Journal of Morphological Sciences
J Morphol Sci
Brazilian Society of Anatomy

Original Article
J Morphol Sci 2023;40:2-230-236

# Structural Changes of the Thymus Parenchyma Under the Condition of General Dehydration

**Olha Prykhodko[1], Vitalii Sikora[1]**

[1]Department of Morphology, Sumy State University, Sumy, Ukraine

**Disclose and conflicts of interest: none to be declared by all authors**

## ABSTRACT

**Introduction:** dehydration is an extremely dangerous condition of the body that affects all tissues and organs. The purpose of the research was to study submicroscopic changes in the thymus parenchyma of rats under the condition of general dehydration of the body.

**Material and Methods:** the study was conducted on 40 white male rats of reproductive age. The microanatomy of the structural components of the thymus of white rats under physiological conditions was studied on 10 intact animals. The experimental animals were dehydrated for 6 days.

**Results:** after six days of the experiment, the absolute weight of the rats was lower than the control by 30.98% ($p<0.001$), the absolute weight of the thymus of the rats decreased by 16.77% ($p<0.001$). In the thymus parenchyma, numerous cells are in a state of apoptosis at various stages and necrosis (karyopyknosis, karyorrhexis, karyolysis). Cortical and medullary thymocytes are mainly represented by medium T-lymphocytes. They have a nucleus with a predominance of euchromatin, there is a splitting of contours with pronounced intussusceptions of the nuclear envelope. There is an overflow of the intercellular interstitium with cell remnants. Violations of contacts between epithelial reticular cells and other cells of the thymus were noted.

**Conclusions:** therefore, under conditions of general dehydration of an average degree, which develops in 6 days, signs of accidental transformation with inversion of its layers were found in the parenchyma of the thymus (III).

**Keywords:** Dehydration; Thymus; Rat; Thymocytes; Epithelial reticular cell.

## Introduction

Dehydration is an extremely dangerous state of the body[1]. This is a process characterized by the loss of water by the body, which leads to its deficiency. It is impossible to overestimate the role of water for the body. Water makes up to 70 percent of the human body weight. It provides transport of nutrients and oxygen to all organs and tissues of the body, protects vital organs. It is the basis of all fluids in the body[2]. Recently, much attention has been paid to the study of the impact of various stress conditions, which is important for the population that works in harsh environmental conditions (for example, cold and hypoxia). It has been proven that dehydration syndrome leads to a significant deterioration of the body's condition. Human cannot control environmental conditions; however, since a state of dehydration can cause further deterioration of all processes, adequate fluid intake is an effective tactic[3].

Acute dehydration can cause both physical and cognitive impairment, as well as heat stroke, exhaustion, and death. Mild chronic dehydration is most often associated with kidney disease, however, if it goes on for a long time without treatment, the course becomes more complicated. In addition to infants and people with certain medical conditions, athletes, military personnel, physically active individuals, and the elderly are at particular risk for dehydration due to their physical activity, environmental exposures, and problems maintaining fluid homeostasis[4].

The problem of dehydration is expected to gain more and more relevance in connection with climate changes, in which more and more people will face the need to prevent and overcome the consequences of heat stress, the emergence of new diseases, the prevention and treatment of which will require special attention to the issue of adequate hydration of the body[5].

Dehydration is common among patients with ischemic stroke and is associated with early neurologic deterioration. Dehydration syndrome leads to a decrease in cerebral perfusion and exacerbation of ischemic brain damage[6]. Impaired hydration is common among older adults who are medically hospitalized for any reason[7]. Elderly patients admitted with a primary diagnosis of dehydration had a 30-day mortality rate of 17% and a 1-year mortality rate of 44%, compared with 7% and 25%, respectively, in patients without dehydration. Patients who were diagnosed with dehydration during hospitalization were twice as



DOI: 10.51929/jms.40.230.2023
ISSN 2177-0298

likely to die in the hospital, regardless of age, sex, and comorbidities[8].

Studying the state of immune organs under the influence of various exogenous factors is an important task for morphologists, since these organs provide homeostasis and protection of the body[9-11]. One of the primary lymphoid organs is a thymus[12,13].

Considering the above, further studies of the effect of dehydration on the morphology of the thymus, as the central organ of immunogenesis, will contribute to a better understanding of the structural basis of compensatory and adaptive mechanisms and pathological processes in the body under conditions of dehydration.

The purpose of the study: to study submicroscopic changes in the thymus parenchyma of rats under the condition of general dehydration of the body.

## Materials and Methods

The study was conducted on 40 white male rats of reproductive age weighing 111,81±5.16–162.00±6.00 g.

