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O. Ye. Kuziv *https://orcid.org/0000-0001-6185-928X*
A. F. Slyva *https://orcid.org/0000-0003-2385-4001*
I. I. Yuryk *https://orcid.org/0000-0002-0008-6276*
Ya. I. Yuryk *https://orcid.org/0000-0001-7690-9307*

AUTOPHAGY AS A KEY ADAPTIVE MECHANISM IN THE STRUCTURAL REMODELING OF THE THYMUS UNDER CONDITIONS OF PROLONGED TOTAL FASTING IN THE EXPERIMENT

Ivan Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine, Ternopil, Ukraine

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Under conditions of prolonged total fasting, a profound restructuring of the cellular composition and stromal elements of the thymus occurs; however, the role of autophagy in these processes remains insufficiently elucidated.

Objective is to determine the role of autophagy in the structural remodeling of the thymus under conditions of prolonged total fasting in rats.

Materials and methods. The experiment was conducted on 32 white outbred laboratory rats of both sexes and 8 intact animals. The rats were sacrificed after 1, 3, and 7 days of complete fasting and after 7 days of refeeding. Thymic tissue for histological examination was stained with hematoxylin and eosin and with azure II and eosin, and studied using a SEOSCAN microscope. For ultrastructural examination, thymus tissue samples were fixed in OsO_4, contrasted with uranyl acetate, embedded in epoxy resin, and ultrathin sections were examined with a PEM-125K electron microscope.

Results. Prolonged total fasting is characterized by marked depletion of the cortical lymphoid population, apoptosis of thymocytes, and destructive changes in epithelial reticular cells. Changes in the medullary substance are less pronounced; however, its relative "enlargement" is observed due to cortical zone reduction. Hassall's corpuscles retain their typical structure. The most pronounced structural alterations of the thymus are detected after 7 days of complete fasting, manifested by severe lymphoid depletion in the cortex and large Hassall's corpuscles in the medulla with signs of keratinization and hyalinosis. Morphological markers of autophagy (cytoplasmic vacuoles, increased lysosome and autophagosome content, and residual bodies) are clearly identified at the early stages of deprivation and progressively intensify with fasting duration. During the recovery period, cortical repopulation occurs, accompanied by increased mitotic activity of thymocytes. The presence of autophagy during this phase represents an important mechanism of restoration of the structural organization of the thymus.

Keywords: thymus, autophagy, total fasting, morphology, electron microscopy.

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О. Є. Кузів, А. Ф. Слива, І. І. Юрик, Я. І. Юрик

АУТОФАГІЯ – КЛЮЧОВИЙ АДАПТАЦІЙНИЙ МЕХАНІЗМ У СТРУКТУРНІЙ ПЕРЕБУДОВІ ВИЛОЧКОВОЇ ЗАЛОЗИ ЗА УМОВ ПОВНОГО ТРИВАЛОГО ГОЛОДУВАННЯ В ЕКСПЕРИМЕНТІ

Тернопільський національний медичний університет імені І. Я. Горбачевського Міністерства охорони здоров'я України, Тернопіль, Україна

З аналізу літературних джерел відомо, що вилочкова залоза є ключовою ланкою специфічного імунітету, характеризується високою проліферативною активністю тимоцитів та є надзвичайно чутливою до голодування. Проведене дослідження присвячене вивченню ролі аутофагій у структурній перебудові тимуса за умов повного тривалого голодування в експерименті.

З'ясовано, що повне тривале голодування характеризується вираженим клітинним спустошенням кіркової речовини, апоптозом тимоцитів і деструктивними змінами епітеліоретикулоцитів. У мозковій речовині зміни виражені менше, однак спостерігається відносне її «збільшення» через редукцію кіркової зони. Тільця Гассаля мають типову структуру. Найвираженіші структурні зміни вилочкової залози виявляються через 7 діб повного голоду, що проявляється суттєвою лімфоїдною деплецією кіркової речовини, в мозковій – виявляються великі тільця Гассаля з явищами кератинізації та гіалінозу.

Ключові слова: тимус, аутофагія, повне голодування, морфологія, електронна мікроскопія.

