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# METABOLIC PROFILES AND SPERM PRODUCTION IN IMPORTED HOLSTEIN BULL SIRES UNDER DIFFERENT CLIMATIC AND GEOCHEMICAL CONDITIONS OF RUSSIA AND KAZAKHSTAN

**A.I. ABILOV[1], N.A. KOMBAROVA[2] ✉, Kh.A. AMERKHANOV[3], S.A. SHEMETYUK[2], A.S. SHAMSHIDIN[1], S.V. MYMRIN[4], E.A. PYZHOVA[5], N.V. BOGOLYUBOVA[1], A.A. GUDILINA[4], S.F. ABILOVA[1], P.G. KOMBAROV[5], O.S. MITYASHOVA[1]**

[1]*Ernst Federal Science Center for Animal Husbandry,* 60, pos. Dubrovitsy, Podolsk District, Moscow Province, 142132 Russia, e-mail ahmed.abilov@mail.ru, 270180@mail.ru, 652202@mail.ru, info@vij.ru, mityashova_o@mail.ru;
[2]*Head Center for Reproduction of Farm Animals AO*, 3, ul. Tsentralnaya, pos. Bykovo, Podolsk Region, Moscow Province, 142143 Russia, e-mail komnina@list.ru (✉ corresponding author), csio-secr@yandex.ru;
[3]*Timiryazev Russian State Agrarian University—Moscow Agrarian Academy,* 49, ul. Timiryazevskaya, Moscow, 127550 Russia, e-mail h.amerhanov@rgau-msha.ru;
[4]*Uralplemcentr OAO*, 21 km, Siberian tract, Ekaterinburg, 620913 Russia, e-mail mymrinsv@yandex.ru, gudilina.vet@mail.ru;
[5]*Lomonosov Moscow State University, Faculty of Geography*, 1, *Leninskie gory*, Moscow, 119991 Russia, e-mail Lena.pyzhova@gmail.com, pavel.kombarov@mail.ru
ORCID:
Abilov A.I. orcid.org/0000-0001-6236-8634
Kombarova N.A. orcid.org/0000-0003-3861-4465
Amerkhanov Kh.A. orcid.org/0000-0001-7680-3748
Shemetyuk S.A. orcid.org/0000-0002-1280-102X
Shamshidin A.S. orcid.org/0000-0001-5457-1720
Mymrin S.V. orcid.org/0000-0001-5173-984X
Pyzhova E.A. orcid.org/0000-0001-5719-3075
Bogolyubova N.V. orcid.org/0000-0002-0520-7022
Gudilina A.A. orcid.org/0000-0002-7962-5315
Abilova S.F. orcid.org/0000-0002-3340-1631
Kombarov P.G. orcid.org/0000-0001-6713-1855
Mityashova O.S. orcid.org/0000-0002-0401-5088
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Abstract

Currently, the potential of highly productive animals adapted to industrial farming should be used most effectively and not depend on the geographical location and agro-climatic resources of the region. Our study showed that the observation of required technologies minimizes effects of regional climatic and geochemical factors. Our findings give more understanding on the metabolic peculiarities of the sire bulls in various geo-climatic conditions of the 55.86°N and 51.18°N zone. This may be of interest for the practice of breeding the Holstein breed in countries with similar geo-climatic factors. We compared the influence of climatic and geochemical conditions of the Central Russia (the Head Center for the Reproduction of Farm Animals, Moscow Province), the Middle Urals (JSC Uralplemcenter, Sverdlovsk Province), and the Northern Kazakhstan (RCPZh JSC Asyl-Tulik, Akmola region) on the adaptive status of the imported Holstein 3-9-year-old bull sires ($n$ = 122). Blood levels of bioelements Ca, P, Mg, Ca:P, Fe, chlorides, Se, Cu, and Zn were recorded. To assess protein-lipid metabolism parameters and blood enzyme activity, the total protein, albumin, globulins, urea, creatinine, total bilirubin, urea, triglycerides, cholesterol, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were measured. The endogenous hormone levels (testosterone, estradiol, thyroxine, and cortisol) were measured. The volume of ejaculate, the concentration of spermatozoa in the ejaculate, and the number of spermatozoa in the ejaculate were assessed to evaluate sperm productivity. Climatic and geochemical characteristics of the regions were a temperate climate with sod-podzolic soils for the Moscow region, a sharply continental climate with bedrock rocks with sandy-clayey and sod-podzolic soils for the Middle Urals, and sever sharply continental climate with dark chestnut soil for the Northern Kazakhstan. The study revealed that the balance of macroelements was within the permissible limits and did not have significant differences between regions, i.e., 2.34-2.53 mmol/l Ca, 1.47-2.01 mmol/l P (Ca:P 1.20-1.65), and 0.79-0.98 mmol/l Mg. The iron supply in the Moscow region was within the normal range (23.82±6.18 μmol/l), reached the upper limits in the Northern Kazakhstan (30.74±6.97 μmol/l) and exceeded the physiological level (40.32±7.30 μmol/l) in the Middle Urals. The balance of Se (0.72-1.13 μmol/l) and Cu (12.6-16.0 μmol/l) was within allowed limits. On the soils of the Moskvoretsko-Oka geochemical province (the Head Center for the Reproduction of Farm Animals), the bulls were 65.8 % provided with Zn compared to 95.9 % provision (of that minimum allowed) observed in the dry steppe zone on dark chestnut soils of the Northern Kazakhstan. The enzymatic activity (as per the de Ritis coefficient) increased 2-fold in bulls of the Moscow region and the Northern Kazakhstan. All the sires had a sufficient concentration of both total protein and its fractions. The sires of the Moscow region fed an excessive amount of protein, as evidenced by the urea concentration at the upper limit (7.57±2.82 mmol/l) and creatinine 147.45±37.94 μmol/l). The bulls of the Northern Kazakhstan showed iron overload syndrome of 30.74±6.97 μmol/l with an increased bilirubin of 9.15±3.42 μmol/l. The balance of blood steroid hormones indicates a slight testosterone deficiency (39.17±5.06 nmol/l) and an excess of cortisol (226.75±45.62 nmol/l) in bulls of the Moscow region compared to the Middle Urals (50.36±5.80 and 138.81±21.48 nmol/l) and Kazakhstan (52.79±4.14 and 190.50±50.30 nmol/l); the differences are not statistically significant. The average level of blood thyroxine was within the physiologically permissible values, from 66.65±3.52 nmol/l in the Middle Urals to 91.13±3.35 and 95.39±1.86 nmol/l in the Moscow region and the Northern Kazakhstan, respectively. The level of estradiol varied from 0.197±0.02 nmol/l in the Moscow region to 0.234±0.02 and 0.276±0.04 nmol/l in the Northern Kazakhstan and the Middle Urals, which fit into physiological norms of 0.2-0.4 nmol/l for bull sires. The average ejaculate volume varied from 3.72 to 4.87 ml, with an average sperm concentration of 1.21-1.52 billion/ml. The total number of spermatozoa in the ejaculate was 5.32-6.00 billion; the differences were not statistically significant. Therefore, stable keeping conditions, strict control of the requirements in nutrients and mineral elements, and proper light regime (morning-day solar insolation, darkness at night) make it possible to avoid the negative influence of climatic and geochemical factors on breeding animals.

