# Morphological and functional blood parameters in the comorbid course of endometritis and purulent-necrotic diseases of the hoof area in highly productive cows

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Abstract. In veterinary medicine, there is a problem of the comorbid course of reproductive function disorders and purulent-necrotic lesions in the toe area of cows. The research was carried out on the basis of Voskresenskoye JSC, Voskresensky district, Moscow region, with a total population of 1,450 heads of cattle, including 830 cows. The material for the study was cows with endometritis (n=28), animals with orthopedic pathology (n=25) and with a comorbid course of postpartum endometritis and purulentinflammatory processes in the toe area (n=27). Indicators obtained from clinically healthy animals (n=23) were used as control. From animals in the control and experimental groups, blood was taken in the morning before feeding from the jugular vein for morphofunctional studies. In experienced cows that had lesions in the limbs before or after birth, the likelihood of gynecological diseases associated with morphological disorders in the ovaries increased. The significant spread of these types of pathology is the direct cause of prolonged anaphrodisia of cows and a decrease in the level of reproduction of the herd with a high incidence of limb diseases. It has been established that the clinical manifestation of the comorbid course of orthopedic and obstetric-gynecological pathology has a more severe clinical manifestation than in the course of individual diseases. The study was supported by the grant from the Russian Science Foundation No 24-26-00172, https://rscf.ru/project/24-26-00172/.

### 1 Introduction

In veterinary medicine, there is a problem of the comorbid course of reproductive function disorders and purulent-necrotic lesions in the toe area of cows. It is known that postpartum endometritis most often develops in highly productive cows with purulent-necrotic lesions in the distal part of the limbs that occur before birth or in the first weeks after calving [1-4].

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The comorbid course of gynecological and orthopedic pathology in cows leads to significant economic damage associated with a decrease in milk productivity and the cost of diagnostic, therapeutic, and preventive veterinary measures [2, 5-9]. The problem of a significant spread of reproductive dysfunction and purulent-necrotic lesions in the toe area of cows requires the search for new ways of early diagnosis and correction of this pathology [10, 11]. Impact of stress factors, significant anthropogenic pressure and inconsistency of living conditions with the physiological needs of animals, unbalanced feeding, violation of the operating regime, unsatisfactory sanitary and hygienic condition of the premises, uncontrolled use of antimicrobial drugs, the formation of farm parasitocenoses, violation of artificial insemination technology, lack of regular exercise, defective start-up animals lead to the development of a significant range of pathologies of a non-contagious nature in cows [7, 12-16]. Internal pathology in highly productive cows mainly becomes a prerequisite for the development of orthopedic, obstetric, gynecological diseases and their associated manifestations [17, 18-22]. The problem of orthopedic pathology is quite acute, since in highly productive cows its level increases to 18–80%. At the same time, the milk productivity of the herd decreases by 40-50%, and up to 37% of cows are prematurely culled, which altogether leads to significant economic losses in livestock farming [23-26]. When a herd is significantly affected by orthopedic diseases, a sharp drop in its reproductive potential is noted due to low fertility, prolonged postpartum anaphrodisia and a general increase in the number of infertile cows [27-30].

The above facts indicate the existence of etiological connections and certain pathogenetic patterns of the associated manifestations of disorders of reproductive processes and diseases of the extremities. The problem is not considered holistically and systemically, and therefore the fragmentation of therapeutic and preventive measures significantly reduces their effectiveness [31, 32]. The study of their etiological relationships, common triggers and pathogenetic mechanisms is relevant, since it will allow us to establish diagnostic and prognostic criteria for the associated course of orthopedic, obstetric and gynecological pathologies, develop appropriate treatment and preventive measures, and improve the level of health and reproductive function of cows.

#### 2 Materials and methods

The study was supported by the grant from the Russian Science Foundation No 24-26-00172, https://rscf.ru/project/24-26-00172/. The experiment was approved by the bioethical commission of the Department of Veterinary Medicine of the Russian Biotechnological University in terms of humane treatment of experimental animals. The research was carried out on the basis of Voskresenskoye JSC, Voskresensky district, Moscow region, with a total population of 1,450 heads of cattle, including 830 cows. The material for the study was cows with endometritis (n=28), animals with orthopedic pathology (n=25) and with a comorbid course of postpartum endometritis and purulent-inflammatory processes in the toe area (n=27). Indicators obtained from clinically healthy animals (n=23) were used as control.

