

ОРИГІНАЛЬНІ ДОСЛІДЖЕННЯ

DOI 10.64108/imh.2025.1.1.6

UDC 616-07+616.157+612.592

MORPHOFUNCTIONAL STUDY OF TISSUE BASOPHILS ACTIVITY WITH GENERAL DEEP HYPOTHERMIA

O. V. Antymys, O. Y. Zhurakivska*, N. T. Sahan, V. A. Miskiv, U. M. Dutchak

*Ivano-Frankivsk National Medical University, Department of Human Anatomy, Ivano-Frankivsk, Ukraine*ORCID ID: [0000-0001-6040-8137](https://orcid.org/0000-0001-6040-8137), e-mail: oantymys@ifnmu.edu.ua,ORCID ID: [0000-0002-1041-4237](https://orcid.org/0000-0002-1041-4237), e-mail: ozhurakivska@ifnmu.edu.uaORCID ID: [0000-0002-5474-195X](https://orcid.org/0000-0002-5474-195X), e-mail: nsahan@ifnmu.edu.uaORCID ID: [0000-0002-3924-1544](https://orcid.org/0000-0002-3924-1544), e-mail: vmiskiv@ifnmu.edu.uaORCID ID: [0000-0002-3715-5650](https://orcid.org/0000-0002-3715-5650), e-mail: udutchak@ifnmu.edu.ua*Correspondence: e-mail: ozhurakivska@ifnmu.edu.ua

Abstract. The absence of a complex morphofunctional approach to the study of tissue basophils when exposed to cold factors has not allowed for the revelation of many aspects of the pathogenesis of changes in this influence.

Therefore, the purpose of this study was to establish the morpho-functional state of tissue basophils of different layers of skin with general deep hypothermia.

Immediately after cold exposure, a massive degranulation of tissue basophils, especially those located directly near the wall of vessels, is noted. The most pronounced changes we have noted from the third day of the posthypothermic period manifested almost 100% of the degranulation of tissue basophils, which were directly close to the wall of the vessels, to a strong degree. 59,96% of degranulating cells were found in the papillary layer of the dermis. Of these, 8,53% with low degranulation, 12,93% with moderate and 38,42% with strong degranulation. The mesh layer also increases the processes of secretion, especially to a strong degree. It can detect 70,2% of degranulating tissue basophils, 11,02% with a weak degree, 13,73% – with an average, and 45,67% – with a strong degree of degranulation. In the hypoderm, almost all cells, located close to microvessels, are degraded (96,63%), with 16,08% – poorly degraded, 21,65% – degraded moderately, and 58,91% – strongly. Degranulation indices are in the papillary layer 0,62, in the retina – 0,72, and in the hypoderm – 0,97. At the electron microscopic level, you can see swelling of all structural components of the microvascular wall, which leads to hypoxia and subsequent deepening of disorders of blood-binged and transcapillary metabolism. You can also see a significant decrease in the size of tissue basophils and the mass exit of the granules beyond them. Almost all cells delay, resulting in the appearance of a small cell with a swollen nucleus and a small number of granules. In the cytoplasm of mitochondria with destroyed crystals, vacuolated tubes of granular endoplasmic reticulum and single-shaped tanks of the Golgi apparatus are destroyed. There is a considerable amount of macropinocytosis vesicles, multivesicular bodies, and vacuoles. In other tissue basophils, the processes of granulolysis are observed. The cells look diminished, with single granules and a large number of large vacuoles. Many cells die, accompanied by the destruction of the cytoskeleton, resulting in the nucleus and granules lying freely, scattered, mitochondria, endoplasmic reticulum, and Golgi apparatus being destroyed.

Conclusions. Thus, in the study of the effect of general deep hypothermia on tissue basophils of different skin layers, we concluded that immediately after cold exposure, massive degranulation of tissue basophils, especially those located directly near the vascular wall, occurred.

We noted the most pronounced changes from the third day of the posthypothermic period, which was manifested by almost 100% degranulation of tissue basophils located close to the vessel wall, and to a severe degree. At the electron microscopic level, swelling of all structural components of the microvascular wall can be seen, which leads to hypoxia and further aggravation of blood circulation and transcapillary metabolism disorders.

