Ukrainian Journal of Ecology

Ukrainian Journal of Ecology, 2021, 11(3), 145-152, doi: 10.15421/2021_157

ORIGINAL ARTICLE

Autogenous vaccines are an effective means of controlling the epizootic process of mastitis in cows

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Received: 11.04.2021. Accepted 24.05.2021

Prevention of mastitis remains one of the most critical problems in dairy farming. The basis of further pathogenesis is the interaction of the macroorganism and the microorganism/s. The infectious process's latent or clinical form should be considered one of the links in the epizootic process. We examined the dairy herd of a dairy farm and bacteriological examination to set the reasons for mastitis, endometritis, and diseases of newborn calves. The associative content of the microbiota of the udder of sick animals was determined, antibacterial preparations were selected on the principle of targeted use. Production tests were carried out of an experimental series of vaccines made from indigenous microflora, showed that it has a stimulating influence on the cellular and humoral immunity of vaccinated cows, which as the final result, prevents postpartum complications in cows, has a beneficial influence on the condition of the breast and milk quality, as well as on the health of newborn calves. In order to break the epizootic chain, it is essential to effectively influence all three of its links -the source of the pathogen, the mechanism of transmission of the pathogen, and susceptible animals. On dairy farms with organic farming, the most effective is to create a 100% layer of the dairy herd immune to pathogenic and conditionally pathogenic microflora through the use of autogenous vaccines.

Keywords: subclinical mastitis, autochthonous microflora, antibiotic sensitivity, autogenous vaccines, immunity.

Introduction

Formulation of the problem. From year to year, our country is growing requirements for milk and dairy products (Saienko, 2002; Borshch et al., 2020; Grymak et al., 2020; Bashchenko et al., 2021; Fedorovych et al., 2021). The leading indicators of evaluating the quality and safety of milk are the level of bacterial contamination and the number of somatic cells. No less important are other indicators that influence the quality characteristics of this product (Kryzhanivskyi, 2004; Kulyaba et al., 2019; Palchykov et al., 2020; Slivinska et al., 2021). The disease of dairy cows with various forms of mastitis negatively influences the quality of milk (Danylenko, 1973; Korol, 2013).

Mastitis is one of the main reasons for the reduced productivity of cows (up to 30%) and the deterioration of the sanitary quality of milk. Milk from sick cows loses its nutritional properties and becomes unsuitable for technological processing. Young animals that have received milk from cows with mastitis develop poorly, suffer from dysbacteriosis or dyspepsia, and often die. Heifers who were sick in the early postnatal period have 20-30% lower milk production than those who did not. In addition, the secret of patients with mastitis in cows contains microorganisms that negatively influence the quality of dairy products and can also cause various human diseases (Khomyn & Dmytriv, 1999; Nelson et al., 1999; Kukhtyn, 2007).

These data and researches by other scientists testify that mastitis is one of the most difficult veterinary problems. This disease can get sick from 20% to 50% of cows (Roman et al., 2020). Therefore, the prevention of mastitis in cows is one of the most critical problems of dairy farming. Despite the wide range of therapeutic and prophylactic veterinary preparations, mastitis continues to cause significant economic losses to the dairy industry.

The main etiological factor (80% of cases) of mastitis in cows is pathogenic microflora (streptococci, staphylococci, *Escherichia coli*, *Pseudomonas aeruginosa*, corynebacteria, mycoplasmas) or their associations, which are usually activated under the

