



Contemporary approaches to assessment of the body's condition of dogs with gastrointestinal pathologies based on the intensity of the inflammatory process and the level of endogenous intoxication

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Abstract

Due to the existing methods of diagnosing diseases of domestic animals are ineffective and imperfect, our goal was to develop a technology for assessing the state of the body of dogs to be able to diagnose the occurrence of diseases at an early stage. The article provides data on the development of technology to assess the state of the body, as well as to check its functioning in practice by determining the presence of such typical pathological processes (TPP) as inflammation and endogenous intoxication of the German Shepherd dogs. Clinical, laboratory, and statistical methods were used for the study. As a result of the study, an effective method of assessing the condition of the dog's body was developed and based on two algorithms for determining the intensity of the inflammatory process and endogenous intoxication. This method is effective, sensitive, and fully reproducible in practice, which allows the veterinarian to correctly diagnose and effectively carry out therapy and rehabilitation of sick animals.

Key words: assessment of the body's condition, inflammatory process, endogenous intoxication, absolute, integral numbers, algorithms.



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1. Introduction

Nowadays, the veterinary doctor is responsible for the health of the animal at all stages of his life, regardless of age, gender, etc. To make a responsible decision while choosing adequate therapy, prevention, or rehabilitation by a veterinary specialist requires deep knowledge, professional experience, skills, as well as much more.

Therapeutic algorithms generally accepted in veterinary medicine are based on a subjective assessment of the results of laboratory and functional tests. In a complex with indicators of clinical examination, they allow the veterinary doctor to diagnose and prescribe treatment. But it is more complicated, and sometimes it is impossible to use clinical and diagnostic approaches to identify before pathological changes; obtaining criteria for the forecast of therapy, assessing the state of a healthy animal, etc. So, for instance, standard approaches and diagnostic methods are often ineffective in

detecting pre-disease, since most functional and laboratory markers are within the reference values, and the clinical picture of the disease is absent. In the current case, the veterinary doctor states the fact of the lack of any clinical ideas changes in the body of the animal, which may have serious consequences in the future. The standard clinical diagnostic approach also doesn't give a veterinary doctor ability to determine the condition of a healthy animal correctly, evaluate the dynamics of recovery objectively, and make the forecast of the therapy, and so on so forth. Moreover, without having significant deviations in the indicators of the animal surveyed (clinical, laboratory, etc.) For veterinary doctors, it is extremely difficult to carry out rehabilitation, as well as preventive measures.

Thus, the development and implementation of a simple, accessible, efficient, and unified technique in the practice of the work, which allows assessment condition of the body of

the animal realistically, and it doesn't depend on age, gender, clinical status, etc.

At present, contemporary veterinary practice requires publicly available techniques to determine the condition of the body as a holistic biological system. The veterinarian must follow the basic principle – to treat the patient's organism but not a disease. It means that he needs to be able to assess the condition of a holistic organism in the dynamics, and not to track the symptoms, the level of functional, laboratory, and other numbers, control the function of organs or systems. An effective technology assessment of the body's condition is fundamental to a veterinary doctor, either for solving therapy problems or prevention and rehabilitation.

Any animal disease is created by typical pathological processes (TPP), such as inflammation, endogenous intoxication, impaired immune protection, metabolism disorder, power supply, etc. (Kryzhanovskij, 2002; Borgarelli et al., 2004; Borgarelli et al., 2012; Varkholiak & Gutj, 2020; 2021; Stybel et al., 2021; Konstantinidis et al., 2021). Effective and timely detection of the presence and determination of the direction of the TPP is the key to success in the prevention, treatment, and rehabilitation of multiple diseases. It was this approach that was based on the technology to the evaluation of the body's condition. It was certainly difficult to make development for the absence of unified algorithms for estimating the intensity of the inflammatory process and endogenous intoxication of animals.

