

# Features of clinical flow of traumatic illness on a background chronic stress

Stepan S. Filip, Rudolf M. Slivka, Andrii M. Bratasiuk, Yuriy P. Skrypynets, Antonina V. Varvarynets  
UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

## ABSTRACT

**Aim:** To focus on the dependence of the severity of the clinical features of traumatic illness on stress components and chronic stress in particular.

**Materials and Methods:** Analysis of data on the results of existing studies assessing the impact of chronic stress on the course of traumatic illness.

**Conclusions:** The introduction of a therapeutic complex of immunotherapy and sedatives for traumatic illness with a pronounced stress component, with the possible development of severe complications, will make it possible to improve the results of treatment and rehabilitation of patients with traumatic illness.

**KEY WORDS:** traumatic illness, chronic stress, clinical course, stress mechanisms, immunity, recovery

Wiad Lek. 2025;78(4):908-914. doi: 10.36740/WLek/203903 DOI

## INTRODUCTION

Traumatic illness is a complex process that includes not only mechanical damage to tissues, but also secondary disorders that arise as a result of stress reactions of the body. In this case, there is a general response of the body to injury, which is manifested by a number of adaptive and pathological reactions, as well as local and general symptoms that are characteristic of a particular injury. Traumatic illness greatly affects the outcome of the injury, determines the prognosis for the course of the pathological process, the results of treatment and performance.

Of great importance are changes in the psycho-emotional sphere, metabolic processes and hemostasis, the state of the immune system, the work of the heart, lungs, digestive organs and the central nervous system.

## AIM

The aim of our study was to focus on the dependence of the severity of clinical features of traumatic illness on stressful components and chronic stress in particular. Pay attention to the importance of analyzing the functioning of the immune, nervous and endocrine systems in this category of patients. To emphasize the importance of psychological support and immunocorrection in the treatment process of patients with traumatic illness against the background of stressful manifestations.

## MATERIALS AND METHODS

Analysis of data on the results of existing studies assessing the impact of chronic stress on the course of traumatic illness.

## REVIEW AND DISCUSSION

### CLINICAL FEATURES OF THE COURSE OF TRAUMATIC ILLNESS AGAINST THE BACKGROUND OF CHRONIC STRESS

The clinical picture in traumatic illness depends on the severity of the injury. In patients with mild injuries, the disease is erased, with the absence of characteristic periods and complications. In patients with a severe clinical course and, especially, with a traumatic illness, the stages and symptoms are more pronounced, since in this case there is a mutual encumbrance syndrome - a situation in which pathological factors not only «add up» with each other, but also mutually burden each other.

One of the main components of a traumatic illness is a wound. A wound is a mechanical injury accompanied by a violation of the integrity of the outer integumentary tissues, primarily the skin. The wound process is the body's reaction to trauma, characterized by a sequence of stages that have their own anatomical, pathohisological, biochemical, clinical features. The essence of the wound process

is to mobilize general and local protective reactions aimed at wound healing [1-4].

Acute stress disorder is an intense, unpleasant reaction to a severe traumatic incident that begins shortly after it and lasts less than a month. The symptoms of acute stress disorder are similar to post-traumatic stress disorder and can include feelings of detachment from reality or feelings of disconnection from themselves and their experiences. After a traumatic event in a person's life, psychological changes first occur in his body, but in the later stages this is very strongly reflected in physical health, and this can manifest itself even decades after the injury [5-8].

From the standpoint of immune distress syndrome, the course of a traumatic disease is characterized by a stage in which four periods are distinguished.

The first period of traumatic illness begins immediately after the traumatic injury and lasts 6-12 hours. This period is characterized by neuroendocrine reactions with activation of the sympathoadrenal system, impaired vascular tone, signs of traumatic shock or a terminal condition. The main cause of death of patients during this period is life-threatening injuries, IV degree shock and massive blood loss with the development of DIC syndrome.