influence of unfavorable factors caused by poor quality feed, poor care and keeping animals (Dmytriv, 2000; Brylin, 2001; Boiko & Boiko, 2014).
The absence of systemic preventive measures, irrational use of antibacterial preparations for treatment and prevention is the leading factor of formation in conditionally-pathogenic microbiota of the mammary gland of stable antibiotic resistance, which is a problem not only of a particular dairy farm but also a global problem of humane and veterinary medicine (Zhelavskyi et al., 2005; Perkii, 2007; Stetsko, 2018). Therefore, effective prevention of mastitis, based on approaches, which provide limitations on antibacterial preparations, is vital in preventing the formation of antibiotic resistance of microorganisms. Finally, modern requirements regarding organic farming prohibit the use of dairy farms many antibacterial preparations, which, in turn, complicates the prevention of mastitis (Gorbenko et al., 2013). Therefore, the development of new approaches to preventing mastitis, based on the use of the potential of cows' immune system, is an urgent problem of modern dairy farming. This approach, in our opinion, is to study the microbial scape of the breast in clinically healthy cows and for mastitis, the identification of priority pathogens, the identification of possible synergistic relationships between them, and based on these data, the design of autogenous vaccines, which would contain the essential immunogenic substances of each autochthonous pathogen.
In recent years, there have been increasing reports in the scientific literature of the successful use of autogenic vaccines for this purpose (Ryzhenko et al., 2004; Stehnii et al., 2018; Pinchuk et al., 2018). The research aimed to study the effectiveness of the experimental and research series (ERS) of autogenous vaccines to prevent mastitis in cows in one dairy farm in the Lviv region.

Materials and Methods

Biomaterial (secret of the udder from cows with mastitis, discharge from the uterus with postpartum complications, feces from sick calves), stabilized blood and blood serum from cows vaccinated with autogenous vaccine, clinical and epidemiological, immunological, bacteriological, statistical methods. A sampling of biomaterial, isolation, and isolates' identification was performed according to methodological recommendations and guidelines (Skorodumov et al., 2005; Vlizlo et al., 2012).
The ERS of the autogenous vaccine was produced based on the Institute of Veterinary Medicine of the National Academy of Agrarian Sciences (Ukraine). The vaccine is a concentrated aqueous suspension of formalin-inactivated (0.2% formaldehyde by volume of culture) and aerosil adsorbed brand A-300 (1.5 mg/cm^3 inactivated culture) exotoxins and microbial cells of autochthonous strains of *Escherichia coli, Streptococcus pneumoniae, Str. dysagalactiae* and *Staphylococcus aureus* at a concentration of 1.5±0.3×109 for each microorganism species in 1 cm^3 of the vaccine. The preparation is a suspension of light brown color with significant loose sediment, easily broken by shaking into a homogeneous suspension.
The vaccine was warmed to 25-30 °C before introduction, shaken, and introduced intramuscularly in the croup area, twice: the first injection - 2.0 cm^3, the second - 3.0 cm^3 with an interval between the first and second injection - 10-14 days. Blood for the research of vaccinated cows was taken on the 21st day after the second injection of the vaccine, one month and two months after calving. Unvaccinated cows served as controls. Blood was stabilized in one syringe, which was stabilized with heparin, and in the other - not stabilized blood. Bactericidal (BASK) and lysozyme (LASK) activity and antibody titers in the expanded agglutination reaction to surface antigens of bacteria were determined in blood serum, which was taken as immunogens for vaccine production; phagocytic activity of neutrophils and the phagocytic index was determined in stabilized blood (Ivchenko & Pavlenko, 2003).

Results and discussion

The dairy herd of the dairy commodity farm counts 600 cows. The incidence of clinical mastitis during the last three years was 12%, subclinical - 25%, the specific weight of cows with excess somatic cell content in milk was 48%, postpartum complications in the form of delayed manure and purulent-catarrhal endometritis - 26%, morbidity of newborn calves for gastrointestinal disorders - 32%.
Milk samples from cows with clinical and subclinical forms of mastitis were selected for bacteriological examination, the uterine contents from cows with postpartum endometritis, and fecal samples from patients with signs of digestive disorders in newborns calves. Samples of biomaterial were taken before treatment with antibacterial preparations. The research results are given in Table 1.
We determined that 13 isolates were isolated and identified from 12 biomaterials, of which *E. coli* - 6, *Str. pneumoniae* - 3, *Str. dysagalactiae* - 2, *S. aureus* and *S. intermedius* - 2 isolates.
The received data indicate that the microbial landscape of pathogenic and conditionally-pathogenic microorganisms on a separate farm is inhomogeneous in species composition. As a rule, two pathogens were isolated from each pathological biomaterial, each of which belongs to a morphologically and phylogenetically different genus. Therefore, strategic and tactical approaches to preventing and treating such associative infectious diseases require a differentiated approach to selecting antibiotics and specific means of prevention.
Excretion of enteropathogenic by serological typing and biological testing on white mice isolates of E. coli from the secretion of the udder of cows with mastitis and the feces of patients with diarrhea of newborn calves indicates a cause-and-effect relationship of both types of pathology, where the enteropathogenic strain of Escherichia coli plays, in our opinion, a leading role. This is indicated by the isolation of *E. coli* isolates of the same type by antigenic structure, biochemical and enteropathogenic properties from all studied biomaterials.

