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## ALLERGIC MARCH IN CHILDREN OF UKRAINE

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**Key words:** children, allergic march, bronchial asthma, atopic dermatitis, allergic rhinitis, morbidity, prevalence, pollutants

**Ключові слова:** діти, алергічний марш, бронхіальна астма, атопічний дерматит, алергічний риніт, захворюваність, поширеність, поллютанти

**Ключевые слова:** дети, аллергический марш, бронхиальная астма, атопический дерматит, аллергический ринит, заболеваемость, распространенность, поллютанты

**Abstract.** Allergic march in children of Ukraine. Volosovets O.P., Bolbot Yu.K., Beketova G.V., Berezenko V.S., Umanets T.R., Rechkina O.O., Mitiuriaeva-Korniuko I.O., Volosovets T.M., Churylina A.V. Allergic diseases with a certain stage in their development from food allergy to bronchial asthma / allergic rhinitis, are much more common in children than in adults. The aim of this study was to analyze data on the prevalence and incidence of atopic dermatitis, bronchial asthma and allergic rhinitis as components of the allergic march in children of Ukraine from 1994 to 2017, to determine the possible impact of adverse environmental factors on their development. During the same period due to the influence of a number of factors, in particular environmental, there were significant changes in the structure of allergic diseases making up stages of the allergic march due to an increase in the proportion of allergic rhinitis against the reduced one of asthma and atopic dermatitis. Within 24 years the incidence of atopic dermatitis in children aged 0-6 years including, increased by 27.6%, in adolescents - by 40.5% and significantly decreased by 39.5%

*in children aged 7-14 years including. Most cases of allergic rhinitis and bronchial asthma were observed in schoolchildren (47.6 and 54.0%, respectively) with a slight decrease compared to 1994. In general in recent years allergic diseases have become more common in children aged from 0 to 6 years and their detection has decreased in schoolchildren and adolescents. Over the past 24 years, in children of Ukraine a steady increase in the incidence and prevalence of allergic diseases which form an allergic march has been noted: the prevalence of bronchial asthma has increased by 69.3% and the incidence has increased by 22.9%; the prevalence of atopic dermatitis has increased by 43.9% and the incidence – by 8.3%; the prevalence of allergic rhinitis has increased by 488.3% and the incidence of allergic rhinitis – by 380.3%, with a predominance of detection of this pathology in children from regions with developed infrastructure and industry, with significant emissions of pollutants into the atmosphere that have a direct moderate effect on the increase in the prevalence of bronchial asthma, the incidence and prevalence of allergic rhinitis in children.*

**Реферат. Аллергический марш у детей Украины. Волосовец А.П., Больбот Ю.К., Бекетова Г.В., Березенко В.С., Уманец Т.Р., Речкина Е.А., Митюреева-Корнейко И.А., Волосовец Т.Н., Чурилина А.В.** В детском возрасте гораздо чаще, чем у взрослых, встречаются аллергические болезни, имеющие определенную стадийность в своем развитии от пищевой аллергии к бронхиальной астме / аллергическому риниту. Целью этого исследования был анализ данных распространенности и заболеваемости атопическим дерматитом, бронхиальной астмой и аллергическим ринитом, как составляющими аллергического марша, у детей Украины с 1994 по 2017 г. для определения возможного влияния на их развитие экологических факторов. За этот же промежуток времени вследствие влияния ряда факторов, в частности экологических, произошли значительные изменения в структуре аллергических болезней, составляющих этапы аллергического марша из-за роста удельного веса аллергического ринита на фоне уменьшения бронхиальной астмы и атопического дерматита. В течение 24 лет заболеваемость атопическим дерматитом у детей в возрасте 0-6 лет включительно возросла на 27,6%, у подростков – на 40,5% и существенно уменьшилась на 39,5% у детей в возрасте 7-14 лет включительно. Больше всего случаев аллергического ринита и бронхиальной астмы наблюдалось у школьников (47,6 и 54,0% соответственно), с небольшим уменьшением по сравнению с 1994 годом. В целом аллергические болезни в последние годы стали чаще регистрироваться у детей от 0 до 6 лет и уменьшилось их выявление у детей школьного возраста и подростков. За последние 24 года у детей Украины наблюдается устойчивый рост заболеваемости и распространенности аллергической патологии, формирующих аллергический марш: на 69,3% увеличилась распространенность бронхиальной астмы и на 22,9% заболеваемость ею; на 43,9% выросла распространенность атопического дерматита и на 8,3% – уровень заболеваемости детей атопическим дерматитом; на 488,3% выросла распространенность аллергического ринита у детей и на 380,3% – уровень заболеваемости детей аллергическим ринитом с преобладанием выявления этой патологии у детей из крупных регионов с развитой инфраструктурой и промышленностью, где наблюдаются значительные выбросы загрязнителей в атмосферу, которые имеют прямое влияние умеренной силы на увеличение распространенности бронхиальной астмы, заболеваемости и распространенности аллергического ринита у детей.

