*Медицинская иммунология*
*2023, Т. 25, № 4,*
*стр. 891-898*

***Краткие сообщения***
***Short communications***

*Medical Immunology (Russia)/*
*Meditsinskaya Immunologiya*
*2023, Vol. 25, № 4, pp. 891-898*

# ДИФФЕРЕНЦИРОВАННЫЕ НАРУШЕНИЯ ИММУННОЙ СИСТЕМЫ ПРИ ОСТРОМ ГЕМАТОГЕННОМ И ОСТРОМ ПОСТТРАВМАТИЧЕСКОМ ОСТЕОМИЕЛИТАХ У ДЕТЕЙ

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Резюме. Остеомиелит – воспаление кости и костного мозга, вызванное распространением *S. aureus* из локального очага гематогенным путем или из открытого травматического перелома, которое трудно поддается лечению и остается серьезной проблемой. Условиями распространения инфекционного процесса в кости является влияние *S. aureus*, нарушение его элиминации из-за дисфункции иммунной системы (ИС). Разноречивые данные об иммунопатогенетических механизмах развития острого остеомиелита требуют изучения, позволяющего разработать обоснованную иммунотерапию. Цель исследования – уточнить варианты нарушений противобактериальной иммунной защиты у детей с острым гематогенным и острым посттравматическим остеомиелитами. Исследованы дети 8-15 лет (n = 22): группа исследования 1 (ГИ1) – 12 пациентов с острым гематогенным остеомиелитом (ОГО); группа исследования 2 (ГИ2) – 10 детей с острым посттравматическим остеомиелитом (ОПО). Группу сравнения (ГС) – 13 здоровых детей соответствующего возраста. Тестировали Т-лимфоциты ($CD3^+CD19^-$, $CD3^+CD4^+$, $CD3^+CD8^+$, $CD3^+CD4^+/CD3^+CD8^+$), В-лимфоциты ($CD3^-CD19^+$), NK ($CD3^-CD16^+CD56^+$) и TNK ($CD3^+CD16^+CD56^+$) лимфоциты, CD16, CD32, CD64 рецепторы на нейтрофильных гранулоцитов (НГ) (FC-500 Beckman Coulter, США); уровень сывороточных IgA, IgM, IgG (ИФА). Оценивали фагоцитарную функцию НГ по отношению к *S. aureus*: количество активно фагоцитирующих НГ (%ФАН), процессы захвата (ФЧ, ФИ) и киллинговую активность (%П, ИП). В группах ОГО и ОПО выявлено снижение количества Т-лимфоцитов, Т-хелперов, TCTL и NK ($p_{1\text{-}4} < 0{,}05$). Также установлено, что при ОГО уровень IgA, IgM, IgG не отличался от показателей ГС, тогда как при ОПО отмечалось повышение уровня IgA и IgG ($p_{1,2} < 0{,}05$). Показано, в группах с ОГО и ОПО отмечается разная плотность экспрессии рецепторов CD64, CD16, CD32 на НГ, предопределяющая несостоятельность фагоцитарной функции. Дефекты фагоцитоза, при ОГО в первую очередь, связанны с нарушениями захвата и киллинга, а при ОПО только с процессами переваривания бактериального антигена. Выявленные комбинированные дефекты функционирования ИС диктуют

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**Образец цитирования:**

*Г.А. Чудилова, В.А. Тараканов, Е.А. Чичерев, Ю.В. Тетерин, Н.К. Барова, М.Н. Митропанова «Дифференцированные нарушения иммунной системы при остром гематогенном и остром посттравматическом остеомиелитах у детей» // Медицинская иммунология, 2023. Т. 25, № 4. С. 891-898.*
*doi: 10.15789/1563-0625-DDO-2759*



**For citation:**

*G.A. Chudilova, V.A. Tarakanov, E.A. Chicherev, Yu.V. Teterin, N.K. Barova, M.N. Mitropanova "Differentiated disorders of the immune system in acute hematogenic and acute posttraumatic osteomyelitis in children", Medical Immunology (Russia)/Meditsinskaya Immunologiya, 2023, Vol. 25, no. 4, pp. 891-898.*
*doi: 10.15789/1563-0625-DDO-2759*



**DOI:** 10.15789/1563-0625-DDO-2759

необходимость разработки новых подходов в лечении ОГО и ОПО у детей, патогенетически обосновывающих использование иммунотерапии в комплексном этиопатогенетическом лечении, что будет способствовать восстановлению противоинфекционного иммунитета, улучшению клинического течения заболеваний, а также препятствовать хронизации воспалительного процесса и усугублению дисфункции ИС.

