

Patterns of pathomorphological alterations in the respiratory tract segments of experimental animals following exposure to pesticides.

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Abstract: *In the study conducted at the Department of Histology and Biology of the Fergana Medical Institute of Public Health, histopathological methods were employed to analyze the respiratory tissue of rabbits subjected to aeroallergen intoxication with the pesticide Nurinol-D. After one month of experimentation, the animals were euthanized, and their tissues were obtained for analysis. Histological examination was performed on samples from the nasal cavity, trachea, lungs, and tracheobronchial lymph nodes. The results revealed changes in the structure and condition of the rabbits' respiratory tissues, including mucosal edema and hyperemia, infiltration by inflammatory cells, and other pathomorphological alterations. The study also identified the presence of bean-shaped tracheobronchial lymph nodes on both sides of the trachea, characterized by enlarged size and dark brown coloration. Aeroallergenic insecticides have been found to lead to modifications in tracheobronchial lymph nodes manifesting*

as lymphadenopathy. Cortical growth is observed as a result of active cellular proliferation, which includes adipocytes, and at the same time, the number of immature cellular bureaucracy and mitotic activity decreases. Pathomorphological examination revealed various modifications inside the nasal cavity and tracheal tissues. The nasal cavity showed mucosal edema, hyperemia, dilatation of small blood vessels, hypertrophy of the ciliated epithelium, and an improved number of goblet cells with submucosal infiltration by various inflammatory cells. In the trachea, infiltration of inflammatory cells, reduced density of cilia on the surface of the epithelium and changes in the length of glandular cells were observed, indicating disturbances in access to epithelial exfoliation and glandular function.

Key words: insecticides, aeroallergens, lymph nodes, lymphadenopathy, nasal cavity, trachea, bronchi, alveoli

Introduction: The term "pesticide" is the maximum that is usually used to consult goods designed to eliminate dangerous diseases, parasites or weeds that affect vegetation, people or animals. Some authors also use the term "biocide" to refer to capacity toxicity to other organisms. Despite their known toxicity, pesticides remain in use due to economic feasibility [1]. Their use is becoming more and more widespread in developing countries, which represents a particularly high chance for professional users of pesticides, together with those involved in practice and application [2].

In developed countries, protection is highly ensured through current legislation; however, challenging situations arise regarding product residues and their distribution in various ecosystems and biocenoses, even at a certain stage of technological processing. In growing international locations, these problems are becoming particularly acute, and people and rural residents are not adequately protected from the toxic consequences of pesticides [3].

Currently, a mixture of the organophosphate insecticide chlorpyrifos and the artificial pyrethroid insecticide cypermethrin is widely used in horticulture and horticulture in the Republic of Uzbekistan. Chlorpyrifos works by inhibiting the activity of acetylcholinesterase, which leads to the accumulation of acetylcholine in the synaptic clefts and subsequently to paralysis and death of the pests [4].

The majority of research (79%) found high-quality institutions in pesticide promotion and respiratory and allergic effects in children, along with bronchial asthma, wheezing, cough, acute respiratory infections, hay fever, rhinitis, eczema, persistent productive cough, and lung function. damage [5].

A study examining the impact of pesticide exposure on respiratory fitness among workers in the pesticide industry showed a higher incidence of persistent respiratory symptoms in pesticide workers as well as an increase in acute symptoms during painting

shifts. Checks of lung characteristics revealed extensive decreases compared to predicted values, indicating deterioration of lung function. Gender differences were found in the results of smoking and lung function work. Overall, a look at shows that prolonged exposure to pesticides can also lead to acute and continuous respiratory symptoms and disorders characteristic of the lungs, especially in combination with smoking [6].

A 20-year survey of pest control workers in Florida, USA revealed that long-term occupational exposure (greater than 18 months) to chlorpyrifos was associated with prolonged worker mortality from most lung cancers [7].

Some insecticides can cause irritation of the nasal mucosa, allergies, rhinosinusitis, rhinitis and other nasal and paranasal diseases, especially in people frequently exposed to these chemical compounds, which include farmers or commercial workers [8].