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Стаття поширюється на умовах ліцензії

Introduction

One of the most relevant areas of modern morphology and immunology is the study of the structure and function of lymphoid tissue as a morphological substrate of the immune system. The thymus plays a key role in the development of adaptive immunity, as it ensures the maturation and selection of T lymphocytes – the main effector cells of the cellular immune response [1–3]. Autophagy is a universal mechanism of intracellular homeostasis that ensures cell survival under stressful conditions, in particular, during food deprivation. Autophagy is an evolutionarily developed mechanism for the degradation and recycling of internal cell components, which is important both for cell survival under stressful conditions and for the control of immune processes. It affects cell self-renewal, differentiation, and long-term survival by coordinating the balance between energy needs and the removal of damaged organelles [4–8]. Starvation is the strongest inducer of autophagy [7; 9]. However, the mechanisms of this process's participation in the structural and functional remodeling of the thymus under conditions of complete prolonged starvation remain insufficiently understood. Thymus involution is accompanied by increased autophagic activity [10], but the relationship between these processes under conditions of complete prolonged starvation has not yet been adequately explained morphologically.

Studying the dynamics of autophagy in the structural components of the thymus during complete prolonged starvation is promising for understanding the adaptive capabilities of the body's immune system under conditions of extreme metabolic stress [4; 10]. The results obtained may become the structural basis for further research into the effects of metabolic stress on the immune system and the search for new approaches to its correction.

The aim of the study is to determine the role of autophagy in the structural remodeling of the thymus under conditions of complete prolonged starvation in rats.

Materials and Methods

The study involved 32 white outbred rats of both sexes laboratory rats aged three months with an average body weight of 180–200 grams, which were kept under complete starvation with free access to water and were placed individually in exchange cages. The animals were removed from the experiment after 1, 3, and 7 days of complete starvation and after 7 days of recovery feeding. The control group consisted of 8 intact animals.

The thymus tissue for histological examination was stained with hematoxylin and eosin and azure II and eosin and examined under a SEOSCAN microscope using a VISION Color CCD Camera and InterVideoWinDVR software. For ultramicroscopic examination, thymus tissue was fixed in a 2.5 % solution of glutaraldehyde, and the material was fixed in a 1 % solution of osmium tetroxide in Milonga buffer. Further processing of the material (dehydration in alcohols and acetone, staining with uranyl acetate, and embedding in epoxy resin) was performed according to the standard procedure [11]. Ultrathin sections were prepared on an LKB-3 ultramicrotome (Sweden) and studied in a PEM-125 K electron microscope. The experimental study and maintenance of rats were carried out in accordance with the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), the rules for the treatment of experimental animals in accordance with EU Council Directive 2010/63/EU on compliance with the regulations, laws, and administrative provisions of EU Member States on the protection of animals used for scientific purposes [11].

Research results and their discussion

In intact animals, the thymus gland has a well-defined capsule and connective tissue trabeculae that divide it into lobules. The area of the cortex significantly exceeds the medulla of the organ. The main mass of the parenchyma consists of small lymphocytes, the density of which in the cortical substance is significantly higher than in the medulla, which causes a sharp boundary between them. The medulla is composed mainly of epithelioid reticular cells, which form its stroma with a small number of lymphoid elements. The number of Hassall's corpuscles is small, which correlates with the data of R. Mikušová and J. Mokrý [12].

Small lymphocytes are regularly round in shape with round or oval nuclei in the center. Chromatin is dense, collected in large clumps located along the karyolemma. One or two nucleoli are outlined in the nucleoplasm. The cytoplasm forms a narrow band around the nucleus, in which small spherical mitochondria with clearly defined cristae, a few ribosomes and polysomes, and isolated microvesicles are located.

In medium lymphocytes, the cytoplasm forms a wider band than in small lymphocytes, containing multiple mitochondria, ribosomes, polysomes, short tubules of the granular reticulum, and occasionally the Golgi complex. Immunoblasts (large lymphocytes) have a large oval-shaped light nucleus, in the nucleoplasm of which euchromatin dominates, with only small clumps of heterochromatin near the karyolemma. The cytoplasm is wide and contains large mitochondria of round or elongated shape with a moderately electron-dense matrix and multiple cristae, numerous ribosomes, polysomes, and quite a lot of short tubules of the granular endoplasmic reticulum.