In recent decades, the prevalence of allergic pathology worldwide has increased significantly [3, 4, 11]. Allergic march belongs to the natural course of allergic diseases, in the development of which T-helpers type 2 (Th2) participate [3, 11]. It is important that the presence of one allergic disease increases the risk of developing others, which leads to the development of allergic march [3, 8].

Allergic disease usually begins in children with the development of atopic dermatitis, then asthma and, finally, allergic rhinitis [1, 3, 7]. In a systematic cohort study Hill et al. found that food allergy is directly related to the development of asthma and rhinitis [10]. The influence of the environment on the health of children is undeniable [6, 9]. The growing prevalence of diseases in children is determined by changes in lifestyle and nutrition and the amount of pollutants contaminating the environment [6, 13, 14]. The impact of polluted air

on the body of pregnant women and fetuses and infants may contribute to the development of allergic rhinitis and lung dysfunction in children [12, 13].

The aim of our work was to determine the trends in the prevalence and incidence of allergic diseases constituting the part of the allergic march in the dynamics from 1994 to 2017, to assess the impact of pollutant emissions in the region of residence on the level of allergic diseases and their prevalence in children of Ukraine.

#### MATERIALS AND METHODS OF RESEARCH

A study of 24-year trends in the incidence and prevalence of allergic diseases in children aged 0-17 years living in regions with different pollutant emissions from different sources of pollution was done. Statistical and epidemiological assessment of data from the Ministry of Health of Ukraine from 1994 to 2017 was conducted [5]. Pollutant emissions

into the atmosphere in 2015 were determined according to state statistics [14].

In order to compare the incidence of children with allergic diseases from the same regions of Ukraine from 1994 to 2017, the U-criterion of sign ranks (Wilcoxon-Mann-Whitney test) was used [2]. Spearman's rank correlation coefficient was used to determine the relationship and the degree of correlation between pollutant emissions and the incidence and prevalence of allergic diseases in children. Excel-2010 and STATISTICA 6.1 (StatSoftInc., No. AGAR909E415822FA) were used to calculate the results of the work.

## RESULTS AND DISCUSSION

As a rule, the first step in the "allergic march" in childhood is atopic dermatitis (hereinafter – AD), which affects 10-20% of children worldwide [4, 14]. In 80% of cases it is first diagnosed in young children and in a third of patients the disease continues to persist in adulthood. According to the data of the Ministry of Health of Ukraine in 2017 the incidence of AD in children aged 0-17 years including was 27,803 of new cases or 3.65 of cases per 1,000 of the child population (hereinafter – 1,000 children), and the prevalence of AD was 66,389 or 8,72 cases per 1,000 children.

