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Research article

THE RISK OF IMBALANCE IN THE POPULATION COMPOSITION OF LYMPHOCYTES AND SPECIFIC SENSITIZATION IN CHILDREN LIVING UNDER EXPOSURE TO AIRBORNE BENZO(A)PYRENE IN THE ARCTIC ZONE OF RUSSIA

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Climatic and geographical determinants of the Arctic zone can aggravate effects of technogenic chemical factors and induce health disorders in children even at low exposure levels.

1291 children aged 3–6 years were examined. Group A included 608 children living in an urbanized area in the Arctic zone. Group B consisted of 204 children from a conventionally clean area of the Arctic zone. Group C included 308 children from an urbanized middle latitude area. Group D consisted of 171 children from a conventionally clean middle latitude area. Benzo(a)pyrene levels in ambient air and in blood were determined by HPLC. Identification of T-($CD3^+$) and B-lymphocytes ($CD19^+$) was carried out by flow cytofluorometry.

Exposure to airborne benzo(a)pyrene (0.6 average daily MPL) in the Arctic zone in a daily dose equal to $7.11 \cdot 10^{-3}$ μg/(kg·day) results in blood of exposed children being contaminated with benzo(a)pyrene and in lower levels of T-lymphocytes ($CD3^+$) (OR (CI) = 2.99 (2.00–4.46); RR (CI) = 1.94 (1.47–2.56); p = 0.024) against hyperexpression of B-lymphocytes ($CD19^+$) (OR (CI) = 2.55 (1.83–3.56); RR (CI) = 1.68 (1.36–2.06); p = 0.019) and IgG to benzo(a)pyrene (OR (CI) = 53.33 (27.56–103.20); RR (CI) = 15.11 (8,24–27.72); p = 0.001) in comparison with children living on a conventionally clean territory (p < 0.05). Similar disorders are identified in children in case benzo(a)pyrene is introduced in a dose equal to $87.6 \cdot 10^{-3}$ μg/(kg·day) under airborne exposure (7.4 average daily MPL) in the middle-latitude zone (p > 0.05).

Thus, children who live in the Arctic zone and are exposed to airborne benzo(a)pyrene in an average daily dose equal to $7.11 \cdot 10^{-3}$ μg/(kg·day) face an elevated risk of imbalance in the population composition of lymphocytes as per basic cell differentiation clusters (CD3+ and CD19+; RR = 1.68–1.94; p = 0.024–0.019) and specific sensitization (IgG to benzo(a)pyrene; RR = 15.11; p = 0.001). This risk is comparable with effects of exposure to airborne benzo(a)pyrene in an average daily dose equal to $87.6 \cdot 10^{-3}$ μg/(kg·day) in the middle-latitude zone. These findings confirm the hypothesis on effects of technogenic chemical factors being potentiated by specific climatic and geographic conditions (low average annual temperatures and photoperiodic asymmetry). Their additive effects induce early manifestations of pathological phenotypic health disorders in children even under low levels of exposure to benzo(a)pyrene.

Keywords: *benzo(a)pyrene, airborne exposure, immunity, lymphocytes, Arctic, children, IgG to benzo(a)pyrene, sensitization.*

Technogenic chemical factors produce negative effects on public health. Chronic exposure to them causes early deadaptation, immunologic, and nuerohumoral disruptions of homeostasis, which, in their turn, create elevated risks of ecology-dependent diseases in future [1]. Benzo(a)pyrene is one of the most widely spread environmental pollutants. The chemical belongs to the hazard class 1, is highly toxic for the immune system and a powerful carcinogen; it also has very strong ability to bioaccumulate [2].

However, effects produced by any technogenic factors are not isolated. They occur under specific climatic and geographical conditions on a given territory able to aggravate toxic effects of haptens [3, 4]. Thus, climatic and geographical conditions in the Arctic zone are considered extreme since air temperatures tend to be low all year round (long frosty winters and short cool summers) and there is apparent photoperiodic seasonal asymmetry (the midnight sun in spring and summer and polar night in autumn and winter). Even without any

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technogenic burdens, such conditions considerably affect adaptation potential and facilitate development of so called 'polar stress syndrome' or 'northern' stress [5].