An independent view of the proven development of olfactory disorder observed using irreversible anosmia during acute and excessive pesticide attention [9].

In addition, an observation made on rats exposed to insecticides confirmed a high index of apnea in a certain stage of sleep and a longer exit time [10].

The study of results of pesticides on the respiratory apparatus remains a relevant issue due to their significant use in agriculture and in areas where soil and plant processing is carried out. These chemicals can have an adverse effect on the respiratory health of both professional customers and residents living near the affected regions. Research in this area is essential to identify potential health hazards and develop appropriate measures to protect the population and workers from the adverse effects of pesticide propagation on the respiratory tract. It is also important to conduct more in-depth research to better understand the mechanisms of pesticide action on the respiratory system and to develop effective techniques to manage public health hazards.

Thus, the study of the consequences of numerous pesticides on the morphofunctional modifications of the respiratory mucosa and tracheobronchial lymph nodes is insufficiently investigated.

Aim of the research: The aim of the research was to investigate the patterns of pathomorphological changes in sections of airways and tracheobronchial lymph nodes in experimental animals exposed to pesticides.

The survey was carried out at the department of histology and biology of the Medical Institute of Public Health of Fergana. Methods of histopathological studies were used. Animal dissections are performed in accordance with European Parliament and European Union Directive 2010/63EC on the safety of animals used for scientific purposes. Material from the histological examination preserved parts of excised tissues from the nasal cavity, trachea, lungs and tracheobronchial lymph nodes of experimental animals, especially male rabbits weighing 2.4-2.7 kg (n = 28). For a period of one

month, the animals were exposed to acute aeroallergen intoxication with the pesticide Nurinol-D containing chlorpyrifos and cypermethrin. Nurinol-D is diluted with cooled boiled water at a ratio of 1:50 and the mixture is sprayed every three days, twice in the afternoon, in the closed terrarium where the rabbits were kept.

After one month of the test, the animals were sacrificed and tissues of the respiratory apparatus were obtained. The tissues were then fixed in 10% neutral formalin solution. After fixation and rinsing, the tissue pieces were crossed with alcohols of increasing awareness from 60°C to 100°C and then embedded in paraffin. Subsequently, histological sections with a thickness of 7-8 µm were obtained using a microtome. After deparaffinization, the sections were stained with such stains as Hematoxylin-Eosin, Van Gieson and Schiff's reagent. Histological arrangements were tested using an MT 5300L medium microscope with a digital virtual digicam at magnifications ranging from × hundred to × four hundred as designs for morphometric studies.

Results and analysis: The results of our view show that in rabbits, the cranial airways are divided into the area of the nostril and its walls, the nasopharynx, the larynx, the trachea, the bronchi, and the attractive in the bronchioles. The caudal element belongs to the respiratory segment of the respiratory tract, i.e. respiratory bronchioles, alveolar ducts and alveolar sacs, each of which has its own personal features in histological form. The results determined the presence of normal tracheobronchial lymph nodes to the right and left of the trachea. According to their proximity, they were divided into 3 enterprises: own (predominant) tracheobronchial lymph node, left (relevant) tracheobronchial lymph node, and peripheral nodes located cranially and caudal to the right and left tracheobronchial nodes. The proper and left lymph nodes were located individually, while the peripheral ones were determined in small corporations of three to five units, cranial and caudal to the important lymph nodes. The lymph nodes were enlarged and dark brown in color.

Pathomorphologically, the nasal cavity showed mucosal edema, hyperemia, and dilatation of small blood vessels in the mucous membranes and submucosal membranes. In addition, the hypertrophy of the ciliated epithelium changed to citable, and detachment of the mucosal and membranous epithelial layers was found in several areas. Most specimens showed a boom within the giant goblet cell type, a thickening of the submucosal layer richly saturated with migrating cells that include eosinophils, basophils, neutrophils, macrophages, plasma cells, and adipocytes (submucosal infiltration) (Fig. 1).