For comparison, in 1994 for the first time 38044 cases of AD or 2.88 cases per 1,000 children were detected (Fig. 1). The prevalence of AD was then 63,326 or 5.18 reported cases per 1,000 children aged 0 to 17 years including. In general, the growth rate of prevalence of AD over 24 years was 1.5 times greater than the rate of increase in the prevalence of diseases in children in the country [9].

In 2017, 40,209 children with AD were under dispensary supervision, which is only 62.69% of the complete coverage. In general, such statistic data may indicate defects in the completeness of the register of children with AD and, accordingly, delayed diagnosis, especially in children aged 0-6 years, which can lead to the realization of allergic (atopic) march and development of bronchial asthma (hereinafter – BA) or allergic rhinitis (hereinafter – AR). The incidence of asthma in children aged 0-17 in 2017 according to state statistics was 4513 new cases or 0.59 per 1,000 children, and the prevalence was 37246 or 4.91 per 1,000 children [5]. For comparison, in 1994, 5,544 cases of asthma were detected for the first time, or 0.46 per 1,000 children. The prevalence of asthma was then 40,424 or 3.0 per 1,000 children aged 0 to 14 years. The proportion of asthma in the structure of children's morbidity is

0.32%, which does not reduce the socio-medical significance of this complex pathology.

As illustrated in Figure 1, over 24 years the incidence of asthma increased by 22.9% ( $p>0.05$ ), the prevalence of asthma – by 69.3 ( $p<0.05$ ). Bronchial asthma was characterized by the highest index of accumulation of chronic pathology (hereinafter – IACBP) among other allergic diseases – 8.3 against similar indicators of 2.4 and 2.5, respectively, for AD and AR. These data correspond to the global trend of increasing asthma in most countries [10]. Another important step in the allergic march is AR, which often occurs in schoolchildren after AD and may precede or develop asthma. According to state statistics, the incidence of allergic rhinitis in children aged 0-17 years including was 17,669 new cases or 2.32 cases per 1,000 children. The prevalence of this disease was 43,571 cases or 5.72 cases per 1,000 children and was lower than the indicators of AD and exceeded the prevalence and incidence of children with asthma. In the structure of the prevalence of childhood diseases, the proportion of AR is only 0.33%, which does not reduce the importance of this pathology, being an important part of the allergic march in general. For comparison, in 1994, 7,986 newly diagnosed cases of AR were registered, or 0.61 per 1,000 children. The prevalence of AR was then 15,452 or 1.17 per 1,000 children aged 0 to 17 years including. The proportion of AR among all childhood diseases was 0.11%.

A retrospective analysis of the incidence and prevalence of AR in children from 1994 to 2017 shows that in Ukraine there is a significant increase in cases of AR ( $p<0.01$ ). Thus, for 24 years of observations, the prevalence of AR in children of Ukraine increased by 488.9% ( $p<0.01$ ), and the incidence – by 380.3% ( $p<0.01$ ). These data correspond to the global trend of increasing detection of AR in children [1, 4]. In general, the growth rate of the prevalence of AR in children in Ukraine over the past 24 years exceeded the growth rate of the overall prevalence of diseases in children in the country by 8 times. Figure 2 shows the dynamics of changes in the incidence of children with allergic diseases, which are stages of the allergic march, where AD dominated by the incidence and prevalence, being essentially the start of the allergic march in children. The dynamics of the increase in the incidence of AR in children (by 127.7%) was observed against the background of a decrease in AD (by 24.2%) and asthma (by 22.5%) in the proportion of overall incidence of children with allergic diseases.