The lymphoid elements of the thymus have high proliferative activity. The highest number of mitoses occurs in the cortical substance, specifically in its subcapsular zone. There are two types of epithelioid cells that form the stroma of the organ: epithelioid cells of the cortical substance and epithelioid cells of the medullary substance of the thymus.

A submicroscopic examination of the epithelial reticulocytes of the thymus cortex revealed that they have a star-shaped form with long cytoplasmic processes. The nucleus is elongated, often irregular in shape, with small clumps of heterochromatin located along the inner layer of the karyolemma. Thin fibrils, ribosomes, polysomes, mitochondria, and small light vacuoles are outlined in the cytoplasmic processes (Fig. 1).

Epithelial cells of the medulla against the cells of the cortex have a light oval-shaped nucleus. The extensive cytoplasm has short projections, in which thin fibrillar structures, mitochondria, Golgi complexes, multiple ribosomes, and microvesicles are outlined. A characteristic feature of these cells is the presence of large light-colored cluster-like vacuoles in their cytoplasm with a single osmiophilic granule at the periphery (Fig. 2).



Fig. 1. Fragments of thymus cortex from an intact rat:
1 – epithelioid cells with long cytoplasmic processes that contact lymphocytes. Magnification: × 7500

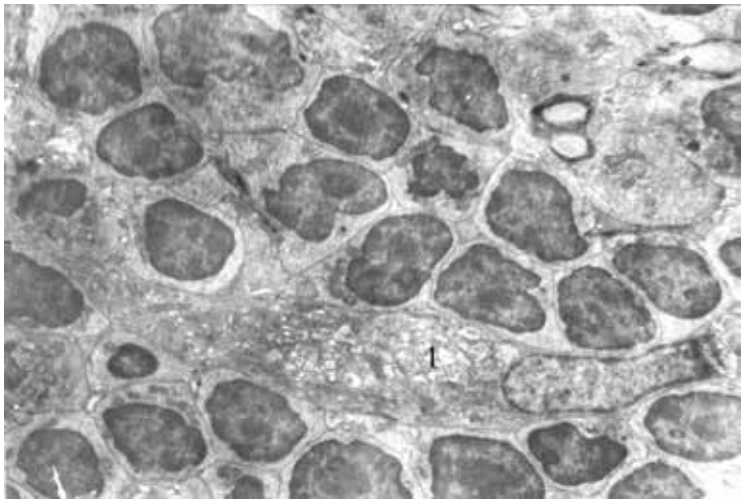


Fig. 2. Fragments of the medulla of the thymus of an intact rat:
1 – epithelioid cell of the medulla. Magnification: × 2500

Macrophages of the cortex of the thymus are functionally active. The nuclei of macrophages are oval in shape, dominated by euchromatin, with heterochromatin forming a narrow band along the inner layer of the nucleolemma. The cytoplasm contains well-defined general-purpose organelles: small multiple mitochondria, canaliculi of the granular and agranular endoplasmic reticulum, the Golgi complex, and, in particular, numerous lysosomes. The cytoplasm contains lymphocyte nuclei at various stages of degradation.

Analysis of histological preparations showed that after 1 day of complete fasting of experimental animals, the capsule and interlobular connective tissue trabeculae and the cross-sectional area of the thymus significantly increased compared to those in intact rats.

A redistribution between the parenchyma and the connective tissue capsule and trabeculae is noted, accompanied by a decrease in the area of the cortex substance with a simultaneous increase in the area of medullary substance. The mosaic pattern of the gland lesion is noteworthy. There are isolated lobules with well-preserved cortex, some completely replaced by adipose tissue, and in most lobules there is blurring of the boundary between the cortical and medullary substances and accumulation of adipose tissue in them. In the medullary substance of the thymus lobules, areas of lymphocyte destruction are visible.

