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PECULIARITIES OF CELLULAR AND HUMORAL IMMUNITY IN 3–12 MONTHS OLD INFANTS WITH ATOPIC DERMATITIS

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The increasing frequency and severity of allergopathology in childhood dictate the need to deepen theoretical knowledge about the pathogenesis of immune reactions in allergies. **The aim** of the work is to analyze the indicators of cellular and humoral immunity in children of the first year of life suffering from atopic dermatitis. **Materials and methods.** 61 children were examined. Three groups were formed: group 1 – children aged 3–5 months (30 children), group 2 – 6–9 months (19 children), group 3 – 10–12 months (22 children). The study of the immune status was carried out by immunological tests of the first level. Immunophenotyping of lymphocytes-by flow cytometry. **Results.** The subpopulation composition of lymphocytes revealed some age-related features: children of group 1 are characterized by the development of T-lymphocytopenia, group 2 – B- and T-cell lymphocytopenia, group 3 – B-lymphocytopenia. In all age groups, there is a decrease in the content of activated NK-lymphocytes, HLA-DR$^+$ T-lymphocytes, and an increase in γδ-T-lymphocytes. Decrease in the immunoregulatory index in group 1 – 23.3% of cases, in group 2 – 26.3%, in group 3 – 45.5%. Violation of the process of phagocytosis is noted in 22.4% of children. All examined children have hyperimmunoglobulinemia E, which is ten times higher than the age norm. In group 3, a strong negative correlation was found between the value of the immunoregulatory index and the concentration of total IgE (r = –0.6). The content of immunoglobulins A, M, G in the blood serum tends to develop of hyperimmunoglobulinemia. However, more than 40% of children older than 6 months have a deficiency in the synthesis of one or two classes of immunoglobulins. **Conclusion.** The detected changes in the immune status are predisposing for the development of a secondary immunodeficiency state in the future. The study of the immune status in children with atopic dermatitis is necessary for individual immunocorrection in order to increase the effectiveness of basic therapy, reduce the severity of the disease, the frequency of exacerbations.

Keywords: atopic dermatitis; lymphocyte subpopulations; immune status; immunoglobulins; phagocytosis.

ОСОБЕННОСТИ КЛЕТОЧНОГО И ГУМОРАЛЬНОГО ИММУНИТЕТА ПРИ АТОПИЧЕСКОМ ДЕРМАТИТЕ У ДЕТЕЙ ПЕРВОГО ГОДА ЖИЗНИ

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Рост частоты и тяжести аллергопатологии в детском возрасте диктуют необходимость углубления теоретических знаний о патогенезе иммунных реакций при аллергии. **Цель работы** — анализ показателей клеточного и гуморального иммунитета у детей первого года жизни, страдающих атопическим дерматитом. **Материалы и методы.** Обследован 61 ребенок. Сформированы три группы: 1-я группа — дети в возрасте 3–5 мес. (30 детей), 2-я группа — 6–9 мес. (19 детей), 3-я группа — 10–12 мес. (22 ребенка). Исследование иммунного статуса проводилось иммунологическими тестами первого уровня, иммунофенотипирование лимфоцитов — методом проточной цитометрии. **Результаты.** В субпопуляционном составе лимфоцитов выявлены некоторые возрастные особенности: для детей 1-й группы характерно развитие Т-лимфоцитопении, 2-й группы — В- и Т-клеточной лимфоцитопении, 3-й группы — В-лимфоцитопении. Во всех возрастных группах наблюдается снижение содержания активированных NK-лимфоцитов, HLA-DR$^+$ Т-лимфоцитов, повышение γδ-Т-лимфоцитов. Снижение иммунорегуляторного индекса в 1-й группе составило 23,3 %, во 2-й группе — 26,3 %, в 3-й группе — 45,5 %. Нарушение процесса фагоцитоза отмечается у 22,4 % детей. У всех обследованных детей обнаружена гипериммуноглобулинемия Е, в десятки раз превышающая возрастную норму. У детей 3-й группы выявлена сильная отрицательная корреляционная связь между значением иммунорегуляторного индекса и концентрацией общего IgE (r = –0,6). Содержание иммуноглобулинов А, М, G в сыворотке крови имеет тенденцию к развитию гипериммуноглобулинемии. Однако более 40 % детей старше 6 мес. имеют дефицит синтеза одного или двух классов иммуноглобулинов. **Заключение.** Обнаруженные изменения в иммунном статусе являются пред-

располагающими для развития в дальнейшем вторичного иммунодефицитного состояния. Исследование иммунного статуса у детей с атопическим дерматитом необходимо для проведения индивидуальной иммунокоррекции с целью повышения эффективности базовой терапии, снижения тяжести заболевания, частоты обострений.

