

# Geoecological-endemic and technogenic aspects of metabolic disorders in breeding cows in the conditions of Uzbekistan

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**Abstract.** The article presents the results of scientific research which is aimed at studying the type, etiology and pathogenetic features of hipomicroelementosis in breeding cows in the conditions of the Takhtakupir and Muynak districts of the Karakalpakstan Republic, the Altinkul and Pakhtaabad districts of the Andijan region, the Sariasia and Angara districts of the Surhandarya regions of Uzbekistan in connection with different levels salinity and trace element composition of the soil, as well as the technogenic properties of the area. The article proves that due to the inferiority of the diet in terms of energy and vitamin-mineral components against the background of high salinity of the environment and iodine-manganese endemicity, liver dystrophy and orthopedic pathology with an obligatory decrease in reproductive qualities develop in the body of breeding cows.

## 1 Introduction

Animal diseases associated directly with geo-ecological and endemic environmental conditions in imported breeding livestock are one of the main inhibitory factors in fulfilling the tasks provided for in the Law of the Republic of Uzbekistan Law of the President N4576 on January 29, 2020 “On additional measures for state support of the livestock industry”, as well as in other regulatory documents aimed at improving the living standards of the population of the Republic through the comprehensive development of livestock farming and ensuring the epizootic situation in veterinary medicine [1].

Research has established that in some farms with a relatively low standard of animal husbandry, diseases of metabolic disorders affect on average up to 50-70% of the dairy cow population and, at the same time, due to a sharp drop in fatness and milk productivity, deterioration in reproductive qualities, the birth of low-viable young animals, as well as an increase in cases of forced slaughter cause great economic damage to the Republic's farms, which dictates the development of a set of measures, including methods of early diagnosis, modern therapy and effective group prevention of this pathology [2-3].

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It was noted that productive cattle primarily suffer from hypotony and atony of the rumen with a transition to rumen acidosis. The incidence rate of this illness in productive livestock is 18.9-72.9%, including in summer - 18.9-28.8 %, in autumn - 31.0-42.5%, in winter - 49.4-72.9% and in spring 42.9-63.1% respectively. Highly concentrated feeds, based on the dominant role of grain feeds rich in starch, are the main cause of rumen acidosis in 50-60% of cases, and in 40-50% of cases - low-nutrient feeding of productive cows [2-3, 5].

Secretion of hydrogen ions in the rumen content to the acidic direction (pH decreasing from 5.88 to 5.38) and an increase in the amount of lactic acid on the average of up to 14 mmol/l, as well as pungent odour, brown colour and mash-like consistency of rumen content are observed in productive cows with rumen acidosis. The ciliates' vitality and activity in the forestomach are sharply disrupted, and their number decreases to 198-192 thousand/ml (normal in healthy cows it is on average around 700 thousand/ml). The composition of the ciliates species also changes - a decrease in the number of the genus *Isotricha* and *Dasytricha* from 4 to 0.5%, *Entodinium* - from 70 to 62-44%, and an increase occurs in the number of ciliates from the genus *Diplodinium* - from 25 to 42-32% and *Ophryoscolex* - from 1 to 2-13.5%. The species composition of beneficial bacteria in the forestomach changes dramatically. In particular, the proportion of bacteria synthesizing lactic acid from the genus *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* reaches 94.37%, the proportion of bacteria that digest lactic acid will decrease to 5.42% of the total number of lactic acid bacteria [4, 7].

For group prevention of rumen acidosis in productive cows, it is recommended, in addition to the main diet, to use a preventive complex consisting of internal use of sodium bicarbonate ( $\text{NaHCO}_3$ ) at a dose of 30 g and a premix of a particular microbial composition GELAMIN VARIO FERM at a dose of 150 g per day, intramuscular administration every 25 days Multivit + minerals in a dose of 20 ml [5, 10].

It is recommended to carry out the early diagnosis of endemic goiter in cows, considering the endemic characteristics of the area. According to the clinical examination methodology, this must be done through zootechnical analysis of the feed, clinical studies of animals aimed at identifying a specific oval physique, folding of the skin, roughness, ruffled skin and alopecia of the skin, "false eyebrows" and "false manes", retardation in growth and development muscle tissue, morphometric enlargements of the thyroid gland, as well as laboratory blood tests should be provided to detect thyroid pathology (T4, TSH, T3) and liver markers [6, 8-10].