Table 1. The results of the bacteriological examination of biomaterial from cows and calves

Type of material	Number of samples	Type and number of isolates	Features of antigenic structure, biochemical and biological properties
The secret of the udder, SCM *	4	*Escherichia coli, 2*	O9: K99, enteropathogenic by bioassay on white mice
		Streptococcus dysagalactiae, 2	α-hemolysis, non-pathogenic for white mice
The secret of the udder, CM **	4	*Escherichia coli, 2*	O8, enteropathogenic by bioassay on white mice
		Staphylococcus aureus, 2	Plasma coagulating
The contents of the uterus	2	*Staphylococcus intermedius, 2*	Not plasma coagulating
		Streptococcus pneumoniae, 2	α-hemolytic, virulent for white mice
Faeces	2	*Escherichia coli, 2*	O9: K99, enteropathogenic by bioassay on white mice
		Streptococcus pneumoniae, 1	α-hemolytic, virulent for white mice

Note: SCM * - subclinical mastitis; CM ** - clinical mastitis.

A similar conclusion can be drawn concerning α-hemolytic virulence for white mice strains of *Str. pneumoniae*, excreted from the contents of the uterus on endometritis of cows and feces of sick newborn calves. The biological properties of both isolates of streptococcus (hemolytic and virulence for white mice) indicate their role as virulent pathogens of endometritis in cows and dysbiosis in calves. Analyzing the microbiota of the secretion of the cow's udder with both subclinical and clinical forms of mastitis, it should be noted the leading role of *E. coli* as a pathogen or as a biological factor that aggravated the course of mastitis caused by other factors.

The study of the antigenic structure of dedicated isolates of *E. coli* indicates their belonging to the group of enteropathogenic strains of *Escherichia coli* both in antigenic structure (O9: K99) and in biological properties.

The results (Table 1), show that the causative agents of calf dysbacteriosis were *E. coli* and *Str. pneumoniae*. Escherichia coli as a pathogen entered the organism of calves with colostrum or cow's milk, as evidenced by the results of a bacteriological examination of the udder secretion of cows with mastitis. *Streptococcus pneumoniae*, being the root cause of postpartum endometritis or aggravating postpartum trauma to the birth canal, usually enters the organism of newborn calves during birth. The bacteriological indication and identification of cattle infectious pathology (mastitis - endometritis - dysbacteriosis) indicate its biological polytropicity (Nezhdanov & Zinkevich, 1999; Dmytriv, 2000). Are not excluded that other microorganisms (viruses, mycoplasmas, candidiasis, and others) may participate in this consortium of bacterial agents. Therefore, bacteriological diagnosis of mastitis and endometritis in cows and dysbiosis in newborn calves should be compulsory and comprehensive. Thus, it could use all available methods, in particular microscopic (painting by Gram, Stamp, Main-Grunwald, Rebiger, if possible, specific immunofluorescent globulins), culture using a wide range of differential diagnostic chromogenic media, as well as biological tests on laboratory animals to confirm the virulence of the selected isolates.