Ключевые слова: атопический дерматит; субпопуляции лимфоцитов; иммунный статус; иммуноглобулины; фагоцитоз.

INTRODUCTION

In various regions of the Russian Federation, approximately 10 to 15% of pediatric patients in the general population suffer from allergic diseases and also, approximately 20–30% of children are at risk of allergopathology [4, 7]. Atopic dermatitis (AD) is one of the most common skin diseases, which starts at an early age in pediatric patients and is characterized by a chronic relapsing course with increasing severity. Atopic dermatitis is often accompanied by complications, affecting many internal organs and systems and with the development of multivalent sensitization [15].

In young pediatric patients, AD occurs due to a genetic predisposition to allergies, maternal diseases during pregnancy, and maternal and fetal exposures to unfavorable environmental factors [1, 5, 6, 8, 10, 17]. The pathogenesis of an allergic disease is usually triggered by disorders at the regulatory level of the immune, endocrine, and nervous systems. In addition, an immunosuppressive state of the immune system is commonly noted in this disease, which includes suppression of all cellular reactions, with a decrease in the reserve capacity of neutrophils when there is a decrease in the local immune activity [2, 10, 15].

Antigen presentation is the first event in the development of the immune response. An interaction occurs between the T-cell receptor of the lymphocyte and the MHC-antigen molecule complex (major histocompatibility complex) on the antigen-presenting cell. MHC class I functions as a receptor for $CD8^+$ lymphocytes (cytotoxic T cells) while MHC class II molecules functions as a receptor for $CD4^+$ lymphocytes (T-helpers) [1, 3, 10, 16]. With an atopic allergic reaction, the activity of class II T-helpers increases, synthesizing cytokines IL-4, IL-13, and IL-5, and stimulating the production of immunoglobulin (Ig) E and IgG_4 by B-lymphocytes. Reaginic antibodies induce the activity and proliferation of eosinophils, increasing the expression of MHC class II, and serve as a growth factor for mast cells. Mast cells mediate the early phase of an allergic response by ejecting mediators of allergy and tryptase, which activates specific receptors on endothelial and epithelial cells. Activation of these receptors triggers a cascade of reactions that increase the expression of adhesion molecules, causing chemotaxis of eosinophils; which in turn triggers the late phase of an allergic response and are involved in maintaining the inflammatory response in tissues [7, 10, 12, 13]. γδ-T cells are able to enhance the immune response, producing large quantities of γ-interferon, TNF-β, and chemokines, which have effector (cytotoxic) activities. They are able to recognize non-peptide antigens, regardless of the MHC. An increase in the relative level of γδ-T cells is characteristic of AD in childhood [18, 20]. Natural killer (NK) lymphocytes are able to recognize and lyse foreign cells upon initial contact without prior sensitization, even in the absence of inflammatory signals. Interaction with antigenic structures occurs due to the receptors that recognize MHC class I molecules. NK cells are an early source of γ-interferon at the site of the immune response [9, 18, 19]. NKT lymphocytes are phenotypically true T cells having TCR αβ and CD3, although NK1.1 receptor that is characteristic of NK cells is also noted on their surface. The NKT lymphocyte T cell receptor recognizes lipid/glycolipid antigens represented by the antigen-presenting cell in complex with the CD1d molecule. Activation of NKT cells is accompanied by rapid secretion of a large number of cytokines including IL-2, IL-5, IL-6, IL-10, IL-17, IL-31, TNF-α, and GM-CSF [9, 14, 18].

Thus, the pathological process of hypersensitivity depends on the formation of an imbalance between subpopulations of lymphocytes. Even among conditionally healthy individuals, the state of "latent sensitization" is widespread, which is detected by determining the allergen-specific immunoglobulin E (IgE) in blood serum to a wide panel of allergens [11].

An increase in the frequency and aggravation of the severity of allergic diseases in childhood necessitates profound theoretical knowledge about the causes and the pathogenesis of immune reactions in various types of allergies.

This study aimed to analyze the indicators of cellular and humoral immunity in **3–12-month-old infants** with atopic dermatitis.

MATERIALS AND METHODS

We examined 61 pediatric patients diagnosed with AD, aged 3 months to 1 year. These patients were divided into three groups according to age: group 1 consisted of pediatric patients age 3–5 months (30 children), group 2 of patients aged 6–9 months (19 children), and group 3 patients aged 10–12 months (22 children).