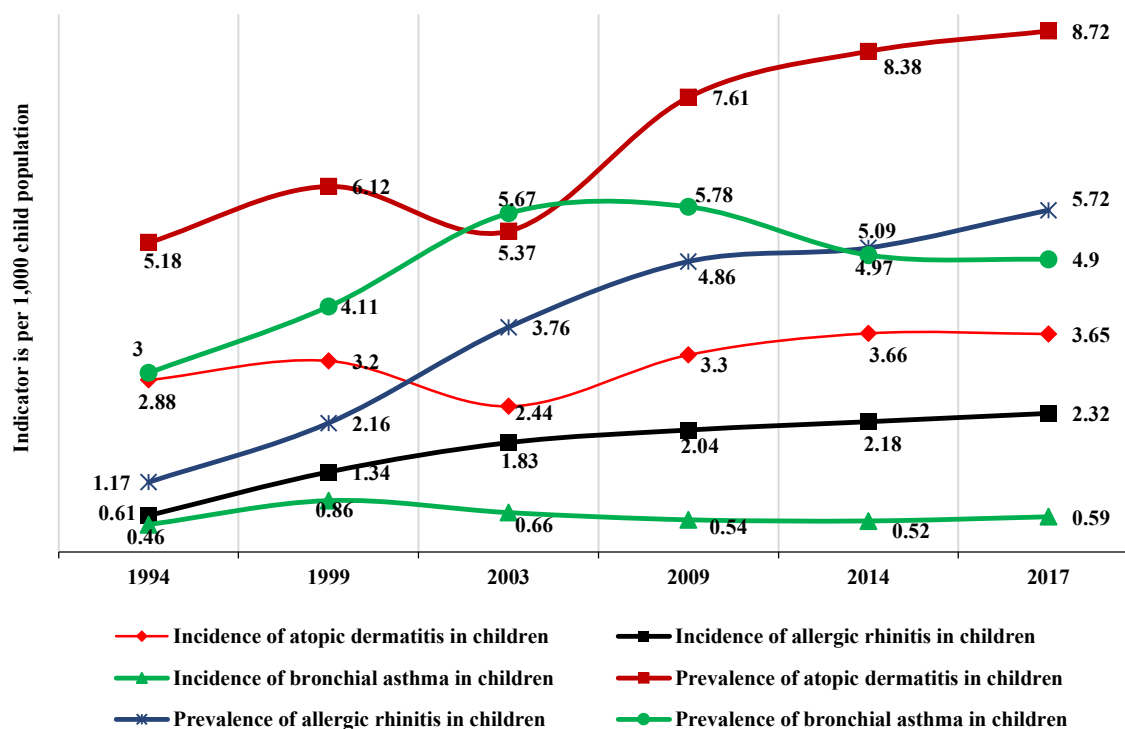


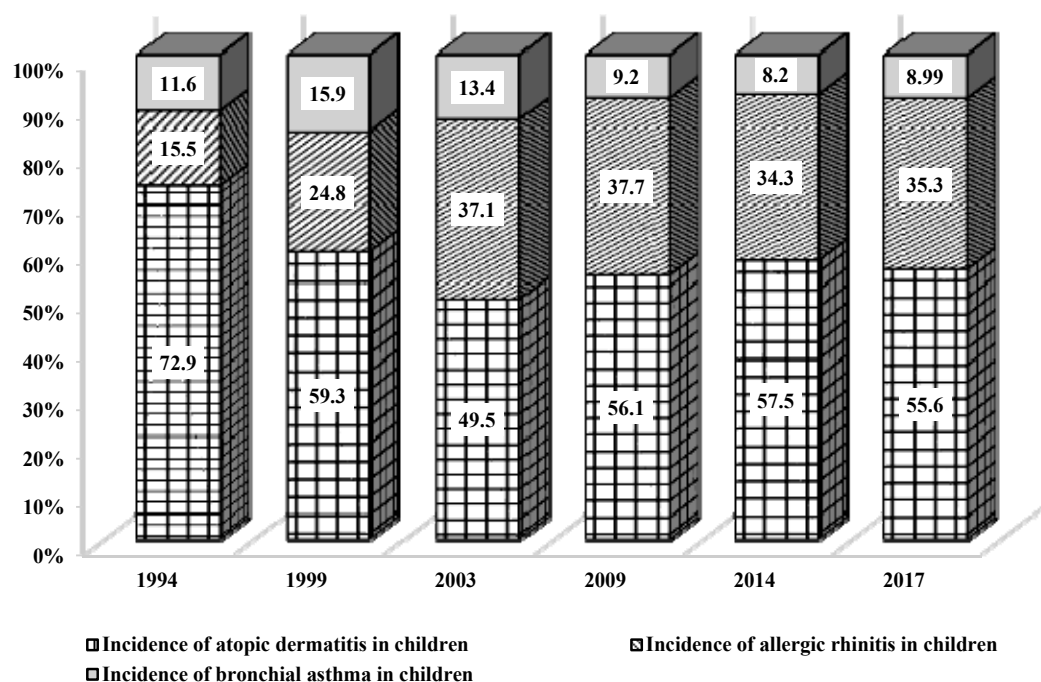
Fig. 1. Dynamics of increase in prevalence and incidence of atopic dermatitis, allergic rhinitis and bronchial asthma in children (1994-2017)

