

## CLINICAL AND LABORATORY DIAGNOSTIC CRITERIA OF IMMUNE RESISTANCE OF HEALTHY AND SICK WITH PNEUMONIA CHILDREN OF DIFFERENT AGE

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**Background.** The universality of the general adaptation syndrome and the need to study the impact of general adaptive responses on the occurrence and consequences of pathological processes, as well as detection of early signs of disadaptation, have been proven by numerous works.

**Objective.** The aim of study was to explore the peculiarities of general non-specific adaptive reactions in pediatric population and to discuss the diagnostics effectiveness of general nonspecific adaptive reactions in early detection of health disorders in children of different age.

**Methods.** The paper presents the results of laboratory and clinical tests, conducted in 185 healthy children age 4-12 years and 42 children of the same age with community-acquired pneumonia. The characteristics and prevalence of general nonspecific adaptative reactions in healthy children of different age were given. Determination of adverse adaptative reactions (stress, training and overactivation) based on analysis of the general blood analysis is an early diagnostic criterion of individual health reduction of children.

**Results.** The features of clinical course, the nature and direction of immune disorders of children with community-acquired pneumonia, depending on their adaptive systems, were revealed. The influence of conventional treatment regimens of children with pneumonia on the state of adaptation processes was determined. Clinical diagnostic criteria for prognosis and treatment efficacy based on diagnostics of nonspecific adaptive responses in the dynamic of pneumonia were established. The proportion of morphometrically different blood lymphocytes in healthy children was determined. It was revealed that the blood of preschool age children dominated with type I cells ( $61.3 \pm 1.7$  %). The relative content of lymphocytes (morphological type II) ( $28.7 \pm 1.6$  %), type III – ( $6.1 \pm 0.6$  %), type IV – ( $3.9 \pm 0.6$  %) was observed.

**Conclusions.** General nonspecific adaptative reactions of mild and increased activation, as the most conducive to children's age, demonstrate a balance of the relative content of different types of lymphocytes according to morphometrical data.

KEY WORDS: children, cell-mediated immunity, adaptive reactions, community-acquired pneumonia.

### Introduction

Currently, it is not possible to assess the health of the child without taking into account the processes of adaptation to the external environmental factors, indicators of physical and mental health of an individual [1]. The universality of the general adaptation syndrome and the need to study the impact of general adaptive responses on the occurrence and consequences of pathological processes, as well as detection of early signs of disadaptation have been proven by numerous works [2, 3, 4]. According to the previous studies, poor adaptation processes are the background for the implementation of specific pathogenic factors [5, 6].

Resistance and adaptation are provided with blood components, which serve as a clinical indicator of the organism status, provide immune supervision and act as effectors at various adaptive-trophic effects [7]. Lymphocytes represented by a diverse in form and functions cell population are recognized

as central cells of the immune system. Damaging factor may cause activation or depression of the immune system that necessarily is reflected in the number and structure of lymphocytes.

The objective of the study is to explore the peculiarities of general non-specific adaptive reactions in pediatric population and to discuss the diagnostics effectiveness of general nonspecific adaptive reactions in early detection of health disorders in children of different age and to improve the treatment control and prognosis depending on the immune resistance in case of community-acquired pneumonia.

### Methods

185 healthy children age four to twelve years were examined. The sample was formed on the basis of pre-schools and secondary schools in Ternopil and Ternopil region. Only children without congenital malformations or chronic disease, during the physical well-being and not less than three weeks after the last acute illness or vaccination were involved into the research. The general totality was formed by probabilistic method (during the general dispensary

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examinations), thus excluding the element of subjectivity. Distribution of surveyed children by age and sex is shown in Fig. 1. Type of the general nonspecific adaptive reactions (GNAR) was determined by the indexes of lymphocytes as white blood count (WBC).

Also, the study involved 42 children of the relevant age with community-acquired pneumonia who were treated in the pulmonological department of Ternopil Regional Children's Hospital (TRChH). All patients in the hospital underwent clinical, laboratory and instrumental examination in accordance with approved Protocols of treatment in the specialty "Children's Pulmonology" (Ministry of Health of Ukraine № 18 from 13.01.2005). In all cases the diagnosis of pneumonia was confirmed radiographically.