To prevent endemic goiter in cows, it was recommended the daily use of activated iodized salt in a dose of 50 g, the universal premix "Blattin Premium" in a dose of 5 g and intramuscular injections of 10% thyroid extract (at a dose of 5 ml/100 kg, a total of five times at 1st, 3rd, 8th, 18th and 33rd days of the experiment) and Trivit following the instruction [7].

Based on the above, there is no consensus on the spread, diagnostic approach, treatment and prevention of the more common diseases of imported livestock. Therefore, etiology, early diagnosis, treatment methods, and preventive measures for the common non-contagious diseases of imported livestock in the Republic of Uzbekistan are still relevant.

The aim of the study. Determination of prevailing pathologies, study of pathogenesis, development of early diagnosis, effective therapy and prevention in imported breeding cattle in the conditions of alimentary-geoecological and endemic-technogenic zones specific to Uzbekistan.

## 2 Materials and methods

The experiments were carried out in 2021-2023 on cows of the Goldstein and Simmental breeds in the Seyit Sharua farm of the Takhtakupir and Kazakhdyra agro-industrial complex of the Muynak region of the Republic of Karakalpakstan and the district of Pakhtabad, in the farm "Kelajak Omadi" of the Altinkul district of the Andijan region, in the farm "Kulpista" of the Sariasia and the farm "Chorvador Normumin" of the Angora district of the Surkhandarya region of Uzbekistan. Organoleptic observations of the liver and thyroid gland of culled cows and seasonal clinical examination of live cows were carried out. Clinical-physiological and hemo-morpho-biochemical parameters and the trace element content in the soil in different areas where clinical experiments were carried out were considered.

## 3 Results and Discussion

The results of clinical studies in the near Aral Sea region (the Republic of Karakalpakstan) show that of the examined breeding cows, 5-27.5% had a decrease in appetite (some of these had licking), 19.0-33.5% had hypotony and atony of the forestomach, 36.2-88.0% - diarrhea, 15.0-42.3% - ruffled skin and decreased skin elasticity, 13.7-22.0% - varying degrees of icterus and anemia of the mucous membranes, 19.3-44.0% - increased heart rate, 17.0-52.2% - increased breathing, 12.0-30.2% - enlarged liver, and 19.0-36.2% - pain in the liver area, 17.0-25.0% have diseases of the extremities, such as laminitis, pododermatitis, etc.

The results of laboratory blood tests show the number of red blood cells was 4.22-5.15 million/ $\mu$ l, hemoglobin - 87.2-107.0 g/l, total protein - 65.46-68.5 g/l, glucose - 2.18-2.48 mmol/l, total bilirubin - 1.59-1.74  $\mu$ mol/l, conjugated bilirubin - 0.30-0.38  $\mu$ mol/l and unconjugated bilirubin - 1.30-1.39  $\mu$ mol/l, activity of ALT - 2.48-2.75 mmol/l and AST - 1.59-2.29 mmol/l, total calcium - 9.7-10.8 mg%, inorganic phosphorus - 4.98-5.63 mg%, copper - 0.211-0.242%/of the pulp, manganese - 0.027-0.055%/ of the pulp, zinc - 0.121-0.132%/ of the pulp, iron - 9.21-11.78%/ of the pulp, potassium - 3, 07-5.61%/ of the pulp, chlorine - 37.2-41.9%/ of the pulp, and magnesium, cobalt, iodine and sodium were almost not foundable in blood or were found in traces. The results of chemical studies of feed showed that the acidity in wheat straw was 1.35% (with a norm of 0.8-5.0%) and in corn silage - 2.7% (with a norm of 2.7-5.0%), the chloride content was, respectively, 1.77% (with a norm of 1.0-1.5%) and 3.5% (with a norm of 1.0-1.5%).

The results of biogeochemical soil studies showed that in the soils taken from the territories of the Kazakhdyra farm in the Muynak region, the manganese content was in the range of 20-25 mg/kg, in the Bozatau region, it was 100-130 mg/kg, and in the Kungrad region 50-55 mg/kg respectively.

In the conditions of the Andijan region, the organoleptic studies of the cow gall bladder revealed - fullness in 8% of cases and poor filling or absence of bile in 64% of cases.

