Influence of biopreparations on the postnatal period of highly productive cows

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Abstract. The article describes the results of comparative studies on the influence of new immunostimulants on the course of postnatal recovery of the cows under conditions of intensive milk production technology. Injections of PS-2 (group 1) and Prevention-N-E (group 2) at a dose of 10 ml forty, twenty and ten days before calving, and a injection of PDE at a dose of 20 ml with E-Selemium of 10 ml (group 3) twenty days before calving prevent the occurrence of obstetric and gynecological pathology, improve reproductive qualities, as compared to the control group, where no biologics were injected. This fact impacts the acceleration of the first heat onset by 13.7-21.1 days, the conception rate by 0.5-0.7 times, the service period by 16-29.9 days. A positive effect of the tested agents on metabolic processes, morphological and biochemical blood parameters, nonspecific immunological reactivity of the organism was also established. All these factors led to an increase in milk productivity for 305 days of lactation by 186-478 kg, at the same time, milk quality indicators improved correspondingly. Thus, biological preparations PS-2 and Prevention-N-E are highly effective means of preventing obstetric and gynecological pathology.

1. Introduction
Black-and-white breed of cattle is one of the most numerous all over the world. The genetic potential of Holstein cattle is widely used for the purposes of the breed enhancement, this fact results in the
accelerated creation of new populations of specialized dairy animals that are characterized by high productivity and effectiveness.

In several countries the high-priority features for Holstein breed selection have been studied, among them 59.5% – productivity, 28.0% – longevity and 12.5% – health and reproduction [1]. The result of this selection is an effective milk production and low immune status.

Further livestock breeding intensification requires intensive use of the breeding stock. This task can be solved when the occurrence of obstetric and gynecological pathology is reduced to minimum; however, the level of this pathology significantly increases with an increase in the productivity of animals. It impacts the incidence of complications at calving and the postnatal process, leading to extension of the recovery period and conception decrease. It is noted that most often infertility occurs in highly productive cows [2-4].

Due to peculiarities of the physiological state, the cattle breeding stock is characterized by a low immune status, which, in its turn, becomes lower under the influence of external limiting factors. As a result, farm animals productivity decreases by 10-35%, breeding capacity – by 15-30% [5].

Endometritis, subinvolution of the uterus, mastitis, leading to infertility and forced culling, are most often recorded among obstetric and gynecological pathologies in cows [6, 7].

The immediate causes of birth and postnatal pathologies are lack of exercise, cow overfeeding during the dry period followed by gross obesity, large fetus or twins leading to severe stretching of the uterus, due to which the force in labors is reduced significantly; intrauterine development abnormalities in the fetus, the birth canal damage in the process of calving causing general weakness and ineffective uterine contractions for the placenta and lochia removal. But most scientists give the primary role to the uterine infections [8, 9].

It is possible to maintain health, reproduction, and resistance to environmental and technogenic pressure in high-productive animals only when optimal conditions for animal immunodefenses against the pathological process are provided [10, 11]. Consequently, the immune status of the animal body is very important, particularly, in gynecological diseases. Therefore, the search for the ways to reduce these negative effects in cows of high-productive herds is an urgent issue of modern livestock farming.

The purpose of this work is prevention of diseases in the postnatal period and realization of the cows productive qualities by activating the nonspecific resistance of the organism with biologicals PS-2, Prevention-N-E and PDE+E-selenium.

2. Materials and methods
The experimental part of the research work on studying influence of the biologicals on the cattle breeding capacity and milk productivity have been carried out under conditions of the livestock breeding complex at the farming enterprise Agrofirma Oldeevskaya, JSC, the Chuvash Republic; materials processing have been carried out at the Chuvash Republican Veterinary Laboratory of the State Veterinary Service of the Chuvash Republic and at the Laboratory of Clinical and Hematological Research at the Chuvash State Agrarian University during the period from 2017 to 2019.