*Ключевые слова: острый гематогенный остеомиелит, острый посттравматический остеомиелит, дети, иммунная система, дисфункции, противобактериальный иммунитет*

# DIFFERENTIATED DISORDERS OF THE IMMUNE SYSTEM IN ACUTE HEMATOGENIC AND ACUTE POSTTRAUMATIC OSTEOMYELITIS IN CHILDREN

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**Abstract.** Osteomyelitis is an inflammation of bone and bone marrow caused by the spread of *S. aureus* from a local focus by the hematogenous route or from an open traumatic fracture; it is difficult to treat and remains a serious problem. The condition for spreading of the infectious process into bone is the effect of *S. aureus* and its impaired elimination due to immune system (IS) dysfunction. Controversial information on the immunopathogenetic mechanisms of acute osteomyelitis needs study, which would allow the development of sound immunotherapy. Purpose of the study: to specify the variants of antibacterial immune protection disorders in children with acute hematogenous and acute posttraumatic osteomyelitis. Materials and methods. Children 8-15 years old (n = 22) were studied: Study Group 1 (SG1, n = 12) – with acute hematogenous osteomyelitis (AHO); Study Group 2 (SG2, n = 10) – with acute post-traumatic osteomyelitis (APTO). The comparison group (CG) – 13 healthy children. Tested: T lymphocytes ($CD3^+CD19^-$, $CD3^+CD4^+$, $CD3^+CD8^+$), B lymphocytes ($CD3^-CD19^+$), NK ($CD3^-CD16^+CD56^+$) and TNK ($CD3^+CD16^+CD56^+$) lymphocytes, neutrophil granulocytes (NG, CD16, CD32, CD64) (FC-500 Beckman Coulter, USA); the level of serum IgA, IgM, IgG (ELISA). Phagocytic function of NGs in relation to *S. aureus* was assessed: the number of actively phagocytizing NGs (%PhAN), capture processes (PhN, PhI) and killing activity (%D, DI). Results. In both groups was revealed a decrease of T lymphocytes, T helpers, $T_{CTL}$ and NK quantity ($p_{1-4} < 0.05$). In AHO, the levels of IgA, IgM, IgG did not differ from that in GS, while in APTO the levels of IgA and IgG increased ($p_{1, 2} < 0.05$). The density of CD64, CD16, CD32 receptor expression on NG in the studied groups has been a different equipping, predetermining an incompetence of the phagocytic function: in AHO associated with abnormalities in the function capture and killing, in APTO only with the *S. aureus* digestion. Conclusion. The revealed combined defects of IS functioning necessitate the development of new approaches in the treatment of AHO and APTO in children, pathogenetically substantiating the use of immunotherapy in the complex etiopathogenetic treatment. This approach will contribute to the restoration of mechanisms of anti-infective immunity, timely elimination of pathogens, improve the clinical course of the diseases, prevent the chronic inflammatory process.

*Keywords: acute hematogenous osteomyelitis, acute post-traumatic osteomyelitis, children, immune system, dysfunctions, antibacterial immunity*

The study was carried out as part of the state assignment of the Ministry of Health of the Russian Federation (No. 121031000071-4).