Keywords: bulls, Holstein breed, spermatozoa, metabolic balance, protein-lipid balance, bio-element balance, endogenous hormones, climatic zones, adaptation

Currently, when milk production is concentrated at large enterprises, the potential of highly productive animals adapted to industrial farming should be used most effectively and not depend on the geographical location and agro-climatic resources of the region [1, 2].

In Russia, the development of dairy farming is determined and limited by a certain set of agro-climatic factors [3—5]. It is known that the breed zoning of cattle is based on the specifics of fodder and climatic features of ecological and biogeochemical provinces, which is largely related to the bio-element status and body functions [6, 7]. Traditionally, dairy cattle breeding tends to areas of intensive agriculture. The territories of the Russian Federation with developed dairy cattle breeding are geographically located between 60 and 50 °N and are bounded by the Sayans from the east. According to the All-Russian Research Institute of Breeding (VNIIplem, Moscow Region) for 2018, 70.0% of the judged dairy livestock of the Russian Federation is concentrated on the East European Plain in the second climatic zone. The southern part of the West Siberian Plain, belonging to the third climatic zone, accounts for only 20.4% of the dairy cattle population. The potential of these territories can be used for the development of dairy cattle breeding in the Russian Federation.

In dairy cattle breeding, in terms of productivity and adaptability to industrial conditions, the world popularity belongs to Holstein cattle [8-11], despite the limited period of production [12-14]. According to VNIIplem data for 2018, in Russia, this period averages 2.0-2.3 lactations.

The spread of Holstein cattle in Russia began in the 1970s when in the advanced farms of the USSR, imported Holstein bulls were used to improve the dairy productivity of black-and-white cattle [15]. Since the 2000s, breeding stock has been actively imported to complete large high-tech agricultural holdings that have replaced inefficient farms [16]. Due to the enlargement of dairy production, the displacement of zoned breeds has accelerated due to the influx of blood, as well as the import of heifers and spermatozoa of highly productive Holstein cattle [17]. As a result, breeding enterprises in various regions of the Russian Federation began to massively abandon the bulls of zoned breeds, replacing them with imported Holstein sires from countries with developed dairy farming — Canada, the USA, France, Germany, the Netherlands; their share in the structure of the herd of bull sires of the Russian Federation is 60% [18].

However, the exploitation of highly productive Holstein cattle (including bull sires) revealed difficulties associated with the diversity of natural and climatic conditions in Russia and an unusual fodder base for animals [19]. The Russian Federation has accumulated considerable experience in studying the processes of adaptation of productive breeding stock and bull sires in various climatic conditions [20, 21].

When transferring highly productive animals to conditions different from their typical habitat, with a sharp change in climate and time zones, the body experiences adaptive stress, expressed in a shift in metabolic processes [22–26]. During long-term breeding in the conditions of the specific climate of Sakhalin, an adaptive decrease in the productive potential of Holstein cattle was noted [27]. There is evidence that Holstein cattle adapt to hypothermia faster than to hyperthermia [28, 29]. One of the reasons for metabolic adaptation syndrome in highly productive Holstein cattle is an unbalanced diet and feed of inadequate quality [20, 30, 31].

Bull sires of the Holstein breed, obtained from highly productive mothers [32], are also sensitive to changes in environmental conditions, feed quality, farming and operation technology. With an increase in the genetic potential of productivity in cows, adaptive stress is increasingly noted, which develops into a metabolic syndrome in their calves. When acclimatizing bull sires, it is important to minimize the consequences of changes in time zones, climatic, and feeding conditions [33] to avoid prolonged adaptation and persistent decline in spermatozoa quality as a stress response [34].

The quality of the spermatozoa depends on the physiological status of the bull sire and determines its role in the reproduction of offspring, which is not limited to the actual fertilization of the cow. It was found out that the nature of the stress response in the next generation was determined by nine types of miRNAs that are present in spermatozoa [35, 36]. Changes caused by external factors are inherited from fathers through DNA methylation of spermatozoa, modification of proteins involved in DNA packaging, as well as through epigenetic modifications caused by changes in the composition and structure of RNA contained in spermatozoa, therefore, males under chronic stress produce offspring with a significantly weakened stress response in adulthood [37]. The quality of spermatozoa affects both the efficiency of female fertilization and the ability of the embryo to survive throughout pregnancy [38]. Individual differences in gene expression in bull sires and the coherence of such differences with the effectiveness of artificial insemination were determined [39]. The presence of aberrant RNA in defective spermatozoa can affect and even disrupt early embryogenesis [40]. Thus, oxidative stress of spermatozoa, neuropathy, and androgen deficiency induced by the metabolic syndrome are the most significant mechanisms for the realization of its neuroendocrine and reproductive consequences [41].