The second period of traumatic illness, or immunotoxicosis with the possible development of immunoparalysis, lasts 12-48 hours. Patients are in the intensive care unit of the intensive care unit, where they are given intensive anti-shock therapy. According to vital or absolute indications, urgent surgical interventions are carried out during this period: operations on the brain and spinal cord, main vessels, abdominal and chest organs, spine, bones.

The treatment plan, volume and method of surgical interventions are determined individually, taking into account the nature of injuries, the likelihood of developing dangerous complications, the age and general condition of the patient, the presence of acute and chronic diseases. The main cause of mortality of victims during this period is multiple organ failure.

The third period of traumatic illness is characterized by late manifestations of dystrophic and sclerotic processes. This period is characterized by the development of complications. Complications occur at a certain frequency. So, lung disorders in traumatic illness are usually detected on the 3-4th day, on the part of the abdominal cavity, as well as local infectious complications - on the 6-10th day. Treatment tactics are determined individually. Intensive detoxification therapy and antibiotic therapy are carried out, immunotherapy in some cases there are indications for surgical interventions.

The duration of the fourth period of traumatic illness - the rehabilitation period, depends on the location and severity of the injury, as well as the presence and nature of complications. The condition of the body gradually improves, all vital functions are normalized. During this period, planned operations are carried out to restore damaged organs and tissues, conservative treatment is prescribed, and rehabilitation measures are carried out.

Along with traditional medical measures, at this stage, work on normalizing the psychological state of patients is of great importance. Since the stressful component of a traumatic illness persistently does not lose its relevance. Acute stress disorder is an intense, unpleasant reaction to a severe traumatic incident that begins after it and lasts up to thirty days. The symptoms of acute stress disorder are similar to post-traumatic stress disorder and include a feeling of detachment from reality, a feeling of disconnection from oneself and one's experiences. After a traumatic event in a person's life, psychological changes occur in the body, which later significantly affects physical health, and this can manifest itself even decades after the injury. Of course, stress can be caused by the presence of a wound surface on the body. Wounds can cause stress for a variety of reasons. Thus, trauma, accompanied by a loss of the ability to self-care, a change in living conditions and social status, is a severe stress not only for the body, but also for the psyche. And long-term treatment further aggravates these changes. There may be a loss of motivation, increased aggressiveness, emotional lability, depression, the presence of a secondary benefit effect, etc. Stress is a strong tension of the body that does not go away without a trace. The negative impact of stress on health is very large and has the worst consequences. It is the stressful situation that causes many diseases that will manifest themselves later - both physical and mental [9-13].

Chronic or «long-term traumatic» stress, in turn, can cause disorders in many physiological systems, including nervous, endocrine and immune. This worsens the results of the treatment of traumatic injuries, contributing to the development of inflammatory processes, deterioration of wound healing, and even an increase in the likelihood of infectious complications. Chronic stress has a complex pathophysiological mechanism that includes the activation of the sympathetic-adrenal system and the release of stress hormones such as cortisol and adrenaline. They are able to change microcirculation in tissues, impairing the supply of oxygen to damaged areas and increasing the inflammatory process. The term «long-term traumatic stress» was coined in the context of political violence and social conflict, and refers to both social and individual conditions.

There are three levels of response of body systems to stress, and it depends on their reactivity: 1) cognitive-emotional level (involved cortical and limbic structures located above the hypothalamus), which is responsible for individual psychological differences in the cognitive-emotional response; 2) autonomous-endocrine level (involved anatomical structures localized in the hypothalamus and brain stem), which connects information received from the upper centers with endocrine organs and the autonomic system; 3) the peripheral level, which is responsible for the individual reactivity of the periphery (for example, structural changes in the arteries can alter the response to information coming from the central nervous system) [9,10].

Chronic stress leads to an imbalance in the immune response, reduces the activity of cells responsible for protecting the body from infections and contributes to the chronicity of inflammatory processes. In the context of traumatic illness, this leads to a slowdown in healing and an increased risk of developing infectious and inflammatory complications such as sepsis or osteomyelitis. Statistics show that 30-40% of patients who experience severe injuries due to chronic stress have a higher risk of developing infectious and inflammatory complications, namely wound infections, impaired healing or even sepsis [1].