After 3 days of complete starvation, interstitial expansion is observed, and there is a marked decrease in thymocytes in the cortex with the appearance of “empty” areas. The medulla appears enlarged against the background of a decrease in the cortical zone. Cortico-medullary inversion occurs. Hassall’s corpuscles are formed in the exposed areas of the medulla.

The significant decrease in thymocyte density in the cortical substance after 3 days of complete starvation that we observed correlates with data in the literature on rapid thymus involution during stress or deprivation [7; 13]. The most pronounced destructive changes, including atrophy of epithelioid cells and reduction of the cortical zone, are observed after 7 days of complete starvation.

After 7 days of complete starvation, the stroma is characterized by interstitial expansion. There are no clear boundaries between the cortex and medulla. The cortex undergoes pronounced lymphoid depletion: the density of thymocytes is sharply reduced, and the structure of the zone is fragmented.

Large Hassall's corpuscles with signs of keratinization and hyalinosis are found in the medulla.

A characteristic feature of thymus epithelial reticulocytes in animals that have been completely starved is a sharp increase in their secretory activity and enhanced autophagy. Epithelial reticulocytes retain their stellate shape with an irregularly shaped nucleus due to frequent invaginations, which can vary in depth. The nucleus has a mottled appearance due to the presence of multiple euchromatin clumps. The nucleolus is usually absent. The signs of autophagy are manifested by the localization of vacuoles and lysosomes of various sizes (from small to large). The manifestations we have described of increased secretory activity of the epithelial reticulocytes of the thymus cortex and autophagy during complete starvation, as well as the appearance of Hassall's corpuscles with signs of keratinization and hyalinosis, coincide with the data of other scientists [4; 6; 12; 14]. At the same time, the content of lysosomes in the cytoplasm of lymphocytes increases (Fig. 3).

The reaction of epithelial reticulocytes of thymus parenchyma cells to complete starvation manifests itself in organelle hypertrophy and hyperplasia. Such epithelial reticulocytes have large, irregularly shaped light nuclei dominated by euchromatin, with one or two nucleoli, usually ectopic. The cytoplasm contains a hypertrophied Golgi complex, short multiple endoplasmic reticulum tubules, and numerous secretory granules ranging from small to large with light contents and a single osmiophilic granule at the periphery. Mitochondria are small, round in shape with a small number of cristae. The cytoplasm contains a large number of small vacuoles, vesicles, lysosomes, and autophagosomes, multiple ribosomes, and polysomes.

After 3 days of complete starvation, an increase in the functional activity of cortical epithelioid cells is observed. The nucleus is irregular in shape, and the nucleoplasm is mottled due to numerous small clumps of heterochromatin. The cytoplasmic processes show an increase in the content of light vacuoles, autophagosomes, lysosomes, and residual bodies. Autophagic vacuoles are more common in cortical cells, indicating the activation of mechanisms for the utilization of intracellular components (Fig. 4).

The nuclei of the epithelial reticulum cells of the thymus medulla are light, oval in shape, and outlined in the middle of the cytoplasm. In the wide, long processes with light cytoplasm, which are in close contact with the cytosomes of lymphocytes over a significant part of their

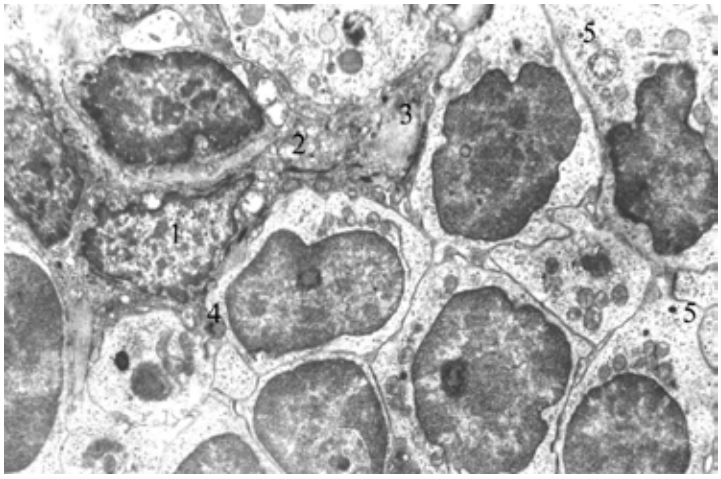


Fig. 3. Fragment of thymus cortex. Epithelial reticulocytes: 1 – nucleus, 2 – vacuoles, 3 – lysosomes, 4 – autophagosomes, 5 – lysosomes in the cytoplasm of lymphocytes. Magnification × 5000