Deviations from the physiological norm in terms of protein-lipid and bioelement status reflect the functional state of organs and systems of the body, serve as an early marker of metabolic syndrome before its clinical manifestations [42]. Earlier, the authors of this paper analyzed in detail the protein-lipid [43] and trace element [44] status of bull sires in connection with sperm production and spermatozoa quality. Metabolic syndrome is accompanied by dysfunction of the endocrine system, including androgen deficiency in males [45, 46]. The authors' previous studies have described in detail the hormonal status of highly productive bulls of modern breeding [47-50]. The endocrine system is the most important regulatory link that supports homeostasis. In male mammals, the content of hormones in the peripheral blood varies depending on the region of habitat. This indicator is influenced by many factors, in particular, the length of daylight as the most stable value for a particular latitude in the same periods of the year. The length of daylight determines the cyclicity of processes in the body, including at the level of regulatory systems [51-55]. It changes throughout the year, most clearly it is noticeable with a change in geographical latitude [56]. The direct dependence of the content of thyrotropin, prolactin, cortisol, and insulin in the blood and the reverse – for somatotropin, thyroxine, and triiodothyronine on the duration of daylight has been established [57].

The latitude factor is determined by the angle of sun rays, but their distribution depends on cloudage, surface relief, and the degree of air transparency. Radiation balance is one of the main climate-forming factors. It forms and determines the natural heat turnover, seasonal changes in air and soil temperature, the rate of evaporation, and some other important ecological and climatic characteristics of the area. Thus, geographical points located at the same latitude but different longitudes are in different climatic conditions [58].

Different studies provide data on the effects of ultraviolet radiation, the intensity of which is closely related to the latitude factor. In particular, with the displacement of the place of habitat from the equator to the poles, ultraviolet radiation decreases, a lack of vitamin D occurs in the body [59]. The role of this vitamin is not limited to the regulation of phosphorus-calcium metabolism, and the development of the metabolic syndrome and obesity is associated with a decrease in its amount [60, 61].

Constant exposure to climatic factors (along with seasonal fluctuations in the amount of hormones), daylight duration, and solar insolation can cause changes in the functional reserves of the endocrine system [62].

It should also be taken into account that even within the natural zone, the adaptability of animals of the same breed, but imported from countries with different climatic conditions, may be different and depend on many factors, including the chemical characteristics of water and soil cover [7]. In the work by Krymova *et al.* [63], a pattern of fluctuations in the concentration of trace elements with zonal gradation in tissue samples depending on the place of residence or birth of an individual was found. The content of strontium, lead, copper, and zinc in water, soil and plants increases zonally from humid (wet) to arid (dry) climatic zones. The reverse pattern is typical for manganese: the highest concentrations are observed in wet zones, the lowest in steppe dry zones. An increase in the concentration of lead and copper in geochemical provinces is associated with high man-made pollution. Mineral exchange and its significance for bull sires are described in more detail earlier in the work [44].

Thus, the quantitative and qualitative indicators of sperm are determined not only by the genotype but also by the peculiarities of the individual's metabolism and hormonal status. These features, in turn, depend on natural and climatic factors, which are determined by the geolocation of the individual. However, in the practice of animal husbandry, these circumstances, as a rule, are not considered entirely. In this work, for the first time, the authors conducted a comprehensive (by 33 parameters) study of the influence of climatic and geochemical conditions of Central Russia, Middle Urals, and Northern Kazakhstan on the enzyme status, macro- and microelement balance, protein-lipid metabolism, endogenous hormone production and the formation of the adaptive status of Holstein bull sires of foreign breeding in connection with sperm production. It is established that the negative effect of regional climatic and geochemical factors can be minimized if all technological regulations are observed. The study results expand the understanding of the peculiarities of the metabolism of bull sires in various geoclimatic conditions of a moderate circulation zone between 55.86 and 51.18 °N, which may be of interest for the practice of breeding Holstein breed in countries with similar natural factors.

The purpose of the study is to compare the influence of climatic and geochemical conditions of Central Russia, Middle Urals, and Northern Kazakhstan on the formation of the adaptive status of imported Holstein bull sires.

*Materials and methods.* The study was carried out in 2017-2018 on 122 Holstein bull sires of foreign origin aged 3 to 9 years: 20 bulls — JSC Head Center for Reproduction of Farm Animals (JSC HCR, Moscow Region), 56 bulls — JSC Uralplemcenter (Sverdlovsk Region), 46 bulls — JSC RCPZh Asyl-Tulik (Akmola Region, Republic of Kazakhstan). The conditions of feeding and farming the animals corresponded to the requirements of the National Technology of freezing and using the sperm of bull sires [64].

Blood for analysis was taken from the jugular vein (September 2017) in the morning hours after taking the semen. After separating the serum from the formed elements, the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), the concentration of albumin, creatinine, urea, total bilirubin, as well as total protein and cholesterol were determined. Macronutrients (Ca, P, Mg, Fe) were determined in blood serum using a ChemWell 2902 biochemical analyzer (Awareness Technology, Inc., USA), trace elements (Cu, Zn, Se, Mn) — in whole blood using a Quantum-2A atomic absorption spectrometer (CJSC CORTEC, Russia). The concentration of endogenous hormones was measured by enzyme immunoassay in 2-fold repetition using laboratory reagents (CJSC Immunotech, Russia) for estradiol, thyroxine TT4, cortisol, and testosterone on a UNIPLAN device (AFG-01) (CJSC Pikon, Russia). Cholesterol content was evaluated on an automatic analyzer ChemWell 2902 (Awareness Technology, Inc., USA) following the manufacturer's instructions.

Spermological parameters (volume of ejaculate, ml; concentration of sperm in the ejaculate, billion/ml; the total number of sperm in the ejaculate, billion) were studied following the National Technology of freezing and using sperm of bull sires [64] and the instructions for the organization and technology of work with sires of different types of animals in breeding centers of the Republic of Kazakhstan.

Statistical processing was carried out in Microsoft Excel. The tables show the mean values (*M*) and standard errors of means (±SEM). Statistical significance of the differences was assessed by Student's *t*-criterion (at significance levels $p < 0.05$; $p < 0.01$; $p < 0.001$) and with the use of IBM® SPSS® Statistics (https://www.ibm.com/ru-ru/analytics/spss-statistics-software).