In order to determine the extent of influence of the biological products PS-2 and Prevention-N-E, developed by the scientists of Chuvash State Agrarian University, Federal State Budgetary Educational Institution of Higher Education, on the implementation of the potential biological resource of cows, we have studied their clinical and physiological state, hematological and biochemical blood profiles, parameters of the organism nonspecific resistance, milk productivity. These studies have been carried out in comparison with PDE (denatured emulsified placenta) and E-selenium, which are widely used in the veterinary practice.

The objects of research were pregnant (45 days before calving) and newly-calved (3-5 days after calving) cows of the Holsteinized Black-and-White breed. In the scientific and economic experiment, four groups of dry cows (control, the 1st experimental, the 2nd experimental and the 3rd experimental) have been selected according to the principle of analogue groups, taking into account clinical and physiological state, age and live weight of 10 animals in each group. Cows of the 1st experimental group have been injected intramuscularly in the middle third of the neck with PS-2 at a dose of 10 ml three
times 45-40, 25-20 and 15-10 days before the expected calving date, the 2nd experimental group have been injected with Prevention-N-E during the same period and at the same dose, the animals of the 3rd experimental group have been injected subcutaneously with a tissue-engineered product at a dose of 20.0 ml and intramuscularly with a complex mineral and vitamin preparation E-selenium – 10.0 ml 20 days before calving; no biologicals have been used in the control group.

PS-2 is a biological product intended for animal nonspecific resistance and immunogenesis activation; it is an aqueous suspension containing 2.5% of a polysaccharide complex of yeast cells immobilized in an agar gel with the addition of 3.55% benzimidazole derivative. Development center – Chuvash State Agrarian University, Federal State Budgetary Educational Institution of Higher Education (Cheboksary, Russia).

Prevention-NE is a complex preparation for activating nonspecific resistance of the cattle organism, for enabling breeding and productive qualities of farm animals; it is an aqueous suspension containing 2.5% of a polysaccharide complex of yeast cells immobilized in an agar gel with the addition of 1.5% benzimidazole derivative and bactericidal drugs of the penicillin and aminoglycoside group. Development center – Chuvash State Agrarian University, Federal State Budgetary Educational Institution of Higher Education (Cheboksary, Russia).

PDE (denatured emulsified placenta) is a tissue-engineered preparation made of the placenta. Contains a complex of biologically active substances: 20 amino acids, low molecular weight peptides, proteins, lipids, Q10 coenzyme, cytokines (interleukins, interferons, growth factors), alpha-fetoprotein, higher fatty acids, balanced natural complex of vitamins, as well as macro- and microelements. It is used for postnatal diseases prevention and treatment, stimulating the immune system in farm animals and birds. Development center – NPP Farmaks, CJSC, Russia, Kirov.

E-selenium is a medicinal product in the form of a solution for injection and oral administration, intended for prevention and treatment of the diseases caused by a lack of vitamin E and selenium. The drug contains sodium selenite and tocopherol acetate (vitamin E) as the active substances, benzyl alcohol and distilled water as the excipients. Development and production of the veterinary pharmaceuticals for professional use – Nita-Pharm, LLC, Russia, Saratov.

Tests of the clinical and physiological state, morphological and biochemical blood profiles, cellular and humoral factors of nonspecific resistance of the cows organism have been carried out 35-30, 15-10 and 10-5 days before the expected calving date, as well as 3-5 days after calving.

Research work have been carried out using the following methods:

- clinical and physiological – monitoring over the animals behavior and appetite, studying their general physiological state, measuring body temperature rectally using an electronic thermometer, the pulse rate was evaluated by palpation along the tail artery, breathing - by auscultation using a phonendoscope;
- zootechnical - the first heat onset, service period, conception rate, breeding efficiency during the first conception and milk productivity records were analyzed in the automated system “Selex. Dairy Cattle”;
- veterinary – when the fetal membranes are not expelled within 8 hours after calving, retention of the placenta was recorded. Reproductive diseases (endometritis, uterine subinvolution) and the conception result were diagnosed by means of rectal ultrasound diagnostics with DRAMINSKI iScan scanner. The diagnosis of clinical mastitis was made when the concomitant clinical signs (hyperemia, inflammation, tenderness, increased local or general temperature, discharged caseous clots and other atypical discharge) are observed, taking into account medical history. Somatest rapid test was used to diagnose subclinical mastitis. Blood samples were taken from the tail vein using a double-ended needle and Vacutainer test tubes containing coagulant to obtain serum and anticoagulant to extract the blood plasma. Subclinical ketosis was diagnosed by measuring beta-hydroxybutyrate (BHB) in the blood of fresh cows on the 5th day after calving with the WellionVet BELUA device;
- hematological – erythrocytes count, hemoglobin concentration and leukocytes count in the blood of cows were determined with PCE 90 Vet automatic hematological analyzer;
• biochemistry - the levels of total protein and its fraction, ALT, AST, glucose, carotene, calcium, phosphorus, alkaline reserve were measured with Chem Well Combo automated biochemistry and EIA analyzer;
• veterinary and sanitary milk inspection was carried out using Klever 2, No. 1213, Termoscan mini, and Somatos-Mini visometric analyzer. Milk samples were taken each month during one lactation period (305 days) at morning milking into the milk collectors installed on the milking machines.
• Processing of the digital data on the research results was carried out by the method of variation statistics as for the reliability of differences between the compared indicators (P<0.05-0.001) using Microsoft Office Excel application software.

3. Results and discussion
Before conducting the research, we analyzed the rate of occurrence of birth and postnatal diseases in cows and the most frequent forms of their manifestation at the livestock complex of Agrofirma Oldeevskaya, JSC, during the period from 2017 to 2019. For the purposes of the analysis, we used the statistical data of the primary reports in Form No. 2-Vet, the register of sick animals, as well as obstetric and gynecological clinical examination. The most common postnatal diseases are mastitis (24.5-28.5%), endometritis (21.1-27.0%) and uterine subinvolution (23.1-25.2%). Retention of placenta was found in 6.1-8.2% of cows, ovarian pathologies were diagnosed in 16.4-18.5% of cows, while ovarian hypofunction was recorded more often – 8.7-11.6%, persistent corpus luteum was found in 6.9-7.8% of cows, and vestibulo-vaginitis – in 16.4-18.2%.

The high incidence rate of reproductive pathologies is explained by large fetuses (an average live weight of calves at birth is 38.0 kg), leading to damage of the birth canal mucous membranes and their subsequent infection with pathogenic microorganisms. Among metabolic disorders, postnatal paresis is recorded – in 4.7-5.9% of cows, as well as subclinical ketosis in 11.6-18.5%, which is apparently associated with the adaptive mechanisms of the body, since the first days after calving milk production is more intensive than dry matter consumption, and this leads to a negative energy balance and hypocalcemia.

Table 1. Gynecologic condition of cows.

| Parameter                          | Control | 1<sup>st</sup> experimental | 2<sup>nd</sup> experimental | 3<sup>rd</sup> experimental |
|------------------------------------|---------|-----------------------------|-----------------------------|-----------------------------|
| Number of animals                  | 10      | 10                          | 10                          | 10                          |
| Placenta expulsion period, h       | 11.9±1.02| 6.2±0.58<sup>*</sup>         | 5.5±0.66<sup>*</sup>         | 7.1±0.62<sup>*</sup>         |
| Placenta retention                 | 3       | -                           | -                           | 1                           |
| Uterine subinvolution              | 3       | 2                           | 1                           | 3                           |
| Endometritis                       | 2       | 1                           | -                           | 1                           |
| Mastitis                           | 3       | 1                           | 2                           | 2                           |
| Ketosis, incl.:                    | 4       | 1                           | 2                           | 1                           |
| 1.2 – 2.5 mmol/L                   | 2       | 1                           | 2                           | 1                           |
| 3.0 – 4.5 mmol/L                   | 2       | -                           | -                           | -                           |
| Over 4.5 mmol/L                    | -       | -                           | -                           | -                           |

<sup>*</sup>P<0.05

In cows of the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> experimental groups the fetal membranes expulsion period was reduced by 5.7 h, 6.4 h and 4.8 h respectively. The risk of uterine subinvolution, endometritis and mastitis decreased in cows of the experimental groups. In presence of the diagnosis of subclinical ketosis, a decrease in the number of cows with metabolic disorders by 4.0 times in the 1st and 3rd experimental groups and by 2.0 times in the 2nd experimental group was established. At the same time, the cows of the experimental groups had ketosis in mild form (BHB = 1.2-2.5 mmol/l), as opposed to the control...
animals (table 1).

