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**Growth and formation of the adrenal cortex in the offspring under conditions of intrauterine exposure to pesticides through the maternal body
(Review article)**

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Abstract: One of the current problems of modern biology and medicine is the study of the state of the neuroendocrine system under various conditions. Numerous experimental and clinical observations have established that the neuroendocrine system undergoes significant changes during the individual development of the organism (B.V. Aleshin, F.Z. Meerson). In the adult body the development of adaptive reactions, in response to various influences (Petrov I.P., Boyko R.T.). Currently, the protection of the environmental health of the population is an urgent problem on a global scale. The predominant part of environmental pollutants are pesticides, without the use of which the prospective development of agriculture is impossible. According to the World Health Organization (WHO), between 500,000 and 2 million people worldwide are poisoned by pesticides each year, and 40,000 of these poisonings are fatal. The use of highly toxic organophosphorus or organochlorine pesticides is now banned or restricted and is being replaced by pesticides derived from pyrethroid, pyrazole and other classes. Their advantages are relatively low toxicity to animals and humans, high efficiency against insects when exposed to relatively small doses. It has been established that an important role in stress reactions caused by the action of damaging factors, in particular hypoxia, belongs to the cortical layer of the adrenal glands (V.N. Korostovtseva, I.D. Horizontov). The use of pesticides to increase crop yields on a global scale makes it extremely important to develop measures to prevent the negative effects of their effects on human and animal organisms.

Keywords: pesticides, pyrethroids, adrenal cortex, stress, postnatal development

Target: Identification of structural and functional features of early postnatal formation of the adrenal cortex in offspring produced under conditions of chronic maternal exposure to pesticides. At the present time, research works on the following priority directions of revealing the toxic effects of intrauterine and early postnatal exposure to pesticides continue in different countries of the world, including: development of ways to prevent endocrine-destroying effects of pesticides in the postnatal period based on the study of their mechanisms to determine the

concentration of marker hormones of the anterior pituitary, thyroid, and adrenal glands; to substantiate the morphological mechanisms of the toxic effects of small doses of pesticides in early postnatal ontogenesis; to identify the state of cell proliferation and apoptosis processes in the organs and tissues of the offspring under conditions of maternal exposure to pesticides; to improve the quality of life in different population groups through the formation of a healthy lifestyle and improvement of evidence-based methods of prevention, early diagnosis and pathogenetic treatment of the negative effects of intrauterine and early postnatal exposure to pesticides.

Studies of scientists from near (N.V. Yaglova, V.V. Yaglov, 2012) and far abroad (Pine M.D. et al., 2008; Mnif W. et al., 2011; Gore A.C. et al., 2015) showed the importance of exposure to endocrine-destroying modern pesticides in the pathogenesis of obesity, atherosclerosis, hypertension and ischemic disease, malignancies, fertility disorders and other [29; p.p.56-61. 91; p.p.1093. 134; p.p.2265-2303. 148; p.p.1243-1247]. Of these, pyrethroid pesticides represent for approximately one-quarter of the entire global insecticide market and are widely used in agriculture and public health [75; pp.7297-7305]. It is shown that several pyrethroid pesticides (lambda-cyhalothrin, deltamethrin) have an antiandrogenic effect, disrupting hormonal regulation of reproductive function [74; pp. 58-66. 143; pp. 794-800]. Evidence has emerged that the endocrine-disrupting effect of lambda-cyhalothrin is largely due to its antagonism to glucocorticoid receptors of steroid hormones [206; p.p.435-443]. The endocrine-destroying effect of lambda-cyhalothrin on the pituitary-thyroid axis has not been adequately studied and is manifested mainly as a decrease in the level of thyroid hormones in the blood [165; p.265-270. 179; p.876-885]. The other most common pyrazole pesticide is fipronil, which has high insecticidal activity at low doses and is widely used worldwide. [53; p.p.35-67]. Fipronil is another most common pesticide of the pyrazole class, which has high insecticidal activity at low doses and is widely used throughout the world [53; pp.35-67]. The endocrine-disrupting effect of fipronil is mainly manifested in the form of thyroid gland dysfunction and is associated mainly with the toxic action of its metabolites [77; pp. 3697-3710; 121; pp. 38-44. 123; pp. 51-57. 160; pp. 29-41. 172; pp. 5-34]. The works of Professors P.I. Tashkhodjaev (2006), T.I. Iskandarov (2008), G.T. Iskandarova (2004) and Doctor of Science M.A. Khamrakulova (2014) are devoted to toxicological and biochemical changes in acute and chronic poisonings with pyrethroid pesticides [7; pp.65-67. 8; pp.121-122. 18; pp.84-86. 25; p.70. 26; p.66]. It should be emphasized that the vast majority of studies on mechanisms and effects of modern pesticides on the endocrine system have been conducted on sexually mature animals or in adult humans. Nevertheless, it is the fetal and early postnatal periods that are the most critical stages of life in terms of development of severe consequences of pesticide exposure. Studying the effect of widespread modern pesticides on the growth and formation of endocrine glands would provide new data