Usually, when it comes to laboratory methods of indication and identification of pathogens of mastitis or endometritis in cows, we do not have to talk about mono-infection because we deal with at least three types of pathogenic microbiota (Boiko & Boiko, 2014; Boiko, 2015). In our case, determining which of the selected microorganisms initiated the first alternative changes, i.e., are the primary pathogens and secondary to the infectious process, is complicated and mostly impossible. Finally, at this stage of the organization of anti-epizootic measures aimed at reducing the tension of the epizootic situation with mastitis and endometritis of cows and dysbiosis in newborn calves, this issue is not decisive. The main thing is that we have identified the primary pathogens of all three pathologies and that the latter is infectious; that is, we are dealing with a polyetiological epizootic process on a particular farm. Because of this, the strategy of antibiotic therapy should be aimed primarily at all pathogenic and conditionally-pathogenic isolates selected from the materials of all three biotypes. In Table 2, we presented the sensitivity of isolates to antibiotics.

The isolates of *E. coli* were the most sensitive to ciprofloxacin, enrofloxacin, insensitive to cefuroxime and gentamicin. Isolates of streptococci *Str. pneumoniae* and *Str. dysagalactiae* showed the highest sensitivity to ciprofloxacin, enrofloxacin, cefotaxime, and neomycin, less sensitive to tetracycline and oxacillin (Table 2). Staphylococcal isolates of *S. aureus* and *S. intermedius* were the most sensitive to enrofloxacin, neomycin, and ciprofloxacin. Thus, it can be considered that the most effective antibiotics against autochthonous pathogenic and conditionally-pathogenic microflora in our case were enrofloxacin and ciprofloxacin, less effective - cefotaxime and neomycin.

To overcome the epizootic process in mastitis and endometritis of cows and dysbacteriosis of newborn calves on a separate farm, caused by a consortium of bacteria in which the sources of infectious agents are sick cows and calves, with the help of antibiotics only and even subtracted to each pathogen, with no influence on other links in the epizootic chain, is not possible (Nezhdanov & Zinkevich, 1999; Boiko, 2015).

Table 2. Results of bacteriological research of susceptibility of isolates to antibiotics

№	Antibiotic (group)	Diameters of growth retardation zones, in mm				
		E. coli	***Str. dysagalactiae***	***Str. pneumoniae***	***S. aureus***	***S. intermedius***
1	Benzylpenicillin	12±0.4	18±0.3	21±0.3	16±0.3	14±0.3
2	Oxacillin	15±0.3	21±0.2	23±0.3	19±0.2	15±0.2
3	Cefuroxime	14±0.3	16±0.2	19±0.2	21±0.2	19±0.3
4	Cefotaxime	22±0.2	28±0.2	27±0.2	24±0.2	19±0.2
5	Neomycin	11±0.4	28±0.2	30±0.3	26±0.3	24±0.3
6	Gentamicin	19±0.2	16±0.2	19±0.3	15±0.2	13±0.3
7	Polymyxin B	22±0.4	17±0.3	20±0.2	21±0.3	17±0.2
8	Tetracycline	12±0.3	21±0.2	24±0.2	21±0.2	16±0.3
9	Ciprofloxacin	32±0.2	28±0.2	31±0.2	26±0.2	22±0.2
10	Enrofloxacin	33±0.2	30±0.2	33±0.2	32±0.2	31±0.2