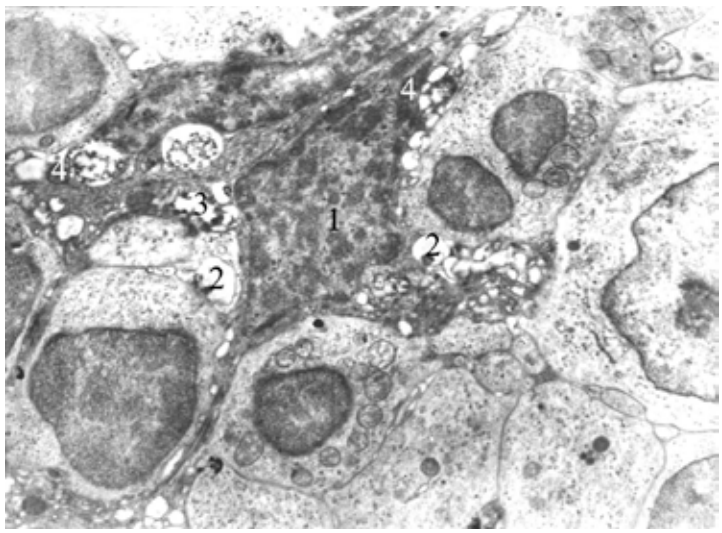


Fig. 4. Fragment of thymus cortex after 3 days of complete starvation. Epithelial reticulum cells in the cytoplasm of which are localized: 1 – nucleus, 2 – vacuoles, 3 – residual bodies, 4 – autophagosomes. Magnification: × 4000

length, the number of secretory granules, lysosomes, endoplasmic reticulum tubules, ribosomes, polysomes, small mitochondria, and a hypertrophied Golgi complex.

Electron microscopic examination of the thymus cortex of rats after 7 days of complete starvation showed increased atrophy in the epithelioid reticulocytes. Large and small vacuoles were found in the cytoplasm of these cells as a result of the destruction of mitochondria, lysosomes, autophagosomes, and residual bodies. Karyopyknosis and karyorhexis occur in epithelial reticulocytes (Fig. 5).

In functionally active epithelioid cells, there was an increase in the content of mitochondria, ribosomes, short endoplasmic reticulum tubules, small and large light vacuoles, lysosomes, and autophagosomes, indicating increased autophagy, which contributes to the positive selection of T cells [15].

After 7 days of starvation, the number of hypertrophied epithelioid cells significantly increases in the thymus parenchyma: these are large light cells with a significant cytoplasm content, which have short and long cytoplasmic processes in the cytoplasm of which large cluster-like light vacuoles are found, each of which contains one osmiophilic granule localized at the periphery (Fig. 6).

The number of small light vacuoles, lysosomes, and autophagosomes increases in their cytoplasm. Autophagy in these cells serves to present tissue-specific antigens and to carry out negative selection of T cells [15].

Submicroscopic examination of macrophages revealed a sharp increase in their functional activity under the influence of complete starvation. Macrophages have well-developed general-purpose organelles: numerous large round mitochondria with well-defined cristae, endoplasmic reticulum, Golgi complex, and especially lysosomal apparatus. After 3 days of complete starvation, the content of macrophages in the cortex and at its border with the medulla increases, in the cytoplasm of which multiple lysosomes, phagosomes of various sizes, and residual bodies are localized. The number of macrophages that phagocytose apoptotic bodies increases. The nuclei of macrophages are irregular in shape due to deep invaginations of the karyolemma. Euchromatin dominates in the nucleoplasm, while heterochromatin forms a narrow band along the inner layer of the karyolemma (Fig. 7).

