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MORPHOCHARACTERISTICS OF THE THYMUS IN CHRONIC POISONING WITH ENTO DEFOL

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Abstract: The article presents morphological changes in the thymus of rats during chronic poisoning with the pesticide Ento Defol. At high doses of Ento Defol (1/20 LD50), reactive thickening of collagen fibers in interstitial barriers and perivascular zones was observed after 3–7 days. These changes were assessed as a compensatory response developing against a background of interstitial edema and microcirculatory disturbances. By days 14–30, high doses resulted in a significant increase in the relative area of collagen fibers, as well as an increased predominance of stromal elements against a background of disruption of the corticomedullary architecture. After 90 days, fibrotic processes stabilized, manifesting themselves in combination with an atrophic reduction in the lymphoid parenchyma. At this dose, the mast cell response was moderate: whereas activation was observed in the early periods, their numbers stabilized in later periods, and by day 90, a downward trend was observed.

Key words: thymus, rat, pesticide, Ento Defol, chronic poisoning, morphological changes.

Introduction. The thymus is responsible for the formation and maintenance of the body's biological defenses (Abaeva T.S., 2017) [1]. Specialists in the field of immunomorphology define the immune system as a set of organs, tissues, and cells whose function is to protect the body from various diseases and eliminate foreign substances that have already entered the body (Perez Y.E., Moran C.A., 2022) [8].

The immune system protects against infections (bacterial, viral, fungal) and toxins. When the immune system is not functioning properly, the likelihood of exposure to various factors increases, which also leads to the development of autoimmune diseases (Rozhkova I.S., Teply D.L., 2016; Verma R.S., Srivastava A.K., 2017) [5,9].

Цель исследования. Изучение морфологических изменений в тимусе крыс при хроническом отравлении Энто Дефолом.

Various experimental and clinical observations demonstrate dramatic changes in the morphofunctional state of the thymus under the influence of pesticides. However, morphological and histochemical changes in the thymus after the application of different doses of pesticides are not comparable. Furthermore, complete information on the processes occurring in the gland under the influence of various pesticides is lacking. The literature lacks comprehensive information on the state of adaptive reactions in the thymus after exposure to pesticides, including Ento Defol. All this justifies the need for a detailed study of morphofunctional changes in the gland after exposure to different doses of pesticides, which is very important in terms of its significance (Mukhamedzhanov A.Kh., 2024; Khasanova D., 2021; Maletin N. et al., 2025) [3,6,7].

Study objective. To study morphological changes in the thymus of rats chronically poisoned with Ento Defol.

Research materials and methods.

The experimental study was conducted on adult male rats weighing 150–200 g. Ento Defol was administered intragastrically, in solution, on an empty stomach at various doses. The pesticide was dissolved in distilled water. Accordingly, a dose of 1/20th the LD50 was selected. A standard syringe with a metal probe was inserted deep into the rat's mouth, and the drug was slowly injected. Oral administration of the defoliant was chosen given that, according to some authors, pesticides enter the body through food and water in 85–90% of cases.

The LD50 (median lethal dose) of the pesticide was selected based on the data specified in the "Safety and Environmental Protection Requirements" data sheet for the use of pesticides (2022). For rats, this dose is 3520 mg/kg body weight. A pesticide dose equal to 1/100 LD50 for rats corresponds to the threshold value; this dose is often encountered by humans and mammals in areas with intensive pesticide use, making its use of defoliant of practical significance. To compare the obtained data with those obtained with exposure to the product at a dose of 1/100 LD50, doses of the defoliant equal to 1/20 LD50 were used, which is 5 times higher than the threshold value. Such doses may have an impact on people involved in pesticide production and defoliation.

On this basis, the following fractions were selected:

- 1/100 LD_{50} (35.2 mg/kg) – as the limit dose, as this amount is close to the level that humans and mammals may encounter in areas of intensive pesticide use;
- 1/20 LD_{50} (176 mg/kg) – correspondingly 5 times higher, allowing the effect to be compared with 1/100 LD_{50}.

Repeated applications are carried out for 3 months, which corresponds to 1/10 of the animal's life.

