

# MEDICAL AND BIOLOGICAL ASPECTS OF THE ASSESSMENT OF THE RISK FACTORS

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## ASSESSMENT OF CORRELATION BETWEEN LEUCOCYTES MIGRATION REACTION AND LEVEL OF INHALATION EXPOSURE TO PRIORITY AIR CONTAMINANTS

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*Nowadays each fourth person suffers from allergic diseases and allergic pathology prevalence is constantly growing. There are compounds in air which are generally toxic, or have sensitizing or allergenic effects on a body. For example, we can name formaldehyde and nitrogen dioxide. Our research goal was to reveal a correlation between reaction of leucocytes migration inhibition to formaldehyde and level of inhalation exposure to the examined chemicals. We examined 410 teenagers who permanently lived in industrial cities in Irkutsk region. We studied individual load as per formaldehyde and nitrogen dioxide. We estimated eosinophils content in nasal mucus and determined indexes of leucocytes migration inhibition to formaldehyde. Index of formaldehyde effects danger was detected to exceed 1 in 54% teenagers. The greatest value of danger coefficient in terms of exposure to this substance was equal to 1.76. anger index in terms of exposure to nitrogen dioxide didn't exceed 0.7 in the examined teenagers. The obtained results prove that inhalation formaldehyde load influences teenagers from industrial centers as sensitization to this substance evolves in them. We found out that true inhibition reaction of leucocytes migration in a reaction with formaldehyde more frequently occurred in people with danger index in terms of exposure to this substance being lower than 1. We obtained models which described correlation between level of sensitization to formaldehyde and a number of eosinophils in nasal mucus and it allowed us to detect that sensitization depended on the examined contaminants content in the air. The sensitization to chemical air contaminants which we revealed in teenagers calls for necessary activities aimed at reducing risks of allergic pathology evolvement in them.*

**Key words:** teenagers, formaldehyde, nitrogen dioxide, inhalation load, reaction of leucocytes migration inhibition, rhinocytogram, eosinophils.

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Allergic diseases prevalence has been growing over the last decades; nowadays each fourth person suffers from them [11, 14]. Allergic pathologies are proved to be more frequent in industrial cities and territories with adverse ecological situation [5,

7, 11, 15, 17, 18]. At the same time allergic intolerance to various chemicals, including inert ones [4], occurs more often; and it is also detected that ecological pollutants are able to act as allergens and sensitizers [2, 12]. Formaldehyde is undoubted-

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ly one of such pollutants as it exerts overall toxic, sensitizing, and allergenic impacts on a body [5, 13, 16, 18, 19]. It was revealed that 28 - 36% of children living in industrial cities located in East Siberia where 14% of the total inhalation exposure danger index belonged to nitrogen dioxide, and 9 - 18% to formaldehyde [6], suffered from allergic rhinitis or bronchial asthma [1]. We should also take into account that nowadays there are no data which can prove that nitrogen dioxide as one of priority ecological pollutants has any sensitizing effects; however, when sensitivity to it evolves it can be determined by oxidation stress development and consequent variety of pro- and anti-inflammatory processes caused by the impacts exerted by the substance. The earlier research revealed that sensitization to formaldehyde and sodium nitrite occurred quite frequently in children living in industrial cities where allergenic pathologies prevailed [3]. At the same time, there are no proofs that such ecological factors play any important role in the evolvement of such diseases.

In relation to that our research goal was to detect correlation between reaction of leucocytes migration inhibition to formaldehyde and level of inhalation exposure to chemicals.

**Data and methods.** Our research was performed on 410 teenagers aged 14-17 who permanently lived in industrial cities located in Irkutsk region (Angarsk and Sayansk), after their parents (legal representatives) gave their informed consent.