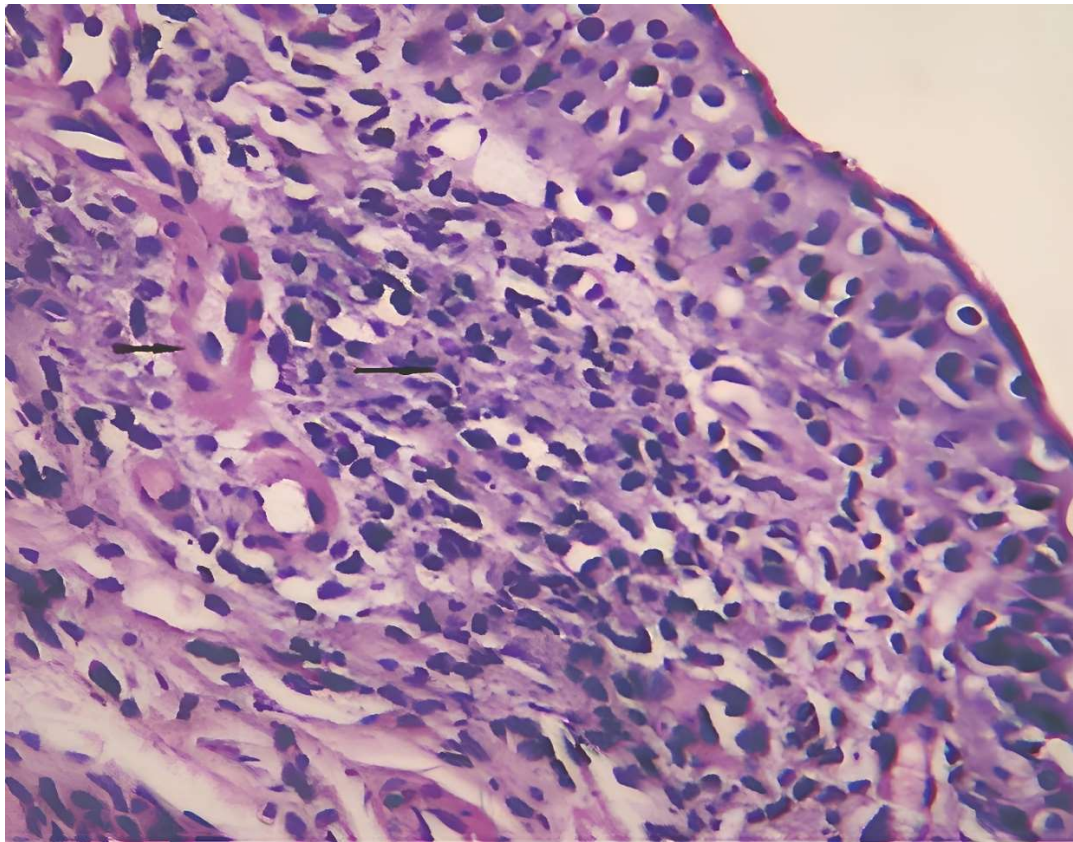


Figure 1. Morphostructural modifications of the nasal mucosa after exposure to pesticides. In the go-phase of the nasal vestibule, there is thickening, edema of mucous membranes and submucous membranes, vasodilatation and glandular hyperplasia of the submucosal layer with infiltration of granular leukocytes (arrows). Stained with hematoxylin and eosin, magnification $\times 160$.

In the trachea, infiltration of inflammatory cells inside the mucosal and submucosal layers is reported. On the surface of the pseudostratified columnar ciliated epithelium is a lower variety of cilia, observed by growth within the length of tracheal gland cells in the submucosal layer. Disruption of epithelial exfoliation tactics in the trachea is also discovered on the side of infiltration and growth within the number of goblet cells.

