Chapter 7

DETERMINATION OF THE IMMUNOLOGICAL STATUS OF ANIMALS DURING THE PERIOD OF FETAL DEVELOPMENT

Prosyanyi Sergiy, Horiuk Yulia
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INTRODUCTION

Reproductive immunology includes all stages of the reproduction process: fertilization, implantation of embryos, development of the placenta, both in the early and late stages of pregnancy, childbirth[1, 2]. Scientists pay considerable attention to this direction, but it is still not fully understood how the process of semialogenous fetal transplantation occurs, when the mother's immune system avoids rejection of the embryo[3].

It has been established that the feto-maternal interface is a complex system of specific immune processes, both on the part of the mother and the fetus. In the mother's womb, the fetus undergoes complex morphological and physiological changes, both from the mother's body and under the influence of various environmental factors, which occur with a certain speed and sequence[4], [5]. Thus, during the first four months of cattle embryogenesis, a fetus with a zygote of 0.000003 g and a diameter of 125 μm reaches a mass of one kilogram[6].

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[3] Genetic parameters for production, health, fertility and longevity traits in dairy cows / T. Pritchard et al. *Animal*. 2013. Vol. 7, no. 1. P. 34–46. https://doi.org/10.1017/s1751731112001401

[4] Characterization of Bioactive Recombinant Human Lysozyme Expressed in Milk of Cloned Transgenic Cattle / B. Yang et al. *PLoS ONE*. 2011. Vol. 6, no. 3. P. e17593. https://doi.org/10.1371/journal.pone.0017593

[5] Changes in antioxidant enzyme activities and metabolic parameters in dairy cows during different reproductive periods / S. Sayiner et al. *Theriogenology*. 2021. Vol. 159. P. 116–122. https://doi.org/10.1016/j.theriogenology.2020.10.024

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The body of the fetus is extremely plastic in the initial phase of its development, when its individual organs are formed and all biochemical reactions take place most intensively[7, 8]. Their feature is the manifestation of a leading component for a certain period of pregnancy with clearly defined functions, and there is a permanent change in the leading component as it develops, which ensures its normal course. The dependence of the prenatal development of fetuses on the state of the immune system of females and the negative impact on the viability of embryos of an immunodeficient state in the mother's body has been determined[9, 10].

Antibodies are natural proteins in the body of animals, and their structure is safe for the fetus. The transfer of maternal antibodies is an important mechanism of protection for fetuses and newborns, since their immune system is not yet endowed with a humoral response[11, 12]. Transport of all nutrients across the placental membrane can involve one of four major transport mechanisms: simple diffusion, facilitated diffusion, active transport, and pinocytosis. In addition, the maternal-fetal barrier depends on many other factors, including the thickness and type of the placenta, the concentration of substances, the activity of transport mechanisms, etc.[13, 14].

Immunoglobulins are antibodies that belong to the family of globular proteins and make up a group of glycoproteins that are present in blood

[7] Fetal programming in dairy cows: Effect of heat stress on progeny fertility and associations with the hypothalamic-pituitary-adrenal axis functions / E. Huber et al. *Animal Reproduction Science.* 2020. Vol. 216. P. 106348. https://doi.org/10.1016/j.anireprosci.2020.106348

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[11] Natural Antibodies Related to Energy Balance in Early Lactation Dairy Cows / A. T. M. van Knegsel et al. *Journal of Dairy Science*. 2007. Vol. 90, no. 12. P. 5490–5498. https://doi.org/10.3168/jds.2007-0289

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[13] The Role of Innate Immune Response and Microbiome in Resilience of Dairy Cattle to Disease: The Mastitis Model / V. Bronzo et al. *Animals.* 2020. Vol. 10, no. 8. P. 1397. https://doi.org/10.3390/ani10081397

[14] Heat stress and immune response phenotype affect DNA methylation in blood mononuclear cells from Holstein dairy cows / A. M. Livernois et al. *Scientific Reports*. 2021. Vol. 11, no. 1. P. 11371. https://doi.org/10.1038/s41598-021-89951-5

serum and tissue fluids of all mammals[15, 16]. Currently, there are five classes of antibodies (IgG, IgA, IgM, IgD and IgE), each of which has its own characteristics. Yes, each class differs in size, electrical charges, carbohydrate and amino acid content. The main biological function of antibodies is to bind antigens, which helps to remove them from the body[17, 18].

Cows have a cotyledonary synepitheliochorial placenta, which prevents direct transfer of antibodies from mother to fetus[19]. This explains why calves have agammaglobulinemia at birth, and the acquisition of immunity occurs only with adequate consumption of high-quality colostrum. In addition, the amount of Ig in the colostrum and blood serum of the offspring can vary between different breeds[20].Therefore, it is important to know the influence of different genotypes of animal breeds on the formation of the immune status of animals during the period of intrauterine development.