Normalization in the microcirculatory system begins on the fourteenth day of the posthypothermic period, which correlates with an increase in the number of tissue basophils with a simultaneous tendency to a decrease in degranulation processes.

Keywords: skin layers, tissue basophils, general deep hypothermia, microcirculatory system, transcapillary exchange, cell.

Introduction. According to the literature, the skin is not only the body's integument, but also an insufficiently

studied organ that is located at the boundary of the external and internal environment, is closely connected with all internal organs and is the first to respond to various external and internal changes. According to the literature, the skin actively responds to external factors [1].

Data on the effect of various factors on the population of tissue basophils are of great practical importance. They are also called “short-acting regulators of tissue homeostasis” because it has been proven that tissue basophils actively respond to external and internal influences [2, 3, 4]. At present, the state of tissue basophils in various diseases has been largely studied, but their changes under the influence of the cold factor have been studied little. The absence of a comprehensive morphofunctional approach to the study of tissue basophils under the influence of cold factors has not yet allowed us to reveal many aspects of the pathogenesis of the development of changes under this influence.

Therefore, this study aimed to determine the morphological and functional state of tissue basophils of different skin layers under general deep hypothermia.

Object and methods of the research. The material for the study was the skin of the back and blood of 70 white outbred male rats (to level the hormonal effect) weighing 180-200 g. The choice of white rats is explained by their sensitivity to extreme factors and the possibility of reproducing adaptive reactions inherent in humans. At the same time, it is difficult to objectively analyze morphological changes in human skin due to the traumatic nature of the biopsy method of examination.

Groups of animals: Group I - control (kept in standard vivarium conditions and not involved in any experiments) (n=10);

Group II - experimental - under conditions of general deep hypothermia (n=20). Animals were withdrawn from the experiment immediately after the exposure;

Group III - experimental - under conditions of general deep hypothermia (n=20). Animals were withdrawn from the experiment on day 3;

Group IV - experimental - under conditions of general deep hypothermia (n=20). Animals were withdrawn from the experiment on day 14.

The animals were kept, fed and manipulated under the provisions of the European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes (Strasbourg, 1986), Council Directive 86/609/EEC (1986), the Law of Ukraine “On Protection of Animals from Cruelty” of December 15, 2009 and orders of the Ministry of Health of Ukraine No. 690 of 23.09.2009, No. 616 of 03.08.2012. Animals were euthanized by injection of sodium thiopental (2% solution at a dose of 25 mg/kg body weight). For sampling, animals were decapitated under anesthesia (2% sodium thiopental solution at a dose of 25 mg/kg intraperitoneally). The following research methods were used to solve the tasks: modeling of general deep hypothermia, biochemical blood tests, histological and electron microscopic examination of tissue basophils, and statistical analysis of morphometric and biochemical parameters.

Results of the study and their discussion. It was found that immediately after exposure to total deep hypothermia, we observed a layer-by-layer change in degranulation, especially in cells located near the vascular wall. That is, it can be assumed that degranulation leads to the release of biologically active substances, such as histamine, which will subsequently lead to changes in the vascular bed of the skin layers and structural changes in the organ [5, 6].

In the papillary layer of the dermis, the number of degranulating tissue basophils located close to the vessels was 35.21%, with 14.25% of their number having a weak degree of degranulation, 8.53% - with a moderate degree and 12.41% - with a strong degree. In the reticular layer, the number of secretory cells increased to 56.39%, of which 20.45% were of a weak degree, 20.95% were of a moderate degree, and 14.99% were of a strong degree. In the hypodermis, the degree of degranulation increased to 59.18%, 20.35% - mild degranulation, 21.53% - moderate, and 17.34% - severe. The indices of degranulation of tissue basophils also increased accordingly, which in the papillary layer was 0.35, in the reticular layer - 0.56, and in the hypodermis - 0.58.

The secretion of tissue basophils located at a distance of 10-12 μm from the vessels increased, but to a somewhat lesser extent than in the previous cells and amounted to 26.76% in the papillary layer, of which 12.01% was mild, 7.87% was moderate, and 8.15% was severe. In the reticular layer, degranulation amounted to 47.48% (18.10% - mild, 20.18% - moderate, 10.85% - severe). In the hypodermis, the degree of degranulation increased to 49.58%, weak degranulation - to 13.28%, medium - to 18.01%, and strong - 10.19%. The degranulation index was 0.28 in the papillary layer, 0.49 in the reticular layer, and 0.51 in the hypodermis.