## Introduction

Deep infections, such as osteomyelitis, which are difficult to treat, remain a serious health problem worldwide [2, 11]. Osteomyelitis is an infectious inflammation of the bone and bone marrow caused by the spreading of an agent from a local focus by hematogenous route and/or from an open fracture to all parts of the bone and its surrounding soft tissues, which ultimately leads to progressive destruction of the bone [7]. Acute osteomyelitis is predominantly a childhood disease with a peak incidence occurs at 10-14 years (60-80%) [3]. In difficult cases of acute

osteomyelitis, children continue to die, even in our era of significant advances in surgical procedures and the strongest antibiotics. The causative agents of osteomyelitis are commensal staphylococci, *S. epidermidis*, and the most common etiological agent is *S. aureus* [6]. *S. aureus* is highly virulent, expressing immunomodulatory proteins, adhesins, toxins, and superantigens, and is able to adapt to the immune response and evade it.

In addition, *S. aureus* has many mechanisms promoting tolerance to antibiotic treatment [9]. In particular, it is able to create three-dimensional conglomerates consisting of bacteria surrounded by neutrophilic granulocytes (NGs) and macrophages. *S. aureus* forms biofilms on necrotic bone; it secretes SpA proteins that bind to IgG Fc-fragments and block antibody-mediated phagocytosis, or to Fab-domains of the VH3 chain of IgM antibodies, which causes proliferative expansion of B cells ending in apoptosis [9]. Recently, the mechanism of *S. aureus* evasion from the response of the immune system (IS), which leads to its persistence, was discovered: the invasion into submicron channels deep in the bone cortex, where bacteria can survive for many years, dissolving the surrounding bone mineral matrix [4].

On the other hand, it has been established that the most important condition for the spread of the infectious process in the bone is both the negative impact of *S. aureus* itself and the violation of its elimination, and IS dysfunction [8, 12]. The imbalance of the immune system in AHO in young children has been confirmed in various studies [1, 3, 12]. There is the information of the presence of immune deficiency before the onset of the disease, which caused the onset and progression of a focus in the bone tissue in chronic osteomyelitis [1]. At the same time, there are many conflicting facts of the pathogenetic mechanisms in the development of acute osteomyelitis, which, from our point of view, remain insufficiently studied. It should be noted that an in-depth approach to the study of the immunopathogenesis of acute osteomyelitis is needed, which would allow to develop the pathogenetically substantiated immunotherapy.

**Purpose of the study:** to clarify the variants of violations of antibacterial immune defense in children with acute hematogenous and acute post-traumatic osteomyelitis.

## Materials and methods

The study included children aged 8-15 years with acute osteomyelitis (n = 22) hospitalized at the Regional Children's Clinical Hospital of the Ministry of Health of the Krasnodar Krai.

Based on clinical and laboratory data, 2 study groups were formed. Study group 1 (SG 1) included 12 patients (1 girl, 11 boys) with acute hematogenous osteomyelitis (AHO). For patients from SG1, at the time of admission to the hospital the febrile temperature was for the 4 (2.5-6.5) days from the onset of the disease, a high level of CRP – 60 (13-158) mg/L. Before hospitalization, 1 person took antibiotics.

Study group 2 (SG2) consisted of 10 children (2 girls, 8 boys) with acute post-traumatic osteomyelitis (APTO). In SG2 patients, at 9 (7-14) from the onset of the disease, subfebrile temperature was noted, the level of CRP was 8 (5-30) mg/L. Prior to hospitalization, 5 people were taking antibiotics (a broad-spectrum synthetic penicillin antibiotic with a beta-lactamase inhibitor or a third-generation cephalosporin with a beta-lactamase inhibitor). The comparison group (CG) consisted of 13 conditionally healthy children of the corresponding age.

We have determined the content of T lymphocytes ($CD3^+CD19^-$, $CD3^+CD4^+$, $CD3^+CD8^+$, $IRI_1$ – $CD3^+CD4^+/CD3^+CD8^+$), and B lymphocytes ($CD3^-CD19^+$), as well as NK lymphocytes ($CD3^-CD16^+CD56^+$), TNK lymphocytes ($CD3^+CD16^+CD56^+$), CD16, CD32, CD64 NGs receptors on Cytomics FC-500 cytometer (Beckman Coulter, USA) using monoclonal antibodies (Beckman Coulter, USA). The level of serum IgA, IgM, IgG was determined (ELISA, test systems of CJSC Vector-Best, Russia). The phagocytic activity of NG was assessed with the determination of the number of actively phagocytic NG (%PhAN) uptake processes (PhN, PhI) and the degree of completion of the phagocytic act with an assessment of the digestive activity (% D, DI) in relation to *S. aureus* (strain 209)

The conducted study complies with the requirements of the WMA Declaration of Helsinki (DoH), approved by the Social Ethics Committee of the Kuban State Medical University of the Ministry of Health of Russia.

