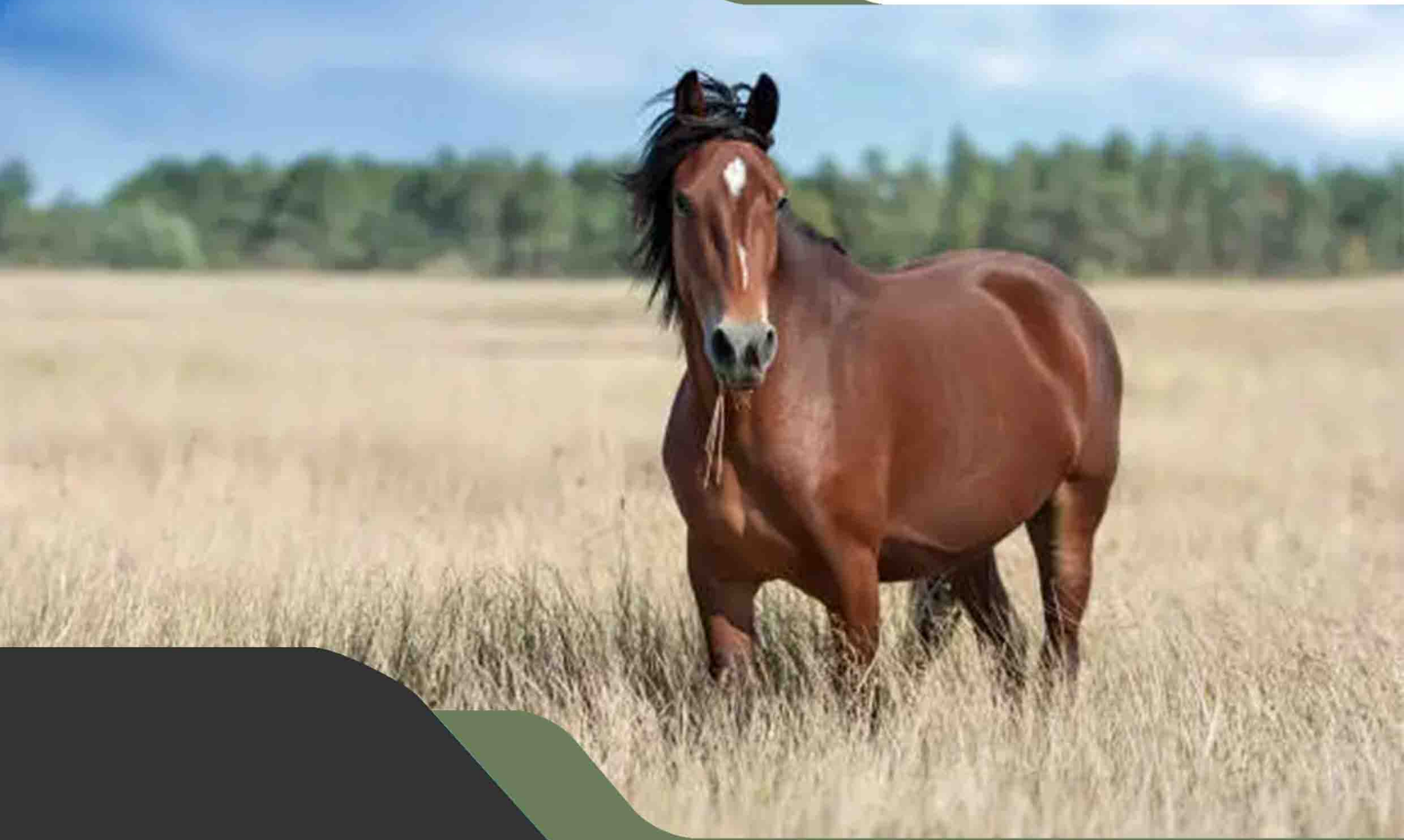




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HORSES' MINERAL METABOLISM DISORDERS AND ITS PREVENTION

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**Tsvilikhovsky M., Sharandak P., Pavelytsia O., Drobot M., Zemlianskyi A.,
Klymkovetska L., Dubin R.**

HORSES' MINERAL METABOLISM DISORDERS AND ITS PREVENTION

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This monograph focuses on the characteristics of macro- and micronutrient metabolism in horses, the diagnosis, treatment, and prevention of related disorders, as well as an evaluation of the efficacy of the drug “Lactachos” in treating mineral metabolism disorders in these animals.

For scientists, faculty members, doctoral candidates, graduate students, and undergraduates at higher education institutions, as well as veterinary medicine specialists and researchers.

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FOREWORD

For many centuries, there has been and continues to be a special relationship between horses and humans, which has changed significantly over time. Thus, from the middle of the last century and at the beginning of this century, due to the rapid development of scientific and technological progress, the number of domestic horses has significantly decreased, as their main role, which was to transport passengers and cargo, perform agricultural work, supply the army, etc., has been taken over by mechanical means.

However, today there is a revival of human interest in horses, due to their use in sports, recreation, rehabilitation therapy for children with cerebral palsy (hippotherapy), etc. In addition, horses are used for the production of meat, milk from which kumis is made, blood serum from pregnant mares, gastric juice, gamma globulin, horsehair and hoof horn. Horses are also used for public order protection, in various equestrian sports, national equestrian games and tourism.

Due to the development of equestrian sports in our country and the expansion of international relations, there is an increased demand for high-quality, strong, well-developed and hardy horses.

Breeding and sport horses are highly valuable animals. When raising, using, and caring for these animals, it is important to obtain high-quality offspring from them. Under normal conditions of mare pregnancy, there is a close relationship between the metabolic processes of the mother and the foetus [106]. Foetal development largely depends on the strengthening or weakening of the functions of the mother's organs, which have a correlative effect on its condition [19]. Therefore, all measures for the effective reproduction of a healthy horse population should begin not at the moment of the foal's birth, but with the targeted care of pregnant mares. This, to a large extent, allows the development of prenatal and postnatal pathologies in foals to be avoided.

Unfortunately, in recent years, science has moved away from the problems of horse breeding, which has now had a negative impact on this industry. At the same time, there are many problems in creating proper conditions for keeping, feeding and

training horses, because even minor violations of these three factors can lead to the emergence of various diseases that affect many organs and systems. Bio-geocenotic pathology in adult horses and foals has become widespread in Ukrainian stud farms. It is particularly acute during periods of greatest physiological stress on the organism (growth, pregnancy, lactation) [14]. This affects the course of pregnancy, the health of the mare and foal, and subsequently its growth, development and athletic performance. Biogeocenotic pathology manifests itself in metabolic disorders, the development of immunodeficiency, respiratory tract diseases, and the birth of non-viable, poorly developed young with congenital or acquired diseases in the first months of life. Such animals are subsequently culled. One of the main aetiological factors in the occurrence and development of biogeocenotic pathology in horses is the deficiency (or excess) of macro- and microelements in the soils of the corresponding biogeochemical zones of Ukraine, as well as in feed, water and, accordingly, in the animals' bodies [25, 32], metabolism disorders in pregnant mares and foals, as well as the search for and creation of effective therapeutic and prophylactic agents, is a pressing issue in the horse breeding industry of our country, which requires an effective solution.

1. SPECIFICITY OF HORSE DIGESTION

The total time it takes for feed to pass through the digestive tract of horses is approximately 35–50 hours. Approximately 85% of this time, the chyme is in the large intestine, where, with the help of bacterial microflora and protozoa, cellulose, hemicellulose and pectin substances are digested. The microflora of the horse's caecum and the microflora of the rumen of ruminants are practically identical in terms of quality. The bacteria in the horse's caecum can synthesise a significant amount of B vitamins. To date, the efficiency of the horse's utilisation of B vitamins has not been sufficiently studied. However, provided that the large intestine is functioning normally, horses do not experience a deficiency of B vitamins. The same cannot be said for minerals, the supply of which to horses depends on many factors and whose deficiency often leads to general metabolic disorders in these animals.

The gestation period in horses lasts about 11 months (320–345 days) and also requires a special approach to feeding these animals. During the first 8 months of gestation, mares need a maintenance diet. At this time, it is necessary to improve the condition of weakened animals and control mares that are overweight.

Breeding mares must be provided with a high-quality balanced diet. The main focus should be on providing mares with energy, proteins, minerals and vitamins. It should be noted that when feeding high-quality feed and in the absence of digestive tract pathology, vitamin deficiency is practically not observed in horses.

At the same time, the mineral supply of pregnant mares depends on a number of factors, namely their availability in soil and water, their digestibility by plants and the animal's own body, the antagonism and synergism of individual minerals, etc. That is why horses often experience metabolic disorders, which can be caused by a deficiency or excess of certain macro- and microelements in their bodies.

1.1. The role of macro- and microelements in the animal organism

Minerals are components of tissues and fluids in living organisms, forming a complex physiological system that participates in the regulation of vital functions at all stages of organism development [2, 4, 29, 90, 100, 103].

Of the 92 elements found in nature, 81 are found in the human body and higher vertebrates. Fifteen elements are structural. These include calcium, phosphorus, magnesium, sodium, chlorine, potassium, sulphur, iodine, zinc, manganese, molybdenum, selenium, iron, copper and cobalt [2, 27, 99, 100, 107, 113].

Depending on their content in the body of animals, mineral elements are divided into macroelements (calcium, phosphorus, magnesium, sodium, chlorine, potassium, sulphur), which are contained in amounts ranging from 9 to 0.09% of body weight, and microelements (iodine, zinc, manganese, molybdenum, selenium, iron, copper, cobalt, etc.), which are found in the human and animal body in amounts ranging from 10⁻³ to 10⁻¹²% [2, 47].

In terms of their importance for the vital functions of organisms, trace elements are divided into: essential (essential, biogenic): Fe, I, Cu, Zn, Co, Mo, Se, Mn; conditionally essential: As, B, Br, F, Li, Ni, V, Si; toxic: Al, Cd, Pb, Hg, Be, Ba, Vi, Tl; potentially toxic: Ge, Au, In, Rb, Ag, Ti, Te, U, W, Sn, etc. [2, 27, 52, 99].

There are five criteria for the biogenicity of a chemical element, namely:

- the presence of a chemical element in the tissues of a healthy organism;
- a slight difference in the relative content of a chemical element in different organisms;
- when a particular chemical element is excluded from the diet, clinical changes caused by its deficiency are clearly recorded in the animal organism;
- specific disturbances in biochemical processes during hypoelementosis;
- the identified disturbances are eliminated by introducing the element into the organism [27, 51].

The biogenicity of elements is confirmed by three principles: first, the selective absorption of certain elements; second, their selective concentration in certain organisms, organs, tissues, cells and their organelles; third, the selective elimination of mineral substances. It is the interaction of these mechanisms that ensures the maintenance of mineral homeostasis in the body of animals [2, 52, 103].

The body is a complex dynamic polyligand system, the functioning of which requires the maintenance of metalloligand homeostasis. The exchange and transport of

substances and the deposition of metal ions in the human and animal body are determined by their ability to participate in complex formation processes with natural endogenous (nucleic acids, carbohydrates, amino acids, peptides, proteins, hormones) and exogenous (medicines, etc.) ligands [29, 51, 52, 99].

Recently, the role of macro- and microelements in the processes of growth, differentiation, repair, regeneration, necrosis and cell survival, as well as in the pathogenesis of various chronic, inflammatory, degenerative and neoplastic diseases, has been proven [1, 2, 29, 46, 69, 98].

Thus, in the case of inflammatory, degenerative and neoplastic processes, a deficiency of zinc, selenium and magnesium develops, manifested by increased permeability of the basement membranes, endothelial dysfunction, disruption of the cell cycle, namely cell growth and differentiation, and inhibition of their mitosis [69, 136, 276].

Macro- and microelements are indispensable participants in virtually all physiological processes in the body, as they are part of enzymes (copper-containing oxidases, zinc-containing carbonic anhydrases and carboxypeptidases, molybdenum is a component of the enzyme xanthine oxidase), hormones (zinc is a cofactor of thymulin), vitamins (cobalt is a component of the vitamin B12 molecule) and other biologically active compounds [95, 96, 102].

Chemical elements are also necessary for the activity of other enzyme systems. For example, Mg^{2+} is necessary for phosphotransferases, K^{+} and Mg^{2+} for pyruvate kinase, Na^{+} , K^{+} and Mg^{2+} for membrane transport Na^{+} , K^{+} -ATPase, Ca^{2+} for Ca^{2+} -ATPase of the sarcoplasmic reticulum [95, 144].

Macro- and microelements in compounds with proteins form organometallic complexes, among which metalloenzymes play an important role in the body, for example, mitochondrial Mn^{2+} -superoxide dismutase, selenium-dependent glutathione peroxidase, etc. [22, 51, 169, 276].

Metals can be part of the active centre of an enzyme or function as a link that binds the enzyme to the substrate, being in a compound with both and thus holding the substrate in the active centre of the enzyme [51].

Metal ions can displace the inhibitor contained in the enzyme complex, as well as the ineffective metal ion from its compound with the active site of the enzyme or with the functional groups of the substrate [51, 52].

Ions of some metals bind the substrate to the enzyme, others activate enzymes, others are a permanent component of the enzyme's active site, and others form a bond between the enzyme and the substrate [52, 113].

By forming compounds with chemical regulators of metabolism or acting in a free state, metal ions are essential participants in biochemical transformations that affect the metabolism of energy, proteins, carbohydrates, and lipids [10, 20, 95, 169].

Ions of some metals interact with organic substances (amino acids, peptides, proteins). This is when chelation occurs. Chelates of manganese, iron, cobalt, copper, molybdenum and zinc catalyse redox reactions and participate in the formation of the active centre of the enzyme [113, 275, 286].

Metals absorbed by living organisms and contained in tissues and fluids can be activators or inhibitors of enzymes [47].

Metals ensure the stability of osmotic pressure and acid-base balance and are involved in various metabolic reactions.

With the participation of minerals, processes of absorption, secretion, blood formation and excretion of metabolites from the body occur [47, 61, 274]. Without them, muscle contraction, nerve conduction and tissue respiration are impossible [7, 8].

Minerals are involved in the creation of various structures (bone and muscle tissue, cell membranes, etc.), in biochemical processes, muscle regulation, nerve impulse transmission, etc. [18, 20, 29, 47, 94].

Performing catalytic, structural and regulatory functions, minerals interact with enzymes, hormone precursors and biological membranes [1, 2, 3, 20, 46, 252].

Minerals play an important role in the processes of digestion, absorption, secretion, assimilation of nutrients and excretion of end products of metabolism from the body [29, 47, 102, 191]. They ensure bacterial digestion in the rumen of cattle and the caecum of horses. Rumen and caecum bacteria require various trace elements –

manganese, copper, iodine, iron, molybdenum and zinc. Cobalt is essential for bacteria that produce vitamin B12 [47, 114, 286].

The addition of macro- and microelements to the diet has been shown to increase the number and activity of certain rumen microorganisms [47].

Mineral nutrition affects the reproductive function of animals and humans from the moment of maturation and fertilisation of sex cells to the birth of offspring [6, 16, 53, 58, 93, 102, 110, 155, 281].

Studies show that the levels of zinc, copper and manganese were several times higher in foetal tissues than in reproductive tissues, indicating selective accumulation of these elements by the foetus. At the same time, it has been established that a deficiency of copper, iodine, iron, manganese, selenium and zinc affects the level of embryonic mortality and foetal survival in mammals [207].

The involvement of macro- and microelements in the mechanisms of cell apoptosis is well known. Thus, they play a significant role in the regulation of cell growth and metabolism. It is also assumed that there is a regular system of interaction between macro- and microelements and the programme of cell death [29, 51, 52, 69, 276].

According to current understanding, the intracellular pool of microelements is the most stable and is important for the functioning of enzymes involved in antioxidant protection of cells [23, 51, 69, 260, 267, 276].

During the destabilisation of endogenous metals (zinc, iron, copper), the processes of lipid peroxidation and nitrogen oxide synthesis are intensified, which inactivates enzymes containing iron, zinc and cobalt and contributes to cell death [51, 69, 180].

Recently, research on the effect of minerals on cellular and humoral immunity and key immunoregulatory functions has been of particular interest [11, 12, 45, 80, 180Error! Source link not found.]. Thus, for the immune system, some researchers distinguish between essential (zinc, iodine, lithium, copper, cobalt, chromium, molybdenum, selenium, manganese, iron) and immunotoxic (aluminium, arsenic, boron, nickel, cadmium, lead, hydrargyrum, beryllium, vanadium, thallium,

germanium, aurum, stannum) [51, 52, 174].

The significant role of various metals (beryllium, hydrargyrum, chromium, nickel, platinum, aurum, argentum, stibium) in the development of allergic diseases (contact dermatitis, eczema, bronchial asthma, etc.) has also been established [29, 32, 103, 111, 117].

Anthropogenic pollution of the environment leads to disturbances in the metabolism of trace elements in animals [29, 103, 125].

In addition to the above, the problem of the pathological effect of heavy metals on the frequency and severity of environmentally-related diseases resulting from anthropogenic pollution of the biosphere is becoming increasingly relevant. First of all, these are metals such as hydrargyrum, cadmium, plumbum, nickel, aluminium, beryllium, strontium, etc., which have genotoxic, teratogenic, carcinogenic and mutagenic effects [1, 2, 104, 125]. Thus, minerals play an important role in ensuring the vital functions of living organisms. At the same time, each species of animal has its own characteristics in terms of mineral nutrition and the processes of macro- and microelement metabolism during certain physiological periods.

1.2. Characteristics of macro- and microelement metabolism in horses

The effectiveness of horse breeding, their service life and the production of healthy offspring are determined by the extent to which these animals' needs for nutrients, minerals and vitamins are met [14, 20, 44, 94, 120, 126].

Thus, feeding young horses an unbalanced diet in terms of macro- and microelements leads to disturbances in the growth of bone and muscle tissue and the functioning of certain body systems. In this case, unfavourable and often irreversible changes in the constitution of the animals' bodies occur [5, 49, 87, 120].

Unlike other farm animals, mineral metabolism in horses has not been sufficiently studied. Researchers have mainly used data obtained from other farm animals.

At the same time, unlike other farm animals, horses have a higher individual value and are bred for entertainment, sporting purposes and work. Horses are used for

a longer period of time than other animals. They should not be overweight, and their feeding should be aimed at ensuring the stability of the nervous and muscular systems, temperament, liveliness, athleticism, and in mares – at normal pregnancy and lactation [17, 20, 26, 74, 83, 94, 97].

The peculiarities of the horse's organism include the ability to accumulate significant amounts of toxic trace elements with age, as well as active digestion in the large intestine and the need for specific nutrients, which is caused by the nature of the loads, individual development and reproduction [9, 62, 94].

Unlike other animal species, horses are most sensitive to mineral deficiencies or excesses in their feed. This is due to the peculiarities of digestion in horses. Thus, a horse's stomach is 9 times smaller than that of cattle, its digestive tract is 46% shorter, the absorptive surface of its intestines is 30% smaller, and feed components pass through the horse's gastrointestinal tract 5-6 times faster [49, 94, 112, 176].

Microbial activity in the horse's stomach is relatively low, while in the rumen of ruminants it is quite high [47].

In the digestive tract of ruminants and horses, areas with high microflora activity occupy different positions in relation to the small intestine. Thus, the rumen of ruminants, which has a fairly high microflora activity, is located in front of the small intestine. At the same time, in horses, the cecum is located outside it. Therefore, the efficiency of absorption of nutrients synthesized by microorganisms in the digestive tract of horses is lower than in ruminants [190, 150, 260].

Horses digest fibre worse than ruminants: only 18–30% compared to 50–60% in cattle. Horses utilise phytin phosphorus worse [6, 7, 274, 297].

The nutritional needs of horses can be met by balancing their diet. At the same time, vitamin deficiency in horses is very rare. Water-soluble vitamins are easily synthesised in the horse's body: vitamin C from glucose, B vitamins during bacterial fermentation of the contents of the large intestine [94, 154, 285, 286]. Water-soluble vitamins are also found in sufficient quantities in high-quality fodder.

Vitamins A, D and E are supplied in sufficient quantities with feed, but only if it is of high quality, while vitamin K in horses is synthesised by microorganisms in the

large intestine. Therefore, a deficiency of fat-soluble vitamins in horses can only be observed in cases of diseases that disrupt the absorption of lipids or when these animals are fed poor-quality feed [20, 94].

This cannot be said about macro- and microelements, since they cannot be synthesised in the body or replaced by other nutrients. Microelements enter the animal's body only with feed and water, and the horse's supply of them also has a number of features [14, 33, 47, 160].

Horses obtain most of the necessary minerals from roughage, which accounts for up to 77% of their diet, or from grain in a concentrate-type diet, which accounts for up to 65% of their diet [18, 20, 38, 94, 163]. However, according to N. F. Cymbaluk [163], such diets usually contain either too little (up to 0.24%) or too much (up to 1.06%) phosphorus.

Depending on the type of feed, the calcium-phosphorus ratio in the blood serum of horses changes. Thus, when horses eat alfalfa, the calcium-phosphorus ratio is 2.4:1, and when they eat meadow fescue, it is 0.9:1 [160].

The mineral content of feed and its availability for absorption by the horse's body depend on many factors, namely the concentration of minerals in the soil and water, the type of grass, the stage of plant growth and conditions of feed harvesting, the absorption of minerals by plants and animals, the synergism or antagonism of minerals, etc. [14, 83, 106, 108, 120, 260].

Microelements can enter into antagonistic interactions. Thus, zinc and copper, cobalt and iron inhibit each other's absorption in the intestine, and calcium inhibits the absorption of zinc and manganese [113, 116, 286].

Antagonistic interactions occur between copper and molybdenum, magnesium and manganese, copper and zinc in tissue metabolism processes; between iron and zinc in the blood during binding to plasma transferrin [55, 113].

The absorption of minerals is often determined by the interaction between different mineral elements or between other components of the diet. For example, the absorption of calcium and phosphorus depends on the ratio of these elements in the feed and the animal's vitamin D supply. The absorption of calcium, magnesium and

zinc by the body can be influenced by phytate anion [47, 95, 297].

According to many researchers, horses are affected by more stress factors than other animal species. These arise as a result of training, competitions, trials, transport, regrouping, crowding and other adverse environmental factors. As a result, horses' need for nutrients and minerals increases significantly [3, 42, 43, 60, 94, 97].

It is more difficult to provide a horse's body with macro- and microelements than the body of other animals. Thus, for a horse, these needs do not remain constant over time. They are determined individually, and many factors are important in this regard [173, 177].

The diet for mares is divided into a diet for young, unmated mares, unmated mares in the service period, mares up to 8 months of pregnancy and from 8 to 11 months of pregnancy, respectively. The needs of a mare's body vary depending on the physiological period [6, 20, 38, 94, 127].

The age of horses also affects the absorption of minerals. It has been established that young horses absorb nearly 100% of calcium, phosphorus and magnesium, while with age this gradually decreases and in adult animals is only 50% for calcium and 20% for magnesium [146].

Older horses have a reduced ability to retain phosphorus in the body, mainly due to a decrease in fibre absorption [94].

Shellow J.S., Jackson S. G. et al. [276] found lower levels of selenium and glutathione peroxidase activity in the blood serum of older horses compared to younger animals.

The physiological condition of mares also significantly affects the supply of macro- and microelements to their bodies. The gestation period of a mare after fertilisation lasts 11 months (approximately 335–345 days for thoroughbred mares and slightly less for horses of other breeds) [94]. The main growth of the foetus occurs in the last three months of the mare's gestation. At this time, 60–65% of the foetal tissues grow and develop [20, 94]. Therefore, the mare's need for nutrients and biologically active substances during this period increases by 20%, and for mares whose gestation falls in the period from winter to early spring, by 40–50% [20, 94].

A well-developed skeleton is the main criterion that determines a horse's suitability for trials or competitions. Skeletal growth during intrauterine development determines the future of the foal, and the growth of the foal after birth determines the format of the adult animal [33].

Within a few hours after birth, a healthy foal can run as fast as its mother, and the length of its legs is almost equal to that of an adult animal. This indicates the intensity and significance of bone tissue formation in the foetus in the mare's womb [144].

Unlike other farm animals, a foal does not lose body weight during the first days after birth, but actively grows. At the age of one year, a foal reaches approximately 90% of the height of an adult horse, while its body weight at this stage is approximately 60-75% of the body weight of an adult animal. The active growth of foal bone tissue during this period determines the need for minerals, which significantly exceeds the needs of adult horses that consume a diet to maintain their condition [20, 62, 162].

The mare's body in the middle and at the end of lactation, as well as up to the 8th month of pregnancy, requires only a diet to maintain the mare's condition [94]. At the same time, after foaling, a mare begins to produce milk in an amount equal to 3-4% of her body weight, which is a heavy load on the metabolic processes in her body. Therefore, the mare's need for nutrients and minerals at this time increases by approximately 30%, and for mares that foal in December–April, by 60% [20, 94].