*Results.* The observations made over the past 20 years have made it possible to apply previously made preliminary conclusions to the analysis of the obtained data. In this work, carried out within the framework of the EurAsEC, when determining the degree of influence of climatic and geochemical factors on the adaptation and metabolism of imported Holstein bull sires, their bio-element, protein-lipid, enzymatic, and hormonal statuses were taken into account. For the survey, the most typical and well-known breeding centers were selected, located within the middle latitude (deviations of no more than 5.67 °N), but distant from each other in east longitude, which affects the climatic and geochemical conditions of geographical points where breeding centers are geographically located (all of them are in a moderate circulation zone) (Table 1).

**1. Geographical, physical and climatic characteristics of the studied regions**

| Climate zone | Region | Geographic coordinates | | ASLE, m | AAP, mm |
|---|---|---|---|---|---|
| | | ° N | ° E | | |
| II (East European Plain) | Moscow (JSC Head Center for Reproduction of Farm Animals) | 55.42 | 37.55 | 162 | 668 |
| III (West Siberian Plain) | Middle Urals (OJSC Uralplemcenter) | 56.85 | 60.11 | 255 | 497 |
| | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) | 51.18 | 71.44 | 358 | 308 |

N o t e. ASLE — above sea level elevation, AAP — average annual precipitation. The data are taken from the Scientific and Applied reference book "Climate of Russia" (http://aisori-m.meteo.ru/climsprn /) and the National Atlas of Russia ( https://национальныйатлас.рф/cd2/about.html) .

The Moscow Province is located in the zone of domination of the continental climate of temperate latitudes, characterized by relatively mild winters with rare thaws and warm relatively humid summers, belongs to the zone of sufficient moisture. In the Moscow Region, observations of recent years show an increase in average annual and seasonal air temperatures, increased aridity in summer, and warming in winter [65]. The main climate-forming factor in the Middle Urals is its geographical location. The Ural Mountains are divided by natural synoptic areas; zonal patterns of distribution of various meteorological elements, especially air temperature and precipitation, are violated here, which serves as the basis for the allocation of this territory into a separate climatic region with a sharp change in weather. The climate is close to moderately cold with a significant amount of precipitation. As a result of the rhythmic features of the climate, winter and spring increases in air temperature have been typical for recent years [66]. The territory of Northern Kazakhstan belongs to the continental steppe of the West Siberian climatic region with a flat relief and a sharply continental climate with a shortage of moisture [67]. Despite the low agro-climatic potential, characterized by a short growing season and expressed seasonality of agriculture [68], crop production remains the main specialization of the region, but prospects for the development of milk and cattle meat production are being considered [69]

The biochemical analysis showed (Table 2) that the average values of concentrations of macronutrients in the blood plasma of the examined animals in all regions were mainly within the reference values [70] and had no significant differences in Ca, P, Ca:P, Mg. Macronutrients, in particular calcium, phosphorus, and magnesium, enter the animal's body with the main diet, and their blood concentration in ruminants depends on the initial quality of feed, vitamin D availability, and solar insolation [71]. The obtained results (see Table 2) indicate that the supply of bull sires with the listed macronutrients at all enterprises corresponds to regulatory indicators with a certain zonal variability.

**2. The blood content of macroelements in the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** ($M$±SEM, 2017)

| Element | Region | | | Reference values |
|---|---|---|---|---|
| | Moscow (JSC HCR) ($n$ = 20) | Middle Urals (OJSC Uralplemcenter) ($n$ = 56) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) ($n$ = 46) | |
| Ca, mmol/l | 2.43±1.17 | 2.34±0.14 | 2.53±0.23 | 2.06-3.16 |
| P, mmol/l | 1.47±0.21 | 2.01±0.36 | 1.98±0.33 | 1.13-2.91 |
| Ca:P | 1.65±0.26 | 1.20±0.23 | 1.31±0.23 | 0.82-2.39 |
| Mg, mmol/l | 0.79±0.12 | 0.92±0.15 | 0.98±0.35 | 0.75-1.34 |
| Fe, μmol/l | 23.82±6.18 | 40.32±7.30 | 30.74±6.97 | 12.90-37.10 |
| Chlorides, mmol/l | 100.45±2.86 | 97.61±4.28 | 95.69±9.28 | 90-108 |

N o t e. JSC HCR stands for JSC Head Center for Reproduction of Farm Animals.

When harvesting coarse fodder in the Southern Moscow Region, it is necessary to take into account the peculiarity of loamy soils on low-carbonate covering deposits of the Podolsk-Kolomna high plains with low natural fertility and insufficient content of available magnesium (less than 120 mg/kg). Acidic and strongly acidic sod-podzolic soils are characterized by the leaching of magnesium, which, with sufficient moisture, moves to the lower horizons of the soil, creating a deficit in the root zone of plants [72]. Soil deficiency of Mg (0.79±0.12 mmol/l) indirectly affected the availability of bull sires at the lower limit of the norm for this element. In the Middle Urals, the main part of agricultural land (69.9%) falls on sod-podzolic soils formed on rocks rich in calcium and magnesium, which differ from the same soils of Central Russia by an increased content of humus, increased capacity of cation exchange, and the entire absorbing complex [73]. As can be seen from Table 2, Mg content in the blood serum of bull sires from JSC Ural-plemcenter is close to the average normative indicators and is 0.92±0.15 mmol/l with values for phosphorus and calcium 2.01± 0.36 and 2.34±0.14 mmol/l, respectively. Fodder crops in the North Kazakhstan region can accumulate significant amounts of Ca and Mg carbonates from upper arable horizons with low mobility of these compounds along the soil profile since they are cultivated in moderately arid areas on chernozems and dark chestnut soils [74]. Bull sires in this region are well provided with Mg due to the basic diet (the concentration of Mg and Ca in the blood serum was 0.98±0.35 and 2.53±0.23 mmol/l, respectively) with a relatively reduced supply, in particular, with phosphorus (1.98±0.33 mmol/l).

