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**THE BALANCE OF REGULATORY CYTOKINES IN THE BLOOD SERUM IN THE OFFSPRING OF RATS WHO WERE KEPT ON A HYPOCALORIC DIET DURING PREGNANCY**

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**Introduction.** Pancreatic pathology is one of the urgent problems of medicine and occupies a significant place in the structure of morbidity in children and adults. Every year there is a tendency to increase the incidence not only in Ukraine and around the world, especially in highly developed countries.

What factors have the main influence on the occurrence of damage to the pancreas is not fully understood. It is known that the complex of local and systemic protective responses develops in the organism in response to exogenic and endogenic influences of different nature. Activation of a non-specific link in the systemic immune response is directly related to local, inflammatory tissue damage.

 Interaction of the immune and neuroendocrinal systems is provided from the side of the immune system, mainly with help of cytokines by changing the concentration of which it is possible to track the direction of the realization of the immune response. The peculiarity of the action of cytokines is their specificity, broad spectrum and pleiotropic biological action, which depends on their effect on many cell types and the type of target cells.

 Taking into consideration the scattered data of the literature, dedicated to the peculiarities direction of immune responses, which arise against the background of pathological influences during post-natal development of the organism, the clarification of the role of the immune system in the mechanisms of damage of the pancreas structure and function is important.

**Purpose.** Determination of the content of cytokines IL-12 and IL-4 and their ratio in blood serum in the offspring of rats that were kept on a hypocaloric diet during pregnancy.

**Materials and methods.** The scope of the study included experiments on the offspring of rats (the WAG/G Sto population) that received a hypocaloric diet during pregnancy due to an unbalanced diet with a reduced content of proteins and carbohydrates: 1-month-old (10 specimens) and 2-month-old rats (10 specimens). All the rats after their birth received a physiologic (balanced) nutrition and were in the usual conditions of a vivarium. The removal of animals from the experiment as far as they reached the age of 1 and 2 months by decapitation was made under anesthesia. The levels of interleukin-4 (IL-4) and interleukin-12 (IL-12) in the blood serum were determined by the immunoenzymatic - standard method. The results of the study are processed by means of the analysis package of Microsoft Excel program, Biostat.excel-2008 computer program.

**Results and discussion.** The important regulatory role of cytokines is known. IL-4 induces the proliferation of T-helpers of the 2-nd type (Th2) which mediate the reactions of humoral immune response (stimulation of B-lymphocytes and production of antibodies) and is also an antagonist of gamma interferon inhibiting the proliferation of T-helpers of the 1-st (Th1) type while IL-12 enhances the proliferation and differentiation of T-helpers of the 1-st (Th1) type which mediate the reactions of cellular immunity and at the same time inhibit the proliferation of T-helpers of the 2-nd type (Th2).

In the blood serum of 1-month-old infant rats, the decrease of the content of not only IL-4 but also IL-12 was observed that mediately indicates the disturbance of functional activity of macrophages – the cells of effectors and modulators of an immune response, a source of regulatory cytokines (one of them is IL-12) which are known to be in close cooperative interaction with Th potentiating the differentiation of Th1 followed by Th1 and macrophage mutual activation of each other. In the blood serum of 2-month-old infant rats the increase of IL-12 content and the essential (by 4 times) decrease of the average level of IL-4 compared with control.

The data obtained are indicative not only of the existence of an essential imbalance of regulatory cytokines in infant rats, as compared with control, and thus about the prevalence of a nonspecific cellular link of the immunologic reactivity increases the risk of developing chronic pancreatitis in infant rats in the future, and about that the hypocaloric nutrition of female rats during pregnancy is one of the important risk factors for the development of pancreatic pathology (exo- and endocrine apparatus) in their offspring in the future, despite a balanced diet after birth.

**Conclusions**

1. In 1-month-old infant rats that were born by the mothers that had a hypocaloric diet during their pregnancy despite their normal nutrition in the blood serum the inhibition of immunologic reactivity was revealed to what the decrease of both IL-4 and IL-12.

2. In the blood serum of 2-month-old infant rats, in the dynamics of cytokine content, unidirectional changes are observed: an increase in the content of IL-12 and a decrease in the content of IL-4, but the changes are more pronounced.

3. The imbalance of regulatory cytokines offspring indicates the participation of a specific (Th 1) and nonspecific (macrophagic) cellular link of immunity to the pathogenesis of the pancreas damage, which is possibly bound to the disturbance of activity of main effectors and modulators of an immune response and a source of regulatory cytokines - macrophages.

**Keywords.** cytokines, nonspecific immunologic reactivity, pancreas