After 7 days of complete starvation, large and small lysosomes, phagosomes of various sizes, and a significant

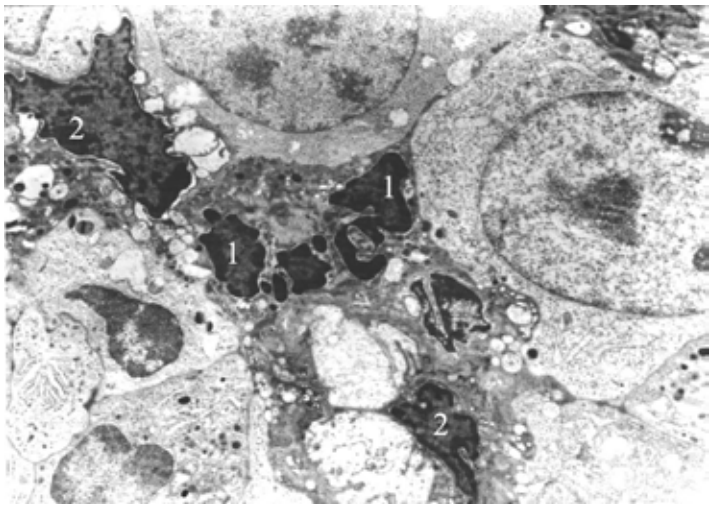


Fig. 5. Fragment of thymus cortex after 7 days of complete starvation: 1 – karyorhexis, 2 – karyopyknosis of epithelioid reticulocytes. Magnification × 6500

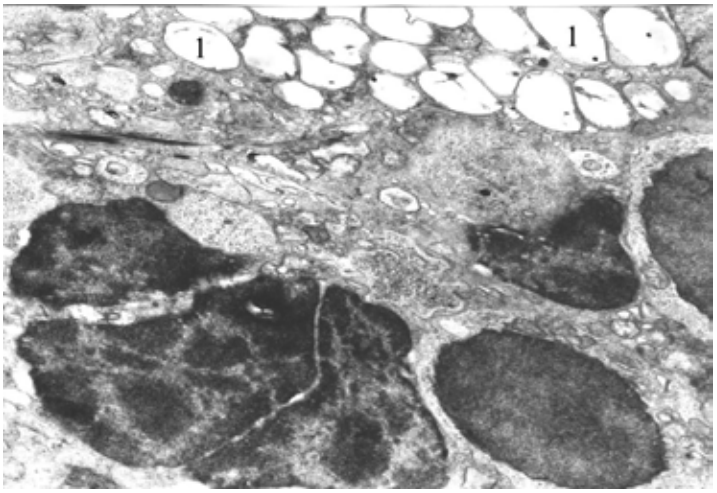


Fig. 6. Fragment of an epithelioid reticulocyte of the thymus medulla after 7 days of complete starvation: 1 – cluster-like light vacuoles with an osmiophilic granule. Magnification × 6000

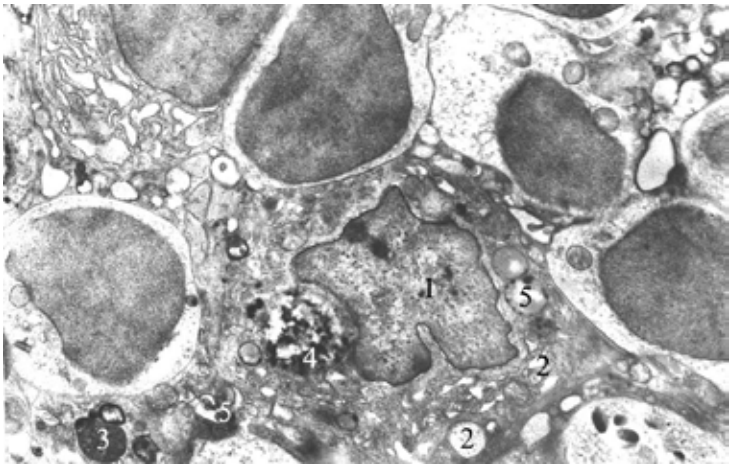


Fig. 7. Fragment of rat thymus cortex after 3 days of complete starvation. Ultrastructure of a macrophage: nucleus (1), vacuoles (2), lysosomes (3), residual bodies (4), autophagosomes (5). Magnification × 4500

number of vacuoles, among which there are light ones filled with lipids and light ones with an osmiophilic core, are outlined in the cytoplasm of macrophages. Therefore, autophagy in macrophages mediates the efferocytosis of apoptotic thymocytes [15].