The determination of GNAR was done by analyzing the correlation of different types of leukocytes in WBC [2]. The character of GNAR (harmonious or strained) was determined on the basis of adaptation index, calculated as the ratio of relative values of lymphocytes to segmented neutrophils. The level of GNAR reactivity (low, medium, high) was determined by the presence and severity of strain signs at WBC. These strain signs include an increase or decrease in the number of white blood cells, the relative levels of band neutrophils, eosinophils, monocytes, and the emergence of young and immature forms of leukocytes. As a marker of the state of perfect health in children, we accepted GNAR of increased activation at a high level of reactivity.

Studies of the cellular immunity was conducted by determining the number of lymphocytes and their subpopulations (CD3+, CD4+, CD8+, CD16+, CD22+) in venous blood by indirect immunofluorescence using monoclonal antibodies ("Granum", Kharkiv). Indicators of endogenous intoxication were determined by colorimetric method over the serum content of molecules of medium mass (MMM) using the technique of Gabrielian, N.I. and Levitsky, E.R. (1984).

Statistical processing of the research results was performed by parametric analysis with the calculation of Student's t-test using the software package "Microsoft EXCEL 5.0".

**Results**

We have found that among children of pre-schools and secondary schools of the Ternopil region and Ternopil only 41 children were healthy (22.2 %) (1<sup>st</sup> group). In 144 children (77.8 %), who were considered healthy as well (2<sup>nd</sup> group), some insignificant deviations were found, including functional minor pathology of the respiratory system (61.6 %) and digestive system (42.7 %) at leading positions (Fig. 2).

The GNAR values of increased activation (51.3 %) and over-activation (25.2 %) in preschool children were detected. We have revealed reactions of mild activation (11.3 %) and training (12.2 %) with somewhat less frequency in the same group of children. In children of the 1<sup>st</sup> group, the reaction of high activation predominated (64.7 %) (Fig. 3).

In the group of younger pupils the GNAR of mild and increased activation (29.4 % and 38.2 % respectively) were predominant. Simultaneously, GNAR of mild activation (50.2 %) was registered in the majority of the 1<sup>st</sup> group children. In the age group 10-12 years, the same GNAR (high activation (39.0 %), mild activation (25.0 %), and training (25.0 %)) were identified; in the 1<sup>st</sup> group the prevailing finding was GNAR of training (45.4 %) (Fig. 3).

It was found that general nonspecific adaptive reactions differ in the parameters of the immune response based on the subpopulations of lymphocytes results. Thus, the GNAR of stress and over-activation are characterized by a low content of CD3+ ((37.5±0.3) % and (42.0±1.3) %, respectively) and CD8+ lymphocytes ((11.7±0.2) % and (12.8±0.5) %, respectively), showing a pronounced tendency to immunosuppression. The reactions of mild and increased activation and training are characterized by minor changes of immune cells quantitative indicators that testify to active functioning of all components of the immune system.

Among the clinical peculiarities of children hospitalized in the pulmonary department of TRChH, we detected prevailing focal (91.3 %) forms of community-acquired pneumonia that coincides with the literature data. The prevalence of bilateral forms of community-acquired pneumonia (in 69.0 %) was determined that differs from the reference data

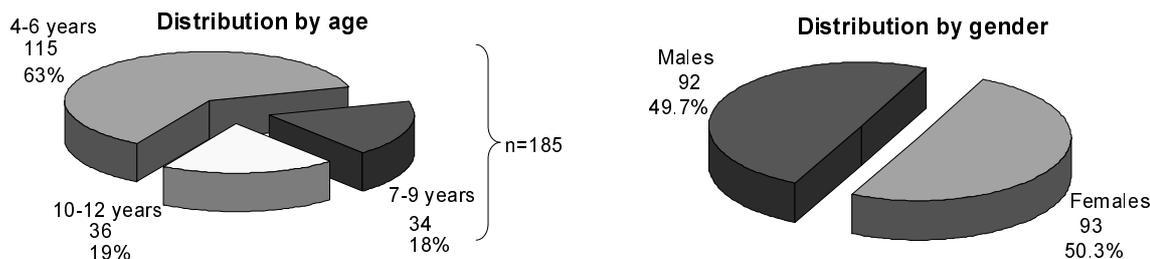


Fig. 1. Distribution of surveyed children by age and gender.

