INTRODUCTION

Bronchial asthma (BA) is considered to be a multifactorial disease characterized by recurrent episodes of reverse variable bronchial obstruction, which are based on the increased airway hyperresponsiveness (AHR) to various stimuli [5, 6]. Nonspecific AHR to direct and indirect triggers may be considered as a key phenomenon of asthma, which is the basis of formation of its clinical symptoms, frequency and severity of exacerbations. AHR determines the course, severity, and controllability of the disease in general [8]. Bronchoconstriction caused or induced by exercise (EIB) often manifests among the first symptoms of BA, which may be a possible sign of bronchial hyperreactivity, which, in turn, is a diagnostic marker of BA [2, 4]. EIB is a transient narrowing of the inferior respiratory tract after significant physical activity with a decrease in forced expiratory volume in the first second by 10-15 % as compared to the basic value. EIB prevalence among patients with asthma is up to 90 % [10, 11]. Contradictory relationship exists between nature and severity of chronic inflammation of the bronchi, their hypersensitivity and hyperreactivity, which even starts to be doubtful in case they are used for clinical purpose [9]. There is a lack of scientific research on the evaluation of the diagnostic value of bronchial lability and hyperreactivity for verification of clinical subphenotypes of the different variants of the disease in order to determine the optimal therapeutic approaches in children [12].

OBJECTIVE. To assess the indicators of nonspecific airway reactivity in children with asthma and EIB.

MATERIAL AND METHODS. To achieve this goal according to the principles of bioethics in the Pulmonology Department of the Regional Pediatric Hospital (Chernivtsi) using simple random sample a cohort of school children with BA was generated and two clinical groups were formed. The first (I) group consisted of 30 children with asthma phenotype, accompanied by EIB (manifestation of bronchoconstriction during exercise in anamnesis, and index of bronchospasm (IBS) after dosed physical exercise (DFE) equal to at least 15 %), or "exercise induced asthma". IBS was determined according to the recommendations [3] by assessing the response to DFE:

\[
\text{IBS} = \frac{(\text{FEV}_1\text{initial} - \text{FEV}_1\text{after DFE})}{\text{FEV}_1\text{initial}} \times 100\%
\]

The II clinical group (control) included 30 patients, diagnosed with asthma whose phenotype was not characterized by above mentioned signs. At the average, the indices of bronchospasm in children in basic clinical group (according to both FEV$_1$ and MEF$_{25,75}$) were 3-5 times higher in comparison with the control group and nearly twice higher than the threshold of 15 %.

According to the main clinical features the groups of comparison were not significantly different. There were 63,3 % of boys in both clinical groups. There were 63,3±8,0 % of inhabitants of the rural region among the children with asthma phenotype with EIB vs 66,7±8,8 % in the control group; the average age of the members of the first clinical group was 12,0±3,3 years, in children of the group of comparison – 11,1±3,4 years (p>0,05).

Bronchial lability was determined according to the recommendations [7] by assessing their response to DFE and inhalation of short acting β2-agonists (200 mcg of salbutamol) followed by calculation of bronchial lability as the sum of the components – IBS and bronchodilation index (IBD). A bronchomotor test to salbutamol was considered to be positive if IBD increased by more than 12 %.

Research of the bronchial hypersensitivity was performed using standardized spirometric test of histamine inhaling [2] on the basis of recommendations for standardization of the study [3]. Assessing the threshold concentration of histamine (PC$_{20}$H) was used to determine airway hypersensitivity [3].

Statistical analysis of the data was carried out from the position of Biostatistics [1]. The evaluation of the diagnostic value of tests was determined using sensitivity, specificity, positive predictive value and negative results and likelihood ratio test results. Risk assessment of the event realization was held on the basis of probability values of relative risk, odds ratio and post-test probability, as well as their confidence intervals.
Results and discussion. The estimation of parameters of bronchial lability in children of the groups of comparison, including IBD after the inhalation of salbutamol and mean values of the integrative indicator of the bronchial lability (ILB), are presented in table 1.

Thus, the significant difference between the values of the dilatation of the bronchi in response to the test with inhaled short-acting β₂-agonist was revealed in patients of the main group: in children with exercise-induced asthma phenotype IBD and IBL were almost three times higher. Indices of the bronchial dilatation more than 15 % to confirm exercise-induced asthma were characterized by the specificity – 87 %, predictive value of a positive result – 73 %, but a significant proportion of false negative results – 58 %. The relative risk of asthma phenotype with EIB (in the case of IBD which exceeded 15 %) was 1,7 (95 % CI: 0,6-4,8) with odds ratio of 3,8 (95 % CI: 1,0-13,7).

Evident bronchial lability (IBL over 12 %) was observed in 90 % of patients of the main clinical group and only in 50 % of children with asthma without EIB (Pφ<0,05). Significantly increased bronchial lability (IBL more than 20 %) more frequently was recorded among patients with asthma phenotype accompanied by EIB (in 83,3 %) as compared to the second clinical group (13,3 %, Pφ<0,05). Risk indicators of the presence of ILB over 20 % were higher in patients with exercise-induced asthma phenotype as compared to the second group: relative risk – 5,3 (95 %CI: 2,1-13,5) and odds ratio – 32,5 (95 %CI: 7,8-135,1).