The morphological manifestations of autophagy during complete 7-day fasting of experimental animals are autophagic vacuoles and autolysosomes in the epithelial reticulocytes of the cortex and medulla of the thymus and macrophages, which we have identified, indicating the activation of self-digestion mechanisms, which, in our opinion, is a key adaptive mechanism for maintaining cell viability under conditions of deprivation which has been confirmed in the works of other authors. The literature sources known to us indicate that autophagy in thymus cells not only promotes the utilization of damaged organelles, but may also participate in antigen presentation, influencing the maturation processes of thymocytes [2; 4; 6].

Nowadays, three main types of autophagy for the degradation of cytoplasmic substrates are distinguished: microautophagy (direct uptake of small parts of the cytoplasm by lysosomes), macroautophagy (formation of autophagosomes and their subsequent delivery to lysosomes for degradation), and chaperone-mediated autophagy (chaperone proteins direct specific substrates to lysosomes) [16].

Our electron-microscopic studies confirm the predominance of microautophagy and macroautophagy in thymus cells during complete, prolonged starvation. The main function of autophagy in T lymphocytes is to ensure their survival, proliferation, and maintenance of their energy homeostasis [17–19].

The 7th day of the recovery period is characterized by thymocyte repopulation and increased mitotic activity, indicating the activation of proliferative processes. Epithelioid cells of the cortex and medulla of the thymus and macrophages acquire the features of the electron microscopic structure of intact tissues, while retaining signs of active autophagy, which can be considered as a mechanism for the restoration of cellular structures after metabolic stress [10; 12; 20]. Thus, autophagy performs a dual function: on the one hand, during complete starvation, it ensures cell survival, and on the other hand, during the recovery phase of nutrition, it promotes the restoration of the thymus structure [5; 10].

Conclusions

1. Complete starvation causes profound structural changes in the thymus, manifested by lymphoid depletion of the cortical substance, thymocyte apoptosis, and destructive changes in epithelioid reticulocytes.

2. The most pronounced structural changes in the thymus are observed after 7 days of complete starvation: marked depletion of the cortex, activation of epithelioid reticulocytes and macrophages, keratinization and hyalinosis of Hassall's corpuscles of the medulla.

3. Morphological signs of autophagy are already evident in the early stages of deprivation and progress with the duration of complete starvation, indicating the leading role of autophagy in maintaining cellular homeostasis.

4. During the recovery period, repopulation of the cortical zone and activation of thymocyte mitotic activity occur. Maintaining autophagic activity during this period is an important mechanism for restoring the structural organization of the thymus after metabolic stress.

5. Autophagy is a key adaptive mechanism in the remodeling of the thymus both under conditions of complete prolonged starvation, ensuring cell survival and restoration of the morphofunctional integrity of the organ.

Practical significance. The results expand the current understanding of the mechanisms underlying structural and functional restructuring of the thymus under conditions of prolonged metabolic stress and refeeding, and deepen understanding of the role of autophagy as a universal mechanism of adaptation in immune system cells. The observed findings may form the basis for the development of new strategies for immunorehabilitation in patients after prolonged fasting, severe infections, multiple trauma, burns, major surgical interventions, chemotherapy, and other conditions accompanied by thymus involution.

REFERENCES

1. Shichkin VP, Antica M. Key Factors for Thymic Function and Development. *Front Immunol.* 2022;30(13):926516. doi: 10.3389/fimmu.2022.926516.

2. Dinges SS, Amini K, Notarangelo LD, et al. Primary and secondary defects of the thymus. *Immunol Rev*. 2024;322(1):178–211. doi: 10.1111/imr.13306.