The results of the histopathological examination of the bronchi of the rabbit subjected to aerosol intoxication confirmed that the bronchial tree branched into extrapulmonary bronchi and intrapulmonary bronchi. Edema and hypertrophy of pseudostratified columnar ciliated epithelium were noted in the bronchial mucosa (Fig. 2), occasionally with signs and symptoms of exfoliation and separation of the mucosal and membranous epithelial layers. Additionally, increases within the goblet cell range and basement membrane thickening have been cited.

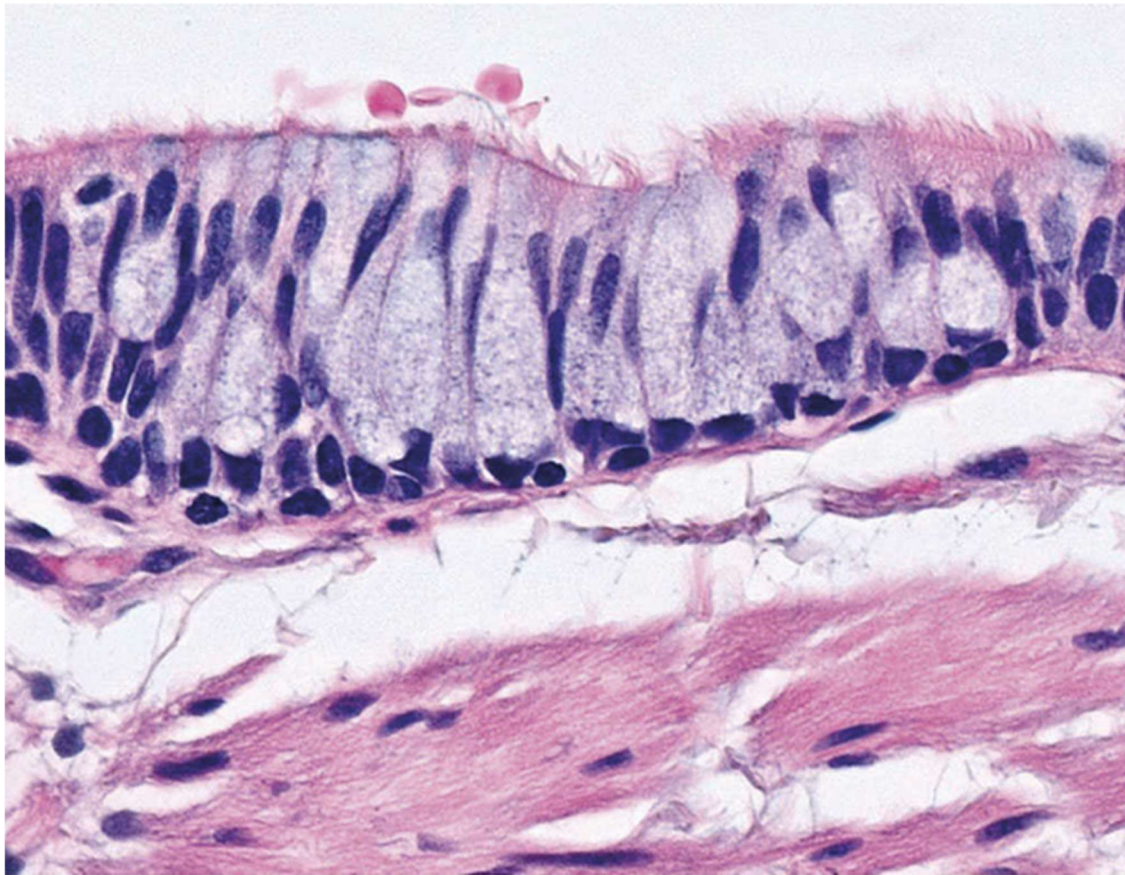


Figure 2. Cross-section of bronchial mucosa showing signs of goblet cell hyperplasia exceeding the abundance of ciliated cells. The cell is filled with mucinous vacuoles that push the nucleus closer to the basement membrane. H&E staining. $\times 400$ magnification.