Even though the concentration of available iron in soil solutions depends on the composition of the parent rock and increases with increasing acidity of the soil [75], the bull sires in all the studied regions did not lack Fe. The concentration of iron in the blood of bulls in the Moscow Region did not exceed the norm, in Northern Kazakhstan corresponded to its upper limit, and in the Middle Urals, exceeded the norm. In the technogenic territories of the Urals and Northern Kazakhstan, Fe as a heavy metal accumulates in the soil-plants-animals system on dark gray forest, chernozems, and dark chestnut clay-loamy soils with an alkaline reaction of the medium [76]. When a large amount of iron is supplied with feed and water, ferritin accumulates in the villi of the mucous membrane and the so-called mucosal blockade develops, iron absorption stops [77]. In the blood serum of bull sires from the Moscow Region, the concentration of iron (23.82 ± 6.18 mmol/l) did not exceed the regulatory limits, despite the contamination of water with iron (its concentration in some sources can reach 10 mg/l) compared with water of deeper occurrence [78].

Thus, no significant differences have been revealed in the availability of macronutrients for bull sires, despite the diversity of geochemical zones and agroclimatic conditions in the regions where the surveyed breeding centers are located.

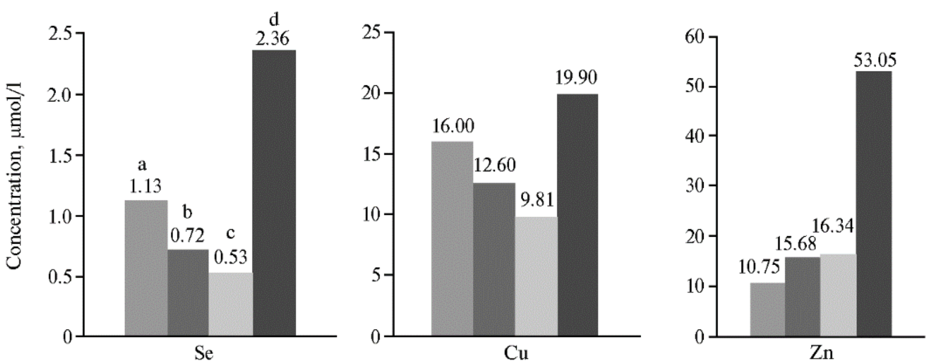


**Fig. 1. Blood concentration of trace elements in the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** (2017): a — Moscow Province (JSC Head Center for Reproduction of Farm Animals, *n* = 20), b — Northern Kazakhstan (JSC RCPZh Asyl-Tulik, *n* = 46), c — lower limit of the norm, d — upper limit of the norm.

Biogenic trace elements are necessary for the formation of full-fledged spermatozoa and to increase the efficiency of the use of bull sires. Trace elements are part of enzymes, vitamins, hormones, respiratory pigments, cell structures and significantly affect the qualitative and quantitative characteristics of ejaculate and sperm fertility [44, 79–82]. The availability of microelements for animals (Fig. 1) depends on the feed set of the main diet and the geochemical conditions of the area.

The change in the concentration of trace elements in the blood of Holstein bull sires of foreign breeding is demonstrated in the example of the Moscow Region and Northern Kazakhstan. For the analyzed regions, the average values for Se and Cu in the blood serum of bull sires were in the range of reference values, exceeding the minimum threshold concentration (see Fig. 1), for Zn – were below the permissible minimum. It is known that the amount of zinc in soils increases from tundra landscapes to steppe arid soils [63]. The same pattern can be traced by the concentration of this element in the blood serum of bull sires. Thus, in the Moscow Region (JSC HCR) at the border of the distribution of sod-podzolic and gray forest soils, the concentration of zinc in the blood serum of bulls was 65.2% of the threshold reference value that ensures normal metabolism. In the dry steppe zone on dark chestnut soils (Northern Kazakhstan, JSC RCPZh Asyl-Tulik) zinc content in the blood of bull sires was 95.7% of the minimum threshold value, which is significantly higher than in animals in the central part of the East European (Russian) plain (JSC HCR). Copper concentration in the blood of bulls, while remaining within the reference values, was 21% higher in the Moscow Region than in Northern Kazakhstan. It is shown that for copper, the distribution in soils is similar to that for zinc, strontium, and lead [63]. However, due to industrial pressure, Cu content in the soil, water, and plants may increase, the consequences of which was noted in the south of Moscow suburbs. Selenium belongs to trace elements, its content in soils is mainly due to the parent rock and climatic features of the region. The accumulation of Se in plants is determined by its quantity and forms in the soil, its type, acidity, precipitation, and ambient temperature, the stage of growth of the plant itself [83]. Currently, there are no systematic data on the content of selenium in various types of soils [84]. The concentration of selenium in the blood serum of bulls in the south of the Moscow Region was 63.7% higher than in Northern Kazakhstan, although, according to biogeochemical surveys, the soils of the Moscow Region can be attributed to selenium deficiency [85].

Trace elements as cofactors are involved in all vital metabolic processes. The activity of many enzymes is manifested only in the presence of metal ions ($Zn^{2+}$, $Mg^{2+}$, $Mn^{2+}$, $Fe^{2+}$, $Cu^{2+}$, $K^{+}$, $Na^{+}$) [86].

**3. Cellular enzyme activity** (IU/л, $M$±SEM) **in blood of the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** ($M$±SEM, 2017)

| Enzyme | Norm | Region | | |
|---|---|---|---|---|
| | | Moscow (JSC HCR) ($n$ = 20) | Middle Urals (OJSC Uralplemcenter) ($n$ = 56) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) ($n$ = 46) |
| Alanine aminotransferase (ALT) | 10-36 | 40.15±15.34 | 68.45±16.38 | 37.47±11.96 |
| Aspartate aminotransferase (AST) | 41-107 | 132.55±74.61 | 104.00±15.95 | 111.35±14.09 |
| AST ALT | 1.3-1.5 | 3.03 | 1.51 | 2.97 |
| Alkaline phosphatase | 31-163 | 72.7±75.66 | 125.25±45.43 | 232.02±119.77 |

The presence of cellular enzymes — AST, ALT, and alkaline phosphatase in the blood above the norm is a sign of cytolysis and a marker of some diseases [87-89]. As a rule, an increase in activity for AST often coincides with a decrease for ALT and vice versa. ALT is more specific for the diagnosis of hepatic pathologies, an increase in its activity in plasma indicates more damage to cells than a violation of liver function in general. In the current survey, the highest ALT index — 68.45±16.38 IU/l, which is 2 times higher than the regulatory activity, was found in bull sires in the Middle Urals (JSC Ural-plemcenter), in animals from the Moscow Region (JSC HCR) and Northern Kazakhstan (JSC RCPZh Asyl-Tulik), ALT activity (40.15±15.34 and 37.47±11.96 IU/l, respectively) was at the upper limit of the norm (Table 3). According to AST, indicators corresponding to the upper limit of the norm were recorded in bulls in JSC Ural-plemcenter, excess of the norm in JSC RCPZh Asyl-Tulik and JSC HCR (see Table 3). The value of the De Ritis ratio in these animals was 2 times higher than the standard value (see Table 3), which indicates the predominance of the tricarboxylic acid cycle in the metabolism [90, 91]. The activity of alkaline phosphatase in bulls in Northern Kazakhstan (JSC RCPZh Asyl-Tulik) exceeded the upper limit of reference values by 30%, which, with normal calcium-phosphorus metabolism, serves as a marker of high functional loads on the liver and heart and the active work of young bone cells [92, 93].