An orthopedic medical examination was carried out monthly, which made it possible to determine the degree and nature of deformities, the intensity of destruction of the hoof horn, as well as the dynamics of hoof diseases in cows during the calendar year. In this case, special attention was paid to the condition of the hooves (the presence of deformations) and the hoof horn (the presence of pockets, shells, delaminations, cracks), as well as the position of the thoracic and pelvic limbs. In animals with purulent-necrotic lesions in the area of the fingers in the postpartum period, an obstetric-gynecological medical examination was performed according to clinical manifestations using transrectal palpation and ultrasound scanning of the genital organs with a Scanner Falco apparatus with a frequency of 8 MHz, according to the methods adopted in veterinary reproductive medicine. During the clinical examination of

the animals, attention was paid to the condition of the vulva, pain, local temperature, the presence or absence of discharge from the genital organs, their quantity, color, smell and consistency. A vaginal examination was carried out using a vaginal speculum, taking into account the condition of the mucous membrane of the vagina and cervix, its integrity, rigidity, topographic location of the cervix and the degree of its dilatation, as well as the nature and volume of uterine discharge. When examining the ovaries, their size, shape, tissue consistency, and the presence of follicles and corpora lutea were recorded. Ultrasound examination determined the size and echo density of tissues, their homogeneity, and the echo character of functional and pathological structures.

From animals in the control and experimental groups, blood was taken in the morning before feeding from the jugular vein for morphofunctional studies. At the same time, hematocrit (HCT), % was determined; hemoglobin level (HGB), g/l; red blood cells (RBC),  $10^{12}$ /l; platelet count (PLT),  $10^{9}$ /l; leukocytes,  $10^{9}$ /l; measured mean erythrocyte volume (MCV),  $\mu$ m³; average hemoglobin content in an erythrocyte (MCH), pg; average erythrocyte hemoglobin concentration (MCHC), (g/l); erythrocyte distribution width by volume (RDW), %; thrombocytocrit (PCT), %; mean platelet volume (MPV), fl. and erythrocyte sedimentation rate (ESR) mm/h, by conventional methods.

The results obtained were processed statistically and presented in the form of tables.

## 3 Results and discussion

Veterinary practice confirms the existence of a clinically pronounced associated relationship between the manifestation of obstetric diseases and orthopedic pathology in highly productive cows. In particular, postpartum metritis most often develops in cows with purulent-necrotic lesions in the distal limbs that occur before birth or in the first weeks after calving. Morphological blood parameters in the comorbid course of endometritis and purulent-necrotic diseases in the claw area of highly productive cows are shown in Table 1. Using one-way analysis of variance (ANOVA), significant changes in hematocrit were established (F = 47.48; p < 0.001). In this case, we can reject the null hypothesis that the hematocrit indicator in animals of different groups belongs to the same general population. Subsequently, Tukey's multiple comparison analysis was performed to provide detailed statistical analysis of differences between experimental groups of animals. Thus, a highly significant (p <0.001) decrease in hematocrit in cows of groups I, II and III was established by 1.10; 1.08 and 1.19 times, respectively, when compared with the indicators of animals in the control group. It should be noted that when comparing the indicators of animals of groups I and III, we found a significant (p < 0.001) decrease in cows with comorbid endometritis and orthopedic pathology in the hematocrit index by 1.08 times, from 38.08±2.18% to 35.00±2.42%, when compared with output data. In addition, we identified significant (p <0.001) differences between the indicators of cows of groups II and III – a decrease in hematocrit by 9.88%, from  $38.84\pm1.62\%$  to  $35.00\pm2.42\%$ .