A layer-by-layer increase in degranulation processes was observed in remote tissue basophils, although at a much lower rate than in the previous cells. Thus, in the papillary layer, the number of degranulating cells was 26.76% (12.71% - mild, 6.32% - moderate, 7.73% - severe). In the reticular layer of tissue basophils, there were 47.78% degranulating cells, of which 17.45% were of mild degranulation, 18.87% were of moderate degranulation, and 14.79% were of strong degranulation. In the hypodermis, the number of actively secreting tissue basophils was 49.58%, with 18.05% being weakly degranulating, 18.15% moderately degranulating, and 13.38% strongly degranulating. The degranulation index in the papillary layer was 0.27, in the reticular layer - 0.47, and in the hypodermis - 0.52.

Ultramicroscopically, a layer-by-layer change in degranulation was observed, especially in cells located near the vascular wall. They are expressed in the intensification of degranulation processes, especially severe degranulation. As a result, wide perigranular spaces appear, the volume increases the structure of the granules is disturbed, and condensation of the granule contents is noted with the formation of a conglomerate of small lumps. In tissue basophils, there is a marked violation of the membrane

integrity and the release of granules outside the cell. At the same time, a nucleus with a wide perinuclear space is manifested. Chromatin forms small lumps. Single mitochondria of small size, some with matrix clearance and destruction of individual cristae. The granular endoplasmic reticulum is characterized by dilated tubes with uneven contours and losing ribosomes, most of which are freely located in the cytoplasm. The Golgi apparatus consists of small elongated cisternae and small vesicles. Some cells are characterized by cytoplasmic vacuolization and a decrease in the number of granules, the nucleus is well contoured. The cytoplasmic membrane remains intact. Mitochondria with matrix enlightenment.

On the third day of the posthypothermic period, the most statistically significant difference in the diameters of tissue basophils was observed ($P < 0.01$). Their volume, area, and number significantly decreased. Particularly pronounced changes were observed in cells located at a small distance from the vascular wall. Thus, in the papillary layer of the dermis, the number of these tissue basophils decreases by half and amounts to 2.08 ± 0.83 per arterioles, and in the reticular layer - 2.15 ± 0.71 . In the hypodermis, the number of closely spaced tissue basophils decreases threefold (2.38 ± 0.68). The secretory activity of closely spaced tissue basophils also increases significantly. Thus, 59.96% of degranulating cells were found in the papillary layer of the dermis. Of these, 8.53% were mildly degranulated, 12.93% were moderately degranulated, and 38.42% were severely degranulated. In the reticular layer, secretion processes also increase, especially to a high degree. Here, 70.42% of degranulating tissue basophils can be detected, 11.02% - with a weak degree, 13.73% - with a moderate degree, and 45.67% - with a strong degree of degranulation. In the hypodermis, almost all cells located close to microvessels are degranulated (96.63%), with 16.08% being slightly degranulated, 21.65% being moderately degranulated, and 58.91% being severely degranulated. Degranulation indices are 0.62 in the papillary layer, 0.72 in the reticular layer, and 0.97 in the hypodermis.

Cells located at some distance from the vessels also significantly decreased in number, although at a slower rate than previous tissue basophils. Functional activity, on the contrary, increased significantly, but to a lesser extent than in previous tissue basophils. 53.21% of all tissue basophils were degranulated. Of these, 7.35% in the papillary layer were slightly degranulated, 12.12% were moderately degranulated, and 33.74% were severely degranulated. In the reticular layer, the degree of degranulation was 67.35%, 10.51% - with weakly expressed secretion, 13.14% - with moderately expressed, and 43.43% - with strongly expressed. In the hypodermis, 88.35% of tissue basophils were found in the state of secretion, with 15.92% of them being of a weak degree, 21.06% of them of a moderate degree, and more than half of them of a strong degree (51.37%). The index of degranulation, respectively, was 0.53, 0.67, 0.88 in layers.