Atmospheric air quality was assessed as per data collected at Hydrometeorological service stationary posts located in Angarsk and Sayansk. Air samples in houses and educational establishments were taken by experts from East-Siberian Institute of Medical and Ecological Research (Candidates of Biological Sciences L.G. Li-

setskaya and N.A. Taranenko); contents of sulfur dioxide and nitrogen dioxide, carbon monoxide, formaldehyde, and suspended substances, were examined in the samples. When calculating individual chemical load exerted by formaldehyde and nitrogen dioxide on teenagers' bodies, we used data on admixtures content in atmospheric air, in the air in houses and educational establishments, information on educational processes organization and students' rest (questioning was performed by an expert from East-Siberian Institute of Medical and Ecological Research, Candidate of Medical Sciences I.V. Melnikova), anthropometric and spirometric parameters (as per data obtained via medical examination performed by physicians in the clinic of East-Siberian Institute of Medical and Ecological Research) [8]. Individual danger coefficients of inhalation exposure to chemicals were calculated in conformity with Guide to health risk assessment when exposed to chemicals polluting the environment 2.1.10.1920-04 [8, 10].

Nasal mucus examination (rhinocytogram) was accomplished via microscopy, a conventional examination technique. Eosinophils quantity in swabs was calculated per 100 calculated cells. Reaction of leucocytes migration inhibition was performed with the use of Costar pads as per a procedure described earlier when a chemokinetic factor, formaldehyde, was added [9]. Concentrations of a chemical mitogen to perform reaction of leucocytes migration inhibition were adjusted via experiments. Migration index (MI) was calculated as per ratio of tested samples colonies size to intact control and given in per cents. MIs which were beyond (-20% - +20%) range were considered to be positive.

Research results were analyzed with «STATISTICA 6.0» program software, and such non-parametric techniques as

Spearman's rank correlation and U-criterion by Mann - Whitney were applied. We compared frequencies of deviations from standards in the examined parameters with the use of abundance of a character in a sampling. To assess influence exerted by chemical factors on MI value in the reaction of leucocytes migration inhibition we applied non-linear regression with step-by-step introduction. Discrepancies were considered to be statistically significant in all cases when  $p < 0.05$ .

**Results and discussion.** There had previously been research performed on the territories of the examined cities and as a result it had been revealed that formaldehyde and nitrogen dioxide made the greatest contribution into immune system disorders risk [6, 8]; allowing for the results of the above-mentioned research we calculated individual exposure load exerted by the said substances on teenagers' bodies.

Danger coefficients (HQ) of formaldehyde effects varied from 0.6 to 1.76, nitrogen dioxide, from 0.05 to 0.59. The examined teenagers were divided into groups as per HQ values for air pollutants impacts. Teenagers with HQ value for formaldehyde effects being lower than 1 made up the IFA group (190 teenagers), with value being 1 and higher, IIFA group (220 teenagers).

We detected that quantity of eosinophils in nasal mucus increase in which was the evidence of a body allergic orientation didn't have any discrepancies between groups of teenagers with different level of inhalation formaldehyde load (Table 1). It is quite interesting that a body reaction to formaldehyde was detected in 40% of the examined teenagers which indicated there was sensitization to the substance in them. At the same time average group value of MI to formaldehyde in teenagers with HQ of the exposure to the toxicant being  $\geq 1$

was statistically significantly higher than in teenagers with HQ being lower than 1. We should note that leucocytes migration inhibition occurred statistically significantly more frequently (33.9%) and activation occurred two times more rarely (10.7%) in group IFA than in group IIFA (17.0%,  $p=0.01$  and 21.8%,  $p=0.08$  correspondingly).

The examined teenagers were divided into two groups as per HQ value of nitrogen dioxide (NO<sub>2</sub>) effects in the following way: 104 teenagers with the said parameter value being lower than 0.3 made up the group INO<sub>2</sub>, 306 teenagers with inhalation nitrogen dioxide load being 0.3 and higher made up the group IINO<sub>2</sub>.

As we analyzed relative content of eosinophils in nasal mucus taken from teenagers with different HQ values of nitrogen dioxide effects, we revealed that their quantity in teenagers from group IINO<sub>2</sub> was higher than in another one (Table 2).