Consequently, the purpose of our study was to develop technology for assessment of the body's condition, as well as to test its functioning in practice by defining the presence of such TPP as an inflammatory process and endogenous intoxication of the German Shepherd dogs.

2. Materials and methods

The research was taken in the veterinary clinic and the laboratory "Four paws" (Kyiv).

According to the research, 20 German Shepherd breed dogs were chosen between 5 to 8 years, which were divided into two groups. An experimental group of animals (10 head of animals) – made animals with the gastroenterological pathology, most common in the conditions of the city of Kyiv, the therapy (group № 1) and the control group (10 head of animals) are healthy animals (group № 2).

In 10 dogs with gastroenterological pathology (group № 1), blood was picked on the first day of the study (before treatment) and in two weeks, after the end of treatment, 10 healthy dogs – blood was selected only once at the beginning of the study (group № 2).

In animal groups № 1 and № 2, the following indicators of the complete blood count (CBC) were identified: the percentage of neutrophils, lymphocytes, monocytes, eosinophils, as well as erythrocytes sedimentation rate (ESR) (International Council..., 1993). Moreover, animals of groups № 1 and № 2 identified such biochemical indicators as the activity of aspartate transaminase (AST) and alanine transaminase (ALT), the concentration of C-reactive protein (CRP) (Provan & Krentz, 2002).

On the basis of results of the absolute and relative research, integral hematological indicators were calculated: the leukocyte index of intoxication (LII) index of the ratio of leukocytes and the ESR (IRLESR), Index of the ratio of lymphocytes and monocytes (IRLM), blood leukocyte shift

index (BLSI), The Garkavi Index (GI), the allergy index (AI) (Mustafina et al., 1999; Suhorukov et al., 2007; Gabunshhina, 2012; Speranskij et al., 2009; Zhukov et al., 2017). Using unique biochemical numbers, the coefficient where the De Ritis Ratio (AST/ALT) was calculated, as well as the measure of the activity of transaminase AST+ALT (Panchyshyn et al., 2014).

To define the level of one of the central TPP as inflammation, the integral algorithm was created (Table 1), the prototype that is given in the article (Smiiian et al., 2020). The effect of endogenous intoxication was determined using the integral level of intoxication (LII) (Akalaev et al., 2013). To the evaluation of LII, the arithmetic averages were managed from the calculation of the changing degree of the analyzed indicators (Table 2). An assessment of the intensity of endogenous intoxication was transferred using the criteria shown in chart 3. The prototype of this algorithm is added to the article (Akalaev et al., 2013).

The statistical process of the results was invented using the student's t-test, as well as nonparametric criteria of signs G (Lapach et al., 2001). For all types of analysis, obtained data was experimentally estimated as statistically reliable at $P < 0.05$.

Table 1

Integral assessment of the intensity of the inflammatory process in dogs in terms of the level of the SRP, ESR and the leukocyte formula

Indicator	Description
CRP 0-6 mg/l, ESR, but the leukocyte formula in norms	No inflammatory process
CRP 6-35 mg/l or a slight deviation of the ESR or any indicator of the leukocyte formula at the normal level of the CRP and ESR	Low inflammatory process
CRP 35–300 mg/l	Inflammatory process of medium intensity
CRP >300 mg/l	Inflammatory process of high intensity

Table 2

Integral assessment of the level of endogenous intoxication

Indicator	Degree of change of indicators (score)			
	0	I	II	III
LII, c.u.	0–2.03	2.04–3.05	3.06–5.05	>5.05
IRLESR, c.u.	0–0.39	0.40–1.05	1.06–2.05	>2.05
IRLM, c.u.	≥5.01	5.00–3.70	3.71–1.50	<1.50
ALT, U/l	0–60	61–75	76–83	>83
AST, U/l	0–75	76–85	86–93	>93

Table 3

Identification and assessment of the intensity of endogenous intoxication depending on LII