In the submucosal layer, there is a picture of venous stasis and hypertrophy of protein-mucosal glands with copious secretion of mucus. In addition, the submucosal layer is infiltrated by granular leukocytes, the majority of which are eosinophils, forming a mixed inflammatory infiltrate (Fig. 3).

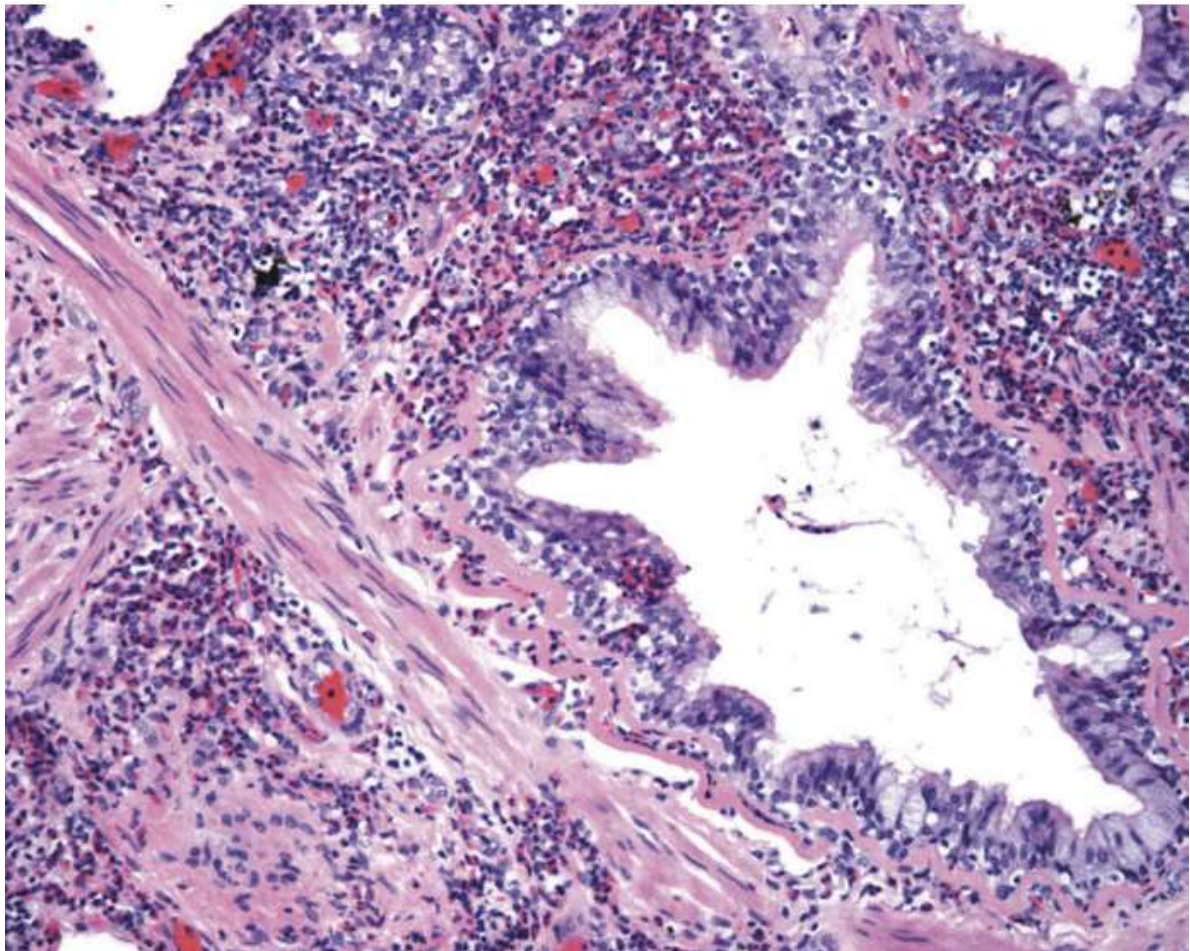


Figure 3. Cross-section of lung tissue. Bronchiolar mucosa and submucosa are abundantly infiltrated by inflammatory eosinophils. H&E staining. $\times 160$ magnification.