### Table 2. Reproductive qualities of cows.

| Parameter                  | Control | 1<sup>st</sup> experimental | 2<sup>nd</sup> experimental | 3<sup>rd</sup> experimental |
|----------------------------|---------|------------------------------|----------------------------|----------------------------|
| Number of animals          | 10      | 10                           | 10                         | 10                         |
| Time of the first heat onset, days | 58.2±1.36 | 42.8±0.93<sup>*</sup>  | 37.1±0.71<sup>*</sup>  | 44.5±0.93<sup>*</sup>  |
| Conception rate            | 2.4±0.43 | 1.8±0.24<sup>**</sup>    | 1.7±0.19<sup>**</sup>    | 1.9±0.32<sup>**</sup> |
| Service period, days       | 119.2±3.05 | 95.8±1.94<sup>**</sup> | 89.3±1.50<sup>**</sup> | 103.2±0.87<sup>**</sup> |

- *P<0.05; **P<0.01.

Under the exposure of the tested biological preparations in cows of the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> experimental groups, the first heat started earlier by 15.4 days, 21.1 and 13.7 days, a decrease in the cows conception rate by 1.3, 1.4 and 1.2 times, respectively, was recorded. The service period in cows from the experimental groups decreased by 23.4 days, 29.9 and 16.0 days, and the breeding efficiency after the first conception increased by 2.5, 2.5 and 2.0 times, respectively (P<0.05-0.01) (table 2).

Three injections of biologicals PS-2 and Prevention-N-E, as well as single injection of PDE and Selenium helped to improve the blood morphological parameters in the experimental cows. Thus, erythrocytes count at the final stage of observation (3-5 days after calving) in cows of the experimental groups was higher, as compared to the control group, by $0.54 \times 10^{12}/l$, 0.70 and $0.41 \times 10^{12}/l$, hemoglobin concentration was higher by 4.1 g/l, 5.0 and 3.4 g/l, and leukocytes count – by $0.69 \times 10^{9}/l$, 1.14 and 0.56 $\times 10^{9}/l$, respectively (P<0.05-0.01). The above-mentioned qualitative changes in the erythrocytes count and hemoglobin level demonstrate hematopoiesis improvement, and the increase in leukocytes count within the reference values indicates the activation of cellular factors of nonspecific resistance of cows under the exposure of the tested biologicals.

Cow immune system correction using biologicals results in hematopoiesis improvement. At the final stage of the study (3-5 days after calving), erythrocytes count in the blood of the cows of the 1<sup>st</sup> (6.64 ± 0.13), 2<sup>nd</sup> (6.80 ± 0.09) and 3<sup>rd</sup> (6.51 ± 0.11) experimental groups was higher than in the control group (6.1 ± 0.22) by 8.9, 11.5 and 6.5%, respectively. The concentration of hemoglobin in the experimental cows exceeded the control ones by 3.9, 4.8 and 3.3%, leukocytes count – by 7.8, 12.8 and 6.3%, respectively.

Animals of all groups had a decrease in the count of eosinophils before and after calving, it means that calving is a technological stress factor for cows. But at the same time, the count of these formed elements after calving was higher in the blood of animals of the 1<sup>st</sup> (5.0 ± 0.51), 2<sup>nd</sup> (5.5 ± 0.51) and 3<sup>rd</sup> (5.2 ± 0, 50) experimental groups as compared to the control group (4.7 ± 0.8%). It can be claimed that immune stimulants reduce the adverse stress effect on cows.