Combined exposure to adverse climatic and geographical determinants and technogenic factors in the Arctic zone causes early health disorders in local population even if levels of certain chemicals in ambient air are within hygienic standards on this territory [6]. In addition, preschoolers are affected by various environmental factors to a much greater extent than adults due to their adaptive and detoxification systems being underdeveloped [7].

The immune system plays a key role in protective and adaptive responses of the body and determines its integral reactivity under modified environmental conditions. It is a primary target under climatic, geographical and technogenic exposures. Consequently, changes in the population composition of lymphocytes can be early informative markers of combined exposure to various stressor factors. They describe disruption of the innate (NK-cells) and adaptive (T- and B-lymphocytes) immune response [8, 9].

Therefore, it seems relevant to perform a complex comparative assessment of the population composition of lymphocytes and specific sensitization in children living under exposure to airborne benzo(a)pyrene in the Arctic zone and in a middle latitude area. Its results can be useful for developing a system of indicators describing early health disorders in children that occur due to technogenic burdens on territories with specific climatic and geographical conditions.

The aim of this study was to perform a comparative assessment of the population composition of lymphocytes and specific sensitization in children exposed to airborne benzo(a)pyrene in the Arctic zone of the Russian Federation.

Materials and methods. We conducted clinical-laboratory examination of children living in the Eastern Siberia. Overall, 1291 preschoolers aged between 3 and 6 years took part in the research. The examined children were divided into four groups according to levels of exposure to airborne benzo(a)pyrene and climatic and geographic features of a territory where they lived. The Group A included 608 children who lived on a territory with developed industry in the Arctic zone (69° north latitude) and were exposed to airborne benzo(a)pyrene. The Group B was made of 204 children who lived on a conditionally clean territory in the Arctic zone (69° north latitude). The Group C included 308 children who lived on a territory with developed industry in a middle latitude area (56° north latitude) and were exposed to airborne benzo(a)pyrene. The Group D was made of 171children living on a conditionally clean middle latitude territory (51° north latitude).

The study complied with the ethical requirements stated in the WMA Declaration of Helsinki (2000) and the Protocol of the Convention on Human Rights and Biomedicine of the Council of Europe (1999). The study was approved by the Local Ethics Committee of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing (the Meeting Report No. 23 dated December 20, 2021). Informed consent was provided for each participant in the research.

Benzo(a)pyrene levels were identified in ambient air on the territories where the examined Groups (A, B, C, and D) lived by using high performance liquid chromatography (HPLC) on Agilent 1200 (Agilent Technologies Inc., USA) in accordance with the Methodical Guidelines MUK 4.1.1273-03 Measurement of Mass Concentration of Benzo(a)pyrene in Ambient Air and Workplace Air by Using HPLC with Fluorometric Detection.

Benzo(a)pyrene levels were identified in the examined children's blood by using high performance liquid chromatography (HPLC) on Agilent 1200 (Agilent Technologies Inc., USA) in accordance with the Methodical Guidelines MUK 4.1.3040-12 Determination of Mass Concentration of Benzo(a)pyrene in Blood by Using HPLC.

The population composition of lymphocytes was explored in the examined children as

per T- ($CD3^+$), B-lymphocytes ($CD19^+$) and NK-cells count by using flow cytometry on FACSCalibur (Becton Dickinson, USA) and with CellQuestPrO software.

The results were statistically analyzed by using descriptive mathematical statistics in Statistica 10.0 applied software package (StatSoft, USA). Distribution of data in the analyzed samples was examined with the Shapiro – Wilk test. In case the data were normally distributed, we estimated authenticity of differences using the parametric Student's t-test; the Mann – Whitney U-test was applied for the data that were not normally distributed. The study findings are presented as simple mean (*X*) and standard error (*SE*) of the values of the analyzed indicators. We calculated odds ratio (*OR*), relative risk (*RR*), and their 95 % confidence intervals (*CI*) to evaluate relationships between examined responses and exposure to a given factor. Cause-effect relations between exposure to benzo(a)pyrene and detected body responses were established by using pair regression analysis together with calculating the determination coefficient R^2. Differences between the samples were considered authentic at $p < 0.05$.

