



THE EFFECT OF PESTICIDES ON THE STATE OF THE MICROVASCULATURE AND TISSUE STRUCTURES OF THE OVARY

Khozhanazarova Saulekhan Jubatirovna

Ph.D., Associate Professor of the Department of human anatomy and clinical anatomy of the Tashkent Medical Academy. Phone: +998-88-166-19-68.

Shamsiyev Shakhzod Jabbor ugli
Student of Tashkent Medical Academy

Article history:	Abstract:
<p>Received: 10th October 2022 Accepted: 10th November 2022 Published: 20th December 2022</p>	<p>The aim of the study is to study the postnatal morphogenesis of tissue structures and intraorganic vessels of the ovary of the offspring, under conditions of chronic toxic effects of the "Vantex" pesticide on the mother's body.</p> <p>Material and research methods. The experiments were carried out on white outbred rats. The animals were divided into 2 groups of 30 individuals each: group 1 (control) - intact animals, i.e. rat pups born from intact mother rats, group 2 - rats, which, in order to create a model of chronic pesticide poisoning</p> <p>Results: It has been established that chronic intoxication of the mother with the "Vantex" pesticide negatively affects the processes of postnatal growth, development and formation of the vascular tissue structures of the reproductive organs, in particular the ovary of the offspring, i.e. The pesticide "Vantex" has a reproductively toxic chemical. Chronic intoxication of the mother with the pesticide "Vantex" leads to the development of inflammatory-reactive changes in the vascular tissue structures of the ovaries in the early periods of postnatal development of the offspring.</p> <p>Conclusions: Pathomorphological changes in the vascular tissue structures subsequently at later stages of postnatal ontogenesis lead to atrophic processes and delay in the processes of postnatal formation and development of the ovaries of the offspring.</p>

Keywords: chronic intoxication with pesticides, "mother-offspring", ovary, tissue, blood vessels.

BACKGROUND. The protection of the ecological health of the population is an urgent problem on a global scale. The predominant part of environmental pollutants are pesticides, without which the perspective development of agriculture is impossible [1,3]. Currently, a number of large-scale research projects are being carried out aimed at developing and improving methods for preventing, early diagnosing, and treating the negative effects of pesticides on offspring under conditions of intrauterine and early postnatal exposure through the mother's body [4]. All of the above allows us to conclude that the study of macroscopic and microscopic studies of postnatal ontogenesis of the ovaries in offspring [2,5,6], born under conditions of chronic toxic effects on the mother's body, is an urgent problem that has both scientific fundamental and applied significance.

MATERIAL AND RESEARCH METHODS. To solve the tasks set, white outbred female rats were used, which were divided into 2 groups: 1 - Control (n=30), 2 - Experimental (n=30). Experimental groups of

female rats daily, until the end of the experiments, received "Vantex" pesticides at a rate of 4.0 mg/kg. The morphological features of the development and formation of intraorganic vessels and tissues of female genital organs in mothers and in the dynamics of offspring were studied. On days 7, 14, 21 and 30 after birth, both control and experimental rats were slaughtered by decapitation under light ether anesthesia.

To study the angioarchitectonics of the ovary, Gerota's mass was slowly introduced through the abdominal aorta, the resulting material was clarified according to the method of T.A. Sagatov, and after appropriate wiring, they were poured into paraffin. For histological preparations, sections of 0.3-0.6 mm in size were isolated from different parts of the uterus and ovary, which were fixed in Carnoy's fluid, 10% neutral formalin. After appropriate wiring, the pieces were embedded in paraffin. Sections 5-7µm thick were stained with hematoxylin-eosin. Immunohistochemical methods were used to identify marker substrates.



Proliferating cells were identified using monoclonal rabbit antibodies Ki-67, and apoptotic cells were detected using monoclonal rabbit antibodies BcL-2. Sections were counterstained with methylene blue and neutral red.

RESULTS. The results of our studies show that on the 3rd day in the ovary, both in control and experimental rats, there is no clear boundary between the cortical and medulla, the albuginea of the ovary of the rat is formed by thin bundles of collagen and elastic fibers. They are directed mainly longitudinally. Outside, the protein membrane of the ovaries is covered with cells of the germinal epithelium. In the cortical substance, primordial follicles are revealed, a high density of their location is found in the region of the ovary poles. The study of the ovary in offspring with the introduction of "Vantex" in this period did not reveal significant morphological differences compared with the control group.