Indicator of LII	Assessment of the level of endogenous intoxication
0	Norme
0–0.99	Low
1–1.99	Medium
2–2.99	High
3	Critical

3. Results and discussion

The huge majority of animal diseases are TPP such as inflammation and endogenous intoxication (Kryzhanovskij, 2002). In our experiment, we carried out the determination and assessment of the TPP data using the proposed algorithms (tables 1, 2, 3). For their development and approbation, a literary search was accomplished (Kryzhanovskij, 2002; Speranskij et al., 2009; Akalaev et al., 2013; Smiian et al., 2020), as well as an analysis of absolute and relative hematological and biochemical parameters. Some of the results of our research are included in this article and are shown in table 4. Their statistical analysis made it possible to reveal in the blood of sick animals (group №1 before treatment) an increased content of stab neutrophils by 2.4 times. Two weeks later, after the therapy, this indicator stabilized at the control level, it became possible to decrease it by a factor of 2.2 times (table 4). Such dynamics may indicate the presence of an inflammatory process of sick experimental animals. Unfortunately, this conclusion can only be drawn from a change in one indicator with a certain

degree of probability. However, the assumption has been confirmed in other changes of CBC. In particular, a significant increase in ESR was revealed in sick dogs in the first group before treatment by 3.3 times. After the therapy, this indicator decreased 2,6 times to achieve the control level (table 4). It is important to emphasize that ESR has been recently assigned the role of a “marker of inflammation” in the body. However, the versatility of this role is now being questioned.

The concentration of C-reactive protein in the blood is considered by some authors to be one of the markers of the inflammatory process of various etiology, localization, and strength (Korppi et al., 1997; Sivaraman et al., 2004; Weitkamp & Achner, 2005). That's why this indicator was used by our team in the study, as one of the markers of the presence of this TPP. As a result, a significant excess of CRP in the blood of animals of group № 1 before treatment was revealed (by 7.7 times). This may indicate the dog's intense inflammatory process in this group. Treatment led to the concentration of CRP (5.8 times) to the level of control in animals group № 1 after treatment (Table 4).

Table 4

The value of absolute blood counts of the German Shepherd breed dogs ($M \pm m$, $n = 10$)

Blood counts	Group № 1 animals before treatment	Group № 1 animals after treatment	Group № 2 healthy animals (control)
Stab neutrophil, %	8.09 ± 1.55 ^{##}	3.60 ± 0.72 [#]	3.31 ± 0.79
Segmentonuclear neutrophils, %	61.96 ± 6.92	68.30 ± 2.84	67.85 ± 2.63
Lymphocytes, %	21.48 ± 6.07	22.10 ± 2.52	23.69 ± 2.44
Monocytes, %	3.78 ± 1.91	3.00 ± 1.20	2.08 ± 0.73
Eosinophils, %	4.87 ± 2.22	3.00 ± 0.80	3.15 ± 1.14
ESR, mm/h	12.96 ± 2.73 ^{##}	4.90 ± 2.32 [#]	3.92 ± 0.72
ALT, U/l	61.27 ± 10.89 ^{##}	33.78 ± 5.66 [#]	28.52 ± 4.04
AST, U/l	48.57 ± 6.62 ^{##}	30.51 ± 6.65	24.33 ± 4.60
CRP, mg/l	54.32 ± 18.36 ^{##}	9.31 ± 1.22 [#]	7.07 ± 0.60

Note: # – $P \leq 0.05$ – significant difference between the mean values of blood counts of dogs before and after treatment; ## – $P \leq 0.05$ – significant difference between the mean values of blood counts of dogs, group № 1 before treatment and group № 2 (control)