The microanatomy of the structural components of the thymus of white rats under physiological conditions was studied on 10 intact animals. Experimental animals (20 animals) were exposed to general dehydration by maintaining the animals on a completely water-free diet for 6 days. Controls were 10 white rats that received a standard vivarium diet and water regimen for six days. The degree of dehydration was determined by the difference of the dried carcass. According to the indicator of water deficit, three degrees of dehydration are distinguished: light (water deficit reaches 2-5%), middle (5-10%) and severe (more than 10%).

All experimental animals were kept in the vivarium of Sumy State University. The research was conducted in accordance with the provisions of the European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), Council of Europe Directives 86/609/EEC (1986), Law of Ukraine No. 3447-IV "On the Protection of Animals from Cruelty handling", general ethical principles of experiments on animals, adopted by the First National Congress of Ukraine on Bioethics (2001). Before taking the material, the animals were anesthetized with ether anesthesia. Material was collected in accordance with generally accepted rules. Thymus tissue samples were fixed in glutaraldehyde according to Karnovsky, then in 1% osmium tetroxide according to Palade. It was then passed through alcohols of increasing concentration (50%, 70%, 80%, 96%, absolute alcohol) and poured into a mixture of epoxy resins and polymerized. Ultrathin sections were prepared on an UMTP-4 ultramicrotome. Studying and photographing objects was carried out with the help of a PEM-125 microscope at an accelerating voltage of 90 kV and magnifications on the microscope screen of 4050x–10000x.

Statistical processing of quantitative data was carried out using the Statistica v.10 program (StatSoft Inc., USA). Descriptive analysis of each sample was performed with calculation of Mean (M) and Standard Deviation (SD). The non-parametric Mann-Whitney U-test was used to assess the differences between the two samples according to the studied indicators. A difference of $p<0.05$ was considered significant. On semi-thin sections of thymus tissue in the cortical and medullary substance of lobules of the thymus, the absolute number of lymphoid cells in the field of view corresponding to an area of 0.009 $mm^2$ (magnification x1000) was determined using the program «ImageJ» (USA).

## Results

The submicroscopic structure of the thymus of white male rats of reproductive age of the intact and control groups corresponds to the species norm. From the outside, the organ is surrounded by a capsule, which, showing partitions in the parenchyma, divides it into lobules. Each of lobules include cortical and medullary substance. The framework of the organ is formed by epithelial reticular cells, which are connected to each other by processes. The space between them is occupied by thymocytes, macrophages, fibroblasts, myofibroblasts, and basophils. The nucleus of epithelial reticular cells is large, bright because euchromatin prevails. Cytoplasm contains ribosomes, bundles of tonofilaments, mitochondria, vacuoles, granular endoplasmic reticulum. Cortical substance of the lobules of thymus is made of small and middle lymphocytes, macrophages. The medullary substance is made up of small, middle and large lymphocytes, macrophages, and epithelial reticular cells. The structure of all cells is typical, unchanged (Fig.1, 2). Lymphoblasts are located in the subcapsular

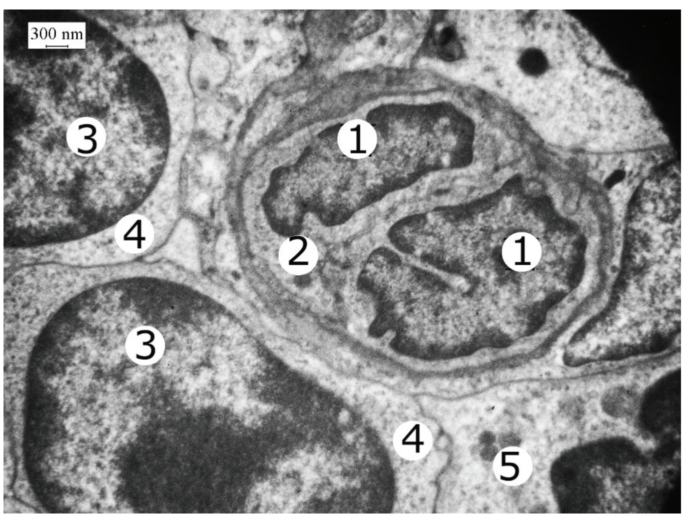

**Figure 1.** Hassal's corpuscle in the medullary substance of the thymus lobules of the rat male of intact group. Electron micrograph. Magnification: ×8000. Symbols: 1 – nucleus of epithelial reticular cell; 2 – cytoplasm of epithelial reticular cell; 3 – nucleus of thymocyte; 4 –cytoplasm of thymocyte; 5 – mitochondria.