Effective measures of general and specific influence on other epizootic chain links are required, particularly on the pathogen's mechanism and on susceptible animals. Therefore, at this stage of the fight against mastitis and endometritis in cows and dysbacteriosis in calves, we have introduced several measures to reduce microflora in all farm premises. In particular, we used disinfection of stalls, feed, and technological passages, cages for calves, equipment using the new disinfectant "Epidez", according to its use. All objects were treated with the preparation in working dilution at the rate of 0.3±0.2 l/m^2. The actively acting substance of the preparation "Epidez" is polyhexamethylene guanidine hydrochloride (PHMG) - a preparation that belongs to the group of slightly toxic, odorless, and irritating properties, there is no corrosive influence on metals and other materials, and therefore we used it in the presence of animals (Lysytsia et al., 2012; Mandyhra et al., 2018). The use of this disinfectant significantly reduced the microbial load on the organism of animals and thus had a positive influence on the dynamics of the epizootic process. On the effectiveness of the influence on the mechanism of transmission of the pathogen as one of the links in the epizootic chain in the system of preventive measures regarding mastitis and endometritis in cows, numerous developments by both domestic and foreign authors testify (Brylin, 2001; Kurtasov & Kriukova, 2018).
As a result of these and several other investigations on dairy farms, standard operating procedures for preparing the udder of cows for milking have been developed, conservation of teats after milking, sanitation of the mammary gland during dry periods (Dmytriv, 2000; Zhelavskyi et al., 2005). Nevertheless, mastitis remains a major problem in dairy farming because their occurrence is due to many factors, such as biotic nature (circulation on the farm of specific pathogenic and conditionally-pathogenic microflora, individual susceptibility of cows to these pathogens), and the negative influence on the organism of cows of several abiotic contributing and predisposing factors. It is possible to increase the specific resistance of cows to pathogens circulating in a particular form only with the help of inactivated vaccines made from autogenous (autochthonous) strains. Bacterial autogenic vaccines are now de facto and should become a de jure complete alternative to antibiotics in most cases of diseases of bacterial etiology of any localization (Ryzhenko et al., 2001; Boiko, 2016).
Autogenic vaccines are made from strains of microorganisms isolated from sick animals within a single farm (not even a farm if it has several farms) and are used for animals of that particular farm (Ryzhenko et al., 2001; Stehnii et al., 2018; Pinchuk et al., 2018). Autogenous vaccines are made from strains of microorganisms isolated from sick animals within a single farm (not even a farm if it has several farms). We made an experimental and research series of autogenous vaccines used in cows in the dry season (Table 3).
The highest antigenic activity was possessed by the immunogen *E. coli* (1: 1024±307) and *S. aureus* (1: 576±102), and the lowest - immunogens *Str. pneumoniae* (1: 144±26) and *Str. dysagalactiae* (1: 72±13). High antigenicity and immunogenicity of *E. coli* are associated with its surface morphological structures, particularly flagella and villi (Lin et al., 2013; Duan et al., 2017). The more villi have vegetative cells at the time of their inactivation, the stronger is the organism's immune response to this immunogen; herewith, the level of antigenic response correlates with protective (Tiels et al., 2005).
The antigenicity of *E. coli* is significantly influenced by a well-defined lipopolysaccharide complex, which is often used as a powerful stimulant of the immune system (Katz, 1986; Tiels et al., 2005). Because of these data, as well as the results of our previous research, inactivated young (12-14-hour-old) cultures of all three *E. coli* isolates were used as an immunogen for the autogenous vaccine, which was grown in tryptone-soy yeast bouillon (TSYB) with active aeration of the culture (1 l/h) (Mandyhra et al., 2015). Due to the high nutritional qualities of this medium and active aeration of cultures, we achieved a high concentration of microbial mass (3±2×109 microbial cells/cm^3).
The low antigenic activity of streptococci and staphylococci was caused by microcapsules, even though their concentration in microbial cells was the same as Escherichia coli. The latter is built from polysaccharides, which have fragile antigenic properties. Perhaps the weak antigenicity of staphylococci in the vaccine may be due to other mechanisms that are not yet fully understood.

Table 3. Dynamics of agglutinin titers to surface antigens of bacteria, which were taken as immunogens for the production of autogenous vaccines, in the blood serum of cows vaccinated with the vaccine from autogenous strains, in 21 days after the second injection of the vaccine (before calving), in one month and two months after calving (n=5)

The period of taking blood for research	Titers of antibodies to mastitis pathogens, in particular:				
	E. coli	***S. aureus***	***S. intermedius***	***Str. pneumoniae***	***Str. dysagalactiae***
Before calving	1:1024±307*	1:576±102**	1:64±14**	1:144±26**	1:72±13**
1 month after calving	1:576±102**	1:224±77*	1:32±12*	1:64±12**	1:32±10*
2 months after calving	1:224±77*	1:112±38*	1:28±9*	1:40±16*	1:20±8*

Note: ** - p<0,01; * - p<0.05.