1. The problem's prerequisites emergence and the problem's formulation

Information on establishing the immune status of the fetus, especially of cattle, is rather scarce and contradictory[21, 22] A number of scientists note that in the process of intrauterine development, the animal body produces cells that carry out phagocytosis and molecules with a pronounced antimicrobial effect – lysozyme, complement, properdin, immunoglobulins

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[15] The Impact of Heat Stress on Immune Status of Dairy Cattle and Strategies to Ameliorate the Negative Effects / S. Gupta et al. Animals. 2022. Vol. 13, no. 1. P. 107. https://doi.org/10.3390/ani13010107

[16] Prospects of toll-like receptors in dairy cattle breeding / M. Maurić Maljković et al. *Animal Genetics*. 2023. Vol. 54, no. 4. P. 425–434. https://doi.org/10.1111/age.13325

[17] The association of immune response and colostral immunoglobulin G in Canadian and US Holstein-Friesian dairy cows / T. E. Altvater-Hughes et al. *Journal of Dairy Science*. 2023. Vol. 106, no. 4. P. 2857–2865. https://doi.org/10.3168/jds.2022-22562

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[22] Chebel R. C. Predicting the risk of retained fetal membranes and metritis in dairy cows according to prepartum hemogram and immune and metabolic status. *Preventive Veterinary Medicine.* 2020. P. 105204. https://doi.org/10.1016/j.prevetmed.2020.105204

and other factors of natural resistance[23, 24]. The concentration of lysozyme in fetal blood plasma depends on the ratio between the main producers – neutrophils and monocytes and the function of the kidneys as an organ responsible for its elimination[25]. There is information that blood serum of fetuses of 4–8-month-old cattle contains complement in incredible quantities and only at 9 months of age it was constantly detected. At the same time, no correlation was found between the level of complement in the blood of fetuses and their mothers, which indicates a possible autonomous synthesis of it by fetuses[26]. It has also been proven that fetal properdin in the blood serum of 3-month-old fetuses of cows does not always show specific activity in hemolytic tests due to the absence of a beta-polypeptide that determines it, but its amount gradually increases and by the end of gestation was 3.55±0.29 units/ Jr. However, in the blood serum of mother cows, this indicator did not undergo significant fluctuations during pregnancy. According to the amount of properdin in blood serum, fetuses at the last stage of the prenatal period exceed their mothers, which indicates the autosynthesis of this factor, especially since this indicator is absent in the amniotic fluid of pregnant cows[27, 28].

Numerous studies have established that the content of immunoglobulins of various classes in humans and animals in the postnatal period undergoes age-related changes and has certain features[29]. As for fetuses and newborn calves of cattle, some researchers consider it a proven fact that there is no gamma globulin in their blood[30, 31]. However, others still find

[23] Feasibility and accuracy of using different methods to detect pregnancy by conceptus-stimulated genes in dairy cattle / P. A. Ferraz et al. *JDS Communications*. 2021. Vol. 2, no. 3. P. 153–158. https://doi.org/10.3168/jdsc.2020-0062

[24] Stress and inflammatory response of cows and their calves during peripartum and early neonatal period / F. Arfuso et al. *Theriogenology*. 2022. Vol. 196. P. 157–166. https://doi.org/10.1016/j.theriogenology.2022.11.019

[25] A comparative study on various immunological parameters influencing embryo survivability in crossbred dairy cows / B. S. K. Panda et al. *Theriogenology*. 2020. Vol. 157. P. 140–148. https://doi.org/10.1016/j.theriogenology.2020.05.041

[26] Ott T. L. Immunological detection of pregnancy: Evidence for systemic immune modulation during early pregnancy in ruminants. *Theriogenology*. 2020. Vol. 150. P. 498–503. https://doi.org/10.1016/j.theriogenology.2020.04.010

[27] A comparative study on various immunological parameters influencing embryo survivability in crossbred dairy cows / B. S. K. Panda et al. Theriogenology. 2020. Vol. 157. P. 140–148. https://doi.org/10.1016/j.theriogenology.2020.05.041

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immunoglobulins in fetuses[32]. Thus, a gradual increase in the share of gamma-globulin secretion in fetuses of cows was established, which reaches a maximum by the 9th month of pregnancy. In newborn calves, it is possible to detect Ig G1 Ig G2 in minimal concentrations before receiving colostrum[33]. Therefore, some scientists indicate that before colostrum intake, immunoglobulins are contained in the body of newborn calves in the form of traces[34], while others have found a significant amount of them[35].

Conducted experiments on the study of cytochemical indicators of neutrophils in the blood of fetuses of cattle testify to the manifestation of their activity already at the age of 7 months[36]. During the period of intrauterine development, the phagocytic activity of monocytes dominates the activity of neutrophils in the blood of fetuses[37].

