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**Gushchin M.Yu., Barkhina T.G., Polner S.A., Gumeniuk S.A.**

# Bronchial asthma and allergic rhinitis in different age groups

*Aim: to study the epidemiological, clinical, and morphological features of allergic rhinitis (AR) and bronchial asthma (BA). Materials and methods: common clinical, allergological, morphological (cytological and electron-microscopic methods) examination of patients with AR and BA. Results: the study was conducted among 685 adolescents with AR and BA between the ages of 14 to 18 years and 870 adults aged 18 to 65 years who were divided into groups. Divided by severity of adults: light level - 23%, medium - at 72%, and severe degree - at 5%. Divided by severity of teenagers: light level - 33,1%, medium - at 42,1%, and severe degree - at 24,8%. In the group of adolescents onset of the diseases occurred mostly from 5 to 15 years, and also a hormonal imbalance was detected that increased the severity of illness at this age. The results of allergological examination in the spectrum of allergens in patients with more severe BA revealed sensibilization to multiple allergen groups. In adolescents with AR and BA, there was found unique clinical and morphological changes in the mucous membranes of the respiratory tract. It was installed expressed morphological changes that have a direct relationship to the severity of the diseases. Conclusion: revealed similarities and differences in the clinical course, allergy data and morphological changes in patients of all ages with AR and BA.*

In the structure of respiratory pathology allergic rhinitis (AR) and bronchial asthma (BA) are playing the leading roles. Also these diseases involve both the upper and lower airways, and have similar pathogenesis [1,5]. Despite the fact that the initial contact with the allergen occurs in the mucous membrane of the nose, the further process of AR and BA affects the entire respiratory tract.

Nowadays the number of patients with these diseases is increasing worldwide; this process affects negatively quality of life, efficiency in work and study. Also other organs and systems are involved in this pathological process [5]. All these aspects make scientific investigations of great social sharpness in the 21st century.

AR and BA are similar allergic diseases, which are based on an inadequate response of airways on foreign agent (allergen). Hyperresponse leads to increased release of inflammatory mediators that lead to the clinical manifestations (reduced air speed and difficulty of passing it through airways, secretion hyperproduction, spasm of the respiratory muscles) [3]. The degree of foreignness of allergen-specific characteristics is determined individualy; the nature of this determination remains unknown.

Recurrent and long-lasting acute respiratory viral diseases (ARVD), insufficient diagnostics of allergic diseases, environment and appearance of new allergens leads in childhood to development of the AR, and in juvenile period to possibility to transformation in asthma [4,6]. All of these conditions have motivated us to investigate the morphology of the nose cavity in patients with BA and patients with AR. It should also be noted that in juvenile period AR and BA are very closely related. However, the mechanisms of these phenomena are not well investigated.

## MATERIALS AND METHODS.

Epidemiology of the diseases was studied, clinical data of outpatients of different age

groups was analyzed. The triggers and clinical characteristics of the diseases were assessed, as well as laboratory tests and instrumental methods results. Also we analyzed claiming rate for medical service, when the AR and BA were diagnosed, the basic therapy competence and adequacy. Studied the causes of onset and clinical features, the results of clinical, laboratory and functional studies, in seeking medical care, the timing of diagnosis of AR and BA, the amount and adequacy of standard therapy. Depending on age and clinical criteria patient were divided in to clinical groups. In our work we used standard laboratory tests and instrumental methods. Special laboratory tests included immunogram, assessment of hypothalamic-pituitary-thyroid system hormone level in the serum (T3, T4, TG, insulin, cortisol, testosterone, somatotropin, TPO, TTH, ACTH) using radioimmunoassay and enzyme immunodetection methods. Provocative nasal and inhalation tests with carbaholinum were carried using existing protocols. Morphological examination of scrapings of the nasal cavity (SNC), bronchoalveolar lavage (BAL) was performed by scanning and transmission electron microscopy (SEM, TEM) using conventional methods, the same methods were used for semithin sections (STS) assessment. STS were made by using ultratome LKB (Sweden) and stained with methylene blue combined method - azure II - basic fuchsin.

Specific allergy assessment of patients included getting the natural history, performing prick - tests with atopic allergens, determination of allergen-specific IgE - antibodies to the main groups of non-bacterial allergens in blood serum. Allergen-specific immunotherapy (ASIT) was held in the hospital using allergens Dermatophagoides pteronissinus. The average total dose was 6000 PNU for one ASIT course. Evaluation of clinical efficacy was carried out after the end of each course using generally accepted standards; the morphological evaluation (re-study SNC) was carried out only after the end of the third year of ASIT. All data were analyzed with Sigma Stat 3.5 (Systat Software, Inc.). A value of $P \leq 0.05$ was considered significant.

