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## CONDITION OF IMMUNE STATUS IN ADULTS WITH ENTEROBIASIS INVASION

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The purpose of the present project was to study the immune status condition in patients with enterobiasis. The immune status condition was studied in 39 cadets with primary and repeated invasion with seatworms and 12 clinically healthy cadets. During the primary invasion, the immunogram indices did not differ from those of the control group and were within the reference values of the norm. The redistribution of T-helpers and T-suppressors concentrations was found during the repeated enterobiasis with a marked decrease in the level of immunoregulatory cells possessing the T-helper activity, which is, in our opinion, a significant factor leading to the development of stable immunocomprometation and may further lead to reinvasion. Changes in the macrophage-phagocytic system indicate a decrease in the killing effect of phagocytic neutrophils in the peripheral blood against the background of their compensatory stress during repeated enterobiasis invasions.

**Key words:** enterobiasis, seatworms, reinvasion, immune status, adults.

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## СТАН ІМУННОГО СТАТУСУ У ДОРΟΣЛИХ З ЕНТЕРОБІОЗНОЮ ІНВАЗІЄЮ

Метою дослідження було вивчення стану імунного статусу у хворих на ентеробіоз. Досліджено імунологічний статус у 39 курсанта, з первинною і повторною інвазією гостриками і у 12 клінічно здорових курсантів. При первинній інвазії показники імунограм не відрізнялися від контрольної групи і знаходилися в межах референтних значень норми. Виявлений перерозподіл концентрації Т-хелперів і Т-супресорів при повторному ентеробіозі з вираженим зниженням імунорегулюючого рівня клітин, які мають Т-хелперну активність, є, на нашу думку, істотним фактором, який веде до розвитку стійкої імунокомпрометації, що може надалі приводити до реінвазії. Зміни в макрофагально-фагоцитарній системі вказують на зниження килінгового ефекту фагоцитуючих нейтрофілів периферичної крові на фоні їхньої компенсаторної напруги при повторних ентеробіозних інвазіях.

**Ключові слова:** ентеробіоз, гострики, реінвазія, імунний статус, дорослі.

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Enterobiasis remains the most common helminthiasis in Ukraine, which is of great medical and social importance, exerting a multifaceted pathological effect on the human body. Noteworthy, the high incidence of enterobiasis in adults [4, 5, 7, 10, 12].

General pathological effect of helminthiases on the host is allergization and immunosuppression [6]. The long-term course of enterobiasis in connection with frequent reinvasions should be regarded as a violation of mutual relations in the parasite-host system in favor of the helminth. Attention is drawn by the immunological homeostasis disorder during parasitic invasions [9]. It is a well-known fact that common intestinal parasitoses create secondary immunodeficiency states, even in the form of carriage [3, 4, 8]. It has been established that pinworms suppress the development of post-vaccination immunity against diphtheria and measles [1, 4]. It has been shown the hyperactivity of the B immune system which leads to an increase in the synthesis of immunoglobulins (a significant increase in the concentration of IgA and IgM) in patients with ascariasis and enterobiasis of low intensity of invasion, and, in the same time, the formation of circulating immune complexes (CIC), and the failure of systems that eliminate the CIC [1].

The peculiarity of pinworm biology - the rapid development of eggs and resistance in the environment - determines the recurrence of infection and the long course of enterobiasis. In the available literature sources, we did not come across publications concerning the immune system's status during persistent enterobiasis invasion in adults. From our point of view, the study of impaired immunological status in this category of patients is essential to determine the degree of seatworms pathogenic effect on the human body and the choice of the correct treatment strategy.

The current data on the immunoreactivity of patients with enterobiasis are fragmentary and sometimes contradictory. This is due not least to the fact that the study of this issue is carried out on patients of different ages, with the presence of comorbidities, in the adult population or in children, among them being frequently ill ones [7, 10, 12]. Therefore, the study of the immune status in enterobiasis in cadets without concomitant pathology performed in our study is of fundamental importance.