Regarding the influence of endogenous and exogenous factors on the establishment of immunological reactivity of the fruits of agricultural animals, the research here is at the initial level and is small in number. In particular, it was found that in the blood serum of piglets that did not receive colostrum, some activity of antibodies is observed, but it is not clear whether they are transferred from the sow or synthesized by the fetus[38]. Some researchers believe that the level of fetal antibodies is directly dependent on their concentration in the mother's body. Neutrophils and monocytes have

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[31] Chebel R. C. Predicting the risk of retained fetal membranes and metritis in dairy cows according to prepartum hemogram and immune and metabolic status. *Preventive Veterinary Medicine*. 2020. P. 105204. https://doi.org/10.1016/j.prevetmed.2020.105204

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[33] Dahl G. E., Tao S., Laporta J. Heat Stress Impacts Immune Status in Cows Across the Life Cycle. *Frontiers in Veterinary Science*. 2020. Vol. 7. P. 116. https://doi.org/10.3389/fvets.2020.00116

[34] Natural antibodies in bovine milk and blood plasma: Variability among cows, repeatability within cows, and relation between milk and plasma titers / T. C. W. Ploegaert et al. *Veterinary Immunology and Immunopathology*. 2011. Vol. 144, no. 1–2. P. 88–94. https://doi.org/10.1016/j.vetimm.2011.07.008

[35] Heat treatment of bovine colostrum: I. Effects on bacterial and somatic cell counts, immunoglobulin, insulin, and IGF-I concentrations, as well as the colostrum proteome / S. Mann et al. *Journal of Dairy Science*. 2020. Vol. 103, no. 10. P. 9368–9383. https://doi.org/10.3168/jds.2020-18618

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[37] Fluctuation in the number, type and activity of blood neutrophils in cows exhibiting successful and unsuccessful completion of gestation cycle / S. Mohammed et al. *Biological Rhythm Research*. 2017. Vol. 48, no. 6. P. 855–865. https://doi.org/10.1080/09291016.2017.1311984

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the ability to capture test microbes from 3-month-old fetuses, and eosinophils from 5-month-old fetuses[39].

In general, the study of the formation of the immunological status of fetuses during intrauterine development and the influence of various factors on it is an important issue that significantly affects the stability and viability of newborns, especially in the early postnatal period. In particular, the question of the influence of heredity on the immune status of fetuses remains relevant.

The purpose of the research was to investigate the influence of hereditary factors on the immunological parameters of the fetuses of the black-spotted dairy cows.

2. Research material and methodology

In this study, the data obtained on four dairy farms of the Podil region, Ukraine were analyzed. The size of the herd varied, on average, from 100 to 400 cows. Animals were kept loose, fed with mixed rations, milking was carried out twice a day. Vaccinations and treatments against parasites were carried out in accordance with the protocols for their use. The study was conducted from 2019 to 2023.

To conduct the experiment, according to the principle of analogues, taking into account breed, age, live weight and clinical and physiological state, four groups of fat cows of the black and spotted breed, 15 heads each, were formed. In the I (control) group there were fruits of the purebred black-spotted breed, II – fruits of the genotype 5/8 black-spotted (Ch) x 3/8 Holstein (G), III – fruits of the genotype 7/16 Ch x 9/16 G and IV – fruits of genotype 5/16 Ch x 11/16 G. All animals were kept on a 24-hour starvation diet before slaughter. Blood from calving cows was taken from the jugular vein. Fruits with uteruses were collected in a specially mounted container. All manipulations with uteruses and fetuses, including taking blood from the umbilical cord of the fetuses, were performed in the conditions of a laboratory box.

The level of lysozyme, class G and M immunoglobulins, bactericidal and lysozyme activity was determined in the blood of fetuses and their mothers. Concentrations of immunoglobulins G, M, and A were determined by simple radial immunodiffusion using a commercial kit[40]. Plates with agar added to anti-bovine immunoglobulin G, M, and A were used. Bactericidal activity

[39] Early post-partum hematological changes in Holstein dairy cows with retained placenta / P. Moretti et al. *Animal Reproduction Science.* 2015. Vol. 152. P. 17–25. https://doi.org/10.1016/j.anireprosci.2014.11.019

[40] Mancini G., Carbonara A. O., Heremans J. F. Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry.* 1965. Vol. 2, no. 3. P. 235–IN6. https://doi.org/10.1016/0019-2791(65)90004-2

in blood serum samples was studied according to the method of Markov, lysozyme activity – using the diffusion method[41].

During the experimental research, the international requirements of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986) and the corresponding Law of Ukraine "On the Protection of Animals from Cruelty Treatment" No. 3447-IV dated June 21 were observed. 2006

The obtained digital material was statistically processed using a computer program to determine the arithmetic mean (M), the statistical error of the arithmetic mean (m), the probability of the difference (p) between the arithmetic means of two variational series according to the Student's probability criterion (t). The difference between the two values was considered significant at $P<0.05$.

3. Research results and their discussion

The immunobiology of the animal body during intrauterine development is characterized by a number of features. In particular, it is suggested that the mother's immune response to antigens of the embryo of the paternal haplotype is a necessary part of normal embryogenesis, determines the growth, development, formation, differentiation of tissues and organs of the embryo, that is, the immune system exhibits an immunotrophic effect on it. There are also reports of so-called "enhancement antibodies", which are apparently blocking immunoglobulins of the mother with sufficiently high activity and have the ability to stimulate fetal growth[42, 43].