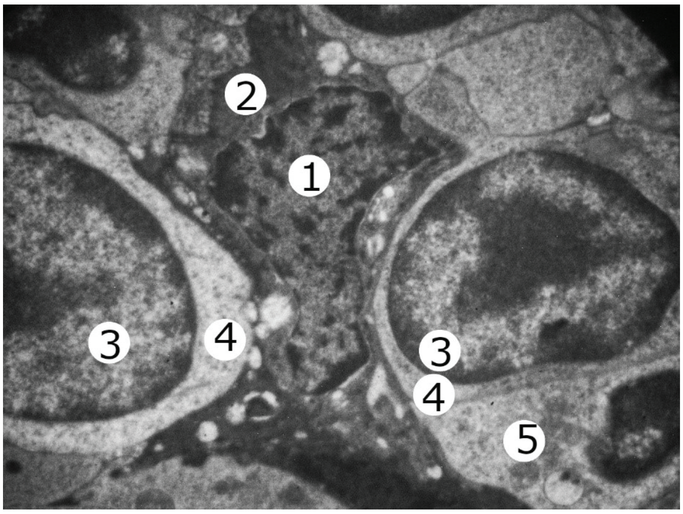


**Figure 2.** Electron-microscopic organization of the medullary substance of the thymus lobules of the of the rat male of intact group. Electron micrograph. Magnification: ×8000. Symbols: 1 – nucleus of epithelial reticular cell; 2 – cytoplasm of epithelial reticular cell; 3 – nucleus of thymocyte; 4 – cytoplasm of thymocyte; 5 – mitochondria.

substance. There are many postcapillary venules in the medullary substance of lobules.

On the 6th day from the beginning of the experiment, an average degree of general dehydration developed. After 6 days of dehydration the absolute mass of rats is lower than the control by 30.98% ($p<0.001$), the absolute mass of the thymus of rats decreased by 16.77% ($p<0.001$) (Table 1). The length of the thymus is lower than the control indicators by 10.39% ($p<0.001$), the middle indicator of the width of the thymus decreases by 5.02% ($p=0.002$), the thickness decreases by 13.84% ($p<0.001$). The density of lymphocytes in the cortical substance of the thymus lobules decreases than the control by 36.97 % ($p<0.001$) and in medullary substance by 31.13 % ($p<0.001$) (Table 1).

Accidental transformation of the thymus with inversion of its layers is observed (III). At the same time, in the lobules of the thymus, there is not a clear border between the cortical and medullary substance, besides, the cortical substance looks lighter, and the medulla, on the contrary, is somewhat dark, compared to the control group, which is due to a change in the density of thymocytes in both areas. During the study of ultrathin sections of the thymus of rats, active plasma cells of an elongated shape were found. Such cells have a nucleus with wavy contours, areas of lysis and a well-defined perinuclear zone. The ultrastructure of these cells is characterized by the presence in the cytoplasm of a well-developed and expanded granular endoplasmic reticulum (ESR), represented by short discontinuous tubules with a low electron density, occupying most of the cell cytoplasm (Fig. 3). The cytoplasm also contains ribosomes of different diameters, centrioles are located in the perinuclear area, surrounded by Golgi

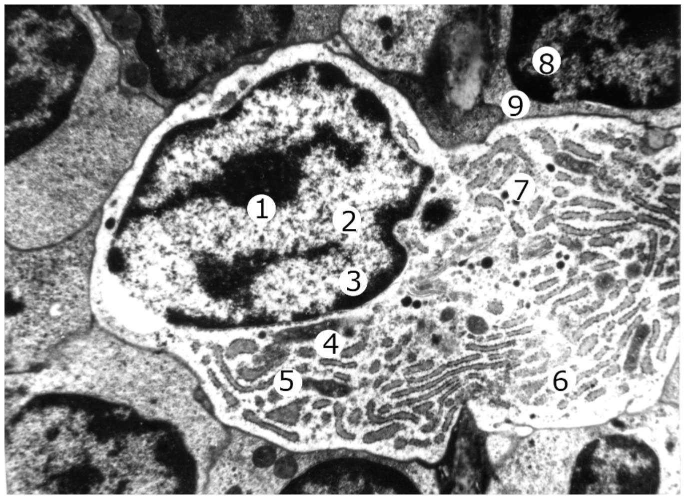


**Figure 3.** Electron microscopic organization of a fragment of a thymus of a rat male on the 6th day of general dehydration. Electron photography. Magnification: ×10000. Symbols: 1 – nucleus of plasma cell; 2 – euchromatin and heterochromatin (3) in the nucleus of plasma cell; 4 – deformed mitochondria; 5 – Golgi complex; 6 – expanded tubules of the granular endoplasmic reticulum with ribosomes; 7 – lysosomes of different diameters; 8 – nucleus of thymocyte; 9 – a thin rim of cytoplasm.