Therefore, the increase in antigenicity and immunogenicity to staphylococci and streptococci requires further investigation from the point of view of the accumulation of active biomass of autochthonous isolates and selection of inactivators of these cultures. After all, the means and methods of inactivation of immunogen cultures significantly influence the antigenicity and projective power of immunogens (Stegnij & Sosnickij, 2010).

Analysis of the dynamics of agglutinin titers in the serum of vaccinated cows shows that it has a steady tendency to decrease sharply concerning all immunogens. Thus, antibody titers to *E. coli* antigens in the second month were decreased by 4.6 times, to *S. aureus* antigens - by 3.5, *S. intermedius* - by 2.3, *Str. pneumoniae* - in 4.7 and *Str. dysagalactiae* - 4 times.

On the one hand, this testifies that, despite the relatively high titer of postvaccinal agglutinins, their level after 50-60 days is significantly reduced in order to maintain a sufficient level of immune protection of the mammary gland from possible infection during intensive milk yields, in our opinion, it is necessary to conduct an additional (third) injection of the vaccine.

However, analyzing the overall immune response of vaccinated cow organisms to a 2-times injection of a polyvalent inactivated vaccine, it should be noted that it was powerful, judging by the level of agglutinins, and had a pronounced protective effect. This is evidenced by the research results of phagocytic activity and phagocytic index of blood neutrophils, bactericidal, and lysozyme activity of serum-vaccinated cows (Table 4).

Table 4. Dynamics of phagocytic activity and phagocytic index of blood neutrophils, bactericidal and lysozyme activity of serum of cows in 3 weeks (before calving), in one and two months (after calving) after their vaccination with the autogenous vaccine (n=5)

The period of taking blood for research	Indicators			
	Phagocytic number,%	**Phagocytic index**	**Bactericidal activity of serum, %**	**Lysozyme activity of serum, %**
Before calving	74.4±1.8*	12.5±0.6*	79±8.6*	26.6±0.9*
1 month after calving	60.7±1.4*	11.2±0.4*	68±7.3*	24.1±0.7*
2 months after calving	54.3±1.1*	10.1±0.3*	57±6.6*	22.3±0.5*
Control	40.9±0.9*	7.5±0.7*	43±5.7*	18.4±0.8*

Note: * p<0.01.

Analyzing Table 4, it should be noted that the high level of phagocytic activity of neutrophils, which compared with that in control animals on the 21st day after the second injection of the vaccine, is higher by 33.5% and is 74.4%. However, it gradually decreases, and in a month after calving is 60.7%, two months after calving - 54.3%.

Analyzing the dynamics of the phagocytic index of neutrophils, it should be noted that it is highest in the first three weeks after the second injection of the vaccine (in our case before the calf) and also tends to decrease with increasing post-vaccination period gradually and is closely correlated (ρ=0.94) with phagocytic activity.

Analysis of indicators of the bactericidal and lysozyme activity of the serum grafted with the autogenous vaccine shows that both of these indicators are highest on the 21st day after the second injection of the vaccine and are 79±8.6% and 26.6±0.9%, respectively, indicating the stimulating influence of the vaccine on both indicators of nonspecific humoral activity of serum of cows. With the prolongation of the period from the last injection of the vaccine, the bactericidal and lysozyme activities gradually decrease.

Thus, the analysis of immunological indicators of vaccinated cows shows that they are highest on the 21st day after re-injection of the vaccine. Because of this, we consider that the optimal vaccination period is one in which the period between the second vaccination of pregnant cows and the expected calving date should be 21-28 days. After all, just during this period, the indicators of the intensity of immunity in vaccinated cows are the highest, significantly influencing the protection of the mammary gland from the negative influence of autochthonous pathogenic and conditionally pathogenic microflora, as well as to protect newborn young.