Another factor that determines the specifics of providing horses with macro- and microelements is physical work, during which the horse loses a significant amount of minerals through sweat and as a result of energy generation, and free radicals accumulate in the animal's muscles, damaging the body's tissues (exhaustion syndrome) [30, 56, 73, 94]. Thus, during intense physical exertion, the mineral metabolism indicators in the body of sport horses are significantly reduced [25, 40, 42, 44]. It has been established that a horse can lose 200.0 mg of calcium, 150.0 mg of phosphorus, 200.0 mg of magnesium, up to 5.0 g of sodium, 7.5 g of chlorine, and 2.5 g of potassium per 1 kg of sweat [59]. During several hours of intense training, a horse can lose 50.0 g of sodium and 75.0 g of chlorine [20].

In horses that are easily excitable, a decrease in the magnesium content in blood plasma is recorded. Therefore, it is recommended that they be fed a diet high in this element [94].

A shift in the phosphorus, calcium and magnesium content in the blood of horses in one direction or another may be an indicator of their level of training [97].

Thus, the literature data indicate the peculiarities of mineral metabolism in horses compared to other animal species. At the same time, there are factors that affect mineral metabolism in horses and, in some cases, cause its disruption.

1.3. Disturbance of mineral metabolism in organism of the horses

Plants, animals and humans living in different biogeochemical zones use nutrients that differ in chemical composition. This determines the corresponding chemical composition of their organisms [104].

Only under conditions of harmonious combination and mutual influence of factors on each other in the soil-plant-animal chain are the necessary conditions formed to ensure the vital activity, working capacity and health of the animal [71].

The concentration of macro- and microelements in a warm-blooded organism is maintained at a stable level from the moment of its birth and throughout its life. An imbalance of macro- and microelements can lead to significant disturbances in metabolism and bodily functions [2, 64, 124, 126, 170].

At the same time, special attention should be paid to the study of anthropogenic, technogenic and ecosystem factors, the disruption of which leads to the emergence of biogeocenotic pathology of non-infectious aetiology in adult horses and newborn foals [14, 83]. Thus, metabolic disorders in horses often arise as a result of disturbances in the biogeocenosis, inadequate feeding, and violations of animal husbandry conditions and technology [81, 109, 118, 120, 172].

The spread of diseases characterised by mineral metabolism disorders in horses at stud farms and racecourses is associated with uniform feeding of animals and the lack of pastures. With uniform feeding based on feed rations, it is impossible to satisfy the horses' need for minerals [59, 120]. In addition, diets do not always correspond to the age of the animals, their physiological condition, the intensity of physical activity,

etc. [43, 97].

In this regard, horses are often diagnosed with disorders of the metabolism of macroelements (most often calcium, phosphorus, magnesium, sodium, chlorine, potassium) and microelements (cobalt, copper, iodine, zinc, manganese, iron, selenium) [77, 77–83, 101, 108, 164].

Several macro- and microelements are most often involved in the disruption of mineral metabolism in animals. This is due to a deficiency or excess of not one but several elements in the biosphere, which can blur the clinical signs of a particular mineral deficiency. Therefore, clinical signs of mineral metabolism disorders in horses associated with a deficiency or excess of a single element are rarely recorded. The only exception may be iodine deficiency [83, 120].

Mineral metabolism disorders in horses are most often recorded in the form of polyopathologies. The main syndromes are growth and development disorders in young animals, decreased reproductive function in mares and stallions, birth of defective offspring, damage to the skin and hair, skeleton, nervous, cardiovascular and immune systems [83, 90, 118, 105, 120].

The symptoms of some mineral metabolism disorders in animals become visible after birth. It has been established that insufficient feeding of animals affects the development of different parts of the skeleton in different ways. Thus, with a deficiency of mineral elements, those parts of the skeleton that grow more rapidly over a certain period of time are more likely to be underdeveloped. In particular, under the influence of mineral deficiency in the diet of mares during pregnancy, the growth of tubular bones is disrupted in newborn foals [47, 73, 140].

In recent years, there has been a significant increase in diseases of the musculoskeletal system in young horses, which is associated with an imbalance of minerals such as calcium, phosphorus, copper, manganese and zinc. These include diseases such as tendon contracture, rickets, osteochondrosis, and, in adult horses, osteodystrophy [101, 119, 164, 251].

In foreign literature, bone diseases in young horses are classified as orthopaedic growth disorders, which is a general term for many disorders that interfere with the

physiological development of bones. These disorders are based on the pathology of cartilage and bone tissue development, which weakens the overall bone structure [73, 87, 94].

Studies show that thoroughbred horses and fast-growing breeds are most affected. This is due to rapid bone development, and one of the main factors is a deficiency or excess of minerals in the horse's body [73, 87, 94].

The main causes of bone tissue pathology in horses are imbalances in calcium, phosphorus, magnesium, manganese, copper and zinc [20, 108, 120, 161, 164, 250]. There is evidence of the positive effect of silicon on bone mineralisation in foals during the critical period of their development [225].

Research results indicate that the use of manganese, zinc, copper, and cobalt in growing horses aged 340–350 days significantly improves bone mineralisation, although other production indicators (growth, body weight, girth, and torso length) did not differ from the control group [254].

Most often, calcium-phosphorus metabolism disorders are recorded in the pathogenesis of bone disease in horses [37, 101, 105, 314].

Calcium accounts for approximately 35% of bone structure [20]. It is involved in muscle contraction, nerve impulse transmission, blood clotting, regulation of many enzymes, and acts as an intracellular messenger [95, 144].

Studies have shown that one of the factors contributing to musculoskeletal disorders in foals is an imbalance of calcium and phosphorus. Thus, at horse farms with the lowest incidence of such diseases, the calcium content in the diet of foals was $1.16 \pm 0.09\%$, and phosphorus – $0.72 \pm 0.08\%$, which corresponds to the horses' need for these elements [90].

A link has been established between calcium consumption and the degree of bone pathology in foals of the same age. Thus, foals of the same age that received a diet containing 1.2% calcium had the lowest incidence of bone diseases, while foals of the same age that received a diet containing 0.2% calcium had the highest percentage of such diseases [314].

A significant calcium deficiency in lactating mares causes eclampsia, which

manifests itself as depression, increased sweating, ataxia, general weakness, and muscle tremors [73].

Phosphorus makes up 14–17% of the skeleton. In addition, it is necessary for many energy conversion reactions involving adenosine diphosphate (ADP) and adenosine triphosphate (ATP), for the synthesis of phospholipids, nucleic acids and phosphoproteins [95].

Inadequate phosphorus content in the diet, as well as calcium and vitamin D, causes rickets in foals and bone softening in adult horses [127].

Phosphorus imbalance affects metabolic processes in bone tissue. With a simultaneous deficiency of phosphorus and fibre in foals, skeletal damage and taste distortion were recorded [73].

Horse diseases manifested by bone tissue damage (lameness caused by tendon tears, ligament tears and microfractures, thickening of the flat bones of the skull, which occurs with prolonged consumption of large amounts of wheat bran containing high levels of phosphate relative to calcium) is recorded in stud farms where horses are fed porridge and mash with a high bran content, or large amounts of grain with a significant phytic acid content. As a result, the phytic acid, which is found in large quantities in wheat bran, makes calcium unavailable for absorption by the body. As a result, horses develop secondary hyperparathyroidism, known as ‘big head’, osteofibrosis and osteodystrophy. The disease is characterised by lameness during movement and, in chronic cases, enlargement of the upper and lower jaws and facial crest [73]. Fibrous osteodystrophy has also been reported in horses grazing on pastures where the grass contains large amounts of oxalates, which make calcium unabsorbable by the body [59].

The calcium-phosphorus ratio is an important criterion for evaluating a horse's diet. A ratio of less than 1:1, i.e. when the phosphorus requirement exceeds the calcium requirement, can be harmful (destructive) for calcium absorption in the intestines of horses. Even if calcium requirements are met, excessive phosphorus consumption causes abnormal skeletal formation. A calcium-phosphorus ratio of 6:1 in the diets of growing horses did not cause any disorders, provided that phosphorus was consumed

in appropriate amounts [94, 127].

Magnesium accounts for approximately 0.05% of a horse's body weight. 60% of magnesium is found in the skeleton [20]. Unlike ruminants, which absorb 10 to 40% of magnesium, the level of magnesium absorption from feed in horses ranges from 40 to 60% [198]. The average daily requirement of magnesium for a horse is 15 mg/kg of body weight [20].

Magnesium activates cholinesterase and accelerates the hydrolysis of acetylcholine. When there is a deficiency of magnesium, cholinesterase activity decreases, while acetylcholine concentration and nervous excitability increase, leading to clonic and tetanic convulsions (pasture tetany, hypomagnesaemia) [71].

Magnesium deficiency is not often observed in horses. For example, ruminants grazing on pastures poor in magnesium developed pasture tetany, while this was not observed in horses [54].

There is evidence of a decrease in immunoglobulin levels in the blood serum of horses with low magnesium levels in their bodies. At the same time, an increase in magnesium levels led to the normalisation of immunoglobulin levels in the blood serum of horses [71].

Studies have shown that experimentally induced hypomagnesaemia in foals fed a diet containing 7.0–8.0 mg of magnesium per 1 kg of feed for 150–190 days led to the development of nervous symptoms in foals, muscle tremors, ataxia, and subsequently collapse [54].

It has also been established that magnesium deficiency in horses leads to focal deposition of minerals, in particular calcium and phosphorus, in the aorta [198].

Potassium is the main intracellular cation involved in maintaining acid-base balance and osmotic pressure, and supports the polarisation of the cell plasma membrane [61].

Horses need approximately 0.05 g of potassium per 1 kg of body weight per day, or approximately 0.4% of the diet. Roughage, which forms the basis of a horse's diet, usually contains 1-2% potassium on a dry matter basis, which easily meets the horse's potassium requirements [20].

In experiments on foals that were fed a potassium-deficient diet, it was found that the animals gradually refused to eat, resulting in weight loss, poor appearance, and a decrease in potassium concentration in their blood serum [9].

Excess potassium is easily excreted from the body of horses, mainly in urine, provided that the animals have a normal water supply [198].

Sodium is necessary for muscle contraction and bile formation. It is the main electrolyte involved in the regulation of acid-base balance and osmotic regulation of fluids in the body [61, 95].

Chlorine is necessary for muscle contraction and is involved in the formation of hydrochloric acid and gastric secretions necessary for the digestion of feed [90].

The sodium content in natural horse feed is less than 0.1%, and the chloride content ranges from 0.05% in concentrates to 3.0% in molasses [33].

Sodium chloride (table salt, salt lick) is often added to the diet. For horses, it is both a supplement and a nutrient. Therefore, sodium chloride deficiency is usually recorded in cases of mismanagement [127].

Most often, sodium and chlorine deficiency manifests itself during physical exertion of horses in hot weather, when they lose a significant part of them with sweat [36].

Chronic sodium chloride deficiency leads to a decrease in skin turgor. Horses begin to lick objects that are contaminated with sweat (harness, equipment), eat slowly, have a distorted appetite, tire quickly, consume less water and, ultimately, refuse to eat [36, 105].

With a significant deficiency of sodium chloride in horses, uncoordinated muscle contractions and chewing disorders were recorded, the animals had an unsteady gait, and their blood serum had reduced sodium and chlorine content, while the potassium concentration was higher than normal [59]. At the same time, studies conducted on ponies have shown that with limited access to sodium chloride for 4 weeks, the animals did not experience digestive disorders or changes in blood parameters. However, the animals were restricted in their movement and no sodium loss was detected in their sweat [7].

On the other hand, the risk of excessive salt consumption by horses is low, but only in cases where the animals do not experience prolonged salt starvation or if they have sufficient water supply [127].

Copper is necessary for the body to absorb iron, synthesise haemoglobin, and for the maturation of red blood cells [113, 124]. Copper is a component of many metalloenzymes involved in amino acid metabolism [113].

Copper is a component of the protein ceruloplasmin, which is involved in the degradation of amines and helps protect lung surfactant from lipid peroxidation [28].

Copper is important for cellular respiration, as it is a component of cytochrome oxidase, increases the intensity of haemoglobin synthesis processes, and is involved in the formation of bones, cartilage and elastin [65, 95, 178].

The absorption of copper is influenced by manganese, zinc, molybdenum, sulphur, lead, strontium, cadmium, and silver [103, 113].

Molybdenum-induced hypocuprosis (copper deficiency) is often recorded in various species of farm animals, including horses [315].

Currently, there are enough studies that indicate a link between the onset of osteochondrosis and osteogenesis disorders with copper deficiency in horses and other animal species [161, 250].

Ott E.A [250] established a correlation between the copper content in the diet of weaned foals and the degree of their metabolic diseases. It was found that when mares were given 13 and 32 mg of copper per 1 kg of feed, and their foals were given 15 and 55 mg of copper per 1 kg of feed, all foals were healthy, grew normally and had no symptoms of lameness or ataxia.

At the same time, E. Gee [178], in experiments on 22 thoroughbred riding horses aged 160 days, found that even when Cuprum preparations were administered to pregnant mares in the last third of gestation, histological changes in the cartilage occurred in clinically healthy foals.

Foals with copper deficiency have congenital abnormalities that resemble rickets in their clinical presentation. These changes develop due to insufficient collagen synthesis and decreased osteoblast activity [127].

It has also been established that copper deficiency in foals leads to stunted growth and development, swelling and stiffness of the joints, and deformation of the limbs [73].

A significant decrease in copper content in the blood serum of mares with age is associated with foetal rupture of the uterine artery [278]. Copper deficiency in mares leads to an increase in the number of abortions [9], and in horses, the pigment melanin is disrupted, since copper is necessary for its synthesis. The coat becomes coarse and stiff, and depigmentation occurs on dark areas of the body [85, 108].

Experimental studies have shown that in calves fed a copper-deficient diet, macrophage activity decreases and neutrophil phagocytic activity decreases [180]. Experimentally induced copper deficiency in mice caused a decrease in the T-helper population and suppression of T- and B-lymphocyte activity [212].

Copper deficiency is also possible with an excess of iron or molybdenum, which can inhibit the absorption and storage of copper [107, 302].

Iodine is a component of the thyroid hormones thyroxine and triiodothyronine, which play an important role in reproductive function and basal metabolic rate regulation [61]. In adult horses, iodine deficiency is most often chronic and without visible clinical signs, unlike in foals, in which it has an acute course [31, 73].

Iodine is important for ensuring the physiological course of pregnancy. Thus, iodine deficiency in the body reduces female fertility, leads to stillbirths, abortions, congenital developmental abnormalities, increased perinatal mortality, etc. [13, 27, 103, 107].

Mares with iodine deficiency give birth to stillborn or weak foals that are unable to be nursed, often without a coat of hair, even if the mothers have no clinical symptoms of iodine deficiency [31, 85, 127]. Such foals have a significantly enlarged neck in the anterior trachea due to hyperplasia of the thyroid gland [87].

Iodine deficiency during mare pregnancy leads to goitre in foals, as well as visible changes in the condition of the coat, ossification of bones, contracture of the tendons of the front limbs, and arthrosis [73, 85].

Mares with iodine deficiency do not come into heat on time and their sexual

instincts are reduced. However, mares do not usually show an enlargement of the thyroid gland [73, 120].

Iodine deficiency is also observed when eating plant feeds containing goitrogens, which inhibit the binding of iodine ions in the thyroid gland. Such plants include white clover, cabbage, soybeans, etc. [72, 113]. In addition, iodine deficiency in horses occurs when there is an excess of calcium, manganese, lead, fluorine, and bromine, which are antagonists of iodine [107].

Excess iodine is extremely toxic to horses. Therefore, it is recommended not to exceed its maximum content, which is 5 mg/kg of feed [20].

In case of iodine deficiency or excess in the diet of pregnant mares, symptoms of iodine deficiency are observed in foals. Thus, excess iodine inhibits the stimulation of the thyroid gland and prevents the transition of thyroid hormones from an inactive to an active form [47, 61].

It has been established that foals with developmental abnormalities and premature foals with bone ossification disorders were born to mares with excess iodine in their bodies. Such foals often had goitre, drowsiness, muscle weakness, limb deformities, and long hair. Even foals born at term showed signs of prematurity, i.e., physiological immaturity [73, 85, 126].

Adult animals most often showed no signs of thyroid enlargement or changes in the skin or coat [73].

According to S. N. Aukhatova [11], a decrease in phagocyte activity was found in the bodies of piglets with iodine deficiency.

Zinc is an essential trace element that is an important component of finger proteins, which regulate the level of transcription of other intracellular proteins [110].

Zinc is a component of enzymes such as lactate dehydrogenase, alkaline phosphatase and carboxypeptidase [3, 90].

Zinc activates the hormones of the gonads, pituitary gland and pancreas. It is closely linked to enzymes and vitamins and has a regulatory effect on reproductive function, carbohydrate, protein and lipid metabolism, the haematopoietic system, and the growth and development of the body [27, 159, 194].

Zinc participates in the processes of cellular respiration and carbohydrate oxidation, increases overall energy metabolism, and the level of carbohydrate, protein, and lipid metabolism [2, 191].

Recently, many studies have been devoted to investigating the effect of zinc on the immune system. Thus, zinc is a cofactor of thymulin and an essential element for the conversion of prethymulin to thymulin, which regulates the activity of mature T-lymphocytes in peripheral blood and stimulates the maturation of T-lymphocytes [35, 63, 173, 194, 244].

Zinc deficiency is characterised by impaired reproductive function in females and delayed growth and development in young animals [120, 142, 303, 304].

Research by P. J. Bentley, B. R. Grubb, et al. [142] on rabbits showed that animals consuming a diet with reduced zinc content develop alopecia, skin lesions, and become susceptible to infections, in particular pasteurellosis. All animals experienced a reduction in the size of the thymus gland, and males also experienced a reduction in the size of the testicles.

With zinc deficiency in the body of foals receiving 5 mg/kg of zinc in their diet, loss of appetite, growth retardation, parakeratosis (especially of the lower limbs), alopecia, and poor hair retention in the hair follicles were observed [90].

In Ukraine, zinc deficiency in horses was recorded by M. O. Sudakov [108]. In this case, no clear clinical signs of zinc deficiency were found in horses, but functional and structural changes occurred in their bodies due to metabolic disorders, primarily of nitrogen and carbohydrates. Stallions showed impaired spermatogenesis, and mares showed infertility. Zinc deficiency has been found to inhibit sexual desire, disrupt ovulation and reduce sperm quality [9].

It has been proven that treating animals with zinc-containing drugs potentiates cell-mediated immune responses directed against bacteria, viruses, and tumour cells [194, 244].

Reduced zinc levels were found in the blood of women who gave birth to children with hypotrophy [102].

Foals exposed to high doses of zinc (90 g of zinc per day, equal to 2% of their

diet) developed lameness, enlarged epiphyses and stiffness of movement [40, 90].

The absorption of zinc by the body can be influenced by the phytic acid anion, which binds zinc [95, 47, 274], and calcium, which is an antagonist of zinc [107, 120, 274].

Iron plays an important role in respiratory processes; it is a component of the gene locus responsible for the synthesis of haemoglobin, myoglobin and, partially, the respiratory enzyme cytochrome oxidase [95].

In vitro and in vivo experiments on mice have shown that low iron content in the body of animals leads to a weakening of the immune system, a decrease in the saturation of tissues with granulocytes and macrophages, and inhibits phagocytosis, the response of lymphocytes to antigen stimulation, and antibody formation [27].

It has been established that in adult horses, a small amount of iron is excreted from the body, since they have a closed iron metabolism cycle in the bone marrow-erythrocyte system, which means that 90% of the released iron is not excreted from the body but re-enters the bone marrow cells [120].

A horse's diet usually contains 100–250 mg of iron/kg of feed. The iron requirement is 50 mg/kg of dry feed per day for growing horses, pregnant and lactating mares, and 40 mg/kg for adult horses. Thus, normal feed should fully meet the iron requirements of horses [94, 126].

The body of a horse weighing 500 kg contains 33 g of iron, distributed as follows: 60% in haemoglobin, 20% in myoglobin, 20% in reserve and transport forms, and 2% in cytochromes and other enzymes [90].

There is also evidence that a decrease in the iron content in the body of horses can occur because of significant physical exertion [25].

Research results show that adding iron salts to the diet is not effective in increasing haemoglobin content and improving the ability of erythrocytes to transport oxygen. Feeding ponies a diet high in iron did not increase daily weight gain, red blood cell count, haemoglobin content, or serum iron, calcium, copper, and manganese levels. The use of dextrin in horses caused a syndrome like anaphylactic shock [90].

When animals consumed excess iron, its toxic effect was observed, which was

particularly evident in young animals. Thus, foals that were given iron in the form of ferrous fumarate in doses recommended by the manufacturer after birth and at the age of 3 days were found to have duodenal erosion, pulmonary haemorrhages, massive iron deposits in the liver and impaired liver integrity [90].

It should be noted that an excess of Ferrum in the diet impairs the absorption of manganese, causing symptoms of manganese deficiency in animals [9].

Cobalt is a cofactor of tetrahydropteroyl-glutamate-methyltransferase, methylmalonyl-CoA mutase and other enzymes involved in haematopoiesis, tissue regeneration, thyroid hormone production and myelin biosynthesis. Cobalt stimulates leukocytopoiesis and the production of tumour necrosis factor [2].

Cobalt is a component of the vitamin B12 molecule, which is synthesised by the microflora of the large intestine of horses. Therefore, the physiological role of cobalt in the body of animals is associated with the function of vitamin B12 [20, 61, 90, 105, 131, 286].

It has been established that 10–50 mg of vitamin B12 is synthesized daily in the large intestine of horses under the action of microorganisms [96].

In in vitro experiments, 47% of 97 microorganisms isolated from the horse intestine (mainly intestinal anaerobes) produce vitamin B12. Thus, a positive correlation was found between the level of cobalt in the diet and the concentration of vitamin B12 in the blood serum of sheep and horses [96].

In the literature available to us, we did not find any described cases of cobalt deficiency or excess in horses. However, domestic literature describes hypocobalteaemia in horses in biogeochemical zones where the soil contains less than 0.4–1.8 mg/kg of cobalt. Hypocobalcaemia in horses manifested itself in the form of impaired erythropoiesis, hyperchromic anaemia, anisocytosis and poikilocytosis of erythrocytes [105, 108].

The antagonists of cobalt are manganese, strontium, and boron [107].

Manganese is a component of hydrolases, carboxylases, and transferases, and is also involved in the synthesis of glycoproteins and proteoglycans [3, 61].

Manganese is associated with hormones and vitamins, activates phosphatases in

blood and other tissues, and participates in the regulation of the metabolism of proteins, carbohydrates, vitamins, lipids, and minerals [90, 120].

One of the metalloenzymes directly related to the functioning of the immune system is Mn-superoxide dismutase. Manganese is an activator of RNA polymerase, DNA polymerase and many other kinases [52].

There is evidence that after the administration of manganese chloride to mice, the number of NK cells increased 2–4 times, mainly due to the activation of IFN- α , IFN- β and IFN- γ [52].

Manganese is necessary for the activation of glycosyltransferase, which is involved in the synthesis of glycosaminoglycans and glycoproteins in bones and cartilage [127], as well as for the metabolism of carbohydrates and lipids and the synthesis of chondroitin sulphate [64].

Manganese deficiency leads to skeletal growth retardation, limb deformation with shortening and curvature, and joint enlargement [9, 90, 124]. It is suggested that manganese deficiency in mares may lead to congenital contractures in newborn foals [126].

There is evidence that manganese deficiency in stallions leads to impaired spermatogenesis, followed by testicular degeneration. Manganese deficiency in mares leads to silent oestrus, an increase in the number of abortions, delayed sexual maturity and deterioration of reproductive qualities [9, 120].

When horses were grazed on fields that had been treated with lime, resulting in poor manganese uptake by plants, mares experienced slow oestrus, reduced reproductive capacity and abortions. Foals were born with skeletal deformities and shortened muscles. Other signs included skull asymmetry, spinal curvature, shortened limb bones and enlarged joints, resulting in a peculiar head position in foals due to excessively short neck muscles [90].

In humans, manganese has been shown to have a positive effect on foetal growth and development and on the development of newborns [102].

Selenium is a cofactor of Se-dependent glutathione peroxidase, which is involved in the detoxification of peroxides formed as a result of the oxidation of

unsaturated fatty acids and are toxic to the cell membrane [20, 61, 94, 136, 276, 156].

It has been established that selenium plays an important role in iodine metabolism, DNA repair, and in ensuring the functioning of the immune system, which is most likely also related to its antioxidant properties [63, 52].

Selenium deficiency is associated with a wide variety of immunodeficiency conditions, oncological, autoimmune and allergic diseases [52]. Selenium stimulates NK activity, increases IL-1 and IL-2 production, potentiates cellular and humoral immune responses, and modulates the phagocytic function of polymorphonuclear leukocytes in both laboratory and farm animals [63, 219, 167].