Lysozyme has a bactericidal effect on almost all body fluids. Resistance was found only in lactic acid and propionic acid bacteria. In addition, its activity increases in the presence of immunoglobulins[44]. As it was established as a result of our research, the bactericidal activity of blood serum of fetuses of cows from 3 to 7 months of gestation was detected only in some samples and at a rather low level (Table 1). In particular, in the control group of 7-month-old fetuses, the bactericidal activity of blood

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[41] Current Diagnostic Methods for Assessing Transfer of Passive Immunity in Calves and Possible Improvements: A Literature Review / R. S. de Souza et al. Animals. 2021. Vol. 11, no. 10. P. 2963. https://doi.org/10.3390/ani11102963

[42] Natural antibodies in bovine milk and blood plasma: Variability among cows, repeatability within cows, and relation between milk and plasma titers / T. C. W. Ploegaert et al. *Veterinary Immunology and Immunopathology*. 2011. Vol. 144, no. 1–2. P. 88–94. https://doi.org/10.1016/j.vetimm.2011.07.008

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[44] The bovine neutrophil: Structure and function in blood and milk. *Veterinary Research.* 2003. Vol. 34, no. 5. P. 597–627. https://doi.org/10.1051/vetres:2003024

serum was observed only in 2 samples out of 5 (40.0%), and in the fetuses of cows of the Ukrainian black-spotted dairy breed – in 4 samples out of 15 (26.7%).

Table 1

Immunological indicators of the blood of the fetuses of different genotypes of black and spotted cattle, M±m

Indicator	Group of animals (n = 5 in each group of each age period)				On average for II–IV groups in each age period (n=15)
	I	II	III	IV	
3 months					
SBA, %	10,59 (1)	-	-	-	-
Lysozyme, µg/ml	1,76±0,14	2,10±0,10	1,99±0,16	2,06±0,12	2,05±0,06
SLA, U/mL	35,73±2,74	42,63±2,06	40,40±3,26	41,82±2,42	41,62±1,28
IgG, мг/мл	-	0,01 (1)	0,03 (1)	0,04±0,01 (2)	0,03±0,01 (4)
IgM, мг/мл	0,29±0,01	0,31±0,02	0,38±0,04	0,32±0,05	0,33±0,02
5 months					
SBA, %	7,39 (1)	10,09 (1)	-	-	10,09 (1)
Lysozyme, µg/ml	2,10±0,12	2,45±0,19	2,84±0,14	2,84±0,08	2,71±0,09
SLA, U/mL	42,63±2,46	49,74±3,87	57,65±2,92	57,65±1,54	55,01±1,72
IgG, мг/мл	±	±	±	±	±
IgM, мг/мл	±	±	±	±	±
7 months					
SBA, %	±	±	±	±	±
Lysozyme, µg/ml	±	±	±	±	±
SLA, U/mL	±	±	±	±	±
IgG, мг/мл	±	±	±	±	±
IgM, мг/мл	±	±	±	±	±

However, the level of lysozyme was detected in fetuses throughout the entire period. This indicator in blood serum of 3-month-old fetuses of the control group was lower than that of fetuses of the II group by 19.31%; III – by 13.07; IV – by 17.05% and on average for II-IV groups – by 16.48%. At the same time, a significant difference ($P<0.05$) was observed only between the control (I) and II experimental groups and the fruits of the Ukrainian black-spotted dairy breed (together for II–IV groups).

The level of lysozyme and lysozyme activity in blood serum of 5-month-old fetuses was lower in the control group of animals. The difference according to the indicated indicators was statistically significant between I and II groups, I and III, and I and on average across II-IV groups. At the 7th month of gestation, an increase in lysozyme and lysozyme activity of blood serum was found in fetuses of groups II and IV by 27.35% ($P<0.05$), group III and fetuses of the Ukrainian black and spotted dairy breed (together in groups II-IV) – respectively by 10.04 and 21.79% ($P<0.05$), compared to the fruits of the control group. In connection with the increase in blood volume in the Holstein breed, the above-mentioned indicators had a wave-like character throughout the body.

Immunoglobulin G (IgG) is one of the main types of antibodies because of its protective role in infectious diseases. IgG is responsible for neutralizing viruses and bacterial toxins, promoting phagocytosis and lysis of bacteria. It accounts for approximately 80% of total circulating immunoglobulins. IgG can be transferred from mother to fetus through colostrum or through the placenta. For example, the transfer of this class of immunoglobulins has been described in horses [45], cows[46, 47], humans[48, 49].

Our research revealed that immunoglobulins of class M are constantly circulating in the blood serum of 3-month-old fetuses of all groups, and immunoglobulins of class G were absent in almost all samples. Only

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[45] Quality-Related Properties of Equine Immunoglobulins Purified by Different Approaches / S. Mateljak Lukačević et al. *Toxins.* 2020. Vol. 12, no. 12. P. 798. https://doi.org/10.3390/toxins12120798

[46] Factors associated with the concentration of immunoglobulin G in the colostrum of dairy cows / M. Conneely et al. *Animal.* 2013. Vol. 7, no. 11. P. 1824–1832. https://doi.org/10.1017/s1751731113001444

[47] Changes in biomarkers of metabolic stress during late gestation of dairy cows associated with colostrum volume and immunoglobulin content / R. M. Rossi et al. *Journal of Dairy Science.* 2022. Vol. 106, no. 1. P. 718–732. https://doi.org/10.3168/jds.2022-22240