As we can see, individual indicators of the CBC (the content of stab leukocytes and ESR), as well as the concentration of CRP in the blood, only with a certain degree of probability can reveal the presence of an inflammatory process to a greater or lesser extent. Moreover, all of them, separately from each other, are unable to determine the intensity of a given TPP. In addition, today, none of the existing indicators can be considered an effective marker of inflammation. It is also important to note that at present, there is no generally accepted universal algorithm that would determine the presence and assess the intensity of the inflammatory process of any etiology and localization in dogs. It was assumed that an integrated approach would help to solve this problem. Certain steps have already been taken in this direction. So some authors, the role of universal marker indicators of inflammation are assigned to integral hematological indices (Suhorukov et al., 2007; Pisarev et al., 2008). The work we have done, shows no pretext for us to agree with this. As part of our study, the dynamics of six hematological indices of dogs were assessed. Integral hematological indicators such as LII, IRLM, BLSI, GI, and AI did not change. Only one of the hematological indices, the IRLESR of dogs in group № 1 for treatment exceeded the control values (group № 2 – healthy animals). According to our theory, the key role in this was played not by the hema-

tological index itself – IRLESR, but by the ESR, which is used in its calculation (table 5). Therefore, today, integral indicators (indices and coefficients) cannot be considered as effective markers of the presence and assessment of the intensity of the inflammatory process. To figure out the problem, we have chosen further integration.

That is why an algorithm for the integral assessment of the intensity of the inflammatory process in dogs was developed and proposed using the integrated use of individual indicators of the CBC (leukocyte formula and ESR), as well as the concentration of CRP in the blood (table 1). All of them were not chosen by chance. As noted above, each of the indicators which were mentioned before was assigned the role of an indicator of inflammation to a greater or lesser extent. However, none of them can be considered an effective marker of the inflammatory process. In our opinion, the combination of separate indicators of the CBC (leukocyte formula and ESR), as well as the concentration of CRP in one algorithm for assessing inflammation, should ensure its reliable reproduction and assessment of intensity.

The results of the study of the integral definition of the inflammatory process, using the proposed algorithm (table 1), indicate the absence of inflammation in 10 healthy dogs of group № 2 (table 6). At the same time, all animals with gastroenterological pathology (group № 1) had an

inflammatory process before treatment. Simultaneously, in 7 dogs of this group, inflammation of low intensity was found, and in 3 dogs, replenishment was found of medium intensity (Table 6).

This was fully consistent with the clinical picture that was observed when the animals were admitted to the clinic. Signs and symptoms of various gastroenterological diseases were pronounced. The treatment that was carried out for 2

weeks gave positive results. The clinical picture significantly improved in 8 dogs (group № 1 after treatment), which can be characterized as complete recovery. On the one hand, using the algorithm for the integral assessment of the intensity of inflammation, this TPP was not detected in them. On the other hand, in two dogs from group № 1 after treatment, there were signs of a further course of the disease against the background of an inflammatory process (table 6).

Table 5

Values of integral indicators of the German Shepherd dogs ($M \pm m$, $n = 10$)

Indicator	Group № 1 animals before treatment	Group № 1 animals after treatment	Group № 2 healthy animals (control)
LII	2.42 ± 0.68	2.62 ± 0.35	2.50 ± 0.31
IRLESR	12.93 ± 2.47 ^{##}	6.90 ± 1.32 [#]	3.93 ± 0.72
IRLM	9.75 ± 7.72	9.50 ± 4.10	14.71 ± 7.10
BLSI	0.36 ± 0.11	0.34 ± 0.05	0.35 ± 0.05
GI	0.37 ± 0.14	0.33 ± 0.05	0.36 ± 0.05
AI	0.37 ± 0.11	0.34 ± 0.05	0.37 ± 0.04
AST+ALT	109.84 ± 17.01 ^{##}	64.29 ± 11.95 [#]	52.85 ± 8.31
AST/ALT	0.81 ± 0.06	0.90 ± 0.13	0.85 ± 0.10

Note: # – $P \leq 0.05$ – significant difference between the mean values of blood parameters of dogs before and after treatment; ## – $P \leq 0.05$ – significant difference between the mean values of blood parameters of dogs group № 1 for treatment and group № 2 (control)