## RESULTS AND DISCUSSION.

According to the results of retrospective analysis in juvenile patients atopic asthma (88.2%) is the most common form. Debut of asthma in juvenile period occurs in 73.8% patients under the age of 15 years. We clarified that that juvenile have moderate severity of asthma (40.3%), mild severity was observed in 32.8% of patients and the severity stage of the disease was observed in 26.9% of patients. In adults (from 20 to 55 years) the severity was observed in 20%, 50% and 30% of patients respectively. Gastrointestinal tract diseases, endocrine system diseases and vegetative-vascular dystonia were the comorbidities which were found in the half of patients (tabl. 1).

Furthermore, 78% of patients with BA possessed strong family allergic history, a history of frequent ARVD, the presence of bad habits (smoking - 42.2%, alcohol abuse - 10.6%, all the data according the juvenile group).

Positive skin prick-tests with different groups of allergens were detected in 87% of the patients (Table 2).

The widest range of domestic and epidermal allergens was found in patients with more severe BA and with combination with the AR. Nevertheless in patients with AR or mild asthma were found significantly low number of allergens. These data suggest maintaining persistent allergic inflammation in patients with a wide variety of year-round allergies. In patients with more severe asthma polisensibilization was more common. In this group of patients the leading role played dust mites, pollen of trees, compositae and gramineae. Despite the fact that the pollen sensibilization was prevalent, a significant percentage of patients had domesic, epidermal and fungal sensibilization.

In 84% of patients with BA was diagnosed 3rd or 4th class of allergen-specific IgE

**Table 1. Comorbidities in the examined groups of patients**

| Diseases | 1 Group n=195 | 2 Group n=250 | 3 Group n=425 | 4 Group n=57 |
|---|---|---|---|---|
| | % | % | % | % |
| Gastrointestinal tract diseases | 65 | 53 | 46 | 45 |
| Chr. tonsillitis | 8 | 9 | 8 | 40 |
| Sinusitis | 10 | 8 | 12 | 33 |
| Polypoid rhinosinusitis | 10 | 6 | 11 | 5 |
| Vegetative-vascular dystonia | 53 | 47 | 36 | 46 |
| Endocrinopathy | 7 | 9 | 10 | 16 |
| Atopic Dermatitis | 25 | 32 | 27 | 37 |
| Alimentary allergy | 15 | 23 | 22 | 25 |

antibodies in the serum of different groups of allergens, corresponding with a history of clinical symptoms and results of skin testing.

Important diagnostic value have assessment of respiratory function and provocative tests with carbaholinum, cold air, exercise.

The most significant changes in respiratory function parameters (obstructive type changes) reported in juvenile and adults without remission. Obstructive changes were observed mainly at the level of small and medium-sized bronchi and respiratory function parameters match the clinical data: history and auscultation of the lungs.

While examining the levels of hormones most significant deviations were observed in juveniles with BA compared to adults. There was a statistically significant ($p < 0.05$) increase in testosterone levels and decrease of cortisol levels in half the patients (52.4%) with acute and severe stage (fig. 1).

Morphologic study of the nasal mucosa in patients of all ages groups with BA showed changes, which are characterized as a destructive process, and abnormal secretion process. These changes were followed by the activation of immunocompetent cells, the severity of which

**Table 2. The spectrum of positive reaction on allergens.**

| Positive prick-tests with allergens | 1 Group n=195 | 2 Group n=250 | 3 Group n=425 | 4 Group n=57 |
|---|---|---|---|---|
| | % | % | % | % |
| Dust mites | 76 | 80 | 70 | 70 |
| Feather pillows | 53 | 41 | 47 | 15 |
| Library dust | 43 | 39 | 38 | 30 |
| Cats hair | 53 | 41 | 40 | 36 |
| Dog hair | 15 | 14 | 13 | 23 |
| Sheep wool | 9 | 8 | 6 | 6 |
| Horse dander | 1 | 3 | 1 | 7 |
| Tree group | 11 | 13 | 14 | 20 |
| Gramineae group | 13 | 15 | 17 | 16 |
| Weeds group | 31 | 28 | 29 | 25 |