Distribution of animals into groups (a total of 66 male rats):

1. Intact group – 6 rats.

2. Control group – 30 rats (they were administered distilled water; 30 animals – for 3, 7, 14, 30, 90 days).

3. Group 1/20 LD_{50} – 30 rats (daily for 3 months, examination on days 3, 7, 14, 30, 90).

The care and slaughter of laboratory animals were conducted in strict accordance with bioethical standards adopted for experimental research in the Republic of Uzbekistan.

The following general histological methods were used for the study: hematoxylin and eosin staining of sections to examine the general structure of the thymus, van Gieson staining to assess the condition of connective and muscle tissue, and toluidine blue staining.

Results of the study and their discussion.

Characteristics of microscopic changes in the thymus after 3 days of exposure to Ento Defol at a dose of 1/20 the LD50. The thymus is surrounded by a capsule composed of dense connective tissue on the outside. The capsule is intact, and segments directed from the capsule to the interior of the organ divide the parenchyma into smaller segments. The intersegmental barrier is preserved, although in some areas, the intersegmental barrier is less clearly defined. The morphological relationship between the cortex and medulla is maintained in the thymus segments, but certain changes in their cellular composition are noted. The density of lymphoblasts and thymocytes in the cortex is reduced, and in some areas, lymphoid cell sparseness is observed. Some thymocytes exhibit initial signs of nuclear pyknosis, chromatin condensation, and a decrease in the cytoplasmic ratio, indicating the activation of apoptotic processes. In this case, morphological integrity is preserved in many cells, and in some areas proliferative activity with a relatively reduced number of cells in a state of mitosis is detected. The reticular structure of the epithelial cells is preserved, and in some of them minor vacuolization of the cytoplasm and morphological changes characteristic of dystrophy are observed. The border between the cortex and medulla layers is slightly blurred, but the difference in intensity is preserved. In the

medulla, the density of thymocytes is relatively low, epithelial reticulocytes and macrophages predominate. Thymic corpuscles (Hassall's corpuscles) of various sizes and shapes are detected in this area, most of them are morphologically preserved, in some corpuscles a slightly uneven arrangement of concentric layers and an increase in the number of hyaline elements are detected. In the vascular system, capillary dilation, venous plethora, and perivascular edema are noted in some places [10]. A slight increase in the number of macrophages indicates activation of the processes of phagocytosis of apoptotic thymocytes (Fig. 1).

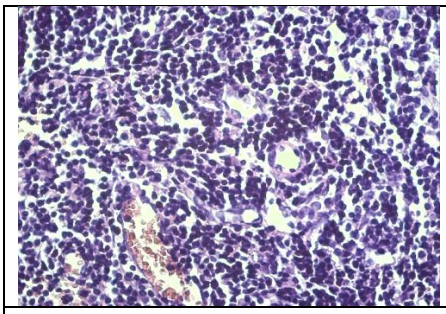
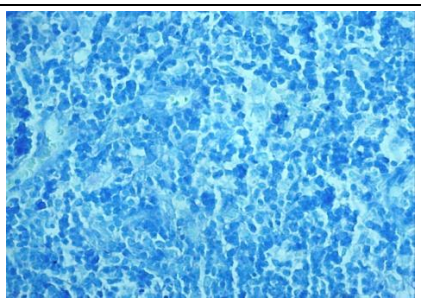
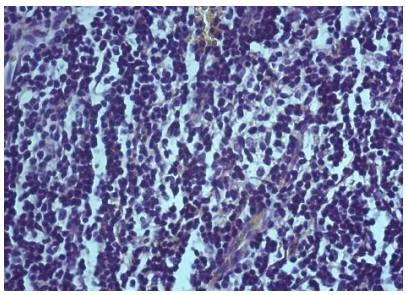
		
Staining – Hematoxylin and eosin. (400. X)	Staining – Toluidine blue. (400x).	Staining – according to Van Gieson. (400x).

Fig. 1. Microscopic changes in the thymus of rats exposed to Ento Defol at a dose of 1/20 LD50 for 3 days.