Horses require 0.1–0.2 mg of selenium per 1 kg of dry matter in their diet. With this amount, the concentration of selenium in the blood serum of adult horses reaches 140 ng/ml [22, 90, 169].

Stowe H. D., Herdt T. H [287] recommend the following normative values for selenium content in blood serum: in newborn calves and sheep – 50–80 ng/ml, in foals and pigs – 70–90 ng/ml With age, this indicator gradually increases and in adult cattle it is 70–100 ng/ml, in sheep – 120–150 ng/ml, in horses 130–160 ng/ml, and in pigs 180–220 ng/ml.

The vitamin E status affects the selenium content in the body of animals [94, 236].

Selenium-responsive diseases in horses are characterised by damage to the skeletal and cardiac muscles. They are associated with a decrease in glutathione peroxidase activity to below 0.25 U/ml [219] and a decrease in serum selenium levels to below 60 ng/ml [152, 287].

Studies conducted in Ohio (USA) have shown that selenium deficiency is the main cause of retained placenta in mares [91], while experiments on a farm in New York showed that selenium deficiency is the cause of reduced horse reproduction and foal mortality [22].

Selenium deficiency-induced myopathy (white muscle disease) in horses leads to weakness, slow movement, difficulty swallowing, respiratory diseases and heart problems [91].

Recently, there has been increased interest among researchers in selenium deficiency and exercise tolerance in horses [267].

Some foals with severe selenium deficiency have been found to have dilated cardiomyopathy [22], tachycardia, colic, and signs of intestinal damage, which may be caused by dysfunction of the smooth muscles of the intestine and heart muscle disorders [90].

Canadian scientists have found low selenium levels in the blood serum of horses with skeletal muscle disease, which showed signs of heart failure and colic syndrome. In contrast, other horses that did not show signs of muscle disease but suffered from colic had normal selenium levels in their blood serum [23]. The blood serum of these horses showed increased activity of creatine kinase and aspartate aminotransferase, as well as high levels of potassium and urea [23].

During pregnancy and lactation, mares are recommended to be given approximately 1.3 mg of selenium per animal weighing 450 kg per day. In mares, only a small amount of selenium can pass to the foetus through the placenta [90].

The selenium content in the blood serum of foals born to mares with sufficient selenium content in their blood serum was lower than in mares and ranged from 70 to 80 ng/ml. If the selenium content in the blood serum of foals is lower than 65 ng/ml, this indicates a deficiency. Such foals may be susceptible to alimentary and muscular dystrophy, especially if they have low vitamin E status [126].

Selenium is one of those elements whose blood level is directly related to its content in the diet [74]. The maximum permissible level of selenium for horses is 2 mg/kg of dry matter in the diet, and the LD-50 for oral administration of selenium-containing preparations is 3.3 mg of selenium (in the form of sodium selenite)/kg of animal body weight [90].

Acute selenium poisoning in animals most often occurs as a result of eating plants that are capable of accumulating selenium, or due to the irrational use of feed additives containing selenium [73].

Selenium poisoning in horses manifests itself in hair loss in the mane and tail area, laminitis with detachment of the hoof capsule, and symptoms of nervous system

disorders characterised by blindness, weakness, and movement disorders (ataxia) [73, 90].

Stowe H. D., Herdt T. H. [287] observed hair loss and hoof damage in horses with a serum selenium content of 928 ng/ml, compared to the normal range of 140–160 ng/ml.

Recently, one of the areas of increased attention of scientists in the fields of human and veterinary medicine has been the study of the effect on the human and animal body of elements of technogenic origin, such as heavy metals (cadmium, lead, hydrargyrum), as well as an excess of essential trace elements (zinc, copper, molybdenum, fluorine, chlorine, nickel, etc.) in the environment caused by human activity [86]. Undoubtedly, they can affect the metabolic processes, working capacity and health of horses [9].

For example, an excess of cadmium in the body of animals leads to anaemia, liver damage, cardiomyopathy, pulmonary emphysema, osteoporosis and skeletal deformation [103].

An excess of lead primarily affects the blood-forming organs and leads to anaemia, as well as the nervous (encephalopathy and neuropathy) and urinary systems, especially the kidneys (nephropathy) [103].

1.4. Diagnostics disturbances of mineral metabolism in horse organism

The state of mineral metabolism in horses is studied using clinical, laboratory, radiographic and osteometric methods [57].

In order to identify mineral metabolism disorders in horses, twice a year (in spring and autumn) a medical examination is carried out, which consists of three stages: diagnostic, therapeutic and preventive [57].

The diagnostic stage of medical examinations includes an analysis of the herd's symptoms, hygiene, feeding, and the level and nature of metabolism in the animals' bodies. The entire horse population is examined. Particular attention is paid to brood mares and stallions. Laboratory tests of blood, urine, and faeces are performed [57].

When diagnosing mineral metabolism disorders in animals, it is necessary, first

of all, to take into account the characteristics of the geochemical zone or biogeochemical province and to conduct comprehensive clinical and biochemical studies of animals to determine the content of macro and microelements in their bodies (blood, milk, internal organs), as well as in soils, water sources and feed [107, 113, 120, 124].

Particular attention is paid to the balance of minerals in the diet according to the needs of horses, considering their age, physiological condition, intensity of physical activity, etc. [37, 94].

When diagnosing mineral metabolism disorders in horses, clinical signs that appear during the development of the pathology are considered, when morpho-functional changes in the animal's body are already occurring, which are often irreversible. Therefore, it is necessary to diagnose mineral metabolism disorders in horses at an early stage of their development, which is quite difficult to do.

Disorders of mineral metabolism in foals lead to changes in their growth and development, and subsequently to reproductive disorders, reduced working capacity, reduced productivity, non-specific resistance of the body, changes in the condition of the skin, coat and hoof horn [73, 107, 120].

Symptoms of mineral metabolism disorders in horses develop gradually, making them difficult to diagnose. Most often in adult horses, unlike other farm animals, mineral deficiencies are hidden [81, 83, 107, 108, 120].

In hidden forms of mineral metabolism disorders, which often occur with micronutrient deficiencies, mares experience reproductive dysfunction, have difficulty coming into heat and becoming pregnant, they experience silent oestrus and give birth to weak foals that are susceptible to diseases, especially of the respiratory and gastrointestinal tracts. Foals lag behind in growth and development and subsequently perform worse than their peers in racetrack trials [37, 120].

The basis for diagnosing the latent course of mineral metabolism pathology in animals is the determination of the content of macro- and microelements in feed, water sources and biological substrates (blood, milk, urine, hair, etc.) using spectrographic and biochemical research methods [51, 68, 77, 83].

The following methods are used to determine the content and identify macro- and microelements in soils, feed and biological substrates [51, 68]:

- spectrometric or spectrographic determination of the content of macro- and microelements in various substrates: emission spectrography, atomic absorption spectrometry, chromatography-mass spectrometry studies;
- nuclear magnetic resonance using magnetic relaxation markers;
- radioisotope studies, which include radioimmunological methods in combination with other molecular biological and immunological techniques (ELISA, immunoblotting);
- ionometric method, which allows the determination of microconcentrations of the ionised fraction of microelements;
- cell culture methods and intact animal models;
- ion exchange compounds and chelators.

Recently, research on the content of macro- and microelements in hair has become relevant. This method is non-invasive and is considered the most objective and informative in terms of the content of minerals in the body of animals [58, 79, 86, 159, 314]. At the same time, it was found that the calcium and phosphorus content in the diet of Shetland ponies did not correspond to the level of these elements in their hair, which may be related to the phases of hair growth activity [314].

On the other hand, it should be noted that, in addition to diet, many factors influence hair composition: season, animal age, certain medications, and contamination of hair with feed, soil, and other substances [52, 79, 130].

When studying the content of macro- and microelements in blood, factors such as stress, infectious and parasitic diseases, neoplasms, the use of corticosteroids in animals, etc. should be taken into account [34, 40, 118, 119, 126].

1.5. Treatment and prevention pathology of horses' mineral metabolism

Treatment of mineral metabolism disorders in horses should be comprehensive, taking into account the specific clinical condition of the animal and the results of biochemical, morphological and spectrometric blood tests [113].

In case of mineral metabolism disorders, replacement therapy is carried out,

aimed at eliminating them by introducing macro- and microelements into the animal's body [113].

Prevention of mineral metabolism disorders is aimed at preventing possible macro- and microelement deficiencies in animals by constantly providing their bodies with the necessary macro- and microelements [107, 113].

Prevention of mineral metabolism disorders in animals is based on the principles of general prevention and therapy using feed additives, premixes, specific preparations and drugs for pathogenetic and replacement therapy [15, 107, 120].

The development of a plan of therapeutic and preventive measures for mineral metabolism disorders in animals should take into account the characteristics of clinical manifestations and the severity of the disease, the nature of changes in the geochemical situation in the agricultural landscape (biogeocenosis), the content of minerals in the diet and the animals' need for them, which depends on age, physiological state, exploitation, etc. [107, 113, 120].

In some cases, urgent medical care should be provided to sick animals, while in others, appropriate preventive measures should be taken. Most often, a situation arises in which therapeutic and preventive measures must be carried out simultaneously [107, 113].

Given that the clinical manifestation of mineral metabolism disorders in horses is most often accompanied by morphological and functional changes in their bodies, which are often irreversible, prevention plays a key role in combating them. The theoretical basis for non-specific prevention of mineral metabolism disorders in horses is the general biological law of the unity and interconnection of the organism with the environment [114].

The most rational approach to the prevention of mineral metabolism disorders in animals is to add depleted forms of minerals to the soil. However, due to the insufficient quantity of such substances and the difficulty of their use, the main therapeutic and preventive measure is to administer mineral substances that are lacking in the diet to animals in the form of feed additives or veterinary preparations [107, 120].

For the treatment and prevention of mineral metabolism disorders, therapeutic

and prophylactic doses of minerals are administered to the animal's body. Macro- and microelements are not used in their native form, but in the form of their salts, which requires the determination of the appropriate dose [107, 113, 127, 171].

Various sources of minerals are used for the prevention and treatment of mineral metabolism disorders in horses.

Thus, to eliminate sodium and chlorine deficiency, horses are provided with access to table salt or a salt lick. For calcium and phosphorus deficiency, horses are given crushed limestone or shell flour, bone meal, dicalcium phosphate, monosodium phosphate, and sodium tripolyphosphate. Magnesium is given to horses in the form of magnesium sulphate and oxide; potassium in the form of potassium chloride; cobalt in the form of chloride, sulphate, oxide or carbonate; copper in the form of copper sulphate or carbonate. To provide horses with iodine, iodised salt, calcium or potassium iodide is used. Iron is used for horses in the form of iron sulphate, but iron oxide is not used because horses do not absorb it well. Manganese is used for horses in the form of mineralised salt containing 0.25% manganese; selenium – in the form of sodium selenate and selenite; zinc – in the form of zinc carbonate and sulphate [47, 83, 127, 152].

If there is more than the required amount of a particular element in the feed, the animals need to be given a chemical element – an antagonist [107].

If there is a deficiency of trace elements in the feed, it is advisable to reduce the calculated doses of feed supplements by 1.5–2.0 times. At such doses, trace elements are better absorbed and deposited. In this case, animals can be fed for a long time without interruption. When feeding animals with average and maximum prophylactic doses, a 15-day break should be taken every 1.5–2.0 months. Therapeutic doses should be twice as high as prophylactic doses [107, 120].

Thus, mineral metabolism disorders in horses occur during the most stressful physiological periods, when the animals' need for minerals increases significantly. Such periods include the last third of a mare's pregnancy, lactation, growth, physical stress, etc.

The clinical manifestation of mineral metabolism disorders in horses is most

often accompanied by morphological and functional changes in their bodies. Quite often, these changes are irreversible. Therefore, early diagnosis and prevention of mineral metabolism disorders in horses are quite relevant issues.

Mineral metabolism disorders in horses should be diagnosed at an early stage of their development. From a diagnostic point of view, this is a difficult task and requires a comprehensive approach, including analysis of soil cartograms, determination of the mineral content in the diet, as well as in blood, hair and other biological substrates.

Early diagnosis of mineral metabolism disorders is particularly important for pregnant mares. Mineral metabolism disorders in mares result in foals being born with clinical signs of mineral deficiency.

Mineral metabolism disorders in foals have quite serious consequences. Such foals are born weak, susceptible to various diseases (rickets, tendon contracture, osteochondrosis, etc.), they grow and develop slowly and must be culled.

In conclusion, it should be noted that macro- and microelements are indispensable participants in virtually all physiological processes in the animal organism. Their deficiency or imbalance leads to the development of mineral metabolism pathology, which is registered in horses all over the world.

The occurrence of mineral metabolism disorders depends primarily on the supply of minerals to the horse's body. Mineral metabolism disorders lead to changes in the growth and development of foals, reduced working capacity, productivity, non-specific resistance of the body and the occurrence of microelementosis in adult horses.

In modern conditions, the classic manifestation of a deficiency of certain macro- and microelements is rare. However, mineral metabolism disorders in horses are increasingly manifested in the form of polyopathologies. Their prevalence, severity and symptoms depend on a number of factors, the level and nature of the disorders. A particularly relevant issue is the pathology of mineral metabolism in broodmares during pregnancy.

2. MODELLING OF MINERAL METABOLISM DISORDERS IN HORSES

The work was carried out between 2006 and 2010 at the Department of Therapy and Clinical Diagnostics of the National University of Life and Environmental Sciences of Ukraine (NULES of Ukraine). Some studies were conducted at the Institute of Occupational Medicine of the Academy of Medical Sciences of Ukraine, the diagnostic department of the Kyiv City State Laboratory of Veterinary Medicine, and the Bald Animal Disease Diagnostic Centre (Kyiv).

The experimental part of the work was carried out at the Horse Farm in the Poltava region on pregnant mares of the Russian trotting breed, aged 7 to 12 years, and their foals, aged 1 month. This Farm specialises in breeding Russian and Orlov trotters for racing, as well as Novoaleksandrivsky heavy horses for the dairy industry (kumis production). The stud farm has a total of 282 horses, of which 87 are brood mares of trotting breeds, 7 are stallions of trotting breeds, 24 are brood mares and 3 are stallions of heavy breeds. All horses are kept in individual stalls, with mares and young stock grazing in the summer and staying in stables in the winter.

All animals undergo routine deworming twice a year with fenbendazole at a dose of 10 mg per 1 kg of body weight orally, vaccination against anthrax and equine influenza, and diagnosis of infectious diseases such as glanders, equine infectious anaemia, and dourine.

An analysis of the farm's documentation was carried out, which indicates cases of foals born to clinically healthy mares with signs of mineral metabolism pathology: without hair cover, dying within a few days, with tendon contracture, which were subsequently culled. Foals with rickets, growth retardation and hair loss were also registered. The farm often diagnoses respiratory tract diseases in one-month-old foals, which may be associated with a decrease in their immune status during this period.

During the research, we analysed the ecological and agrochemical characteristics of the soils of this farm and the Poltava region, as well as the main diet of pregnant mares during the grazing and stabling periods. We studied the nutritional value of the diet and, using spectral analysis, the content of macroelements (calcium,

phosphorus, chlorine, magnesium) and microelements (iron, manganese, zinc, copper, cobalt, selenium, molybdenum, nickel, lithium, chromium, barium, vanadium, aluminium, cadmium, lead, arsenic, boron, strontium, silver and tin) in feed (straw, hay, oats) and water.

A dispensary examination of the population of trotting horses at the horse farm was conducted, as a result of which clinically healthy and sick animals with signs of mineral metabolism disorders were selected.

During the dispensary examination, the clinical condition of the horses was studied. The habitus, condition of the hair coat, skin, hoof horn, subcutaneous tissue, visible mucous membranes, lymph nodes, and the condition of the cardiovascular, respiratory, digestive, and genitourinary systems were determined. Laboratory blood tests were performed, namely morphological, biochemical, immunological, and spectrometric.

During the study of general clinical blood parameters, the number of erythrocytes and leukocytes was determined, a leukogram was calculated, and the erythrocyte sedimentation rate (ESR) and haematocrit value were determined.

The serum of pregnant mares and foals was tested for macronutrients (calcium, phosphorus, magnesium, sodium, chlorine, potassium) and microelements (iron, cobalt, copper, manganese, zinc, selenium), biochemical indicators (total protein content, its fractions and their ratio, concentration of haemoglobin, glucose, urea, creatinine, bilirubin, triglycerides, cholesterol), as well as the activity of alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), gamma-glutamyltranspeptidase (GGT), α -amylase.

The indicators of the immune status of animals were studied, namely the number of T-lymphocytes, T-helpers, T-suppressors, PK cells, B-lymphocytes, O-lymphocytes, HST-spontaneous, HST-induced, RBLT-spontaneous, RBLT-induced, and circulating immune complexes (CIC).

During the adjustment period, the diet of pregnant mares was corrected to meet their nutritional needs.

Experimental studies on animals were conducted in three stages:

At the first stage of the research, a dispensary examination of the population of trotting horses at the horse farm was conducted, as a result of which clinically healthy and sick animals with signs of mineral metabolism disorders were selected.

In the second stage of the research, a control group and two experimental groups of pregnant mares with impaired mineral metabolism were formed, which were in the 8th month of pregnancy, with 5 animals in each group.

The mares in the control group received a basic diet consisting of 6.0 kg of cereal and mixed grass hay, 8.0 kg of oat straw and 4.0 kg of oats. During the day, each animal consumed approximately 35.5 ± 5.0 litres of water extracted from an artesian well.

The mares in the first experimental group received a basic diet with the addition of the KM L2 premix at a rate of 15 g per animal, once a day for 42 days, during the morning feeding period. The KM L2 premix contains a complex of fat- and water-soluble vitamins, as well as macro- and microelements, at a rate of 1 kg of premix: Mg – 5.5%, Na – 9.9%, P – 6.95%, Ca – 12.65%. Cu – 810 mg, Zn – 4100 mg, Mn – 3400 mg, Fe – 951 mg, Co – 18 mg, I – 65 mg, Se – 16 mg.

The mares in the second experimental group received their basic diet and the drug ‘Lactahos’, which was developed by us in the research laboratory for non-contagious internal diseases of animals at the Department of Therapy and Clinical Diagnostics of the National University of Life and Environmental Sciences of Ukraine. The feed with the Lactahos preparation was administered once a day for 42 days, during the morning feeding, at a rate of 5 g per animal. The Lactahos preparation contains the following components, %: zinc lactate – 4.0, copper lactate – 2.0, cobalt lactate – 0.06, manganese lactate – 2.0, starch iodine – 3.0, triethanolamine salt of selenic acid – 0.03, organosilicon immunomodulator ‘Mival’ – 0.3, opoka – 88.61.

In the third stage, foals from mares in the control and experimental groups were studied. For this purpose, a control group and two experimental groups of foals were formed, with 5 foals in each group.

The foals in the control group were born to mares that received the basic diet.

The foals in the first experimental group were born to mares that received the

basic diet with the addition of the premix KM L2.

The foals in the second experimental group were born to mares that received the basic diet and the drug Lactahos.

During the study period, pregnant mares were kept in individual stalls in compliance with sanitary and hygienic standards according to the technological parameters for horses.

The clinical condition of pregnant mares and their foals was examined using methods commonly accepted in veterinary medicine. The habitus, condition of the coat, skin, hoof horn, subcutaneous tissue, visible mucous membranes, lymph nodes, cardiovascular, respiratory, digestive and urogenital systems were determined, and thermometry was performed.

Blood and blood serum were used as material for laboratory studies. Blood from the experimental animals was obtained from the jugular vein in the morning, before feeding, with a simultaneous clinical examination. Blood was collected in sterile polypropylene tubes from Sarstedt (Germany) using needles from BD Drogeda (Ireland). Blood serum and whole blood stabilised with heparin were used in the studies.

General clinical, biochemical and immunological blood tests were performed.

The number of erythrocytes was determined using a microscope in a Goryaev chamber; the number of leukocytes was determined by counting under low magnification of a microscope in 100 large squares of the Goryaev chamber. The leukogram was obtained by counting leukocytes in blood smears stained according to Romanovsky-Giemsa. The erythrocyte sedimentation rate (ESR) was determined using the method of T.P. Panchenkov, and the haematocrit value was determined using the method of Y. Todorov [48, 122].

The concentration of haemoglobin in the blood was determined using the haemoglobin cyanide method. The total protein content in blood serum was determined using the biuret method; albumin – by reaction with bromcresol green; globulins and protein coefficient – by calculation; urea – by the urease method; creatinine – by the Popper method; total bilirubin was determined using the Jędraszzyk-Kleghorn-Grof

method; glucose was determined using the glucose oxidase method [43, 45]; cholesterol was determined using the enzymatic method; triglycerides were determined using the colorimetric method according to Gottfried and Rosenberg; AST and ALT activity – using the Wrightman-Frenkel method; GGT activity – using the G. Szasz method; α -amylase activity – using the W.T. Caraway method; alkaline phosphatase (ALP) activity – using the Kings-Armstrong method [39, 41].

The study of serum protein fractions – albumins, alpha-, beta- and gamma-globulins – was carried out using electrophoresis in 7.5% polyacrylamide gel (Laemmly U. K., 1970) [224].

The number of T and B lymphocytes and PK cells was determined from blood immunological parameters by lymphocyte phenotyping in rosette formation tests with particles coated with monoclonal antibodies [41]. This method was used to determine the number of T lymphocytes, which was equal to the number of rosette-forming lymphocytes with CD3 diagnosticum, the number of T helpers – with CD4 diagnosticum,

T-suppressors – with CD8-diagnosticum, B-lymphocytes – with CD22-diagnosticum, PK cells – with CD16-diagnosticum. The number of O-lymphocytes was determined by calculation by subtracting the number of T-lymphocytes,

B-lymphocytes and PK cells from 100%. The phagocytic activity of neutrophils was assessed using the neutroblue tetrazolium reduction test (NST test). The activity of neutrophils was determined in two variants – basal and stimulated (stimulated with staphylococci $5 \cdot 10^8$) [41]. The indicator of blast transformation of lymphocytes was determined using the Chernushenko method [121]. The content of circulating immune complexes (CIC) was determined by the precipitation method in 3.75% polyethylene glycol by spectrophotometry with polyethylene glycol – 6000, followed by photometric measurement of the precipitate density (in optical units) [121].

The content of macro- and microelements in feed, blood serum and hair was studied by optical emission spectrophotometry with induced plasma binding using an OPTIMA 2100 DV spectrometer from Perkin Elmer, USA [68].

The research results were statistically processed using Excel-2003 software,

assessing the reliability of the indicators ($p < 0.05$, $p < 0.01$, $p < 0.001$) according to Student's criterion.

2.1. The mineral supply of pregnant mares and the diagnosis of mineral disturbances

The deficiency or excess of macro- and microelements in the soils of the respective biogeochemical zones of Ukraine, as well as in water, feed and animal organisms, is one of the main aetiological factors in the occurrence and development of biogeocenotic pathology in horses.

Disruption of mineral metabolism in horses leads to a decrease in working capacity, productivity, non-specific resistance of the organism and the occurrence of microelementosis, and in foals – to growth and development delays.

When diagnosing mineral metabolism pathology in horses, it is necessary, first of all, to take into account the characteristics of the geochemical zone or biogeochemical province, to conduct comprehensive clinical and biochemical studies of animals, determining the content of macro- and microelements in their bodies (in blood, urine, hair, milk, internal organs), as well as in soils, water sources and feed. Timely detection of mineral metabolism disorders in horses, even before their clinical manifestation, makes it possible to carry out prevention and therapy of animals at an early stage and avoid economic losses in the horse breeding industry.

Based on the content of mobile forms of microelements in the soil, the territory of Ukraine is divided into four biogeochemical zones: western, north-eastern, central and southern [109].

The soils and water sources of the western zone (Rivne, Volyn, Lviv, Ternopil, Chernivtsi, Ivano-Frankivsk and Zakarpattia regions) are depleted in mobile forms of iodine, cobalt, zinc, molybdenum, and in some places copper and manganese.

The north-eastern biogeochemical zone includes the northern regions of Kyiv, Sumy, Chernihiv, Vinnytsia, as well as Zhytomyr and Khmelnytskyi regions. The soils and water sources of this region are characterised by low levels of mobile forms of iodine, cobalt, zinc, and in some places manganese and copper.

The southern biogeochemical zone includes the Mykolaiv, Kherson,

Dnipropetrovsk, Zaporizhzhia, Donetsk, and Luhansk regions, the southern regions of the Kharkiv region, the southern and central regions of the Kirovohrad and Odesa regions, and the Autonomous Republic of Crimea [109].

The central biogeochemical zone of Ukraine includes Cherkasy and Poltava regions, the southern regions of Vinnytsia, Kyiv, Chernihiv and Sumy regions, as well as the northern regions of Odesa, Kharkiv and Kirovohrad regions. The soils of the central and southern biogeochemical zones of Ukraine are better supplied with microelements than other biogeochemical zones, but they are deficient in absorbable forms of zinc and cobalt. The soils of some localities have an excess of manganese [109].