**The purpose** of the present project was to study the immune status condition in patients with enterobiasis.

**Materials and methods.** The cellular and humoral immunity indices was studied, as well as the neutrophils phagocytic activity of peripheral blood in 51 cadets of the Kharkiv Institute of Air Force aged 18

to 24 years, among them 24 persons being diagnosed with enterobiasis (group 1), 15 – with seatworms reinvasion (group 2) and 12 clinically healthy cadets formed the control group.

Parameters of the immune status were studied: the main populations and subpopulations of peripheral blood lymphocytes (CD3+; CD4+; CD8+; CD19+) were determined using a monoclonal antibodies panel by means of the indirect surface immunofluorescence method, the relative number of 0-lymphocytes was calculated by the formula: % 0-lymphocytes = 100 – (%CD3 + %CD19+), the level of circulating immune complexes in the peripheral blood serum was determined by the spectrophotometric method, the concentration of immunoglobulins of the main classes (A, G and M) – by the method of simple radial immunodiffusion. In the study of the neutrophils' phagocytic function, the parameters characterizing the absorption (phagocytic index and phagocytic number) and digesting (index of phagocytosis completeness) ability of peripheral blood neutrophils were calculated [13].

The diagnosis of enterobiasis was established when seatworm eggs were found in the perianal folds using adhesive tape (Graham method). To exclude other helminthiasis, the presence of their eggs in feces was determined by the Fulleborn enrichment method [1, 5].

Statistical processing was carried out using generally accepted methods with the calculation of percentages, mean values and their errors using computer programs Statgraphics Plus for Windows 2.1. When assessing the reliability of differences in samples, Student's t-test was used.

**Results of the study and their discussion.** The mean group and individual analysis of immunograms (table 1) revealed some changes in the studied immunity parameters, more pronounced in the group of patients with repeated enterobiasis invasion.

Table 1

**The immune status of the host during primary and repeated invasion by seatworms**

Studied parameters	Primary invasion (n = 24)	Repeated invasion (n = 15)	Control group (n = 12)	Normal reference values
	(M±m)	(M±m)	(M±m)	
Lymphocytes, %	34.6±2.5	37.9±6.5	30.2±1.2	19÷40
CD 3+, %	57.5±3.9*	47±2***	60.4±2	45÷70
CD 4+, %	35.5±4.5*	21.7±3.0***	41.0±2	35÷49
CD 8+, %	21±3.2	29.0±4.0*	19±0.9	14÷24
IRI, CU	1.74±0.2***	0.9±0.07***	1.9±0.2	1.1÷2.5
CD 19+, %	6.8±0.9	7.5±1.2	7.3±0.6	5÷15
0-cells, %	35.1±2.6*	45.5±3.5***	29.5±1.4	23÷37
CIC, CU.	68.0±3.9	64.4±3.5	58.9±4.5	40÷80
Ig G, g/l	14.2±1.8	15.01±1.9	12.8±0.5	8.5÷16.5
Ig A, g/l	2.3±0.6	1.85±0.7	2.05±0.09	1.2÷2.6
Ig M, g/l	1.04±0.3	0.84±0.1**	1.19±0.07	0.7÷1.8
PN, CU	3.4±0.3	4.1±0.8	3.6±0.2	2÷5
IPC, CU.	1.01±0.07	0.85±0.08**	1.16±0.04	≥1

Note. Reliability of differences by the Student's t-test: \* – p<0.05; \*\* – p<0.01; \*\*\* – p<0.001 in comparison with the control group; • – p<0.05; •• – p<0.01; ••• – p<0.001 when comparing patients with primary and repeated invasion.

The immunological profile of cadets diagnosed enterobiasis with primary and repeated invasion, as compared to clinically healthy persons, is shown in fig. 1, 2.

Data on the expression level of mature thymus-dependent lymphocytes detected by CD3+ monoclonal antibodies showed a significant decrease in their number in peripheral blood upon repeated invasion. The mean group content of this peripheral blood lymphocytes population was at the lower reference limits level of the physiological norm and was significantly lower than that in the control group and in the group with primary enterobiasis, amounting 47±2%. Moreover, an individual analysis of immunograms in patients with repeated invasion by seatworms showed that 60% of them had a relative content of CD3+ cells below the lower limit of the confidence interval for the mean statistical norm.

