

TNF $\alpha$ ) and lymphokines of Th1-type (IFN $\gamma$  and IL-2) were studied in serum of patients with chronic obstructive and nonobstructive bronchitis on the background of secondary immunodeficiency state (IDS), also patients with subacute and chronic rheumatoid arthritis (RA) in the course of immunorehabilitation (IR). Disorders in activation processes of immunocompetent cells in peripheral blood of patients with chronic bronchitis (CB) were revealed that manifested in a decreased quantity of activated T-lymphocytes expressing CD25 and CD45RO antigens, as well as significant increase in the number of CD95-cells. The levels of IFN $\gamma$  and IL-2 were shown to decrease in blood serum of patients with CB, thus evidencing lower functional activity of Th1. Proinflammatory cytokines were demonstrated to prevail in blood of these patients. A step-by-step scheme for IR of CB patients with secondary IDS is suggested which can be also applied when treating patients with other immunopathological states. High efficiency of combined application of immunomodulators for system and local use in patients with CB of various severities was shown.

It was shown that RA patients are characterized by an elevated expression of activation markers on the surface of T-lymphocytes (CD25 and HLA-DR), significant increase in the number of activated CD45RO-bearing T-memory cells and CD95-cells thus evidencing increased readiness to apoptosis. Direct correlation between the number of T-lymphocytes which express the marker of prolonged activation (HLA-DR) and duration of the disease in RA patients was established. It was shown that in serum of RA patients, proinflammatory cytokines prevail. Positive correlation between the levels of IL-1 $\beta$  and IL-6 in serum and activity of the process was revealed.

Immunological monitoring at all IR stages of IDS patients was substantiated. The level of TNF $\alpha$  was shown to positively correlate with the number of CD95-cells in patients with chronic pathologic processes. Comprehensive clinical immunological analysis of a huge amount of clinical materials allowed elaborating technical approaches and tactics of IR of patients with disorders in immune system. It was shown that the choice of immunomodulators, scheme and methods of IR are determined by peculiarities of the clinical course of the disease, its severity, activity of inflammation process and immune state indices.

Results of ambulatory and sanatorium-resort IR programs were analyzed. They proved to be more efficient as compared to routine pharmaceutical and therapy measures. It was demonstrated that these complex IR programs should include adequate basic medicamentous therapy, set of immunomodulators of directed action, methods of nonmedicamentous treatment, as well as resort and preformed physical factors taking into account clinical immunological and pathogenic peculiarities of a person at every stage of IR. It was shown that step-by-step IR restores not only the number of regulatory immune cells, but also their

functional activity and the level of proinflammatory cytokines which play an important role in the chronic inflammatory processes. It also provides stable clinical remission. It was demonstrated that prolonged, rational, complex, step-by-step IR allows to decrease the number of recurrences (by 95-98% in average), prolong remission by 4-to 5-fold, reduce drug uptake and improve ability for work and quality of life.

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#### IMMUNOLOGICAL ADAPTATION OF NEWBORN INFANTS WITH RESPIRATORY DISTRESS-SYNDROME OR PNEUMONIA

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The main peculiarities of neonatal immune system are:

1. The prevalence of immature CD5+ B-lymphocytes with high expression of sIgM and lack of sIgD which are able to produce polyreactive IgM, IgG1 and IgG<sub>3</sub>; massive antigen binding with sIgM leads to immature B-cell apoptosis.

2. Low expression of CD40L on neonatal T-lymphocytes decreases their ability to differentiate to Th1 and to intensify macrophage reactions, to cooperate with B-cells and to be typically switch immunoglobulin classes synthesis.

3. Insufficiency of B7 expression on antigen-presenting cells (APC) which leads to non-professional antigen presentation to naive T-cells. Ratio of professional and non-professional APC has influence on priming or tolerance as a result of neonatal immune response. Small amounts of antigen can interact with a few mature B-cells and can be a base for specific humeral immunity development.

4. Heterogeneity of CD4+ lymphocyte subpopulation, the priority of CD45RA+ naive T-cells which act as suppression inductors and produce mainly interleukin-2.

The aim of our research work was to investigate dynamical changes of main immunological parameters (such as IL-1, TNF- $\alpha$ , IL-4, TGF- $\beta$  serum concentrations (ELISA), lymphocyte phenotype (flow cytometry) and chemiluminescent response of peripheral blood phagocytes) during the early postnatal period in physiological conditions and in infants suffered from respiratory distress-syndrome (RDS) or pneumonia. We investigated 48 full-term newborn infants from moderate and high risk pregnancies during the first month of life.