The Poltava region is considered a conditional reference point for the content of mobile forms of microelements in water, soil and feed. At the same time, animals in the Poltava region are diagnosed with microelementosis, which occurs as a result of a deficiency or excess of certain microelements in their bodies [109].

Based on the above, one of the tasks of our work was to study the supply of macro- and microelements to horses in the conditionally standard biogeochemical zone of Ukraine, which includes the horse farm in the Poltava region.

The daily ration of pregnant mares consisted of cereal and mixed grass hay (6.0 kg), oat straw (8.0 kg) and oats (4.0 kg) (Table 2.1). During the day, each animal consumed approximately 35.5 ± 5.0 litres of water extracted from an artesian well.

Analysis of the diet of pregnant mares shows an excess of feed units (1.16 times), metabolisable energy (1.44 times), fibre (2.0 times), calcium (1.68 times) and a deficiency of phosphorus (1.21 times).

Table 2.1

Diet of a Russian trotting mare weighing 450 kg in last trimester of pregnancy

Feed	Amount of feed, kg	Feed units	Metabol. energy, MJ	Digestible protein, g	Cellulose, g	Ca, g	P, g
Cereal and mixed grass hay	6,0	2,64	38,7	336,0	1542,0	49,8	12,0
Oat straw	8,0	2,48	43,0	136,0	2592,0	27,2	8,0

Continuation of table 2.1

Oats	4,0	4,0	36,8	316,0	388,0	6,0	13,6
Total	18,0	9,12	118,5	788,0	4522,0	83	33,6
Norm		7,89	82,32	787,5	2250,0	49,4	40,7
± to norm		+1,23	+36,18	+0,5	+2275,0	+33,6	-7,1

The feed and water were tested for calcium, phosphorus, chlorine, magnesium, iron, manganese, zinc, copper, cobalt, selenium, molybdenum, nickel, lithium, chromium, barium, vanadium, aluminium, cadmium, lead, arsenic, boron, strontium, silver, and tin were determined in feed and water.

In the water from the artesian well used to water the horses at the horse farm, we have established levels of biogenic macro- and microelements that are lower than the maximum permissible levels according to the sanitary rules and norms of Ukraine (SanPiN), namely: Calcium by 1.95 times, phosphorus – 97.2 times, magnesium – 1.97 times, cobalt – 5.0 times, zinc – 263.0 times, copper – 14.3 times, manganese – 1.25 times, iron – 150.0 times, and molybdenum – 31.3 times. At the same time, the water was found to contain 2.2 times more arsenic, 3.0 times more barium and 6.8 times more chlorine than the permissible levels according to Ukrainian sanitary rules and standards, which may be due to anthropogenic factors and technogenic pollution of the territories. (tabl. 2.2).

Table 2.2

The content of macro- and microelements in water for watering horses at the horse farm in the Poltava region

Element	Water from artesian well, mg/l	Water according to SanPiN indicators, mg/l/l	Difference (±) from the norm (SanPiN)	Element	Water from artesian well,	Element	Water from artesian well,
Biogenic elements				Technogenic elements			
Ca	51,3	100	-48,7	Pb	0,003	0,03	-0,027
P	0,036	3,5	-3,464	Cd	0,0006	0,001	-0,0004
Mg	25,4	50	-24,6	As	0,11	0,05	+0,06

Continuation of table 2.2

Cl	2375,23	350	+2025,2	Sr	7,0	7,0	0
Co	0,02	0,1	-0,08	Sn	0,0013	0,67	-0,669
Cu	0,07	1,0	-0,93	B	0,0014	0,5	-0,499
Fe	0,002	0,3	-0,298	Al	0,006	0,5	-0,494
Mn	0,08	0,1	-0,02	Ba	2,07	0,7	+1,37
Se	0,01	0,01	0,00	V	0,0004	0,1	-0,1
Zn	0,019	5,0	-4,981	Li	0,085	0,03	+0,055
Mo	0,008	0,25	-0,242	Ni	0,01	0,1	-0,09
Cr	0,04	0,05	-0,01	Ag	0,002	0,05	-0,048

Other indicators of the mineral composition of water did not exceed the permissible levels specified by the current sanitary rules and regulations of Ukraine [24].

The results of studies of the feed ration of pregnant mares for mineral content showed that per day, each animal receives 38.3% less phosphorus, 32.5% less manganese, 71.4% less zinc, 55.8% less copper, and 69.0% less selenium from water and feed. At the same time, the calcium and iron content in the feed of pregnant mares exceeded the norm by 1.32 and 3.47 times, respectively (table 2.3).

Table 2.3

The content of macro- and microelements in feed and water for pregnant mares at the Horse Farm in the Poltava Region

Ratio feed	Amount of feed, kg	Ca, g	P, g	Mg, g	Mn, mg	Zn, mg	Fe, mg	Co, mg	Cu, mg	Se, mg
Cereal and mixed grass hay	6,0	32,3	7,9	1,77	125,2	79,7	645,8	0,09	23,5	0
Oat straw	8,0	28,8	7,8	5,73	120,0	19,2	1235,9	0,22	15,4	0
Oats	4,0	2,45	5,37	2,57	57,8	30,0	86,7	0,02	8,76	0
Water	35,0	1,80	1,26	0,89	2,80	0,67	0,07	0,70	2,45	0,35
Total	53,0	65,3	22,33	10,97	305,9	129,7	1968,5	1,03	50,1	0,35
Norm		49,4	36,2	10,90	453,5	453,5	566,9	1,13	113,4	1,13
± to norm		+15,85	-13,87	+0,07	-147,6	-323,8	+1401,0	-0,10	-63,3	-0,78

During the study of the content of microelements of technogenic origin in feed and drinking water for pregnant mares, it was found that within 24 hours, each animal receives 4.2 mg of lead, 291.2 mg of barium, 12.1 mg of arsenic, 1.78 g of aluminium, 56.3 mg of nickel and 513.5 mg of strontium (Table 2.4).

It should be noted that the harmful effect of technogenic chemical elements on the body of animals depends on many factors. The most important of these is the concentration of a particular chemical element in the animal's body and the period of its exposure. The ability of the body to excrete technogenic elements plays a significant role. This function is performed by the kidneys, liver, and digestive system. The level of harmful effects of technogenic elements also depends on the body's ability to recover after their destructive action.

Table 2.4

**The content of technogenic elements in the feed ration of pregnant mares
at the Horse Farm**

Ratio feed	Amount of feed, kg	Pb, mg	Cd, mg	Sr, mg	V, mg	Ni, mg	As, mg	Al, mg	Ba, mg	Ag, mg
Cereal and mixed grass hay	6,0	2,03	0,138	124,2	0,15	16,54	-	448,9	63,36	-
Oat straw	8,0	1,56	0,12	110,3	0,3	22,4	-	1290,8	150,1	-
Oats	4,0	0,48	0,03	9,5	0,09	17,0	8,24	36,8	5,26	-
Water	35,0	0,11	0,02	24,5	0,014	0,35	3,85	2,1	72,5	0,07
Total	53,0	4,18	0,31	268,5	0,55	56,2	12,09	1778,6	291,2	0,07

Technogenic chemical elements tend to accumulate in parenchymal organs, primarily in the liver, kidneys, and pancreas. With prolonged exposure, technogenic elements can also be deposited in other tissues. For example, lead and aluminium can accumulate in nerve tissue, and cadmium in hair follicles [52].

In view of the above, it can be assumed that the body of a pregnant mare and her foal bear a double burden in terms of providing their bodies with minerals. On the one hand, there is a deficiency of essential macro- and microelements, and on the other,

there is a significant intake of technogenic elements into the animal's body.

Thus, even in the conditionally standard biogeochemical zone of Ukraine, to which the Poltava region belongs, the influence of ecological, technogenic and anthropogenic factors leads to changes in the ecosystem, resulting in a significant reduction in the content of (soil – plant – animal organism) of vital biogenic macro- and microelements, with a simultaneous increase in the content of technogenic elements.

As is well known, constant anthropogenic and technogenic pollution of the environment causes metabolic disorders in animals [14]. This indicates the relevance of research into mineral metabolism disorders in horses, especially during the gestation period of mares. The results of these studies can be used to develop new methods for the diagnosis and prevention of biocenotic pathology in horses.

Therefore, the next stage of our work was to study the clinical condition of pregnant mares and determine the content of macro- and microelements in their blood.

2.2. Clinical condition of pregnant mares and macro- and microelement content in their blood in cases of mineral metabolism disorders

Symptoms of mineral metabolism disorders in horses develop gradually, making diagnosis difficult. Most often in adult horses, unlike other farm animals, mineral deficiency is hidden, but in this case, the foetus and newborn foals are most affected [83, 108, 120].

In our opinion, the biocenotic pathology of horses in the biogeochemical zones and provinces of Ukraine has been little studied for two main reasons. One of them is the complexity and severity of biogeochemical diagnostic methods, and the second is the absence of pathognomonic symptoms in polypathologies.

During the clinical study, the mares were found to be in satisfactory condition. The mucous membrane of the animal's conjunctiva was pale pink in colour. No clinical signs of acute or chronic diseases were observed in the mares. We did not find any disorders of the digestive system; the animals consumed their feed and water well. However, during auscultation, we recorded weakened intestinal motility; the faeces were formed, but undigested oat grains were found in them. During the examination of

the cardiovascular system, it was established that the heartbeat in animals was of moderate strength, heart tones were rhythmic, with a clear timbre, without extraneous noises, and the coefficient of reverse filling of blood vessels, which was determined on the mucous membrane of the gums, was within the normal range.

The results of the urogenital system studies showed that the mares came into heat and foaled on time. During urination, the animals assumed a natural posture, and urination was painless.

The body temperature of the mares was $37.8 \pm 0.05^{\circ}\text{C}$, the heart rate was 32.1 ± 0.07 beats/min, and the respiratory rate was 12.3 ± 0.14 breaths/min, which corresponds to optimal physiological values.

At the same time, all mares selected for the study showed changes in their coat: dullness, matting, dullness of the mane and tail, dandruff flakes at the base of the hair roots, poor hair retention in the skin, delayed moulting in most animals, dry, uneven, dull hooves, and cracks in the hooves. Most animals showed coprophagia and distorted taste (animals licked foreign objects, walls and floors).

The above symptoms indicate a disturbance in the metabolism of minerals in the body of pregnant mares. This is also evidenced by the symptoms we have identified, which characterise a deficiency of magnesium, manganese, zinc, cobalt and selenium in the body of pregnant mares. Namely, changes in the coat and its derivatives, weakened intestinal peristalsis, poor feed digestion and taste distortion.

It should be noted that mineral deficiencies in adult horses occur in a hidden, veiled form. In addition, during the last three months of pregnancy, a large part (60–65%) of the foetus's tissues develop. A mare's need for nutrients and biologically active substances during pregnancy increases by 20% in summer and by 40–50% in winter and early spring [94]. Therefore, ensuring that pregnant mares have sufficient macro- and microelements makes it possible to maintain their health and reproductive qualities and obtain well-developed, viable offspring. Only under such conditions will the foal be able to fully realise its genetic and athletic potential in the future.

During the study of the content of macro- and microelements in the blood serum of pregnant mares with mineral metabolism disorders compared to clinically healthy

animals, a violation of the calcium-phosphorus ratio was established, with a significantly lower content of magnesium – 1.65 times, manganese – 3.0 times, zinc – 1.36 times, cobalt – 3.94 times, and selenium – 1.46 times. It should be noted that the content of magnesium, manganese, cobalt, and selenium was lower than the normative values, while iron exceeded them (Table 2.5).

It should be noted that calcium-phosphorus metabolism disorders in pregnant mares are likely caused by excessive calcium intake. This negatively affects metabolic processes in bone tissue in both the mother and the foetus [20].

Low magnesium content in the blood serum of pregnant mares with mineral metabolism disorders may be associated with the active use of this element in metabolic processes in the mother's and foetus's bodies, since the diet was not deficient in this element (see Table 2.3).

Table 2.5

The content of macro- and microelements in the blood serum of pregnant mares, $M \pm m$, $n=15$

Indexes	Pregnant mares	
	Clinically healthy, $n=15$	Under mineral metabolism disorders, $n=15$
Total calcium, mmol/l	3,16±0,03	3,27±0,04
Inorganic phosphorus, mmol/l	1,14±0,05	1,01±0,04
Ca:P ratio	2,85: 1	3,30: 1
Potassium, mmol/l	4,18±0,09	4,00±0,09
Sodium, mmol/l	142,41±0,67	141,19±1,06
Choline, mmol/l	103,22±0,45	102,85±0,58
Magnesium, mmol/l	1,08±0,03	0,66±0,01***
Manganese, $\mu\text{mol/l}$	0,51±0,01	0,17±0,01***
Iron, $\mu\text{mol/l}$	28,55±2,4	31,03±1,3
Copper, $\mu\text{mol/l}$	18,79±1,5	16,11±1,3
Zinc, $\mu\text{mol/l}$	17,55±0,28	12,88±0,1***
Cobalt, $\mu\text{mol/l}$	0,80±0,01	0,20±0,01***
Selenium, $\mu\text{mol/l}$	0,76±0,01	0,52±0,014***

Note.

*** $p < 0,001$, compared to clinically healthy mares

On the other hand, a deficiency of manganese, zinc, cobalt and selenium was found both in the diet and in the body of pregnant mares with mineral metabolism

disorders (see Tables 2.3 and 2.4).

Analysing the data we obtained, we can conclude that in pregnant mares with mineral metabolism disorders, compared to clinically healthy pregnant mares, polymicroelementosis is recorded, the main cause of which is a deficiency of manganese, zinc, cobalt and selenium, and an excess of calcium and iron in their diet.

Mineral elements play an important role in metabolic reactions in animals due to their physical and chemical properties and their inclusion in the structure of organic compound molecules, thereby ensuring their functional activity. Thus, the participation of metal cations, primarily macro- and microelements, in metabolic processes in the human and animal body is associated with the provision of enzymatic transformations of metabolites. On the other hand, the metabolism of macro- and microelements is regulated by organic components and depends on many body systems. Therefore, the next stage of our work was to study the morphological, biochemical and immunological indicators of the blood of pregnant mares.

2.3. General clinical, biochemical and immunological blood parameters of pregnant mares with mineral metabolism disorders

Blood parameters are an indicator of changes occurring in pathology, and they reflect the intensity of metabolic processes in the animal's body.

The study of general clinical, biochemical and immunological blood parameters in mares during pregnancy is important for monitoring the health of the mother and the development of the foetus.

Based on the results of general clinical, biochemical and immunological blood tests in pregnant mares with mineral metabolism disorders, we have identified changes in the indicators of haematopoiesis, protein, carbohydrate and lipid metabolism, and indicators of non-specific resistance of the body.

Thus, our results indicate that most general clinical blood parameters in mineral metabolism disorders in pregnant mares were at the lower limit of physiological values and, compared to clinically healthy pregnant mares, were characterised by a significantly lower number of leukocytes (1.12 times) erythrocytes (1.10 times) and lower haemoglobin content (1.16 times) (table 2.6).

This may be due to a deficiency of cobalt, zinc and, especially, copper in the diet and body of pregnant mares. The latter enhances the mobilisation of deposited iron in the bone marrow and ensures the transition of inorganic forms of iron into organic ones, thereby catalysing its incorporation into the haem structure and promoting the maturation of erythrocytes in the early stages of development.

Table 2.6

General clinical blood parameters of pregnant mares,

M±m, n=15

Indexes		Pregnant mares	
		Clinically healthy, n=15	Under mineral metabolism disorders, n=15
Haematocrit, %		39,0±1,00	38,0±1,00
RBC, T/l		8,40±0,15	7,74±0,08**
ESR, mm/hour		36,81±1,36	34,14±1,63
Haemoglobin, g/l		150,00±1,31	128,71±1,04***
WBC, G/l		8,78±0,12	7,84±0,08***
Leucogram, %	Basophils	0	0
	Eosinophils	6,0±0,29	6,0±0,43
	Neutrophils:		
	Young	0	0
	Stab	3,0±0,20	3,0±0,22
	Segmented	53,0±0,70	54,0±0,76
	Lymphocytes	34,0±0,52	33,0±0,70
	Monocytes	4,0±0,30	4,0±0,23

Note.

p<0,01; *p<0,001 compared to clinically healthy mares

The gestation period in mares is extremely important for the formation and development of the foetus. Although gestation is a physiological process, changes that border on pathological occur in the mare's body during this time. The mare's body mobilises to ensure normal growth and development of the foetus, preparation for foaling and subsequent lactation. Therefore, during this period, it is extremely important to monitor the biochemical indicators of the blood of a pregnant mare in order to predict the state of her health and the health of the newborn foal in the future. At the same time, the results of our research on feed and water sources showed the

following content of certain technogenic elements (lead, barium, arsenic, aluminium, nickel, strontium), which can accumulate in parenchymal organs, primarily in the liver, kidneys and pancreas, which can also affect the biochemical indicators of the blood of a pregnant mare.

In the blood serum of pregnant mares with mineral metabolism disorders, we found a significantly lower content of total protein (1.12 times) and albumin (1.12 times) (Table 2.7).

The data obtained can be explained by the use of protein as a plastic material for foetal growth and a decrease in the protein-synthesising function of the liver.

Table 2.7

Biochemical indexes of pregnant mares, M±m, n=15

Indexes	Pregnant mares	
	Clinically healthy, n=15	Under mineral metabolism disorder, n=15
Total protein, g/l	68,7±0,80	61,39±0,96***
Albumin, g/l	31,28±0,29	28,04±0,58***
Globulin, g/l	37,41±0,71	33,34±0,60***
Glucose, mmol/l	4,26±0,07	3,44±0,03***
Urea, µmol/l	7,15±0,17	7,48±0,12
Creatinine, µmol/l	108,47±1,82	103,41±1,40
Total bilirubin, µmol/l	22,51±0,40	16,66±0,44***
Triglycerides, mmol/l	0,25±0,01	0,68±0,03***
Cholesterol, µmol/l	2,26±0,03	2,84±0,07***
ALP, U/l	327,3±1,52	497,3±16,3***
ALT, U/l	12,61±0,17	17,9±0,62***
AST, U/l	312,93±2,59	364,2±9,99***
GGT, U/l	22,84±1,51	25,64±1,12
α-Amylase, U/l	23,75±0,37	22,29±0,89

Note.

***p<0,001 compared to clinically healthy mares

A 1.12-fold decrease in globulin content in the blood serum of pregnant mares with mineral metabolism disorders indicates a decrease in the immune status of these animals.

Indicative tests for assessing the state of carbohydrate and lipid metabolism in animals are the concentration of glucose, triglycerides, cholesterol and bilirubin in

blood serum.

Our results showed that in cases of mineral metabolism disorders, the concentration of glucose in the blood serum of pregnant mares was 1.24 times lower than in clinically healthy animals. Given that this indicator was at the lower limit of normal values, this may be due to a physiological decrease in blood glucose levels in mares during pregnancy [39] (see Table 2.7).

In the blood serum of pregnant mares with mineral metabolism disorders, compared to clinically healthy pregnant mares, the triglyceride content was found to be 2.75 times higher and the cholesterol content 1.27 times higher. This may be associated with hypothyroidism in animals with mineral metabolism disorders, caused by an excess of calcium in the diet and in the body of pregnant mares, which is known to be an antagonist of iodine. Thus, experiments on horses have shown that with artificially induced hypothyroidism, the concentration of total cholesterol and triglycerides in the blood of animals increased over a period of 4 weeks [66].

The total bilirubin content in the blood serum of pregnant mares with mineral metabolism disorders was 1.35 times lower than in clinically healthy animals. However, this indicator was within physiological limits. It should be noted that the bilirubin content in the blood serum of horses is a highly variable indicator, which changes under the influence of a number of factors, including the physiological state of the animals [41].

High ALP activity during pregnancy in females can be explained by the increased activity of its placental isoform, which is produced by the microvilli of trophoblast cells. Therefore, some researchers [41, 291] regard LF activity indicators as a test for assessing the condition of the placenta during pregnancy in females. However, when studying animals with mineral metabolism disorders, we found a significantly higher LF activity (1.16 times) compared to clinically healthy animals, which is probably associated with metabolic disorders in bone tissue as a result of metabolic disorders [151, 213].

The 1.42 times higher activity of ALT and 1.16 times higher activity of AST in the blood serum of pregnant mares with mineral metabolism disorders compared to

clinically healthy pregnant mares indicates the destruction of hepatocyte membranes, as well as kidney and heart cells in this pathology.

During the study of serum protein fractions in pregnant mares with mineral metabolism disorders compared to clinically healthy animals, a significantly lower A/G ratio was found, which may indicate a decrease in the protein-synthesising function of the liver.

A significant decrease in the content of γ -globulins in the blood serum of pregnant mares (1.17 times) indicates a decrease in the immune status of their organism in the pathology of mineral metabolism (table 2.8).

The results obtained indicate an increase in the intensity of metabolic processes in mare tissues during pregnancy, as well as the use of a significant portion of nutrients to meet the needs of the foetus when there is a deficiency of minerals in the pregnant mare's body.

During the foaling period, the average level of immunoglobulins in mare colostrum is approximately 2.5 times higher than the content of immunoglobulins in her blood serum. Thus, literature data indicate that in the last months of mare pregnancy, selective delivery of immunoglobulins from the circulatory system to the mammary gland occurs (part of type A immunoglobulins (IgA) can be produced in the mammary gland itself). This selective delivery of immunoglobulins occurs under the influence of the mare's hormonal level, which characterises the final stage of foetal development. The level of oestrogen plays a significant role in these processes [92].

Table 2.8

Protein fraction content in the blood serum of pregnant mares, $M \pm m$, $n=15$

Indexes	Pregnant mares	
	Clinically healthy, $n=15$	Under mineral metabolism disorder, $n=15$
Albumin, %	47,76 \pm 0,47	45,57 \pm 0,53
Globulin, %	52,19 \pm 0,48	54,43 \pm 0,53
α 1- globulin, %	4,14 \pm 0,08	5,21 \pm 0,15***
α 2- globulin, %	12,05 \pm 0,11	12,64 \pm 0,20
β - globulin, %	14,76 \pm 0,18	18,29 \pm 0,53***
γ - globulin, %	21,43 \pm 0,31	18,29 \pm 0,35***
A/G ratio	0,92 \pm 0,02	0,84 \pm 0,02**

Note. ** $p < 0,01$, *** $p < 0,001$ compared to clinically healthy mares

The immune system is one of the main homeostatic systems of the body, which determines the degree of health of animals and the adaptive capabilities of their bodies. It is an indicator of ecological well-being and is very sensitive to changes in the environment [42, 75, 76, 89, 115, 123].

In modern veterinary medicine, particular importance is attached to the search for new approaches to the diagnosis of immune status disorders in animals. Interest in the problem of the immune status of animals is due to the fact that various pathologies are, to one degree or another, the cause or consequence of immunological disorders that contribute to the transition of major diseases into a chronic form or lead to their complications [146, 148, 157, 158].

The study of the immune status of horses in breeding is particularly relevant. This is due to the fact that these animals are valuable, have a delicate nervous system and are very sensitive to various environmental factors that are stressful for them. All this leads to a decrease in the immune status of horses and their susceptibility to diseases [42, 21, 89, 115, 147].

At the same time, the formation of the immune status of a foal begins long before the end of the mare's pregnancy. During the mare's pregnancy, the foal's immune system develops quite rapidly and is fully formed by the 8th month of pregnancy. However, the active growth and development of the foal's immune system begins precisely in the 8th month of the mare's pregnancy. At the same time, the foal's immune system remains unstimulated until the mare foals [19, 149].

At the beginning of the perinatal period, the mare's resources are mobilised to ensure normal foetal growth, preparation for foaling and lactation. Non-specific changes in immune responses and proliferation of T and B lymphocytes occur in the mare's body. This is associated with increased haemocytopoiesis activity. The proliferation of B lymphocytes is particularly enhanced to increase immunoglobulin synthesis [26, 143].

In view of the above, we studied blood parameters that characterise the immunocompetent state of the mare's body in the last third of gestation, as well as in cases of mineral metabolism pathology.

It has been established that in pregnant mares with mineral metabolism disorders, compared to clinically healthy pregnant mares, blood immunological indicators are characterised by a significantly lower number of T-helpers (1.25 times), PK cells (1.18 times) and B lymphocytes (1.14 times), as well as a significantly higher number of T suppressors (1.13 times) and O lymphocytes (1.14 times) (Table 2.8).

The study of phagocytosis indicators is important for assessing the state of the immune system of animals and predicting the development of an infectious inflammatory process. Phagocytosis is the main mechanism for eliminating immune complexes from the body. Therefore, its effectiveness is closely related to the activity of the complement system, the concentration of Ig-G and other opsonising factors. The indicators of complete phagocytosis, which give an idea of the activation of the biocidal activity of neutrophils in the blood of pregnant mares with mineral metabolism disorders compared to clinically healthy pregnant mares, were characterised by a significantly lower percentage of NST-spontaneous (1.15 times), NST-induced (1.11 times) and NST-reserve (1.10 times) (table 2.9).