Organoleptic studies of the liver tissue of slaughtered cows revealed hepatitis in 24% of cases, dystrophy in 40% of cases, cirrhosis in 20% of cases, abscess in 12% of cases, echinococcosis in 16% of cases, and fascioliasis in 16% of cases.

The results of the clinical examination of breeding cows revealed that 35-50% had a decreased appetite (some of these had licking), 30-35% had hypotony and atony of the forestomach, 13.7 - 22% had diarrhea, 30 - 40% - ruffled skin and decreased skin elasticity, 15-25% - varying degrees of icterus and anemia of the mucous membranes, 30-35% - increased heart rate, 35-40% - increased breathing rate, 5-25% - enlarged liver, and 20-45% painful the liver area, in 10-20% there was the sharpness of the incisor teeth and resorption of the last caudal vertebrae, in 13.7-20% there were diseases of the extremities,

such as laminitis, pododermatitis, etc. Average cow fatness was noted in 50– 60%, below average - in 20-30, and obesity - in 20% of animals.

The results of the laboratory blood tests showed that the number of red blood cells was 4.95-5.45 million/ $\mu$ l, hemoglobin - 95.32-101.7 g/l, total protein - 60.30-65.8 g/l, glucose - 2.28-2.44 mmol/l, total bilirubin - 1.78-1.96  $\mu$ mol/l, conjugated bilirubin - 0.41-0.63  $\mu$ mol/l and unconjugated bilirubin - 1.32-1.33  $\mu$ mol /l, activity of ALAT - 2.54-2.60 mmol/l and ASAT - 1.88-1.98 mmol/l, total calcium - 2.7-2.57 mmol/l, inorganic phosphorus - 1.54 - 1.59 mmol/l, ketone bodies - 4.78-5.6  $\mu$ mol/l (Table 1).

The results of the laboratory blood tests for microelements showed that the potassium content in the blood was 3.22-3.46% of the pulp, iron was 1.62 - 11.18% of the pulp, copper - 0.225 - 0.250% of the pulp and zinc - 0.122 - 0.125% of the pulp. The blood's magnesium, cobalt, iodine, selenium and sodium content were almost not detectable or found in trace amounts.

The results of studying soil samples from different areas of the Andijan region for macro and micro elements showed that magnesium, selenium, iodine and sodium were completely absent in all soil samples.

Regarding phosphorus content, the highest content (0.553%/ of the pulp) was observed in the Markhamat region, and the lowest (0.193%/ of the pulp) in the Asaka region. The sulfur was detected (3.10%/ of the pulp) in Altinkul region and less (0.327%/ of the pulp) in the city of Andijan (0.327%/ of the pulp). The chlorine - in the Shakhrikhan region (0.8840%/ of the pulp) and in the city of Andijan (0.0916% of the pulp).

**Table 1.** Morphological and biochemical parameters in investigated cows' blood.

No	Parameters	Farm "Kelajak Omadi" Altinkul district	
		11.05.23	18.08.23
1.	Red blood cells, million/ $\mu$ l	4.95	5.45
2.	Hemoglobin, g/l	95.32	101.7
3.	Total protein, g/l	60.30	65.8
4.	Glucose, mmol/l	2.44	2.28
5.	Total calcium, mg%	2.37	2.57
6.	Inorganic phosphorus, mg%	1.54	1.59
7.	Ketone bodies mmol/l	5.06	4.78
8.	Bilirubin, $\mu$ mol/l:		
	- total	1.96	1.78
	- conjugated	0.63	0.41
	- unconjugated	1.328	1.33
9.	ALAT, mmol/l	26.0	25.4
10.	ASAT, mmol/l	19.8	18.8

The lowest indicators for potassium (3.58%/ of the pulp) were found in the Asaka region and for calcium (25.1%/ of the pulp) in Markhamat district. In the samples from Shakhrikhan, was found manganese (0.202%/ of the pulp), iron (10.2%/ of the pulp), copper (0.0135% of the pulp), zinc (0.0327%/ of the pulp), cobalt (0.0070%/ of the pulp) and silicon (37.5%/ of the pulp). In Altinkul region sample, aluminum was detected at 8.48%/ of the pulp.

In Surkhandarya region, the organoleptical study of samples of cow liver tissue revealed that in the conditions of the Angar district, infection with hepatitis was 20%, the average weight of the thyroid gland was 90-130 g, but in the conditions of Sariasia district, it was 40% and 100-550 g respectively.