An increase in the content of total and direct bilirubin, high activity of AST and ALT can serve as a diagnostic test of liver diseases of alimentary etiology [94] and characterize protein metabolism [81]. At the same time, Shkuratova et al. [95] believe that a high level of inorganic phosphorus and alkaline phosphatase can be attributed to the peculiarities of the metabolic profile of bull sires. In addition, the formation of high-quality spermatozoa capable of enduring a "cold shock" is impossible without the inclusion of animal feed rich in protein and phospholipids in the diet of bulls [96, 97]. The scarcity of protein in the diet of bull sires leads to hormonal imbalance, an increase in secondary immunodeficiency, and a decrease in the quantitative and qualitative characteristics of the ejaculate [43].

**4. Parameters of protein-lipid metabolism in the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** (*M*±SEM, 2017)

| Parameter | Region | | | Reference values |
|---|---|---|---|---|
| | Moscow (JSC HCR) (*n* = 20) | Middle Urals (OJSC Uralplemcenter) (*n* = 56) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) (*n* = 46) | |
| Total protein, g/l | 90.44±6.14 | 84.83±4.05 | 88.81±6.72 | 70-92 |
| Albumin (A), g/l | 32.40±2.77 | 33.20±1.56 | 29.22±3.40 | 25-36 |
| Globulin (G), g/l | 59.08±6.13 | 51.18±4.45 | 59.60±7.55 | 40-63 |
| A/G | 0.55 | 0.64 | 0.50 | 0.4-0.9 |
| Urea, mmol/l | 7.57±2.82 | 3.90±1.39 | 3.40±0.65 | 2.4-7.5 |
| Creatinine, μmol/л | 147.45±37.94 | 121.04±30.90 | 146.66±34.01 | 62-163 |
| Bilirubin, μmol/l | 2.26±0.51 | 2.36±1.30 | 9.15±3.42 | 1.16-8.15 |
| Triglycerides, mmol/l | 0.55±0.07 | 0.14±0.09 | 0.35±0.11 | 0.09-0.37 |
| Cholesterol, mmol/l | 2.37±0.49 | 3.46±0.61 | 2.93±0.50 | 2.1-8.2 |

In bull sires, the main indicators of protein-lipid metabolism were mainly within the reference values (Table 4). Some differences are caused by small feeding errors. The content of total protein and protein fractions in the blood of animals was sufficient to maintain normal metabolism and the formation of full-fledged ejaculates. The concentration of urea and creatinine in the blood serum at the upper limit of the norm (7.57±2.82 mmol/l and 147.45±37.94 mmol/l respectively) was a consequence of the fact that bulls from the Moscow region received an excessive amount of protein with feed. In males, an increase in the concentration of triglycerides is due to the active secretion of testosterone [98], but their excess can lead to metabolic syndrome [99]. In bull sires from the Moscow Region (JSC HCR), this indicator was 0.55±0.07 mmol/l, which exceeded the upper limits of the norm by 32%. Bulls from Northern Kazakhstan (JSC RCPZh Asyl-Tulik) have a high bilirubin index (9.15±3.42 mmol/l) which in combination with an increased iron content (30.74±6.97 mmol/l) (see Table 2) may indicate additional hemoglobin release with excessive destruction of red blood cells. As a consequence, iron overload syndrome [100-102] may form, which occurs when erythropoiesis is impaired, in the case of liver diseases, hereditary defects and serves as the main factor predisposing to the accumulation of iron in liver cells.

Optimal indicators of protein-lipid metabolism were typical for bull sires in the Ural region, which indicates the balance of their diet.

Cholesterol concentration in the blood serum of bull sires in all studied regions was at the lower limit of the reference values and amounted to 2.37−3.46 mmol/l. Since cholesterol is a precursor of steroid hormones (including sex hormones), its low level may be a signal of hormonal status disorders. It is known that hormones of the pituitary-thyroid gland and pituitary-adrenal cortex systems represent a key link in the hormonal regulation of adaptive metabolic processes [102, 103]. It has been established that the aromatase enzyme is present in adipose tissue, under the influence of which androgens are converted into estrogens [104]. Metabolic changes associated with the size of fat cells serve as a trigger for a decrease in testosterone levels [105, 106].

Tables 5 and 6 show the average and maximum concentrations of endogenous hormones characterizing reproductive and adaptive function in Holstein bull sires kept in two different geographical locations in Russia and Northern Kazakhstan.