Table 2.9

Immunological blood indexes of pregnant mares,

M±m, n=15

Indexes	Pregnant mares	
	Clinically healthy, n=15	Under mineral metabolism disorder, n=15
T-lymphocytes, CD3, %	40,43±2,30	38,70±0,47
T-helpers, CD4, %	22,72±0,21	18,0±0,35***
T-suppressors, CD8, %	17,71±0,22	20,7±0,25***
PC-cells, CD16, %	13,86±0,19	11,79±0,21***
B-lymphocytes, CD22, %	8,19±0,18	7,21±0,19**
O-lymphocytes, %	37,52±0,39	42,93±0,53***
HST-spontaneous, %	13,00±0,21	11,43±0,20***
HST-induced, %	48,43±0,79	43,79±0,69***
HST-reserve, %	35,43±0,81	32,36±0,73**
RBLT-spontaneous, %	7,67±0,16	4,43±0,14***
RBLT-induced, %	31,52±0,65	21,00±0,51***
CIC, Units opt. density	40,48±0,66	52,49±1,22***

Note **p<0,01,***p<0,001 compared to clinically healthy mares

The lymphocyte blast transformation reaction (LBRT) laboratory test allows the functional activity of the entire lymphocyte pool to be assessed. The ability of lymphocytes to form blasts in the blood of pregnant mares with mineral metabolism disorders was significantly lower than in clinically healthy animals. Thus, the BLTR index for spontaneous transformation in cases of mineral metabolism disorders in pregnant mares was 1.73 times lower, and the BLTR index for induced transformation was 1.50 times lower (see Table 2.9).

In cases of mineral metabolism disorders in pregnant mares, an increase in the CIC index (1.30 times) was observed compared to clinically healthy animals (see Table 3.8). This may indicate a decrease in the activity of the reticuloendothelial system in pregnant mares with mineral metabolism disorders, which is responsible for the removal of circulating immune complexes from the body and the accumulation of the antigen-antibody-complement complex, which can settle in tissues and on the surface of the vascular wall, causing disturbances due to the activation of the complement system.

Thus, the results of morphological, biochemical and immunological studies of the blood of mares in the 8th month of pregnancy allow us to conclude that mineral metabolism disorders in these animals cause changes in metabolism and non-specific resistance, which can affect the mare's body, foetal development and the quality of offspring. This is further confirmation of the need to develop and apply effective means of treatment and prevention of mineral metabolism disorders in pregnant mares.

3. TREATMENT AND PREVENTION OF MINERAL METABOLISM DISORDERS IN THE BODIES OF MARE AND FOALS

The results we obtained regarding the physiological state of pregnant mares, data from clinical examinations of the animal population, morphological, biochemical and immunological studies of their blood, taking into account the mineral content of pregnant mares and the state of metabolic disorders in their bodies, have allowed us to develop a new domestic preparation, Lactahos, which contains lactate compounds of essential microelements (zinc, manganese, copper), as well as starch iodine, triethanolamine salt of selenic acid, the organosilicon immunomodulator Mival and Opoka.

During the development and application of Lactahos to pregnant mares, the results of studies of soils, feed and water sources, the physiological need of mares for certain elements, the compatibility of the elements in the composition of the drug, and the biological synergy or antagonism of their action in metabolic processes in the body of animals were also taken into account.

The effectiveness of Lactahos in cases of mineral metabolism disorders in pregnant mares was studied in comparison with the indicators of pregnant mares with the same pathology who received the basic diet, as well as the basic diet with the addition of the KM L2 premix produced by Kremiks LLC (Poltava region).

3.1. Clinical condition of the body and content of macro- and microelements in the blood serum of pregnant mares when using the drug "Lactakhos"

The clinical condition of pregnant mares in the control and first experimental groups on the 21st day of the experiment did not differ significantly from the clinical condition of the animals at the beginning of the experiment. Body temperature, heart rate and respiratory rate in pregnant mares in the control and first experimental groups were within physiological limits.

No significant changes in the coat and skin were observed in the mares of the control group compared to the beginning of the experiment.

In the mares of the first experimental group, a slight improvement in the

condition of the coat and skin was noted, namely a reduction in skin flakes and the beginning of moulting, but the hair on the tail, torso and mane remained dull.

At the same time, in pregnant mares of the second experimental group, which were given Lactahos, unlike the animals of the control and first experimental groups, some improvement in clinical indicators was observed on the 21st day of the experiment. Namely, in animals of this group, the hair was better retained in the skin, evenly and densely covering the skin, tightly adhering to it, the hair on the torso, mane and tail had a shiny appearance, and there were significantly fewer flakes on the skin compared to the beginning of the experiment. In 80% of pregnant mares in the second experimental group, moulting was complete.

On the 42nd day of the experiment, the body temperature, heart rate and respiratory rate of the mares in the control and both experimental groups were within physiological limits, with no clinical signs of acute or chronic diseases.

In 100% of mares in the second and 80% of mares in the first experimental groups, on the 42nd day of the experiment, the completion of moulting was established, no scales were found on the skin, the hair was well attached to the skin, evenly and densely covering the skin, tightly adhering to it, and the hair on the torso, mane and tail had a shiny appearance. In all mares of the first and second experimental groups, there were no cases of coprophagia or licking of foreign objects.

In addition, the pregnant mares in the second experimental group showed regrowth of new hoof horn, which had a smooth and shiny surface, which was not observed in animals from other groups.

In pregnant mares of the control group, on the 42nd day of the experiment, a delay in moulting and the presence of scales on the skin were recorded. The hair on the body, mane and tail was dull. The hoof horn was dry, uneven, dull, and in some animals cracked. These animals exhibited coprophagia and continued to lick the walls and floor.

Thus, the results of clinical studies indicate that the use of Lactahos in pregnant mares with mineral metabolism disorders produces positive results as early as on the 21st day. On the 42nd day of using Lactahos in pregnant mares, the clinical signs of mineral metabolism disorders disappeared. However, when using the KM L2 premix,

the recovery of certain clinical indicators in pregnant mares with mineral metabolism disorders is somewhat slower. Our data indicate a faster and more effective effect of Lactahos components on the restoration of clinical indicators in pregnant mares with mineral metabolism disorders in their bodies.

Changes in the clinical condition of pregnant mares during the course of the study were confirmed by the study of the content of macro- and microelements in their blood, which we determined at all stages of the experiment.

Determining the levels of macro- and microelements in the blood serum of pregnant mares allowed us to establish the main trends in the effect of the agents we used on the state of mineral metabolism and the patterns of mineral accumulation in the mares' bodies during pregnancy.

In the blood serum of pregnant mares in the control group, which received only the basic diet, changes in the content of certain microelements were established on the 21st day of the experiment, which, compared to the beginning of the experiment, were characterised by a significantly higher content of manganese (1.41 times) and lower levels of iron (1.15 times), zinc (1.23 times), cobalt (1.33 times) and selenium (2.26 times) (Table 2.9).

Our data indicate a deepening of the processes of macro- and microelement metabolism disorders in the body of pregnant mares with an increase in the gestation period in the absence of additional mineral supplements to the basic diet or the administration of mineral preparations to animals.

On the other hand, when using the KM L2 premix, a significantly higher content of magnesium (1.39 times), manganese (2.12 times) and cobalt (2.30 times), lower levels of zinc (1.16 times) and selenium (1.49 times), and compared to pregnant mares in the control group, a significantly higher content of magnesium (1.33 times), manganese (1.50 times), iron (1.17 times), copper (1.20 times), cobalt (3.07 times) and selenium (1.52 times) (see Table 3.1).

The content of macro- and microelements in the blood serum of pregnant mares on the 21st day of the experiment, $M \pm m$, $n=5$

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OR	First experimental group, OP+ Premix KM L2	Second experimental group, OP+ Laktakhos
Common calcium, mmol/l	3,27±0,04	3,35±0,10	3,34±0,07	3,20±0,07
Non-organic phosphorus, mmol/l	1,01±0,04	1,08±0,06	1,12±0,06	1,12±0,04
Ca:P ratio	3,30 : 1	3,12 : 1	2,98 : 1	2,86 : 1
Potassium, mmol/l	4,00±0,12	3,88±0,10	3,84±0,12	3,60±0,13
Sodium, mmol/l	141,2±1,06	139,9±5,43	135,6±4,80	140,2±5,48
Chlorine, mmol/l	102,9±0,58	97,95±5,35	99,22±5,54	101,5±4,42
Magnesium, mmol/l	0,66±0,01	0,69±0,03	0,92±0,02 ^{***,♦♦♦}	1,35±0,05 ^{***,ΔΔΔ,♦♦♦}
Manganese, μmol/l	0,17±0,01	0,24±0,008 ^{♦♦♦}	0,36±0,01 ^{***,♦♦♦}	0,52±0,03 ^{***,ΔΔΔ,♦♦♦}
Iron, μmol/l	31,03±1,30	26,90±1,11 [♦]	31,52±1,65 [*]	25,24±1,86 ^{Δ,♦}
Copper, μmol/l	16,11±1,30	15,78±0,50	18,86±0,43 ^{***}	20,74±1,03 ^{***,♦}
Zinc, μmol/l	12,88±0,10	10,48±0,50 ^{♦♦♦}	11,10±0,49 ^{♦♦}	22,98±1,41 ^{***,ΔΔΔ,♦♦♦}
Cobalt, μmol/l	0,20±0,01	0,15±0,012 ^{♦♦}	0,46±0,017 ^{***,♦♦♦}	0,41±0,018 ^{***,♦♦♦}
Selenium, μmol/l	0,52±0,014	0,23±0,012 ^{♦♦♦}	0,35±0,016 ^{***,♦♦♦}	1,27±0,017 ^{***,ΔΔΔ,♦♦♦}

Note:

- ♦ - $p < 0,05$, ♦♦ - $p < 0,01$, ♦♦♦ - $p < 0,001$ compared to beginning of experiment
- * - $p < 0,05$, ** - $p < 0,01$, *** - $p < 0,001$ compared to control group
- Δ - $p < 0,05$, ΔΔ - $p < 0,01$, ΔΔΔ - $p < 0,001$ compared to first experimental group

The results obtained indicate, on the one hand, a significant positive effect of the KM L2 premix on mineral metabolism indicators in pregnant mares, while on the other hand, its compensatory effect is insufficient in relation to certain microelements, such as zinc and selenium.

In the blood serum of mares in the second experimental group, which received the Lactahos preparation in addition to their basic diet, on the 21st day of the experiment, compared to its beginning, a significantly higher content of magnesium

(1.96 times), manganese (2.17 times), copper (1.31 times), zinc (2.19 times), cobalt (3.04 times) and selenium (5.52 times), and compared to the mares of the first experimental group, a significantly higher content of magnesium (1.47 times), manganese (1.44 times), zinc (2.07 times), selenium (3.63 times) and lower iron content (1.25 times) (see Table 3.1.).

Thus, the results of the studies indicate significant changes in the content of macro- and microelements in the blood serum of pregnant mares on the 21st day of the experiment. However, the data obtained are not sufficiently informative given the short duration of the experiment, during which it is difficult to achieve stable normalisation of mineral metabolism indicators. In addition, the mineral requirements of pregnant mares increase significantly with the duration of pregnancy, which is explained by their necessity for ensuring the growth and development of the foetus. Therefore, the results regarding the content of macro- and microelements in the blood serum of pregnant mares on the 42nd day of the study are more objective and reliable.

In the blood serum of pregnant mares in the control group on the 42nd day of the experiment, compared to its beginning, a trend similar to the previous stage of research (21st day) was observed in the content of certain macro- and microelements, which was characterised by a significantly higher content of magnesium (1.17 times), manganese (2.41 times), zinc (1.54 times) and lower iron (1.16 times) and selenium (2.36 times) content (Table 3.2).

Table 3.2

Content of macro- and microelements in the blood serum of pregnant mares on the 42nd day of the experiment, $M \pm m$, $n=5$

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group, OP+ Laktakhos
Common calcium, mmol/l	3,27±0,04	3,25±0,06	3,28±0,06	2,51±0,10***, $\Delta\Delta\Delta$, $\blacklozenge\blacklozenge\blacklozenge$
Non-organic phosphorus, mmol/l	1,01±0,04	1,04±0,06	1,06±0,05	1,22±0,07*
Ca:P ratio	3,30 : 1	3,16 : 1	3,13 : 1	2,08 : 1
Potassium, mmol/l	4,00±0,09	4,10±0,11	4,26±0,10	4,12±0,06
Sodium, mmol/l	141,2±1,06	139,7±1,50	139,0±2,25	138,0±3,64

Continuation of table 3.2

Chlorine, mmol/l	102,9±0,58	99,28±2,07	99,84±3,08	102,0±1,33
Magnesium, mmol/l	0,66±0,01	0,77±0,02 ^{***}	0,92±0,02 ^{***,♦♦}	1,34±0,06 ^{***,ΔΔΔ,♦♦}
Manganese, μmol/l	0,17±0,01	0,41±0,02 ^{***}	0,82±0,03 ^{***,♦♦}	1,01±0,05 ^{ΔΔ,***,♦♦}
Iron, μmol/l	31,03±1,30	26,78±0,67 [*]	26,101±1,18 [*]	25,34±1,50 [*]
Copper, μmol/l	16,11±1,30	16,33±0,40	16,807±0,90	20,14±0,70 ^{***,Δ,♦}
Zinc, μmol/l	12,88±0,1	8,34±0,48 ^{***}	13,89±0,27 ^{***,♦}	22,27±1,10 ^{***,ΔΔΔ,♦♦}
Cobalt, μmol/l	0,20±0,01	0,23±0,013	0,48±0,029 ^{***,♦♦}	0,70±0,024 ^{***,ΔΔΔ,♦♦}
Selenium, μmol/l	0,52±0,014	0,22±0,006 ^{***}	0,32±0,016 ^{***,♦♦}	1,34±0,031 ^{***,ΔΔΔ,♦♦}

Note:

1. ♦ -p<0,05, ♦♦ -p<0,01, ♦♦♦ -p<0,001 compared to beginning of experiment
2. * -p<0,05, ** -p<0,01, *** -p<0,001 compared to control group
3. Δ -p<0,05, ΔΔ -p<0,01, ΔΔΔ -p<0,001 compared to first experimental group

The results obtained indicate a further deepening of mineral metabolism pathology in mares with an increase in the duration of pregnancy. Thus, during this period, a significant part of the foetal tissues (about 65%) is formed, and a significant amount of minerals is used to build its organs and tissues.

In the blood serum of pregnant mares in the first experimental group, which were given the KM L2 premix, compared to the control group, on the 42nd day of the experiment, significantly higher levels of magnesium (1.20 times), manganese (2.0 times), zinc (1.66 times), cobalt (2.04 times) and selenium (1.47 times), and compared to the beginning of the experiment, higher levels of magnesium (1.39 times), manganese (4.85 times), zinc (1.08 times), cobalt (2.38 times) and lower iron (1.19 times) and selenium (1.63 times) (see Table 3.2.).

At the same time, the selenium content in the blood serum of pregnant mares in the first experimental group was almost 3.0 times lower than the normative values. This may indicate an insufficient supply of selenium to pregnant mares during the use of the KM L2 premix. Given the importance of selenium in ensuring peroxidation processes, it can be assumed that its deficiency will lead to the accumulation of peroxide oxidation products in the body of a pregnant mare, which will negatively affect the health of the mare and the development of the foetus.

In the blood serum of broodmares in the second experimental group, which were given Lactakhos, an optimal calcium-phosphorus ratio for their physiological state was established, which was not observed in broodmares in the control and first

experimental (premix 'KM L2') groups, in which this indicator was slightly elevated. This could have been due to better absorption of phytin phosphorus under the influence of the Lactakhos drug.

In addition to the above, the blood serum of pregnant mares in the second experimental group, compared to pregnant mares in the control group, showed a significantly higher content of magnesium (1.74 times), manganese (2.46 times), copper (1.23 times), zinc (2.67 times), cobalt (2.99 times), selenium (6.12 times) and a lower content of calcium (1.29 times), and compared to the pregnant mares of the first experimental group, a significantly higher content of magnesium (1.45 times), manganese (1.23 times), copper (1.20 times), zinc (1.60 times), cobalt (1.47 times), selenium (4.18 times) and lower calcium content (1.31 times).

Compared to the data at the beginning of the experiment, the mineral metabolism indicators in the blood serum of pregnant mares in the second experimental group on day 42 were characterised by a significantly higher content of phosphorus (1.21 times), magnesium (2.02 times), manganese (5.96 times), copper (1.25 times), zinc (1.73 times), cobalt (3.48 times), selenium (2.58 times) and lower calcium (1.30 times) and iron (1.22 times) (see Table 3.2.).

The better mineral content indicators in the blood serum of pregnant mares in the second experimental group are due to the action of the components of the Lactakhos preparation. Thus, the lactate compounds of trace elements included in this preparation are absorbed by 80–100%. Therefore, the concentration of macro- and microelements in the blood serum of pregnant mares during the use of the Lactakhos preparation significantly increased already on the 21st day of the experiment. In contrast, well-known mineral supplements for horses contain mixtures of inorganic salts of macro- and microelements together with a filler. They are traditionally used for horses with a lack of macro- or microelements in their diet. The pharmacological action of such supplements is aimed at ensuring the daily requirement of horses for minerals, normalising metabolic processes, improving the metabolism of proteins, lipids and carbohydrates, activating redox processes and stimulating the body's defences.

The disadvantage of such supplements is the insufficient balance of their mineral compound structure, in the form in which they are introduced into the horse's body with feed, especially given the mineral content of the diet, the daily requirement for them and the physiological state of the animal. In addition, inorganic salts of biogenic elements in such supplements are absorbed by the body by 20-30%, while organic compounds of these elements are absorbed by 80-100%, and become toxic during long-term storage.

Therefore, the next stage of the work was to study the morphological, biochemical and immunological indicators of the blood of pregnant mares under the conditions of using the drug 'Lactachos' and the premix 'KM L2'.

3.2. General clinical, biochemical and immunological blood parameters of pregnant mares when using the drug "Lactakhos"

The results of the studies indicate changes in certain general clinical blood parameters of pregnant mares as early as on the 21st day of administration of the KM L2 premix and Lactahos.

Thus, during the administration of the KM L2 premix to pregnant mares on the 21st day of the experiment, compared to its beginning, a significant decrease in the number of leukocytes (1.12 times) was established, and compared to the control group of pregnant mares, a significant increase in haemoglobin concentration (1.10 times) (Table 3.3).

Table 3.3

General clinical blood parameters of pregnant mares on the 21st day of the experiment, $M \pm m$, $n=5$

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group, OP+Lactakhos
Haematocrit, l/l	0,38±0,01	0,40±0,01	0,39±0,01	0,39±0,01
RBC, T/l	7,74±0,08	7,9±0,15	7,6±0,24	8,2±0,19*
ESR, mm/hour	34,14±1,6	26,5±3,23	32,2±2,65	32,0±2,70
Haemoglobin, g/l	128,7±1,4	117,0±2,08***	128,2±2,07***	133,6±2,21***, Δ , $\Delta\Delta$, $\Delta\Delta\Delta$
WBC, G/l	7,84±0,1	7,1±0,28**	7,0±0,23**	7,8±0,25 Δ

Continuation of table 3.3

Leucogram, %	Basophils	0	0	0	0
	Eosinophils	6,0±0,43	5,0±0,85	5,0±0,45	5,0±0,60
	Neutrophils:				
	Young	0	0	0	0
	Stab	3,0±0,22	3,0±0,29	3,0±0,32	3,0±0,20
	Segmented	54,0±0,76	55,0±1,22	54,0±1,03	55,0±1,17
	Lymphocytes	35,0±0,7	33,0±1,04	33,0±0,93	33,0±0,80
Monocytes	5,0±0,23	4,0±0,48	5,0±0,73	4,0±0,51	

Note:

1. \diamond - $p < 0,05$, $\diamond\diamond$ - $p < 0,01$, $\diamond\diamond\diamond$ - $p < 0,001$ compared to beginning of experiment
2. * - $p < 0,05$, ** - $p < 0,01$, *** - $p < 0,001$ compared to control group
3. Δ - $p < 0,05$, $\Delta\Delta$ - $p < 0,01$, $\Delta\Delta\Delta$ - $p < 0,001$ compared to first experimental group

‘Lactakhos’, on the 21st day of the experiment, compared to its beginning, a significantly higher concentration of haemoglobin (1.04 times) and a greater number of erythrocytes (1.06 times) were found; compared to the pregnant mares in the control group, there was a significantly higher haemoglobin content (1.14 times), and compared to the pregnant mares in the first experimental group, there was a significantly higher haemoglobin content (1.04 times) and a higher number of leukocytes (1.11 times) (see Table 3.3).

On the 21st day of the experiment, some changes were also found in the blood of pregnant mares in the control group, which, compared to the beginning of the experiment, were characterised by a significantly lower haemoglobin concentration (1.10 times) and a lower number of leukocytes (1.10 times) (see Table 3.3).

Thus, the results of general clinical blood tests of pregnant mares indicate insignificant changes in indicators between the control and experimental groups of animals on the 21st day of the experiment, which may indicate the existence of powerful compensatory mechanisms in the mare's body that maintain blood homeostasis during pregnancy.

The general clinical blood parameters of pregnant mares in the control group on the 42nd day of the experiment, compared to its beginning, were characterised by a lower haemoglobin concentration (1.12 times), a lower number of leukocytes (1.10 times), a lower relative number of lymphocytes (1.18 times) and a higher number of segmented neutrophils (1.08 times) (Table 3.4).

Our data indicate that as the gestation period of mares increases, mineral metabolism disorders in their bodies intensify, and even compensatory mechanisms are unable to maintain blood homeostasis in animals at a stable level.

The general clinical blood parameters of pregnant mares in the first experimental group on the 42nd day of the experiment, compared to its beginning, were characterised by a significantly lower number of leukocytes (1.09 times), lymphocytes (1.15 times) and a higher number of segmented neutrophils (1.08 times). Compared to the pregnant mares of the control group, the general clinical blood parameters of the mares of the first experimental group on the 42nd day of the experiment did not differ significantly (Table 3.4).

Table 3.4

General clinical blood parameters of pregnant mares on the 42nd day of the experiment, M±m, n=5

Indexes		Pregnant mares			
		Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group OP+Laktakhos
Haematocrit, %		0,38±0,01	0,38±0,01	0,39±0,01	0,38±0,02
RBC, T/l		7,74±0,08	7,6±0,09	7,7±0,12	8,1±0,17*
ESR, mm/hour		34,14±1,63	32,0±3,34	33,2±2,54	32,4±1,44
Haemoglobin, g/l		128,7±1,04	115,0±4,49 [♦]	124,6±3,60	132,8±2,31**
WBC, G/l		7,84±0,08	7,1±0,13 ^{♦♦♦}	7,2±0,10 ^{♦♦♦}	7,9±0,25 ^{**} , ^Δ
Leucogram, %	Basophils	0	0	0	0
	Eosinophils	6,0±0,43	6,0±0,87	5,0±0,71	4,0±0,49
	Neutrophils:				
	Young		0	0	0
	Stab	3,0±0,22	4,0±0,29	4,0±0,24	3,0±0,32
	Segmented	54,0±0,76	58,0±1,22 ^{♦♦}	58,0±1,24 [♦]	55,0±1,12
	Lymphocytes	33,0±0,70	28,0±1,11 ^{♦♦♦}	28,0±0,75 ^{♦♦♦}	33,0±0,84 ^{**} , ^{ΔΔ}
Monocytes	4,0±0,23	4,0±0,48	5,0±0,37	4,0±0,40	

Note:

1. [♦] -p<0,05, ^{♦♦} -p<0,01, ^{♦♦♦} -p<0,001 compared with beginning of experiment
2. * -p<0,05, ** -p<0,01, *** -p<0,001 compared with control group
3. ^Δ -p<0,05, ^{ΔΔ} -p<0,01, ^{ΔΔΔ} -p<0,001 compared with first experimental group

Almost all general clinical blood parameters of pregnant mares in the second

experimental group, which were given Lactahos, were within the optimal normal range on the 42nd day of the experiment and showed no significant differences compared to the beginning of the experiment.

However, the general clinical blood parameters of pregnant mares in the second experimental group, compared with the animals in the control group, were characterised by a significantly higher number of erythrocytes (1.10 times), leukocytes (1.11 times) and lymphocytes (1.19 times) and a higher haemoglobin content (1.15 times), and compared to the animals of the first experimental group, they had a significantly higher number of leukocytes (1.11 times) and a higher number of lymphocytes (1.16 times) (see Table 3.4).

Thus, the results of general clinical studies of the blood of pregnant mares indicate a positive effect of the drug 'Lactakhos' on the processes of haematopoiesis.

During the study of biochemical indicators of blood serum in pregnant mares of the control group on the 21st day of the experiment, compared to its beginning, a significantly lower content of globulins (1.12 times), cholesterol (1.42 times), higher glucose content (1.34 times), lower ALP activity (1.24 times), AsAT (1.23 times) and α -amylase (1.24 times) (Table 3.5).