In the stroma of the ovary of a 7-day-old rat in the control group, the density of the fibrous structures of the connective tissue increases. The boundary between the medulla and cortex is distinguishable. Connective tissue layers between the cortical substance separate the ovarian follicles from each other. At this age, an oocyte is formed in the primordial follicles. It is located in the center of the follicle. They are larger than primordial follicles. Around the oocyte is not one, but two layers of follicular epithelial cells. In the center of the oocyte there is one nucleus, the space is filled with follicular fluid. Secondary follicles are located in the central areas of the cortical substance. They are larger in size. The oocyte has a larger diameter. The secondary membrane, consisting of cells of the follicular epithelium, is adjacent to the oocyte of these follicles. The follicular epithelium becomes stratified. The inner one is formed by oval-shaped cells, the outer one consists of spindle-shaped cells. In the experimental

groups in rats on the 7th day under the action of Vantex pesticides, secondary follicles were not found in the ovary. By day 14, in the rats of the control group, bundles of collagen and elastic fibers in the stroma of the ovary have different arrangement densities. Large networks of reticular fibers were found on the periphery of the cortex. Connective tissue layers in the cortex have clear boundaries. In the cortical substance of the ovary of rats, primordial, primary and secondary follicles are revealed. When exposed to Vantex pesticides in rats on the 14th day in the stroma of the ovary, compared with the control, the density of bundles of collagen and elastic fibers increases, pronounced inflammatory-destructive changes in vascular tissue structures are observed, and the processes of folliculogenesis are also accelerated. They adhere tightly to the blood vessels in the center of the medulla and to the follicles. The effect of pesticides on the follicular apparatus of the rat ovary in the early stages of breastfeeding causes various morphological changes. A decrease in the increase in the height of the follicular epithelium is associated with thickening of the basement membrane, which is associated with the manifestation of trophic disorders. Similar phenomena were found in the mucous membrane of various organs of rat pups under the action of small doses of pesticides that passed through mother's milk into the growing organism. The toxic effect of "Vantex" is due to the fact that it destroys the lipid membrane of cells. This is due to the fact that they quickly penetrate into organs and tissues. In the control group, on day 21, the number of primordial follicles in the cortical substance of the ovary of rats decreases. A greater increase in the diameter of the oocyte than the primordial follicle itself, the slowdown in the growth of the height of the follicular epithelium, from our point of view, is associated with a structural reorganization of the follicular apparatus and a change in its function (Fig. 1).

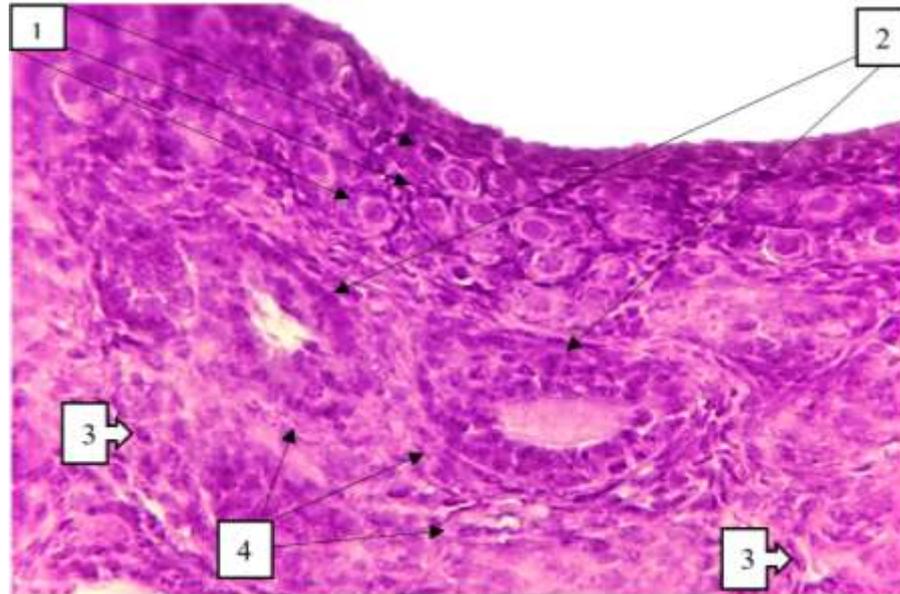


Figure 1. Ovary exposed to "Vantex" on the 21st day. Immature primordial follicles (1), atretic eggs (2), proliferative foci in interstitial cells (3), immature primordial follicles (4). Stained with hematoxylin and eosin. SW. 40x10.