The study of the immune status was performed with first level immunological tests. Immunophenotyping of lymphocytes was performed using flow cytometry by direct immunofluorescence of whole peripheral blood and a no-wash procedure (Epics XL flow cytometer, Beckman Coulter, USA). To assess the different subpopulations of lymphocytes, the cells were stained with three-color combinations of monoclonal antibodies conjugated with FITC/PE/PC5 fluorescent dyes such as CD45/CD3/CD19, CD45/CD3/CD4, CD45/CD3/CD8, CD45/CD3/CD(16^+56), CD45/CD3/CD25, and CD45/CD3/HLA-DR (Beckman Coulter, USA). Cell populations were isolated using heterogeneous gating. Absolute lymphocyte counts were calculated using reference particles. Statistical processing of the results obtained was performed using Microsoft Excel.

RESULTS AND DISCUSSION

In infant aged 3–12 months, distinctive features of the differentiation of lymphocytes in the various age groups were revealed (Tables 1, 2; Figs. 1–3).

A large scatter of indicators is noteworthy, which may be due to an individual response to the development of the disease, concomitant pathology, and various stages of the pathological process.

The differentiation of lymphocytes in the group 1 pediatric patients was characterized by the development of absolute T-lymphocytopenia (33.3% of cases), due to a decrease in the absolute number of T-helper cells (13.3%) and cytotoxic T-lymphocytes (23.3%). A decrease in the relative and absolute content of activated T-cells with HLA-DR activation markers (40.0 and 60.0% of cases, respectively), an increase

Table 1 / Таблица 1

Subpopulation composition of lymphocytes in young children with atopic dermatitis
Субпопуляционный состав лимфоцитов у детей раннего возраста с атопическим дерматитом

Lymphocyte subpopulations / Субпопуляции лимфоцитов	Возраст, месяцев / Ages, months					
	3–5		6–9		10–12	
	Relative content (min–max) / Относительное содержание	Absolute number (min–max) / Абсолютное количество	Relative content (min–max) / Относительное содержание	Absolute number (min–max) / Абсолютное количество	Relative content (min–max) / Относительное содержание	Absolute number (min–max) / Абсолютное количество
B-lymphocytes $CD19^+$ / В-лимфоциты $CD19^+$	15.96–39.8	453–3337	7.0–48.3	493–3937	1.72–40.72	61–5914
T-lymphocytes $CD3^+$ / Т-лимфоциты $CD3^+$	55.7–75.71	1735–5072	48.5–82.5	1580–7477	45.1–89.57	1333–7465
T-helpers $CD3^+CD4^+$ / Т-хелперы $CD3^+CD4^+$	33.7–58.7	1069–6255	28.8–57.4	914–4679	20.7–52.8	936–4999
T-cytotoxic $CD3^+CD8^+$ / Т-цитотоксические $CD3^+CD8^+$	8.49–29.3	247–2336	10.19–31.6	309–3212	10.88–40.1	323–3858
Activated NK cells $CD8^+CD3^-CD(16^+56)^+$ / Активированные NK-клетки $CD8^+CD3^-CD(16^+56)^+$	0.68–4.9	22–594	0.37–6.1	11–639	0.2–5.57	6–318
NK-lymphocytes $CD3^-CD(16^+56)^+$ / NK-лимфоциты $CD3^-CD(16^+56)^+$	1.7–14.79	53–1486	1.5–19.9	74–1806	1.7–28.49	50–1189
NKT-cells $CD3^+CD(16^+56)^+$ / NKT-клетки $CD3^+CD(16^+56)^+$	0.1–5.51	4–213	0.1–3.05	4–198	0.2–4.83	8–156
Activated T-lymphocytes $CD3^+HLA\text{-}DR^+$ / Активированные Т-лимфоциты $CD3^+HLA\text{-}DR^+$	0.0–5.1	0.0–324	0.2–1.73	8–258	0.1–4.0	10–175
Activated T-lymphocytes $CD3^+CD25^+$ / Активированные Т-лимфоциты $CD3^+CD25^+$	0.15–7.5	9–675	0.4–5.5	15–386	0.97–6.5	52–637
γδ-T cells / γδ-Т-клетки	0.18–7.33	6–387	0.01–11.6	0–773	0.8–10.6	44–582

Table 2 / Таблица 2

The average number of lymphocytes in different age periods in children of the first year of life with atopic dermatitis
Среднее количество лимфоцитов в различные возрастные периоды у детей первого года жизни с атопическим дерматитом