Results and discussion. We performed comparative hygienic assessment of ambient air quality on the territories where the examined children lived. As a result, we established that benzo(a)pyrene levels equaled 0.6 average daily maximum permissible level (MPL) on the urbanized territory in the Arctic; 0.01 average daily MPL on the conditionally clean territory in this region; 7.4 average daily MPL on the urbanized middle latitude territory; 0.7 average daily MPL on the conditionally clean middle latitude territory[1]. Consequently, hygienic standards are violated as per benzo(a)pyrene levels on the territory where the Group C lives whereas quality of ambient air on three other territories (the Groups A, B, and D) corresponds to sanitary-epidemiological requirements and norms. An average dose of inhalation exposure to airborne benzo(a)pyrene is 60.3 times higher for the children living on the territory with developed industry in the Arctic zone (the Group A) than for their counterparts living on the conditionally clean territory in this region (the group B) ($p = 0.001$). This dose is also 12.3 times lower against that identified for the children living on the middle latitude territory with developed industry (the Group C) ($p = 0.001$) and 1.2 times lower against that identified for the children living on the conditionally clean middle latitude territory (the Group D).

An average dose of inhalation exposure to airborne benzo(a)pyrene is 12.3 times higher for the children living on the middle latitude territory with developed industry (the Group C) than that identified for children living on the territory with developed industry in the Arctic zone (the Group A) and 38.2 times higher than that identified for the children living on the conditionally clean middle latitude territory (the Group D) ($p = 0.001$) (Table 1).

We performed chemical analysis of the examined children's blood. As a result, we established that benzo(a)pyrene contamination was 1.8 times higher in the children living and in the Arctic and exposed to airborne benzo(a)pyrene (the Group A) than in the children living on the conditionally clean territory in this region (the Group B) ($p = 0.049$). In their turn, benzo(a)pyrene levels were 2.2 times higher in blood of the children living on

[1] O sostoyanii i ob okhrane okruzhayushchei sredy Rossiiskoi Federatsii v 2018 godu: Gosudarstvennyi doklad [On the state and the protection of the environment in the Russian Federation in 2018: The state report]. Moscow, The RF Ministry of Natural Resources and Environment; NPP Kadastr, 2019 (in Russian); Sostoyanie zagryazneniya atmosfery v gorodakh na territorii Rossii za 2017 g.: Ezhegodnik [Levels of ambient air pollution in cities in Russia in 2017: the annual bulletin]. St. Petersburg, 2018 (in Russian); Ob utverzhdenii Programmy kompleksnogo razvitiya transportnoi infrastruktury munitsipal'nogo obrazovaniya «Gorod Dudinka»: reshenie Dudinskogo gorodskogo soveta deputatov ot 14.09.2017 № 10-0358 [On Approval of the Complex Program of the development of transport infrastructure in Gorod Dudinka Municipality: the decision by the Dudinka Town Deputy Council dated September 14, 2017 No. 10-0358]. *The official legal web-site of Dudinka*. Available at: http://www.pravo-dudinka.ru/download/rgs/rgs_2017-09-14_10-0358.pdf (July 25, 2023) (in Russian).

Table 1

Average daily doses of airborne benzo(a)pyrene and benzo(a)pyrene contamination in blood of the children living in the Arctic zone and in the middle latitude area

Group A (n = 608)	Group B (n = 204)	Group C (n = 308)	Group D (n = 171)
Daily airborne benzo(a)pyrene doses under inhalation exposure, μg/(kg·day)			
$7.11 \cdot 10^{-3}$	$1.18 \cdot 10^{-4}$	$8.76 \cdot 10^{-2}$	$2.29 \cdot 10^{-3}$
Benzo(a)pyrene levels in blood, μg /dm^3 (the reference level is 0 μg /dm^3			
0.002244 ± 0.000416	0.001277 ± 0.000258	0.00242 ± 0.000378	0.001094 ± 0.000382

Table 2

The Immune profile of the children exposed to airborne benzo(a)pyrene in the Arctic zone and in the middle latitude area

