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## **INFLUENCE OF ADVERSE FACTORS OF LOW INTENSITY ON THE FREQUENCY OF MALFORMATIONS IN FETUSES AND NEWBORNS**

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### **Abstract**

Extreme anthropogenic and technology-related environmental factors are known to have an adverse influence on the development of fetal and newborn malformations. The subject has been studied fully enough and is also practically assured. At the same time, the long-term impact of low-intensity factors (each of which does not exceed the maximum permissible concentration) both on the body of parents and the frequency of development (sentinel) structural changes in children has not been discussed in sufficient detail. Based on this, the analysis of the malformations frequency in fetuses

and newborns was conducted from 2004 to 2014 if their parents lived in 5 districts of Chernivtsi region and the districts were known as technogenic polluted (ERF 2,0 or more). The obtained data has been compared to the malformations frequency in fetuses and newborns whose parents constantly lived in more favorable environmental conditions (ERF less than 2,0).

Accordingly, the data provided make us consider that if parents lived where there was an increased risk of environmental factors influence their body, their children had major (sentinel) malformations more often than the comparison group. These malformations are recommended for mandatory registration in the EUROCAT register. Since these malformations with a fixed phenotype reflect the interaction of genetic and environmental factors, the data obtained, in particular, indicates the correctness of the selected group forming criteria.

**Key words: environmental factors; malformations; fetuses; newborns.**

**Introduction.** Adverse environmental influences, especially in sensitive periods of fetal development, can cause structural, metabolic and genetic changes that increase the susceptibility to infectious diseases after birth [1, 2, 3]. According to the EUROCAT special report, the formation of congenital malformations is largely influenced by adverse environmental stimuli. In turn, many of the so-called "modal" developmental defects can act as markers of environmental distress.

### **Material and methods**

The proposed environmental risk factor (ERF), taking into account the environmental situation in the regional centers, was a criteria for group formation to assess the long-term load of anthropogenic air, water and soil pollution on the organism of newborns' parents in the regions. For instance, the first clinical group (the main one) included patients with neonatal sepsis, whose parents were permanent residents in places with ERF 2.0 or more and with unfavorable environmental characteristics of the regional center. This clinical group will hereinafter be referred to as the "main one" or "high environmental risk" (HER) group. The second group (the comparative one) was formed by newborns with sepsis, whose parents resided permanently in territories with low risk of adverse influence of these environmental factors on their body (ERF <2.0). This clinical group will be referred to as the "Comparison Group" or the "Low Environmental Risk" Group (LER). The environmental situation in the place of residence of the parents was evaluated in accordance with the methodological recommendations [4]. Complex anthropo-technogenic load on the environment, taking into

account the bioavailability of soil, water and air pollutants in some areas of the region, by the magnitude of the proposed environmental risk factor (ERF).

The results of the study were analyzed using the Statistica 6 software package Stat Soft and Excell XP for Windows on a personal computer using parametric and non-parametric calculation methods.

### Discussion

Table. 1 shows the data of the development frequency of congenital malformations dates from 2004-2014, depending on the environmental characteristics of parents' residence in Chernivtsi region.

Table 1. - The frequency of congenital malformations in the districts of Chernivtsi region for the years 2004-2014

Districts	ERF *	Number of observations				Frequency of malformations (‰)	
		Newborns	N malformations	Deadborn	N malformations	Congenital**	Total number***
Novoselytsia	3,2	8823	508	55	17	57,5	59,1
Sokyryany	2,9	6634	333	46	8	50,1	50,3
Zastavna	2,6	6626	342	64	14	51,6	53,2
Kitsman	2,1	8653	306	59	18	42,2	44,1
Storozhynets district	2,0	16142	627	85	35	38,8	40,0
Hlyboka	1,8	11084	334	110	33	30,1	32,8
Vyzhnytsia	1,7	9060	308	75	21	34,0	36,0
Hertsia district	1,6	4876	180	50	14	36,9	39,3
Khotyn district	1,3	7744	349	35	14	45,1	46,7
Kelmentsi	1,1	4231	127	40	11	30,0	32,3
Putyla district	1,05	4713	200	90	4	42,4	43,0

Note: \* ERF - environmental risk factor

\*\* Number of malformations among live births/number of labours

\*\*\* Number of malformations among live births, deadborn/number of live births + deadborn

The table suggests that the frequency of malformations in children of the population increases as the number of ERF goes up in the places where their parents live. The exceptions are Khotyn and Putyla districts. In general, there has been a strong correlation between ERF and the number of congenital malformations ( $r=0,73$ ,

P<0,05). The ERF has shown more pronounced character except some of the specified districts( $r=-0.65$ ,  $P>0.05$ ).

The frequency of malformations in the newborns of parents who were living in conditions of ecological problems ( $ERF \geq 2,0$ ) showed 48.0%, and the total number of such malformations was 50.36%. If parents lived in a more favorable environment ( $ERF < 2,0$ ), the frequency of malformations was 36,3% and 39,0% ( $p<0.05$ ). The odds ratio (OR) for the developing of congenital malformations in newborns whose parents permanently lived in areas of environmental risk to the comparison group was 1,62 (95% CI 1-2,6), and the total number of their OR-1,59 (95% CI 1-2,8).