In the blood serum of animals in the first experimental group on the 21st day of the experiment, compared to its beginning, the content of glucose (1.42 times) and albumin (1.07 times) was significantly higher, the content of globulins (1.11 times), creatinine (1.09 times), cholesterol (1.46 times), lower activity of ALP (1.35 times), AST (1.25 times) and GGT (1.43 times). Compared to the pregnant mares in the control group, the biochemical parameters of the blood serum of the mares in the first experimental group on the 21st day of the experiment did not show any significant differences (see Table 3.5).

On the 21st day of the experiment, the blood serum of pregnant mares in the second experimental group showed a significantly higher content of glucose (1.47 times) and albumin (1.08 times), lower cholesterol (1.24 times), lower activity of ALP (1.41 times), AST (1.36 times), GGT (1.54 times) and α -amylase (1.38 times).

Biochemical blood parameters of pregnant mares on the 21st day of the experiment, M±m, n=5

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
Glucose, mmol/l	3,44±0,03	4,60±0,16 ^{***}	4,90±0,29 ^{***}	5,04±0,20 ^{***}
Total protein, g/l	61,39±0,96	58,1±1,60	60,12±0,78	62,08±1,29
Albumin, g/l	28,04±0,58	28,3±0,89	30,06±0,40 [*]	30,78±0,87 [*]
Globulin, g/l	33,34±0,60	29,9±0,73 ^{**}	30,06±0,82 ^{**}	31,30±0,72
Urea, µmol/l	7,48±0,12	7,0±0,53	7,42±0,53	7,94±0,36
Creatinine, µmol/l	103,4±1,40	96,0±4,08	95,02±3,43 [*]	101,9±5,23
Total bilirubin, µmol/l	16,66±0,44	17,7±0,75	16,34±1,31	19,14±1,09
Triglycerides, mmol/l	0,68±0,03	0,6±0,05	0,59±0,04	0,69±0,05
Cholesterol, µmol/l	2,84±0,07	2,0±0,14 ^{***}	1,95±0,02 ^{***}	2,29±0,05 ^{ΔΔ,***}
ALP, U/l	497,3±16,3	399,8±29,60 [*]	367,9±25,44 ^{***}	351,8±17,19 ^{***}
ALT, U/l	17,9±0,62	22,3±2,06	21,82±1,90	16,68±0,59 ^{*,Δ}
AST, U/l	364,2±9,99	295,8±11,2 ^{***}	290,2±10,3 ^{***}	268,3±12,1 ^{***}
GGT, U/l	25,64±1,12	21,3±2,50	17,88±0,61 ^{***}	16,66±0,72 ^{***}
α-Amylase, U/l	22,29±0,89	18,0±2,55 ^{**}	23,36±5,47	16,20±1,41 ^{***}

Примітки:

1. ^{*} -p<0,05, ^{**} - p<0,01, ^{***} -p<0,001 compared with beginning of experiment
2. ^{*} -p<0,05, ^{**} - p<0,01, ^{***} -p<0,001 compared with control group
3. ^Δ -p<0,05, ^{ΔΔ} -p<0,01, ^{ΔΔΔ} -p<0,001 compared with first experimental group

Compared to mares in the control group, on the 21st day of the experiment, significantly higher ALT activity (1.34 times) was found in the blood serum of these animals, and compared to the mares in the first experimental group, higher ALT activity (1.31 times) and higher cholesterol content (1.17 times) (see Table 3.5).

On the 42nd day of the experiment, the biochemical parameters of the blood serum of pregnant mares in the control group, compared with the beginning of the experiment, were characterised by a significantly higher glucose content (1.25 times), lower total protein content (1.05 times), globulins (1.14 times), cholesterol (1.42 times) and lower activity of ALP (1.55 times), AST (1.37 times) and GGT (1.63 times) (Table 3.6).

Table 3.6.

**Biochemical indexes of blood pregnant mares on 42nd day of experiment, M±m,
n=5**

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OI	First experimental Group, OP+ Premix KM L2	Beginning of experiment
Glucose, mmol/l	3,44±0,03	4,30±0,11 ^{♦♦♦}	4,38±0,15 ^{♦♦♦}	4,26±0,12 ^{♦♦♦}
Total protein, g/l	61,39±0,96	58,4±0,31 ^{♦♦}	58,88±0,49 [♦]	64,60±0,24 ^{***, ΔΔΔ, ♦♦}
Albumin, g/l	28,04±0,58	29,1±0,64	30,38±0,69 [♦]	36,24±0,57 ^{***, ΔΔΔ, ♦♦}
Globulin, g/l	33,34±0,60	29,3±0,52 ^{♦♦♦}	28,50±0,67 ^{♦♦♦}	28,36±0,72 ^{♦♦♦}
Urea, μmol/l	7,48±0,12	7,1±0,27	7,48±0,62	7,28±0,17
Creatinine, μmol/l	103,41±1,40	103,8±4,85	116,68±3,75 ^{♦♦}	108,68±3,24
Total bilirubin, μmol/l	16,66±0,44	19,7±2,45	19,84±1,30 [♦]	21,54±2,00 [♦]
Triglycerides, mmol/l	0,68±0,03	0,60±0,06	0,72±0,02	0,74±0,02
Cholesterol, μmol/l	2,84±0,07	2,0±0,09 ^{♦♦♦}	2,35±0,11 ^{*, ♦♦}	2,68±0,14 ^{**}
ALP, U/l	497,3±16,3	320,7±19,23 ^{♦♦♦}	321,96±8,98 ^{♦♦♦}	313,28±17,5 ^{♦♦♦}
ALT, U/l	17,9±0,62	20,1±2,37	18,10±0,82	18,48±1,11
AST, U/l	364,2±10,0	266,5±15,7 ^{♦♦♦}	258,3±16,9 ^{♦♦♦}	264,8±11,5 ^{♦♦♦}
GGT, U/l	25,64±1,12	15,7±0,53 ^{♦♦♦}	14,32±0,32 ^{♦♦♦}	15,42±0,94 ^{♦♦♦}
α-Amylase, U/l	22,29±0,89	20,4±1,43	25,86±2,57	19,28±2,43

Notes:

1. ♦ -p<0,05, ♦♦ - p<0,01, ♦♦♦ -p<0,001 compared with beginning of experiment
2. * -p<0,05, ** - p<0,01, *** -p<0,001 compared with control group
3. Δ -p<0,05, ΔΔ -p<0,01, ΔΔΔ -p<0,001 compared with first experimental group

Biochemical indicators of blood serum of pregnant mares in the first experimental group on the 42nd day of the experiment, compared with its beginning, were characterised by a significantly higher content of glucose (1.27 times), albumin (1.08 times), creatinine (1.13 times), bilirubin (1.19 times) and lower levels of total protein (1.04 times), globulins (1.17 times), cholesterol (1.21 times) and lower activity of LF (1.54 times), AST (1.41 times), GGT (1.66 times), and compared to the control group, a significantly higher cholesterol content (1.18 times) (see Table 3.6).

In the blood serum of animals in the second experimental group on the 42nd day of the experiment, compared to its beginning, a significantly higher content of glucose (1.24 times), total protein (1.05 times), albumin (1.29 times), bilirubin (1.29 times), as well as lower globulin content (1.18 times), lower LF activity (1.59 times), AST (1.38 times), GGT (1.66 times), and compared to the control group animals, a significantly

higher content of total protein (1.11 times), albumin (1.25 times) and cholesterol (1.34 times). At the same time, the biochemical parameters of the blood serum of pregnant mares in the second experimental group, compared with those in the first experimental group, were characterised by higher levels of total protein (1.10 times) and albumin (1.19 times) (see Table 3.6).

A significant decrease in serum cholesterol levels in pregnant mares of the control and first experimental groups, which were already in the 10th month of pregnancy on the 42nd day of the study, is noteworthy. This may be due to the fact that cholesterol is a precursor of progesterone, which in the late stages of pregnancy is produced by the placenta 30–40 times more than by the corpus luteum. It should be noted that the placenta cannot synthesise cholesterol on its own and must obtain it from the mother's body [61], which leads to a decrease in cholesterol content in the mares' bodies in the last months of pregnancy. At the same time, the use of the drug 'Lactakhos' in pregnant mares ensures a stable cholesterol content in the blood serum of pregnant mares, as evidenced by the results we obtained (see Table 3.6).

In the blood serum of mares of all groups at the 10th month of pregnancy, compared to the beginning of the experiment, a significantly higher glucose content and lower activity of ALT, AST, GGT and LF were found. The data obtained may indicate a decrease in the intensity of certain biochemical processes (glycolysis, amino acid transamination, etc.) in the body of pregnant mares before foaling. During this period, a decrease in the content of globulins in the blood serum of mares was also found, which may be associated with their transport to the mammary gland.

During foaling, the average content of immunoglobulins in mare colostrum is approximately 2.5 times higher than their content in her blood plasma [19]. Thus, the literature indicates that in the last months of pregnancy, selective transport of immunoglobulins from the circulatory system to the mammary gland occurs (some type A immunoglobulins (IgA) may be produced in the mammary gland itself). This selective transport of immunoglobulins to the mare's mammary gland occurs under the influence of hormones, which characterises the final stage of foetal development. The level of oestrogen plays a decisive role in these processes [92]. The decrease in the

intensity of biochemical processes in mares before foaling, as evidenced by the results of our studies, may also occur under the influence of hormones.

During the study of protein fractions in the blood serum of pregnant mares in the control group on the 21st day of the experiment, compared to its beginning, significantly lower levels of globulins (1.06 times), β -globulins (1.18 times) and higher albumin content (1.06 times) and a higher A/G ratio (1.12 times) (Table 3.7).

Table 3.7

Protein fractions content in serum blood of pregnant mares on 21st day of experiment, $M \pm m$, $n=5$

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental Group, OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
Albumin, %	45,57 \pm 0,53	48,50 \pm 0,29 ^{***}	50,00 \pm 0,89 ^{***}	49,40 \pm 0,81 ^{**}
Globulin, %	54,43 \pm 0,53	51,50 \pm 0,29 ^{***}	50,00 \pm 0,89 ^{***}	50,60 \pm 0,81 ^{**}
α 1- globulin, %	5,21 \pm 0,15	5,0 \pm 0,58	4,60 \pm 0,24	4,80 \pm 0,37
α 2- globulin, %	12,64 \pm 0,20	12,0 \pm 0,29	11,40 \pm 0,40 [*]	11,0 \pm 0,45 [*]
β - globulin, %	18,29 \pm 0,53	15,50 \pm 0,25 ^{***}	14,20 \pm 0,50 ^{***}	14,40 \pm 0,68 ^{***}
γ - globulin, %	18,29 \pm 0,35	19,00 \pm 0,41	19,80 \pm 0,58	20,40 \pm 0,40 ^{*,**}
A/G ratio	0,84 \pm 0,02	0,94 \pm 0,04 [*]	1,00 \pm 0,04 ^{**}	0,98 \pm 0,03 ^{**}

Notes:

1. ^{*} - $p < 0,05$, ^{**} - $p < 0,01$, ^{***} - $p < 0,001$ compared with beginning of experiment
2. ^{*} - $p < 0,05$ compared with control group

On the 21st day of the experiment, a significant decrease in the content of globulins (1.09 times), α 2-globulins (1.11 times), β -globulins (1.29 times), an increase in albumin content (1.10 times) and a higher A/G ratio (1.19 times) (Table 3.7).

In the blood serum of pregnant mares in the second experimental group on the 21st day of the experiment, compared to its beginning, a decrease in the content of globulins (by 1.08 times), α 2-globulins (by 1.15 times), β -globulins (by 1.27 times), and γ -globulins (1.12 times), an increase in the content of albumins (1.08 times) and a higher A/G ratio (1.17 times), and compared to the mares of the control group, a higher content of γ -globulins (1.07 times) (Table 3.7).

On the 42nd day of the experiment, almost all indicators of protein metabolism in pregnant mares of the second experimental group were within the optimal normative

values.

On the 42nd day of the experiment, compared to its beginning, the blood serum of pregnant mares in the control group showed a significantly higher albumin content (1.09 times), a higher A/G ratio (1.18 times) and a lower globulin content (1.08 times) (Table 3.8).

On the 42nd day of the experiment, the blood serum of pregnant mares in the first experimental group showed significantly higher levels of albumin (1.12 times higher) A/G ratio (1.25 times) and lower globulin content (1.11 times), α 2-globulin content (1.13 times) compared to the beginning of the experiment, while no significant differences were found compared to the pregnant mares of the control group (Table 3.8).

Table 3.8

Protein fractions content in serum blood of pregnant mares on 42nd day of experiment, M \pm m, n=5

Indexes	Preganant mares			
	Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Beginning of experiment
Albumin, %	45,57 \pm 0,53	49,75 \pm 1,03 ^{♦♦}	51,00 \pm 1,26 ^{♦♦}	55,80 \pm 0,80 ^{***, $\Delta\Delta$, ♦♦}
Globulin, %	54,43 \pm 0,53	50,25 \pm 1,03 ^{♦♦}	49,00 \pm 1,26 ^{♦♦}	44,20 \pm 0,80 ^{***, $\Delta\Delta$, ♦♦}
α 1- globulin, %	5,21 \pm 0,15	5,250 \pm 0,85	4,80 \pm 0,66	4,40 \pm 0,24 [♦]
α 2- globulin, %	12,64 \pm 0,20	12,25 \pm 0,85	11,20 \pm 0,49 [♦]	8,40 \pm 0,68 ^{**$\Delta\Delta$, ♦♦}
β - globulin, %	18,29 \pm 0,53	17,0 \pm 1,08	16,20 \pm 0,97	14,40 \pm 0,68 ^{♦♦}
γ - globulin, %	18,29 \pm 0,35	15,75 \pm 1,49	16,80 \pm 1,02	17,00 \pm 0,32 [*]
A/G ratio	0,84 \pm 0,02	0,99 \pm 0,04 ^{♦♦}	1,05 \pm 0,06 ^{♦♦}	1,27 \pm 0,04 ^{***, $\Delta\Delta$, ♦♦}

Примітки:

- ♦ -p<0,05, ♦♦- p<0,01, ♦♦♦ -p<0,001 compared with beginning of experiment
- * -p<0,05, **- p<0,01, *** -p<0,001 compared with control group
- Δ -p<0,05, $\Delta\Delta$ -p<0,01, $\Delta\Delta\Delta$ -p<0,001 compared with first experimental group

In the blood serum of pregnant mares of the second experimental group on the 42nd day of the experiment, compared to its beginning, a higher content of albumins (1.10 times), a higher A/G ratio (1.51 times), a lower content of globulins (1.23 times), α 1-globulins (1.18 times), α 2-globulins (1.50 times) and β -globulins (1.27 times); compared to the pregnant mares of the control group, there was a significantly higher content of albumins (1.11 times), higher A/G ratio (1.28 times), γ -globulins (1.08

times) and lower globulin content (1.14 times), α 2-globulins (1.46 times), and compared to mares in the first experimental group – significantly higher albumin content (1.10 times), higher A/G ratio (1.21 times), lower globulin content (1.11 times) and α 2-globulin content (1.33 times) (Table 3.8).

Thus, the results of electrophoretic separation of serum protein fractions of pregnant mares indicate an increase in albumin content and a decrease in globulin content with an increase in gestation period, which confirms our results obtained during biochemical studies of the serum of these animals (Table 3.8).

The next stage of our work was to study the immunological indicators of the blood of pregnant mares with mineral metabolism disorders and the use of the mineral premix 'KM L2' and the mineral preparation Lactahos in order to find new approaches to correcting the immune status in animals, which is particularly important at the current stage of development of veterinary science.

Interest in the problem of studying the immune status in animals is primarily due to the fact that any pathology is the cause or consequence of immunological disorders that contribute to the transition of the underlying disease into a chronic form or its complication. This problem also applies to mineral metabolism pathology.

Secondly, the immune system is one of the most important homeostatic systems of the body, which determines the level of health of animals and their adaptive capabilities. It is an indicator system of ecological well-being and is very sensitive to changes in the environment.

The issue of ensuring a stable immune status in purebred and thoroughbred horses is particularly relevant. These animals have a delicate nervous system and are quite sensitive to various external stimuli, especially stress and physical exertion. This leads to a decrease in the immune status of the body and increased susceptibility of animals to diseases.

The formation of the immune status in foals begins long before the end of the mare's pregnancy. Thus, various organs of the foal's immune system develop quite rapidly and are fully formed by the 8th month of the mare's pregnancy [19]. At the same time, the foal's immune system remains unstimulated until the mare foals. It

should also be taken into account that the diffuse epitheliochorial attachment of the placenta in mares does not provide transplacental transfer of immunoglobulins. Therefore, a newborn foal receives immune bodies only through passive transfer with colostrum [19, 92]. Thus, the immune status of a newborn foal depends entirely on the content of immunoglobulins in the mother's colostrum, which it can receive in the first hours of its life.

It is during this period that a deficiency of trace elements essential for the immune system (manganese, zinc, copper, cobalt, iodine, selenium) negatively affects the immune status of both the pregnant mare and the newborn foal [80].

For example, zinc is a component of the hormone thymulin and influences the production of B-lymphocyte nuclear cells in the bone marrow of the mare, which subsequently produce immunoglobulins [52].

Copper deficiency reduces the CD4 (T-helper) subpopulation and suppresses the functional activity of T and B lymphocytes [51, 52].

Manganese activates the production of α -INF, b-INF and g-INF and increases the activity of natural killer cells in relation to any target cells [51, 52].

Based on the above, early diagnosis and timely correction of immune status disorders in pregnant mares caused by mineral deficiencies (especially in the last third of gestation), will prevent a number of diseases of the respiratory and digestive systems, which are quite common in young foals, and reduce the incidence of infectious diseases in horses in breeding. These measures will result in healthy and well-developed foals, which will subsequently be able to realise their sporting and genetic potential.

During the study of immunological indicators in the blood of pregnant mares in the control group on the 21st day of the study, compared to the beginning of the study, a significantly higher number of PC cells (1.10 times) a higher level of RBLT-induced (1.20 times) and a lower number of O-lymphocytes (1.11 times) (Table 3.9).

Table 3.9.

Immunological blood indexes of pregnant mares on 21st day of experiment,

M±m, n=5

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
T- lymphocytes, %	38,7±0,47	40,80±1,11	44,00±1,3 ^{***}	50,60±0,60 ^{***, ΔΔΔ, ***}
T- helpers, %	18,0±0,35	19,50±0,65	23,60±0,51 ^{***, ***}	28,60±0,51 ^{***, ΔΔΔ, ***}
T- supresors, %	20,7±0,25	21,30±0,48	20,40±1,11	22,00±1,00
PC-cells, %	11,79±0,21	13,00±0,41 [♦]	15,00±0,85 ^{**}	14,60±0,51 ^{*, ***}
B- lymphocytes, %	7,21±0,19	7,50±0,29	7,60±0,51	16,60±0,60 ^{***, ΔΔΔ, ***}
O- lymphocytes, %	42,93±0,53	38,80±1,85 ^{**}	33,40±2,29 ^{**}	18,20±1,80 ^{***, ΔΔΔ, ***}
HCT- spontaneous, %	11,43±0,20	11,0±0,82	10,60±0,6 ^{***}	14,60±0,40 ^{** , ΔΔΔ, ***}
HCT- induced, %	43,79±0,69	41,50±1,71	48,20±1,69 ^{*,♦}	65,80±2,85 ^{***, ΔΔΔ, ***}
HCT- reserve, %	32,36±0,73	30,50±1,50	37,60±1,21 ^{**,♦♦}	51,20±3,02 ^{***, ΔΔΔ, ***}
RBTL- spontaneous, %	4,43±0,14	4,50±0,29	3,60±0,25 ^{*,♦}	5,20±0,37 ^{ΔΔ}
RBTL- induced, %	21,00±0,51	25,25±1,49 [♦]	20,20±0,73 ^{**}	34,00±1,38 ^{***, ΔΔΔ, ***}
CIC, Units opt. density	52,49±1,22	55,37±4,30	55,00±2,70	55,00±3,45

Note:

- ♦ -p<0,05, ♦♦ -p<0,01, ♦♦♦ -p<0,001 compared with beginning of experiment
- * -p<0,05, ** -p<0,01, *** -p<0,001 compared with control group
- Δ -p<0,05, ΔΔ -p<0,01, ΔΔΔ -p<0,001 compared with first experimental group

On the 21st day of the experiment, compared to its beginning, the blood of pregnant mares in the first experimental group contained a significantly higher number of T-lymphocytes (1.14 times), T-helpers (1.31 times), PC cells (1.27 times), a higher HST-induced index (1.10 times), HST reserve (1.16 times) and a lower number of O lymphocytes (1.29 times), a lower HST spontaneous index (1.08 times), RBLT-spontaneous (1.23 times), and compared to the control group of mares, a significantly higher number of T-helpers (1.21 times), HST-induced (1.10 times), higher HST-reserve index (1.23 times) and lower RBLT-spontaneous and RBLT-induced indices (1.25 times in both cases) (Table 3.9).

In the blood of pregnant mares in the second experimental group, on the 21st day of the experiment, compared to its beginning, a significantly higher number of T-lymphocytes (1.31 times), T-helpers (1.59 times), PC cells (1.24 times), B lymphocytes (2.30 times), higher indicators of spontaneous HST (1.28 times), induced HST (1.50 times), HST reserve (1.58 times), RBL-induced (1.62 times) and a lower number of O-

lymphocytes (2.36 times). In these animals, compared with the control group mares, a significantly higher number of T lymphocytes (1.24 times), T helpers (1.47 times), PK cells (1.12 times), B-lymphocytes (2.21 times), higher NST-spontaneous (1.33 times), HST-induced and NST-reserve (1.56 and 1.68 times, respectively), as well as RBLT-induced (1.35 times) and a lower number of O-lymphocytes (2.13 times), and compared to mares in the first experimental group – significantly higher number of T lymphocytes (1.15 times), T helper cells (1.21 times), B lymphocytes (2.18 times), higher HST-spontaneous (1.38 times), NST -induced (1.37 times), HST-reserve (1.36 times), RBLT-spontaneous and induced (1.44 and 1.68 times, respectively) and a lower number of O-lymphocytes (1.84 times) (Table 3.9).

Thus, our data indicate higher immunomodulatory properties of the drug ‘Lactakhos’ compared to the premix ‘KM L2’ already on the 21st day of the experiment, characterised by high lymphocyte differentiation and better indicators of neutrophil phagocytic activity.

On the 42nd day of the study, a significantly higher number of T-lymphocytes (1.18 times), T-helpers (1.31 times), PC-cells (1.19 times), B lymphocytes (1.25 times), higher indicators of HST-induced (1.10 times), HST reserve (1.13 times), RBLT-induced (1.24 times) and a lower number of O-lymphocytes (1.36 times) (Table 3.10).

In the blood of pregnant mares in the first experimental group on the 42nd day of the experiment, compared to its beginning, a significantly higher number of T-lymphocytes (1.34 times), T-helpers (1.70 times), PK cells (1.26 times), B lymphocytes (1.55 times), higher levels of spontaneous HST (1.31 times), induced HST (1.34 times), HST reserve (1.35 times) and significantly fewer O-lymphocytes (1.95 times), and compared to the control group of mares, a significantly higher number of T-lymphocytes (1.14 times), T-helpers (1.30 times), higher levels of spontaneous HST (1.28 times), HST-induced (1.21 times), HST-reserve (1.27 times), higher CIC content (1.22 times) and fewer O-lymphocytes (1.43 times) (see Table 3.10).

Table 3.10.