For a more detailed analysis of the sensitivity of the respiratory tract to DFE and bronchodilator effect of the short-acting β₂-agonists, the indicators of bronchial lability at different bronchial calibers were evaluated (table 2).

Thus, more expressive bronchial lability in patients with exercise induced asthma does not depend on the caliber of the bronchi, and is defined by both bronchospasmic and bronchodilative components. Negative bronhomotor test with salbutamol at the level of small bronchi was observed only in 6,7 % of patients with exercise-induced asthma and almost in every third representative of the second clinical group (27 %, Pφ<0,05). However, excessive bronchodilation (IBD over 30 %) significantly more often was recorded in children with asthma and EIB (30 %) than in patients with asthma phenotype without EIB (16 %, Pφ<0,05).

The trend towards greater severity of the bronchial hyperresponsiveness was revealed in children with exercise-induced asthma phenotype. In particular, PC₂₀H was 1,2±0,4 mg/ml in patients of the main group versus 2,3±0,8 mg/ml in the representatives of the group of comparison (p>0,05). It was noted that the expressive bronchial hyperresponsiveness (PC₂₀H <4 mg/ml) was observed in more than half of the patients of the main clinical group (56 %) and only in 22 % of children of the group of comparison (pφ>0,05) and increased the relative risk of the exercise-induced asthma phenotype by 1,9 (95 %CI: 0,8-4,4) with odds ratio of 4,3 (95 %CI: 1,2-15,4). Post-test probability of detecting of the exercise-induced phenotype of asthma in excessive airways hypersensitivity was equal to 71 % at moderate specificity (77,3 %). Diagnostic value of the indicators of the bronchial lability and hypersensitivity in confirming the exercise-induced bronchial asthma as compared
Diagnostic value of parameters of nonspecific bronchial hyperreactivity in confirming BA with EIB

<table>
<thead>
<tr>
<th>Indices of bronchial lability and hyperresponsiveness</th>
<th>Diagnostic value, %</th>
<th>predictive value</th>
<th>Likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>positive result</td>
</tr>
<tr>
<td>IBD &gt;20%</td>
<td>92</td>
<td>60</td>
<td>37</td>
</tr>
<tr>
<td>IBL &gt;30%</td>
<td>26</td>
<td>84</td>
<td>71</td>
</tr>
<tr>
<td>PC20H&lt;0.4 mg/ml</td>
<td>56</td>
<td>77</td>
<td>49</td>
</tr>
</tbody>
</table>

to the opposite phenotype of asthma is shown in the table 3.

Consequently, indicators of the bronchial lability and hyperresponsiveness for confirming the exercise induced bronchial asthma as compared to its opposite phenotype were highly specific, but with a significant proportion of false negative results.

Conclusions
1. Excessive bronchial lability is typical for children with exercise-induced asthma. IBL over 30 % was highly significant with high proportion of false negative results to confirm asthma with EIB as compared to the opposite phenotype.

2. IBD which exceeds 20 % is the most sensitive indicator in detecting exercise-induced asthma with a significant level of likelihood ratio, which reflects a high lability of the airways in exercise testing.

3. Indicators of the bronchial hypersensitivity to inhaled histamine in a concentration less than 0.4 mg/ml with moderate specificity, post-test probability and significant odds ratio confirm exercise-induced asthma phenotype.

Prospects for future research – identifying the main paraclinical characteristics of the disease which reflect inflammation and bronchial hyperresponsiveness in children with BA and EIB.

References
Резюме. Результати аналізу показників гіперреактивності бронхів у 60 дітей, хворих на бронхиальну астму з бронхоконстрикцією фізічного зусильля та без бронхоконстрикції фізичної напруги, представлені в статті. Встановлено, що дітям, хворим на бронхиальну астму фізічного зусильля, притаманна виразніша лабільність бронхів. Показники гіперреактивності бронхів до інгаляцій гістаміну в концентрації менше 0,4 мг/мл зі специфічністю 77 %, постгостео- вою вірогідністю 71 % та з вірогідним співвідношенням шансів свідчать про наявність у дітей фенотипу астми фізічної напруги.

Ключові слова: бронхиальна астма, діти, фенотипи, гіперреактивність, лабільність бронхів.

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РАННЯ ДІАГНОСТИКА ТЯЖКИХ КОМБІНОВАНИХ ІМУНОДЕФІЦІТІВ

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Вступ. Тяжкий комбінований імунодефіцит (Severe combined immunodeficiencies, SCID) – це генетично гетерогена група захворювань, які характеризуються глобальним порушенням функції або відсутністю T- і В-клітин. У роботі представлено досвід роботи з хворими на тяжкі комбіновані імунодефіцити з метою встановлення ранніх клінічних та лабораторних маркерів SCID. Прове- дено клініко-генеалогічний та клініко-лабораторний аналіз 22 хворих на SCID і пацієнтів групи порівняння, визначено найбільш типові ознаки хвороби та час їх появи. Встановлено, що при SCID хворі не мають особливих клінічних симптомів до відбиття інфекції, а ранніми ознаками хвороби можуть бути об'єднані випадки смерті дітей у ранньому віці імунодефіциту.

Ключові слова: тяжкий комбінований імунодефі- цит, діти, інфекційні ускладнення, рання діагностика.

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