In animals of the control group (4.4 ± 0.20%) the level of banded neutrophils after calving was higher than in the experimental groups by 0.8, 1.0 and 0.6%, respectively. At the same time, the number of segmented neutrophils in the blood of cows of the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> experimental groups was higher by 5.0, 8.4 and 2.0%, respectively, as compared to the control group (19.0 ± 0.60%). The revealed qualitative changes are characteristic of the neutrophilic nucleus shift to the right, thus, cellular factors of nonspecific resistance are stimulated (table 3).

Comparative studies of the blood biochemistry in cows made it possible to discover that the tested biologicals have a significant effect on the total protein synthesis, as its content during the entire observation period was higher in the 1<sup>st</sup> (76.0 ± 0.75 g/l), 2<sup>nd</sup> (76.6 ± 0.35 g/l) and 3<sup>rd</sup> (74.8 ± 0.64 g/l) experimental groups than in the control group (71.0 ± 0.69 g/l) by 5.0 g/l, 5.6 and 3.8 g/l. The albumin
concentration was higher by 7.3, 8.7 and 7.8 g/l, and γ-globulins – by 0.8 g/l, 2.3 and 0.7 g/l, respectively.

Table 3. Dynamics of the cow’s blood leukogram.

| Group of animals | Observation period, days | BA | EO | NEU | agranulocytes, % |
|-----------------|--------------------------|----|----|-----|-----------------|
|                 | before calving | after calving |     |     | banded | segmented | LYM | MO |
| Control         | 35 – 30        | 1.5±0.20       | 5.2±0.32 | 4.3±0.45 | 18.5±1.14 | 52.8±1.24 | 6.0±0.37 |
|                 | 15 – 10        | 1.4±0.24       | 5.0±0.20 | 4.8±0.37 | 19.8±0.37 | 54.6±1.17 | 5.6±0.58 |
|                 | 10 – 5         | 1.6±0.37       | 4.7±0.37 | 4.1±0.37 | 19.4±0.93 | 56.2±1.11 | 5.8±0.40 |
|                 | 3 – 5          | 1.2±0.32       | 4.7±0.80 | 4.4±0.20 | 19.0±0.60 | 57.8±0.60 | 6.0±0.51 |

| 1st experimental | 35 – 30        | 1.6±0.20       | 5.4±0.37 | 3.8±0.37 | 19.0±0.51 | 55.0±0.55 | 5.9±0.40 |
|                 | 15 – 10        | 1.5±0.32       | 5.9±0.20 | 3.6±0.24 | 22.4±0.24 | 56.7±0.32 | 4.8±0.40 |
|                 | 10 – 5         | 1.2±0.20       | 5.3±0.81 | 3.4±0.24 | 24.5±0.92 | 57.4±1.20 | 4.6±0.32 |
|                 | 3 – 5          | 1.1±0.24       | 5.0±0.51 | 3.6±0.24 | 24.0±0.92 | 58.2±0.81 | 4.6±0.51 |

| 2d experimental | 35 – 30        | 1.8±0.32       | 5.7±0.37 | 3.8±0.24 | 19.3±0.45 | 55.4±0.51 | 5.7±0.32 |
|                 | 15 – 10        | 1.5±0.24       | 6.5±0.24 | 3.5±0.24 | 25.2±0.37 | 57.6±0.40 | 4.8±0.37 |
|                 | 10 – 5         | 1.5±0.24       | 5.8±0.51 | 3.0±0.20 | 27.4±1.33 | 58.4±0.93 | 5.1±0.84 |
|                 | 3 – 5          | 1.4±0.24       | 5.5±0.51 | 3.4±0.24 | 27.4±0.97 | 59.6±1.00 | 4.6±0.80 |

| 3d experimental | 35 – 30        | 1.5±0.22       | 5.6±0.25 | 3.6±0.35 | 18.9±0.32 | 56.9±0.35 | 5.0±0.61 |
|                 | 15 – 10        | 1.4±0.33       | 5.0±0.37 | 3.3±0.23 | 21.3±0.73 | 58.0±0.90 | 5.0±0.67 |
|                 | 10 – 5         | 1.4±0.32       | 5.2±0.50 | 3.8±0.20 | 21.0±0.50 | 59.2±0.72 | 4.8±0.55 |

* P<0.05; ** P<0.01.