[48] How to estimate time of infection with Toxoplasma gondii in pregnant women. Use of specific IgG and IgM kinetics by 7 techniques on 691 sera / H. Fricker-Hidalgo et al. *Diagnostic Microbiology and Infectious Disease*. 2020. Vol. 96, no. 4. P. 114987. https://doi.org/10.1016/j.diagmicrobio.2020.114987

[49] Prevalence of human parvovirus b19 igg and igm antibodies among pregnant women attending antenatal clinic at federal teaching hospital ido-ekiti, Nigeria. / R. Y. Akele et al. *African journal of infectious diseases*. 2021. Vol. 15, no. 2. P. 10–15. https://doi.org/10.21010/ajid.v15i2.3

4 samples out of 15 (26.27%) of fetuses of the Ukrainian black and spotted dairy breed contained small amounts of Ig G, but with rather high variability of this indicator (Cv = 72.01%). A statistically significant difference was observed between the level of Ig M in the blood serum of the fetuses of the I group compared to the III and in the average of the II-IV groups ($P<0.05$).

The level of Ig M in blood serum of 5-month-old fetuses of groups II and III and on average in groups II-IV was higher by 11.90%, and IV by 9.52% compared to fetuses of group I. At the same time, a probable difference according to this indicator existed between the fruits of groups I and II, groups I and III, and between fruits of the Ukrainian black and spotted dairy breed in general. Class G immunoglobulins were absent in the vast majority of blood serum samples of 5-month-old fetuses. Again, a high variability of this indicator was observed in the fruits of the Ukrainian black and spotted dairy breed (Cv = 98.15%).

Compared with 3- and 5-month-old fetuses, the number of positive samples for Ig G in the blood serum of 7-month-old fetuses increased – in 2 samples out of 5 (40.00%) in the control group and in 7 samples out of 15 (46.67%) in the fruits of the Ukrainian black and spotted dairy breed with a high coefficient of variation – 28.28 and 83.32%, respectively. There was no significant difference in the level of Ig M in blood serum of 7-month-old fetuses of the control and experimental groups.

The conducted experimental studies prove that humoral factors of natural resistance are not expressed in calves during intrauterine development, in particular, complement and bactericidal activity of blood could not be detected in them[50]. However, it is known that the calf's blood in the first hours of life before receiving colostrum has an increased number of leukocytes that have phagocytic activity[51, 52]. Research conducted by scientists on the effect of maternal blood plasma on the phagocytic activity of fetal leukocytes and vice versa, indicates the set or level of humoral factors in fetal blood serum that opsonize the activity of bovine leukocytes, as well as the presence of phagocytosis inhibitors in it, or a change in receptors on leukocytes of cows[53, 54].

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We established that, regardless of the age of the fetuses, the bactericidal activity of their blood serum was manifested only in some samples. The amount of lysozyme in the blood serum of fetuses from 3 to 5 months of age increased in the control (I) group by 1.19 times, and from 5 to 7 months of age it decreased by 1.17 times. In the Ukrainian black-spotted dairy breed, a similar pattern is observed, that is, an increase from 3 to 5 months of fruit age by 1.32 times and a decrease of lysozyme from 5 to 7 months of age by 1.24 times. Therefore, the peak level of lysozyme in the blood serum of the fetuses, regardless of the groups, falls on the 5-month age of the fetuses. The dynamics of changes in the lysozyme activity of fetal blood serum varied similarly to the level of lysozyme.

Literary data are quite different regarding information on the presence of gamma globulins of classes A and M in the circulating blood of late fetuses of cattle and calves before receiving colostrum[55, 56]. Experimental studies confirm the constant presence of immunoglobulins of class M and probably registered immunoglobulins of class G in the blood serum of fetuses of cattle, while immunoglobulins of class A were absent in fetal serum at all. Moreover, the maximum Ig M was observed in 5- and 9-month-old fetuses, the minimum in 3- and 7-month-old fetuses.

We established that in all studied groups, the highest level of Ig M was observed in the blood serum of 5-month-old fetuses. They prevailed according to this indicator of 3-month-old fetuses of the I group by 1.45 times; II – in 1.52; III – in 1.24; IV – by 1.42 times, and 7-month-olds – by 1.11, respectively; 1.15; 1.27; 1.18 and 1.21 times ($P<0.05$). It can be assumed that the synthesis of Ig M in the blood serum of fetuses occurs unevenly and with a certain periodicity. In the blood of fetuses of all age groups, Ig G was mostly absent, although with increasing age of the fetus, the number of positive samples increases approximately twice.

In the blood serum of pregnant mothers, the general pattern is that the content of lysozyme, immunoglobulins G and M, as well as the level of bactericidal and lysozyme activity were significantly higher than in the blood serum of their fetuses (Table 2). At the 3rd month of gestation, the bactericidal activity of blood serum of cows of the II group was higher by 5.20%, III by 14.11%, and on average by II-IV groups by 4.88%, compared

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to the cows of the I (control) group. At the same time, the cows of the IV group were inferior to the animals of the I group by 4.86% in terms of this indicator. At the same time, the difference was statistically significant only between animals of the I and III groups ($P<0.05$).