Tissue basophils far from the microvessels decreased somewhat less in number. On the contrary, the processes of degranulation increased significantly, especially its strong

degree, although to a lesser extent than in the previous cells, and in the papillary layer the number of degranulating cells was 52.76%, in the reticular layer - 64.22%, in the hypodermis - 86.82%. Tissue basophils with mild degranulation amounted to 6.08% in the papillary layer, 10.15% in the reticular layer, and 15.03% in the hypodermis. With moderate degranulation, respectively, in layers - 12.01%, 13.02% and 20.89%. With severe degranulation in the papillary layer of tissue basophils there were 16.08%, in the reticular layer - 21.65% and in the hypodermis most of the cells were degranulated (58.9). Layer-by-layer degranulation indices increased, which in the papillary layer was 0.53, in the reticular layer - 0.64, and in the hypodermis - 0.87.

At the ultrastructural level, one can also see a significant reduction in the size of tissue basophils and a massive release of granules outside of them. Almost all cells are degranulated, resulting in the appearance of a small cell with a swollen nucleus and a small number of granules. In the cytoplasm, there are mitochondria with destroyed cristae, vacuolated tubes of granular endoplasmic reticulum, and destroyed single cisternae of the Golgi apparatus. A significant number of micropinocytotic vesicles, multivesicular bodies, and vacuoles are noted. In other tissue basophils, processes of granulolysis are observed. The cells look reduced, with single granules and a significant number of large vacuoles. Many cells die, which is accompanied by destruction of the cytomembrane, as a result of which the nucleus and granules lie free, scattered, mitochondria, endoplasmic reticulum, and Golgi apparatus are destroyed.

Such massive degranulation of tissue basophils leads to the release of active amines (heparin, histamine), which prevent blood clotting, dilate blood vessels, and promote cell migration to the site of injury. In combination with leukotrienes and other mediators, they cause the main clinical symptoms of allergy: flushing, itching, urticaria, and bronchospasm [5]. The process of releasing active amines occurs when IgE binds to antigenic cellular determinants, complement activation, platelet aggregation, or activation of the kinin system, which likely leads to thrombocytopenia. Polynuclears damage small blood vessels as part of this process. This releases endogenous pyrogens, which often cause an increase in body temperature.

On the 14th day of development after the posthypothermic period, a further increase (compared to the previous values) in the size of tissue basophils is observed. Moreover, in the papillary layer, the average diameter, volume, and area of cells increase faster, in contrast to the reticular layer and hypodermis. There is an increase in the number of tissue basophils, especially those located close to the vascular wall in the papillary layer. The number of tissue basophils distant from the walls of microvessels increases slowly.

There were changes in the functional activity of various tissue basophils. A decrease in degranulation processes was observed compared to the previous study period, especially strong degranulation, with some increase in weak secretion. The most pronounced changes could be observed in cells located close to the vascular wall. At the

ultrastructural level, granules in the cytoplasm of tissue basophils have different shapes, sizes, and electron densities. Small-sized secretory granules with a granular matrix are already appearing, indicating their new formation.

In other types of tissue basophils, secretory activity decreased at a slower rate. In addition, during the layer-by-layer study in the papillary layer, the number of degranulating tissue basophils decreased almost twice compared to the previous period, while in the deeper layers of the dermis and hypodermis, degranulation processes decreased slowly. The morphometric study of tissue basophils located directly near the microvessels revealed that 38.15% of them degranulated in the papillary layer, 57.13% in the reticular layer, and 67.11% in the hypodermis. Whereas, 11.15% of them were found in the papillary layer, 12.05% in the reticular layer, 12.98% in the hypodermis, respectively, 12.03%, 13.69%, 15.73% with a weak degree, and 14.97%, 31.39%, 38.47% with a strong degree.

In other types of tissue basophils, the secretory activity of degranulating tissue basophils located at a distance of 10-12 μm from the vessel decreases in number, and the papillary layer make up 3.67%, in the reticular layer - 52.02%, in the hypodermis - 61.93%. Of these, 11.11% can be found in the papillary layer, 1.59% in the reticular layer, and 12.71% in the hypodermis, respectively, with a mild degranulation in layers of 1.07%, 13.11%, 15.21%, and with a strong degranulation - 10.49%, 29.42%, and 39.21%.

