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# МИКРОЦИРКУЛЯТОРНЫЕ И ВЕГЕТОСОСУДИСТЫЕ ИЗМЕНЕНИЯ У ДЕТЕЙ С АЛЛЕРГИЧЕСКИМ РИНИТОМ В ЗАВИСИМОСТИ ОТ СРЕДЫ ПРОЖИВАНИЯ

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**Резюме.** В последнее время актуальность изучения влияния экологической составляющей среды на формирование общественного здоровья детского населения возрастает [1, 12, 20].

В последние десятилетия отмечается бурный рост аллергических заболеваний, в том числе и аллергического ринита среди детского населения. Большое количество исследований связывают увеличения числа аллергических заболеваний с влиянием окружающей среды, с техногенным развитием и урбанизацией [4].

Аллергический ринит (АР) представляет одну из наиболее актуальных проблем аллергологии и иммунологии [2]. АР является одной из наиболее распространенных хронических патологий у детей [6, 21].

Так, установлено, что патогенез АР представляет собой сложный механизм, который не ограничивается сугубо аллергической реакцией и воспалительным процессом в области носа. Он включает в себя сложные механизмы нейрогенного воспаления с участием основных нейропептидов и нейромедиаторов, которые находятся в тесной связи с состоянием эндокринной, иммунной систем человека, и во многом определяется состоянием слизистых оболочек носа и дыхательных путей в целом. На патогенез АР в первую очередь оказывает воздействие состояние микроциркуляторного русла слизистой оболочки, а также качественные и количественные характеристики микробиоценоза носовой полости, носо- и ротоглотки, верхних и нижних дыхательных путей. Все эти параметры напрямую определяются нейровегетативными механизмами [5, 7, 9, 16].

Важное место в патогенезе развития аллергических заболеваний занимают изменения в системе микроциркуляции, с участием которых реализуются все клинические проявления. Нарушения микроциркуляции играют важную инициально-триггерную роль в патогенезе аллергических ринитов.

Вегетативная нервная система обеспечивает связь организма с окружающей и внутренней средой, регулируя обмен веществ и функции органов и тканей в соответствии с изменениями этой среды, она также обеспечивает интеграцию всех органов в единое целое, являясь одной из главных адаптационных систем организма [13].

Так как во главе регуляции функционирования организма и гомеостаза стоит вегетативная нервная система, объединяющая отдельные патогенетические звенья развития заболеваний и обуславливающая структурное и функциональное единство [3, 19]. Механизм регуляции реализуется нервно-рефлекторным путем с помощью различных нейрогуморальных факторов, сущность которых изучена в экспериментальных условиях и на сегодняшний день не подвергается сомнению [8].

*Ключевые слова: аллергический ринит, урбанизация, вегетативная нервная система, микроциркуляция, капилляроскопия, мегаполис*

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# ENVIRONMENT-DEPENDENT MICROCIRCULATORY AND AUTONOMIC NEUROVASCULAR CHANGES IN THE CHILDREN WITH ALLERGIC RHINITIS

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**Abstract.** Recently, the studies of environmental effects upon public health of children become quite relevant [1, 12, 20]. Over last decades, there is a rapid increase in allergic diseases, including allergic rhinitis, among the child population. A large number of studies connect this increment in pediatric allergies with influence of environment, technogenic development and urbanization [4]. Allergic rhinitis (AR) is one of the most pressing problems in allergology and immunology [2], being among the most common chronic disorders in children [6, 21]. Thus, it was found that the pathogenesis of AR is a complex mechanism that is not limited to a purely allergic reaction and inflammation in the nasal region. It includes complex mechanisms of neurogenic inflammation under participation of the main neuropeptides and neurotransmitters, which are closely related to the individual condition of endocrine and immune systems, being largely determined by the state of mucous membranes of the nasal cavity and respiratory tract in general. The pathogenesis of AR is primarily influenced by the state of microvasculature of the mucous membrane, as well as dictinct qualitative and quantitative characteristics of microbiocenosis of the nasal cavity, nasopharynx and oropharynx, upper and lower respiratory tract. All these parameters are directly determined by neurovegetative mechanisms [5, 7, 9, 16].

An important place in the pathogenesis of the development of allergic diseases belongs to changes of the microcirculation system which is involved into all the clinical manifestations observed. The microcirculation disorders play an important initial triggering role in pathogenesis of allergic rhinitis. Likewise, the autonomic nervous system is responsible for setting links between the body, ambient and internal environment *via* regulation of metabolism, functioning of organs and tissues based on changes in this environment; it also provides integration of all organs into a single entity, acting as one of the main adaptive systems in human body [13].

Therefore, the autonomic nervous system regulates the body and homeostasis by unifying the separate pathogenetic links of disease progression and setting basis for structural and functional unity [3, 19]. This regulatory mechanism is implemented *via* nerves and reflexes by different neurohumoral factors. Their nature has been established under experimental conditions and is beyond doubt to date [8].