As indicated by Besh LV (2010), the allergic march in most patients (87.2%) begins with food allergies or AD in children of the first three years of life. There are cases when allergic march develops in children aged 7 to 14 years and adolescents (11.2% of cases), which is manifested in the form of AR or a combination of AR and asthma. During 24 years, there was a certain transformation of the allergic march: with a decrease in the prevalence of atopic dermatitis and asthma, the proportion of AR almost doubled, this became more common in schoolchildren and children aged 0 to 6 years.

It is the severe course of hypertension in young children is a risk factor for further development of asthma. According to Okhotnikova OM and Gladusha YI (2015), in children aged 0 to 6 years including the combination of AR with broncho-obstructive syndrome was observed in 27.4% of children, and the combination of asthma and AR – in 23.9%. The combination of AD with AR was noted in only 19% of cases, the combination of AR with asthma and AD – in 80.3%, which decreased to 67% in children aged under 12 years

[1]. Patients with allergic rhinitis are 2 times more likely to suffer from asthma compared with children without AR [4, 11], although a close correlation between these pathological conditions we could not find (Spearman's correlation coefficient ( $\rho$ ) was only 0.210). The relationship between the incidence of children with allergic rhinitis and the incidence of children with bronchial asthma was direct, and the closeness (strength) of the relationship by Chaddock scale was determined as weak ( $p > 0.05$ ). A closer direct relationship was found between atopic dermatitis and bronchial asthma, where  $\rho$  was 0.293. But the strength of the relationship by Chaddock scale was weak and statistically insignificant ( $p \geq 0.05$ ). Weak direct correlation was also observed between the incidence of AD and AR –  $\rho = 0.178$  ( $p > 0.05$ ).

As shown in the Table, most cases of AD were observed in infants and children under 6 years. This corresponds to modern ideas about the early debut of an allergic march developing from food allergy, which in the absence of adequate measures can bring into action atopic dermatitis.



**Fig. 2. Changes in the specific weight of atopic dermatitis, allergic rhinitis and bronchial asthma in the overall incidence of allergic diseases from 1994 to 2017 (in %)**

Interestingly, that during the 24 years of follow-up, the incidence of AD in children aged 0-6 years increased by 27.6%, in adolescents - by 40.5% and significantly decreased by 39.5% in children aged 7-14 years including. The highest number of cases of AR and asthma was observed in schoolchildren (47.6 and 54.0%, respectively), with a slight decrease compared to 1994. In recent years in adolescents a decrease in the incidence of allergic rhinitis and asthma was observed. An alarming fact is the increase in the incidence of these diseases in children aged 0-6 years including, which reflects the epigenetic changes and the growth of ecotoxic load

on children from the very beginning of life. As shown in the table, the lowest number of newly diagnosed cases of AR was observed in adolescence – 18.3% (in 1994 – 21.2%), but the incidence and prevalence of AR in this age cohort reached maximum values (9, 21 and 3.02 per 1,000 children, respectively). Obviously, this pattern is due to the increase in IACBP from 1.67 in children aged 0-6 years up to 3.05 in children aged 15-17 years including. It should be noted that the incidence of AR in adolescence significantly exceeded the incidence of atopic dermatitis and bronchial asthma.

