ABSTRACT:
The morphological features of immune system development of the offspring born to female rats with chronic hepatitis were studied. Maternal heliotrin hepatitis contributed to rat pups' mortality increase on 1-3 days after birth. Disorders in development of thymus in peripheral immunal organs have been established during the period of early postnatal development.

Keywords: hepatitis, mother, offspring, development, thymus, spleen. Peyer's plaques.

INTRODUCTION:
The frequency of various extragenital diseases among women of childbearing age has been increasing recent years. First of all, this refers to lesions of the hepatobiliary system due to past viral hepatitis [3].

Chronic lesions of the mother's liver cause various changes in hematological parameters, cellular and humoral immunity in the offspring [4,5]. It was hard to find an information about the way chronic maternal liver damage affects the structural foundations of progeny immunogenesis organs formation in available literature. Meanwhile, a solution to this problem would make the mechanisms of children immunodeficiency born to mothers with liver lesions understandable and would lead to substantial preventive collection and prevention of possible diseases of children.

The purpose of the study was to explore in an experimental way the effect of chronic heliotrin hepatitis on female rat reproductive function and the structural state of the immune system organs of their offspring.

MATERIALS AND METHODS:
The experiments were carried out on 50 sexually mature females of white outbred rat weighing 170-190 g. Animals were divided into 2 groups (25 rats each): experimental and control. A model of heliotrin hepatitis was obtained by weekly injection of 0.05 mg of heliotrin per 1 g of body weight for 6 weeks. The control group received sterile saline instead of heliotrin. After 10 days after the last injection, males were joined to the females, which pregnancy was observed subsequently.

There was a firm evidence of significant negative effect of toxic hepatitis on fertility and pregnancy. All animals of the control group became pregnant which successfully ended with childbirth. 84% of rats in the experimental group got pregnant, 64% of those pregnancies ended with childbirth and 8% miscarriages. The rest died during pregnancy.

The average number of pups of one mother in the control group was 9.7 ± 0.5, though in the experimental group 6.3 ± 0.6. With toxic hepatitis in the mother, the postnatal mortality of the offspring increased to 39.6% (4.2% in the control). Moreover, the highest mortality rate (28.7%) was observed on the 1st - 7th day after birth (3.4% in the control). The dead pups were excluded from the experiment, hi total, 84 cubs from control females and 61 from females of the experimental group were included in the studies.
The pups were dissected under mild ether anesthesia on the 1st, 3rd, 7th, 14th, 21st, and 30th days after birth. Pieces of the thymus, mesenteric lymph nodes, spleen and Peyer's patches were fixed in 12% neutral formalin or Buen's fluid and after the corresponding wiring were poured into paraffin. Sections 5 thick were stained with hematoxylin and eosin and used for morphological and morphometric studies.

According to morphological studies the thymus of the newborn rat pups of the control group is quite formed. The cortical and medulla can be clearly differentiated. Cells distribution density in the cortical substance is greater than in the brain. Thymocytes, macrophages and reticuloepithelial cells neatly differentiate among other cells. Reticuloepitheliocytes predominate in the medulla and much less thymocytes. Gassal bodies are very rare.

Lymph nodes are represented by diffuse accumulations of lymphocytes and other mononuclear cells in the reticular stroma. Lymphoid follicles are not formed yet. The absence of formed structural-functional zones is also typical for the other peripheral organs of immune system. The spleen in this period is mainly an organ of erythro- and thrombocytopoiesis. The organ parenchyma mainly consists of red pulp, in which numerous erythroblastic islets are located. The former white pulp is absent, hi Peyer's plaques, diffuse distribution of mononuclear cells throughout the stroma is also observed in the absence of clear boundaries of lymphoid follicles.

Differentiation of the cortical and medulla in the lymph nodes is noted on the 7th-14th days of the postnatal period. Lymphoid follicles form at the same time.

Formation of lymph nodes and the differentiation of their marginal and periarterial zones in the spleen are also observed. Lymphoid follicles form in Peyer's plaques.

Immunogenesis peripheral organs structural and functional zones' formation is completed on the 21st-30th day of postnatal ontogenesis, where the processes of lymphocyte, plasmacytopoiesis and antibody production occur.

Chronic hepatitis in the experimental group leads to severe structural disorders in the processes of postnatal organ formation in the immune system of the offspring.

Thymus of newborn rats evidently differentiate into cortical and medulla. However, the distribution. The scientific heritage density of cells in the cortical substance is markedly reduced.

He comparison with the control group, the number of lymphoblasts decreased by 15%, small lymphocytes by 20%. This trend continued in the subsequent periods of thymus postnatal development. Noteworthy is the increase in the number of destructive thymocytes, which at various times after birth were 2-3 times higher than the indices of the control group. Along with this, large macrophages with dense inclusions in the cytoplasm were found more frequently on the thymus sections of the experimental group than in the control, apparently also being a sign of enhanced thymocytolysis.

The severity of the described changes decreased only by the 30th day of postnatal ontogenesis.

During the peripheral organs' study of experimental pups' immune system, a significant delay in the postnatal formation of structural and functional zones was noted. On the 7th—14th days of the experiments the lymph node parenchyma consisted mainly of diffuse lymphoid tissue without clear boundaries of the cortical and medulla. Subcapsular sinuses were significantly
expanded. The absence of formed lymphatic follicles during this period is also typical for the spleen and Peyer's plaques. On the 14th day only the formation of small lymphoid follicles in peripheral organs was observed in rat pups of the experimental group, hi the contrary, sufficiently formed lymphatic follicles were detected in the control group during this period. Even by the 21st day of the postnatal period the lymphoid tissue of the lymph nodes, spleen, and Peyer's plaques remained hypoplastic in rat pups of the experimental group and the borders of the various structural zones of the lymphatic follicles were fuzzy. Postnatal formation of lymphoid tissue depends on many internal and external factors, including environmental antigens, which are quite important [1]. Along with exogenous antigenic exposure significant acceleration in lymphatic follicles formation and differentiation of their structural and functional zones was noted [2.6.7]. However, the natural formation of lymphoid tissue under the environmental antigen influence can occur only under the normal process course of embryonic bookmark and intrauterine development of the immune system organs. Undoubtedly, chronic hepatitis accompanied by a number of metabolic disorders in the body changes the natural course of embryonic development of organs and systems, including the immune system.

These violations continue to manifest themselves in the postnatal period of life. Our data indicate a significant delay in the postnatal formation of the immune system organs with toxic hepatitis in the mother.

CONCLUSION:
1. Chronic heliotrin hepatitis in female rats leads to postnatal mortality of offspring increasing by more than 3 times, with the highest mortality observed on the 1st - 3rd day after birth.
2. Rat pups born to mothers with chronic hepatitis suffer significantly slowed down lymphoid tissue formation of peripheral immune organs on the background of thymus hypoplasia.

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