In Angor region, the results of the clinical studies of productive cows were - pulse on average 55.0 times/min, breathing - 14.0 times/min, and rumination - 3.8 times/2 min. In the conditions of the Sariasia region, where there are man-made factors (high fluorine

content in the environment), these indicators were 61.0 times/min, 17.8 times/min, and 3.4 times/2 min, respectively. In addition, in Angor region, the number of animals with signs of chromatism was 20%, resorption of the last caudal vertebrae - 40%, fluorosis - 20%, which in Sariasia region was 40%, 60%, 40%, respectively.

The animals with below-average body condition accounted for 40% of Angor region and 60% of Sariasia region.

The average milk yield per cow in Angor region in the first month of lactation was 15 kg, in the second - 12 kg; in the third - 13 kg, and in the fifth - 11 kg, while in Sariasia region, these parameters were 10, 12, 11 and 8 kg, respectively.

The results of studies of blood samples showed that in the conditions of Angor region, there was a decrease in the number of red blood cells in the blood compared to standard indicators, and so which averaged 80-90%, hemoglobin 70-80%, total protein 70-90%, glucose 60-70%, total calcium 80-90%, inorganic phosphorus 70-80%, ASAT activities 120-140%, ALAT 120-150%, ALP 100-120%, and in the Sariasia region, 70-80%, 60-80%, 60-70 %, 50-60%, 70-80%, 60-7%, 150-160%, 150-180%, 100-140% respectively.

Thus, the research results of many years show that the most often non-contagious etiology diseases which breeding cattle suffer, first of all, are hypotony and atony of the forestomach with the transition to rumen acidosis, nutritional dystrophy, ketosis, osteodystrophy, endemic goiter, hepatosis (metabolic hepato-dystrophy), mixed hypovitaminosis with hypo-microelementoses and other types of metabolic disorders, feed toxicosis, limb diseases, infertility and secondary non-contagious pathologies due to blood parasites, anaerobic-infectious, invasive and radioactive etiology.

In imported breeding cattle in the conditions of Uzbekistan, the predominant non-contagious diseases are complex multi-stage metabolic pathology (CMMP), consisting of diseases that develop in stages, such as hypotony and atony of the forestomach, rumen acidosis, ketosis, alimentary osteodystrophy, hepatosis (metabolic hepato-dystrophy), endemic iodine deficiency, orthopedic diseases, nutritional dystrophy with hypo- and agalactia and infertility. The etiology of these diseases is characterized by multipolarity, which is characterized by the simultaneous action in the development of this pathology of nutritional (inadequate diet) and geo-ecological-endemic (high salinity, iodine endemia, man-made factors) and some secondary (invasion, infection, feed toxicosis) factors. In pathogenetic terms, in almost all these cases, there is a stage of metabolic hepato-dystrophy.

Clinical signs of CMMP in the stage of metabolic hepato-dystrophy are characterized by general metabolic syndrome, special hepato-clinical signs and special hepato-biochemical changes. The general metabolic syndrome is a noticeable decrease in milk production, weight loss, altered appetite (licking), increased incidence of hypo- and atony of the forestomach, obstetric and gynecological diseases (retention of placenta, *coma puerperalis*, congestion, infertility, etc.), diseases of metabolic disorders (ketosis, nutritional osteodystrophy, obesity, nutritional dystrophy) and diseases of young animals (dyspepsia, rickets, etc.), unprofitability of livestock farming.

The specific hepato-clinical signs are characterized by icterus of the mucous membranes and subcutaneous tissue at slaughterhouse, an increase in the border of the liver and its pain on percussion and palpation.