Statistical processing of the study results was carried out using computer programs Microsoft Excel 2016 and StatPlus 2020. Nonparametric statistics methods were used: Me ($Q_{0.25}$-$Q_{0.75}$), Mann–Whitney U test. Differences were determined to be statistically significant at $p < 0.05$

## Results and discussion

An analysis of the total number of leukocytes and their morphology made it possible, already at the level of general clinical studies, to identify an inadequate response to the inflammatory process in AHO and APTO. Thus, in children with AHO in SG1, a slight increase in WBC was found to 9.6 (8.4-10.0) × $10^9$/L *versus* 4.6 (4.1-6.2) × $10^9$/L in CG ($p < 0.05$), by against the background of an unchanged absolute and percentage content of NG with an increase in the proportion of stab forms – 7.0 (5.0-10.3) % ($p_1 < 0.05$; $p_2 > 0.05$), a decrease in the number of lymphocytes (LY) – 29 (19.5-30.0) % *versus* 37,3 (33.4-38.5) %

($p < 0.05$) and 2.1 (1.7-2.9) × $10^9$/L *versus* 2.5 (2.4-2.5) × $10^9$/L in CG ($p > 0.05$) (Table 1).

Evaluation of leukocyte parameters in children with APTO in SG 2 revealed a blockade of the response to the infectious and inflammatory process. Tendencies were noted: an increase in the number of WBCs to the upper limit of the reference values of CG ($p > 0.05$), an increase in the absolute content of NG ($p > 0.05$), against the background of a decrease in the proportion of segmented NG due to an increase in banded NG ($p < 0.05$). At the same time, the indicators of the relative amount and absolute LY did not differ from the values of CG ($p_{1,2} > 0.05$) (Table 1).

In the study of cellular immunity in children with AHO and APTO, unidirectional, but with varying degrees of dysfunction, are revealed. Thus, in SG 1 with AHO, there was a 1.4-fold decrease in the level of T lymphocytes – $CD3^+CD19^-$ to 1.3 (1.1-1.6) × $10^9$/L against 1.9 (1.7-2.0) × $10^9$/L in CG ($p < 0.05$), due to a parallel decrease in T helpers – $CD3^+CD4^+$ by 1.6 times ($p < 0.05$) and 1.9 times the amount of $T_{CTL}$-$CD3^+CD8^+$ ($p < 0.05$), implementation index inversion ($IRI_1$) – 1.3 (0.9-1.6). Also, a pronounced trend of a 2.5-fold decrease in NK-$CD3^-CD16^+CD56^+$ to 0.2 (0.2-0.4) × $10^9$/L *versus* 0.5 (0.3-0.4) × $10^9$/L in CG ($p > 0.05$), while the level of TNK-$CD3^+CD16^+CD56^+$ and the content of B lymphocytes $CD3^-CD19^+$ did not differ from the values determined in the CG ($p > 0.05$) (Table 2).

The SG2 of APTO children also showed a 1.3-fold decrease in Tl-$CD3^+CD19^-$ ($p < 0.05$) and Th-$CD3^+CD4^+$ ($p < 0.05$) and 1.6-fold decrease in $T_{CTL}$-$CD3^+CD8^+$ ($p < 0.05$) and 2,5-fold NK-$CD3^-CD16^+CD56^+$ ($p < 0.05$). In contrast to SG1, there was a 2,3-fold increase in TNK-$CD3^+CD16^+CD56^+$ ($p < 0.05$) in SG2. The content of Bl-$CD3^-CD19^+$ did not differ from that of CG ($p > 0.05$) (Table 2).