Lymphocyte subpopulations / Субпопуляции лимфоцитов	Ages, months / Возраст, месяцев					
	3–5		6–9		10–12	
	Mean ± mean deviation, % cells / Среднее ± среднее отклонение, % клеток	Mean ± mean deviation $\cdot 10^9$ cells/l / Среднее ± среднее отклонение $\cdot 10^9$ кл/л	Mean ± mean deviation, % cells / Среднее ± среднее отклонение, % клеток	Mean ± mean deviation $\cdot 10^9$ cells/l / Среднее ± среднее отклонение $\cdot 10^9$ кл/л	Mean ± mean deviation, % cells / Среднее ± среднее отклонение, % клеток	Mean ± mean deviation $\cdot 10^9$ cells/l / Среднее ± среднее отклонение $\cdot 10^9$ кл/л
B-lymphocytes $CD19^+$ / В-лимфоциты $CD19^+$	26.5 ± 4.1	1637.6 ± 703	24.2 ± 7.3	1399.4 ± 770.5	23.6 ± 9.2	1419.9 ± 828.7
T-lymphocytes $CD3^+$ / Т-лимфоциты $CD3^+$	65.3 ± 5.0	3850.5 ± 1417	68.2 ± 7.1	4062.6 ± 2025.9	66.2 ± 9.2	3708.1 ± 1348.6
T-helpers $CD3^+CD4^+$ / Т-хелперы $CD3^+CD4^+$	45.5 ± 6.2	2648.1 ± 929.5	45.5 ± 6.7	2675.8 ± 1288.6	41.3 ± 8.2	2296.2±827.4
T-cytotoxic $CD3^+CD8^+$ / Т-цитотоксические $CD3^+$ $CD8^+$	16.9 ± 3.9	1042 ± 508	19.8 ± 4.0	1234.1 ± 717.0	20.4 ± 4.9	1159.1±510.5
Activated NK cells $CD8^+CD3^-CD(16^+56)^+$ / Активированные NK-клетки $CD8^+CD3^-CD(16^+56)^+$	2.1 ± 1.1	144.7 ± 99.0	1.6 ± 1.1	109.1 ± 106.3	2.1 ± 1.42	119.4±81.3
NK-lymphocytes $CD3^-CD(16^+56)^+$ / NK-лимфоциты $CD3^-$ $CD(16^+56)^+$	6.2 ± 3.0	421.5 ± 267.2	5.9 ± 3.1	393.4 ± 344.7	8.3 ± 4.0	434.5 ± 271.8
NKT-cells $CD3^+CD(16^+56)^+$ / NKT-клетки $CD3^+CD(16^+56)^+$	1.2 ± 0.8	67.2 ± 50.0	1.0 ± 0.8	51.1 ± 38.4	1.2 ± 0.7	61.0 ± 35.9
Activated T-lymphocytes $CD3^+HLA\text{-}DR^+$ / Активированные Т-лимфоциты $CD3^+HLA\text{-}DR^+$	1.3 ± 0.8	76.5 ± 58.5	1.1 ± 0.5	61.2 ± 31,	1.3 ± 1.0	59.3±34.7
Activated T-lymphocytes $CD3^+CD25^+$ / Активированные Т-лимфоциты $CD3^+CD25^+$	4.2 ± 1.8	231.0 ± 143.2	3.2 ± 1.0	178.1 ± 100.7	3.2 ± 1.6	193.9 ± 118.9
γδ-T-cells / γδ-Т-клетки	3.0 ± 1.2	169.7 ± 77.4	3.7 ± 2.3	196.1 ± 116.6	4.3 ± 1.8	239.0 ± 124.8

in the CD25 content in 26.0% of the pediatric patients examined, and a low relative and absolute level of activated natural killers ($CD8^+NK$) (33.3 and 23.3% of cases, respectively) were registered.

In group 2 patients, absolute B- and T-cell lymphocytopenia were noted (23.5 and 31.5% of the examined pediatric patients, respectively). A decrease in the absolute level of T-helpers (15.8%) and T-cytotoxic (21.0%) lymphocytes was noted, as well as a decrease in the relative and absolute content of activated lymphocytes with the $CD3^+HLA\text{-}DR^+$ phenotype (50.0 and 77.8% of cases, respectively) and a decrease in the relative and absolute content of activated $CD8^+NK$-cells (57.9 and 36.8% of pediatric patients, respectively).

In group 3 pediatric patients, there was a relative and an absolute B-lymphocytopenia (27.3 and 18.2% of cases, respectively), a decrease in the relative and absolute number of activated NK-lymphocytes ($CD8^+NK$) (45.4 and 22.7% of pediatric patients, respectively), and a decrease in the relative and absolute level of $CD3^+HLA\text{-}DR^+$ cells (72.7 and 86.4% of cases, respectively).