Structural changes were found in the respiratory chambers of experimental animals, which indicated signs of irritation of the alveoli and alveolar sacs of the lungs, from time to time with thickening of the alveolar septa. In addition to the above, there was an expansion of the hollow space and the formation of gaps between the mucosal and submucosal layers inside the respiratory bronchioles. All this turned into accompanied by the use of fibrosis surrounding smooth muscle fibers. Inflammatory infiltration, edema, and gaps between the mucosal and submucosal layers of terminal bronchioles were also noted.

Exposure to pesticides in the form of aerosol allergens also induces proliferative changes in the tracheobronchial lymph nodes, particularly lymphadenopathy with signs of inflammation. Meanwhile, the results of histopathological examination revealed the presence of two amazing elements of lymph nodes, which include cortical (as paracortical) and medullary zones. A boom was noted within the area of the cortical

substance, while the area of the medullary substance shrank. In the germinal centers of the secondary lymph nodes of the cortical component, it turned into an observed decrease in the activity of proliferative processes, manifested by a lower interior of a wide range of immature cells of the lymphoid collection and mitoses (Fig. 4).

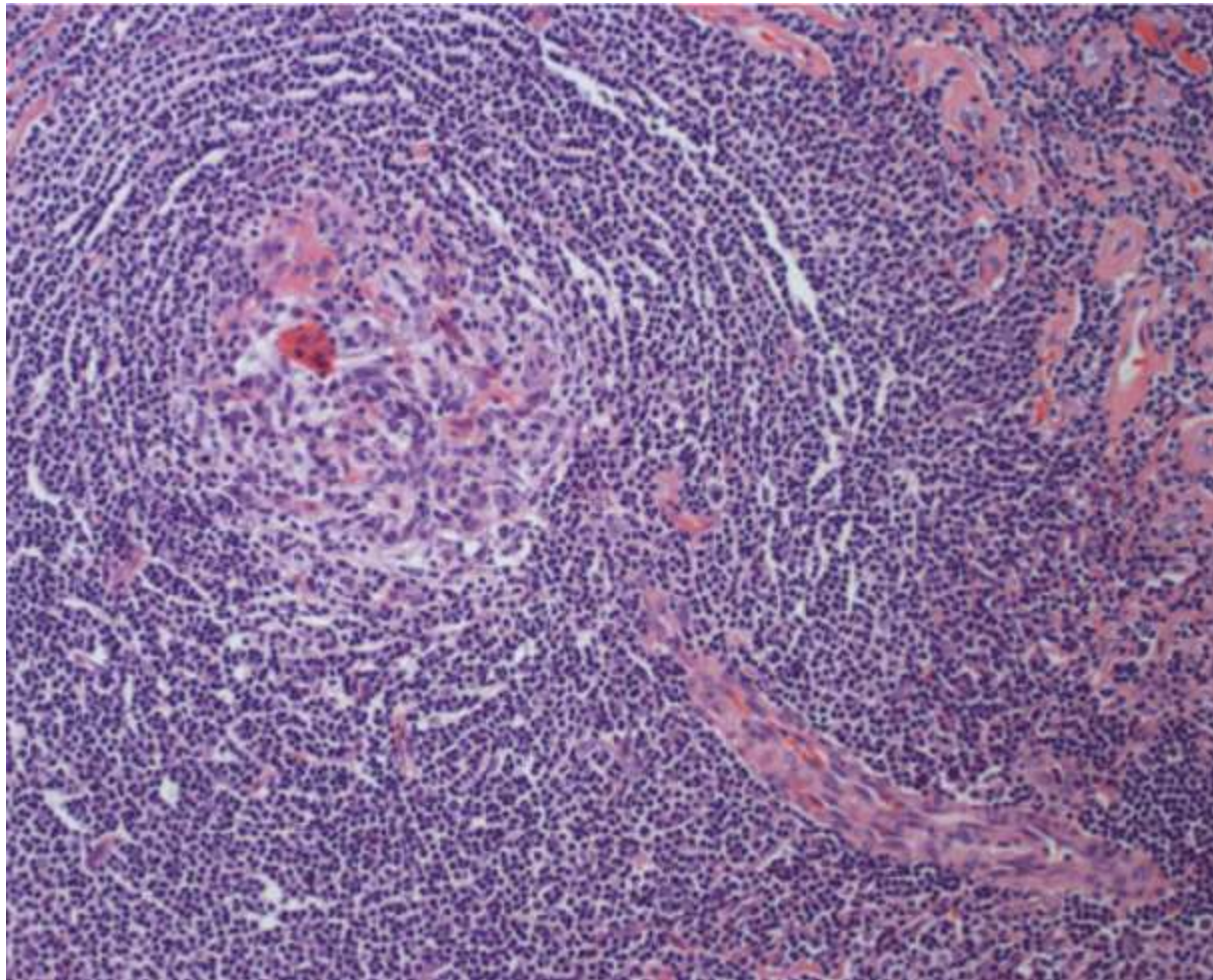


Figure 4. Secondary lymphoid nodule of the tracheobronchial lymph node. H&E staining. $\times 160$ magnification.

At the same time, a wide variety of small lymphocytes increase, although the extent of macrophages increases towards the mantle enlargement history. The cortical part increases due to the paracortical component, in which active mobile proliferation takes place and the presence of fat cells is detected. However, there may be a decrease in the number of immature lymphoid and plasma cells and a decrease in the mitotic hobby of the cells.

Discussion. The inspection carried out at the department of histology and biology of the Fergana Medical Institute of Public Health allowed an in-depth evaluation of

structural changes in the respiratory system of experimental rabbits exposed to aerosol allergenic intoxication with the pesticide Nurinol-D. The histopathological techniques used during the examination made it possible to reveal a wide range of pathological changes in the tissues of the respiratory system, from the nasal cavity to the respiratory part of the respiratory system.