*Keywords: allergic rhinitis, urbanization, autonomic nervous system, microcirculation, capillaroscopy, megapolis*

## Introduction

According to the environmental approach, a long-term impact on the environment resulted in the creation of a new (anthropogenic, urban) ecosystem that haS a diverse impact on a growing body, the consequences of such impact are quite difficult to visualize and assess [11]. Recently, many researchers report an increase in number and change in the ratio of risk factors for health deterioration. The impact of these factors depends on the body's adaptive capacities [1].

The significant difference between the conditions of life for children in megapolises and a rural area has a direct impact on the children's organism features [17]. A study of changes in the functional state of children according to the degree of regulatory systems tension in a megapolis or rural environment will allow to identify functional disorders and diseases in time [9].

The heart rate variability analysis is used to evaluate the body's adaptation to changing environment conditions, it allows to describe the activity of different subsystems of the autonomic nervous system through their influence on the cardiac pacer functions [14]. The nervous system ensures that cells, tissues, organs, and organ systems are integrated into a single whole. It acts as a link connecting all living systems to the environment and ensures their adaptation to its constantly changing components by regulating life activities.

The organism's adaptive activity indicator is the blood circulation system, both central and peripheral. Scholars note that vegetative reactions are

non-specific features of regulatory processes, also in the microcirculatory bloodstream system. The microcirculation system is an important pathogenetic link in the development and progression of many diseases. That is why it is very promising to study methods for objective appraisal of its changes.

The knowledge on vegetative and microcirculatory homeostasis for children living in megapolises and rural areas is scarce and contradictory compared to the findings of the heart rate variability analysis. Meanwhile, the intensity of urbanization and anthropogenic load dictate the relevance of studying their impact on children's health.

## Materials and methods

120 children with allergic rhinitis in the age of 7 to 11 have been examined in the outpatient clinic. All children have undergone the condition of the microcirculatory bloodstream has been examined by computer-aided nail bed capillaroscopy in course of which some parameters such as length of capillaries arterial and venular parts, inequalities of arterial and venular capillary parts caliber; distance between capillaries, diameter of arterial and venular parts of capillaries; distance between arterial and venular parts of capillaries; perivascular zone length have been analyzed. The autonomic nervous system conditions were assessed following the results of heart rate variability (HRV) within 3 minutes by means of Cardiovisor-6C equipment complex (Medical Computer Systems LLC, Russia). In course of HRV study, the standard deviation of NN intervals mean value (SDNN), root mean square of successive differences (RMSSD), regulatory systems stress index (SI, Baevsky's index), centralization index (IC), root mean square deviation of NN intervals duration (PNN50), number of interval values corresponding to the modal values (Amo), two frequency ranges: HF (high frequency component), LF (low frequency component), and their ratios have been calculated.

The study involved 2 groups of patients: the main group included 60 children from a megapolis away from massive green areas, and the comparison group comprised 60 children from rural areas. The results have been processed in SPSS 14.0 software (SPSS Lab, USA).

## Results and discussion

In order to comprehensively assess children's health, generally accepted criteria were used [18]. According to the life history, almost all children in the main group (81%) experienced an increase in the ARI cases in March-April; in the comparison group, number of ARI cases was approximately the same and had no seasonal nature. In the main group, the respiratory disease index amounted to 0.44±0.16, in the comparison group to 0.3±0.14; $p < 0.05$. The children living in megapolises had a later age of ARI onset – 7.9±1.2 months than those living in rural areas 5.8±1.2 months) ($p < 0.05$).

The main group, 21.6% of patients (n = 13) demonstrated an increase in body temperature (above 38.5 °C) when suffered ARI, 51.6% (n = 31) of the study group (sometimes even 26.8% (n = 16)) showed no increase in body temperature. For the comparison group: 41.6% (n = 25), 53.3% (n = 32), and 5.1% (n = 3) of children respectively ($p < 0.05$). There was a high degree of domestic and social history burden in the main group of children ($p < 0.05$).

We looked at heart rate variations as at the result of the activity of different parts of the autonomic nervous system related to the functioning of neurohormonal regulation mechanisms to support homeostasis and different functional systems development under environmental influence.

The HRV analysis revealed that children from urban areas suffer from a regulatory systems deficiency or exhaustion. The analysis of the heart rate at rest shows that the values of SDNN, a parameter that reflects the overall variability of heart rate, were higher in the main group than in the comparison group. The same trend was peculiar to the main group in terms of RMSSD parameters that represent high-frequency heart rhythm components, which exceeded the corresponding index by 1.5 times in the comparison group.

The children from the main group showed a decrease in AMo (24.9±7.1) and an increase in the variation range mean value to 0.36±0.035 sec. This indicates a raise of the autonomic nervous system sympathetic effect on children's regulatory processes. In the comparison group the variation range mean value amounted to 0.3±0.07 sec, and AMo to 34.5±8.3.

The stress index was within normal limits in all groups, but children living in cities and towns had a stress index two times higher than children living in rural areas, 226.5±54.3 and 134.1±44.7, respectively. The centralization index correlating to the central regulation mechanisms stress in course of adaptation was 4 times above the norm in the main group – 10.8±2.1 mainly because of the activation of the ANS sympathetic division, while in the comparison group this index was within normal limits – 2.2±0.9.