Group A (n = 608)	Group B (n = 204)	p (A/B)	Group C (n = 308)	Group D (n = 171)	p (C/D)
$CD3^+$-lymphocytes, % (Reference range is 55–84 %)					
66.00 ± 1.02	70.42 ± 1.62	0.024	67.07 ± 1.92	72.71 ± 1.93	0.039
$CD19^+$-lymphocytes, % (Reference range is 6–25 %)					
16.63 ± 0.73	13.09 ± 0.65	0.019	16.01 ± 0.61	14.04 ± 0.77	0.046
IgG to benzo(a)pyrene, a.u. (Reference range is 0–0.3 a.u.)					
0.204 ± 0.019	0.080 ± 0.005	0.001	0.196 ± 0.02	0.074 ± 0.01	0.001

Note: p (A/B) is the level of significance for differences between the Groups A and B, p (C/D) is the level of significance for differences between the Groups C and D.

the middle latitude territory with developed industry (the Group C) than in their counterparts living on the conditionally clean territory in this region (the Group D) (p = 0.013). It is worth noting that we identified comparable levels of benzo(a)pyrene contamination in blood of the children from the Group A and those from the Group C. The former live under exposure to airborne benzo(a)pyrene in an average daily dose being equal to $7.11 \cdot 10^{-3}$ μg/(kg·day) and under the climatic conditions characterized with low average daily temperatures and photoperiodic asymmetry in the Arctic zone. The latter live under exposure to much higher average daily doses of airborne benzo(a)pyrene, $87.6 \cdot 10^{-3}$ μg/(kg·day), but in the area with moderate climate and the circadian rhythm of natural lighting.

The immunological examination of the children exposed to airborne benzo(a)pyrene identified certain changes in the population composition of lymphocytes as per T- and B-cells count. They occurred against specific hypersensitivity to this PAH (Table 2).

The cellular immune profile of 52.6 % (320) of the children from the Group A and 79.9 % (246) of the children from the Group C is described with lower T-lymphocytes ($CD3^+$) counts against the same indicator in the reference Groups B (*OR* (*CI*) = 2.99 (2.00–4.46); *RR* (*CI*) = 1.94 (1.47–2.56); p = 0.024) and D (*OR* (*CI*) = 15.99 (10.01–25.51); *RR* (*CI*) = 4.01 (2.95–5.45); p = 0.039) accordingly. The values of this indicator in the children living in the Arctic zone (the Groups A and B) were slightly lower than those identified in the children living on the middle latitude territories (the Groups C and D) (p (A/C) = 0.623; p (B/D) = 0.367). The lowest $CD3^+$-lymphocytes count was identified in the children exposed to low doses ($7.11 \cdot 10^{-3}$ μg/(kg·day)) of airborne benzo(a)pyrene and living in in the Arctic zone (the Group A); the maximum count was identified in the children living on the conditionally clean middle altitude territory (the Group D).

On the contrary, 56.1 % (341) of the children from the Group A and 53.3 % (164) of the children from the group C, who were exposed to airborne benzo(a)pyrene, had authentically higher B-lymphocytes ($CD19^+$) count against the Group B (*OR* (*CI*) = 2.55 (1.83–3.56);

RR (*CI*) = 1.68 (1.37–2.07); $p = 0.019$) and D (*OR* (*CI*) = 1.49 (1.02–2.17); *RR* (*CI*) = 1.23 (1.01–1.50); $p = 0.046$) accordingly. This indicator was slightly higher in the children from the Group A who lived in the Arctic zone under exposure to low doses of airborne benzo(a)pyrene against the children from the Group C who lived in the middle latitude area and were exposed to high doses of airborne benzo(a)pyrene ($p = 0.521$). However, the children in the Group B who lived on the conditionally clean territory in the Arctic zone had a slight decrease in B-lymphocytes ($CD19^+$) count against their unexposed counterparts who lived on the conditionally clean middle latitude territory (the Group D) ($p = 0.348$). The highest B-lymphocytes ($CD19^+$) count was identified in the children living in the Arctic zone under exposure to low doses of airborne benzo(a)pyrene (the Group A); the lowest count was identified in the children living on the conditionally clean middle latitude territory (the Group D).