The effects of the studies revealed that pesticide exposure caused full-scale changes in the histological structure of the respiratory tract. Inside the nasal cavity, in addition to hypertrophy of the ciliary epithelium, signs of irritation such as mucosal edema and capillary dilatation were recognized. In the trachea, infiltration of inflammatory cells, reduction in the extent of cilia and enlargement of glandular cells was noted. Similar modifications were additionally determined within the bronchi, in which mucosal edema and epithelial hypertrophy were localized. Mucous edema in the bronchi indicates microcirculation disorders and increased permeability of the vascular wall. Hypertrophy of pseudostratified columnar ciliated epithelium indicates the response of epithelial cells to inflammatory irritants. Signs of desquamation and separation of the epithelial layers indicate damage to the epithelial lining and disruption of its protective function.

An increase in goblet cells is a common response to infection and serves as an indicator of increased mucus secretion to protect tissues from further damage. The thickening of the basement membrane also indicates the activation of remodeling processes and the response of bronchial cells to stressors.

Venous stasis and hypertrophy of protein-mucosal glands were localized in the submucosal layer of the bronchi, which may indicate microcirculation disorders and increased mucus secretion. Infiltration by granular leukocytes, especially eosinophils, indicates the presence of allergic or immune reactions in the bronchial tissues.

One of the essential findings is evidence of necrosis in the alveoli and alveolar sacs of the lungs. The presence of edema and infiltration indicates extreme tissue damage and may cause impairment of fuel exchange and respiration. In addition, thickening of the alveolar septa impairs gas trade by reducing the floor area for diffusion of oxygen and carbon dioxide.

In addition, there is an increase in the cavity and the appearance of gaps between the mucosal and submucosal layers in the respiratory bronchioles. These modifications can also lead to disruption of the structural integrity of the airways, which can exacerbate allergic inflammatory responses and increase the risk of infections.

Fibrosis of the surrounding smooth muscle fibers similarly exacerbates the problem by developing additional limitations in daily respiratory function. The fibrotic way can cause a continuous decrease in tissue elasticity and impairment of ability.