Characteristics of microscopic changes in the thymus after 7 days of exposure to Ento Defol at a dose of 1/20 the LD50. The thymus is surrounded by a capsule of dense connective tissue; its integrity is preserved, but reactive edema and loosening of collagen fibers are observed in some areas. Diffuse edema and changes in the thickness of the interlobular barrier of varying severity are observed. The general morphological structure of the cortex and medulla is preserved; a significant decrease in lymphoid cell density in the cortex, pyknosis, chromatin condensation, and disruption of the nuclear-cytoplasmic ratio are observed in the nuclei of some thymocytes, indicating activation of apoptotic processes. The number of cells in mitosis is reduced, and proliferative activity is preserved in some areas. The reticular structure of epithelioid reticulocytes is generally preserved, but some of them demonstrate vacuolization and moderate degenerative changes. The boundary between the cortical and medullary layers is blurred, which is considered a morphological condition associated with a partial reduction in lymphoid tissue [1]. In the medullary layer, the density of thymocytes is further reduced, with a relative predominance of epithelioid reticulocytes and macrophages. Some thymic bodies found in the medullary region show an uneven arrangement of concentric layers and an increase in hyaline-like elements. In the vascular system, signs of dilated capillaries and venules, venous congestion, and perivascular edema are detected (Fig. 2).

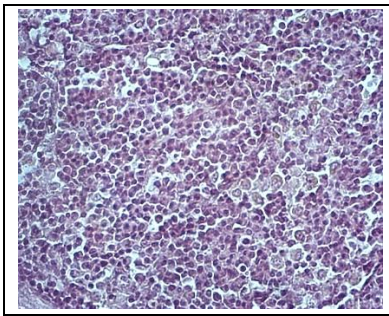
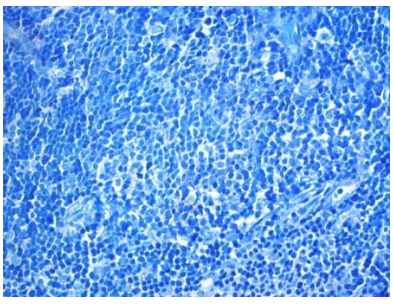
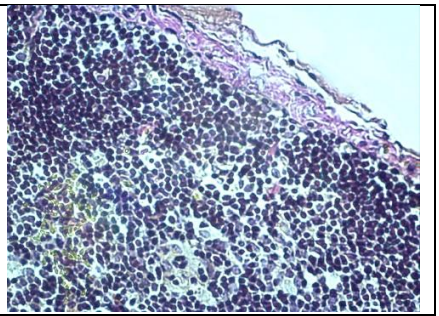
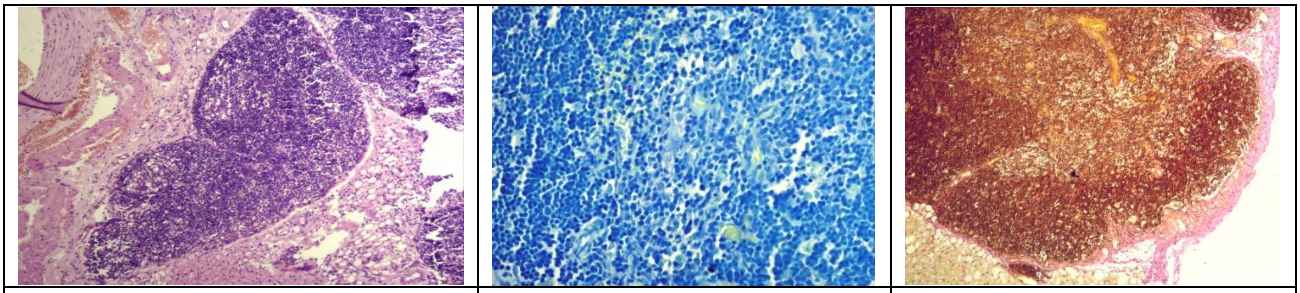
		
Staining – Hematoxylin and eosin. (400x).	Staining – Toluidine blue. (400x).	Staining – according to Van Gieson. (400x).

Fig. 2. Microscopic changes in the thymus of rats exposed to Ento Defol at a dose of 1/20 LD50 for 7 days.