**Table 1.** Dynamics of changes of parameters of thymus of male rats in control and experimental groups (M±SD)

| Parameter, units of measurement | A group of animals | |
|---|---|---|
| | Control | Experimental (6 days) |
| Body weight, g | 162.00±6.00 | 111.81±5.16<br>$p<0.001$ |
| Thymus weight, mg | 301.50±19.13 | 250.95±21.08<br>$p<0.001$ |
| Thymus length, mm | 14.34±0.20 | 12.85±0.24<br>$p<0.001$ |
| Thymus width, mm | 9.17±0.13 | 8.71±0.38<br>$p=0.002$ |
| Thymus thickness, mm | 3.54±0.21 | 3.05±0.17<br>$p<0.001$ |
| Lymphocytes density in the cortical substance, $N_{Lymphocytes}/0.009\ mm^2$ | 247.25±17.87 | 155.85±15.34<br>$p<0.001$ |
| Lymphocytes density in the medullary substance, $N_{Lymphocytes}/0.009\ mm^2$ | 132.72±20.77 | 91.40±13.99<br>$p<0.001$ |

cisternae. These areas alternate with areas of focal lysis. Mitochondria are deformed, with a compacted matrix. In this term of the experiment, plasma cells with lighted cytoplasm are more common.

Cortical and medullary thymocytes are mainly represented by middle T-lymphocytes. They have a nucleus with a predominance of euchromatin. In some thymocytes, the nucleus are hypertrophied, the boundaries of the plasmolemma are not clear. Split contours with pronounced intussusceptions of the nuclear envelope are observed (Fig. 4). Nuclear pores and perinuclear space are not expanded. The number of mitochondria is significant, they are well contoured, some of them have destroyed cristae, most of them are electron-dense. However, in these cells there are areas of disintegration of the cytoplasm. The cytoplasm contains electron-dense lysosomes and relatively weakly developed ribosomes, polysomes, single tanks of the granular endoplasmic reticulum, and centrioles. Along with this, hypertrophied and giant mitochondria were found. In separate areas of the sarcoplasm, mitochondria were located in groups, closely adjacent to each other, pushing myofibrils against the background of the illuminated matrix, while in the control grain, mitochondria were located in the form of a chain at a small distance from each other. Small thymocytes are rare.

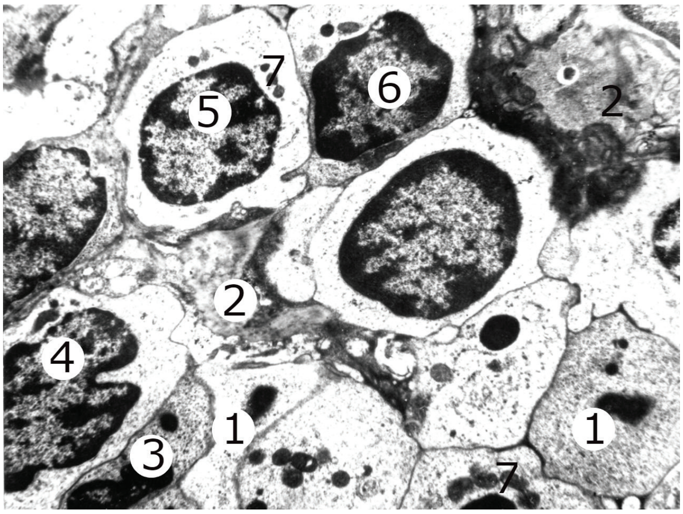


**Figure 4.** Electron-microscopic organization of the cortical substance of the thymus lobules of the rat male on the 6th day of general dehydration. Electron photography. Magnification: ×4000. Symbols: 1 – cell karyolysis; 2 – the area of cell destructuring; 3 – wrinkled thymocyte, the nucleus contains mostly condensed heterochromatin; 4 – invaginated nuclear envelope of the thymocyte nucleus; 5 – nucleus of middle thymocyte; 6 – the nucleus of a "dark" thymocyte, condensation of heterochromatin in the depths; 7 - arrangement of mitochondria in groups.

There were «dark» thymocytes, the diameter of their nuclei was reduced, the chromatin was represented by compact blocks (Fig. 4). The nuclear contour is wavy, the perinuclear space has areas of expansion, mitochondria in dark thymocytes are functionally inactive, usually rounded or elongated, electron-dense. Areas of destruction of the nuclear envelope and release of nuclear material into the cytoplasm are noted. Individual cells are shriveled and deformed. Numerous cells in a state of apoptosis at various stages and necrosis (karyopyknosis, karyorrhexis, karyolysis).