The number of degranulating tissue basophils remote from the vascular wall decreased in the papillary layer to 28.63%, in the reticular layer to 50.68%, and in the hypodermis to 59.66%. At the same time, cells with weak degranulation make up 10.05% in the papillary layer, 11.08% in the reticular layer, 12.03% in the hypodermis, respectively, with moderate degranulation - 19.95%, 12.65%, and 15.06%, with strong degranulation - 8.63%, 30.05%, 39.57%. Degranulation indices also decreased layer by layer, especially in tissue basophils located close to the microvessels of the papillary layer (0.38). The degranulation index was 0.57 in the reticular layer and 0.67 in the hypodermis.

At the ultrastructural level, an increase in the number of granules characterized by significant polymorphism is

noted in the cytoplasm of tissue basophils. Some of them are electronically transparent, others have a dense content. The mitochondria are oval in shape, some of them with areas of lumen. Their number increases significantly. The granular endoplasmic reticulum is well defined and consists of numerous tubules with ribosomes attached to them. The Golgi apparatus looks like cisterns with electron-dense contents. At the same time, degranulation processes are still significantly expressed in tissue basophils. You can also see cells with massive degranulation, intracellular granulolysis, and destroyed tissue basophils.

Conclusions. Thus, in the study of the effect of general deep hypothermia on tissue basophils of different skin layers, we concluded that immediately after cold exposure, massive degranulation of tissue basophils, especially those located directly near the vascular wall, occurred.

We noted the most pronounced changes from the third day of the posthypothermic period, which was manifested by almost 100% degranulation of tissue basophils located close to the vessel wall, and to a severe degree. At the electron microscopic level, swelling of all structural components of the microvascular wall can be seen, which leads to hypoxia and further aggravation of blood circulation and transcapillary metabolism disorders.

Normalization in the microcirculatory system begins on the fourteenth day of the posthypothermic period, which correlates with an increase in the number of tissue basophils with a simultaneous tendency to a decrease in degranulation processes.

Conflict of interest. The authors declare that they have no conflict of interest in relation to this research, including financial, personal, authorship or other nature, which could affect the research and its results presented in this article.

Financing. The study was conducted without financial support.

Author contributions: O.Y. Zhurakivska a) conception and design; c) provision of materials for the study; d) collection and synthesis of data; U.M. Dutchak e) analysis and interpretation of results; N.T. Sahan f) writing of the manuscript; O.V. Antymys b) administrative support; V.A. Miskiv g) editing of the manuscript;

All authors have read and agreed with the published version of the manuscript.

References:

1. [Mangua K, Ferree S, Murase J, Kourosch A](#). The Burden of Air Pollution on Skin Health: a Brief Report and Call to Action. *Dermatol Ther (Heidelb)*. 2024;14(1):251-259. <https://doi.org/10.1007/s13555-023-01080-1>
2. [Yeroshenko, H.A, Hasiuk NV, Kalinichenko MV](#) Morfolohichna kharakterystyka tkanyynykh bazofiliv pry khronichnomu katarl'nomu hinhiviti. *Svit medytsyny ta biologii*. 2011;1:18-21.
3. [Okhotnikova, O.M, Sharikadze OV, Hryshchenko OM](#) Syndrom aktyvatsii mastotsytiv: suchasnyi pohliad na problemu. *Klinichna imunolohiia. Alerholohiia. Infektolohiia*. 2018;2(107):6-14.
4. [Schulman, E.S, Nishi H, Pelleg A](#). Degranulation of human mast cells: modulation by P2 receptors' agonists. *Front Immunol*. 2023;14:1216580. <https://doi.org/10.3389/fimmu.2023.1216580>.
5. [Vorozhbyt. O.B, Hrytsko R.Yu](#) Immunological features of toxocariasis. *Klinichna imunolohiia. Alerholohiia. Infektolohiia*. 2010;1(30):59-61.
6. [Radchenko, O.M](#). Histamine as a vital universal regulator. *Ratsionalna farmakoterapiya*. 2017;4(45):5-9.