Microscopic changes in the thymus after 14 days of exposure to Ento Defol at a dose of 1/20 the LD50. The thymus is surrounded externally by a capsule composed of dense connective tissue; its overall integrity is preserved; signs of reactive edema are detected in the capsule. While interlobular

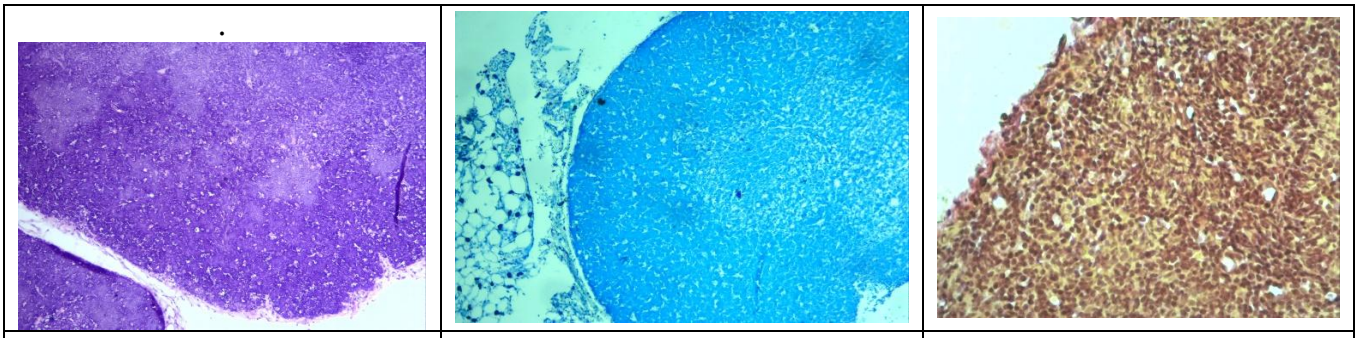
barriers are preserved, changes in their thickness and structure are noted. The ratio of the cortex to medulla in the thymus lobes changed. The cortex ratio decreased in many lobes, and thymocyte density significantly decreased. Lymphoid cells became sparse, with localized cellular relaxation observed, and some thymocytes exhibited morphological signs characteristic of apoptosis, including nuclear pyknosis, severe chromatin condensation, and a decrease in the number of cells in mitosis. Epithelial reticulocytes are mainly located in the cortex, most of which demonstrate vacuolation and mild to moderate degenerative changes. The boundary between the cortex and medulla is blurred or poorly defined in many areas, the amount of lymphoid tissue is reduced, and epithelial reticulocytes and macrophages predominate. Thymic corpuscles (Hassall's corpuscles), located in the medulla, are in different morphological states: some are structurally preserved, while others show signs of disruption of concentric layers, an increase in hyaline-like elements, and partial disintegration [10]. An increase in the number of macrophages indicates activation of phagocytosis of apoptotic thymocytes. The vascular system is plethoraic, and signs of perivascular edema are found in some areas (Fig. 3).



Staining – Hematoxylin and eosin. (100x).	Staining – Toluidine blue. (400x).	Staining – according to Van Gieson. (400x).

Fig. 3. Microscopic changes in the thymus of rats exposed to Ento Defol at a dose of 1/20 LD50 for 14 days.