The method of one-way analysis of variance (ANOVA) also revealed significant changes in hemoglobin levels in animals of different groups (F = 47.00; p <0.001). It was shown that in cows of experimental groups I, II and III there was a highly significant (p <0.001) decrease in hemoglobin level of 1.21; 1.17 and 1.29 times, when compared with the indicators of clinically healthy animals. We also recorded a significant (p<0.05) decrease in hemoglobin when comparing the parameters of animals of groups I and III by 6.35%, from  $79.25\pm4.94$  g/l to  $74.22\pm8.49$  g/l. A significant decrease in the amount of hemoglobin in cows of group III was also established, when compared with the indicators of experimental group II by 8.95%, from  $81.52\pm4.71$  g/l to  $74.22\pm8.49$  g/l (Tukey's criterion).

Using one-way analysis of variance (ANOVA), significant changes in the level of red blood cells (F = 14.63; p <0.001) were also established in animals of different experimental

groups. Thus, we observed a significant (p <0.001) decrease in the level of erythrocytes in the blood of animals of experimental groups I, II and III by 1.24; 1.20 and 1.35 times, when compared with the output data of the control group (Tukey's criterion).

Using the method of one-way analysis of variance (ANOVA), significant changes in the platelet count in the blood of animals from different experimental groups were established (F = 35.92; p < 0.001). The analysis of Tukey's multiple comparisons for a detailed statistical analysis of the differences between the experimental groups of animals allowed us to establish a significant (p < 0.001) increase in the level of platelets in the blood of cows of experimental groups I, II and III at 1.38; 1.42 and 1.79 times, respectively, when compared with the indicators of clinically healthy animals. A significant (p<0.001) increase in the number of platelets was revealed when comparing the parameters of cows of groups I and III by 23.01%, from 449.18 $\pm$ 110.88 109/I to 583.44 $\pm$ 57.86 109/I. A significant (p<0.001) increase in the platelet count in the blood of animals of experimental group III was also established when compared with its level in animals of experimental group II – by 20.74%, from 462.40 $\pm$ 101.25 10 $^9$ /I to 583.44 $\pm$ 57.86 10 $^9$ /I.

**Table 1.** Morphological blood parameters in the comorbid course of endometritis and purulent-necrotic diseases in the hooves of highly productive cows

T., J.,,	Groups of sick cows				ows	ANIONA
Index	Biometri cs	Healthy cows (n=23)	I (n=28)	II (n=25)	III (n=27)	ANOVA test
Hematocrit	M±SD	41.99±1.96	38.08±2.18 ***	38.84±1.62 ***	35.00±2.42 ***ггг <sub>ᢤ</sub> ‡	F = 47.48; p<0.001
	95% CI	41.14 – 42.84	37.23 – 38.93	38.17 – 39.51	34.04 – 35.95	
Hemoglobi n, g/l	M±SD	95.65±7.49	79.25±4.94 ***	81.52±4.71 ***	74.22±8.49 ***「****	F = 47.00; p<0.001
	95% CI	92.41 – 98.89	77.33 – 81.17	79.57 – 83.47	70.86 – 77.58	
Red blood cells, 10 <sup>12</sup> /l	M±SD	6.91±1.03	5.59±0.91 ***	5.76±1.01 ***	5.13±0.96 ***	F = 14.63; p<0.001
	95% CI	6.46 - 7.35	5.24 – 5.94	5.34 - 6.18	4.74 – 5.51	_
Platelets, 10 <sup>9</sup> /l	M±SD	324.30±69.1 5	449.18±110. 88 ***	462.40±101. 25 ***	583.44 ± 57.86 ************************************	F = 35.92; p<0.001
	95% CI	294.40 – 354.21	406.18 – 492.17	420.60 - 504.19	560.55 – 606.33	
Leukocyte s, 10 <sup>9</sup> /l	M±SD	7.04±1.15	11.32±3.04 ***	9.67±2.15 ***◊	14.78±1.78 ***ггг <sub>‡‡</sub> ‡	F = 55.31; p<0.001
	95% CI	6.54 – 7.54	10.14 – 12.50	8,78 – 10,55	14.08 – 15.49	