Table 6

The presence and intensity of the inflammatory process of the German Shepherd dogs

Animals No.	Group № 1 animals before treatment	Group № 1 animals after treatment	Conclusion on the condition of the animal after 2 weeks of treatment	Group № 2 healthy animals (control)
1	+	0	healthy animals	0
2	+	+	it is necessary to continue treatment	0
3	+	0	healthy animals	0
4	+	0	healthy animals	0
5	+	0	healthy animals	0
6	+	0	healthy animals	0
7	+	+	it is necessary to continue treatment	0
8	++	0	healthy animals	0
9	++	0	healthy animals	0
10	++	0	healthy animals	0

Note: 0 – no inflammation; + – inflammation of low intensity; ++ – inflammation of medium intensity

It should be noted that the therapy allowed to reliably reduce the level of inflammation in group № 1 after treatment compared to group № 1 before treatment (criterion of G), up to the absence of this TPP in 80 % of dogs.

So, the results obtained may indicate the sensitivity, efficiency, and reproducibility of the proposed algorithm for the integral assessment of the intensity of the inflammatory process in dogs. In the course of some diseases, endogenous intoxication is no less significant TPP than others. For animals, in particular dogs, to date, there is no developed universal, and even more so a unified method for determining the presence and assessment of the intensity of endotoxiosis.

The cause of the development of endogenous intoxication can be cytolytic processes, impaired detoxification mechanisms, impaired barrier functions in the body, etc (Umanskij et al., 1991; Uzbekov & Misionzhnik, 2000; Allenspach et al., 2019; Sacoor et al., 2021). Transaminases, in particular AST and ALT, are considered markers of cytological processes, as well as endotoxiosis (Umanskij et al., 1991). That is why changes in the functions of these enzymes were studied in our experiment. As a result, there was a 2,1-fold increase in ALT activity in animals of group № 1 before treatment compared with the corresponding indicator in healthy dogs of group № 2 (table 4). After completion of treatment, the ALT function in dogs of group № 1 after

treatment did not significantly differ from the control (healthy dogs of group № 2). The activity of AST had a similar dynamic. In dogs of group № 1 before treatment, this indicator exceeded the control values by 2 times (table 4). As well as the ALT activity, the AST activity, after the treatment of the animals, stabilized to the control values (table 4). Against the background of earlier processes, biochemical integral indicators have changed less. Thus, the De Ritis Ratio of dogs of group № 1 before treatment, as well as dogs of group № 1 after treatment, did not significantly differ from AST/ALT of healthy animals (table 5). Only the AST + ALT indicator had similar dynamics with the activity of the studied transaminases. In dogs of group № 1, before treatment, it significantly (almost 2.1 times) exceeded the control values. Two-week therapy had the following result, because the AST+ALT index in animals of group № 1 decreased to the control level (table 5).

The proposed algorithm for identifying and assessing the intensity of endogenous intoxication (tables 2 and 3) made it possible to study the dynamics of this TPP in our experiment. According to the table 7, all dogs of group № 1 had endotoxiosis before treatment. Nine out of ten animals had an average level of endogenous intoxication and one animal had a high level. This is fully consistent with the clinical picture that was observed in animals before starting treat-

ment. The therapy made it possible to reliably reduce the intensity of endogenous intoxication in experimental dogs (criterion of G). Despite this, the entire group of animals №1 after treatment had endotoxicosis of varying intensity, which indicates their incomplete recovery.

Of no less interest are the results of a study of the presence and degree of endotoxicosis in healthy animals

(healthy dogs of group № 2). Interestingly, nine of them showed a low level of endogenous intoxication, and only one dog did not show this TPP (table 7). In this regard, only one out of ten dogs in group № 2 can be considered healthy, and the above nine animals in this group are not healthy.