The immune profile of 73 % (444) of the children from the Group A and 93.2 % (287) of the children from the Group C had elevated levels of IgG specific to benzo(a)pyrene against the reference level (0–0.3 a.u.), and the reference Group B (*OR* (*CI*) = 53.33 (27.56–103.20); *RR* (*CI*) = 15.11 (8.24–27.72); $p = 0.001$) and D (*OR* (*CI*) = 453.73 (167.94–1225.84); *RR* (*CI*) = 31.86 (13.42–75.62); $p = 0.001$) accordingly. This indicates specific hypersensitivity developing in the children on the analyzed territories with developed industry ($p = 0.001$). It is noteworthy that the levels of IgG to benzo(a)pyrene detected under airborne exposure to this PAH in an average daily dose equal to $7.11 \cdot 10^{-3}$ μg/(kg·day) in the Arctic zone (the Group A) are not only similar to its levels under exposure to this hapten in an average daily dose equal to $87.6 \cdot 10^{-3}$ μg/(kg·day) on the middle altitude territory (the Group C) but even a bit higher ($p = 0.77$). However, the regression analysis within the 'exposure marker – marker of effect' relationship model revealed a stronger correlation between elevated levels of IgG to benzo(a)pyrene as the marker of effect and elevated benzo(a)pyrene contamination in blood (the exposure marker) under exposure to high doses of benzo(a)pyrene on the middle latitude territory ($R^2 = 0.92$, $p = 0.001$) than under exposure to low doses of the chemical in the Arctic zone ($R^2 = 0.87$, $p = 0.001$) (Table 3).

Our research results provide evidence of an authentic decrease in the adaptive cellular immunity as per T-lymphocytes ($CD3^+$) levels against hyperproduction of specific IgG to benzo(a)pyrene combined with excess B-lymphocytes ($CD19^+$) levels in the children from the Groups A and C living on the urbanized territories in comparison with the children from the Groups B and D living on the conditionally clean territories. The study findings indicate that the cellular effector immunity is inhibited and depleting and the process is associated with developing specific hapten hypersensitivity under exposure to airborne benzo(a)pyrene.

Immunotropic effects of benzo(a)pyrene occur due to its ability to get bound to the aryl hydrocarbon receptor Ahr and the following activation of the P450 CYP1A cytochrome enzyme participating in detoxification and elimination of PAHs and their metabolites. However, activation of this enzyme induces formation of more toxic benzo(a)pyrene metabolites, namely, benzo(a)pyrene-7,8-diol-9,10-epoxide (BPDE). This compound produces stronger carcinogenic and immunotoxic effects and is able to disrupt the balance between proliferation and programmed lymphocytes death [10].

Table 3

Parameters of the 'exposure marker – marker of effect' relationship models

Exposure marker	Marker of effect	Direction of indicator change	b_0	b_1	F	p	R^2
Benzo(a)pyrene	Group A + B						
	IgG to benzo(a)pyrene	Increase	-1.835	24.339	3154.24	0.001	0.874
	Group C + D						
	IgG to benzo(a)pyrene	Increase	-0.954	-29.661	4126.32	0.001	0.920

Moreover, CYP1A-mediated PAHs metabolism stimulates ROS formation against inhibited expression of Nrf2, the redox-sensitive transcription factor of antioxidant protection, and, consequently, development of oxidative stress, which, in its turn can also be a reason for the immune response inhibition [11]. Benzo(a)pyrene can have direct effects on the immune regulation by disrupting the $Ca2^{+}$-dependent transfer of signals between immunocytes. Excess benzo(a)pyrene levels facilitate the protein tyrosine kinase (PTK) activation and the following inositol triphosphate (IT3)-dependent abnormal release of free Ca^{2+} ions from the endoplasmatic reticulum against inhibited adenylyl cyclase (AC)-cAMP (AC-cAMP)-signal pathway. This leads to weaker expression of the nuclear transcription factors NF-κb and CREB that regulate inflammation, apoptosis, bacteriolytic activity, and phagocytosis [12, 13].