Note, hereinafter: I – cows with endometritis; II – patients with orthopedic pathology of the cow; III – cows with comorbid endometritis and orthopedic pathology; M – arithmetic mean; SD – standard deviation; 95% CI – 95% confidence interval; ANOVA – one-way analysis of variance; \* (p<0,05), \*\* (p<0,01); \*\*\* (p<0,001) – significance of the difference between the indicators of cows of groups I–III and healthy ones (Tukey's criterion);  $\Diamond$  (p<0,05),  $\Diamond\Diamond$  (p<0,01),  $\Diamond\Diamond\Diamond$  (p<0,001) – reliability of the difference between the indicators of cows of groups I and II (Tukey's criterion);  $^{\Gamma}$  (p<0,05);  $^{\Gamma\Gamma}$  (p<0,01);  $^{\Gamma\Gamma}$  (p<0,001) reliability of the difference between the indicators of cows of groups I and III (Tukey's criterion);  $^{\Gamma\Gamma}$  (p<0,05);  $^{\Gamma\Gamma}$  (p<0,01);  $^{\Gamma\Gamma}$ 

Significant changes in the level of leukocytes in the blood of animals from different experimental groups were also revealed using one-way analysis of variance (ANOVA test F = 55.31; p < 0.001), which made it possible to analyze Tukey's multiple comparisons to identify differences between experimental groups. It was established that in the blood of cows

of experimental groups I, II and III a highly significant (p <0.001) increase in the number of leukocytes was found by 1.61; 1.37 and 2.09 times, respectively, when compared with the indicators of animals in the control group. It was shown that there are also significant (p <0.001) differences between the indicators of cows of groups I and III – an increase in this analyte by 23.4%, from  $11.32\pm3.04\ 109/I$  to  $14.78\pm1.78\ 10^9/I$ . A highly significant difference was also revealed between the indicators of cows of experimental groups II and III – an increase in the level of leukocytes by 34.6%, from  $9.67\pm2.15\ 109/I$  to  $14.78\pm1.78\ 109/I$ . In addition, we established the significance of the difference between the indicators of cows of groups I and II (Tukey's criterion) – a decrease in the level of leukocytes by  $1.17\ times$ , from  $11.32\pm3.04\ 10^9/I$  to  $9.67\pm2.15\ 10^9/I$  (p<0.05).

Functional blood parameters in the comorbid course of endometritis and purulent-necrotic diseases in the area of the hooves of highly productive cows found their imprint in Table 2. It was established that in cows with endometritis, animals with orthopedic pathology and with a comorbid course of postpartum endometritis and purulent-inflammatory processes in the area finger, we did not detect significant changes in the average volume of erythrocytes, the average hemoglobin content in an erythrocyte and thrombocytocrit.

Using the method of one-way analysis of variance (ANOVA), we established significant changes in the MCHC indicator (F = 4.59; p < 0.01). In this case, we can reject the null hypothesis that the average hemoglobin concentration in the erythrocyte in animals of different groups refers to the same general population. Therefore, Tukey's multiple comparison analysis was performed to provide detailed statistical analysis of differences between experimental groups of animals. It was shown that in animals of groups I, II and III, when compared with data obtained from cows of the control group, a significant decrease in the MCHC index of 1.09 (p < 0.01) was revealed; 1.08 (p < 0.05) and 1.07 (p < 0.05) times.

Using one-way analysis of variance (ANOVA), we also established significant changes in the width of distribution of erythrocytes by volume (F = 140.00; p < 0.001). A highly significant (p <0.001) increase in the RDW indicator in animals of experimental groups I, II and III was revealed by 1.18; 1.12 and 1.46 times, when compared with the indicators of clinically healthy animals. It was established that there is a significant difference between the indicators of cows of groups I and III – an increase (p<0.001) by 19.55%, from 22.01 $\pm$ 1.92% to 27.36 $\pm$ 1.95%. We also determined a significant (p<0.001) increase in the RDW indicator in cows of group II when compared with this indicator of experimental group III by 23.21%, from 21.01 $\pm$ 1.09% to 27.36 $\pm$ 1.95% (Tukey's criterion).