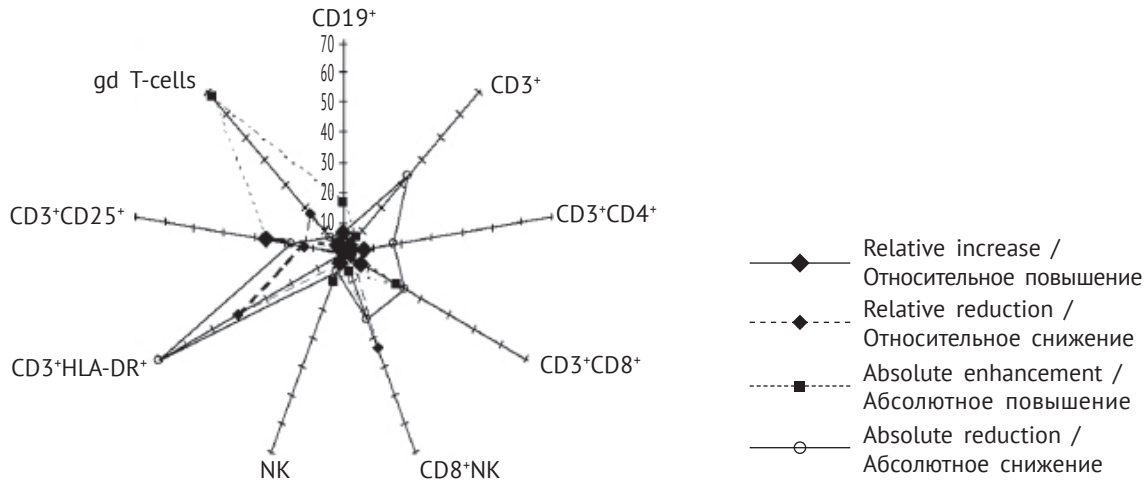

Fig. 1. Changes in the main subpopulations of lymphocytes in children with atopic dermatitis at the age of 3–5 months
Рис. 1. Изменение основных субпопуляций лимфоцитов у детей с атопическим дерматитом в возрасте 3–5 месяцев

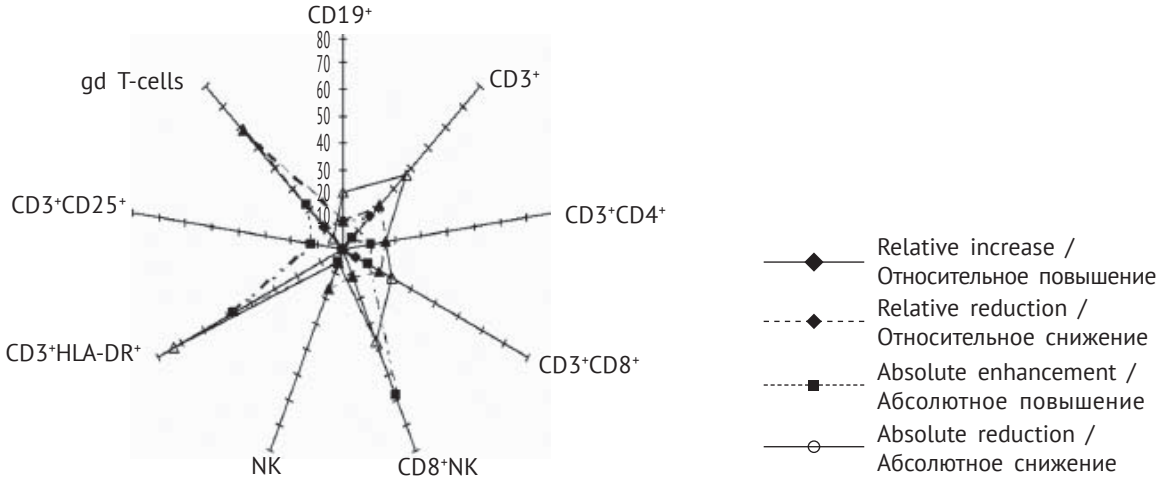

Fig. 2. Changes in the main subpopulations of lymphocytes in children with atopic dermatitis at the age of 6–9 months
Рис. 2. Изменение основных субпопуляций лимфоцитов у детей с атопическим дерматитом в возрасте 6–9 месяцев