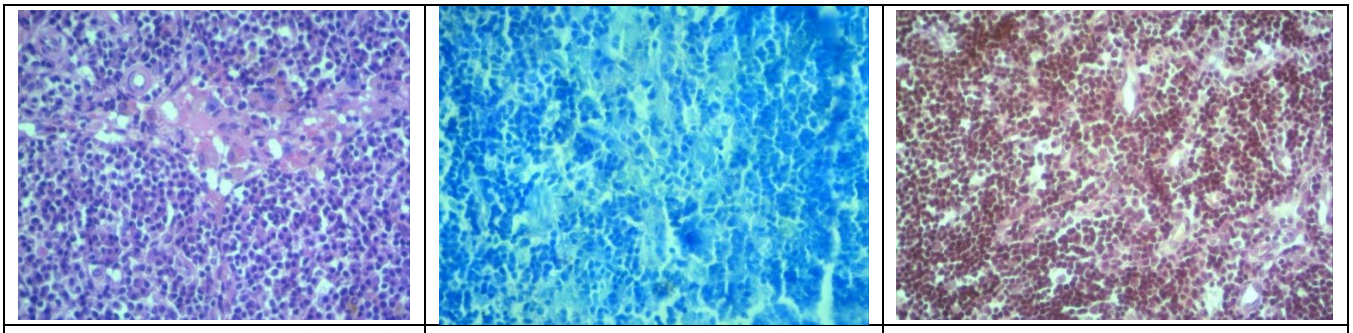
Characterization of microscopic changes in the thymus after 30 days of exposure to Ento Defol at a dose of 1/20 the LD50. The capsule retained its integrity, but an uneven distribution of collagen fibers and softening of the planes were detected in the stroma. The thickness and structure of the interlobular barriers varied, and degenerative changes in the stromal component were clearly visible in some areas. The cortex was significantly reduced, and the lymphoid cell density was significantly reduced. Thymocytes exhibited signs of apoptosis, including nuclear pyknosis, chromatin condensation, and a decrease in cytoplasm. The number of mitotic cells decreased sharply, and lymphopoiesis activity was reduced. The reticular structure of the epithelial reticulocytes is generally preserved, but vacuolization and degenerative changes are detected in the cytoplasm of most of them. In the medulla, the number of thymocytes decreases, and the number of epithelial reticulocytes and macrophages predominates. Gassial bodies are in different morphological states: some are preserved, others have destroyed concentric layers and signs of hyalinosis. The number of macrophages increases, and the processes of phagocytosis of apoptotic cells are activated [2]. In the vascular system, signs of dilation of capillaries and venules, venous filling, and perivascular edema are determined (Fig. 4).



Staining – Hematoxylin and eosin. (100x).	Staining – Toluidine blue. (100x).	Staining – according to Van Gieson. (100x).

Fig. 4. Microscopic changes in the thymus of rats exposed to Ento Defol at a dose of 1/20 LD50 for 30 days.

Characteristics of microscopic changes in the thymus after 90 days of exposure to Ento Defol at a dose of 1/20 the LD50. The capsule is intact, collagen and elastin fibers in the stroma are unevenly distributed, with signs of hypertrophy and degeneration in some areas. Interlobular barriers are absent or deformed in many areas, and the distinction between the cortical and medullary layers is significantly altered. The amount of cortex is reduced, the number of lymphoid cells is minimal, and thymocytes show signs of apoptosis, nuclear pyknosis, chromatin condensation, cytoplasmic shrinkage, and nuclear fragmentation. The number of mitoses is reduced, and lymphopoiesis is impaired. The reticular structure of epithelioid reticulocytes is partially preserved; dystrophic changes and signs of vacuolization predominate. The number of thymocytes in the medulla is small; epithelioid reticulocytes and macrophages predominate. In Hassall's corpuscles, the concentric layers are disrupted, and hyalinosis is evident [4]. The number of macrophages is increased, and the processes of phagocytosis of apoptotic cells are accelerated. In the vascular system, capillaries and venules are dilated, signs of perivascular edema and venous congestion are stable (Fig. 5).



Staining – Hematoxylin and eosin. (400x).	Staining – Toluidine blue. (400x).	Staining – according to Van Gieson. (400x).

Fig. 5. Microscopic changes in the thymus of rats exposed to Ento Defol at a dose of 1/20 LD50 for 90 days.

Conclusion. At high doses of Ento Defol (1/20 LD50), reactive thickening of collagen fibers in interstitial barriers and perivascular zones was observed after 3–7 days. These changes were assessed as a compensatory response developing against a background of interstitial edema and microcirculatory disorders. By days 14–30, under the influence of high doses, a significant increase in the relative area of collagen fibers was noted, as well as an increased predominance of stromal elements against a background of disruption of the corticomedullary architecture. After 90 days, fibrotic processes stabilized, manifesting themselves in combination with an atrophic decrease in the lymphoid parenchyma. The mast cell response at this dose was moderate: whereas activation was observed in the early periods, their numbers stabilized in later periods, and by day 90, a downward trend was observed.

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