**Table 2.** Functional blood parameters in the comorbid course of endometritis and purulent-necrotic diseases in the claw area of highly productive cows

			Groups of sick cows			
Index	Biometri	Healthy	I (n=28)	II (n=25)	III (n=27)	ANOVA
	cs	cows		, ,	, , ,	test
		(n=23)				
MCV, fl	$M\pm SD$	62.22±10.9	69.82±12.0	69.84±15.53	70.41±12.54	F = 2.19;
		3	9			p<0.1
	95% CI	57.49 -	65.13 –	63.43 – 76.25	65.45 - 75.37	
		66.95	74.51			
MCH, pg	M±SD	14.30±2.87	14.43±2.81	14.16±3.31	14.70±4.05	F = 0.13;
	95% CI	13.06 -	13.33 -	12.79 - 15.52	13.10 - 16.30	p<1
		15.54	15.51			
MCHC,	M±SD	227.69±21.	208.11±16.	209.64±13.06	211.85±28.26	F = 4.59;
g/dl		16	76	*	*	p<0.01
			**			
	95% CI	218.54 -	201.61 -	204.25 -	200.67 -	
		236.85	214.61	215.03	223.03	
RDW, %	M±SD	18.70±0.78	22.01±1.92	21.01±1.09	27.36±1.95	F =
			***	***	***[[[***	140.00;

	95% CI	18.37 –	21.27 –	20.55 – 21.47	26.58 – 28.13	p<0.001
		19.04	22.76			_
PCT, %	M±SD	0.19±0.09	0.20±0.11	0.26±0.07	0.24±0.07	F = 3.1;
	95% CI	0.15 - 0.23	0.16 - 0.24	0.22 - 0.29	0.21 - 0.27	p<0.05
MPV, fl.	M±SD	6.01±2.58	4.78±2.75	5.93±2.39	4.03±1.29	F = 4.33;
					*	p<0.01
	95% CI	4.89 - 7.12	3.71 - 5.85	4.94 - 6.92	3.52 - 4.55	
ESR,	M±SD	2.17±1.07	3.92±0.94	5.20±1.66	10.22±2.53	F =
mm/h			**	***	***[[[***	108.65;
	95% CI	1.71 - 2.63	3.56 - 4.29	4.52 - 5.88	9.22 - 11.22	p<0.001

The method of one-way analysis of variance (ANOVA) revealed significant changes in the MPV indicator (F = 4.33; p <0.01). At the same time, when analyzing Tukey's multiple comparisons, it was found that when comparing the average platelet volume in cows with comorbid endometritis and orthopedic pathology with data from control animals, there is a significant decrease of 32.94%, from  $6.01 \pm 2.58$  fl up to  $4.03\pm1.29$  fl (p<0.05), and also when compared with patients with orthopedic pathology – by 32.04%, with  $5.93\pm2.39$  fl up to  $4.03\pm1.29$  fl. (p<0.05).

Significant changes in the erythrocyte sedimentation rate in the blood of animals from different experimental groups were also determined using one-way analysis of variance (F = 108.65; p <0.001), which made it possible to further analyze Tukey's multiple comparisons to identify differences between experimental groups. It was found that in animals of experimental groups I, II and III there was a significant increase in the ESR indicator of 1.81 (p <0.01); 2.39 (p<0.001) and 4.71 (p<0.001) times, when compared with analytes from clinically healthy animals. When comparing the erythrocyte sedimentation rate between cows of groups I and III, a highly significant (p<0.001) increase of 61.64% was revealed, from  $3.92\pm0.94$  mm/h to  $10.22\pm2.53$  mm/h. It was shown that when comparing the ESR indicator of groups II and III, a highly significant (p<0.001) increase of 49.12% was also recorded, from  $5.20\pm1.66$  mm/h to  $10.22\pm2.53$  mm/h. In addition, we determined a significant (p<0.05) increase in this analyte between animals of groups I and II – 1.33 times, from  $3.92\pm0.94$  mm/h to  $5.20\pm1.66$  mm/h.

