INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

IJIMM, Volume 1, Issue 2, 2023 ISSN: XXXX-XXXX
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

Morphological Changes in the Thymus of Rats Exposed to the Endocrine Disruptor Dichlorodiphenyltrichloroethane in the Prenatal and Postnatal Periods

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Abstract: The study of the morphogenesis and histophysiology of the organs that carry out the immune defense of the body has gained particular importance in recent decades due to the increase in the number of allergic, autoimmune and lymphoproliferative diseases. An analysis of the literature shows that the increase in the number of allergic and autoimmune diseases that began after the end of World War II occurred in parallel with an increase in the production and consumption of various classes of chemical compounds. Many of them have the properties of endocrine disruptors - substances that, acting in negligible doses, disrupt any stages of the synthesis and secretion of hormones and their interaction with target cells. Endocrine disruptors have various effects on the immune system. In the scientific literature, there is information about the immunosuppressive effect of disruptors, as well as about the enhancement of inflammatory processes and autoimmune reactions by some of them.
Keywords: thymus, endocrine disruptors, morphology, prenatal and postnatal period

Relevance. Changes in the prenatal and postnatal development of the immune system organs under the influence of endocrine disruptors can also be the causes of impaired functioning of the immune system. Since steroid and thyroid hormones have a significant effect on the morphofunctional state of lymphoid organs and the implementation of immune responses, endocrine disruptors can cause changes in the morphogenesis of immune defense organs. An increase in the number of autoimmune processes has led to an increase in the interest of researchers in the effect of endocrine disruptors on the development and functioning of the thymus. Of the known endocrine disruptors, persistent persistent universal pollutants are of the greatest interest, of which the most common is dichlorodiphenyltrichloroethane (DDT). It was revealed for the first time that the influence of low doses of DDT in the prenatal and postnatal periods of ontogenesis leads to morphological and cytophysiological changes in the rat thymus. It has been established that in the prenatal period, the reticuloepithelial and connective tissue components of the stroma are most sensitive to the disruptive effect of DDT. It has been shown that the greatest changes in postnatal thymus morphogenesis appear in the pubertal period. It has been established for the first time that the impact of low doses of DDT on a developing organism changes the dynamics of proliferative processes in the thymus parenchyma and slows down the development of involutive changes.

A new direction in the research of endocrine disruptors is the study of their effect on the immune defense organs. The immune and endocrine systems function together in response to external influences, and the violation of their signaling systems may underlie some diseases. The available information about the mechanisms of action of endocrine disruptors suggests that they can exert immunomodulatory effects in various ways. First of all, this is a violation of the signaling of steroid hormones. The results of in vitro and in vivo studies show that endocrine disruptors are able to interfere with the implementation of various signals at different levels of immune defense, and thereby change the proliferation, differentiation, production of cytokines of cells, modulating the reactions of both cellular and humoral immunity.

Epidemiological studies show that there is a relationship between exposure to endocrine disruptors and an increase in the number of allergic diseases, and this effect may be due to a change in the development of the immune system of children, since exposure to endocrine disruptors begins in the prenatal period.

The impact of DDT on the body can begin even at the stage of gametogenesis. DDT has a low molecular weight and high lipid solubility. As a result, it easily overcomes the hemato-placental barrier, influencing the development of the embryo. Correlations between maternal and cord blood levels of DDT support these findings.

With birth, the impact of low doses of DDT on the body does not stop, but even intensifies during the first year of life. The main source of DDT for newborns is breast milk. According to researchers, in children of the first two years of life, the level of DDT and its metabolites in the blood is higher than in mothers. Thus, breastfeeding becomes a significant risk factor for newborns, especially in regions with higher levels of DDT and its metabolites in the environment.

Methodology and research methods: Methodology and research methods are based on a comprehensive assessment of the morphological characteristics of the thymus cortex and medulla and cytophysiological parameters of thymocytes in rats that developed under the influence of an endocrine disruptor in the pre- and postnatal periods of ontogenesis. The terms of the study include the main periods in the development of an individual: neonatal, suckling, pubertal and postpubertal (the beginning of an active reproductive period), coinciding with the periods of development and the onset of involutive age-related changes in the thymus. The dosage and method of administration of the DDT solution are based on the analysis of regulatory documents regulating the content of DDT in food products and drinking water, as well as scientific literature on the features of DDT metabolism in the rat body. The dissertation research used morphological. histological preparations, immunohistochemistry with quantitative evaluation of results), cultural, radioisotope and statistical methods.

Results and discussion. The thymus of newborn rats in the control group consisted of two lobes. Outside, the thymus was covered with a capsule, from which connective tissue partitions departed, dividing the lobes into lobules. The cortex and medulla were well distinguished in the lobules. The cortical substance was formed by lymphocytes and accounted for two-thirds, the medulla, represented by reticuloepithelial cells, respectively, one-third of the lobule. The outer part of the cortex was composed of lymphoblasts. In some rats, a narrow, non-epithelial space was found under the capsule. Mitotically dividing lymphocytes were often observed in the cortex. The number of lymphocytes in 1 mm2 of the cortex was small. In the medulla, the content of lymphocytes was 1.7 times less than in the cortex. In the medulla, both individual reticular epithelial cells with increased cytoplasmic oxyphilia and thymic bodies were found. The overwhelming majority were thymic bodies of the 1st stage of development, consisting on average of 3 cells. Venous vessels were well visualized in the medulla. Their gaps were, as a rule, free. venous vessels were visualized.

Conclusion

A review of the data available in the scientific literature shows that the impact of low doses of DDT on a developing organism, in which it exhibits disruptive properties, on morphogenetic processes in the thymus, the acquisition of functional properties by thymocytes, and the development of involutive changes have not been studied. It is not known whether prenatal exposure to DDT can change the program of embryonic and postnatal histogenesis of the parenchyma and stroma of the organ. What is the contribution of the impact of the endocrine disruptor, which began in the prenatal or postnatal periods, to the formation, development and functioning of the thymus is also unknown. In what periods the thymus is most susceptible to the action of the endocrine disruptor has also not been established. To date, there is no doubt that the thymus is both an independent endocrine gland and an organ of immune protection, the development and functioning of which depends both on its own biologically active substances and on the action of various hormones. Exposure to low doses of DDT is ubiquitous, and as a result, it can cause

disturbances in the functioning of the immune system, primarily an increase in the number of allergic and autoimmune diseases.

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