**5. Blood concentration of endogenous hormones in the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** ($M$±SEM, 2017)

| Parameter | Region | | | Average |
|---|---|---|---|---|
| | Moscow (JSC HCR) ($n$ = 19) | Middle Urals (OJSC Uralplemcenter ($n$ = 9) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) ($n$ = 17) | |
| Testosterone, nmol/l | 39.17±5.06 | 50.36±5.80 | 52.79±4.14 | 47.10±2.39 |
| Cortisol, nmol/l | 226.75±45.62 | 138.81±21.48 | 190.5±50.31 | 195.48±27.35 |
| Thyroxine, nmol/l | 91.13±3.35 | 66.65±3.52 | 95.39±1.86 | 81.95±2.26 |
| Estradiol, nmol/l | 0.197±0.02 | 0.276±0.04 | 0.234±0.02 | 0.339±0.02 |

**6. Variability of blood concentration of endogenous hormones in the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** (min-max, 2017)

| Parameter | Region | | | Over the total sample ($n$ = 73) |
|---|---|---|---|---|
| | Moscow (JSC HCR) ($n$ = 19) | Middle Urals (OJSC Uralplemcenter ($n$ = 9) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) ($n$ = 17) | |
| Testosterone, nmol/l | 10.46-81.14 | 28.12-79.12 | 26.27-74.45 | 10.46-81.14 |
| Cortisol, nmol/l | 21.27-728.21 | 43.69-238.41 | 25.60-725.32 | 21.27-728.21 |
| Thyroxine, nmol/l | 53.25-109.43 | 50.20-81.20 | 85.63-109.05 | 32.96-126.92 |
| Estradiol, nmol/l | 0.093-0.350 | 0.100-0.426 | 0.073-0.374 | 0.073-0.909 |

Despite the slight difference in latitude, Moscow (JSC HCR), Yekaterinburg (JSC Ural-plemcenter), and Nursultan (JSC RCPZh Asyl-Tulik) are located in different climatic zones and differ in average annual temperatures and solar radiation (Fig. 2), under the influence of which up to 70% of vitamin D affecting testosterone production [59] is synthesized in the body. Thus, in Northern Kazakhstan, the average annual cross-section of solar radiation exceeded that in the Southern Moscow Region by 24.0%, and the testosterone level in bull sires — by 25.8% (see Table 5) [107]. In males, the participation of testosterone at the molecular level in maintaining bone mineral density (BMD) has been established [108].

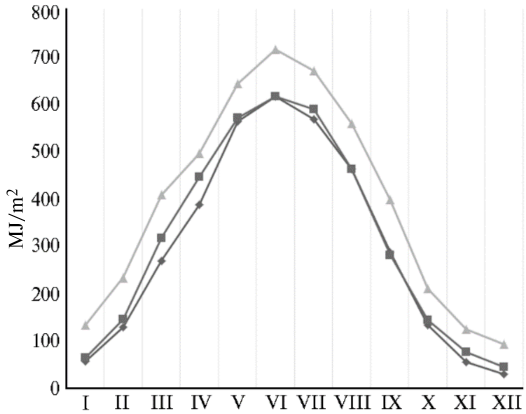


**Fig. 2. The power of total (direct and diffuse) solar radiation on the horizontal surface of the Earth by months during the year under actual cloud conditions in Moscow (♦), Ekaterinburg (□) and Nursultan (▲)** (http://meteo.ru/pogoda-i-klimat/197-nauchno-prikladnoj-spravochnik/).

Testosterone production, as noted, is also characterized by circadian rhythmicity [109]. The highest testosterone peak occurs between $6^{00}$-$8^{00}$, the anti-peak is from $21^{00}$ to $23^{00}$. This physiological cycle is the basis of the technological regime for sperm production. The annual rhythm of the maximum testosterone level falls in August-September with a decrease in the winter months and is also associated with the latitudinal duration of daylight and solar insolation [110, 111]. In the authors' previous studies [47], in the blood of bull sires from the Ural region in December, an average testosterone level of 20.5 nmol/l was detected with variability from 4.8 to 50.6 nmol/l by groups, and low indicators (up to 10 nmol/l) were recorded in 50% of the animals in the herd. In this paper (see Table 5) in September, the average value in bulls from the same region was 50.36±5.80 nmol/l. The obtained results correspond to the annual cycle of changes in the concentration of testosterone. Among bulls in the studied territories, the minimum average level of this hormone (39.17±5.06 nmol/l) was observed in producers from the Moscow region, the maximum (52.79±4.14 nmol/l) — in animals in Northern Kazakhstan (the difference is statistically insignificant).

Cortisol is also characterized by a circadian rhythm with an increase in the level in the morning [112-114]. In the present work, blood was taken for examination in the morning. High (226.75±45.62 nmol/l) cortisol content was registered in bull sires from the Moscow region, in animals in Northern Kazakhstan and the Middle Urals, the average values were slightly lower (by 16 and 39%, respectively, the difference is not statistically significant) (see Table 5). An increase in cortisol concentration is associated with hypertriglyceridemia, increased protein, fat, and carbohydrate metabolism [115, 116]. In stressful situations, the hormone promotes the rapid release of glucose. Excess glucose in the body leads to some metabolic complications: increased blood osmolarity, increased production of carbon dioxide and lactate, as well as fatty liver infiltration due to the conversion of excess glucose into fatty acids [117]. Significant variability of cortisol concentration in the blood of bulls (see Table 6) shows that in the Moscow region and Northern Kazakhstan in the studied groups, there are animals in a state of metabolic stress. Previously, the authors of this paper showed that after a doublet cage, the cortisol level in bull sires significantly increases over the next two days, especially in adult animals [47].

The effect of cortisol on the strengthening or weakening of one or another enzymatic activity complements thyroxine since the presence of another hormone is necessary for the manifestation of the action of one hormone [23]. The average thyroxine content in the examined bulls was within the physiologically permissible norm (51-141 nmol/l) (see Table 5): in the Middle Urals — 66.65±3.52 nmol/l, in the Moscow region and Northern Kazakhstan — slightly higher (91.13±3.35 and 95.39±1.86 nmol/l, respectively). This gives reason to believe that the thyroid gland in these males functions normally and the hormone (thyroxine) secreted by it adequately affects physiological processes, even though the surveyed farms are located in territories that are deficient and moderately deficient in iodine [118].

To identify significant differences in the hormonal background between animals from different regions, the authors conducted pairwise comparisons of indicators using the Mann-Whitney U-test method. The analysis showed a highly significant influence of climatic and geochemical conditions (territorial factor) on the thyroxine content ($p < 0.001$) in the blood serum of the examined bull sires in the compared regional pairs of enterprises: the Southern Moscow suburbs—the Middle Urals, the Middle Urals—Northern Kazakhstan (no significant differences were found in other indicators).