Confirmation of the process of structural reorganization of ovarian follicles at this stage is that at this age we found a large number of primary follicles, in which, in addition to two layers of follicular epithelium cells, there is a third, incomplete layer of cells around the oocyte. In this period of development, there are follicles, in the oocyte of which there are not one, but two nuclei. In the experimental group of rats under the action of "Vantex" on the 30th day in the stroma of the ovary, the arrangement of bundles of collagen and elastic fibers, as well as reticular fibers, is closer to each other. The dense arrangement of the fibrous structures of the connective tissue is more pronounced on the periphery of the cortical substance. In the follicular epithelium, destructive changes occur under the influence of "Vantex", which are manifested by a large decrease in its height. An increase in cell proliferation in the follicular epithelium of primary follicles is associated with their accelerated formation as a result of the accumulation of residual amounts of "Vantex" in the body of rat pups. The increase in cell destruction in the follicular epithelium in the primary follicles in the experiment compared with the control is due to the slight elimination of residual amounts of the pesticide. The blood vessels of the rat ovary are represented by arterioles, capillaries and venules. In the cortical substance of the ovary, arterioles in most cases are found in the peripheral areas of the cortical substance and in the outer shell of the ovary. Capillaries and venules lie next to the ovarian follicles and in the connective tissue layers between them. In the medulla, arterioles are more often detected in its central sections,

closer to the hilum of the ovary. Capillaries and venules are located in connective tissue layers penetrating into the cortical substance.

In the experimental groups under the influence of "Vantex" in the blood vessels of the ovary of the rat, the lumen expands, they are filled with blood cells, the wall of the vessels becomes thicker and thinner. In subsequent periods, the walls of the vessels become denser, against the background of a decrease in their lumen. However, on the 30th day, the lumen in them remains expanded, and the wall is reduced in thickness compared to the control group. In the medulla, the lumen in the venules was 1.3 times greater in the control. When exposed to "Vantex", changes in the blood vessels are observed thinning of all membranes, increased fibrosis and proliferation of connective tissue, as well as small and avascular zones, blind capillaries, especially in areas subject to atrophic changes. Changes in the glandular epithelium are more pronounced. Our results are confirmed in studies. They found that with the development of diseases or the action of harmful factors in the ovary, the density of the arrangement of lymphoid formations decreases and the number of small lymphocytes in them decreases. It has been established that lymphocytes in the ovaries are involved in the regulation of the ovulation process. And changes in these lymphoid formations can cause the development of breast cancer.

Thus, the results of the study show that in the rat ovary, as well as in other organs and systems, regular genetically determined processes develop during early postnatal ontogenesis: the ovarian stroma is

formed, the formation of the stages of folliculogenesis is observed (in parallel with this, physiological selection of follicles occurs, their natural atresia and culling), a system of relationships between blood vessels and the follicular apparatus of the cortex and medulla is being established. In our opinion, in the process of functional development of the rat ovary, the moment of transition to definitive nutrition (14-21 days) is very important and responsible, since tertiary follicles begin to form in the ovary and a significant reorganization of the lymphoid apparatus is observed cells. Most atretic follicles are characterized by the presence of hyperchromia of the nuclei of the primary follicles, nutrient deficiencies around the egg, and are also characterized by the appearance of chromophobic inclusions. Ki-67 rabbit monoclonal antibodies were used to detect proliferating

cell marker substrates, and apoptotic cells were detected with BcL-2 rabbit monoclonal antibodies. Sections were stained with methylene blue or neutral red. In this case, the reaction product in the cells was detected in the form of brown deposits. On the 3rd day after birth, the ovary is surrounded by a protein membrane formed by thin bundles of collagen and elastic fibers. The study of the ovary in offspring with the introduction of "Vantex" in this period did not reveal significant morphological differences compared with the control group. On the 7th day of postnatal development of the ovary, a high proliferative activity is observed (Fig. 2). The proliferative activity of the ovarian cells gradually decreases and by the 30th day is more than half of the initial indicators.

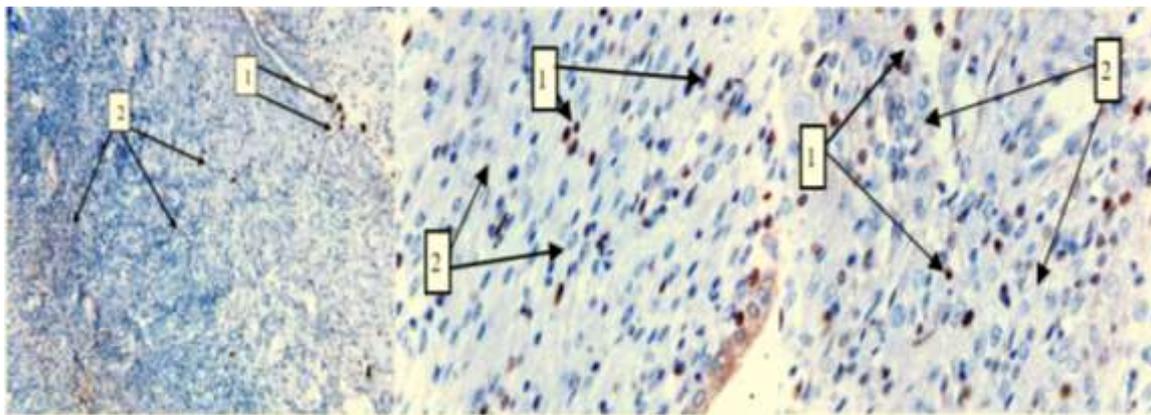


Figure 2. Ovary of the control group on the 14th day. Positive expression of monocellular lymphoid cells (1), negative expression in most stromal structures (2).
 DAB Substrate Kit. Sizes 10x10.

