

Immune and Interferon Status in Schoolchildren Living in Cities with Different Anthropogenic Load

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Examinations of 6-11-year healthy children living in industrial cities of the Orenburg region revealed a close relationship between ecological status of the territory and some immunity parameters such as immune deficiency, interferon content, and formation of postvaccinal immunity with live measles vaccine. The most pronounced changes in the immune status and decreased postvaccinal immunity were found in a city with the greatest anthropogenic load. Changes in interferon status were similar in all cities: a 2-fold increase of serum interferon and suppressed production of interferon- α and interferon- γ .

Key Words: *anthropogenic load; pollutants; immune deficiency; interferon system; children; postvaccinal immunity*

Defense and, probably, pathogenetic role of the immune system in the development of ecologically induced pathologies is beyond doubt [4]. Changes in the immune and interferon systems in populations living in cities with different anthropogenic load are less studied.

The purpose of our study was to analyze the effects of chemical atmospheric pollutants on the immune system and interferon (IFN) status in schoolchildren living in industrial cities of the Orenburg region.

MATERIALS AND METHODS

The study was carried out in Orenburg and Novotroitsk. Serum levels of IgA, IgM, and IgG were measured by immunodiffusion test, IgE by enzyme-linked immunosorbent assay using a Vektor-Best kit (Novosibirsk), and the content of circulating immune complexes (CIC) by polyethylene glycol precipitation. Lymphocyte subsets (CD3, CD4, CD8, CD4/CD8,

CD16, and CD19) were evaluated by flow cytometry (Biorad Bryte HS) using the corresponding monoclonal antibodies (Calted). IFN status was evaluated by serum contents of IFN, IFN- α , and IFN- γ [1].

Antibodies to measles virus were detected by passive hemagglutination test using commercial diagnostic kits. Schoolchildren aging 6-11 years were examined. All children were vaccinated and revaccinated with live measles vaccine in accordance with the current vaccination schedule. Mean body length (128.58 ± 1.59 cm) and weight (26.36 ± 1.04 kg) corresponded to physical development of healthy children [3].

For evaluation of the degree of immune deficiency (DID), the percentage of deviation from the normal was calculated for each immunity parameter in all children [2].

RESULTS

Motor transport, petrochemical and gas industry, power stations, and construction industry are the main sources of air pollution in Orenburg and metallurgical works and construction industry are the sources of pollution in Novotroitsk. Industrial waste exhaust in

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Orsk (South Ural Nickel Plant and petrochemical plant) also contribute to air pollution in Novotroitsk.

Comprehensive hygienic evaluation showed a higher summary anthropogenic effect on atmospheric air and deposition media in Novotroitsk. The primary pollutants in both cities are dust, NO₂, nickel, chromium, tin, cobalt, vanadium, and cadmium compounds. Specific priority pollutants in Orenburg are formaldehyde and copper compounds and in Novotroitsk phenol, ammonium, and beryllium and molybdenum compounds. Results of monitoring of deposition media (soil and snow) showed a higher level of contamination with nickel, chromium, cobalt, and manganese compounds in Novotroitsk and with copper compounds in Orenburg according to all methods of control. Atmospheric exhaust per resident is 5-fold higher in Novotroitsk than in Orenburg, which is due to permanent sources of pollution.

No changes in the composition and levels of neutrophils, eosinophils, lymphocytes, and monocytes were detected in Orenburg children. The leukocytic formula was virtually normal (Table 1). Analysis of the immune status (Table 1) showed a significant decrease in the absolute and relative content of T helpers (CD4), normal content of T suppressors (CD8), decreased CD4/CD8 ratio, normal levels of B lymphocytes (CD19) and natural killers (CD16). The concentrations of IgA, IgG, and IgM were markedly increased, while that of IgE was normal.

Almost all immunity parameters in Orenburg children indicated I-II degree of immune deficiency (DID). The mean DID for all the studied parameters in Orenburg was 35.5%.

Antimeasles antibody log titer was 0.85±0.19 (30% children were seronegative); antibody titers varied from 1:10 to 1:40.

Eosinophilia ($p<0.05$) and monocytosis ($p<0.05$) in the presence of normal absolute and relative counts of lymphocytes and neutrophils were detected in the Novotroitsk children (Table 1). The absolute count of T helpers was decreased ($p<0.05$), that of T suppressors normal, CD4/CD8 ratio decreased, and the count of B lymphocytes (CD19) decreased ($p<0.001$). The content of IgE sharply increased (12-fold vs. the norm, $p<0.001$), while the levels of IgA, IgG, and IgM were normal.

Immunity parameters of children in Novotroitsk were within 2-3 DID. The mean DID value for all studied parameters in Novotroitsk was 62.7%.