Sensitivity of patients to immunotherapy, the effectiveness of different methods of which is not the same in different periods of the disease. Immunotherapy is able to solve both independent tasks - the prevention of purulent complications and generalization of infection, and be a component of the treatment complex, improving the transfer of surgical interventions, the effectiveness of sanitation of destructive foci, the eradication of pathogens and others.

The nervous system, under the influence of chronic stress, can lead to changes in central nervous regulation, which affects the pain threshold, the level of anxiety and depression. Patients with chronic stress often suffer from more severe pain, which can make it difficult for them to recover from an injury. In addition, stress can increase fatigue levels and reduce the overall endurance of the body. Studies show that patients with high levels of stress often need 15-20% more time for rehabilitation compared to patients without stress [3,7,15,16].

Stress affects the release of cortisol, which is the main stress hormone. Chronically elevated cortisol levels slow down the healing process, as cortisol has an anti-catabolic effect, which interferes with tissue regeneration. In addition, under stress, the levels of other important hormones such as testosterone

and insulin decrease, which also slows down the regeneration and healing processes. Studies show that patients with elevated cortisol levels have 25-30% slower healing after injuries [17,18].

Patients with chronic stress have a number of clinical features that can complicate the diagnosis and treatment of injuries. Among them are increased soreness, protracted inflammatory processes, slow wound healing, a tendency to develop depressive and anxiety disorders. Also, chronic stress can cause a shift in the pain threshold, which complicates rehabilitation measures, especially in the postoperative period. According to the results of numerous studies, patients with chronic stress against the background of traumatic injuries have a 20-25% higher level of depression and anxiety, which complicates their post-traumatic psycho-emotional state [19]. Stress and increased cortisol levels lead to an increase in the incidence of opportunistic infections, a decrease in the activity of human growth hormone, which means a slowdown in wound healing, the occurrence of hypertrophic, keloid scars and long-term non-healing (trophic) wounds. Gouin et al. compared the healing rate of a small perforated biopsy wound in a group of dental students. They found that the participants' healing was on average three days slower when they were under the stress of exams, compared to those who were on vacation. This means that the healing time of a small standard wound in young and healthy people has increased by 40%. Older people with numerous comorbidities are also at risk of slowing down wound healing, and stress further increases this risk. People who are stressed are more prone to bad habits that can slow down wound healing, such as drinking alcohol, tobacco or drugs, little physical activity, sleep disturbances, poor diet and not following a medication regimen [11,20-22].

Against the background of all the drama of the impact of stress on the human body, and health in particular, one should not forget about the adaptive capabilities of the body in order to maintain the constancy of functioning. Adaptation of the human body to the action of stress factors occurs as a result of changes in physiological constants with the preservation of the level of metabolic processes – physiological adaptation, which is provided by simultaneous changes in biochemical, namely energy supply of tissues. Regardless of the nature of the stress-inducing effect, this mechanism is universal. The body reacts to stress with a stereotyped set of biochemical and physiological processes, which in turn provide nonspecific or cortical adaptation. Environmental factors, to which the body adapts, acting in different ways, lead to a monotonous general complex of disorders - a deficit of energy supply,

which means the mobilization of energy resources. As a result of these events, the chain of metabolic reactions leads to the expression of marker genes that determine the sensitivity of cells to stressors. Chronic psycho-emotional stress is a consequence of continuous or periodic prolonged exposure to emotionally negative factors [11,16,23,24].

## TREATMENT AND REHABILITATION STRATEGIES

Treatment of patients with traumatic illness against the background of chronic stress requires an integrated approach, which includes not only traditional methods of medical care, but also psychological support. An important part is the correction of stress through psychotherapy, in particular cognitive behavioral therapy, which helps to reduce anxiety and depression. Statistics show that patients receiving psychotherapeutic care recover their psycho-emotional state faster, as well as improve the healing process of trauma [10,25].