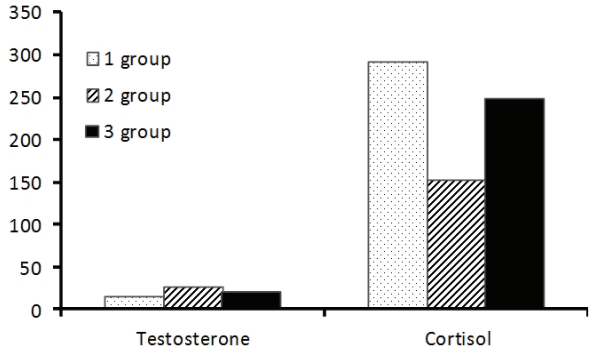
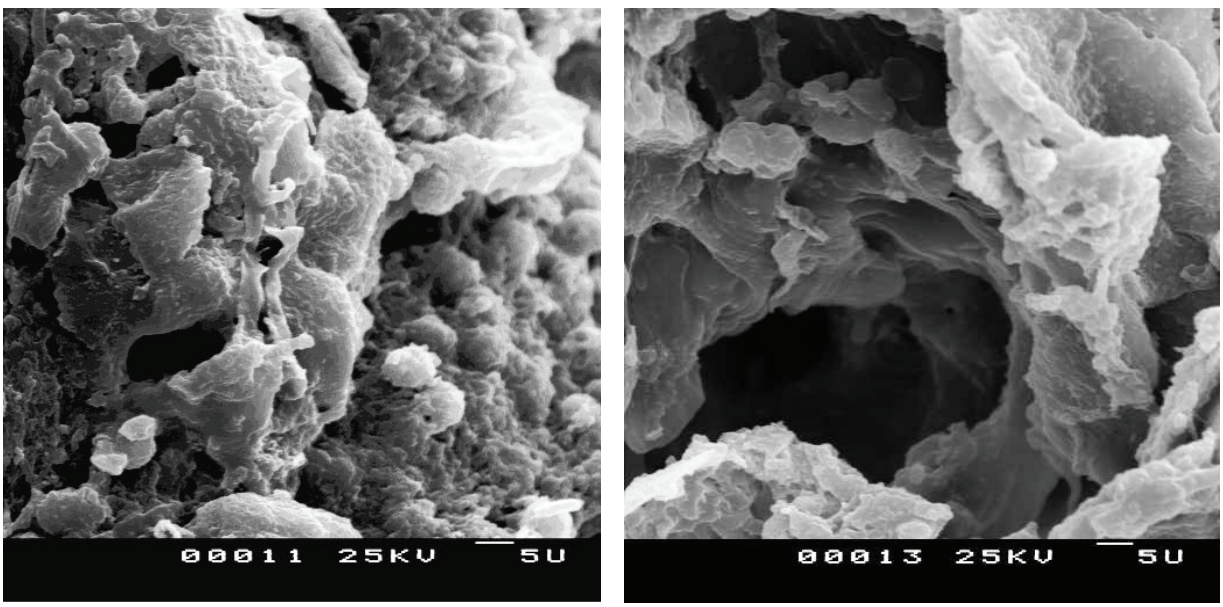



FIGURE 1. Hormone levels in patients examined, nmol / L (n = 33) p <0.05

depends on the severity and duration of asthma.

The STS showed alteration of the epithelial layer and cellular elements of the stroma. In ciliate cells degradation processes in all parts of the cell was observed: the disruption of cilia and their smoothing, increased intercellular spaces and changing the configuration of the cells. A large number of goblet cells were located near the basement membrane, and in the apical part of the epithelium goblet cells were found in the extrusion stage. Many patients, especially in the severe form of the disease, had sharp extrusion of secretion, which is most manifested in the mucosa of the nasal cavity than in the lower respiratory tract.

SEM showed that the surface of the epithelial cells of the upper and lower respiratory tract in AR and BA tend to have the same type of changes, what along with clinical indicators confirms the general pattern of hyperreactivity of these parts, which was determined by provocation tests, proving the similarity of epithelium damage mechanisms [6,8,9]. Using SEM as well as STS we found out that the most damage have the ciliated cells throughout the respiratory tract, but mostly are damaged cells in the nasal mucosa. These changes are characterized by disorientation, deformation of the cilia, up to their smoothing. Using TEM we found intracellular destructive processes in the cell population, which often lead to atrophy. Significant changes are observed in the goblet cells, which playing their protective function, respond to injury by promoted secretion, which we have shown by both light and electron microscopy. This reaction is more expressed in




a b

FIGURE 2. SEM. SNC. Fixation – 2,5% glutaraldehide. Application of Aurum. Patient B. 14. Goblet cells in the process of accumulation. x 1500 (a) and extrusion of secretion. x 1500 (b)

the nasal mucosa, which primarily response to pathological impacts [4,7,9].