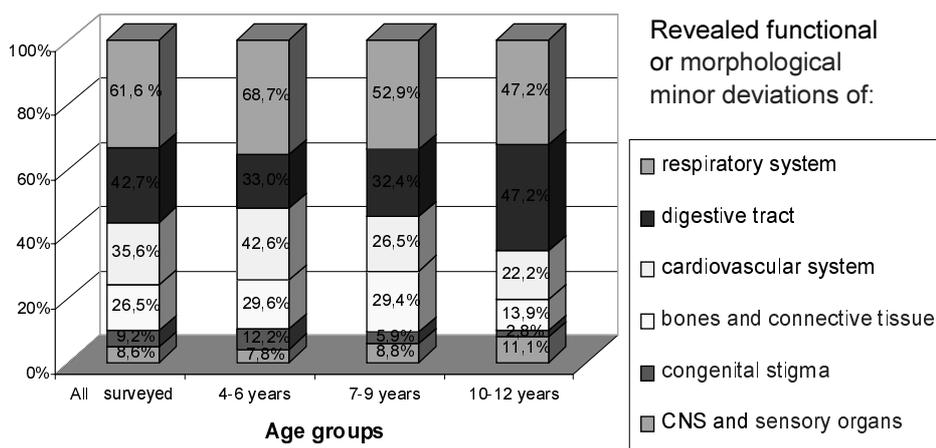


Fig. 2. Minor deviations found in apparently healthy surveyed children

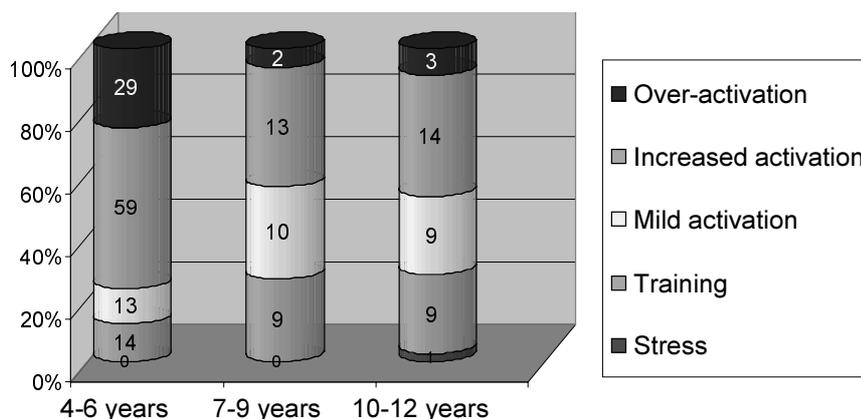


Fig. 3. Types of general nonspecific adaptive reactions in surveyed children from child care institutions of Ternopil region.

testifying the predominance of unilateral pulmonary inflammatory processes in childhood.

Among all analyzed cases, uncomplicated and complicated forms of community-acquired pneumonia were recorded (52.6 % and 58.3 %, respectively). The most commonly observed disorder that complicated the disease was obstructive syndrome (recorded in 26.2 % of cases), with a tendency to increasing the frequency of this complication with age. Allergic history of these patients was not burdened. The most common symptoms of community-acquired pneumonia were cough (95 %), mostly wet and unproductive (50.0 %), respiratory failure events (73,9-78,9 %); objectively dull sound on the lungs percussion in the projection of the inflammatory focus (85.7 %), fine rales (31.0 %) and small-vesicles rhonchi (38.1 %) on auscultation.

Detection of general nonspecific adaptive reactions in patients with community-acquired pneumonia at baseline showed that the GNAR of stress (42.9±1.2) % and training (35.7±1.1) % were recorded more often (Table 1). Consecutive determination of GNAR was conducted on the 7-10<sup>th</sup> day of hospitalization.

Mean values of endogenous intoxication indices in a group of healthy children were within reference

values. The increase of MMM1 and MMM2 was stated at GNAR of stress, training and over-activation; they were significantly lower at activation reaction. In children with community-acquired pneumonia the average values of MMM1 and MMM2 increased by 1.5 and 1.3 times, respectively, in comparison to healthy subjects.