Inflammatory infiltration, edema, and gaps between the mucosal and submucosal

layers of terminal bronchioles are also characteristic responses of respiratory tract damage to pesticide exposure. In addition, these modifications can lead to a deterioration of the patency of the airways and deterioration of the general condition of the animals.

Changes in tracheobronchial lymph nodes should be mentioned separately. In addition to signs of infection and lymphadenopathy, an increase in the length of the lymph nodes was found. Histopathological examination shows the activation of cell proliferation in the cortical part of the lymph nodes, which may also indicate a systemic immune response to aerosol allergen intoxication.

Conclusion. Overall, the results of the studies confirm that the pesticide Nurinol-D has dangerous effects on the respiratory system of rabbits, causing various structural modifications and inflammatory reactions. These findings are important for assessing the health risks to human beings in contact with this pesticide and for developing preventive measures to mitigate its destructive effects. Further studies are needed for a deeper understanding of the mechanisms of pathomorphological changes and the improvement of effective techniques for combating aerosol allergen intoxication.

References

- [1] Warne MStJ, Reichelt-Brushett A. Pesticides and Biocides. In: Reichelt-Brushett A, editor. *Marine Pollution – Monitoring, Management and Mitigation*, Cham: Springer Nature Switzerland; 2023, p. 155–84. https://doi.org/10.1007/978-3-031-10127-4_7.
- [2] MacFarlane E, Carey R, Keegel T, El-Zaemay S, Fritschi L. Dermal exposure associated with occupational end use of pesticides and the role of protective measures. *Safety and Health at Work* 2013;4:136–41.
- [3] Toxics | Free Full-Text | Farmers' Exposure to Pesticides: Toxicity Types and Ways of Prevention n.d. <https://www.mdpi.com/2305-6304/4/1/1> (accessed April 19, 2024).
- [4] Shenouda J, Green P, Sultatos L. An evaluation of the inhibition of human butyrylcholinesterase and acetylcholinesterase by the organophosphate chlorpyrifos oxon. *Toxicology and Applied Pharmacology* 2009;241:135–42.
- [5] Buralli RJ, Dultra AF, Ribeiro H. Respiratory and Allergic Effects in Children Exposed to Pesticides—A Systematic Review. *International Journal of Environmental Research and Public Health* 2020;17:2740. <https://doi.org/10.3390/ijerph17082740>.

- [6] Zuskin E, Mustajbegovic J, Schachter EN, Kern J, Deckovic-Vukres V, Trosic I, et al. Respiratory Function in Pesticide Workers. *Journal of Occupational and Environmental Medicine* 2008;50:1299. <https://doi.org/10.1097/JOM.0b013e3181845f6c>.
- [7] Pesatori AC, Sontag JM, Lubin JH, Consonni D, Blair A. Cohort mortality and nested case-control study of lung cancer among structural pest control workers in Florida (United States). *Cancer Causes Control* 1994;5:310–8. <https://doi.org/10.1007/BF01804981>.
- [8] Krajewska-Wojtys A, Jarzab J, Zawadzińska K, Pyrkosz K, Bozek A. Local Allergic Rhinitis in Adult Patients with Chronic Nasal Symptoms. *Int Arch Allergy Immunol* 2017;173:165–70. <https://doi.org/10.1159/000478656>.
- [9] Gobba F, Abbacchini C. Anosmia after exposure to a pyrethrin-based insecticide: a case report. *Int J Occup Med Environ Health* 2012;25:506–12. <https://doi.org/10.2478/S13382-012-0060-4>.
- [10] Darwiche W, Gay-Quéheillard J, Delanaud S, Sabbouri HEKE, Khachfe H, Joumaa W, et al. Impact of chronic exposure to the pesticide chlorpyrifos on respiratory parameters and sleep apnea in juvenile and adult rats. *PLOS ONE* 2018;13:e0191237. <https://doi.org/10.1371/journal.pone.0191237>.