All children from the main group demonstrated a slight decrease in the low-frequency (LF) spectrum and an increase in the high-frequency (HF) component $p > 0.05$ (Fig. 1, see 3rd page of cover). The

same trend was registered when determining the LF/HF ratio: 3.8±0.7 in the main group, 4.4±0.5, $p > 0.05$ in the comparison group (Fig. 2, see 3rd page of cover).

Positive correlations between IS and residence in the vicinity of industrial enterprises and highways ($r = 0.69$), between LF/HF and viral infections rate ($r = 0.63$), and negative correlation between IS and body temperature increase ($r = -0.6$) have been detected.

Today, it is widely known that microvascular regulation disorder affects inflammatory processes in the body. Due to this, microcirculatory changes of vascular kind genesis indirectly reflect adaptive reactions and act as critical factors that cause pathophysiological disorders leading to frequent ARIs for children living in different conditions.

In contrast to the comparison group, the main group of children showed changes in the microcirculatory bloodstream represented by a minor increase in the capillaries venular part diameter, 52.1±5.9 and 46.8±5.7 $p > 0.05$ respectively in comparison with the control group, while the main group had a reliably smaller arteriolar-to-venular ratio (AVR) indicating the ratio of parallel vessels diameters (0.28±0.02 and 0.35±0.03 respectively; $p < 0.05$). We believe that these changes are compensatory because of the high impact of the autonomic nervous system sympathetic division that reduces at the arterial part due to muscle spasm, increases biochemical active paraendothelial space and leads to perfusion disorders.

Positive correlations between AVR reduction and viral infections rate ($r = 0.72$), AVR and centralization index ($r = 0.72$), SDNN and venular part diameter in the capillaries ($r = 0.6$), negative correlation between stress index and body temperature increase at ARI ($r = 0.61$) have been revealed.

Children living in megalopolises far from massive green spaces tend to have a higher respiratory disease index and certain peculiarities of ARI clinical progression. This fact may serve as a reason for conducting a thorough examination of this group of children for early detection of vegetative dysfunction, before its clinical manifestation, creating a child's "vegetative passport" and determining basic immunological indicators for such children.

According to the findings, we see that children living in urban areas are prone to have changes in autonomic nervous system values and sympathetic division activation in comparison to children living in rural areas, most likely it derives from inadequate regulation in response to the complex impact of anthropogenic and urban factors.

It is known that the age groups examined by us have certain morphofunctional features on the one hand, and on the other hand they are hypersensitive to anthropogenic stress, which is very high at this age, also, as per the heart rate variability data, they have low adaptation reserves. The obtained data show that children living in megapolises have an increased activity of the autonomic nervous system sympathetic division leading, in turn, to vegetative dysfunction and decreased adaptation, which reduces the body's adaptive capabilities and triggers a vicious circle in future. These findings fall in line with the conclusions of Mylnikova IV, Tsibulskaya IS, and others [15, 18].

Also, children living in urban areas display reactive tension in vegetative regulatory mechanisms and have an increased degree of centralization in heart rate control. This may be due to the complex influence of environmental factors on the child's body that results in nonproportional influence of different parts of the autonomic nervous system causing changes in both the microcirculatory bloodstream. In future, this should be studied for different age categories with the consideration of anthropogenic, socio-ecological, and urban stress impact on a child's organism.

Following the concept of vegetative-immunological adaptation to adverse factors, all groups of patients displayed IFNγ within normal values, however children living in the urban environment had this indicator slightly decreased, at the same time the IgE content in blood serum was increased in this group. Perhaps, these changes are adaptive in respect to the urban pathology development under the functional stress mode and serve to prevent the compensatory mechanisms failure.

Most of the children in the main group have changes in the microcirculation system based on the autonomic nervous system influence on microcirculatory vessels arterial section, it also allows to adapt the body's reserve capacity to different surrounding, environmental and hygienic conditions, thereby normalizing the energy, nutrient metabolism, and increased immune response.

## Conclusion

Children living in megapolises far from massive green spaces suffer from various adverse factors, inadequate to their nature and leading to adaptation mechanisms failure and disease onset. The fact that children from rural areas have not been exposed to these changes makes us believe that the factors affecting children in city environment are mostly of urban and anthropogenic origin.

The findings obtained give us grounds to say that children from megapolises have specific changes in the immune and autonomic nervous systems, and in the microcirculatory bloodstream. Urban children

experience reactive changes in their vegetative status toward greater dominance of central regulation mechanisms and a predominance of sympathetic tone, while rural children do not demonstrate an explicit sympathetic effect. This matter shall be considered in planning the personalized follow-up, treatment, and rehabilitation for such children. Also, it is important to outline the urbanization factors with the greatest impact on a child's autonomic nervous system and come up with programs for their mitigation.

One of the important tasks that stands before a future research is to analyze gender indicators of children living under various conditions and examine different age groups of children.

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