

## **Morphological Changes Occurring in the Spleen and Thymus During Chronic Poisoning with Nicotine-Containing Oral Products**

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**Abstract:** Long-term smoking is thought to cause vagal stimulation. The increase in suppressor cells associated with smoking predetermines the disruption of immune surveillance of tumor cell growth and the development of cancer. A significant correlation has been established between the level of morbidity and mortality due to cancer and the amount of tobacco consumed. When determining the nonspecific resistance of the body, it was revealed that tobacco smoke suppresses the phagocytic and degradation functions of the liver and spleen, inhibits the release of lysosomal enzymes and the production of superoxide. Treatment of fresh blood serum with cigarette smoke sharply reduces its bactericidal properties, but the simultaneous use of an antioxidant prevents this effect. In smokers, compared to non-smokers, serum IgE levels are significantly increased. In the blood of the umbilical cord of babies born to smoking mothers, the content of IgE is increased, and in the children themselves, the risk of various symptoms of atony is increased by 4 times.

**Key words:** nicotine, morphology, T- and B-cell components of the immune system, thymus, spleen.

**Relevance.** Smoking can be compared to an epidemic of disease: it spreads from one society to another, from one population to another. Some time after acquiring this habit, an epidemic of smoking-related diseases begins. Tobacco smoke is dangerous not only for the smoker, but also for the people around him. In addition to irritating the eyes and mucous membranes of the throat from tobacco smoke, secondhand smoke has a detrimental effect on the tissues of the respiratory organs and creates an increased risk of developing lung cancer and heart disease in non-smokers. Passive smoking is especially harmful to children. Thus, when talking about women smoking, it is not enough to focus on the impact of tobacco only on their health; they endanger the health of their children. The main component of tobacco is nicotine, an alkaloid that is an integral part of all tobacco products. Nicotine is the main reason people are addicted to tobacco consumption; Nicotine-free tobacco does not meet the needs of those who are addicted to tobacco. It is believed that long-term smoking leads to stimulation of the vagus. The increase in suppressor cells associated with smoking predetermines the disruption of immune surveillance of tumor cell growth and the development of cancer. A significant correlation has been established between the level of morbidity and mortality due to cancer and the amount of tobacco consumed. Profound changes occur in the immune system of smokers. They have a significant increase in the content of T-suppressors and a decrease in the level of T-helpers; decreased activity of natural killer cells and a decrease in their number in the peripheral blood. Due to changes in the ratio of T cells in smokers, the production of immunoglobulins G, A, and M decreases. And the level of IgE increases and remains high in smokers as a result of stimulation by allergens contained in tobacco. Strengthening the processes of lipid peroxidation and the regeneration of free radicals have an

adverse effect on immunocompetent cells, increasing the consumption of antioxidant vitamins A and C. Tobacco smoke suppresses the secretion of immunoglobulin A, reducing the body's resistance to exogenous antigens. This phenomenon explains the susceptibility of smokers to herpes infection. The increase in suppressor cells associated with smoking predetermines the disruption of immune surveillance of tumor cell growth and the development of cancer. Statistics on smoking and tobacco use were collected from 3,625 nationally representative surveys conducted as part of the Global Burden of Disease Study (GBD) project in 204 countries, collected. These statistics show that the number of smokers is increasing overall at the global level and in 2019 it reached 1.1 billion people. At the same time, smoking caused 7.7 million deaths in the world, including every fifth death among men (Global Burden of Disease Study 2019). Scientists are of particular concern about the high level of smoking among young people aged 15–24 years, while more than half of the world's countries are making no progress in reducing smoking among young people. According to the review, every fifth young man and every twentieth young woman in the world smoke, and nine out of ten smokers started smoking before the age of 25 (Melnikova I.M. et al. 2022).

Smoking nicotine-containing products causes vasospasm, which disrupts oxygen supply to tissues, and also causes bad breath, yellow teeth, sore throat, and red eyes from constant irritation from smoke. The spleen is one of the most complex peripheral organs of the immune system. The paucity and inconsistency of information regarding the structure of the spleen is due to the fact that the study of its structure is mainly carried out in various types of laboratory animals with subsequent extrapolation of the data obtained to humans. Single studies performed using histological material from the human spleen do not fully reflect all aspects of the morphometric study of the size of the organ pulp compartments and the state of its cellular composition. Hence it follows that the study of morphological changes in the spleen and thymus during chronic poisoning with nicotine-containing oral products is very interesting and relevant.

### **Purpose of the study**

To study the features of morphological changes that occur in the spleen and thymus during poisoning with nicotine-containing oral products. Nicotine addiction depletes the nervous system and inhibits brain activity. A smoker's reactions slow down and intelligence decreases. Tobacco use reduces the motor function of the stomach and intestines and negatively affects the condition and functional activity of the liver. The mortality rate from diseases of the digestive system - stomach and duodenal ulcers - is 3.5 times higher in smokers than in non-smokers. Nicotine negatively affects appearance, causing deterioration of the skin, darkening of teeth and an unpleasant odor. It has been proven that tobacco use contributes to accelerated biological aging - the functional indicators of the body do not correspond to age.