In some parts of the epithelium there is such great secretion extrusion of goblet cells, that mucin granules cover with a thick layer these damaged areas (fig. 2 a,b).

The intensity of these changes is directly related with the severity of the disease, the period of its debut and duration of the illness. Along with this, the SEM and TEM make it possible to characterize microvascular changes in different parts of the respiratory tract. Observing increased vascular pattern, its roughness, contraction and expansion, unevenly located in different areas we can detect the severity of symptoms and the severity of the pathological process what help us to choose the most efficient method of treatment.

Practical work shows that treatment, which is focused on on-time basic therapy and ASIT realization is the most effective method for the treatment of allergic respiratory diseases. After the ASIT we observe the intensive decrease of reactivity of the mucous membranes of the nose and bronchi, increased regeneration processes of the respiratory epithelial barrier, which are more expressed in young age group compared with adults. These data are confirmed by us using the clinical and morphological methods. Managing ASIT on-time not only reduces the development of clinical symptoms of rhinitis and asthma, but also reduces the amount of consumed drugs and the risk of developing severe forms of the disease and improving the quality of life of the patient.

With the special complex clinical and immunological, allergy and morpho-functional studies in patients with AR and BA in different types of severity, we confirmed the unity of the mechanisms of allergic inflammation of the respiratory tract in AR and BA. We should also note that in the development of AR and BA in juveniles a leading role play: compromised allergic history, inadequacy diagnostics and inadequate treatment of associated allergic diseases, endocrine imbalance, frequent ARVD, bad habits gaining.

It is shown that on-time administration of basic treatment and early ASIT promotes rapid morphological regeneration of the epithelium of the mucous membranes of the respiratory tract. It is important that airways reactivity reducing while using the therapy and regeneration is more intensive in juveniles compared to adult patients. All these promote the most favorable prospects of treatment of AR and BA in patients with on-time and adequate therapy.

**Гущин М.Ю., Бархіна Т.Г., Полнер С.А., Гуменюк С.А.**

**БРОНХІАЛЬНА АСТМА ТА АЛЕРГІЧНІ РИНІТИ В РІЗНИХ ВІКОВИХ ГРУПАХ**

На базі відділення «Бронхіальна астма» ФГБУ «ГНЦ« Інститут імунології »ФМБА Росії і в ФГБУ НДІ морфології людини РАМН проведено поглиблене комплексне клініко-лабораторне, алергологічне, імунологічне та морфо-функціональне обстеження хворих у віці від 14 до 65 років. Залежно від віку та особливостей клінічного перебігу алергічного риніту і бронхіальної астми, пацієнти були розподілені на групи. Виявлено комплекс даних, що свідчать про єдність механізмів розвитку алергічного запалення і гіперреактивності дихального тракту при АР і БА. Представлено аналіз підліткової БА. Показано, що своєчасне призначення базисної терапії та раннє проведення АСИТ сприяє якнайшвидшій морфологічній регенерації епітелію слизових оболонок дихальних шляхів.

**Гущин М.Ю., Бархина Т.Г., Полнер С.А., Гуменюк С.А.,**

**БРОНХИАЛЬНАЯ АСТМА И АЛЛЕРГИЧЕСКИЕ РИНИТЫ В РАЗЛИЧНЫХ ВОЗРАСТНЫХ ГРУППАХ**

На базе отделения «Бронхиальная астма» ФГБУ «ГНЦ «Институт иммунологии» ФМБА России и в ФГБУ НИИ морфологии человека РАМН проведено углубленное комплексное клинико-лабораторное, аллергологическое, иммунологическое и морфо-функциональное обследование больных в возрасте от 14 до 65 лет. В зависимости от возраста и особенностей клинического течения аллергического ринита и бронхиальной астмы пациенты были распределены в группы. Выявлен комплекс данных, свидетельствующих о единстве механизмов развития аллергического воспаления и гиперреактивности дыхательного тракта при АР и БА. Представлен анализ подростковой БА. Показано, что своевременное назначение базисной терапии и раннее проведение АСИТ способствует скорейшей морфологической регенерации эпителия слизистых оболочек дыхательных путей.

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*Institute of Human Morphology, Institute of Immunology, Moscow, Russia; guschin.michail@yandex.ru*