As a result of biochemical studies of blood, its plasma and serum, it was established that intramuscular injection of biologicals to down-calving cows increased the level of total calcium by 0.22, 0.27 and 0.24 mmol/l, inorganic phosphorus – by 0.22, 0.25 and 0.23 mmol/l, alkaline blood reserve – by 3.8, 4.0 and 3.3 vol. % CO₂, glucose – by 0.58, 0.56 and 0.50 mmol/l, respectively (table 4).

The activity of aminotransferases after calving in the blood of cows of the control group was higher than the reference values, which serves as a signal of the initial damage to the liver tissue. At the same time, ALT level was significantly lower in cows of the experimental groups, as compared to the control group, by 11.1 u/l, 8.02 and 9.49 u/l, and AST – by 16.54 u/l, 13.54 and 15.44 u/l, respectively (P<0.05). At the same time, PS-2 and PDE + E-selenium had greater normalizing effect on the tested enzymes synthesis.

Table 5 demonstrates that milk yield from cows of the control group was 8437±44.7, which is less than in the 1st experimental group by 263 kg, 2d experimental – by 478 kg and 3d experimental – by 186 kg or 3.1%, 5.6 % and 2.2%, respectively.

According to the microbiological studies results, QMAFAnM in milk samples from cows of the control group (5.8×10⁵ CFU/cm³) exceeded the normal value by 0.3×10⁵ CFU/cm³. In the experimental groups, this indicator stayed within the normal range and was lower than in the control by 1.0×10⁵, 2.5×10⁵ and 2.1×10⁵ CFU/cm³, respectively.

The lowest count of somatic cells was found in the 2nd experimental group (1.5×10⁵/cm³), where the complex biological product Prevention-NE was used, which is 1.0×10⁵/cm³ less than in the control group (2.5×10⁵/cm³). Injections of PS-2 and PDE + E-selenium resulted also in the somatic cells reduction in milk by 0.6×10³ and 0.7×10³/cm³, respectively.
Table 4. Biochemical parameters of blood.

| Parameter                  | Observation period, days | Group of animals |
|----------------------------|--------------------------|------------------|
|                            | before calving | after calving | Control | 1st experimental | 2nd experimental | 3rd experimental |
| Total calcium, mmol/l       | 35 – 30               |                | 2.46±0.06 | 2.54±0.03 | 2.50±0.04 | – |
|                            | 15 – 10               |                | 2.27±0.07 | 2.40±0.05 | 2.46±0.04 | 2.50±0.07 |
|                            | 10 – 5                |                | 2.12±0.05 | 2.32±0.06 | 2.40±0.03 | 2.39±0.03 |
|                            | 3 – 5                 |                | 2.06±0.04 | 2.28±0.06* | 2.33±0.07* | 2.30±0.05* |
| Inorganic phosphorus, mmol/l| 35 – 30               |                | 1.47±0.07 | 1.50±0.04 | 1.50±0.05 | – |
|                            | 15 – 10               |                | 1.42±0.07 | 1.55±0.03 | 1.54±0.07 | 1.54±0.07 |
|                            | 10 – 5                |                | 1.39±0.08 | 1.61±0.05* | 1.63±0.06 | 1.63±0.05* |
|                            | 3 – 5                 |                | 1.45±0.08 | 1.67±0.04 | 1.70±0.06* | 1.68±0.04 |
| Alkaline reserve, vol.% CO₂ | 35 – 30               |                | 48.6±0.97 | 48.4±1.12 | 48.0±1.09 | – |
|                            | 15 – 10               |                | 47.5±0.84 | 49.2±0.86 | 49.2±0.78 | 48.8±1.07 |
|                            | 10 – 5                |                | 46.8±1.12 | 50.3±1.24 | 50.5±1.03* | 49.8±1.22 |
|                            | 3 – 5                 |                | 46.6±1.20 | 50.0±1.10* | 50.2±1.16** | 49.5±0.94* |
| Glucose, mmol/l             | 35 – 30               |                | 2.48±0.09 | 2.57±0.11 | 2.55±0.10 | – |
|                            | 15 – 10               |                | 2.35±0.10 | 2.60±0.12 | 2.63±0.05 | 2.58±0.16 |
|                            | 10 – 5                |                | 2.26±0.14 | 2.82±0.08 | 2.80±0.12* | 2.76±0.08 |
|                            | 3 – 5                 |                | 2.20±0.07 | 2.78±0.10* | 2.76±0.09* | 2.70±0.08* |
| 1ALT, u/l                  | 35 – 30               |                | 39.30±1.12 | 36.22±1.10 | 38.65±1.12 | – |
|                            | 15 – 10               |                | 41.87±1.09 | 37.15±0.87 | 39.04±1.09 | 38.72±1.10 |
|                            | 10 – 5                |                | 45.25±0.98 | 40.28±1.09 | 40.62±0.98 | 39.44±0.83* |
|                            | 3 – 5                 |                | 56.12±1.03 | 45.02±1.10* | 48.10±1.11* | 46.63±0.95* |
| 2AST, u/l                  | 35 – 30               |                | 98.12±4.22 | 97.24±6.02 | 96.82±3.42 | – |
|                            | 15 – 10               |                | 104.90±3.85 | 99.55±5.55 | 102.36±4.68 | 103.12±4.66 |
|                            | 10 – 5                |                | 111.36±5.08 | 105.93±5.32 | 105.30±4.04 | 104.13±3.82 |
|                            | 3 – 5                 |                | 123.66±4.64 | 107.12±4.05* | 110.12±4.10* | 108.22±5.03* |