Immunological blood indexes of pregnant mares on 42nd day of experiment,

M±m, n=5

Indexes	Pregnant mares			
	Beginning of experiment	Control group, OP	First experimental Group, OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
T- lymphocytes, %	38,7±0,47	45,5±1,85**	52,0±1,70* ^{***}	54,6±1,81** ^{***}
T- helpers, %	18,0±0,35	23,5±1,04 ^{***}	30,6±0,93 ^{***,***}	32,8±1,02 ^{***,***}
T- supresors, %	20,7±0,35	22,0±0,82	21,4±0,93	21,8±0,86
PC-cells, %	11,79±0,2	14,0±0,41 ^{***}	14,8±0,37 ^{***}	15,8±0,58* ^{***}
B- lymphocytes, %	7,21±0,19	9,0±0,71 [♦]	11,2±0,73 ^{***}	17,4±0,51 ^{***,ΔΔΔ,***}
O- lymphocytes, %	42,93±0,5	31,5±2,40	22,0±1,05 ^{***,***}	12,2±1,53 ^{***,ΔΔΔ,***}
HCT- spontaneous, %	11,43±0,2	11,75±0,85	15,00±0,89* ^{**}	15,00±0,71* ^{***}
HCT- induced, %	43,79±0,7	48,25±0,75 ^{***}	58,60±1,66 ^{***,***}	67,0±2,45 ^{***,Δ,***}
HCT- reserve, %	32,36±0,7	36,50±1,26 [♦]	43,60±1,81* ^{***,***}	52,00±1,87 ^{***,ΔΔ,***}
RBTL- spontaneous, %	4,43±0,14	4,75±0,25	5,20±0,37	6,60±0,24 ^{***,ΔΔ,***}
RBTL- induced, %	21,00±0,5	26,0±1,58 ^{**}	23,60±1,36	46,00±3,30 ^{***,ΔΔΔ,***}
CIC, Units opt. density	52,49±1,2	54,88±2,56	66,80±2,37 ^{**^{***}}	60,02±4,17

Note:

1. ♦ -p<0,05, ** - p<0,01, *** -p<0,001 compared with beginning of experiment
2. * -p<0,05, ** - p<0,01, *** -p<0,001 compared with control group
3. Δ -p<0,05, ΔΔ -p<0,01, ΔΔΔ -p<0,001 compared with first experimental group

On the 42nd day of the experiment, a significantly higher number of T-lymphocytes (1.41 times), T-helpers (1.82 times), PC cells (1.34 times),

B-lymphocytes (2.41 times), higher levels of spontaneous HST (1.31 times), induced HST (1.53 times), NST reserve (1.61 times), RBLT spontaneous (1.49 times), RBLT induced (2.19 times) and significantly fewer O lymphocytes (3.52 times) (see Table 3.10). At the same time, in the blood of pregnant mares of the second experimental group on the 42nd day of the experiment, compared with the animals of the control group, immunological indicators were characterised by a significantly higher number of T lymphocytes (1.20 times), T helpers (1.40 times), PK cells (1.13 times), B lymphocytes (1.93 times), higher indicators of spontaneous HST (1.28 times), induced HST (1.39 times), NST reserve (1.42 times), RBLT spontaneous (1.39 times), RBLT induced (1.77 times), and significantly lower number of O lymphocytes (2.58 times), and compared to these indicators in mares of the first experimental group – a significantly higher number of B lymphocytes (1.55 times), higher indicators of NST-

induced (1.14 times), NST reserve (1.19 times), RBLT spontaneous (1.27 times), RBLT induced (1.95 times) and a lower number of O-lymphocytes (1.80 times) (see Table 3.10).

The results of immunological studies confirm that at the beginning of the perinatal period, the mare's resources are mobilised to ensure normal foetal growth, preparation for foaling and lactation. In the last month of pregnancy, nonspecific changes in immune responses and nonspecific proliferation of T- and B-lymphocytes occur in the mare's body. This is associated with increased activity of haematopoietic processes. The proliferation of B lymphocytes is particularly intensified, which is necessary to increase the synthesis of immunoglobulins for their further entry into the mare's mammary gland.

Thus, the results of morphological, biochemical and immunological studies of the blood of pregnant mares indicate positive changes in haematopoiesis, metabolic processes and non-specific resistance in the body of these animals under the influence of the means of prevention of mineral metabolism disorders used by us. The most pronounced changes, indicating the stability of haematopoiesis processes, ensuring an optimal balance of anabolic and catabolic processes and indicators of non-specific resistance in the body of pregnant mares, obtained during the application of the drug 'Lactahos' developed by us to animals for 42 days. The use of the drug 'Lactachos' for the prevention of mineral metabolism disorders in pregnant mares is significantly more effective compared to the premix 'KM L2', which is confirmed by the results of studies of the content of macro and microelements in the blood serum of these animals, as well as data from morphological, biochemical and immunological studies.

3.3. Clinical condition, macro- and microelement content in blood serum and hair of foals

The condition of the mother's body, especially in the last months of pregnancy, determines the future potential of the newborn's body. With this in mind, we studied the clinical condition, haematological, biochemical and immunological indicators of the blood of foals aged 1 month, as well as spectrophotometric studies of the content of macro and microelements in the blood serum and hair of foals of the specified age,

born to mares in the control group and mares that were given the KM L2 premix and our Lactahos preparation during the last third of gestation.

The body temperature, pulse and respiratory rate of foals in all groups were within physiological limits. Foals in the control and first experimental groups showed deterioration in the condition of their coat: dullness, matting, and dullness of the tail and mane hair.

In contrast, in foals from the second experimental group, whose mothers received the drug Lactahos, the tail and mane hair, as well as the coat, were shiny and evenly covered the surface of the animal's body.

During the study of the clinical condition of the foals, it was found that one foal from the control group and one foal from the first experimental group were ill with bronchopneumonia. The disease manifested itself clinically in these foals as depression, elevated body temperature up to 40 °C, tachypnoea, tachycardia, serous and then serous-purulent exudate discharge from the nasal passages, dry cough, and wheezing during auscultation of the lung area.

The next stage of the research was to determine the content of macro- and microelements in the blood serum and hair of foals born to mares in the control and experimental groups.

It should be noted that traditionally, the content of macro- and microelements is studied in body fluids – whole blood, blood serum, urine, cerebrospinal fluid or in tissues. However, determining the content of macro- and microelements in whole blood, its serum or other biological fluids does not always provide accurate information about their content in the body of animals [52, 79, 159, 314].

Firstly, the composition of blood is variable, and the concentration of macro- and microelements measured in it is the result of its equalisation by the body's homeostatic mechanisms using reserves in tissues. Therefore, despite the fact that the concentration of macro- and microelements in blood serum is considered accurate, their content in the body may be insufficient, depending on the mineral content of the animal's diet at the time [52, 86, 314].

Secondly, determining the content of microelements in hair is a non-invasive

diagnostic method that does not cause stress, which is especially important when working with pregnant animals. Hair can be stored and transported for a long time without changing its chemical composition [52, 86, 314].

Determining the content of macro- and microelements in hair provides a detailed description of the metabolic state of the animal's body. Thus, the content of minerals in the animal's body significantly depends on external factors. Depending on the animal's diet, physical activity and the degree of environmental pollution, processes of mineralisation (deposition of minerals), demineralisation (loss of minerals by the body) or transmineralisation (rearrangement of minerals in the body) occur in the body. Macro- and microelements released as a result of metabolic processes can be reused in metabolic transformations.

Significant differences were found between the control and experimental groups in terms of the content of macro- and microelements in hair and blood serum.

Thus, in the hair of foals in the first experimental group, compared with foals in the control group, a significantly lower content of manganese (1.22 times) and a higher content of selenium (1.12 times) were found (Table 3.11).

In the hair of foals in the second experimental group, compared to foals in the control group, a significantly lower content of calcium (1.35 times) and iron (1.68 times) and a higher content of copper (1.17 times), zinc (1.27 times), cobalt (1.45 times) and selenium (2.16 times), and compared to foals in the first experimental group, they had significantly lower calcium (1.33 times) and iron (1.82 times) content and higher copper (1.17 times), zinc (1.27 times), cobalt (1.33 times) and selenium (1.92 times) (see Table 3.11).

Table 3.11

Macro- and microelement content in foal hair, M±m, n=5

Indexes	Foals, 1 month		
	Control group, OP	First experimental group OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
Common calcium, µg/g	9247,8±500,8	9098,0±384,1	6863,5±222,8***, ΔΔΔ
Magnesium, µg/g	1654,6±77,19	1788,9±58,33	1643,8±50,88
Manganese, µg/g	7,71±0,18	6,33±0,32**	7,99±0,36ΔΔ
Iron, µg/g	141,3±19,78	153,7±5,75	84,20±4,24**, ΔΔΔ

Continuation of table 3.11

Copper, µg/g	14,70±0,72	14,49±0,80	17,18±0,77*, ^Δ
Zinc, µg/g	415,5±36,33	346,1±38,41	525,7±28,59**, ^{ΔΔ}
Cobalt, µg/g	0,22±0,01	0,24±0,01	0,32±0,02***, ^{ΔΔ}
Selenium, µg/g	2,28±0,08	2,56±0,02*	4,92±0,14***, ^{ΔΔΔ}

Note:

1. * -p<0,05, ** - p<0,01, *** -p<0,001 compared to control group
2. ^Δ -p<0,05, ^{ΔΔ} -p<0,01, ^{ΔΔΔ} -p<0,001 compared to first experimental group

Thus, the data we obtained indicate that the use of Lactakhos in mares during the last third of gestation is more effective in providing the foetus with minerals compared to the KM L2 premix. This indicates better availability of organic forms of trace elements contained in Lactakhos, which is confirmed by the higher content of trace elements in the hair of foals.

Most of the indicators of macro- and microelement content in the blood serum of foals in the first experimental group, whose mothers received the KM L2 premix, did not show significant differences compared to foals in the control group. At the same time, compared to the control group, the blood serum of these animals had a significantly lower calcium content (1.33 times) and a higher phosphorus content (1.7 times) (Table 3.12).

Table 3.12

Macro- and microelement content in foal blood, M±m, n=5

Indexes	Foals, 1 month		
	Control group, OP	First experimental group, OP+ Premix KM L2	Second experimental group, OP+ Lactakhos
Common calcium, mmol/l	3,43±0,14	2,58±0,17**	3,42±0,08 ^{ΔΔΔ}
Non-organic phosphorus, mmol/l	1,20±0,06	2,04±0,05***	2,14±0,02***
Ca:P ratio	2,86:1	1,26:1	1,60:1
Potassium, mmol/l	3,58±0,31	4,28±0,29	4,34±0,15
Sodium, mmol/l	133,83±4,62	133,72±3,10	136,92±2,14
Chlorine, mmol/l	96,40±3,55	97,90±2,68	100,20±3,05
Magnesium, mmol/l	1,06±0,07	1,11±0,08	1,13±0,06
Manganese, µmol/L	0,21±0,01	0,23±0,01	0,66±0,01***, ^{ΔΔΔ}
Iron, µmol/L	59,49±2,31	62,67±2,46	59,71±2,92
Copper, µmol/L	31,16±1,17	34,05±2,37	31,25±2,22

Continuation of table 3.12

Zinc, $\mu\text{mol/L}$	10,67 \pm 0,87	13,83 \pm 1,28	21,96 \pm 1,00***, $\Delta\Delta\Delta$
Cobalt, $\mu\text{mol/L}$	0,21 \pm 0,01	0,23 \pm 0,01	0,54 \pm 0,02***, $\Delta\Delta\Delta$
Selenium, $\mu\text{mol/L}$	0,39 \pm 0,02	0,40 \pm 0,007	1,19 \pm 0,07***, $\Delta\Delta\Delta$

Note:

1. **- $p < 0,01$, *** - $p < 0,001$ compared to control group
2. $\Delta\Delta\Delta$ - $p < 0,001$ compared to first experimental group

In this regard, the calcium-phosphorus ratio in the blood serum of foals in the first experimental group was significantly lower than the normative values, which may pose a threat to the development of musculoskeletal disorders in these animals.

Our data indicate an optimal calcium-phosphorus ratio in the blood serum of foals in the second experimental group, whose mothers received the drug 'Lactakhos'. This indicator may reflect the stable use of calcium and phosphorus for the formation of the skeleton, muscle and connective tissue in foals during their intensive growth and development in the postnatal period.

Compared to the foals in the control group, the blood serum of the foals in the second experimental group had a significantly higher content of phosphorus (1.78 times), manganese (3.14 times), zinc (2.06 times), cobalt (2.57 times) and selenium (3.05 times), and compared to the foals in the first experimental group, a significantly higher content of calcium (1.33 times), manganese (2.87 times), zinc (1.59 times), cobalt (2.35 times) and selenium (2.98 times) (see Table 3.12).

It should be noted that some indicators of macro- and microelement content (phosphorus, iron, copper) in the blood serum of foals are higher than the standard values generally accepted for adult horses. Given that these indicators are similar in foals of all experimental groups, they can be considered physiological for these animals at the age of 1 month.

Thus, the results of the studies showed the high effectiveness of the Lactakhos preparation we developed in providing foals with macro- and microelements by administering this preparation to mares during the last third of gestation. The data obtained indicate that the components of the Lactakhos preparation are stable, have the ability to penetrate the mother's placenta, are effectively absorbed by the foetus, remain

in sufficient quantities in the foal's tissues for a long time, and support metabolic processes in these animals during their intensive growth and development.

At the same time, our results indicate that not all minerals included in the KM L2 premix are able to accumulate in sufficient quantities in foal tissues. Most likely, they exert their effect in the body of a pregnant mare for a short time and are not able to be absorbed by the foetus.

Our assumptions are confirmed by morphological, biochemical and immunological indicators in the blood of foals.

3.4. General clinical, biochemical and immunological blood parameters of foals

The general clinical blood parameters of foals in the first experimental group, whose mothers received the KM L2 premix, differed significantly from those of foals in the control group only in terms of a higher white blood cell count (1.18 times) (Table 3.13).

Table 3.13

General clinical blood parameters of foals, M±m, n=5

Indexes	Foals, 1 month			
	Control group, OP	First experimental group, OP+Premix KM L2	Second experimental group, OP+Lactakhos	
Haematocrit, %	0,35±0,03	0,36±0,02	0,39±0,01	
RBC, T/l	8,1±0,29	8,4±0,45	9,7±0,30**, ^Δ	
ESR, mm/hour	29,8±2,75	34,4±1,33	33,6±1,29	
Haemoglobin, g/l	116,3±3,01	118,8±4,29	131,4±3,06**, ^Δ	
WBC, G/l	8,0±0,26	9,4±0,54*	10,2±0,35***	
Leucogram, %	Basophils	0	0	
	Eosinophils	3,0±0,25	3,0±0,24	3,0±0,20
	Neutrophils:			
	Young	0	0	0
	Stab	4,0±0,25	4,0±0,24	4,0±0,20
	Segmented	51,0±2,21	50,0±0,80	50,0±1,07
	Lymphocytes	37,0±1,89	38,0±0,97	39,0±0,87
Monocytes	5,0±0,29	4,0±0,24	4,0±0,20	

Note:

1. * -p<0,05, ** - p<0,01, *** -p<0,001 compared to control group
2. ^Δ -p<0,05 compared to first experimental group

On the other hand, the general clinical blood parameters of foals in the second

experimental group, whose mothers received Lactahos during the last third of gestation, were characterised by a significantly higher number of erythrocytes (1.20 times), leukocytes (1.28 times) and higher haemoglobin content (1.10 times), and compared to foals in the first experimental group, whose mothers received the premix KM L2, they had significantly more erythrocytes (1.15 times) and higher haemoglobin content (1.11 times) (see Table 3.13).

During the study of biochemical indicators of blood serum of foals in the first experimental group, no significant differences were found compared to foals in the control group (Table 3.14).

Table 3.14

Biochemical blood indexes of foals, M±m, n=5

Indexes	Foals, 1 month		
	Control group, OP	First experimental group, OP+Premix KM L2	Second experimental group, OP+ Lactahos
Glucose, mmol/l	5,20±0,08	5,28±0,17	5,24±0,16
Total protein, g/l	57,58±0,52	58,26±1,59	64,64±1,00***, $\Delta\Delta$
Albumin, g/l	29,65±0,56	31,36±1,06	34,96±0,63***, Δ
Globulin, g/l	27,93±0,57	26,90±0,74	29,68±0,60 Δ
Urea, μ mol/l	4,80±0,31	4,74±0,09	4,86±0,16
Creatinine, μ mol/l	97,43±2,08	101,34±1,61	103,66±1,91
Total bilirubin, μ mol/l	15,78±0,60	16,30±0,58	19,90±0,92**, $\Delta\Delta$
Triglycerides, mmol/l	0,93±0,08	1,04±0,05	0,77±0,03 $\Delta\Delta\Delta$
Cholesterol, μ mol/l	3,20±0,12	3,18±0,10	2,78±0,09*, $\Delta\Delta$
ALP, U/l	1310,3±19,39	1351,0±49,83	1326,5±48,98
ALT, U/l	14,68±0,50	14,80±1,28	15,22±0,43
AST, U/l	224,48±9,67	238,50±8,28	221,30±3,49
GGT, U/l	19,53±1,55	18,40±2,15	18,62±0,51
α -Amylase, U/l	15,18±0,85	15,54±0,84	15,64±1,11

Note:

- * -p<0,05, ** - p<0,01, *** -p<0,001 compared to control group
- Δ -p<0,05, $\Delta\Delta$ -p<0,01, $\Delta\Delta\Delta$ -p<0,001 compared to first experimental group

At the same time, the biochemical parameters of the blood of foals in the second experimental group, whose mothers received Lactahos during the last third of gestation, were characterised by a significantly higher content of total protein (1.12

times), albumin (1.18 times) and bilirubin (1.26 times) compared to foals in the first experimental group, whose mothers received the KM L2 premix. Compared to foals in the first experimental group, whose mothers received the KM L2 premix, foals in the second experimental group had significantly higher levels of total protein (1.11 times), albumin (1.11 times), bilirubin (1.22 times), lower triglyceride (1.35 times) and cholesterol (1.14 times) content (see Table 3.14).

The biochemical indicators of 1-month-old foals are characterised by triglyceride levels that are higher than the norm for horses (1.8–2.1 times) and higher activity of LF (5.0–5.2 times) and AlAT (1.2–1.3 times), which can be explained by the high intensity of metabolic processes in the body of young animals during their growth and development.

During the study of protein fractions in foal blood serum, it was found that all indicators were within physiological values. At the same time, compared to the control group foals, the blood serum of the second experimental group foals had a higher content of albumin (1.07 times), γ -globulins (1.07 times), a higher A/G ratio (1.11 times) and a lower content of α 2-globulins (1.19 times) (Table 3.15).

Table 3.15

Protein fraction content in the blood serum of foals, $M \pm m$, $n=5$

Indexes	Foals, 1 month		
	Control group, OP	First experimental group, OP+Premix KM L2	Second experimental group, OP+Lactakhos
Albumin, %	50,75±0,75	53,40±0,93	54,20±0,58**
Globulin, %	47,75±0,75	46,20±0,58	45,80±0,58
α 1- globulin, %	5,25±0,25	4,60±0,51	4,80±0,20
α 2- globulin, %	10,75±0,25	9,40±0,81	9,00±0,32***
β - globulin, %	14,75±0,25	14,20±0,20	13,80±0,37
γ - globulin, %	17,00±0,41	18,00±0,45	18,20±0,20*
A/G ratio	1,06±0,03	1,16±0,03	1,18±0,03**

Note.

* - $p < 0,05$, ** - $p < 0,01$, *** - $p < 0,001$ compared to control group

The immunological parameters of the blood of foals in the first experimental group, compared with foals in the control group, were characterised by a significantly higher number of PC cells (1.12 times), higher phagocytic activity of neutrophils –

HST-induced (1.21 times), NST reserve (1.30 times) RBLT spontaneous (1.31 times), RBLT induced (1.23 times) and a lower percentage of CIC (1.91 times) (see Table 3.16).

The immunological indicators of the blood of foals in the second experimental group, whose mothers received Lactahos during the last third of gestation, were characterised by a significantly higher number of T-lymphocytes (1.11 times), T-helpers (1.20 times), PK cells (1.27 times), B lymphocytes (1.22 times), higher phagocytic activity of neutrophils – NST spontaneous (1.20 times), NST induced (1.38 times), NST reserve (1.45 times), spontaneous RBLT (2.18 times), induced RBLT (1.41 times), a lower number of O-lymphocytes (1.74 times) and lower CIC content (2.97 times), and compared to foals in the first experimental group, whose mothers received the KM L2 premix, a significantly higher number of T-lymphocytes (1.11 times), T-helpers (1.15 times), PK cells (1.14 times), B-lymphocytes (1.16 times), higher phagocytic activity of neutrophils – NST-spontaneous (1.26 times), NST-induced (1.14 times), NST-reserve (1.11 times), RBLT-spontaneous (1.67 times) and lower CIC content (1.55 times) (Table 3.16).

Table 3.16

Immunological blood indexes of foals, M±m, n=5

Indexes	Foals, 1 month		
	Control group, OP	First experimental group, OP+Premix KM L2	Second experimental group, OP+Lactakhos
T-lymphocytes, CD3, %	48,0±0,71	48,4±0,93	53,4±0,93 ^{ΔΔ} ,***
T-helpers, CD4, %	26,2±0,63	27,4±0,24	31,6±1,21 ^{ΔΔ} ,**
T-suppressors, CD8, %	21,8±0,25	21,0±0,77	21,8±0,58
PC-cells, CD16, %	11,8±0,48	13,2±0,37*	15,0±0,32 ^{ΔΔ} ,***
B-lymphocytes, CD22, %	12,8±0,48	13,4±0,60	15,6±0,51 ^Δ ,**
O-lymphocytes, %	27,5±1,04	25,0±1,10	16,0±1,22 ^{ΔΔΔ} ,***
HST-spontaneous, %	13,00±0,41	12,40±0,51	15,60±0,68 ^{ΔΔ} ,**
HST-induced, %	48,50±2,75	58,60±1,54**	67,00±1,70 ^{ΔΔ} ,***
HST-reserve, %	35,50±2,72	46,20±1,66**	51,40±1,57 ^Δ ,***
RBLT-spontaneous, %	2,75±0,25	3,60±0,24*	6,00±0,32 ^{ΔΔΔ} ,***
RBLT-induced, %	29,00±1,47	35,80±1,43**	41,00±1,92***
CIC, Units opt. density	48,63±1,30	25,50±0,76***	16,40±0,48 ^{ΔΔΔ} ,***

Note:

- * -p<0,05, **-p<0,01, *** -p<0,001 compared to control group
- Δ -p<0,05, ΔΔ -p<0,01, ΔΔΔ -p<0,001 compared to first experimental group

Thus, the results of general clinical, biochemical and immunological studies indicate the effective impact of Lactahos, administered to mares during gestation, on the foetuses and newborn foals. Organic compounds of trace elements are important for the preventive effect of the drug, aimed at preventing mineral metabolism disorders in horses. As our studies have shown, the optimal use of Lactachos for pregnant mares is the combination of lactate compounds of trace elements, triethanolamine salt of selenic acid, natural mineral opoka and silicon-organic immunomodulator Mival, which effectively act on the body of a pregnant mare, embryo and foal.

4. EFFECTIVENESS OF LAKTAKHOS DRUG FOR MINERAL METABOLISM DISORDERS IN HORSES

Ensuring physiologically normal pregnancy allows maintaining the health and reproductive qualities of the mare and obtaining well-developed, viable offspring that will be able to fully manifest their genetic potential in the future.

The entire reproductive process in horses, from the moment of fertilisation of the mare to the birth of the foal, is a biological component of the unity of the mother's and foal's organisms. In this regard, all measures for the effective reproduction of a healthy horse population should begin not at the moment of the foal's birth, but with the targeted care of pregnant mares. This, to a large extent, allows avoiding the development of prenatal and postnatal pathologies in foals.

During pregnancy, the mare's body mobilises to ensure normal growth and development of the foal, preparation for foaling and subsequent lactation. The development of the foetus largely depends on the strengthening or weakening of the functions of the mother's organs, which have a correlative effect on its condition. It is during this period that it is extremely important to monitor the health of the mother's body and, thus, ensure the normal growth and development of the foetus.

Although pregnancy is a physiological process, changes that border on pathological can occur in the mare's body. Thus, the results of studies by many scientists indicate that the birth of a healthy foal can only occur if the mare's body is in optimal biochemical condition. For normal metabolic processes, a pregnant mare must receive the necessary amount of nutrients from her diet on a daily basis. It is important to note that during pregnancy, a mare's need for biologically active substances increases significantly and certain metabolic changes occur in her body.

Thus, if horses do not receive sufficient mineral substances (macro- and microelements), metabolic disorders occur in their bodies, which alter the transformation of substances in all links of metabolism.

A deficiency or excess of macro and microelements in the soils of the corresponding biogeochemical zones of Ukraine, as well as in feed, water and in the

bodies of animals, is one of the main aetiological factors in the occurrence and development of biogeocenotic pathology in horses, which is particularly pronounced in mares during pregnancy.

Disruption of mineral metabolism in pregnant mares leads to a decrease in their working capacity, productivity and non-specific resistance, as well as changes in the growth and development of foals.

Currently, there are a large number of therapeutic and prophylactic agents containing minerals on the Ukrainian market. However, they have a number of shortcomings that need to be improved. For example, these preparations contain inorganic salts of minerals, which are only partially absorbed (by 20–30%), and do not take into account the characteristics of a particular physiological period of horses, when the needs of these animals for macro- and microelements differ significantly.

Therefore, the development of methods for early diagnosis and effective therapeutic and prophylactic agents for mineral metabolism disorders in pregnant mares and foals is a pressing issue for the horse breeding industry in our country, which requires an effective solution.

The results of our clinical studies of animals and laboratory studies of feed, water, blood, blood serum and hair of pregnant mares and foals with mineral metabolism disorders indicate changes in clinical indicators, protein, lipid, carbohydrate, macro- and microelement metabolism, which has a significant impact on such vital processes as tissue respiration, blood formation, and indicators of non-specific resistance in these animals.