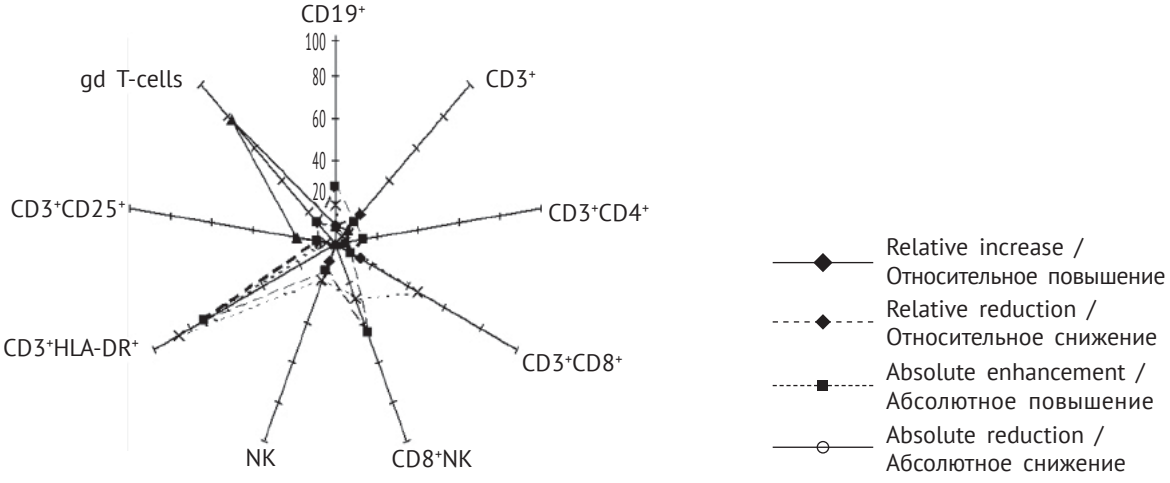

Fig. 3. Changes in the main subpopulations of lymphocytes in children with atopic dermatitis at the age of 10–12 months
Рис. 3. Изменение основных субпопуляций лимфоцитов у детей с атопическим дерматитом в возрасте 10–12 месяцев

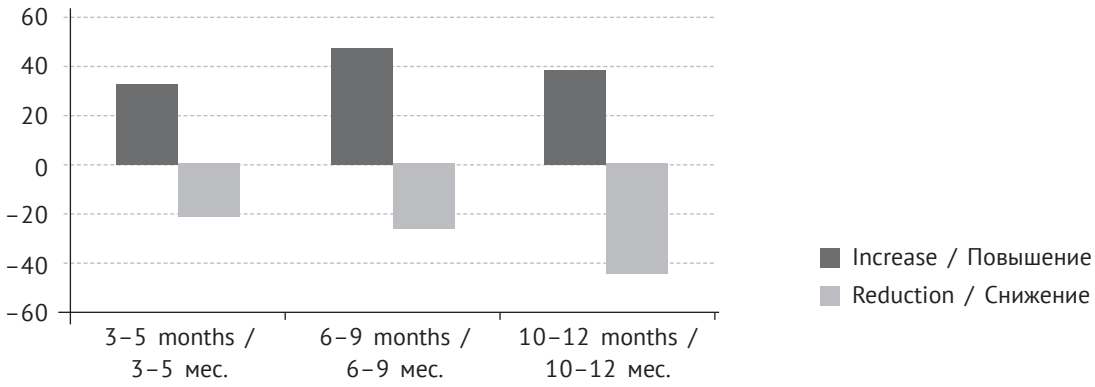

Fig. 4. Dynamics of changes in immunoregulatory index in children of the first year of life with atopic dermatitis
Рис. 4. Динамика изменения иммунорегуляторного индекса у детей первого года жизни с атопическим дерматитом

Table 3 / Таблица 3

Violation of the process of phagocytosis in children of the first year of life with atopic dermatitis (% of examined children)
Нарушение процесса фагоцитоза у детей первого года жизни с атопическим дерматитом (% обследованных детей)

Age groups of children examined / Возрастные группы обследованных детей	Incomplete phagocytosis / Незавершенный фагоцитоз	Violation of phagocytic activity / Нарушение фагоцитарной активности	
		Decrease in phagocytic activity over time / Снижение фагоцитарной активности со временем	"Lazy" phagocytes / «Ленивые» фагоциты
Group 1 (3–5 months) / 1-я группа (3–5 мес.)	4.2	4.2	–
Group 2 (6–9 months) / 2-я группа (6–9 мес.)	14.3	–	21.4
Group 3 (10–12 months) / 3-я группа (10–12 мес.)	13.3	–	20

An increase in the absolute level of γδ-T-lymphocytes protecting the mucous membranes was typical for all the groups of pediatric patients examined; it was revealed in 66.7% of pediatric patients in group 1, 63.1% of pediatric patients in group 2, and 77.3% of pediatric patients in group 3. This is consistent with published data on the activity of this cell population in childhood AD [18].