Consequently, our observations permit to state that a decrease in the relative level of common T-cells during repeated enterobiasis is one of the characteristic features of the cellular component condition of the immune system in this category of patients and may indicate the response of the immune system to an alien one.

We revealed significant changes in the content of regulatory subpopulations of lymphocytes – T-helpers/inducers and T-suppressors/cytotoxic, the severity of which depended on whether patients were initially invaded or re-invaded by seatworms.

With repeated invasion, a significant decrease in the content of CD4+ cells was observed when compared to the control and patients of group 1, which was accompanied by an increase in the level of CD8+ lymphocytes (suppressors / cytotoxic) – 21.7±3% and 29±4% respectively. At the same time, in 58.3% of

patients in group 1, the level of CD4+ lymphocytes was at the lower limit of the confidence interval of the mean statistical norm, however, no significant increase in the number of cytotoxic suppressor cells was observed, unlike in patients of group 2.

The revealed redistribution of T-helpers and T-suppressors concentrations during the repeated enterobiasis with a marked decrease in the immunoregulatory level of cells with T-helper activity is, in our opinion, a significant predisposing factor for the development of stable immunocomprometation, which can lead to reinvasion.

The mean value of the immunoregulatory index (IRI) – T-helpers/T-suppressors ratio – in patients of group 1 was within the reference values of this index in clinically healthy persons, while with repeated invasion this index was significantly lower compared to the mean statistical norm and group 1 surveyed, and amounted to  $0.9 \pm 0.07$  CU. It has been established that seatworms inhibit the development of post-vaccination immunity against diphtheria and measles [4, 8]. In a study conducted by Yu. A. Kopanев, clinical signs of immunological deficiency were observed in 15 of 29 children with enterobiasis or ascariasis. A decrease in the number of T-helper cells was found in all the examined subjects, the helper-suppressor ratio was reduced in 12 children [2].

As for the B-lymphocyte population (CD19+ cells), the latter practically did not undergo any particular changes as compared to clinically healthy cadets and between the comparison groups of patients with enterobiasis invasion, and their relative content in the peripheral blood of patients in both groups was within the reference values for the mean physiological norm.

The imbalance of immunoregulatory lymphocyte subpopulations revealed by us during reinvasion was accompanied by the presence of a large number of lymphocytes in the peripheral blood that do not have antigenic determinants corresponding to the T or B population (the so-called nullers).

The content of 0-lymphocytes during repeated invasion was significantly higher; both if compared to the control group, and compared to patients with primary invasion with seatworms. The mean group number of these cells in group 2 was  $45.5 \pm 3.5\%$  with reference limits of this mean statistical norm index of  $23 \div 37\%$ .

Increase in the concentration of 0-lymphocytes may indicate either disorder in the maturation process (differentiation) of cells in the central organs of immunogenesis, or inhibition of the distant regulators production, ensuring the maturation of cells in the periphery.

In general, it can be concluded that already at the stage of assessing the quantitative parameters of the immunity cellular component in patients with enterobiasis with repeated invasions, pronounced changes in most of them are observed.

Individual analysis of immunograms showed that the production of the main classes of immunoglobulins – G, A, M – was characterized by a high content of IgG in 25% of patients in group 1 and 33.3% in groups 2 and the normal level of IgA in all patients. At the same time, in patients of group 1, the concentration of Ig M remained within the reference values of the physiological norm and practically did not differ from that in the control group. As for patients with reinvasion of enterobiasis, the mean level of serum IgM did not go beyond the lower limit of the normal confidence interval, but was significantly lower than that of healthy cadets.

Indicators of concentration in the peripheral blood of the main classes of immunoglobulins are completely independent parameters, permitting to assess the functional activity of the humoral component in the immune system's work.

