

EFFECTS OF INTRAUTERINE LOW-DOSE CHLORPYRIFOS POISONING ON POSTNATAL DEVELOPMENT OF OFFSPRING.

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Conclusion. *The article presents the results of a study of the hypothalamic-pituitary neurosecretory system in the offspring of rats antenatally induced by the organophosphorus pesticide chlorpyrifos. It is indicated that the effect of chlorpyrifos on rats themselves during different periods of pregnancy and lactation causes various dose-dependent and time-dependent effects on the changes in the morphofunctional characteristics of the HPA axis. Disturbances in the development of the neuroendocrine system that arise in the antenatal period of ontogenesis have long-term negative consequences in postnatal life, as evidenced by the growth retardation of experimental rats, late observation, and high mortality due to antenatal disease.*

Keywords: *Prenatal stress, chlorpyrifos, ontogenesis, hypothalamic-pituitary neurosecretory system, vasopressin, oxytocin.*

Introduction. An acute stress reaction that expresses sympathetic activation. department of the autonomic nervous system. The hypothalamic-pituitary-neurosecretory and immune systems represent an adaptive response that allows the body to maintain its homeostasis in the face of adverse environmental changes. However, when stress factors act chronically, long-term activation of regulatory systems can lead to their maladaptation and have persistent health consequences (1; 4; 6; 8).

Exposure to stress antenatal or in early childhood may have more serious consequences because it may alter the development of brain regulatory systems and lead to long-term health consequences. It is well known that early life adversity can lead to long-lasting changes in physiology and metabolism, which in turn determine the risk of developing diseases in adulthood (3; 5; 7; [11](#)).

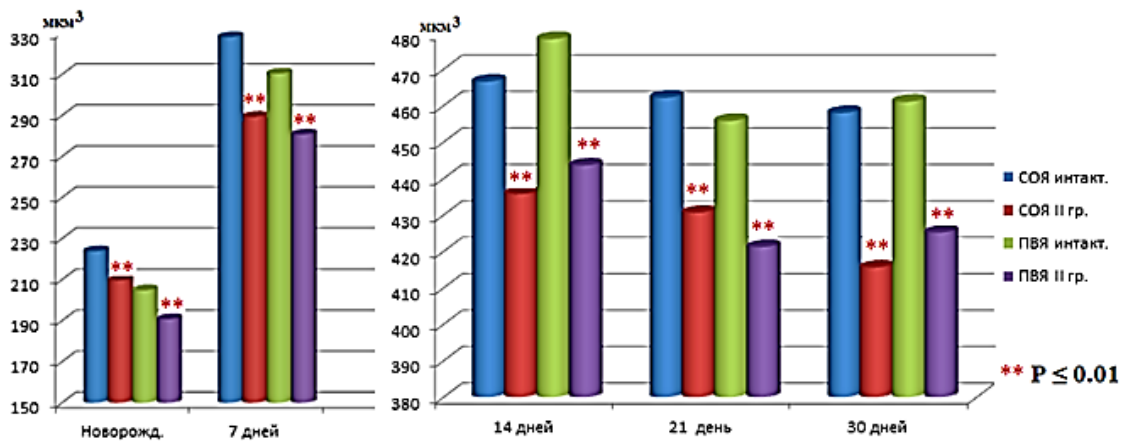
Purpose of the study: the basics of studying morphofunctional changes and features of the formation of the HPA axis in the offspring of animals adopted in accordance with international standards of the organophosphorus preparation chlorpyrifos.

Materials and methods: The study was conducted on outbred white rats weighing 180-200 g and their offspring at different periods of postnatal development. The animals were divided into 3 groups. The first group consisted of intact animals. In the 2nd and 3rd groups, rats were poisoned with chlorpyrifos during the entire period of pregnancy at doses of 1/50 and 1/100 LD₅₀, respectively. The animals were slaughtered on the 1st, 7th, 14th, 21st, 30th days after birth. Pieces of the brain, including the hypothalamus with the physical face, are fixed in hypoen fluid or according to Carnoy. After wiring in alcohol, the pieces were embedded in paraffin, then 5-7 μm thick sections were prepared from them. The sections were stained using one of the following methods: 1) cresyl violet according to Nissl; 2) paraldehyde fuchsin (PAF) according to Gomori-Gab; 3) chrome-kvass

hematoxylin. The study of the hypothalamic-pituitary neurosecretory system was carried out at the level of the hypothalamic nuclei (SON and PVN), median eminence and posterior lobe of the pituitary gland.

Research results. The most significant changes in the HPA axis were observed in offspring animals exposed to chlorpyrifos throughout pregnancy (in series 2 and 3 of experiments), especially when chlorpyrifos was administered at a dose of 1/50 LD50.

In addition to the existence in the hypothalamic-pituitary system in the group of rats, we noted pre- and postnatal death, phenomena of general hypotrophy and later observation of rats. It is likely that in these phenomena the processes of destruction and disintegration of the HPA axis in rats played no role.