Table 7

Presence and intensity of endogenous intoxication of the German Shepherd dogs

Animals No.	Group № 1 animals before treatment	Group № 1 animals after treatment	Conclusion on the condition of the animal after 2 weeks of treatment	Group № 2 healthy animals (control)
1	++	+	healthy animals	+
2	++	++	it is necessary to continue treatment	+
3	++	+	healthy animals	+
4	++	+	healthy animals	+
5	++	+	healthy animals	0
6	++	+	healthy animals	+
7	++	++	it is necessary to continue treatment	+
8	++	+	healthy animals	+
9	++	+	healthy animals	+
10	+++	+	healthy animals	+

Note: 0 – no endogenous intoxication; + – low level of endogenous intoxication; ++ – the medium level of endogenous intoxication; +++ – a high level of endogenous intoxication.

In such way, the obtained results of testing algorithms for detecting and assessing the inflammatory process, as well as endogenous intoxication in dogs in combination, can be used to evaluate the state of the animal's body. In the future, this methodology of assessment of the body's condition may include other algorithms for determining and assessing other TPP.

From our point of view, the most relevant are such TPP as a violation of the body's immune reactivity, changes in metabolism, and many others. But up to today, the developed methodology provides the veterinarian with effective criteria for evaluating the therapy carried out by him, as well as the recovery of animals. In addition, the proposed algorithms make it possible to identify the onset of the pathological process and comprehensively assess the state of a healthy body, which is important while carrying out preventive and rehabilitation measures.

The developed methodology of assessment of the body's condition, which includes algorithms for detecting and assessing the inflammatory process and endogenous intoxication in dogs, is open to changes and additions following further use.

4. Conclusions

1. The proposed algorithm for the integral assessment of the intensity of inflammation makes it possible to identify and determine the level of the inflammatory process in dogs in the dynamics of therapy for gastroenterological diseases at the beginning of the pathological state, as well as in healthy animals.

2. The developed algorithm for the integrated assessment of the level of endogenous intoxication makes it possible to identify and determine the level of endotoxicosis in dogs in the dynamics of therapy for gastroenterological diseases at the beginning of the pathological state, as well as in healthy animals.

3. The results of the conducted studies allow us to assert that the methodology of assessment of the body's condition,

which includes algorithms for detecting and assessing the inflammatory process and endogenous intoxication in dogs, is effective, sensitive and fully reproducible in practice.

4. The developed technique allows the veterinarian to determine the state of the animal's body correctly, including pathological and initial pathological changes, as well as to assess the health level of the dog.

5. The developed technique allows the veterinarian to make a responsible decision on the choice of adequate therapy, prevention or rehabilitation, which is the key to maintaining and increasing the health of the animal.

Conflict of interest

The authors declare that there is no conflict of interest.

References

- Akalaev, R. N., Rizaev, K. S., Stopnickij, A. A., & Hajdarova, S. Je. (2013). Jekstrakorporal'nye metody detoksikacii v kompleksnoj terapii jendogennoj intoksikacii. *Vestnik jekstrennoj mediciny*, 1, 95–100. URL: <https://cyberleninka.ru/article/n/ekstrakorporalnye-metody-detoksikatsii-v-kompleksnoj-terapii-jendogennoj-intoksikatsii> (in Russian).
- Allenspach, K. A., Mochel, J. P., Du, Y., Priestnall, S. L., Moore, F., Slayter, M., Rodrigues, A., Ackermann, M., Krockenberger, M., Mansell, J. et al. (2019). Correlating Gastrointestinal Histopathologic Changes to Clinical Disease Activity in Dogs With Idiopathic Inflammatory Bowel Disease. *Vet Pathol*, 56(3), 435–443. doi: 10.1177/0300985818813090.
- Borgarelli, M., & Buchanan, J. W. (2012). Historical review, epidemiology and natural history of degenerative mitral valve disease. *Journal of Veterinary Cardiology*, 14(1), 93–101. doi: 10.1016/j.jvc.2012.01.011.
- Borgarelli, M., Zini, E., D'Agnolo, G., Tarducci, A., Santilli, R. A., Chiavegato, D., Tursi, M., Prunotto, M., & Häggström, J. (2004). Comparison of primary mitral valve disease in German Shepherd dogs and in small breeds. *Journal of Veterinary Cardiology*, 6(2), 27–34. doi: 10.1016/S1760-2734(06)70055-8.
- Gabunshhina, O. D. (2012). Lejkogramma i lejkocitarnye indeksy v krovi verbljudov kalmyckoj porodny. *Aktual'nye voprosy veterinarnoj biologii*, 1(13), 3–5. URL: <https://cyberleninka.ru/> ar-