When studying the transmission images of sections of light and dark epithelial reticular cells of both the cortical and medullary substance, a characteristic feature on the 6th day of dehydration was that among the morphologically completely preserved epithelial cells, there were cells with a pronounced wrinkled nucleus, with deep and small intussusceptions and partial damage to the integrity of the karyolemma and cytolemmas alternating with increased osmiophilicity of membranes (Fig. 5, 6). Violations of contacts between epithelial reticular cells and other cells of the thymus were noted (Fig. 5). In the cytoplasm of epithelial reticular cells there are destructive mitochondria with flattened and shortened cristae.

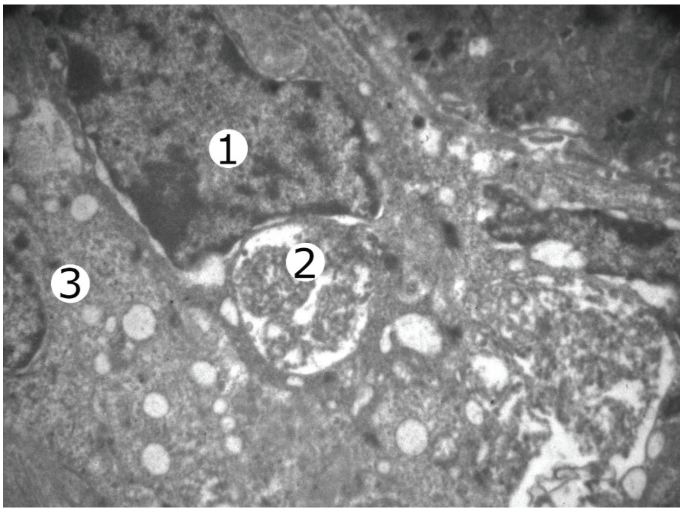


**Figure 5.** Epithelial reticular cell in the medullary substance of the thymus lobules of the rat male on the 6th day of general dehydration. Electron photography. Magnification: ×8000. Symbols: 1 – nucleus with an uneven, not clear karyolemma; 2 – vacuolated cytoplasm; 3 – lack of boundaries and contacts between cells.

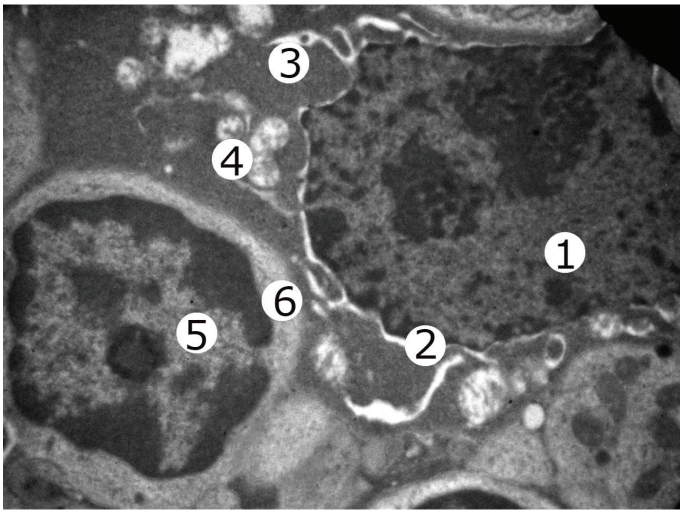


**Figure 6.** Electron-microscopic organization of the cortical substance of the thymus lobules of the rat male on the 6th day of general dehydration. Electron photography. Magnification: ×8000. Symbols: 1 – nucleus of epithelial reticular cell; 2 – expanded perinuclear space, 3 – destruction of cytoplasm of epithelial reticular cell; 4 – mitochondria; 5 – nucleus of thymocyte; 6 – cytoplasm of thymocyte.

They become less osmiophilic (light), a quantitative increase in pinocytotic vesicles is noted (Fig. 5). There is an overflow of the intercellular interstitium with cell remnants, i.e. areas of cytolysis.

Another type of epithelial reticular cells had a completely vacuolated cytoplasm, the source of vacuoles being mitochondria and structural components of the Golgi complex and other cell organelles (Fig. 5). Individual mitochondria are lysed, contain a lighted matrix with remnants of cristae. Altered mitochondria are swollen. There are large vacuoles containing necrotic cytoplasmic material, the cytolemma loses its borders. There are destroyed epithelial reticular cells with a dark nucleus and electron-dense cytoplasm. The nucleus has a discontinuous contour, the perinuclear space is slightly expanded, the cytoplasm of epithelial reticular cells contains scarce membrane components, the absence of organelles and single vacuoles is noted. Flattened epithelial reticular cells with dystrophic changes in the nucleus and cytoplasm with moderate signs of keratinization were observed. The nucleus have jagged contours and deep intussusceptions.