The frequency of malformations detection in the districts of the region has been significantly lower than in the regional center. Thus, on average, malformations of those born alive in the districts of the region occurred in 41,46%, and their total number was 43,42%. In Chernivtsi this frequency of malformations, agreeably, was at the level of 78,7% and 79% cases ( $p>0.05$ ).

Figure 1 shows the risk indicators for malformations development in children whose parents lived in the city of Chernivtsi concerning residents of districts of the region.

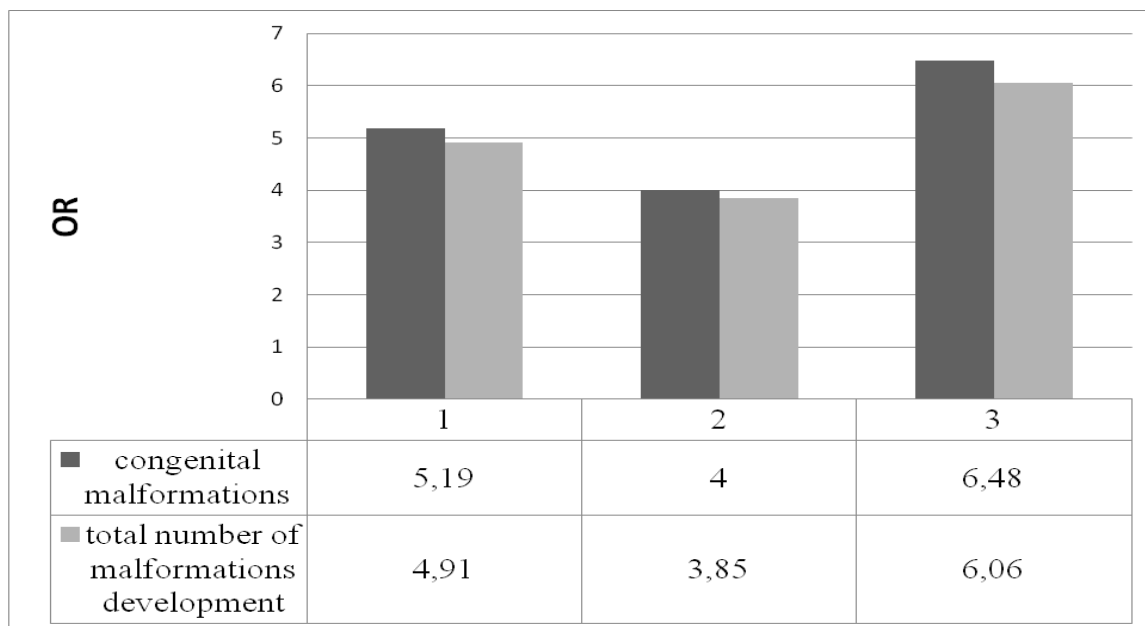


Fig.1-Diagram. The odds ratio of detecting malformations of children in the city as relating to all districts of the region (1), districts with  $ERF \geq 2$  (2) and  $< 2-x$  (3)

These findings suggest that the risk of developing abnormalities in children who lived in the city of Chernivtsi was significantly higher than in those living in districts

of the region. This difference was especially vivid when comparing the corresponding data of residents of the regional center to children of districts of the region with a favorable environmental situation.

We have analyzed the development of malformations in children of Chernivtsi with "fatal" malformations. They were the cause of death in the early neonatal period or deadborn, depending on the geochemical characteristics of their parents' places of residence. Newborn children, whose parents were living in places with the unfavorable environment, were found to have such malformations in 90 cases between 2004 and 2014. Whereas those permanently living in a favorable environment appeared only in 27 cases. The relative frequency of such malformations was 2,97‰ and 0,89‰, respectively ( $p < 0.05$ ). At the same time, the odds ratio of developing such malformations in places with the unfavorable environment comparing to favorable living conditions was 3,41 (95% CI 0,31-37,0).

Fig. 2 shows the structure of sentinel malformations in children of Chernivtsi, resulting in fatal consequences depending on the geochemical characteristics of the residence of newborns' parents.