Although benzo(a)pyrene is a hapten with pronounced immune-suppressive properties, there is also evidence of its role in allergization and development of specific hypersensitivity against compensatory activation of the humoral immune response. Thus, this study has revealed that the immune profile of children under excess exposure to benz(a)pyrene is characterized by excess production of specific IgG to benzo(a)pyrene with simultaneous elevated IgG and IgA antibodies as well as the share of B-lymphocytes ($CD19^{+}$) as plasmatic cells predecessors. Sensitizing properties of benzo(a)pyrene are also combined with its ability to get bound to the AhR-receptor, the latter playing an important role in the immune response modulation, and this induces both pro-inflammatory and anti-inflammatory processes [14]. AhR activation by PAHs is pro-inflammatory in nature, which induces mucus hypersecretion and dysregulation of antigen-presenting cells, Langerhans cell migration, effector T-lymphocytes activation and cytokine hyperproduction (IL-5, IL-13, and IL-17), more intense IgE-mediated histamine release, as well as IL-4 production by basophiles. Exposure to benzo(a)pyrene can reinforce mast cell degranulation and the following histamine release thereby worsening bronchial asthma symptoms. In addition to that, exposure to benzo(a)pyrene can aggravate allergic dermatitis symptoms caused by tick allergens by intensifying the Th2-dependent immune response. PAHs bonding to the AhR-receptors in dendritic cells is associated with effector T-cells inhibiting production of some anti-inflammatory cytokines and, on the contrary, activation of pro-inflammatory tumor-stimulating M2-macrophages able to produce TGF-β and IL-10, tissue growth and reparation factors [15, 16].

In its turn, permanent residence under extreme climatic and geographical conditions in the Arctic zone leads to a considerable decrease in adaptation resources of the human body, even without considering any technogenic burdens. Such resources are based on non-specific phylogenetically programmed stereotype reactions influencing the body homeostasis under unstable environmental conditions. Under such conditions, depletion of the body adaptation potential can induce development of so called ‘polar stress syndrome’ or ‘northern’ stress that usually involves metabolism disruptions, detoxication, endocrine and neurological disorders, biorhythm desynchronization and immunosuppression [5, 17].

It is noteworthy that immunotoxic properties of benzo(a)pyrene have been previously described in detail in observational and experimental studies [10, 18, 19]. However, literature does not provide any data on possible modification of the chemical effects under exposure to additional stress factors, such as low air temperatures and specific lighting. Also, there are few Russian studies that address the immune profile disorders under extreme climatic and geographical conditions of the Arctic zone. However, they predominantly concentrate on adults, either local population or shift workers [9, 20] whereas much less attention has been given to peculiarities of the immune profile in children living in northern regions.

It should be noted that changes in T- and B-lymphocytes count as well as production of IgG-specific to benzo(a)pyrene identified under exposure to this airborne PAH in an average daily dose of $7.11 \cdot 10^{-3}$ μg/(kg·day) in the Arctic zone (the Group A) are comparable to exposure

to this hapten in an average daily dose equal to $87.6 \cdot 10^{-3}$ μg/(kg·day) on the middle latitude territory (the Group C). This confirms the hypothesis that extreme climatic and geographical factors aggravate effects produced by polycyclic aromatic hydrocarbons and induce adverse health outcomes in children exposed to even low doses of such chemicals.