- icle/n/leykogramma-i-leykotsitarnye-indeksy-krovi-verblyudov-kalmytskoy-porody-camelus-bactrianus/viewer (in Russian).
- International Council for Standardization in Hematology (Expert Panel on Blood Rheology) (1993). ICSH recommendations for measurement of erythrocyte sedimentation rate. *J Clin Pathol*, 46(3), 198–203. doi: 10.1136/jcp.46.3.198.
- Konstantinidis, A. O., Adamama-Moraitou, K. K., Pardali, D., Dovas, C. I., Brellou, G. D., Papadopoulos, T., Jergens, A. E., Allenspach, K., & Rallis, T. S. (2021). Colonic mucosal and cytobrush sample cytokine mRNA expression in canine inflammatory bowel disease and their correlation with disease activity, endoscopic and histopathologic score. *PLoS One*, 16(1), e0245713. doi: 10.1371/journal.pone.0245713.
- Korppi, M., Heiskanen-Kosma, T., & Leinonen, M. (1997). White blood cells, C-reactive protein and erythrocyte sedimentation rate in pneumococcal pneumonia in children. *Eur Respir J*, 10(5), 1125–1129. doi: 10.1183/09031936.97.10051125.
- Kryzhanovskij, G. N. (2002). Dizreguljacionnaja patologija. M., Medicina (in Russian).
- Lapach, S. N., Chubenko, A. V., & Babich, P. N. (2001). Statisticheskie metody v mediko-biologicheskikh issledovanijah s ispol'zovaniem Excel. 2-e izd., pererab. i dop. K.: MORION, 143–144 (in Ukrainian).
- Mustafina, Zh. G., Kramarenko, Ju. S., & Kobceva, V. Ju. (1999). Integral'nye gematologicheskie pokazateli v ocenke immunologicheskoj reaktivnosti organizma bol'nyh s oftal'mopatologiej. *Klinicheskaja laboratornaja diagnostika*, 5, 47–48 (in Russian).
- Panchyshyn, Yu. M., Huk-Leshnevska, Z. O., Mostova, O. F., & Shuliuk, Yu. V. (2014). Klinichni osoblyvosti perebihu stabilnoi stenokardii z hipokholesterlemiieiu zalezjno vid velychyny indeksu De Ritisa. *Praktykuiuchyi likar*, 2, 26–30. URL: <https://plr.com.ua/index.php/journal/article/view/354> (in Ukrainian).
- Pisarev, V. V., L'vov, S. E., Oshurkov, V. V., Kaluckov, V. V., Kulygin, V. N., & L'vov, A. S. (2008). Infekcionnye oslozhenija posleoperacionnoj rany pri metallosteosinteze zakrytyh perelomov dlinnyh trubchatyh kostej. *Travmatologija i ortopedija Rossii*, 2, 14–19. URL: <https://cyberleninka.ru/article/n/infekcionnye-oslozheniya-posleoperatsionnoy-rany-pri-metallosteosinteze-zakrytyh-perelomov-dlinnyh-trubchatyh-kostej> (in Russian).
- Provan, D., & Krentz, A., (2002). Oxford Handbook of Clinical and Laboratory Investigation, 2nd ad. Oxford University Press.
- Sacoor, C., Barros, L. M., & Montezinho, L. (2021). What are the potential biomarkers that should be considered in diagnosing and managing canine chronic inflammatory enteropathies? *Open Vet J*, 10(4), 412–430. doi: 10.4314/ovj.v10i4.9.