The value of the immunoregulatory index (IRI) in infants aged **3–12 months old** with AD is ambiguous (Fig. 4).

Immunoregulatory index is the ratio of the relative number of $CD3^+CD4^+$ T helper cells to the relative level of $CD3^+CD8^+$ cytotoxic T cells. In most cases, a decrease in this ratio indicates an immunodeficiency, while an increased value is associated with an autoimmune pathology. A decrease in IRI in the group 1 pediatric patients was noted in 23.3% of cases and its increase was registered in 33.3% of cases. In the group 2 pediatric patients, IRI was decreased in 26.3% and increased in 47.4% of the cases. In the group 3 pediatric patients, a decrease in IRI was detected in 45.5% and its increase was registered in 36.4% of cases, while in pediatric patients aged 10–12 months, there was a strong negative correlation between the IRI value and the concentration of total IgE (r = –0.6). The development of an immunodeficiency state in these patients is directly associated with allergic pathology.

Previous studies have shown that a decrease in the phagocytic activity of peripheral blood leukocytes in children older than 1 year is revealed in 100% of cases [7].

In infant aged 3–12 months, phagocytosis pathology was detected in 22.4% of the examined patients (Table 3).

In pediatric patients of the group 1, a decrease in the phagocytic activity of leukocytes was rare (incomplete phagocytosis in 4.2% of cases, a decrease in the percentage of active cells in 4.2% of cases). In the groups 2 and 3, the phagocytosis pathology was detected more often, namely incomplete phagocytosis in 14.3 and 13.3% of cases, respectively, and "lazy" phagocytes in 21.4 and 20% of cases, respectively.

Table 4 / Таблица 4

Concentration of total IgE in children of the first year of life with atopic dermatitis
Концентрация общего IgE у детей первого года жизни с атопическим дерматитом

Age groups of children examined / Возрастные группы обследованных детей	IgE concentration, IU/ml / Концентрация IgE, МЕ/мл		
	Minimum content / Минимальное содержание	Maximum content / Максимальное содержание	Mean ± mean deviation / Среднее ± среднее отклонение
Group 1 (3–5 months) / 1-я группа (3–5 мес.)	11.51	889.8	239.2 ± 202.5
Group 2 (6–9 months) / 2-я группа (6–9 мес.)	23.77	1200	596.3 ± 377.9
Group 3 (10–12 months) / 3-я группа (10–12 мес.)	192.7	1073	562.3 ± 179.2

Table 5 / Таблица 5

The concentration of immunoglobulins in children of the first year of life with atopic dermatitis
Концентрация иммуноглобулинов у детей первого года жизни с атопическим дерматитом

Age groups of children examined / Возрастные группы обследованных детей	Immunoglobulin concentration, g/l / Концентрация иммуноглобулинов, г/л		
	IgA, mean ± mean deviation / IgA, среднее ± среднее отклонение	IgM, mean ± mean deviation / IgM, среднее ± среднее отклонение	IgG, Mean ± mean deviation / IgG, среднее ± среднее отклонение
Group 1 (3–5 months) / 1-я группа (3–5 мес.)	0.29 ± 0.08	0.52 ± 0.15	5.31 ± 1.28
Group 2 (6–9 months) / 2-я группа (6–9 мес.)	0.38 ± 0.18	0.57 ± 0.16	6.33 ± 2.41
Group 3 (10–12 months) / 3-я группа (10–12 мес.)	0.75 ± 0.26	0.89 ± 0.2	8.03 ± 2.67

The constant exposure of allergens to the body creates a burden on phagocytic cells, which results in disruption of the phagocytic process and a decrease in the elimination of allergens. In turn, this creates the prerequisites for a decrease in the body's resistance to bacterial infections, that is, a secondary immunodeficiency condition occurs.

The concentration of total IgE in the blood serum of infants aged 3–12 months with AD was very high (several times higher than the age norm of 0–15 IU/ml) in 60 pediatric patients. Only one child had IgE blood level corresponding to the age norm. The value of the total IgE concentration in the pediatric patients examined is presented in Table 4.

In pediatric patients aged 3–5 months, the upper limit of the age norm of total IgE was exceeded by 10 or more times in 45.8% of the patients examined; in patients aged 6–8 months, it was noted in 78.6%; and in pediatric patients aged 10–12 months, it was in noted in 100% of cases.

The level of immunoglobulins A, M, G in the blood serum of the pediatric patients examined tended to develop hyperimmunoglobulinemia. Only 6 patients showed different types of dysimmunoglobulinemia (DIG) (Tables 5, 6).