### Discussion

It was found that general nonspecific adaptive reactions differ regarding parameters of the immune response according to the subpopulations of lymphocytes. Thus, the GNAR of stress and over-activation are characterized by a low content of CD3+ (37.5±0.3 % and 42.0±1.3 %, respectively) and CD8+ lymphocytes (11.7±0.2 % and 12.8±0.5 %, respectively), showing a pronounced tendency to immunosuppression. The reactions of mild and increased activation and training are characterized by minor changes of immune cells quantitative indicators that testify to active functioning of all components of the immune system.

In children with community-acquired pneumonia GNAR of stress and training prevailed, that was accompanied by insufficiency of T-cell immunity and increased levels of endogenous intoxication. The

**Table 1. The frequency of GNAR in children with community-acquired pneumonia**

Type of adaptive reaction	At baseline, n=42		After treatment, n=42	
	n	P±m, %	n	P±m, %
Stress	18	42.9±1.2 <sup>5</sup>	3	7.1±0.6 <sup>2*</sup>
Training	15	35.7±1.1 <sup>5</sup>	10	23.8±1.0 <sup>1</sup>
Mild activation	5	11.9±0.8 <sup>1,2</sup>	16	38.1±1.2 <sup>1*</sup>
Increased activation	3	7.1±0.6 <sup>1,2</sup>	10	23.8±1.0 <sup>1,5*</sup>
Over-activation	1	2.4±0.4 <sup>1,2</sup>	3	7.1±0.6 <sup>2,4</sup>

Notes: <sup>1</sup> – statistically significant difference (p<0.05) if compared with stress; <sup>2</sup> – statistically significant difference (p<0.05) if compared with reaction of training; <sup>4</sup> – statistically significant difference (p<0.05) if compared with increased activation; <sup>5</sup> – statistically significant difference (p<0.05) if compared with over-activation; \* – statistically significant difference (p<0.05) in the treatment process.

reactions of stress and training differ from other adaptive reactions by low levels of all subpopulations of lymphocytes. These changes can be interpreted as immunosuppression. We have identified the peculiarities of GNAR types changing in children with community-acquired pneumonia under the influence of treatment. In particular, there was a reduction in the number of patients with reactions of stress to 7.1 % and training to 23.8 % and increased the frequency of GNAR of mild and increased activation (in 38.1 % and 23.8 % of children, respectively) to the 10th day of hospitalization, which indicates an improvement of adaptive processes and satisfactory mobilization of reserve capacity of the organism. However, we observed the prolonged retention of reactions unfavorable to recovery in 7 patients (16.7 %). Devolution on a scale of adaptation reactions was revealed in 2 children (4.8 %) indicating a reduction in the activity of adaptive processes. The detection of GNAR of stress and training by 7–10 day of treatment, even against the normalization of clinical data, may be regarded as criteria of the bronchopulmonary disease treatment inefficiency. Recovery of these patients should not be considered complete. Prolonged retention of the reaction of training, according to the theory of adaptation reactions, creates conditions for chronic pathology.

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#### Conclusions

1. Considering the level of adaptability and resistance of the organism among children surveyed, the condition of perfect health was diagnosed in 13.5 %, the average health – in 58.4 %, the state of preexisting diseases – in 27.6 %, and the state of the vulnerability to the pathological process – in 0.5 %.

2. It was proved that the most common symptoms of community-acquired pneumonia in children age 4–12 years were cough, mostly wet and unproductive, dyspnea, dull sound on percussion in the projection of the inflammatory focus in the lungs, and fine rales on auscultation. Majority of patients had progressing pathological process occurred despite the reduction of immune resistance that was evidenced by GNAR of stress and training, insufficiency of T-cell immunity and increased parameters of endogenous intoxication.

3. The process of recovery with effective treatment occurs against the transition of GNAR of stress into anti-stress reactions of mild and increased activation of a high level of reactivity through reaction of training. Patients with adverse GNAR types (stress, over-activation) are of high risk of a protracted disease course. Detection of the GNAR type allows to identify the risk group of unfavorable community acquired pneumonia course by identifying adaptive reactions of stress and training or over-activation development.

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