*1ALT – Alanine aminotransferase
*2AST – Aspartate aminotransferase
P<0.05; **P<0.01.

Table 5. Milk productivity of cows.

| Parameter                | Group of animals |
|--------------------------|------------------|
|                          | Control | 1st experimental | 2nd experimental | 3rd experimental |
| Number of animals        | 10      | 10               | 10              | 10               |
| Milk yield for 305 days of lactation period, kg | 8437±44.7 | 8700±55.0** | 8915±48.3*** | 8623±51.9*** |
| Average fat content, %   | 4.05±0.06 | 4.18±0.04 | 4.21±0.02 | 4.15±0.02 |
| Average protein content, %| 3.22±0.07 | 3.20±0.02 | 3.32±0.01 | 3.27±0.05 |

**P<0.01; ***P<0.001.

4. Conclusion
For the first time, the effectiveness of using biologics based on the polysaccharide complex of yeast cells PS-2 and Prevention-N-E in comparison with the widely used PDE and E-selenium preparations in veterinary medicine. Based on the studies, we have addressed the multifactorial problem and proposed ways to increase the efficiency of dairy cattle breeding, due to the introduction of environmentally safe biologics PS-2 and Prevention-N-E into the reproduction technology, which contribute to the prevention of postnatal complications, increase the productive and reproductive qualities of dairy cattle in
conditions of intensive milk production technology. Intramuscular injections of biologicals PS-2 and Prevention-N-E at a dose of 10.0 ml 45-40, 25-20, 15-10 days before calving, as well as subcutaneous injection of PDE at a dose of 20.0 ml with intramuscular injection of E-selenium in an amount of 10.0 ml 20 days before calving stimulated hematopoiesis; caused physiological eosinophilia, moderate neutrophylopemia with neutrophilic nucleus shift to the right, and lymphocytosis; selective mobilization of cytotropic serum enzymes; increased protein metabolism, mainly by synthesis of albumin and γ-globulin fractions; increased nonspecific resistance of organism. It was established to increase the productivity of holstinized black-motley cattle and proved the benign quality of milk according to microbiological, spectrometric and physicochemical indicators and, as a result, the safety of the tested preparations. This effect is more significant when Prevention-N-E is used. A promising direction of further scientific work is the correction of metabolic disorders in cows during dry periods and lactation, the development of algorithms for the treatment of breast pathologies and obstetric-gynecological diseases with complex biological products PS-2 and Prevention-N-E.

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