It is quite noticeable that when the examined teenagers were divided into groups depending on HQ values of nitrogen dioxide effects, the nature of leucocytes response to formaldehyde in inhibition reaction had opposite orientation in comparison with groups IFA and IIFA.

Table 1

Parameters of a body allergic orientation and sensitization in teenagers with different inhalation formaldehyde load, Med (LQ-UQ)

Parameters	Group I <sub>FA</sub>	Group II <sub>FA</sub>	<i>p</i>
Eosinophils content in nasal mucus, %	2,00 (0,00– 10,00)	1,00 (0,00 – 10,00)	0,082
Leucocytes migration index in reaction to formaldehyde, %	–9,13 (–26,55 – 1,93)	0,00 (–13,78 – 18,15)	0,001

Table 2  
Parameters of a body allergic orientation and sensitization in teenagers with different inhalation nitrogen dioxide load, Med (LQ-UQ)

Parameter	Group I <sub>NO2</sub>	Group II <sub>NO2</sub>	p
Eosinophils content in nasal mucus, %	0,00 (0,00–8,00)	2,00 (0,00–11,00)	0,00 4
Leucocytes migration index in reaction to nitrogen dioxide, %	3,36 (–8,16–18,15)	–6,62 (–20,09–8,00)	0,00 6

Thus, increase in exposure to nitrogen dioxide led to changes in MI to formaldehyde from values proving leucocytes migration activation (INO2 group) to values which characterized the reaction as being inhibition one (IINO2 group).

Correlations analysis allowed us to detect a weak association between HQ of formaldehyde effects, HQ of nitrogen dioxide values, and MI to formaldehyde ( $R=0.18$ ,  $p=0.01$  and  $R=-0.19$ ,  $p=0.01$  correspondingly). Regression analysis helped to reveal that eosinophils content in nasal mucus taken from teenagers depended on inhalation load both with formaldehyde and nitrogen dioxide. The equation giving this dependence was as follows:  $EOS = 71.57 - 0.13 \cdot HQNO_2 - 2.86 \cdot HQFA + 2.68 \cdot (HQNO_2)^2$ , where EOS was relative eosinophils content in nasal mucus, HQNO<sub>2</sub> was HQ of nitrogen dioxide effects, HQFA was HQ of formaldehyde effects. Other parameters for this model

were:  $F(3.353)=4.923$ ,  $p<0.002$ ,  $R=0.20$ ,  $R^2=0.04$ , adjusted  $R^2=0.03$ .

We also obtained models which described dependence between sensitization to formaldehyde and chemical inhalation load with the examined compounds.  $MIFA = 56.29 + 2.00 \cdot (HQFA)^2 - 0.32 \cdot (HQNO_2)^2 - 1.55 \cdot HQFA$ , where MOFA was MI to formaldehyde, HQNO<sub>2</sub> was HQ of nitrogen dioxide effects, HQFA was HQ of formaldehyde effects. Parameters for the determining model were  $MIFAF(3.197)=3.921$ ,  $p<0.009$ ,  $R=0.24$ ,  $R^2=0.06$ , adjusted  $R^2=0.04$ .

Conclusion. The results we obtained prove that inhalation formaldehyde load influences sensitization to it in teenagers living in industrial cities. True reaction of leucocytes migration inhibition to formaldehyde more frequently occurs in people with HQ of the toxicant being  $<1$ ; to sodium nitrite, in teenagers with HQ of nitrogen dioxide effects being higher than 0.3. Determinacy of leucocytes migration index in reaction to formaldehyde and eosinophils content in nasal mucus are not of linear nature and depend not only on load with formaldehyde but also on nitrogen dioxide introduction into a body; it proves that this pollutant has only indirect effects on a body sensitization and allergization.

The revealed sensitization of teenagers' bodies to chemicals polluting both air indoors and atmospheric air makes it necessary to carry out activities aimed at lowering chemical inhalation load and allergenic pathology risks caused by a lifestyle, nutrition, etc.

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