Of certain value is assessment of the main classes immunoglobulins content for determining the area of predominant injury (mucous membranes or deep layers of tissues). More constant is the change in the immunoglobulin levels ratio in chronic processes or repeated infections, which are often accompanied by an increase of the immunoglobulins concentration in the serum (mainly class G) due to their release from the depot.

When the reaction is associated with the initial contact of the body with the antigen, a normal or slightly elevated, but not exceeding the physiological norm, level of IgM can be observed with a simultaneous increase in the concentration of serum IgG, which we obtained during the examination of patients in group 1. Upon repeated contact (group 2) with this antigen, the increase in IgG level occurs with a simultaneous decrease in the IgM amount. The latter has the greatest ability to binding and activating the complement.

Therefore, a decrease in IgM concentration during repeated invasions can lead to the suppression of the complement system activity, which, in its turn, contributes to blocking the process of helminth antigens lysis and has a significant effect on the immune response of the host.

Immunoglobulin G is polyfunctional, and in the presence of any pathological process, the demand for its products increases, i.e. increased IgG production is a response to excessive accumulation of foreign matter. Experimental and clinical data led to the conclusion that overproduction of IgG4 in helminth infections reduces the sensitizing effect of IgE and contributes to the re-invasion [3].

In the patients examined by us, both with primary and repeated invasions, the mean group level of circulating immune complexes differed slightly from the mean group content of this index in the control group and was within the reference values of the physiological norm.

Normally, the formation of antigen-antibody complexes is a dynamic biological process that plays an important role in immunogenesis and immunoregulation. In healthy people, as a rule, there is a small number of circulating immune complexes. The formation of the CIC is an indispensable stage of any immune response, which is a factor determining the course of the disease, providing neutralization and the degree of pathogenic material elimination (toxins, microorganisms, tissue histolysis products). Under certain conditions, these complexes can become pathogenic for the body. An important condition for the CIC non-pathogenicity is their rapid elimination from the bloodstream, due to the properly functioning MPS.

Peripheral blood phagocytic neutrophils in the patients of the first group examined by us possessed the absorptive capacity analogous to the group of clinically healthy cadets (phagocytic number, PN). However, despite the fact that the number of phagocytic neutrophils in the blood varied during primary invasion within the reference values of the physiological norm, in patients with repeated seatworms invasion, this index exceeded the upper limit of the physiological norm confidence interval ( $93.7 \pm 4.9\%$ ). The latter may be in favor of the compensatory stress in the cells of the macrophage system (MPS) during repeated invasions. At the same time, an increased level of phagocytic neutrophils in the peripheral blood of patients in group 2 was accompanied by a decrease in their digestive activity, compared to clinically healthy cadets and a similar physiological norm index. This is evidenced by a decrease in the index of phagocytosis completeness (IPC) –  $0.85 \pm 0.08$  CU. This fact indicates a decrease in the killing effect of phagocytic neutrophils in the peripheral blood of patients with enterobiasis in the repeated invasion.

N.N. Blagova in her study showed that patients with ascariasis and enterobiasis with weak invasion intensity had some clinical and immunological features: on the one hand, hyperactivity of the B-cells – an increase in IgA and IgM and CIC, on the other hand, the failure of systems eliminating CIC [1].

Such reactions of the MPS correspond to modern ideas about the qualitative and quantitative changes in the parameters of the cytokine network in the immune system under the conditions of the physiological body state and the development of a particular pathology [11].

At the final stages of the antigen processing, namely during its destruction, one of the key mediators of the immune response is identified – interleukin-1. This mediator activates T-helpers/inducers functions and stimulates T-lymphocyte differentiation in the thymus. In their turn, T-helpers with their cytokines, such as gamma-interferon, stimulate the activity of MPS cells.

Consequently, a decrease in the killing ability of the peripheral blood phagocytic neutrophils, which are representatives of the cellular immunity, can cause a cascade of events leading to the disruption of other immune cells function.

This is evidenced by our data that with repeated enterobiasis invasions, a decrease in the quantitative indices of the T-cell immunity component is the most characteristic feature of the immune system's condition.