- Sivaraman, S. K., Zachariah, G., & Annamalai, P. T. (2004). Evaluation of C-reactive protein and other inflammatory markers in acute coronary syndromes. *Kuwait Med J*, 36, 35–37.
- Smiiian, O. I., Sichnenko, P. I., & Moshchych, O. P. (2020). Dosvid zastosuvannia alhorytmu kompleksnoi otsinky stanu orhanizmu u ditei z khronichnoiu hastroduodenalnoiu patolohiieiu. *Skhidnoukrainskyi medychnyi zhurnal*, 1, 43–51. doi: 10.21272/eumj.2020;8(1):52-71 (in Ukrainian).
- Speranskij, I. I., Samojlenko, G. E., & Lobacheva, M. V. (2009). Obs'hij analiz krovi - vse li ego vozmozhnosti ischerpany? Integral'nye indeksy intoksikacii kak kriterii ocenki tjazhesti techenija jendogennoj intoksikacii, ee oslozhenij i jeffektivnosti provodimogo lechenija. *Ostrye i neotlozhnye sostojanija v praktike vracha*, 6(19), 27–36 (in Russian).
- Stybel, V., Gutyj, B., & Said, W. (2021). Effect of fenbenzyl and fenbendazole on peroxide intensity oxidation of lipids in the blood of dogs in experimental toxocariasis. *Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences*, 23(101), 107–112. doi: 10.32718/nvvet10118.
- Suhorukov, V. P., Dvorjanskij, S. A., & Popov, D. V. (2007). Integral'nye gematologicheskie indeksy kak kriterii tjazhesti i jeffektivnosti terapii prejeklampsii. *Klinicheskaja laboratornaja diagnostika*, 11, 47–50 (in Russian).
- Umanskij, M. A., Pinchuk, L. B., & Pinchuk, V. G. (1991). Sindrom jendogennoj intoksikacii. Kiev (in Ukrainian).
- Uzbekov, M. G., & Misionzhnik, Je. Ju. (2000). Nespecificeskij sindrom jendogennoj intoksikacii kak integral'nyj komponent patogeneza psichicheskikh rasstrojstv. *Rossijskij psichiatricheskij zhurnal*, 4, 56–65 (in Russian).
- Varkholiak, I. S., & Gutyj, B. V. (2020). The influence of the preparation “Bendamin” on the morphological and biochemical indices of blood of rats in experimental modeling of heart failure. *Ukrainian Journal of Veterinary and Agricultural Sciences*, 3(1), 38–41. doi: 10.32718/ujvas3-1.07.
- Varkholiak, I., & Gutyj, B. (2021). The effect of the drug “Bendamin” on the biochemical parameters of the blood of dogs in heart failure. *Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences*, 23(101), 93–99. doi: 10.32718/nvvet10116.
- Weitkamp, J-H., & Achner, J. L. (2005). Diagnostic Use of C-Reactive Protein (CRP) in Assessment of Neonatal Sepsis. *Neo-Reviews*, 6(11), 508–515. doi: 10.1542/neo.6-11-e508.
- Zhukov, A. P., Zhambulov, M. M., & Datskij, A. P. (2017). Vozrastnye izmeneniya referentnyh integral'nyh gematologicheskikh indeksov nespecificheskoj reaktivnosti u zdorovyh loshadej. *Izvestija Orenburgskogo gosudarstvennogo universiteta*, 2, 108–113. URL: <https://cyberleninka.ru/article/n/vozzrastnye-izmeneniya-referentnyh-integralnyh-gematologicheskikh-indeksov-nespetsificheskoy-reaktivnosti-u-zdorovyh-loshadej> (in Russian).