Table 2

Immunological indicators of the blood of mothers of fetuses of different genotypes of black and spotted cattle, M±m

Indicator	Group of animals (n = 5 in each group of each age period)				On average for II–IV groups in each age period (n = 15)
	I	II	III	IV	
3 months					
SBA, %	44,02±2,17	46,31±2,89	50,23±1,03	41,98±0,55	46,17±1,25
Lysozyme, µg/ml	8,56±1,34	8,56±0,41	9,00±0,43	9,70±0,50	9,10±0,25
SLA, U/mL	173,77±27,13	173,77±8,30	182,70±8,73	196,91±10,20	184,46±5,05
IgG, мг/мл	16,56±0,67	17,04±0,44	16,74±0,58	16,86±0,72	16,88±0,29
IgM, мг/мл	1,94±0,10	1,90±0,04	1,86±0,13	1,76±0,12	1,84±0,05
5 months					
SBA, %	54,99±2,84	59,75±1,20	52,72±3,18	52,50±1,59	54,99±1,37
Lysozyme, µg/ml	8,94±0,74	10,58±0,56	9,90±0,67	9,80±0,96	10,09±0,37
SLA, U/mL	181,48±14,91	214,77±11,27	200,97±13,66	198,94±19,42	204,90±7,50
IgG, мг/мл	16,32±0,48	17,46±0,50	16,86±0,71	18,06±0,37	17,46±0,29
IgM, мг/мл	1,98±0,09	1,92±0,12	1,98±0,13	1,90±0,12	1,93±0,06
7 months					
SBA, %	50,15±1,46	56,03±3,24	52,63±1,09	49,18±1,23	52,61±1,25
Lysozyme, µg/ml	11,98±0,87	12,90±0,84	12,56±1,14	11,38±0,59	12,28±0,46
SLA, U/mL	243,19±17,59	261,87±16,98	254,97±23,13	231,01±11,89	249,28±9,28
IgG, мг/мл	16,86±0,75	16,62±0,85	16,68±0,41	15,60±0,15	16,30±0,29
IgM, мг/мл	1,76±0,08	1,88±0,09	1,88±0,11	1,80±0,12	1,85±0,05

At 5 months, the animals of the control and experimental groups did not differ significantly in terms of the bactericidal activity of blood serum, which is evidenced by the absence of a statistically significant difference between them. At the same time, cows at 3 months of gestation were significantly inferior to animals that were at 5 months of gestation, namely: Group I – by 1.25 times (24.92%); II – in 1.29 (29.02); III – in 1.05 (4.96); IV – 0 in 1.25 (25.06) and on average in II-IV groups – in 1.19 times (19.10%).

In cows of the I group at 7 months of gestation, the bactericidal activity of blood serum was lower than in the animals of the II group by 11.72%, III – by 4.95%, and on average for the II–IV groups – by 4.91% and higher, than in animals of IV group – by 1.97%, however, the difference between cows of all groups was improbable. An insignificant decrease of this indicator was observed in cows at 7 months of gestation compared to animals at 5 months of gestation in groups I, II, III, IV and on average in groups II–IV by 1.1 times, respectively; 1.07; 1.002; 1.07 and 1.05 times ($P<0.05$).

The amount of lysozyme and, accordingly, the level of lysozyme activity in the blood serum of cows at the 3rd month of gestation in the I and II groups of animals were practically the same, and in the III group they exceeded the control by 5.14%, in the IV group by 13.32%, and on average in animals of the Ukrainian black and spotted dairy breed – by 6.31%. The amount of lysozyme in the blood serum of cows at the 5th month of pregnancy was higher in the II group by 18.34%; III – by 10.74; IV – by 9.62 and on average in II-IV groups – by 12.86%, compared to animals of the I group. In animals at 5 months of gestation, the amount of lysozyme and the level of lysozyme activity in the blood serum of mother cows were significantly higher than in animals at 3 months of gestation in group II by 1.24 times (23.60%), in group III – by 1.10 (10.00) and in general in animals of the Ukrainian black and spotted dairy breed – 1.11 times (11.00%). In groups I and IV, this difference was insignificant – 1.04 times (4.4%) and 1.01 times (1.03%), respectively.

At the 7th month of pregnancy, these indicators in the blood serum of animals of II, III groups and on average in II–IV groups were higher compared to cows of the control group by 7.68%, respectively; 4.84 and 2.50%, and 5.27% lower compared to animals of the IV group of animals. However, this difference between animals of different groups during the studied period of maturity was improbable. We can only talk about the presence of a tendency to increase the level of lysozyme in the blood serum of fat cows, in connection with the increase in the proportion of Holstein blood. The dynamics of changes in the level of lysozyme activity in blood serum of mother cows was similar.

If we compare the given indicators of cows at 7 months of gestation with the indicators of animals at 5 months of gestation, then, regardless of the groups, there is a significant statistically probable increase, in particular, in the 1st group – by 1.34 times; II – in 1.22; III – in 1.27; IV – 1.16 times, and on average for II-IV groups (animals of the Ukrainian black and spotted dairy breed) – 1.22 times. It is natural that there was a gradual increase in the amount of lysozyme and the level of lysozyme activity in the blood serum of mother cows in the period from 3 to 7 months of pregnancy.