On the 6th day of the study, ultrastructural analysis shows that in the cytoplasm of macrophages there is an increased accumulation of phagosomes, a small number of lysosomes, and a well-developed granular endoplasmic reticulum (Fig. 7). Mitochondria of middle and small sizes, in the vast majority of cells are undamaged, the structure of the cristae is preserved, the matrix has a uniform moderate electron density.

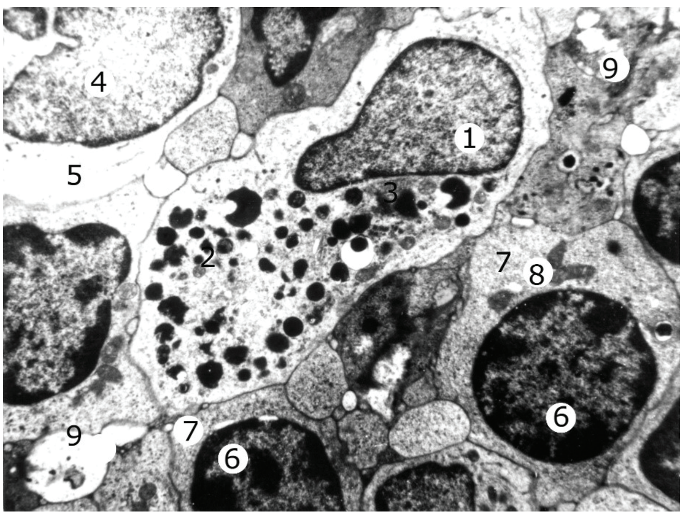


**Figure 7.** Electron-microscopic organization of the medullary substance of the thymus lobules of the rat male on the 6th day of general dehydration. Electron photography. Magnification: ×5000. Symbols: 1 – nucleus of macrophage with signs of pronounced phagocytic activity and pronounced lysosomal reaction; 2 – phagolysosomes; 3 – mitochondria; 4 – nucleus of epithelial reticular cell with deep intussusceptions; 5 – enlightened cytoplasm of epithelial reticular cell; 6 – nucleus of thymocyte; 7 – cytoplasm of thymocyte; 8 – mitochondria with swollen cristae; 9 – areas of destructuring.

Very often, their short cytoplasmic processes, located between other cells, came into view. An increase in the number of monocytes, which is the source of macrophage formation, was noted. They are localized more in the cortical substance of the thymus. Some of the monocytes have destroyed cytoplasm. In some cases, focal necrosis of a part of the cytoplasm and shrinkage of the karyolem with accumulation of chromatin, which formed teeth along it, were observed.

Dendritic cells, which had long cytoplasmic appendages located between other cells, were mature and located in the peripheral parts of the medullary substance. A large number of granules, pinocytotic vesicles and lysosomes attract attention.

During this period of dehydration, the structural changes of hemocapillaries were quite diverse, namely, both empty hemocapillaries and those with a narrow slit-like lumen were observed (Fig. 8). Moderate dehydration was accompanied by an increase in the permeability of the hemocapillary walls, which confirmed the appearance of erythrocytes and plasma cells in the perivascular spaces.