Динамика роста объёмов ядер нейронов СОЯ и ПВЯ при отравлении хлорпирифосом на протяжении всего периода беременности в дозе 1/50 ЛД₅₀

	Newborn	7 days	14 days	21 days	30 days
Control	5.9 ± 0.3	14.4 ± 0.3	21.6 ± 0.5	28.1 ± 0.5	40.5 ± 0.6
II group	4.7 ± 0.4	11.3 ± 0.6	16.7 ± 0.7	22.4 ± 0.7	32.2 ± 0.9
Group III	5.2 ± 0.3	13.2 ± 0.4	18.7 ± 0.6	24.8 ± 0.6	35.7 ± 0.7

Table 2. Dynamics of body weight gain in rat pups

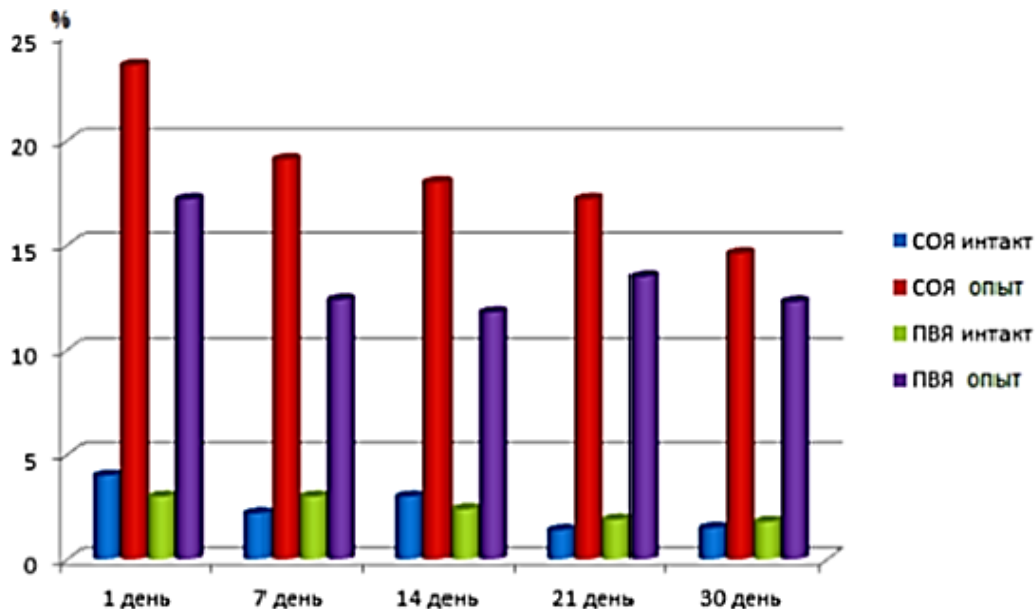


Table 3. The content of destructive forms of neurons in the hypothalamic nuclei upon administration of chlorpyrifos at a dose of 1/50 LD₅₀ throughout pregnancy.

Summary. Thus, chemical compounds on the one hand disrupt the activity in a balanced manner, various changes cause changes in metabolic processes, tissue and cellular metabolism during pregnancy, and such indirect effects can have a negative effect on the fetus. On the other hand, chemical substances can directly accumulate, deposit in the organs of the fetus, passing through the placenta (2; 9). The combination of such effects in the mother-fetus system is the basis of the pathogenetic mechanism of the perinatal system.

For the fetus, if its regulatory principles are imperfect, such a metabolic background can be the cause of abnormal development of organs and body systems that cannot be detected by generally accepted methods of studying embryotoxicity, but which can develop in the postnatal period. These changes are accompanied by long-term, sometimes permanent, disturbances of neuroendocrine and neurochemical signs of reactivity (10; 12). One of the most important factors in eliminating the effects of prenatal stress may be the function of the mother's adrenal gland (13; 14). The increased hormonal background of the matter can contribute to the pathological formation of receptors, which in the perinatal period are immature, plastic, and, therefore, the most vulnerable (2;3;15;). According to Karabaev A.G. (2022) and other authors, neuroendocrine imbalances are an important and responsible part of stress.

Conclusions

1. Poisoning of female rats with the organophosphate chlorpyrifos during different periods of pregnancy and lactation causes various dose- and time-dependent changes in the morphofunctional characteristics of the HPA axis.
2. Long-term, stronger (1/50 LD₅₀) exposure to the pesticide chlorpyrifos leads to delayed development of the HPA axis, rarefaction of cellular fields, and cerebrovascular accidents than with a lower dose (1/100 LD₅₀).
3. The reaction of SON neurons to the toxic effect of chlorpyrifos is more pronounced than the reaction of PVN neurons, which may indicate a greater sensitivity of SON components or a higher resistance of PVN neurons to the conservative, stable effect of this drug.

4. Long-term administration of small doses of chlorpyrifos (1/100 and 1/50 LD₅₀) to the body of pregnant females does not cause phase changes in the morphofunctional state of the HPA axis of the offspring, which are mandatory for sexually mature animals.

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