It is interesting to note that only 1 child from SG1 with AHO and 1 child from SG 2 with APTO had leukocytosis, an adequate increase in the amount of NG necessary to eliminate the bacterial pathogen. Against the background of leukocytosis in patients with AHO and APTO, there were similar changes in the relative parameters of cellular immunity noted in the corresponding groups of SG1 and SG2, which were partially leveled due to an increase in the total number of leukocytes.

In the analysis of humoral immunity in children with AHO in SG1, the concentrations of the main classes of immunoglobulins IgA, IgM, IgG did not differ from the values of GS ($p_{1-3} > 0.05$), and for IgA and IgG, a downward trend was recorded (Table 2). In GI2 of children with APTO, there is an increase in the concentration of IgG to 18.1 (15.9-22.2) g/L ($p < 0.05$) and IgA to the upper limits of the CG

**TABLE 1. LEUKOCYTES IN CHILDREN WITH ACUTE HEMATOGENOUS AND ACUTE POST-TRAUMATIC OSTEOMYELITIS, Me ($Q_{0.25}$-$Q_{0.75}$)**

| Indicators | SG1 acute hematogenous osteomyelitis n = 11 | SGI 2 acute post-traumatic osteomyelitis n = 9 | Comparison group healthy children aged 8-15 years. n = 13 |
|---|---|---|---|
| **WBC, $10^9$/L** | 9.6* (8.40-9.96) | 6.3^ (6.0-7.0) | 4.6 (4.1-6.2) |
| **LY, %** | 29.0* (19.5-30.0) | 36.5 (25.5-40.8) | 37.3 (33.4-38.5) |
| **LY, × $10^9$/L** | 2.1 (1.7-2.9) | 2.3 (1.8-2.8) | 2.5 (2.4-2.5) |
| **NG, %** | 51.0 (36.8-68.3) | 51.5 (46.8-54.8) | 57.8 (54.3-59.8) |
| **NG, × $10^9$/L** | 3.9 (2.6-6.6) | 3.7 (3.3-5.3) | 2.7 (2.6-3.3) |
| **segmented NG, %** | 44.5 (33.3-59.5) | 47.0* (42.5-49.5) | 55.5 (54.1-58.0) |
| **banded NG, %** | 7.0* (5.0-10.3) | 5.00* (3.0-7.0) | 2.5 (1.0-3.5) |
| **MON, %** | 9.0* (7.0-13.3) | 5.00 (4.0-8.0) | 4.0 (3.3-5.8) |
| **EOS, %** | 1.0 (0.1-5.0) | 6.0 (3.0-7.0) | 3.5 (3.0-4.0) |

Note. *, differences in the indicators of study groups with osteomyelitis from those of healthy children; ^, differences between study groups, statistically justified with an error of the 1st kind $p < 0.05$ (Mann–Whitney test).

**TABLE 2. INDICATORS OF CELLULAR AND HUMORAL IMMUNITY IN CHILDREN WITH ACUTE HEMATOGENOUS AND ACUTE POST-TRAUMATIC OSTEOMYELITIS, Me ($Q_{0.25}$-$Q_{0.75}$)**