It was found that serum levels of IL-1 $\beta$  in cord blood of healthy neonates from moderate risk preg-

nancies were significantly higher than in peripheral blood of healthy adults ( $491,4 \pm 49,9$  pg/ml versus  $277,5 \pm 64,4$  pg/ml respectively;  $p < 0,05$ ) but IL-4 serum concentrations in cord blood were significantly lower than those in blood of adults ( $27,4 \pm 10,2$  pg/ml versus  $126,3 \pm 27,2$  pg/ml respectively,  $p < 0,05$ ).

During the first week of life in physiological conditions serum levels of proinflammatory cytokines and IL-4 significantly increased in comparison with cord blood levels. CD3+ and CD4+ cell numbers had the same dynamics while the number of CD8+ cytotoxic T-lymphocytes significantly decreased. The level of zymozan-induced chemiluminescence of peripheral blood leukocytes became significantly lower till the 7th day of life in comparison with cord blood. The values of immunological parameters under the physiological conditions were different from those situations when early postnatal period was complicated with respiratory distress-syndrome (RDS) or pneumonia (significantly lower serum levels of IL-I and TNF, reduced absolute numbers of CD3+, CD4+, CD8+ and B-cells. significantly higher level of spontaneous chemiluminescence in peripheral blood of neonates suffered from RDS or pneumonia versus healthy infants on the 5th-7th day of life. Recovery from pneumonia or RDS was accompanied with restoration of pro- and anti-inflammatory cytokine balance, elevation of absolute lymphocyte number and serum IgM level, reduction of natural killer number and level of expression of CD25+ receptor to IL-2 as well as normalization of spontaneous CL level.

So we describe the mode of normal early postnatal immunological adaptation in healthy full-term newborn infants and immunological distress-syndrome in neonates with RDS or pneumonia. The data are important for the further decisions concerning immunological intervention in neonatal period.

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#### **TERRITORIAL HEALTH DIFFERENCIES IN RUSSIAN FAR EAST POPULATION**

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The health of population is a biosocial phenomenon, as it depends both on the body features of separate people and external conditions. That is why the health level can be thought of as a factor of adaptation of a concrete population group to natural and socioeconomic environment of the territory reflecting how the given environment is comfortable for normal life activity of this group of people [1].

To study the Russian Far East population health we used the factors of life expectancy at birth (LE), men and women separately, in the rural and urban areas, and infant mortality.

The population health and territorial difference definition integral estimations were carried out on the basis of the health index calculated with the help of four LE factors and the infant mortality factor on the method of linear scaling. It is based on the definition of referential points (maximum and minimum values of indicators) and shows the position of a separate region between them. First, the calculation of special indexes on every factor is performed by the formula:

$$Y = (X - X_{\min}) / (X_{\max} - X_{\min}), \text{ to calculate the LE}$$

$$Y = (X_{\max} - X) / (X_{\max} - X_{\min}), \text{ to calculate the infant mortality,}$$

where Y – is a special index, X – the factor of this or that region,  $X_{\min}$  and  $X_{\max}$  – referential points [3]. The Y value varies anywhere from 0 to 1. Zero corresponds to the worst complex estimation, and 1 – to the best one.

The same minimum and maximum values (25 and 85 years accordingly) were chosen as the LE factor referential points. The smallest and largest values of the given factors were chosen as the minimal and maximal referential points for infant mortality in Russia in 2006 – 4,7 (St.-Petersburg) and 33,0 (Koryak AD) per 1000 of newborns accordingly. The spread in values of the chosen factors varied from 1,1 to 3,1 times.

The LE territorial differences manifest themselves considerably stronger in the rural area. A most vivid demographic feature of the FEFD subjects compared to average Russian factors is a tragically low rural area female LE level (Russia – 71,8 years). Even in the safest Republic of Sakha (Yakutia) in the Far East it is lower than the average Russian one (71,3 years). The rural area male LE in 2006 in the majority of FE regions, exclusive of the Republic of Sakha (Yakutia) – 60,2 years, is lower than the average Russian factor. The infant mortality factors in 2006 in the FE regions are higher than the average Russian one (10,2%) and vary from 10,6% in the Republic of Sakha (Yakutia) to 33,0% in the Koryak AD.

When calculating the LE index, first, we calculated and then summarized the indexes on separate components (men and women in town and village) weighted  $\frac{1}{4}$ . At the second stage the final health index was calculated as an arithmetic middling of the two special LE indexes and infant mortality.

We assumed that the health index maximum value fell on Sakha (Yakutia) – 0,73, the minimum value – 0,26 – on the Koryak AD. The difference between the minimum and maximum values of the health indexes among the Far East regions makes 2,8 times.