### **Materials and research methods**

The experiment involved 40 animals - outbred white rats (male and female) four months old with a body weight of 165–200 g, kept under standard vivarium conditions (free access to food and water and 12–14 hour daylight hours). All experiments were carried out in accordance with the "Rules for carrying out work using experimental animals". Two experimental groups of 20 animals each were formed: I – intact animals kept under standard vivarium conditions; II – rats exposed to tobacco smoke, which was modeled as follows: exposure – 1.5 hours. Daily observation of the animals included recording of behavior, appearance, and physiological functions. On the 10th day, the animals were removed from the experiment under ether anesthesia in compliance with the rules of euthanasia, and autopsy material was collected for subsequent histological examination (spleen, thymus). Autopsy material was marked, fixed in 10% buffered formalin, and subjected to

histological examination using standard histological techniques. Quantitative (morphometric) analysis of the studied samples was carried out using specialized software. To study the morphological parameters of the organs of laboratory animals, research methods widely used in experimental studies (anatomical dissection) were used. All histological preparations were viewed using a trinocular microscope HL-19 (China) with software.

### **Result and discussions**

Histologically, in animals of the control group, the structure of the studied organs corresponded to the species norm. The thymus is covered with a thin capsule of dense, unformed connective tissue with a large number of collagen fibers and is divided by trabeculae into vaguely demarcated lobules consisting of the cortex and medulla. In some animals, adipose tissue is detected in the trabeculae. In some preparations, the boundary between the cortex and medulla is not clearly visible. The thymic cortex is represented by weakly oxyphilic epithelioreticular cells, macrophages and basophilically stained, tightly adjacent T-lymphocytes; it contains a small number of capillaries surrounded by epithelioreticular cells. The thymus medulla appears lighter. Lymphocytes, macrophages and epithelioreticular cells are clearly visualized in it. At high magnification, thymic bodies formed by reticuloepithelial cells are revealed. In the connective tissue of the thymic septa, single mast cells are detected. The spleen is the largest peripheral organ of the immune system, responding to any immunopathological process in the body, ensuring the homeostasis of red blood cells and, since some plasma cells migrate to the spleen, it takes part in the effector phase of the humoral immune response. In addition, in acquired hemolytic anemia, the spleen is the organ that carries out intracellular hemolysis of red blood cells. Therefore, we included the study of spleen morphology in our study. The spleen on the outside has a capsule of dense fibrous connective tissue containing numerous collagen and elastic fibers, as well as smooth muscle cells, and is covered with mesothelium. Trabeculae extend from the capsule deep into the organ, in the thickness of which blood vessels, smooth muscle cells and nerves are revealed. The trabeculae are thin, sparsely located, with trabecular arteries of the muscular type and veins of the nonmuscular type having a typical structure. In the spleen of intact animals, two functional zones are clearly visualized - the red and white pulp. The white pulp in sections is represented by spherical formations consisting of lymphocytes surrounding the central (nodular) arterioles, and forms periarteriolar lymphoid couplings (T-dependent zone), as well as lymphoid nodules with light centers (reproduction centers) (B-dependent zone). The red pulp of the spleen consists of sinusoidal capillaries (sinusoids of the spleen) and splenic cords located between them (strands of red pulp), anastomosing with each other. Splenic cords are accumulations of blood cells: red blood cells, macrophage cells, leukocytes, including T and B lymphocytes at different stages of differentiation. The stroma of the red pulp is represented by reticular tissue. In the group with tobacco smoking, by the 10th day of the experiment, primarily vascular disorders (edema of connective tissue and vascular congestion) were noted in the thymus tissue. As for changes in lymphoid tissue, they were expressed to varying degrees in different lobules in the same individuals. In the medulla and cortical layers of the thymus, areas of lymphocyte death were visualized, which appeared optically as a "picture of the starry sky." In 20% of animals, replacement of lymphoid tissue with adipose tissue was noted in the lobules. The blood vessels in the devastated cortex had a structure typical of the vessels of the thymic medulla. It is known that the hemocapillaries of the cortical layer have a relatively thick basement membrane, to which epithelioreticulocytes, macrophages and lymphocytes are often adjacent; The basement membrane of the hemocapillaries of the medulla, on the contrary, is thin.

### **Conclusions**

1. In the thymus of animals exposed to tobacco smoking, a decrease in lymphoid tissue was found, accompanied by the death of lymphocytes in the cortex and medulla.
2. Tobacco smoke entails the appearance in the thymus of a large number of degranulating mast cells and actively functioning epithelial tubules.
3. In the spleen of animals exposed to tobacco smoking, a reduction of lymphoid tissue is noted, confirmed by morphometric methods.

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