| Indicators | SG1 acute hematogenous osteomyelitis n = 11 | SG 2 acute post-traumatic osteomyelitis n = 9 | Comparison group healthy children aged 8-15 years n = 13 |
|---|---|---|---|
| **WBC, × $10^9$/L** | 9.6* (8.40-9.96) | 6.3^ (6.0-7.0) | 4.6 (4.1-6.2) |
| **LY, %** | 29.0* (19.5-30.0) | 36.5 (25.5-40.8) | 37.3 (33.4-38.5) |
| **LY, × $10^9$/L** | 2.1 (1.7-2.9) | 2.3 (1.8-2.8) | 2.5 (2.4-2.5) |
| **T lymphocytes $CD3^+CD19^-$, %** | 60.8* (52.4-67.5) | 58.7* (50.7-66.2) | 75.8 (71.8-78.2) |
| **T lymphocytes $CD3^+CD19^-$, × $10^9$/L** | 1.3* (1.1-1.6) | 1.5 (1.1-1.8) | 1.9 (1.7-2.0) |
| **T helpers $CD3^+CD4^+$, %** | 33.2* (29.5-34.5) | 35.7* (29.0-36.9) | 46.9 (41.3-58.6) |
| **T helpers $CD3^+CD4^+$, × $10^9$/L** | 0.6* (0.5-0.9) | 0.8 (0.5-1.0) | 1.1 (0.9-1.9) |
| **CTL $CD3^+CD8^+$, %** | 27.7* (22.8-30.4) | 22.5* (22.4-24.9) | 34.7 (31.4-38.9) |
| **CTL $CD3^+CD8^+$, $10^9$/L** | 0.5 (0.4-0.8) | 0.6 (0.5-0.7) | 0.9 (0.7-1.0) |
| **IRI CD4/CD8** | 1.3 (0.9-1.6) | 1.4 (1.2-1.6) | 1.8 (1.5-2.0) |
| **NK, % $CD3^-CD16^+CD56^+$** | 11.9* (7.3-15.0) | 7.7* (5.2-11.3) | 19.8 (17.1-19.9) |
| **NK, × $10^9$/L $CD3^-CD16^+CD56^+$** | 0.2* (0.2-0.4) | 0.2* (0.1-0.3) | 0.5 (0.3-0.5) |
| **TNK, % $CD3^+CD16^+CD56^+$** | 0.8 (0.6-2.2) | 2.8* (1.4-3.7) | 0.7 (0.5-0.9) |
| **TNK, × $10^9$/L $CD3^+CD16^+CD56^+$** | 0.03 (0.01-0.05) | 0.06 (0.02-0.06) | 0.03 (0.02-0.06) |
| **B lymphocytes $CD3^-CD19^+$, %** | 17.2 (11.8-19.7) | 10.3 (9.9-14.1) | 11.4 (9.2-7.7) |
| **B lymphocytes $CD3^-CD19^+$, × $10^9$/L** | 0.3 (0.2-0.4) | 0.2 (0.1-0.3) | 0.3 (0.2-0.3) |
| **IgA g/L** | 1.2 (1.1-1.8) | 2.1^ (1.8-2.2) | 1.5 (1.4-2.6) |
| **IgM g/L** | 1.3 (1.1-1.4) | 0.9 (0.8-1.3) | 1.4 (1.1-1.6) |
| **IgG g/L** | 12.5 (11.4-15.6) | 18.1* ^ (15.9-22.2) | 13.2 (12.8-13.6) |

Note. As for Table 1.

quartile zone – 2.1 (1.8-2.2) g/L ($p > 0.05$) against the background of low IgM values of 0.9 (0.8-1.3) g/L ($p > 0.05$) (Table 2).

NG dysfunctions common to all children with AHO and APTO were also found. The functional activity of NG, in particular, the phagocytic function, depends on the number and density of expressed receptors [10]. It is known that CD64 (FcγRI), CD16 (FcγRIII), CD32 (FCγRII) receptors trigger immune phagocytosis and killing processes, antibody-dependent cellular cytotoxicity (ADCC).

It was shown that children with SG1 with AHO, there was a 1,2-fold decrease in the number of NG expressing CD16 ($p < 0.05$), and a 29-fold increase in the level of $CD64^+$NG ($p < 0.05$) against the background of an unchanging quantity of CD32