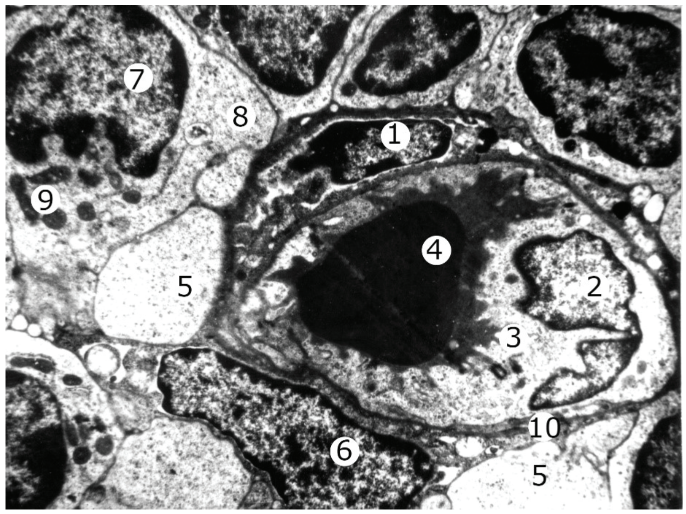


**Figure 8.** Electron-microscopic organization of the cortical substance of the thymus lobules of the rat male on the 6th day of general dehydration. Electron photography. Magnification: ×8000. Symbols: 1 – nucleus of pericyte with condensed chromatin; 2 – deformed nucleus of endotheliocyte; 3 – swelling cytoplasm of endotheliocyte; 4 – erythrocyte in the narrowed lumen of the hemocapillary; 5 – expanded perivascular space; 6 – nucleus of epithelial reticular cell; 7 – deformed nucleus of thymocyte; 8 – enlightened cytoplasm; 9 – mitochondria; 10 – the basement membrane of the hemocapillary.

## Discussion

The above-described data, in particular a decrease in animal body weight of 30.98%, confirm that 6 days of a water-free diet causes general dehydration of experimental animals of an average degree.

The authors conducted a study on 25 male and 14 female rats, in which the animals were dehydrated to the 1st, 2nd and 3rd degree of dehydration by stopping the introduction of water in order to study the condition of the larynx, in particular the vocal folds. Under the condition of a mild degree of dehydration as a result of acute systemic dehydration, no reliable changes in the vocal folds were detected. Under conditions of middle and severe degree, their reliable and significant thinning was revealed. Rehydration restored the condition of the vocal folds only after mild to moderate dehydration. No significant differences between the indicators of male and female rats were found during the experiment[14].

In the study, the authors analyzed the effects of dehydration, hypoxia and hypothermia on the body of rats. It was found that only dehydration significantly reduced the body weight of animals compared to the control group. Only a combination of multiple environmental stressors, such as cold, hypoxia, and dehydration, reliably affected the decrease in core body temperature[3].

Intracellular dehydration was induced in obese and nonobese Zucker rats by replacing the drinking water with hyperosmotic sodium chloride solutions (1.8% and 2.7%, consecutively, for 4 days). Daily food intake, food volume, and number of meals were measured using an automated computerized counter before, during, and after dehydration. After 8 days of hyperosmotic drinking, the body weight of animals decreased by 15% and 10% in lean and obese rats, respectively. Obese rats consumed more food and food volume than lean rats before, during, and after dehydration. Dehydration in obese rats did not affect food intake, but it was reduced in lean rats during 2.7% sodium chloride loading and remained low during refeeding after dehydration when meal size was increased. Thus, dehydration-induced anorexia is present in both obese and lean Zucker rats; however, obese rats are more resistant to dehydration, maintaining meal size and volume intake. These results support the role of diet-related dehydration in the pathogenesis of hyperphagia and obesity[15].

A study conducted on rats with middle cerebral artery occlusion is described. Infarct volume and relative cerebral blood flow after infarction were assessed. The first group of animals was the group of dehydration, the second group of normal hydration. The state of dehydration was achieved by deprivation of water for 48 hours before occlusion of the middle cerebral artery. The results obtained by the authors indicated that the state of dehydration is associated with the progression of the infarct volume and the decrease in cerebral blood flow during the acute stage of ischemic stroke. This study provided a visual clue that a more intensive hydration therapy and reperfusion strategy is needed to treat acute ischemic stroke patients with dehydration status[6].

The changes found in the thymus vessels are somewhat similar to those seen under the opioid nalbuphine. The authors describe an increase in the permeability of the walls of hemocapillaries, the release of erythrocytes into the perivascular space. This is often associated with damage to the integrity of the vessel wall[16].

## Conclusions

As a result of the research conducted on male rats, we found that under conditions of general dehydration of middle degree, which develops in 6 days, signs of accidental transformation with inversion of its layers were found in the thymus parenchyma (III). Numerous cells in a state of apoptosis at various stages and necrosis (karyopyknosis, karyorrhexis, karyolysis). Cortical and medullary thymocytes are mainly represented by middle T-lymphocytes. They have a nucleus with a predominance of euchromatin, there is a splitting of contours with pronounced intussusceptions of the nuclear envelope.