УДК 616-07+616.157+612.592

МОРФОФУНКЦІОНАЛЬНЕ ДОСЛІДЖЕННЯ АКТИВНОСТІ ТКАНИННИХ БАЗОФІЛІВ ПРИ ЗАГАЛЬНІЙ ГЛИБОКІЙ ГІПОТЕРМІЇ

О. В. Антимис, О. Я. Жураківська*, Н. Т. Саган, В. А. Міськів, У. М. Дутчак

Івано-Франківський національний медичний університет, кафедра анатомії людини, м. Івано-Франківськ, Україна

ORCID ID: [0000-0001-6040-8137](https://orcid.org/0000-0001-6040-8137), e-mail: oantymys@ifnmu.edu.ua,ORCID ID: [0000-0002-1041-4237](https://orcid.org/0000-0002-1041-4237), e-mail: ozhurakivska@ifnmu.edu.uaORCID ID: [0000-0002-5474-195X](https://orcid.org/0000-0002-5474-195X), e-mail: nsahan@ifnmu.edu.uaORCID ID: [0000-0002-3924-1544](https://orcid.org/0000-0002-3924-1544), e-mail: vmiskiv@ifnmu.edu.uaORCID ID: [0000-0002-3715-5650](https://orcid.org/0000-0002-3715-5650), e-mail: udutchak@ifnmu.edu.ua*Кореспондуючі автори: e-mail: ozhurakivska@ifnmu.edu.ua

Резюме. За даними літератури, шкіра – це не тільки покрив організму, але ще недостатньо вивчений орган, що знаходиться на межі зовнішнього і внутрішнього середовища, тісно пов'язаний з усіма внутрішніми органами і першим реагує на різні зовнішні і внутрішні зміни. За даними літератури, шкіра активно реагує на зовнішні фактори.

Важливе практичне значення мають дані про вплив різних факторів і на популяцію тканинних базофілів. Їх ще називають «регуляторами тканинного гомеостазу короткодистантної дії», оскільки доведено, що тканинні базофіли активно відповідають на зовнішні та внутрішні впливи. На даний час, в значній мірі вивчений стан тканинних базофілів при різноманітних захворюваннях, однак їх зміни при дії холодового фактора досліджено мало. Відсутність комплексного морфофункціонального підходу до вивчення тканинних базофілів при впливі холодового фактора не дозволило до цього часу розкрити багато аспектів патогенезу розвитку змін при даному впливі.

Тому **метою** даного дослідження було встановити морфо- функціональний стан тканинних базофілів різних шарів шкіри при загальній глибокій гіпотермії.

Відразу після холодового впливу відмічається масивна дегрануляція тканинних базофілів, особливо тих, що знаходяться безпосередньо біля стінки судин. Найбільш виражені зміни ми відмітили з третьої доби постгіпотермічного періоду, що проявлялося майже 100% дегрануляцією тканинних базофілів, які знаходились в безпосередній близькості до стінки судин, причому сильного ступеня. На електронномікроскопічному рівні можна бачити набряк всіх структурних компонентів мікросудинної стінки, що призводить до гіпоксії і подальшого поглиблення порушення кровообігу і трансапілярного обміну. Також можна бачити значне зменшення розмірів тканинних базофілів та масовий вихід гранул за їх межі. Майже всі клітини дегранулюють, внаслідок чого набувають вигляду невеликої клітини з набряклим ядром і незначною кількістю гранул.

Нормалізація в ланках мікроциркуляторного русла починається з чотирнадцятої доби постгіпотермічного періоду, що корелює зі збільшенням кількості тканинних базофілів з одночасною тенденцією до спадання процесів дегрануляції.

Висновки. Досліджуючи вплив загальної глибокої гіпотермії на тканинні базофіли різних шарів шкіри, ми дійшли висновку, що відразу після впливу холоду відбувається масивна дегрануляція тканинних базофілів, особливо тих, що розташовані безпосередньо біля стінки судин.

Найбільш виражені зміни ми відзначали з 3-ї доби постгіпотермічного періоду, що проявлялося майже 100% дегрануляцією тканинних базофілів, розташованих близько до стінки судини, причому у вираженому ступені. На електронномікроскопічному рівні видно набухання всіх структурних компонентів мікросудинної стінки, що призводить до гіпоксії та подальшого погіршення кровообігу та порушень трансапілярного обміну.

Нормалізація в системі мікроциркуляції починається на чотирнадцяту добу постгіпотермічного періоду, що корелює зі збільшенням кількості тканинних базофілів з одночасною тенденцією до зменшення процесів дегрануляції.

Ключові слова: шари шкіри, тканинні базофіли, загальна глибока гіпотермія, мікроциркуляторне русло, трансапілярний обмін, клітина.

Стаття надійшла в редакцію 20.03.2025 р.

Стаття прийнята до видання 02.06.2025 р.