The researchers established fluctuations of lysozyme in fetuses of cattle in the range of 2.03-3.36 μg/ml, and in their mothers – 9.10-14.70 μg/ml, and its maximum level was in 5-month-old fetuses, and in mothers – at 7 months of pregnancy[57, 58, 59]. In our case, the lysozyme content of mothers' blood serum at 3 months of gestation was higher than that of their fetuses of the first group – 4.86 times; II – at 4.08; III – at 4.52; IV – 4.71 times and on average for II–IV groups – 4.43 times; in the 5th month of gestation – 4.26, respectively; 4.32; 3.49; 3.45 and 3.72 times, and in the 7th month of pregnancy – in 6.69; 5.66; 6.38; 4.99 and 5.63 times ($P<0.05$).

The content of Ig G in the blood serum of animals at 3 months of gestation in the II, III, IV experimental groups exceeded this indicator in the cows of the control group by 2.90%, respectively; 1.09 and 1.81%. On average, in groups II-IV, the advantage of this indicator over animals of group I was 1.93%. Therefore, it is possible to note a certain tendency towards an increase in the level of Ig G in the blood serum of cows at 3 months of gestation due to an increase in the bloodiness of the Holstein breed, however, no probable difference in this indicator was found between the animals of the control and experimental groups. The content of Ig M in the blood serum of animals of group I, on the contrary, was somewhat higher than that of cows of groups II, III, IV and on average for groups II–IV by 2.11%, respectively; 4.30; 10.23; and 5.43%, however, the difference between the groups was statistically improbable.

The amount of Ig G in the blood serum of cows at the 5th month of pregnancy was the highest in animals of the IV group, and they prevailed by this indicator of the animals of the I group by 10.66%; II – by 3.44; III – by 7.12 and on average by II-IV groups by 3.44%. In general, the blood serum of the mothers of all experimental groups contains a slightly higher amount of IgG than the animals of the control group. Quite low coefficients of variation of the named indicator (Cv 4.14–8.48%) indicate its insignificant variability in the blood sera of beef cows of all groups.

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At the 5th month of gestation, the animals of the I group had a slight advantage in the amount of Ig M in the blood serum over the animals of the II group by 3.13%; IV – by 4.21% and on average over animals of the Ukrainian black and spotted dairy breed (II-IV groups) – by 2.59%. However, this advantage was statistically improbable. The amount of Ig G in the blood serum of cows of the control group at 5 months of gestation, in contrast to animals of the same group at 3 months of gestation, practically remained at the same level. The biggest difference in this indicator was observed in cows of IV group, where its amount was 1.07 times (7.12%) higher in favor of animals at 5 months of pregnancy, and on average in II–IV groups this indicator was only 1 times higher .03 times (3.44%). The amount of Ig M in the blood serum of cows at the 5th month of gestation was 1.02 times higher in the I group; II – in 1.01; III – in 1.06; IV – by 1.08 and on average by II-IV groups – by 1.05 times, compared to the blood serum of cows at 3 months of pregnancy.

At the 7th month of pregnancy, the content of Ig G in the blood serum of cows of the control group was 8.08% higher than that of animals of the IV group, III – by 1.08%; II – by 1.44 and in general in animals of the Ukrainian black-spotted dairy breed – by 3.44%, but this difference did not acquire statistically significant values. In the blood serum of cows of the control group at 7 months of gestation compared to animals at 5 months of gestation, the content of Ig G was 1.03 times (3.31%) more, and in the cows of the experimental groups, on the contrary, its amount was lower in the II group, respectively – 1.5 times (5.05%); III – in 1.01 (1.08); IV – by 1.16 (15.77) and on average by II-IV groups – by 1.07 times (7.12%). Therefore, a clear regularity of the dynamics of changes in the amount of Ig G in the blood serum of cows of different groups from the 3rd to the 7th month of pregnancy was not found.

In the blood serum of the cows of the experimental groups at 7 months of gestation, compared to purebred black-and-white animals, a slight tendency to increase the amount of Ig M was found. According to this indicator, the cows of the II and III groups prevailed over the animals of the control group by 6.28%; IV by 2.27 and in general animals of the Ukrainian black-spotted dairy breed – by 5.11%. There was slight variability in the mentioned indicator within the groups, as evidenced by the small values of the coefficient of variation (Cv 9.51-13.61%). The amount of Ig M in the blood serum of cows at 5 months of gestation, regardless of the groups, was greater than in animals at 3 and 7 months of gestation. From the 5th to the 7th month of gestation, a slight decrease in the amount of Ig M in the blood serum of animals of the 1st group was found – by 1.13 times; II – in 1.02;

III – in 1.05; IV – by 1.06 and, on average, by II-IV groups (Ukrainian black-spotted dairy breed) – by 1.04 times ($P<0.05$).

It was established that the amount of immunoglobulins G and M in the blood serum of late fetuses is almost equal, but their level is significantly inferior to the concentration in maternal blood serum. In our case, according to the blood serum content of Ig M, cows at 3 months of pregnancy exceeded their fetuses in the first group by 6.69 times; II – at 6.13; III – in 4.89; IV – 5.50 times and, on average, in animals of the black and spotted dairy Ukrainian breed – 5.58 times. At the 5th month of gestation, this advantage was, respectively, 4.71; 4.09; 4.21; 4.13 and 4.11 times, and at 7 months of pregnancy – 4.63; 4.59; 5.08; 4.62 and 4.74 times. According to the content of Ig G, regardless of the month of gestation, the difference was even greater in favor of mothers. In contrast to the fetuses, whose blood serum was dominated by Ig M, their mothers had a consistently high level of Ig G.