## References

1. Hula VI, Sikora VZ, Yarmolenko OS, Bumeister VI, Pernakov MS, Boiko VO. Mikroskopichni ta ultramikroskopichni zminy holovnykh ekzokrynotsytiv slyzovoi obolonky shlunka za umov subletalnoi zahalnoi dehidratatsii orhanizmu [Microscopic and ultramicroscopic changes of the main exocrinocytes of the gastric mucosa under conditions of sublethal general dehydration of the body]. Zaporizkyi medychnyi zhurnal. 2018;20,2(107):193-8. https://doi.org/10.14739/2310-1210. 2018.2.124948.
2. Perry RJ, Rabin-Court A, Song JD, Cardone RL, Wang Y, Kibbey RG, *et al*. Dehydration and insulinopenia are necessary and sufficient for euglycemic ketoacidosis in SGLT2 inhibitor-treated rats. Nat Commun. 2019;10:548. https://doi.org/10.1038/s41467-019-08466-w
3. Uno T, Hasegawa T, Horiuchi M. Combined stimuli of cold, hypoxia, and dehydration status on body temperature in rats: a pilot study with practical implications for humans. BMC Res Notes. 2020;13:530. https://doi.org/10.1186/s13104-020-05375-w.
4. Garrett DC, Rae N, Fletcher JR, Zarnke S, Thorson S, Hogan DB, *et al*. Engineering Approaches to Assessing Hydration Status. IEEE Rev Biomed Eng. 2018;11:233-48. https://doi.org/10.1109/RBME.2017.2776041
5. Perrier ET. Hydration for Health: So What? Ten Advances in Recent Hydration History. Ann Nutr Meta. 2019;74(3):4-10. https://doi.org/10.1159/000500343.
6. Tsai Y-H, Yang J-L, Lee I-N, Yang J-T, Lin L-C, Huang Y-C, *et al*. Effects of Dehydration on Brain Perfusion and Infarct Core After Acute Middle Cerebral Artery Occlusion in Rats: Evidence From High-Field Magnetic Resonance Imaging. Front. Neurol. 2018;9:786. https://doi.org/10.3389/fneur.2018.00786.
7. Sanson G, Marzinotto I, De Matteis D, Boscutti G, Barazzoni R, Zanetti M. Impaired hydration status in acutely admitted older patients: prevalence and impact on mortality. Age and Ageing. 2021;50(4):1151-8. https://doi.org/10.1093/ageing/afaa264.
8. El-Sharkawy AM, Virdee A, Wahab A, Humes DJ, Sahot O, Devonald MAJ, *et al*. Dehydration and clinical outcome in hospitalised older adults: A cohort study. Eur Geriatr Med. 2017;8(1):22-9.
9. Adane F, Asres K, Ergete W, Woldekidan S, Seyoum G. The Developmental Toxicity of Thymus schimperi Essential Oil in Rat Embryos and Fetuses. Journal of Toxicology. 2022;2022:4091839. https://doi.org/10.1155/2022/4091839.
10. Avilova O, Sheyan D, Marakushin D, Erokhina V, Gargin V. Ultrastructural changes in the organs of the immune system under the influence of xenobiotics. Georgian Medical News. 2018;6:132-7.
11. Dires K, Mengiste B, Lulekal E. Evaluation of acute, sub-acute and skin irritation toxicity on essential oil of Thymus schimperi in Ankober, north Shewa, Debre Berhan, Ethiopia. Journal of Clinical Toxicology. 2018;8(3):1-4.
12. Haile T, Cardoso SM, de Oliveira Raphaelli C, Pereira OR, Pereira EdS, Vizzotto M, *et al*. Chemical Composition, Antioxidant Potential, and Blood Glucose Lowering Effect of Aqueous Extract and Essential Oil of Thymus Serrulatus Hochst. Ex Benth. Front. Pharmacol. 2021;12:621536. https://doi.org/10.3389/fphar.2021.621536.

13. Shyian D, Avilova O, Ladnaya I. Organometric changes of rats thymus after xenobiotics exposure. Arch Balk Med Union. 2019;54(3):422-30. https://doi.org/10.31688/ABMU.2019.54.3.04.
14. Oleson S, Cox A, Liu Z, Sivasankar MP, Lu K-H. In Vivo Magnetic Resonance Imaging of the Rat Vocal Folds After Systemic Dehydration and Rehydration. Journal of Speech, Language, and Hearing Research. 2020;63(1):135-42. https://doi.org/10.1044/2019_JSLHR-19-00062.
15. Fetissov SO, Meguid MM. Food intake and meal pattern in response to hyperosmotic-induced dehydration in obese and lean Zucker rats. Nutrition: X. 2020;6:100011. https://doi.org/10.1016/j.nutx.2020.100011
16. Harapko TV, Holovatskyi AS. Nalbuphine-induced submicroscopic changes in the components of the thymus vascular bed. World of Medicine and Biology. 2017;4(62):111-6. https://doi.org/10.26724/2079-8334-2017-4-62-111-116.

Received: January 21, 2023
Accepted: February 7, 2023

Corresponding author
Olha Prykhodko,
E-mail: olha.prykhodko@ukr.net