**TABLE 3. INDICATORS OF RECEPTOR AND PHAGOCYTIC FUNCTIONS OF NEUTROPHILIC GRANULOCYTES IN CHILDREN WITH ACUTE HEMATOGENOUS AND ACUTE POST-TRAUMATIC OSTEOMYELITIS, Me ($Q_{0.25}$-$Q_{0.75}$)**

| Indicators | SG1 acute hematogenous osteomyelitis n = 11 | SG 2 acute post-traumatic osteomyelitis n = 9 | Comparison group healthy children aged 8-15 years n = 13 |
|---|---|---|---|
| **% PhAN** | 51.0* (42.8-58.3) | 67.0* ^ (58.5-71.5) | 54.7 (51.0-57.0) |
| **PhN** | 1.9* (1.7-2.3) | 3.2* ^ (2.4-3.7) | 4.4 (3.8-4.7) |
| **PhI** | 1.0* (0.9-1.5) | 2.0 (1.5-2.3) | 1.9 (1.7-2.2) |
| **% D** | 41.9* (37.8-44.8) | 46.0* ^ (40.3-47.0) | 64.5 (62.6-66.9) |
| **DI** | 0.5* (0.3-0.7) | 1.0* ^ (0.6-1.2) | 1.7 (1.5-2.0) |
| **CD16, % NG** | 86.5* (80.5-96.4) | 93.1^ (91.1-96.0) | 98.3 (96.8-99.4) |
| **CD32, % NG** | 93.8 (90.8-96.9) | 93.7 (92.7-94.3) | 93.1 (91.1-96.6) |
| **CD64, % NG** | 14.5* (5.9-15.7) | 3.4* ^ (2.1-4.7) | 0.5 (0.4-0.7) |

Note. As for Table 1.

($p > 0.05$) in relation to the indicators of CG (Table 3). At the same time, depression of phagocytic activity is observed in SG1 with AHO, which is associated both with a decrease in the number of actively phagocytic NG (% PhAN) ($p > 0.05$), impaired capture functions (PhN, PhI) ($p_{1, 2} < 0.05$) and processes of killing (%D, DI) ($p_{1, 2} < 0.05$) due to impaired NG receptor function.

Meanwhile, in children with AHO in SG1, the content of NGs expressing CD16 and CD32 receptors did not significantly differ from CG values ($p_{1, 2} > 0.05$), while there was a 6,8-fold increase in the level of $CD64^+NG$ ($p < 0.05$) (Table 3). When assessing phagocytic activity in children with SG2, a slight increase in % PhAN to 67.0 (58.5-71.5) % *versus* 54.7 (51.0-57.0) % ($p < 0.05$), however, there was a decrease in 1,4 times the index of PhN reflecting the ability of NG to capture ($p < 0.05$) and, as in SG1, the killing ability of cells was reduced (% D, DI, $p < 0.05$).

Thus, combined defects in the functioning of IS indicators of different severity were revealed in children with AHO s and APTOs aged 8-15 years old.

So, in both studied groups, general dysfunctions of the cellular link of IS were revealed: a decrease in the number of T lymphocytes with a parallel decrease in the proportion of T helpers and $T_{CTL}$ lymphocytes, a decrease in NK cells against the background of an unchanged content of B lymphocytes. At the same time, it was found that in AHO, the level of immunoglobulins of the main classes did not change and did not differ from the CG indicators, while in APTO in SG 2, an increase in the level of IgA and IgG was noted. The received data obtained partly coincide with the trends noted by other authors in children of other age groups with AHO [3, 12].

When analyzing the receptor and phagocytic activity, it was found that the expression levels of the CD64, CD16, CD32, and NG receptors in the studied groups of children with AHO and APTO demonstrate different equipment, which predetermines the failure of the phagocytic function. Defects in phagocytosis, in AHO, are primarily associated with impaired functions of NG capture and killing of the bacterial antigen, and in APTO, only with the completion of the phagocytic act.

## Conclusion

The identified combined defects in the functioning of the immune system necessitate the development of new approaches in the treatment of AHO and APTO in children, pathogenetically substantiating the use of immunotropic medicines in the complex etiopathogenetic treatment of this pathology, which will help restore disturbed mechanisms of anti-infective immunity and, as a result, timely elimination of pathogens, improve clinical the course of diseases, as well as to prevent the chronicity of the inflammatory process and the aggravation of the dysfunction of the immune system.

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*Поступила 13.04.2023*
*Отправлена на доработку 17.04.2023*
*Принята к печати 20.04.2023*

*Received 13.04.2023*
*Revision received 17.04.2023*
*Accepted 20.04.2023*