# 4 Conclusion

In experienced cows with limb damage, the likelihood of gynecological diseases increased. The significant spread of these types of pathology is the direct cause of prolonged anaphrodisia of cows and a decrease in the level of reproduction of the herd with a high incidence of limb diseases. It has been established that the clinical manifestation of the comorbid course of orthopedic and obstetric-gynecological pathology has a more severe clinical manifestation than in the course of individual diseases. Using one-way analysis of variance (ANOVA), significant changes in hematocrit (F = 47.48; p<0.001), hemoglobin (F = 47.00; p<0.001), erythrocytes (F = 14.63; p<0.001), platelets (F = 35.92; p<0.001) were established. p<0.001), leukocytes (F = 55.31; p<0.001), average hemoglobin concentration in an erythrocyte (F = 4.59; p<0.01), distribution width of erythrocytes by volume (F = 140.00; p<0.001), average platelet volume (F = 4.33; p<0.01) and erythrocyte sedimentation rate (F = 108.65; p<0.001). A decrease in hematocrit in cows of groups I-III was found to be 1.10; 1.08 and 1.19 times, when compared with the control group. When comparing the indicators of groups I and III, a decrease in hematocrit was found by 1.08 times. Differences were revealed between the indicators of cows of groups II and III – a decrease in hematocrit by 9.88%. In cows of experimental groups I-III, a decrease in hemoglobin of 1.21 was observed; 1.17 and 1.29 times, when compared with the control. A decrease in hemoglobin was recorded when comparing the parameters of animals of groups I and III by 6.35%. A

decrease in hemoglobin in cows of group III was established, when compared with the indicators of group II by 8.95%. We observed a decrease in the level of erythrocytes in the blood of animals of groups I-III by 1.24; 1.20 and 1.35 times, when compared with the control group. An increase in the level of platelets in the blood of cows of groups I-III was found to be 1.38; 1.42 and 1.79 times, when compared with the indicators of healthy animals. An increase in platelets was revealed when comparing the indicators of cows of groups I and III by 23.01%. An increase in platelets in the blood of animals of group III was established when compared with its level in animals of group II – by 20.74%. It was established that in the blood of cows of groups I-III an increase in the number of leukocytes was found by 1.61; 1.37 and 2.09 times, when compared with the control group. There is an increase of 23.4% between the indicators of cows of groups I and III. An increase in the level of leukocytes between the indicators of cows of groups II and III by 34.6% was also revealed. A decrease in the level of leukocytes between the indicators of cows of groups I and II was established by 1.17 times. It was shown that in animals of groups I-III, when compared with the control group, a decrease in MCHC of 1.09 was detected; 1.08 and 1.07 times. An increase in the RDW indicator in animals of groups I-III was revealed by 1.18; 1.12 and 1.46 times, when compared with the indicators of healthy animals. It has been established that there is an increase of 19.55% between the indicators of cows of groups I and III. An increase in RDW in cows of group II was also determined when compared with this indicator of group III by 23.21%. When analyzing the average platelet volume in cows with comorbid endometritis and orthopedic pathology with data from control animals, there is a decrease of 32.94%, and also when compared with patients with orthopedic pathology – by 32.04%. It was found that in animals of experimental groups I-III there was an increase in ESR of 1.81; 2.39 and 4.71 times, when compared with healthy animals. When comparing the erythrocyte sedimentation rate between cows of groups I and III, an increase of 61.64% was revealed. It is shown that when comparing the ESR indicator of groups II and III, an increase of 49.12% is recorded. An increase in this analyte between animals of groups I and II was also determined -1.33times.