Special hepatobiochemical changes are characterized by:

- *Hypoalbuminemia* (reduction of albumin to  $26.0 \pm 0.50\%$ ).
- *Hypouraremia* (decrease in urea to  $1.8 \pm 0.04$  mmol/l).
- *Hypoglycemia* (decrease in glucose to  $1.48 \pm 0.030$  mmol/l).
- *Hyperbilirubinemia* (increase in bilirubin to  $4.70 \pm 0.14$   $\mu$ mol/l).
- *Hyperlipidemia* (increase in NEFA - up to  $20.5 \pm 0.84$  mg%, volume cholesterol - up to  $3.32 \pm 0.12$   $\mu$ mol/l),

- *Enzymeopathy* (increased activity of ALAT - up to  $0.45 \pm 0.01$  mmol/l, ASAT - up to  $0.92 \pm 0.03$  mmol/l, LDH - up to  $5.01 \pm 0.41$   $\mu$ mol/ml., SDH - up to  $2.0 \pm 0.17$   $\mu$ mol/ml., GGT - up to  $128.4 \pm 4.35$   $\mu$ mol/ml., decrease in ChE activity - up to  $51.4 \pm 1.88$   $\mu$ mol/ml).  
*The amount of ketone bodies* in the blood, milk and urine during MSPOV in the stage of intensive ketosis in an imported highly productive cow (mg%):
- *In the blood* – hyperketonemia, up to 10-50 mg% (a norm 4-6 mg%).
- *In milk* – hyperketonolactia, up to 50-100 mg% (a norm 7-8 mg%).
- *In the urine* – hyperketonuria, up to 100-1000 mg% (a norm 9-10 mg%).

As prophylactic measures were used: *Ketost* (I.P. Kondrakhin, Russia); *Alost* (I.P. Kondrakhin, Russia); *Ultraketost* (B. Bakirov, N.B. Ruzikulov, A.S. Berdiyrov, Uzbekistan); *Gepastimulin* (B. Bakirov, N. B. Ruzikulov, Uzbekistan); *Activated table salt* (B. Bakirov, O.R. Boboev, Uzbekistan); *Thyroid gland extract* (B. Bakirov, O.R. Boboev, Uzbekistan) according to the rules specified in the instructions for each product.

**Table 2.** ULTRAKETOST (Bakirov B., Ruzikulov N.B., Berdiyrov A.S., 2007).

No	Compound	Quantity, g
1.	Bentonite	200.0
2.	Sodium chloride	300.0
3.	Monocalcium phosphate	200.0
4.	Urea	200.0
5.	Sodium bicarbonate	49.7
6.	Cobalt chloride	0.2
7.	Sodium selenite	0.1
8.	HWP (Hydroponic Wheat Powder)	50.0
Total weight		1000.0

Simultaneously with group prevention, nutritious feeding of highly productive cows was organized. The results showed that the most effective option for optimal feeding of breeding cows with an average daily milk yield of 10 kg was a diet where the total nutritional value for each kilogram of milk production per day was, on average, 1.0-1.2 feeding units. Each unit contains 100 - 120 g of digestible protein, 80-100 g of sugar, 6-7 g of calcium, 3 - 4 g of phosphorus, 20 - 30 mg of carotene, 0.3-0.5 g/kg (based on body weight) lipids; the sugar-protein ratio is 0.8, the calcium-phosphorus ratio is 1.5-2.0. In the diet structure, high-quality roughage comprised 18–20%; concentrates 40–50%; root tubers 5–10%; silage-haylage 15-20%; and cotton industry feed 10-20%. Thus, it is recommended to give cows with daily productivity of 8–10 kg of milk per day: 3–5 kg of high-quality hay (of which 2–3 kg of alfalfa hay); 3-5 kg of local roughage; 3-5 kg high-quality concentrated feed; 15 - 20 kg of silage haylage; 3-5 kg of root and tuber crops; 1.0–1.5 kg cotton cake or meal; 50-60 g of activated table salt and premix according to instructions.

## 4 Conclusion

- Among the diseases of breeding cows in the Aral Sea region, the leading place is occupied by complex pathology, including deep metabolic disorders with the dominant manifestation of microelementosis and hepatitis; in the conditions of the Andijan region - hepatitis, developing against the background of deep metabolic disorders, in the conditions of technogenic zones of the Surkhandarya region - displaced pathology, including disorders of protein and mineral metabolism, iodine endemia and liver dystrophy.