CONCLUSIONS

Some features of the immunological indicators of the blood of fetuses and their mothers depending on the blood share of heredity by the Holstein breed have been established. Regardless of the age of the fetuses, the bactericidal activity of their blood serum was observed only in some samples. The peak level of lysozyme in the blood serum of fetuses, regardless of genotype, occurred at 5 months of age. The amount of lysozyme in the blood serum of fetuses from 3 to 5 months of age probably increased by 1.17-1.43 times, and from 5 to 7 months of age – decreased by 1.07-1.44 times. Immunoglobulins were present in the blood of the fetuses, but only Ig M was constantly detected, with the highest level at 5 months of age. They prevailed according to the aforementioned indicator of 3-month-old fruits by 1.24-1.52 times and 7-month-old fruits by 1.11-1.27 times. The synthesis of Ig M in the body of the fetus is uneven and with a certain periodicity. Ig G was mostly absent in the blood of fetuses of all studied age periods, although the number of positive samples increased by approximately twofold with increasing fetal age. An increase in the lysozyme activity (lysozyme level) of the blood serum of fetuses at 5 and 7 months of gestation due to the infusion of Holstein blood was revealed. The content of Ig M was also higher in the blood serum of fetuses with a portion of Holstein blood, but a probable difference was observed only at 5 months of gestation. In terms of bactericidal activity and the level of Ig G, no significant difference between different genotypes of fruits was established. In contrast to the fetuses, all the immunological parameters studied by us were constantly detected in the blood serum of their mothers. A gradual increase in the level of lysozyme (lysozyme activity) in the blood serum of cows during the period from 3 to 7 months of pregnancy was established. In all studied groups, the level of bactericidal activity of blood serum of animals at 3 months of gestation was significantly lower than that of cows that were at 5 months of gestation. With the further increase in the period of conception, an insignificant decrease of this indicator was observed up to 7 months. In general, a clear regularity in the dynamics of changes in the amount of Ig G in the blood serum of cows from 3 to 7 months of gestation was not found in almost all studied groups of animals. In contrast to the fetuses, whose blood serum was dominated by Ig M, the mothers had a significant advantage of Ig G. Cows with a portion of the genotype of Holstein breed fetuses did not differ significantly in terms of the level of bactericidal activity and Ig M from animals with the genotype of black-spotted breed fetuses. According to the level of lysozyme activity (lysozyme) in blood serum, animals with a proportion of blood in the genotype of their fetuses of the Holstein breed prevailed over cows with the genotype of the fetuses of the Black and Spotted breed. The level of Ig G in the blood serum of cows with the fruit genotype of the Ukrainian black-spotted dairy breed was slightly higher than in animals with the black-spotted fruit genotype.

SUMMARY

In the blood of the fetuses, lysozyme and Ig M are constantly present in statistically probable amounts, and not constantly Ig G. A low level of bactericidal activity of the blood serum of the fetuses was manifested in isolated cases. Lysozyme level, Ig M and the manifestation of lysozyme activity in the blood of fetuses undergo significant wave-like fluctuations during pregnancy. Changing the genotype of animals (Holsteinization) affects the quantitative indicators of the level of lysozyme and Ig M in the blood of fetuses. As the age of fetuses increases (from 3 to 7 months), the number of positive samples for Ig G detected in all groups of animals increases by 2.25 times, and by 4 times for bactericidal activity. All studied immunological components of blood serum of cows, in contrast to their fetuses, were characterized by high quantitative indicators. With the development of the fetus, there is a gradual statistically probable increase in the level of lysozyme in the blood serum of mothers by 1.17-1.51 times. The change in the bactericidal activity and content of Ig M in the blood serum of cows has a curvilinear character with the maximum manifestation in animals at 5 months of gestation (52.50-59.75% and 1.90-1.98 mg/ml). During the studied age periods, the level of lysozyme (lysozyme activity) and Ig G in the blood serum of cows whose fetuses had the genotype of the Ukrainian

black-spotted dairy breed was statistically implausibly higher than that of animals with the genotype of the black-spotted dairy breed. In terms of the level of bactericidal activity and the content of Ig M, no significant difference between different genotypes of animals was established.

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Information about the authors:

Prosyanyi Sergiy Borysovych,
Candidate of Agricultural Sciences,
Associate Professor at the Department of Infectious and Invasive Diseases,
Podillia State University
12, Shevchenko Str., Kamianets-Podilskyi, Khmelnytskyi region, 32316, Ukraine

Horiuk Yulia Viktorivna,
Doctor in Veterinary Medicine,
Associate Professor at the Department of Veterinary Obstetrics, Internal Pathology and Surgery,
Podillia State University
12, Shevchenko Str., Kamianets-Podilskyi, Khmelnytskyi region, 32316, Ukraine