### References

- P. Rudenko, Yu. Vatnikov, S. Engashev et al. J. Adv. Vet. Anim. Res., 8(2), pp. 210—217, (2021).
- 2. M.Z. Ali, G. Carlile, M. Giasuddin Open Veterinary Journal, **10(2)**, pp. 178—188, (2020).
- 3. H. Zhang et al., Animals, 9(10), 730, (2019).
- 4. A. Rudenko, I. Glamazdin, V. Lutsay et al., E3S Web of Conferences, **363**, 03029, (2022).
- 5. Yu. Vatnikov, M. Yousefi, S. Engashev et al., Int. J. of Pharm. Res., **12**(S.1), pp. 2731—2742, (2020).
- 6. R.S. Ghallab, D.R.S.G. El-Karim, A.-H. Fayed et al., Tropical Animal Health and Production, **55**(2), 118, (2023).
- 7. D. Enríquez, M.J. Hötzel, R. Ungerfeld, Acta Veterinaria Scandinavica, 53, 28, (2011).
- 8. P.A. Gonzalez-Rivas, S.S. Chauhan, N. Fegan et al., Meat Science, 162, 108025, (2020).
- 9. N. Bugrov, P. Rudenko, V. Lutsay et al., Pathogens, 11(2), 234, (2022).
- 10. K.J. Stafford, N.G. Gregory, New Zealand Veterinary Journal, **56**(6), pp. 274—280, (2008).

- 11. Yu. Vatnikov, I. Donnik, E. Kulikov et al., Int. J. of Pharm. Res., 2020; **12**(S.2), pp. 1481—1492, (2020).
- 12. W. Barański, A. Baryczka, S. Zduńczyk et al., Theriogenology, **192**, pp. 166—171, (2022).
- 13. E.R. Shaykhutdinova, V.A. Palikov, Y.A. Palikova et al., Bull. Exp. Biol. Med., **170**(6), pp. 737—740, (2021).
- 14. S.Yu. Smolentsev, A.H. Volkov, E.K. Papunidi et al., International Journal of Research in Pharmaceutical Sciences, 11(2), pp. 1481—1485, (2020).
- 15. T. Osawa, Journal of Reproduction and Development, 67(5), pp. 291—299, (2021).
- 16. E. Scarsella, A. Zecconi, M. Cintio et al., Animals, 11(5), 1463, (2021).
- 17. V.A. Palikov, Y.A. Palikova, N.A. Borozdina et al. Res. Res. in Pharm., **6**(2), pp. 19—25, (2020).
- 18. S.J. LeBlanc, Animal, **8**(S1), pp. 54—63, (2014).
- 19. A.L. Gazzonis, S.A. Zanzani, G. Aloisio et al., Parasitology International, **91**, 102641, (2022).
- 20. Y. Vatnikov, S. Shabunin, E. Kulikov et al., Int. J. of Pharm. Res., **12**(4), pp. 1108—1117, (2020).
- 21. P.A. Rudenko, A.N. Murashev, Russian J. of Biopharmaceuticals, **9**(6), pp. 40—45, (2017).
- 22. S. Moret-Stalder et al., Preventive Veterinary Medicine, 88(1), pp. 72—76, (2009).
- 23. D.A. Todhunter, K.L. Smith, J.S. Hogan et al., American journal of veterinary research, **52**(2), pp. 184—188, (1991).
- 24. P.A. Rudenko, A.N. Murashev, Russian J. of Biopharmaceuticals, **9**(3), pp. 49—54, (2017).
- 25. Z. Bercovich, Veterinary Quarterly, **20**(3), pp. 81—88, (1998).
- 26. Y. Vatnikov, S. Shabunin, A. Karamyan et al. L, Int. J. of Pharm. Res., **12**(S.1), pp. 723—730, (2020).
- 27. P. Nyabinwa, O.B. Kashongwe, J.P. Habimana et al., Tropical Animal Health and Production, **52**(6), pp. 3135—3145, (2020).
- 28. I. Nicola, F. Cerutti, E. Grego, et al., Microbiome, 5(1), 152, (2017).
- 29. Yu. Vatnikov, S. Shabunin, E. Kulikov et al. Int. J. of Pharm. Res., **12**(S.2), pp. 3064—3073, (2020).
- 30. O.B. Pascottini, C. Aurich, G. England et al., Reproduction in Domestic Animals, **58**(S2), pp. 49—71, (2023).
- 31. C. Ghosh, P. Sarkar, R. Issa et al., Trends Microbiol, 27(4), pp. 323—338, (2019).
- 32. Yu. Vatnikov, I. Donnik, E. Kulikov et al., Int. J. of Pharm. Res., **12**(S.1), pp. 1108—1116, (2020).