- In addition to nutritionally deficient feeding, the main etiological factors of metabolic disorders in breeding cows in the Aral Sea region are high soil salinity and low content of individual microelements such as manganese, zinc and cobalt, as well as high chloride content in feed; in the conditions of the Andijan region - iodine-selenium and sodium-magnesium endemic areas were found, and in the conditions of the Surkhandarya region - iodine endemic deficiency and technogenic salinity of the external environment was detected.
- The pathogenesis of metabolic disorders in breeding cows in different geo-ecological-endemic zones of Uzbekistan is characterized by the development of a complex multi-stage metabolic pathology (CMMP), consisting of hypotony and atony of the forestomach, rumen acidosis, ketosis, nutritional osteodystrophy, hepatosis (metabolic hepato-dystrophy), endemic iodine deficiency, orthopedic diseases, nutritional dystrophy with hypo- and agalactia and infertility.
- Complex multi-stage metabolic pathology (CMMP) with a dominant manifestation of micro-elementosis and hepatosis in breeding cows (Aral zone) is clinically characterised in 5-27.5% of cases by a decrease in appetite (aliened appetite and licking), in 19.0-33.5% of cases - hypotony and atony of the forestomach, in 36.2-88% of cases - diarrhea, in 15-42.3% of cases - ruffled skin and decreased skin elasticity, in 13.7-22% of cases – icterus and anemia of the mucous membranes to varying degrees, in 19.3-44% of cases - increased heart rate, 17.0-52.2% of cases - increased breathing rate, 12.0-30.2% of cases enlarged, and 19.0-36.2% of cases – painfulness of the liver area, 17.0-25.0% of cases - diseases of the extremities, such as laminitis, pododermatitis, etc.
- Complex multi-stage metabolic pathology (CMMP) with a dominant manifestation of hepatosis in breeding cows (Fergana Valley) is clinically manifested in 35-50% of cases by a decrease in appetite (in some of these there is a licking), in 30-35% of cases - hypotony and atony of the forestomach, in 13.7-22% of cases - diarrhea, 30-40% of cases - ruffled skin and decreased skin elasticity, 15-25% of cases - varying degrees of icterus and anaemia of the mucous membranes, 30-35% of cases - increased heart rate, 35-40% of cases - increased breathing rate, 5-25% of cases - enlarged, and in 20 - 45% of cases painfulness of the liver area, 10-20% of cases - moveable incisor teeth and resorption of the last caudal vertebrae, 13.7-20% of cases - diseases of the extremities, such as laminitis, pododermatitis etc. Average fatness was noted in 50-60% of cows, below average was 20-30%, and obesity was noted in 20% of animals.
- Complex multi-stage metabolic pathology (CMMP) with the dominant manifestation of disorders of protein and mineral metabolism, iodine endemic deficiency and liver dystrophy in breeding cows (Surkhandarya region) is also clinically manifested by emaciation, decreased milk production, increased heart rate and respiration, hypo- and atony of the forestomach, fluorosis, resorption of the last caudal vertebrae, enlargement and pain of the liver, enlargement of the thyroid gland, as well as ortho-pedopathy and infertility.
- In case of a complex multi-stage metabolic pathology (CMMP) with a dominant manifestation of micro-elementosis and hepatosis in breeding cows (Aral zone), a decrease in the number of red blood cells, hemoglobin, total protein, glucose, calcium, inorganic phosphorus and an increase in bilirubin of all fractions, as well as an increase in activity, is observed in the blood ALAT and ASAT, in conditions where hepatosis becomes the dominant manifestation (Fergana Valley) - plus to these indicators, an increase in ketone bodies, and in conditions where protein and mineral metabolism disorders, iodine endemic deficiency and liver dystrophy acquire the dominant manifestation (Surkhandarya region) - a noticeable increase in alkaline phosphatase activity in the blood and changes indicating a peculiar thyroid pathology.

- Complex multistage metabolic pathology (CMMP) has the predominant importance among non-contagious diseases in imported pedigree livestock in the conditions of Uzbekistan. Its development mainly includes hypotony and atony of the forestomach, rumen acidosis, ketosis, alimentary osteodystrophy, hepatosis (metabolic hepatodystrophy), iodine endemic deficiency, orthopedic diseases, nutritional dystrophy with hypo- and agalactia and infertility. In pathogenetic terms, in almost all these cases, there is a stage of metabolic hepato-dystrophy, which is clinically characterized by a general metabolic syndrome, special hepato-clinical signs and special hepato-biochemical changes.
- Prevention of complex multi-stage metabolic pathology (CMMP) in the breeding cows must be organized based on the principle of complexity, including routine medical examination, organisation of adequate feeding and preventive therapy, depending on the specific geo-ecological zone and stage of the pathology.

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