on the pathogenesis of a number of diseases caused by pesticides in the prenatal or early childhood period. Unfortunately, this problem, which is of undoubted scientific and applied interest, still remains unsolved.

It is established that in the stress reactions caused by the action of damaging factors, in particular pesticides, the role belongs to the cortical layer of the adrenal glands as well (V.N. Korostovtseva, I.D. Horizontov). Affecting all types of metabolism, hormones of adrenal cortex ensure the maintenance of the internal environment of the organism and its adaptation to adverse conditions (M.I. Mityushev, O.I. Kirilov, A.A. Korolkov, V.P. Petlenko). At the same time, the timing and mechanism of adrenal cortex involvement in the adaptive reactions of the newborn organism remain insufficiently elucidated to date. There are especially few data in the literature on the mechanism of pesticide action on the structure and function of corticocytes in early postnatal ontogenesis (M.A. Zhukovsky et al A.I. Barkalaya, M.A. Verkhotin Research scientists from near (N.V. Yaglova, V.V. Yaglov, 2012) and far abroad (Pine M.D. et al., 2008; Mnif W. et al., 2011; Gore A.C. et al., 2015) showed the importance of exposure to endocrine-destroying modern pesticides in the pathogenesis of obesity, atherosclerosis, hypertension and ischemic disease, malignancies, fertility disorders and others. Of these, pyrethroid pesticides amount for about one-quarter of the global insecticide market and are widely used in agriculture and public health (Elhalwagy M. et al., 2015). A number of pyrethroid pesticides (lambda-cyhalothrin, deltamethrin) have been shown to have an antiandrogenic effect, disrupting hormonal regulation of reproductive function (DuG. et al., 2010; Orton F., et al., 2011). Evidence has appeared that the endocrine-disrupting effect of lambda-cyhalothrin is largely due to its antagonism to the glucocorticoid receptors of steroid hormones (Zhang J. et al., 2016). The endocrine-destroying effect of lambda-cyhalothrin on the pituitary-thyroid axis is poorly understood and manifests itself mainly as a decrease in blood levels of thyroid hormones (Saravanan R., et al., 2009; Tu W., et al., 2016). The other, most common pesticide from the pyrazole class, is fipronil. It has high insecticidal activity at low doses and is widely used worldwide (Bonmatin J.M. et al., 2015). The endocrine-destroying effect of fipronil is mainly manifested in the form of thyroid dysfunction and is mainly related to the toxic effect of its metabolites (Leghait J. et al., 2009, 2010; Roques B. et al., 2012; Ensminger M.P. et al., 2013; Simon-Delso N. et al., 2015).

The endocrine-destroying effects of modern pesticides in the Republic of Uzbekistan have been studied comparatively little. The works of Professor K.R. Tukhtaev (2012, 2014) show the effect of pesticides on the functional state of the thyroid and cortex adrenal glands. The works of Professors P.I. Tashkhodjaev (1993), T.I. Iskandarov (1999, 2002), G.T. Iskandarova (1998) and Dr. M.A. Khamrakulova (2016) are devoted to toxicological and biochemical changes in acute and chronic poisonings with pyrethroid pesticides. It should be emphasized that the vast majority of studies on the mechanisms and effects of modern pesticides on the endocrine

system have been conducted on sexually mature animals or in adult humans. Nevertheless, the fetal and early postnatal periods that are the most critical stages of life in terms of the development of severe effects of pesticide exposure. Studying the effect of widespread modern pesticides on the growth and formation of endocrine glands would provide new data on the pathogenesis of a number of diseases caused by pesticides in the prenatal or early childhood period. Unfortunately, this problem, which is of undoubted scientific and applied interest, still remains unsolved.

Conclusions: Chronic maternal exposure to low doses of pesticides during pregnancy and lactation leads to "endocrine-destroying" effects in the offspring in the early postnatal period.

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