3. Wang L, Das JK, Kumar A, et al. Autophagy in T-cell differentiation, survival and memory. *Int Immunopharmacol.* 2021;96:107569. doi: 10.1111/imcb.12422.

4. Dinges SS, Amini K, Notarangelo LD, Delmonte OM. Autophagy in major human diseases. *EMBO J*. 2021 Oct 1;40(19):e108863. doi: 10.15252/embj.2021108863.

5. Hasan KMM, Haque MA. Autophagy and Its Lineage-Specific Roles in the Hematopoietic System. *Oxid Med Cell Longev*. 2023;3(2023):8257217. doi: 10.1155/2023/8257217.

6. Dikic I, Elazar Z. Mechanism and medical implications of mammalian autophagy. *Nat Rev Mol Cell Biol*. 2018;19(6):349–364. doi: 10.1038/s41580-018-0003-4.

7. Bu T, Xu L, Zhu X, et al. Influence of short-term fasting on oxidative stress, antioxidant-related signaling molecules and autophagy in the intestine of adult Siniperca chuatsi. *Aquaculture Reports.* 2021;21:100933. doi.org/10.1016/j.aqrep.2021.100933

8. Mizushima N, Levine B. Autophagy in human diseases. *N Engl J Med.* 2020 15;383(16):1564–1576. doi: 10.1056/NEJMra2022774.

9. Hordiienko H, Sikora V. Intermittent fasting: literature review with bibliometric analysis. *Eastern Ukrainian Medical Journal.* 2025;13(4): 941–951. https://doi.org/10.21272/eumj.2025;13(4);941-951.

10. Duah M, Teh CE, Parish IA. Thymus degeneration and regeneration. *Front Immunol.* 2021;12:706244. doi: 10.3389/fimmu.2021.706244.

11. Bahrii MM, Dibrova VA, Popadynets OG, Hryshchuk MI. *Methods of morphological research.* In: Bahrii MM, Dibrova VA, editors. Vinnytsia: Nova Knyha; 2016. 328 p. (In Ukrainian).

12. Mikušová R, Mešťanová V, Polák Š, Varga I. What do we know about the structure of human thymic Hassall's corpuscles? A histochemical, immunohistochemical, and electron microscopic study. *Ann Anat.* 2017;211:140–148. doi: 10.1016/j.aanat.2017.02.006.

13. Noda NN. Structural view on autophagosome formation. *FEBS Lett.* 2024;598(1):84–106. doi: 10.1002/1873-3468.14742.

14. Jian F, Wang S, Tian R, et al. The STX17-SNAP47-VAMP7/VAMP8 complex is the default SNARE complex mediating autophagosome-lysosome fusion. *Cell Res*. 2024;34(2):151–168. doi: 10.1038/s41422-023-00916-x.

15. Zhen Y, Shao WH. Experimental Analysis of Apoptotic Thymocyte Engulfment by Macrophages. *J Vis Exp.* 2019;24(147):10.3791/59731. doi: 10.3791/59731.

16. Wolska W, Gutowska I, Wszołek A, Żwierełło W. The Role of Intermittent Fasting in the Activation of Autophagy Processes in the Context of Cancer Diseases. *Int J Mol Sci.* 2025;26(10):4742. doi: 10.3390/ijms26104742.

17. Münz C. Canonical and non-canonical functions of the autophagy machinery in MHC restricted antigen presentation. *Front Immunol*. 2022;13:868888. doi: 10.3389/fimmu.2022.868888.

18. Øynebråten I. Involvement of autophagy in MHC class I antigen presentation. *Scand J Immunol*. 2020;92(5):e12978. doi: 10.1111/sji.12978.

19. Botbol Y, Guerrero-Ros I, Macian F. Key roles of autophagy in regulating T-cell function. *Eur J Immunol*. 2016;46(6):1326–34. doi: 10.1002/eji.201545955.

20. Ueno T, Komatsu M. Monitoring autophagy flux and activity: principles and applications. *BioEssays.* 2020;42(11):e2000122. doi: 10.1002/bies.202000122.

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