Logarithms of antimeasles antibody titers were 0.60±0.17 (40% seronegative children, the rest had the minimum protective titer of antimeasles antibodies -- 1:10).

Similar changes of interferon status were observed in both cities: 2-fold increase of circulating (serum) IFN and suppressed production of IFN- α and IFN- γ , the degree of increase in serum IFN being virtually the same in both cities. As for IFN- α and IFN- γ , their

TABLE 1. Immune Status of Children in Orenburg and Novotroitsk ($M\pm m$)

Parameter	Norm	Orenburg	Novotroitsk
Leukocytes, 10 ⁹	4.97±0.11	5.05±0.13	5.32±0.18
Lymphocytes, 10 ⁹	2.26±0.05	2.26±0.06	2.41±0.09
%	45.45±0.64	44.70±0.79	45.40±1.11
CD3, 10 ⁹	1.32±0.10	1.12±0.06	1.32±0.12
%	58.4±4.1	49.64±2.18	54.34±3.66
CD4, 10 ⁹	1.12±0.20	0.63±0.05**	0.77±0.09
%	49.4±7.7	28.00±1.85**	31.60±2.63**
CD8, 10 ⁹	0.48±0.03	0.50±0.03	0.51±0.04
%	21.3±1.4	22.28±1.61	21.24±1.62
CD4/CD8	2.3±0.3	1.35±0.18**	1.53±0.14**
CD19, 10 ⁹	0.24±0.05	0.20±0.02	0.13±0.02**
%	10.7±0.3	8.87±0.98	5.48±0.89*
CD16, 10 ⁹	0.28±0.05	0.32±0.04	0.25±0.01
%	12.5±1.5	14.38±1.73	10.56±0.55
IgM, g/liter	1.17±0.03	1.61±0.16**	1.42±0.16
IgA, g/liter	1.07±0.03	1.71±0.26**	1.46±0.22
IgG, g/liter	10.41±0.18	14.28±1.07**	10.77±0.52
IgE, U/ml	50.0±5.0	67.35±17.74	727.72±307.23*

Note. * $p<0.01$, ** $p<0.05$ compared to normal.

TABLE 2. Interferon Status of Healthy Children in Orenburg and Novotroitsk ($M \pm m$)

Parameter	Norm	Orenburg	Novotroitsk
Serum IFN, U/ml	≤ 4	7.80 ± 0.81	7.20 ± 2.15
IFN- α , arb. units	$\geq 16-64$	9.49 ± 1.12	13.70 ± 3.31
IFN- γ , arb. Units	$\geq 8-32$	7.70 ± 0.92	12.20 ± 2.0

production was drastically increased in both cities, the greatest drop being observed in Novotroitsk.

Analysis of interferon status and changes in immunity function and formation of postvaccinal immunity showed that IgM, IgG, IgE, and IgA concentrations, total content of T lymphocytes, counts of T helpers, T suppressors, B lymphocytes, and natural killers virtually did not correlate with the titer of antimeasles the antibodies (coefficient of correlation -0.1 to 0.2).

Logarithm of antimeasles antibody titer was in close inverse correlation with DID (Pierson correlation coefficient -0.82).

In Orenburg, changes in immune and interferon status led to disorders in the formation of postvaccinal immunity (30% children vaccinated in accordance with routine schedule remained seronegative), which increased the incidence of infections monitored by specific prevention. The detected disorders in protection from infection seem to manifest during the early inducible response: natural killers were not activated by IFN- α produced by monocytes/macrophages and by IFN- β produced by fibroblasts, and hence IFN- γ synthesis by natural killers was impaired. The second stage of disorders is observed during adaptive immune

response. Suppressed production of IFN- γ leads to impairment of T cell (CD4) differentiation, specifically of T2 helpers, and subsequent impairment of humoral immunity, including the postvaccinal.

In Novotroitsk, the detected disorders in immunity and interferon status were aggravated by pronounced allergization under the effect of pollutants, which closed the circle of functional relationship between immunity and IFN systems, this still more deteriorating the formation of postvaccinal immunity (40% children vaccinated with live measles vaccine remain seronegative and the rest 60% have low protective titers of antibodies, no more than 1:10). Therefore, healthy children living in industrial cities with different degree of anthropogenic load develop more serious disorders in immune status in comparison with the regional norm (2nd-3rd DID). The most pronounced changes in the immune status (DID=62.7%) and decreased postvaccinal immunity were observed in Novotroitsk, a city with the highest anthropogenic load.

A close relationship was revealed between ecological status of residence territory, severity of immune insufficiency, IFN status, and formation of postvaccinal immunity.

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