The previous work [44] found that the content of endogenous estradiol in the blood of bulls depended on the time of year ($p < 0.001$). In spring, the average concentration of estradiol was minimal, in autumn a significant increase in the amount of hormone ($p < 0.001$) was observed in 94% of animals. In this study, estradiol content varied (see Table 5) — from 0.197±0.02 nmol/l in the Moscow region to 0.234±0.02 and 0.276±0.04 nmol/l, respectively, in Northern Kazakhstan and the Middle Urals, which is within the physiological norm (0.2-0.4 nmol/l).

The results of the analysis of the state of bull sires according to the characteristics of native sperm are presented in Table 7 (the qualitative characteristics of cryopreserved sperm are not given since they met GOST requirements).

**7. Characteristics of native semen of the Holstein bull sires of foreign breeding in regions with different climatic and geochemical conditions** (*M*±SEM, 2017)

| Parameter | Region | | |
|---|---|---|---|
| | Moscow (JSC HCR) (*n* = 20) | Middle Urals (OJSC Uralplemcenter) (*n* = 56) | Northern Kazakhstan (JSC RCPZh Asyl-Tulik) (*n* = 46) |
| Ejaculate volume, ml | 4.87±1.8 | 3.72±0.08 | 4.4±0.13 |
| Concentration of spermatozoa, $\times 10^9$/ml | 1.21±0.20 | 1.52±0.02 | 1.29±0.01 |
| Total number of spermatozoa per ejaculate, $\times 10^9$ | 6.00±0.64 | 5.60±0.16 | 5.32±0.27 |

The difference between the indicators shown in Table 7 is not statistically significant.

Thus, the absence of a significant difference in the main indicators characterizing metabolism between animals from different regions that received a balanced diet taking into account the geochemical conditions of the terrain with a similar operating mode according to the regulations provided for by the technology of farming and use indicates minimization of the influence of climatic and geochemical factors and sufficient adaptive ability of Holstein bulls in a moderate circulation zone between 55.86° and 51.18°N. This is evidenced by the comprehensive comparison of the state of protein-lipid, macro- and microelement, enzymatic and hormonal status carried out by the authors for the first time, taking into account the reproductive ability of Holstein bull sires farmed in various geoclimatic conditions.

The results obtained give grounds to conclude that protein-lipid and macronutrient metabolism in producers under the conditions of typical feeding technology and maintenance has no significant geographical differences and mostly depends on the quality of the main feed of the diet.

The deficiency of essential trace elements, in particular Zn, is typical for most of the territory of Russia. Mammals can have Zn from food only. The average daily requirement for a mature bull sire is 300-600 mg, depending on body weight (norms and diets). During the period of intense sexual activity, metabolism of bull sires increases significantly, therefore, the consumption and content of zinc in the body increases [20, 44]. Zinc is mainly secreted by the prostate gland, it is contained in a significant amount in maturing spermatozoa, its concentration correlates with oxygen consumption and the stability of nuclear chromatin [119, 120]. Zinc content in the male reproductive system significantly exceeds that in other organs and tissues; its deficiency can cause disorders of spermatogenesis [121]. Even though iron is irreplaceable in the processes of hematopoiesis, respiration, and cellular metabolism, its excess can initiate lipid peroxidation, toxic damage to proteins and nucleic acids [122], which negatively affects the quality of native sperm [123]. To determine the need of bull sires for essential elements, they should be monitored in the blood serum, taking into account the deficiency or excess intake into the body according to the results of chemical analysis of water, soils, and basic feeds, compensated with targeted premixes. To provide animals with water in regions with high levels of soil iron, it is necessary to use deep-lying wells and water de-ironing stations.

The identified features should be taken into account when farming and using breeding bull sires in various geochemical provinces of Russia, Kazakhstan, and other countries that are members of the EurAsEC. The composition of the diets should be developed taking into account not only the geochemical and climatic conditions of the place of farming but also possible deficits of intrauterine development and postnatal nursery of bull sires.

Taking into account modern studies of neuroendocrine regulation of male sexual development [124, 125], in conditions of large-scale breeding for high productivity with an index evaluation of ancestors, it is necessary to pay attention to prenatal and early postnatal development, which determines the future reproductive health of the animal. A bull with a high genomic prognosis, but sperm not suitable for cryopreservation [126], has no breeding value.

Comparative studies have shown that hormones of the hypothalamic-pituitary-gonadal and thyroid axis of endocrine regulation in bull sires kept at mid-latitude in various climatic and geochemical conditions serve as a key factor in long-term adaptation to external conditions [23].

In the authors' opinion, one of the reasons for the decrease in testosterone status in bull sires from the Moscow region compared to animals in the Middle Urals and Northern Kazakhstan is solar insolation (see Fig. 2). The deficiency of solar insolation and vitamin D synthesis, on the one hand, and the inevitable influence of technological effects, on the other hand, lead to the formation of and increase in metabolic stress [59, 127]. On-duty night lighting in livestock premises disrupts circadian rhythms. It has been shown that the blue component of the spectrum, including artificial lighting, suppresses the production of melatonin hormone significantly, the secretion of which affects the quality of animal sleep [128]. In turn, melatonin indirectly has a regulating effect on the functions of the testicles [129, 130]. Its excess, as well as its deficiency, leads to an imbalance in the secretion of steroid hormones, which is subject not only to circadian but also to infradian rhythms [130]. A complex relationship between circadian rhythm failure and metabolism has been proven, a change in the sleep-wake cycle can lead to the formation of metabolic syndrome and cardiovascular diseases [131]. During sexual activity, testosterone and cortisol levels increase simultaneously in males, which is presumably associated with rivalry, territorial defense, as well as courtship and mating behavior [132].

The authors did not note a significant influence of various climatic and geochemical conditions of the regions on the main indicators of sperm production in bull sires. However, constant exposure to such factors in combination with seasonal fluctuations in the amount of hormones, the influence of daylight hours, and solar insolation can affect the functional reserves of the endocrine system [133, 134]. In this case, the hormonal profile of bull sires can serve as a marker of body plasticity.

So, with the stabilization of farming conditions and strict rationing of the needs of bull sires in nutrients and minerals, as well as the regulation of the light regime (morning-daytime solar insolation, darkness at night), it is possible to minimize the negative impact of climatic and geochemical factors on the body of breeding animals. The obtained data on the total number of spermatozoa in the ejaculate indicate the adaptability of Holstein bull sires in various climatic conditions with the used technologies.

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