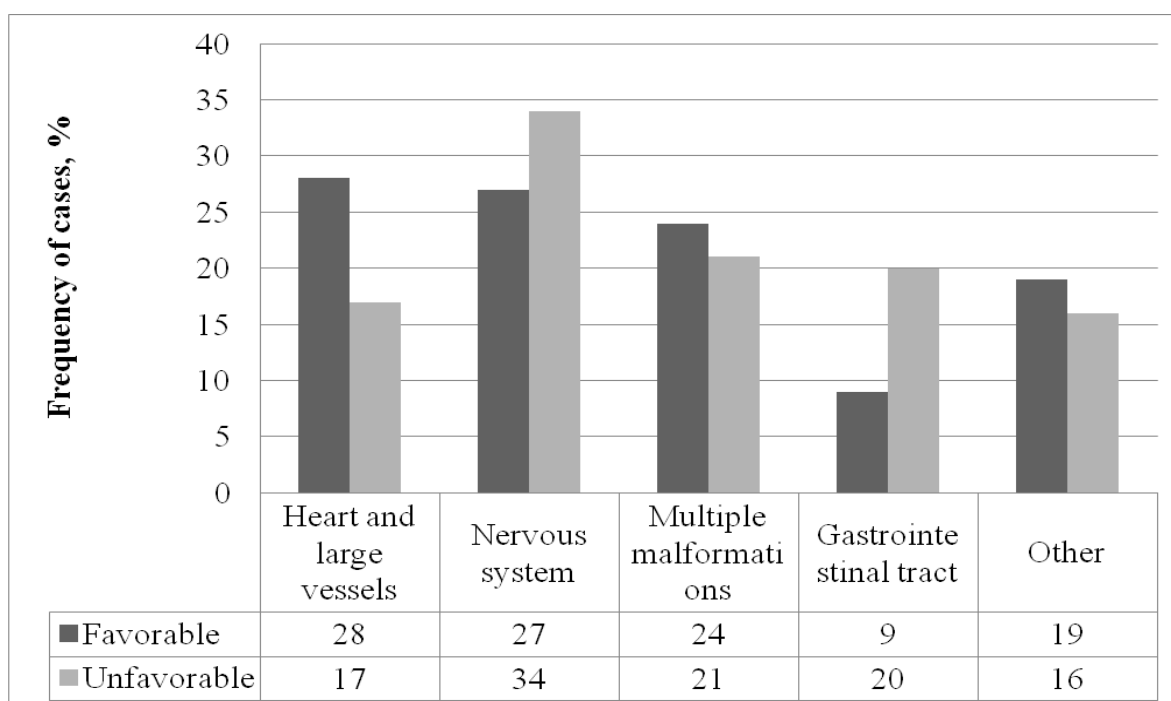


Fig.2-Diagram. The structure of sentinel malformations in newborns depending on the geochemical characteristics of the living place of parents of Chernivtsi during 2004-2014

Even though the structure of fatal malformations in children did not significantly depend on the geochemical characteristics of their parents' places of living, most of these abnormalities occurred in areas of a high content of heavy metal compounds in the soil. Thus, parents of deadborn who were living in the places where the level of heavy metal contamination exceeded the threshold value ( $\geq 2,89 \pm 0,05$  y.o.), "fatal" heart malformations occurred with a frequency of 1,6%, abnormalities of the CNS - 1,4%, multiple malformations - in 1,33%. In places with favorable geochemical conditions, these malformations occurred with a frequency of 0,2%, 0,6% and 1,33% of observations ( $p < 0.05$ ).

Table 2 shows the frequency of congenital malformations in children in the city of Chernivtsi and districts of the region with a different environment for the period of 2010-2018.

Table 2 - Frequency of congenital malformations in children of Chernivtsi and districts of the region (%) for the period of 2010-2018

Environmental characteristics of districts	ERF	The frequency of malformations(‰)								
		Heart and large vessels	Osseomuscular system	Urinary track system	Chromosomal diseases	Gastrointestinal tract	Cleft lip and under-palate	Nervous system	Spina bifida	Other developmental abnormalities
I (Unfavorable)	2,68	11,1	7,8	6,9	2,05	0,8	0,93	0,40	0,33	2,5
II (Favorable)	1,4	6,1	7,0	7,1	1,07	0,6	0,62	0,48	0,05	2,1
III (Chernivtsi)		10,8	34,8	6,8	0,75	3,2	0,60	0,51	0,12	1,9
P		II:I, III <0,05	I:II, III <0,05	>0,05	I:II <0,05	III:I, II <0,05	>0,05	>0,05	II: I,III <0,05	>0,05

Table 2. shows that malformations of the cardiovascular system, osseomuscular abnormalities, chromosomal diseases and abnormalities of the gastrointestinal tract were more often registered in areas of the region with an unfavorable environmental situation, or the city of Chernivtsi

The data provided suggest that the risk of most malformations in children whose parents lived for a long time in areas with unfavorable environmental characteristics was higher. If parents lived in Chernivtsi for a long time, comparing to

the districts of the region, there is a likely risk of abnormalities development of the osseomuscular system, gastrointestinal tract, and cardiovascular system. At the same time, there has been a decrease in the risk of chromosomal diseases and spina bifida. The effect of urbanization on the development of malformations was especially vivid when comparing the residents of the regional center and districts of the region with a favorable environmental situation. It is interesting to observe that the abnormalities development of the nervous system in children did not depend on the place of living of their parents.

### **Conclusions**

Accordingly, the data provided make us consider that if parents lived where there was an increased risk of environmental factors influence their body, their children had major (sentinel) malformations more often than the comparison group. These malformations are recommended for mandatory registration in the EUROCAT register. Since these malformations with a fixed phenotype reflect the interaction of genetic and environmental factors, the data obtained, in particular, indicates the correctness of the selected group forming criteria.

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