Conclusion. We performed comparative hygienic assessment of ambient air quality on the territories where the examined children lived permanently. As a result, we established that exposure to benzo(a)pyrene was equal to 0.6 average daily MPL on the urbanized territory in the Arctic zone; 0.01 average daily MPL on the conditionally clean territory in the Arctic zone; 7.4 average daily MPL on the urbanized middle latitude territory; and 0.7 average daily MPL on the conditionally clean middle latitude territory. Benzo(a)pyrene levels were 1.8 times higher in blood of the children living on the urbanized territory in the Arctic and exposed to this airborne PAH in an average daily dose equal to $7.11 \cdot 10^{-3}$ μg/(kg·day) (the Group A) than the same indicator in the children living on the conditionally clean territory in the same region (the Group B) ($p < 0.05$). Also, the levels identified in the Group A were comparable with those detected in the children living on the urbanized middle latitude territory and exposed to airborne benzo(a)pyrene in a an average daily dose of $87.6 \cdot 10^{-3}$ μg/(kg·day). The immune profile of the children living on the urbanized territory in the Arctic zone (the Group A) has some signs that its T-cell component is inhibited (*OR* (*CI*) = 2.99 (2.00–4.46); *RR* (*CI*) = 1.94 (1.47–2.56); $p = 0.024$) and its humoral component demonstrates specific hypersensitivity as per IgG to benzo(a)pyrene (*OR* (*CI*) = 53.33 (27.56–103.20); *RR* (*CI*) = 15.11 (8.24–27.72); $p = 0.001$) associated with excess B-lymphocytes levels (*OR* (*CI*) = 2.55 (1.83–3.56); *RR* (*CI*) = 1.68 (1.36–2.06); $p = 0.019$) against the children from the Group B who live on the conditionally clean territory in the Arctic ($p < 0.05$). It is worth noting that exposure to low doses of airborne benzo(a)pyrene of $7.11 \cdot 10^{-3}$ μg/(kg·day) on the urbanized territory in the Arctic creates elevated benzo(a)pyrene contamination in blood of the exposed children and this results in an elevated risk, *RR* (1.68–15.11), of developing imbalance in the population composition of lymphocytes (T- and B-cells) and specific hypersensitivity to benzo(a)pyrene as per IgG. The levels of these indicators are comparable to those detected in the children living on the urbanized middle latitude with the circadian rhythm of natural lighting and exposed to airborne benzo(a)pyrene in an average daily dose of $87.6 \cdot 10^{-3}$ μg/(kg·day) (the Group C) ($p > 0.05$). This confirms that adverse climatic and geographical factors are able to potentiate adverse PAH effects. Therefore, the detected changes in the population composition of lymphocytes ($CD3^+$ and $CD19^+$ cell differentiation clusters) and specific reaginic antibodies (IgG to benzo(a)pyrene) indicate the existing risks of immune dysregulation and can be used as eligible indicators within diagnosing and preventing health disorders in children exposed to airborne benzo(a)pyrene in the Arctic zone of Russia.

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References

1. Suzuki T., Hidaka T., Kumagai Y., Yamamoto M. Environmental pollutants and the immune response. *Nat. Immunol.*, 2020, vol. 21, no. 12, pp. 1486–1495. DOI: 10.1038/s41590-020-0802-6

2. Kohno R., Nagata Y., Ishihara T., Amma C., Inomata Y., Seto T., Suzuki R. Benzoo[a]pyrene induces NLRP1 expression and promotes prolonged inflammasome signaling. *Front. Immunol.*, 2023, vol. 14, pp. 1154857. DOI: 10.3389/fimmu.2023.1154857

3. Ilardo M., Nielsen R. Human adaptation to extreme environmental conditions. *Curr. Opin. Genet. Dev.*, 2018, vol. 53, pp. 77–82. DOI: 10.1016/j.gde.2018.07.003

4. Shur P.Z., Khasanova A.A., Tsinker M.Yu., Zaitseva N.V. Methodical approaches to assessing public health risks under combined exposure to climatic factors and chemical air pollution caused by them. *Health Risk Analysis*, 2023, no. 2, pp. 58–68. DOI: 10.21668/health.risk/2023.2.05.eng

5. Petrova P.G. Ecological and physiological aspects of human adaptation to the conditions of the North. *Vestnik Severo-Vostochnogo federal'nogo universiteta im. M.K. Ammosova. Seriya: Meditsinskie nauki*, 2019, no. 2 (15), pp. 29–38. DOI: 10.25587/SVFU.2019.2(15).31309 (in Russian).

6. Karpin V.A., Gudkov A.B., Shuvalova O.I. Impact Analysis of Climate and Technogeneous Pressing on Residents of Northern Urban Land. *Ekologiya cheloveka*, 2018, vol. 25, no. 10, pp. 9–14. DOI: 10.33396/1728-0869-2018-10-9-14 (in Russian).

7. Setko N.P., Setko A.G., Bulycheva E.V. Adaptatsionnaya meditsina detei i podrostkov [Adaptive medicine of children and adolescents]. Orenburg, OrGMU Publ., 2018, 515 p. (in Russian).

8. Morozova O.S., Sergeeva T.B., Shchegoleva L.S. Cellular Immunity in Women Aged 40–60 Years Living in the Far North. *Zhurnal mediko-biologicheskikh issledovanii*, 2020, vol. 8, no. 3, pp. 235–240. DOI: 10.37482/2687-1491-Z014 (in Russian).