The results of our studies of the main diet, water, clinical condition of the body and laboratory blood indicators of pregnant mares showed that in the Poltava region, which is considered a conditional benchmark for the content of macro- and microelements in water, soil and feed, these animals are diagnosed with mineral metabolism disorders resulting from a deficiency or excess of certain macro- and microelements in their bodies.

Thus, during the study of the mineral composition of the diet and water for watering horses at the Poltava region, we found a deficiency of some (phosphorus,

manganese, zinc, cobalt, copper, selenium) and an excess of others (calcium, iron) macro- and microelements, which leads to the development of complex mineral metabolism disorders in pregnant mares and their foals. The development of mineral metabolism disorders in animals is exacerbated by the high content of technogenic elements (arsenic, chlorine, barium, aluminium, nickel, vanadium, chromium, lead) in feed and water. Due to their antagonistic and toxic effects, these elements can negatively affect the animal's body and reduce the absorption of essential elements.

During the study of blood serum from pregnant mares for mineral metabolism pathology in terms of macro- and microelement content, we found a calcium-phosphorus ratio imbalance of 3.30:1. As is known [51, 109], a violation of the calcium-phosphorus ratio in horses (more than 2.0:1) negatively affects the absorption of magnesium, manganese, iron, zinc and iodine [109].

In addition, in the blood serum of pregnant mares with mineral metabolism disorders, compared to clinically healthy animals, a significantly lower content of magnesium, manganese, zinc, cobalt and selenium was found. The deficiency of these elements in the body of pregnant mares was clinically confirmed.

Thus, in pregnant mares with mineral metabolism disorders, defects in the skin and coat were found, namely dullness, roughness and dullness of the mane and tail hair, dandruff flakes at the base of the hair roots, poor hair retention in the hair follicles, in most animals, delayed moulting was recorded, the hoof horn was dry, uneven, dull, cracks in the hoof horn, allotriophagy, weakened intestinal motility and poor feed digestibility were detected.

Disruption of mineral metabolism in pregnant mares leads to changes in the internal homeostasis of the body.

In cases of mineral metabolism disorders in the blood of pregnant mares, haematopoiesis disorders have been identified, which are the result of a deficiency in the animals' diet and their bodies of trace elements essential for haematopoiesis, such as cobalt, zinc and, especially, copper.

Low levels of haemoglobin, total protein and its fractions – albumin and globulin, as well as changes in the ratio of individual globulin fractions in the blood

serum of pregnant mares with mineral metabolism disorders are likely due to toxic phenomena in the body of these animals and, as a result, a decrease in the protein-synthesising function of the liver. This is also confirmed by the high activity of ALP, ALT and AST in the blood serum of pregnant mares with mineral metabolism disorders, which may indicate the destruction of hepatocytes, nephrocytes, osteocytes, possibly cardiomyocytes, as well as a significantly higher content of certain metabolites in the blood serum of these animals: glucose, triglycerides, cholesterol, which may be the result of a hormonal imbalance in mineral metabolism disorders.

There is a significantly lower number of T-helpers, PK cells, B-lymphocytes, a higher number of T-suppressors and O-lymphocytes, lower phagocytic activity of neutrophils (NST-spontaneous, NST-induced, NST-reserve), (spontaneous RBLT, induced RBLT) and higher CIK content in the blood of pregnant mares with mineral metabolism disorders compared to clinically healthy animals confirms the severity of toxic phenomena. As a result, circulating immune complexes accumulate in the blood of pregnant mares with mineral metabolism disorders, and the animals develop an immunosuppressive state.

Thus, the analysis of general clinical, biochemical and immunological indicators of the blood of mares in the 8th month of pregnancy indicates significant changes in metabolism that occur with mineral metabolism disorders in these animals. Changes in the internal homeostasis of pregnant mares can affect foetal development and, subsequently, the growth and development of newborn foals.

Based on the above and taking into account the physiological characteristics of pregnant mares, the state of their mineral supply, the results of clinical and laboratory studies, and metabolic disorders in the body of animals, in the problem scientific laboratory 'Internal Non-Contagious Diseases of Animals' of the Department of Therapy and Clinical Diagnostics of the National University of Life and Environmental Sciences of Ukraine, we have developed the drug Lactakhos, which has been tested on animals in production conditions for the purpose of therapy and prevention of mineral metabolism disorders in them. During the development of Lactakhos, the results of many years of research on soils, feed and water sources in the Poltava region were

taken into account, as well as the results of clinical and laboratory studies of horses from horse farms in the Central Biogeochemical Zone of Ukraine. The physiological need of pregnant mares for certain elements, the compatibility of mineral elements in the composition of the preparation, and the biological synergy or antagonism of their action during metabolic transformations in the animal's body were also taken into account. In addition to biogenic microelements in the form of lactate compounds, triethanolamine salt of selenic acid and the organosilicon immunomodulator 'Mival' were added to the composition of the preparation 'Lactakhos'.

The effectiveness of the Lactakhos preparation for mineral metabolism disorders in pregnant mares was studied in comparison with the use of the KM L2 premix, which has been traditionally used for many years at the Poltava Region Horse Farm to replenish macro- and microelement deficiencies.

Our results showed the stability of haemocytopoiesis processes, ensuring an optimal balance of anabolic and catabolic processes and indicators of non-specific resistance in the body of pregnant mares during the use of Lactakhos. It has been established that the therapeutic use of Lactakhos for mineral metabolism disorders in pregnant mares is significantly more effective than the use of KM L2 premix, as confirmed by the results of studies of the content of macro and microelements in the blood serum of these animals, as well as data from morphological, biochemical and immunological studies.

In particular, the use of Lactakhos for 42 days in pregnant mares with mineral metabolism disorders contributed to the disappearance of clinical signs of mineral metabolism disorders, which did not occur during this period in animals treated with KM L2 premix.

It has been established that Lactakhos effectively meets the needs of pregnant mares for trace elements and normalises the metabolism of macroelements in their bodies.

Thus, in the blood of pregnant mares treated with Lactakhos, the calcium-phosphorus ratio normalised, which, in our opinion, was due to better absorption of phosphorus from phytin in the digestive tract of animals. Thus, if at the beginning of

the experiment, the calcium-phosphorus ratio in the blood serum of pregnant mares treated with Lactakhos was 3.12:1, on the 21st day it was 2.86:1, and on the 42nd day it was 2.08:1. In contrast, in the blood serum of animals treated with the KM L2 premix, this ratio was 3.12:1 at the beginning of the experiment, 2.98:1 on the 21st day, and on the 42nd day – 3.13:1, which exceeds the normative values, which for horses average from 1.5:1 to 2:1.

It should be noted that in the last third of the mare's pregnancy, when the foetus grows most intensively, a significant part of the calcium in the mare's body is used as plastic material for the formation of the foetus's skeleton, which explains the decrease in the content of this element in the blood serum of pregnant mares. At the same time, the calcium-phosphorus ratio in the blood serum of pregnant mares treated with the KM L2 premix did not normalise, although it contains both calcium and phosphorus.

However, during the use of the Lactakhos preparation, the levels of magnesium, manganese, iron, copper, zinc, cobalt and selenium in the blood serum of pregnant mares normalised. The use of Lactakhos in pregnant mares during the last third of pregnancy, when the intensity of metabolism is quite high, contributed to the normalisation of metabolic processes, antioxidant and immune protection in the mares' bodies.

It has been established that with an increase in the duration of gestation, the levels of iron, zinc and selenium in the blood serum of mares decrease significantly. This indicates a further deepening of the pathology of mineral metabolism in the body of pregnant mares during the period of intensive foetal formation. It should be noted that the selenium content in the blood serum of pregnant mares in the control (basic diet) and first experimental (basic diet with the addition of the KM L2 premix) groups was significantly lower than the normative values. The insufficient supply of selenium to pregnant mares may be associated with its deficiency in the diet and low content in the KM L2 premix. Given the importance of selenium in ensuring peroxidation processes, it can be assumed that its deficiency will lead to the accumulation of lipid peroxidation products in the body of a mare, which will negatively affect the health of the mare and the development of the foetus.

At the same time, the use of Lactakhos completely solves the problem of selenium supply in pregnant mares, as proven by our results.

A significantly higher number of erythrocytes, leukocytes, lymphocytes and a higher haemoglobin content in the blood of pregnant mares also indicate the positive effect of the components of the drug 'Lactakhos' on the processes of haematopoiesis in these animals, which was not observed in the case of the use of the drug 'KM L2' in pregnant mares.

In the course of our research, we identified some peculiarities in the biochemical indicators of the blood of mares in their last month of pregnancy. Thus, in the blood serum of mares in the 10th month of pregnancy, compared to the 8th month of pregnancy, a significantly higher concentration of glucose and lower activity of AST, GGT and ALP were found. The data obtained may indicate a decrease in the intensity of metabolic processes in the body of mares before foaling.

The reliable decrease in globulin content in the blood serum of mares at the end of gestation and the resulting changes in the albumin/globulin ratio may be due to the intensive transport of blood serum globulins to the mammary gland in connection with the preparation of mares for foaling.

The use of the drug 'Lactakhos' in pregnant mares contributes to an increase in the content of total protein and albumin in the blood serum, which was not established during the use of the premix 'KM L2'. The results obtained may indicate stimulation of protein biosynthesis processes in the liver and improvement of digestion and absorption of proteins and amino acids in the digestive tract of pregnant mares under the influence of the components of the Lactakhos preparation.

It should be noted that most of the immunological blood parameters we studied, namely the number of T-lymphocytes, T-helpers, PC cells, B lymphocytes, HST-induced, HST-reserve and RBLT-induced values in pregnant mares at 10 months of pregnancy were significantly higher compared to 8 months of pregnancy. Our data allow us to conclude that the immune system of mares is stimulated at the end of gestation. This is also confirmed by data from the literature [19].

At the same time, in the blood of pregnant mares that were given Lactakhos,

compared to those that were given the KM L2 premix, a significantly higher number of T-lymphocytes, T-helpers, PC cells, B lymphocytes, higher levels of spontaneous HST, induced HST, HST reserve, spontaneous RBLT, induced RBLT, and a lower number of O lymphocytes. The results obtained indicate a more active stimulation of non-specific immunity in the body of pregnant mares under the influence of the components of the drug 'Lactakhos' than under the influence of the components of the premix 'KM L2'. Moreover, when using the premix 'KM L2' for pregnant mares, a high content of circulating immune complexes was found in the blood serum of these animals, which have the ability to accumulate in the tissues of internal organs and cause pathological changes in the body of the pregnant mare and foetus.

Thus, the results of our studies indicate positive changes in the clinical condition of pregnant mares and reliable changes in the morphological, biochemical and immunological parameters of their blood, which indicate the normalisation of metabolic processes and non-specific resistance in the body of these animals under the influence of the therapeutic -preventive agents for mineral metabolism disorders. The data obtained reflect the most effective stability of haematopoietic processes, ensuring an optimal balance of anabolic and catabolic processes and indicators of non-specific resistance in the body of pregnant mares during the use of the drug 'Lactakhos'. The use of this drug for the treatment of pregnant mares with mineral metabolism disorders is significantly more effective compared to the premix 'KM L2', which is confirmed by the results of studies of the content of macro- and microelements in the blood serum of these animals, as well as data from clinical, morphological, biochemical and immunological studies.

Currently, there is sufficient data that mineral metabolism disorders in the mother's body are accompanied by disorders of macro- and microelement metabolism in the foetus and newborn animal, leading to delays in its growth and development [27, 52,73, 83, 109].

The results of the use of the drug 'Lactakhos' in mares in the last third of pregnancy with mineral metabolism disorders indicate its positive effect on the foals born to them, in which the absence of diseases, better clinical condition, morphological,

biochemical and immunological blood parameters compared to foals born to mares from other experimental groups. Moreover, foals born to mares in the control group and mares in the experimental group that were given the KM L2 premix showed cases of bronchopneumonia.

An analytical test widely used in the diagnosis of macro- and microelement metabolism disorders is the study of the mineral composition of hair, since the concentration of macro- and microelements in the blood often does not fully reflect their content in the body. This is because the composition of blood serum is highly dependent on homeostatic mechanisms. Therefore, the final concentration of minerals in blood serum is the result of its equalisation by certain homeostatic mechanisms of the animal's body.

Many pathological conditions of the body are closely related to changes in the concentration of macro- and microelements in tissues. The best method for determining the content of macro- and microelements in the human body, which is an alternative to the method of studying the content of macro- and microelements in blood and urine, is to study their concentration in hair and nails [52]. Hair and nails are located outside the skin surface and are excluded from metabolic processes. At the same time, nails are less suitable material than hair due to the difficulty of completely eliminating exogenous contamination. Hair, in turn, is a stable tissue that is not subject to biological changes. The keratin outer shell of the hair completely prevents not only the loss of internal components, but also the entry of external contamination into the hair, ensuring the constancy of its chemical composition. Unlike nails, external contamination can be easily removed from hair, resulting in very good repeatability of analytical results [52].

Thus, studying the content of macro- and microelements in hair allows us to obtain an accurate characterisation of metabolic processes in the body. In this regard, the results of studies of the macro- and microelement composition of hair are increasingly used in the diagnosis of mineral metabolism disorders in humans and animals.

Hair tissue consists of protein with a high cysteine content. This amino acid, due to the presence of a thiol (SH) group, has a chelating ability with regard to macro- and

microelements. This is why the concentration of minerals in hair is approximately 50 times higher than their concentration in blood and urine [51, 52].

Analysis of the macro- and microelement composition of the hair of foals born to mares in the control group, which during the study period received only the basic diet, and foals born to mares in the first experimental group, which received basic feed and the KM L2 premix, showed a significantly higher content of calcium and iron compared to foals born to mares that were fed basic feed and given the Lactakhos preparation. According to the literature [47, 107], excessive calcium and iron content in the body of animals leads to impaired absorption of phosphorus, copper, iodine, reduced vitamin A storage in the liver, and growth retardation. In addition, prolonged excess calcium in the animal's body causes hypertrophy of the thyroid gland [47].

On the other hand, the use of Lactakhos in mares during the last third of gestation ensured stable levels of macro- and microelements (calcium, manganese, iron, copper, zinc, cobalt, selenium) in foal hair.

The levels of macro- and microelements in the blood serum of foals whose mothers received Lactakhos were stable and, compared to similar indicators in foals from other groups, were characterised by an optimal calcium-phosphorus ratio and higher levels of manganese, zinc, cobalt and selenium. The levels of macro- and microelements in the blood of foals whose mothers received the KM L2 premix, although characterised by a significantly higher content of phosphorus and zinc compared to foals in the control group, did not reach the normative values for manganese, cobalt and selenium.

Thus, the content of macro- and microelements in hair and blood serum indicates a highly effective supply of mineral substances to foals through the use of the Lactakhos preparation for mares in the last third of gestation. This indicates that the components of the Lactakhos preparation are stable, have the ability to penetrate the mother's placenta, are effectively absorbed by the foetus, are present in sufficient quantities in the foal's tissues for a long time and ensure metabolic processes in the body of these animals during their intensive growth and development.

At the same time, as shown by the results of our research, not all minerals

included in the KM L2 premix accumulate in sufficient quantities in foal tissues. Most likely, they exert their effect in the body of a pregnant mare for a short time and are only partially absorbed by the foetus.

The use of the drug 'Lactakhos' in pregnant mares in the last third of pregnancy ensured stable morphological blood parameters in their foals, which, compared to foals from other experimental groups, had a significantly higher number of erythrocytes, leukocytes and a tendency to increase the number of lymphocytes.

The indicators of haemoglobin, total protein and albumin fraction in the blood serum of foals born to mares treated with Lactakhos indicate a high intensity of metabolic processes in the red bone marrow and liver of these animals.

The use of Lactakhos in pregnant mares ensured high levels of non-specific resistance in their foals compared to foals from other experimental groups, namely a significantly higher number of T-lymphocytes, T-helpers, PK cells, B lymphocytes, higher phagocytic activity of neutrophils, higher RBLT-spontaneous, RBLT-induced and fewer O lymphocytes in their blood. The results of the studies indicate a high differentiation of lymphocytes and the readiness of these cells to actively engage in immunological reactions in the foals' bodies as early as 1 month of age. The lower content of CIK in the blood of foals obtained from mares that received the drug 'Lactakhos' compared to foals from other groups, indicates the functional maturity of their reticuloendothelial system, which is responsible for removing circulating immune complexes from the body and accumulating the antigen-antibody-complement complex in it. We explain the results obtained by the effect on the immune system of foals of essential microelements and the silicon-organic immunomodulator Mival, which are part of the Lactakhos preparation.

The desired effect was significantly less pronounced in foals born to mares that were fed the premix KM L2, although, compared to the control group, these animals had a higher number of PK cells and higher levels of NST-induced, NST-reserve, RBLT-spontaneous, RBLT-induced and lower levels of CIC in their blood.

Thus, the study of metabolic indicators in pregnant mares and their foals with the aim of preventing metabolic disorders and ensuring the health of these animals is a

pressing issue today.

Most of the feed additives and premixes currently used to prevent mineral metabolism disorders in horses contain a complex of inorganic macro- and microelement salts. Their action is aimed at meeting the needs of horses for minerals that normalise metabolic processes, activate redox processes and stimulate the body's defences. However, one of the significant drawbacks of such feed additives and premixes is the insufficient balance of their mineral compound structure, in the form in which they enter the animal's body with feed, especially given the physiological needs of mares during pregnancy.

Another, no less significant disadvantage of inorganic macro- and microelement salts in feed additives and premixes is that they are only 20–30% absorbed, and their excess has a toxic effect on the animal's body.

In view of this, the development and use of therapeutic and prophylactic agents for animals using biogenic compounds of macro- and microelements creates favourable conditions for the normalisation of metabolic processes in tissues, increases the immune resistance of the body, restores the structural and functional state of organs, and ensures the physiological course of pregnancy and the quality of offspring.

The organic compounds of biogenic elements in our Lactahos preparation are absorbed by animals by 80–100%, and their insignificant residue is easily excreted from the body and has no toxic effect on it. The Lactahos preparation normalises the overall metabolism, metabolic processes in tissues, activates the metabolism of proteins, carbohydrates and lipids, redox processes, stimulates haematopoiesis and the immune system of pregnant mares due to the action of its components, namely organic compounds of biogenic macro- and microelements, natural minerals and the silicon-organic immunomodulator Mival. During the development and formulation of Lactakhos, the specific characteristics of the soil, feed, water and blood of pregnant mares were taken into account under conditions of their commercial use at a stud farm in the Central Biogeochemical Zone of Ukraine. The results obtained allow us to recommend the Lactahos preparation for use in the treatment and prevention of mineral metabolism disorders in pregnant mares, maintaining the health of these animals and

obtaining healthy foals from them.

Thus, based on the results of clinical, spectrophotometric, morphological, biochemical and immunological studies, we provide a theoretical and clinical-experimental justification for the diagnosis, treatment and prevention of mineral metabolism disorders in pregnant mares and their foals using the complex mineral preparation Lactakhos. It has been established that the deficiency (or excess) of macro- and microelements in the soils of the corresponding biogeochemical zones of Ukraine, as well as in feed, water and the organism of animals, is one of the main aetiological factors in the occurrence and development of biogeocenotic pathology in horses, which is particularly severe in pregnant mares kept in stables and fed the same diet during the last third of their pregnancy, when the supply of calcium, phosphorus, manganese, zinc, iron, cobalt, copper and selenium to the animals' bodies is 132.2; 61.7; 67.5; 28.6; 347.2; 96.4; 44.2 and 31.0%, respectively, with an excess of calcium (1.32 times) and iron (3.47 times).

According to the results of clinical studies in pregnant mares, signs of mineral metabolism disorders were found, which manifested themselves in symptoms of skin, hair and hoof horn pathology, as well as allotriophagy, weakened intestinal peristalsis and low feed digestibility, indicating manganese, zinc, cobalt and selenium deficiency.

In the blood serum of pregnant mares with mineral metabolism disorders, compared to clinically healthy pregnant mares, a significantly lower content of magnesium (1.65 times), manganese (3.0 times), zinc by 1.36 times, cobalt by 3.94 times, and selenium by 1.46 times ($p < 0.001$).

Blood parameters of pregnant mares with mineral metabolism disorders, compared to clinically healthy animals, are characterised by a significantly lower number of erythrocytes (1.10 times), leukocytes (1.12 times) and lower haemoglobin content (1.16 times), ($p < 0.01 - p < 0.001$), which indicates suppression of haemocytopoiesis processes.

In the blood serum of pregnant mares with mineral metabolism disorders, compared to clinically healthy pregnant mares, there is a significant decrease in the content of total protein and glucose, an increase in the content of triglycerides and

cholesterol, and an increase in the activity of alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase, and the blood shows a significant decrease in the number of T-helpers, PK cells, B-lymphocytes, an increase in the number of T-suppressors and O-lymphocytes, and a decrease in the indicators of spontaneous HST, induced HST, HST reserve, RBT-spontaneous, RBT-induced, and the content of circulating immune complexes increases ($p < 0.01$ – $p < 0.001$), indicating an immunosuppressive state in mineral metabolism pathology.

After 42 days of using the complex mineral preparation 'Lactakhos' in pregnant mares, the clinical signs of mineral metabolism disorders disappear, the processes of haematopoiesis and the calcium-phosphorus ratio normalise, the content of phosphorus in blood serum increases by 1.21 times, copper – 1.25 ($p < 0.05$), magnesium – 2.02, manganese – 5.96, zinc – 1.73, cobalt – 3.48 times, and selenium – 2.58 times ($p < 0.001$), the level of iron decreases by 1.16 times ($p < 0.05$), calcium – by 1.30 times ($p < 0.001$), the content of total protein increases by 1.05 times, albumin – 1.29 ($p < 0.01$), γ -globulins – 1.08 ($p < 0.05$), the number of T-lymphocytes increases by 1.41, T-helpers – 1.82, PK cells – 1.34 times, B lymphocytes – 2.41 times, HST-spontaneous increases 1.31 times, HST-induced – 1.53 times, HST-reserve – 1.61 times, RBLT-spontaneous – 1.49, RBLT-induced – 2.19 times ($p < 0.001$), and the number of O-lymphocytes reliably decreases by 3.52 times ($p < 0.001$).

The biochemical parameters of blood serum in pregnant mares in the last month of pregnancy were found to be significantly higher in glucose concentration and lower in aspartate aminotransferase activity by 1.38 times, gamma-glutamyltranspeptidase activity by 1.66 times, alkaline phosphatase activity by 1.59 times, and globulin content by 1.18 times ($p < 0.001$), indicating a decrease in the intensity of biochemical processes in the mares' bodies before foaling.

The use of the drug 'Lactakhos' in pregnant mares has a positive effect on their foals, whose hair contains significantly higher levels of copper (1.17 times, $p < 0.05$), zinc – 1.27 ($p < 0.01$), cobalt – 1.45 and selenium – 2.16 times ($p < 0.05$), lower calcium content by 1.35 ($p < 0.001$) and iron by 1.68 times ($p < 0.01$); in blood serum – higher phosphorus content by 1.78 times, manganese – 3.14, zinc – 2.06, cobalt – 2.57,

selenium – by 3.05 times ($p < 0.001$), total protein by 1.12 times, albumin – 1.18 times, γ -globulins – 1.07 times ($p < 0.001$), a higher A/G ratio – 1.11 times ($p < 0.01$), in blood – a significantly higher number of erythrocytes – 1.20 times ($p < 0.01$), leukocytes – 1.28 times ($p < 0.001$), higher haemoglobin content by 1.10 times ($p < 0.01$), a higher number of T-lymphocytes by 1.11 times, PC cells by 1.27 times ($p < 0.001$), T-helpers by 1.20 times, B-lymphocytes by 1.22 times ($p < 0.01$), higher HST-spontaneous indicators by 1.20 times ($p < 0.01$), HST-induced by 1.38 times, HST-reserve by 1.45 times, RBTL-spontaneous (by 2.18 times), induced RBTL (1.41 times), a lower number of O-lymphocytes by 1.74 times and a lower content of circulating immune complexes by 2.97 times ($p < 0.001$), no clinical signs of mineral metabolism disorders were observed in foals.

Thus, the diagnosis of mineral metabolism disorders in horses should be comprehensive and take into account the characteristics of the biogeochemical zone and province, the content of minerals in feed and water in the diet and the animals' need for them, which depends on age, physiological condition, exploitation, etc., as well as the clinical condition of the animals, the results of morphological, biochemical, immunological and spectrophotometric studies of their blood.

For the treatment of pregnant mares with mineral metabolism disorders and the prevention of these disorders in their foals, it is recommended to use the complex biogenic preparation 'Lactahos', which contains zinc lactate, copper lactate, cobalt lactate, manganese lactate, starch iodine, triethanolamine salt of selenic acid, the organosilicon immunomodulator 'Mival,' and plaster. The preparation 'Lactahos' is recommended to be used in the form of a homogeneous mixture with feed, once a day for 42 days, during the morning feeding, at the rate of 5.0 g per 450 kg of body weight, starting from the 8th month of mare pregnancy.

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