Hyperimmunoglobulinemia A and M were most often noted in the group 3 pediatric patients while hyperimmunoglobulinemia G was most often registered in the group 1 pediatric patients. A high level of IgM accompanies the acute phase of the inflammatory process, while IgG is noted with a chronic inflammation or period of convalescence. IgA is often increased when mucous membranes are involved in the inflammatory process.

DIG was not revealed in the group 1 pediatric patients. In group 2 pediatric patients, type IV DIG was noted in 14.2% of cases (hypoimmunoglobulinemia A) and type VII was registered in 7.1% of cases (hypoimmunoglobulinemia M and G). The group 3 pediatric patients had type III DIG in 20% of cases (hypoimmunoglobulinemia G).

According to previous studies, older pediatric patients with AD, are typically characterized by various types of DIG than an increase in immunoglobulins [7].

Table 6 / Таблица 6

Changes in the content of immunoglobulins in children with atopic dermatitis in the first year of life (% of children examined)

Изменения содержания иммуноглобулинов у детей с атопическим дерматитом на первом году жизни (% обследованных детей)

Age groups of children examined / Возрастные группы обследованных детей	↑IgA	↑IgM	↑IgG	Disimmunoglobulinemia / Дисиммуноглобулинемия
Group 1 (3–5 months) / 1-я группа (3–5 мес.)	20.8	33.3	29.2	–
Group 2 (6–9 months) / 2-я группа (6–9 мес.)	28.6	21.4	21.4	IV type — 14.2, VII type — 7.1 / IV тип — 14.2, VII тип — 7.1
Group 3 (10–12 months) / 3-я группа (10–12 мес.)	33.3	46.7	26.7	III type — 20 / III тип — 20

Note. ↑IgA – hyperimmunoglobulinemia A; ↑IgM – hyperimmunoglobulinemia M; ↑IgG – hyperimmunoglobulinemia G; I – gipoimmunoglobulinemia G, type IV – hypoimmunoglobulinemia A, type VII – hypoimmunoglobulinemia M and G.

Примечание. ↑IgA — гипериммуноглобулинемия A; ↑IgM — гипериммуноглобулинемия M; ↑IgG — гипериммуноглобулинемия G; дисиммуноглобулинемия: III тип — гипоиммуноглобулинемия G, IV тип — гипоиммуноглобулинемия A, VII тип — гипоиммуноглобулинемия M и G.

Long-term AD predetermines the development of a humoral-type immunodeficiency state in pediatric patients of older age groups.

Circulating immune complexes, as predictors of autoimmune inflammation, were detected in 4.2%, 14.5%, and 6.7% of cases in the group 1, group 2, and group 3 pediatric patients examined.

CONCLUSIONS

1. The cytometric analysis of the composition of the lymphocyte subpopulations revealed age-related aspects in infants with atopic dermatitis aged 3–12 months, namely the development of T-lymphocytopenia at the age of 3–5 months, B- and T-cell lymphocytopenia at 6–9 months, and B-lymphocytopenia at the age of 10-12 months. In all age groups, the content of activated NK-lymphocytes ($CD8^+NK$) and activated T-lymphocytes with the HLA-DR^+ phenotype was reduced, while the content of γδ-T-lymphocytes was also increased. The immunoregulatory index (T_h/T_{cyt}) was reduced in group 1 in 23.3% of cases, group 2 in 26.3% of cases, and group 3 in 45.5% of pediatric patients.

2. Impairment of the phagocytic process is registered in 22.4% of infants aged 3–12 months old with atopic dermatitis, which predetermines a decrease in the body's resistance to bacterial infections.

3. In all the examined pediatric patients with atopic dermatitis, hyperimmunoglobulinemia E was registered, which was ten times higher than the age norm. Moreover, in group 3 pediatric patients, a strong negative correlation was found between the value of the immunoregulatory index and the concentration of total IgE (r = –0.6).

4. The content of immunoglobulins A, M, and G in the blood serum of 3–12-month-old infants with atopic dermatitis tends to increase, although more than 40% of pediatric patients older than 6 months have a deficiency in the synthesis of one or two classes of immunoglobulins.

5. The revealed changes in the immune status of young pediatric patients with atopic dermatitis predispose to the development of a further secondary immunodeficiency state.

6. The study of the immune status in pediatric patients with atopic dermatitis is necessary to conduct a reasonable individual immunocorrection, in order to increase the efficiency of the basic therapy, reduce the disease severity, the frequency of exacerbations, as well as reduce the likelihood of secondary immunodeficiency due to the atopic process.

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