9. Deng Y.-L., Liao J.-Q., Zhou B., Zhang W.-X., Liu C., Yuan X.-Q., Chen P.-P., Miao Y. [et al.]. Early life exposure to air pollution and cell-mediated immune responses in preschoolers. *Chemosphere*, 2022, vol. 286, pt 3, pp. 131963. DOI: 10.1016/j.chemosphere.2021.131963

10. Abd El-Fattah E.E., Abdelhamid A.M. Benzoo[a]pyrene immunogenetics and immune archetype reprogramming of lung. *Toxicology*, 2021, vol. 463, pp. 152994. DOI: 10.1016/j.tox.2021.152994

11. Huang Y., Zhang J., Tao Y., Ji C., Aniagu S., Jiang Y., Chen T. AHR/ROS-mediated mitochondria apoptosis contributes to benzoo[a]pyrene-induced heart defects and the protective effects of resveratrol. *Toxicology*, 2021, vol. 462, pp. 152965. DOI: 10.1016/j.tox.2021.152965

12. Guan S., Huang Y., Feng Z., Xu L., Jin Y., Lu J. The toxic effects of benzoo[a]pyrene on activated mouse T cells in vitro. *Immunopharmacol. Immunotoxicol.*, 2017, vol. 39, no. 3, pp. 117–123. DOI: 10.1080/08923973.2017.1299173

13. Lei F., Tian Y., Miao J., Pan L., Tong R., Zhou Y. Immunotoxicity pathway and mechanism of benzoo[a]pyrene on hemocytes of Chlamys farreri in vitro. *Fish Shellfish Immunol.*, 2022, vol. 124, pp. 208–218. DOI: 10.1016/j.fsi.2022.04.009

14. Poulain-Godefroy O., Bouté M., Carrard J., Alvarez-Simon D., Tsicopoulos A., de Nadai P. The aryl hydrocarbon receptor in asthma: friend or foe? *Int. J. Mol. Sci.*, 2020, vol. 21, no. 22, pp. 8797. DOI: 10.3390/ijms21228797

15. Wang E., Tu W., Do D.C., Xiao X., Bhatti S.B., Yang L., Sun X., Xu D. [et al.]. Benzoo(a)pyrene Enhanced Dermatophagoides Group 1 (Der f 1)-Induced TGFβ1 Signaling Activation Through the Aryl Hydrocarbon Receptor-RhoA Axis in Asthma. *Front. Immunol.*, 2021, vol. 12, pp. 643260. DOI: 10.3389/fimmu.2021.643260

16. Yanagisawa R., Koike E., Takano H. Benzoo[a]pyrene aggravates atopic dermatitis-like skin lesions in mice. *Hum. Exp. Toxicol.*, 2021, vol. 40, suppl. 12, pp. 269–277. DOI: 10.1177/09603271211036123

17. Solonin Yu.G., Bojko E.R. Medical and physiological problems of the Arctic. *Izvestiya Komi nauchnogo tsentra UrO RAN*, 2017, no. 4 (32), pp. 33–40 (in Russian).

18. Dolgikh O.V., Starkova K.G., Alikina I.N., Chelakova Yu.A., Guselnikov M.A., Nikonoshina N.A. Markers of immune regulation in children exposured to aluminum. *Vestnik Permskogo universiteta. Seriya: Biologiya*, 2019, no. 1, pp. 96–100. DOI: 10.17072/1994-9952-2019-1-96-100 (in Russian).

19. Alikina I.N., Dolgikh O.V. Modification of immunocytes viable parameters in children associated with combined exposure to chemical technogenic and extreme climatic factors. *Health Risk Analysis*, 2021, no. 3, pp. 129–135. DOI: 10.21668/health.risk/2021.3.12.eng

20. Shchegoleva L.S., Sidorovskaya O.E., Shashkova E.Y., Nekrasova M.V., Balashova S.N. The Adaptive Immune Status in Representatives of Various Social and Professional Groups of Inhabitants of the European North of the Russian Federation. *Ekologiya cheloveka*, 2017, vol. 24, no. 10, pp. 46–51. DOI: 10.33396/1728-0869-2017-10-46-51 (in Russian).

Dolgikh O.V., Nikonoshina N.A. The risk of imbalance in the population composition of lymphocytes and specific sensitization in children living under exposure to airborne benzo(a)pyrene in the Arctic zone of Russia. Health Risk Analysis, 2023, no. 4, pp. 68–75. DOI: 10.21668/health.risk/2023.4.06.eng

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