Analysis of zootechnical and economic indicators (Table 5) during the year of vaccine use indicates their positive dynamics, which in turn gives reason to assert the effective influence of vaccination of cows with the autogenous vaccine to reduce the incidence of mastitis in cows (the morbidity decreased by 5.5 times) and endometritis (6 times), reducing the morbidity of newborn calves (8 times).

Table 5. Analysis of zootechnical and economic indicators that characterize the effectiveness of the autogenous vaccine

The use of vaccines	The incidence of mastitis% Clinical	Subclinical	Somatic cells, %	Endometritis, %	Incidence of calves,%
Before	12	25	48	26	32
After	2	5	2.6	4	4

At the same time, the quality of milk by an indicator of the number of somatic cells also improved significantly. Thus, if before the use of the vaccine, the number of cows in the herd with an excess of somatic cells in milk was 48%, then after its use, the percentage of cows with an excess of somatic cells in milk was only 1.6%.
Thus, the use of an integrated approach to the study of the causes of the high incidence of mastitis in cows and endometritis and calves for postnatal diseases and low quality of milk and vaccines from autochthonous strains had a significant favorable influence not only on the condition of the mammary gland and genitive canal after cows calving but also on the health of newborn calves, on the quality of milk and ultimately on the economy of the dairy industry as a whole.

Conclusions

A comprehensive epizootological examination was performed on a dairy farm in the Lviv region due to an increase in the specific clinical weight (12%) and subclinical mastitis (25%), postpartum complications (26%), and gastrointestinal disorders of newborn calves (32%).
Bacteriological research of udder secretion, uterine contents in postpartum complications of cows, and feces of sick newborn calves highlighted and identified the association of pathogenic and conditionally pathogenic microorganisms with the following ratio: *E. coli* - 45%, *Str. pneumoniae* - 20%, *Str. dysagalactiae* - 15%, St. aureus, and *St. intermedius* - 10% each, indicating the causal infectious nature of mastitis and endometritis in cows and neonatal pathology in calves.
The basis of rational antibiotic therapy in patients with mastitis and endometritis of cows and patients with gastrointestinal disorders of newborn calves are the results of antibioticograms of identified pathogens, in particular, it was found that the most effective antibiotics are fluoroquinolones, in particular, enrofloxacin (delay zone 31.8±0.2 mm) and ciprofloxacin (27.8±0.2 mm); beta-lactams - cephalosporins: cefotaxime (24.0±0.2 mm); aminoglycosides: neomycin (23.8±0.3 mm); polypeptides - polymyxin B (19.4±0.28 mm). The highest titers of agglutinins were detected on the 21st day after the second injection of the vaccine against *E. coli* antigens (1:1024±307) and *S. aureus* (1:576±102), the lowest - to *Str. pneumoniae* (1:144±26) and the lowest - to *Str. dysagalactiae* (1:72± 13). With prolongation, the level of agglutinins decreases, and in 2 months after calving decreases significantly, which is an objective reason for the additional (third) injection of the vaccine.
Immunological researches of phagocytic activity and phagocytic index of blood neutrophils, bactericidal and lysozyme activity of serum of cows, vaccinated with an experimental and research series of formalin-inactivated and aerosil-concentrated vaccine from autogenous strains, showed that the highest rates were on the 21st day after the second injection of the vaccine.
The use of laboratory-selected antibacterial preparations, as well as autogenous vaccine, had a significant positive influence not only on the condition of the mammary gland and patrimonial ways after cows calving, but also on the health of newborn calves, on the quality of milk and, ultimately, on the economy of the dairy industry as a whole. This was evidenced by the analysis of zootechnical and economic indicators, which showed a decrease in the proportion of clinical mastitis 6 times and subclinical - in 5 times, postpartum complications - 4 times, and gastrointestinal disorders of newborn calves - 8 times.

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Citation:

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