In the experimental groups, the proliferative activity during all periods of observation remains significantly low in relation to the control. A significant part of the ovarian cell does not reach the level of mature cells and dies inside the ovary through apoptosis and destruction. The decrease in the proliferative activity of ovarian cells in the experimental groups is most pronounced on days 7-21 of the postnatal period. During these observation periods, the proliferation index under the influence of "Vantex" reduces the proliferation index by 27-30% compared with the control. On the 30th day after birth, against the background of a general decrease in the proliferative activity of cells, the decrease in the index during proliferation under the influence of "Vantex" is 12% compared with the control.

All this as a whole indicates a significant inhibition of ovarian cell proliferation during prenatal and early postnatal exposure to pesticides. In particular, each cell has inducers and inhibitors of the apoptosis process. "Vantex" pesticide used in our work induces the process of programmed death in each cell cycle, and these changes are accompanied by increased apoptosis in stromal and parenchymal cells (Fig. 3). In particular, since most of the cells of the parenchyma and stroma of the ovary belong to the group of labile cells. Rapid apoptosis of cells in the reproductive cycle is explained by the simultaneous stimulation of proliferative activity. These proliferative active foci are also found in the parenchymal and stromal cells of the ovary.

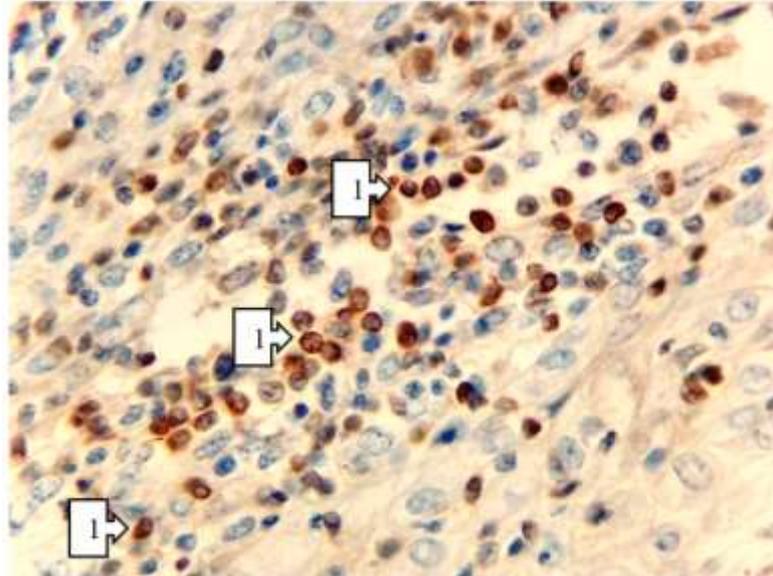


Figure 3. Ovary exposed to Vantex on the 30th day. Positive expression of the Bcl-2 marker (1). DAB Substrate Kit. Sizes 40x10

The positive expression of this marker is mainly a process based on the rapid replacement of the place of apoptotic cells, and the positive expression of the Ki-67 marker in stromal cells increases rapidly, which is explained by the dark brown staining of the cell nucleus and nucleoli. It should be noted that exposure to "Vantex" pesticides leads to a decrease in the proliferation index compared to the control. The decrease in the proliferative activity of ovarian cells in the experimental groups is most pronounced on days 7-21 of postnatal ontogenesis. During these observation periods, the proliferation index under the influence of "Vantex" is reduced by 25-30% compared with the control. All this indicates a significant inhibition of ovarian cell proliferation during prenatal and early postnatal exposure to pesticides.

CONCLUSIONS

1. Chronic maternal intoxication with "Vantex" pesticide in rats in the ovarian stroma compared to the control increases the density of bundles of collagen and elastic fibers, there are pronounced inflammatory and destructive changes in vascular tissue structures, pronounced venous stasis, a large number of avascular zones, which corresponds to development of destructive changes in the wall of ovarian vessels in combination with atrophy of its tissue elements.
2. When exposed to "Vantex" pesticides in the blood vessels of the ovary of a rat, an uneven expansion of the lumen and tortuosity of the course of the vessels occurs, they are filled with blood cells. In subsequent periods, the walls of the vessels become denser,

against the background of a decrease in their lumen.

3. In the experimental groups, the proliferative activity during all periods of observation remains significantly low in relation to the control. A significant part of the ovarian cell does not reach the level of mature cells and dies inside the ovary through apoptosis and destruction.

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