## Conclusion

Thus, the results of the immune status assessment during the seatworms invasion indicate changes in the cellular component of the immune system, the severity of which during repeated invasions clearly goes beyond the so-called “transient” deviations associated with the temporary state of the immune system.

The immunograms indices during the primary invasion do not reliably differ from those of the control group and are within the reference values of the norm. Decrease in the number of T-lymphocytes (CD3+), T-helpers/inducers (CD4+), an increase in the content of T-suppressors/cytotoxic (CD8+) and undifferentiated forms of lymphocytes (0-cells) against the background of reducing Ig M, activation absorption and inhibition of the digestive functions of phagocytic neutrophils in the blood is characteristic of patients with reinvasion. Patients with persistent, long-term enterobiasis are recommended to undergo a detailed study of the immunological status, followed by the appointment of immunomodulating agents.

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### FEATURES OF VESTIBULAR DYSFUNCTION IN PATIENTS WITH HEREDITARY AND ACQUIRED MOTION SICKNESS

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It was established that vestibular dysfunction in patients with hereditary and acquired motion sickness plays one of the leading roles in traffic l-oads. Features of vestibular dysfunction in hereditary motion sickness are characteristic for bilateral symmetrical irritative mixed vestibular syndrome of the I<sup>st</sup> and the II<sup>nd</sup> degree in the stage of subcompensation with hearing acuity within the norm symmetrically on both sides. In acquired motion sickness, the features of vestibular dysfunction are manifested by following variability: unilateral irritative peripheral or mixed vestibular syndrome of the II<sup>nd</sup> degree in the stage of subcompensation or decompensation, as well as asymmetric irritative bilateral mixed syndrome of the II<sup>nd</sup> degree in the stage of subcompensation with different forms and degrees of hearing loss. It was investigated that unilaterality and asymmetry of irritative vestibular syndromes at the acquired motion sickness is one of signs of basic disease development. Certain differences in vestibular dysfunction increase the efficiency of diagnosis, as well as differential diagnosis of hereditary and acquired motion sickness.

**Key words:** hereditary and acquired motion sickness, experimental nystagmus reaction, peripheral and mixed vestibular syndromes.

### Н.С. Міщанчук, О.М. Борисенко, С.Б. Безшапочний, С.В. Кузьменко

### ОСОБЛИВОСТІ ВЕСТИБУЛЯРНОЇ ДИСФУНКЦІЇ У ПАЦІЄНТІВ ПРИ СПАДКОВИХ ТА НАБУТИХ ХВОРОБАХ РУХУ

Досліджені особливості вестибулярної дисфункції приспадкових хворобах руху, які проявляються двобічним симетричним іритативним змішаним вестибулярним синдромом I та II ступеня в стадії субкомпенсації з гостротою слуху у межах норми симетрично з обох боків. При набутих хворобах її особливості проявляється варіабільністю: однобічним іритативним периферичним або змішаним вестибулярним синдромом II ступеня у стадії субкомпенсації чи декомпенсації, а також асиметричним іритативним двобічним змішаним синдромом II ст. у стадії субкомпенсації з різними формами та ступенями зниження слуху. Визначено, що однобічність та асиметричність іритативних вестибулярних синдромів при набутих хворобах руху є однією із ознак розвитку основного захворювання. Визначені відмінності вестибулярної дисфункції підвищують ефективність діагностики, а також диференційної діагностики спадкових та набутих хвороб руху.

**Ключові слова:** спадкові, набуті хвороби руху, експериментальна ністагмова реакція, периферичний та змішаний вестибулярні синдроми.

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Motion sickness occurs with increasing the angular and linear acceleration or deceleration movements during various transport loads, including high-speed and long-term ones. Symptoms of motion sickness have been known since the ancient times, and there are hereditary (congenital) and acquired motion sickness among them.

The physiological mechanisms underlying the onset of motion sickness have been studied for centuries by numerous researchers, but they have not yet been definitively identified and are often contradictory [2, 4 - 8, 12].