**Changes in the age-related structure of incidence of allergic diseases in children from 1994 to 2017**

Nosology	Atopic dermatitis		Allergic rhinitis		Bronchial asthma	
	1994	2017	1994	2017	1994	2017
Specific weight in children aged 0-6 years including	55.8%	67.8%	29.0%	34.1%	29.6%	35.7%
Specific weight in children aged 7-14 years including	36.4%	25.7%	49.8%	47.6%	59.0%	54.0%
Specific weight in children aged 15-17 years including	7.8%	6.5%	21.2%	18.3%	11.4%	10.3%

This is what determines the modern options for the development of allergic march: AD-BA or AD-AR-BA. In a smaller number of cases in adolescents and adults there is the realization of an allergic march in the option: AD-BA-AR. Existing fluctuations in prevalence and incidence can be explained by changes in lifestyle, nutrition, environmental conditions and the appropriate focus of the system of allergy care for children to actively detect disease, not just to register patients.

The highest rates of incidence and prevalence of allergic diseases in all 3 age groups were observed in children of Dnipropetrovsk, Donetsk, Lviv, Mykolaiv, Kharkiv, Zaporizhzhia and Vinnytsia regions. It should be noted that according to state statistics these regions are characterized by the highest volumes of pollutant emissions into the atmosphere due to overdeveloped industrial and agricultural infrastructure [14]. The lowest rates of incidence and prevalence of studied allergic diseases were observed in children from Chernihiv, Cherkasy, Khmelnytsky, Rivne, Odessa and Volyn regions, which do not have significant sources of emissions into the atmosphere. An interesting medical-geographical paradox was observed in children from Chernivtsi region, where low incidence of children with AD and AR was accompanied by high incidence of asthma.

We found a direct effect of moderate strength ( $\rho=0.471$ ) on the relationship between pollutant emissions per capita and the prevalence of asthma in children ( $p<0.05$ ). A direct relationship of moderate strength ( $\rho=0.258$ ) was found between the incidence of children with asthma and pollutant emissions, which was not statistically significant ( $p>0.05$ ). A direct relationship of moderate strength according to the Chaddock scale ( $\rho=0.521$  and  $\rho=0.447$ ) was established between pollutant emissions per capita in 2015 and the prevalence and incidence of children with AR ( $p<0.05$ ). The relationship of moderate strength according to the Chaddock scale ( $\rho=0.345$  and  $\rho=0.372$ ) between the prevalence and incidence

of children with AD and the volume of pollutant emissions into the air per capita was established by us, but the dependence was statistically insignificant ( $p>0.05$ ).

That is, the development of allergic pathology in children in whom allergic march develops directly dependent on the amount of pollutants in the environment, along with other factors. Today it is extremely important to note that such ecological conditionality of the development of allergic diseases, in particular AR and asthma, can significantly complicate the course of COVID-19 in children as well.

### CONCLUSIONS

In Ukraine, over the past 24 years, a steady increase in both the incidence and prevalence of allergic diseases in children has been noted, which, in turn, form an allergic march: the prevalence of bronchial asthma increased by 69.3% and the incidence – by 22.9%; the prevalence of atopic dermatitis increased by 43.9% and the incidence – by 8.3%; the prevalence of allergic rhinitis increased by 488.3% and the incidence – by 380.3%, with the predominance of this pathology in children living in the areas with developed industrial infrastructure with significant emissions of pollutants into the air, the latter have direct impact of moderate strength on the increase in the prevalence of bronchial asthma and prevalence and incidence of allergic rhinitis in children.

Conflict of interest. The authors declare no conflict of interest.

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