In the acute phase of stress, the hypothalamic-pituitary-adrenal system is activated, mediated by cortisol. According to the results of preclinical studies, it is known that according to the type of response to stress, respondents are divided into two categories: whose cortisol levels will be increased or decreased and whose anxiety levels will be high or reduced. An adequate response of the hypothalamic-pituitary-adrenal axis and, as a result, a high level of cortisol is a general adaptation syndrome; It is the body's natural way of experiencing stress. Conversely, low cortisol levels are a phenomenon that leads to a pathological stress response; It is the result of a defect in the hypothalamus. This hypothesis was confirmed in preclinical studies: the injection of high doses of hydrocortisone was effective only if it was used in the first 6 hours («golden hours») after the traumatic event. Taking 100-140 mg of the drug can reduce the incidence of post-traumatic stress disorder from 60% to 16%. Benzodiazepines, enhancing the effect of gammaaminobutyric acid, cause sedative, hypnotic and anxiolytic effects, and actually block the work of the hypothalamic-pituitary-adrenal axis. The medical community opposes the early administration of benzodiazepines and believes that they interfere with the body's natural adaptive response. The fact that early administration of benzodiazepines increases the risk of developing post-traumatic stress disorders is also evidenced by the data of studies. However, the results of a study in rodents, on the contrary, showed that a number of drugs prescribed immediately after exposure to stress helped to reduce the symptoms

of post-traumatic stress disorders. According to the mechanism of action, groups of drugs are distinguished that block the consolidation process (anisomycin), supplement the lack of cortisol (hydrocortisone in high doses, oxytocin) and antidepressants (agomelatine, escitalopram, certraline). The opposite effect was cortisol in small doses, alprazolam, ketamine and alcohol consumption [18,24-26].

It is also necessary to take into account pharmacological correction - the use of anti-stress drugs, adaptogens and means to improve microcirculation, which will contribute to better healing of injuries. Given the negative effects of cortisol, medications are used to correct the level of this hormone in the body, which is an integral part of immunotherapy.

One alternative treatment for anxiety disorders is the use of oxytocin, which mainly affects social behavior. For a long time it was considered a «maternal hormone», but in the 1990s, according to the results of the study, it was found that it is able to reduce anxiety and regulate social behavior (caring for offspring, sexual instinct, social memory). According to the results of preclinical studies, it was found that the administration of oxytocin was as effective in reducing socially determined fear and social withdrawal as the administration of benzodiazepine, or long-term administration of paroxetine. But unlike new psychoactive substances, it did not affect the severity of anxiety and fear caused by sound stimuli; New psychoactive substances were effective in both situations. It should be noted that oxytocin at low doses did not affect either behavioral or physiological manifestations. It demonstrates its effectiveness only when administered in high doses. Reviews on long-term prescription of the drug show that its anxiolytic effect differs depending on gender. Yes, in women, the effect is more pronounced, but further research is needed in this direction. Oxytocin, administered before the onset of stress, slows down the intracellular increase in the production of corticotropin-releasing factor and cortisol. That is, in the future, it reduces the intensity of the activation response, orientation, anxiety, fear, restlessness and tension. Thus, oxytocin and new psychotropic substances are drugs that have a very good prospect in the treatment of anxiety disorders [9,26-28].

The composition of the therapeutic complex of immunotherapy of traumatic illness with a pronounced stress component, with the possible development of severe complications, includes 4 main components in individual combinations:

1. Anticytokine therapy (the goal is the elimination of excess cytokines, the current clinical situation is high cytokineemia, the threat of septic shock).

- Options: hemofiltration with sorption of tumor necrosis factor; Plasmapheresis; introduction of monoclonal anticytokine antibodies; therapy with corticosteroids, hydroxystarch derivatives, aprotinin.
2. Prosthetic therapy: immunoglobulins for intravenous use (the goal is to bind microbial antigens and toxins, enhance opsonization and phagocytosis; the maximum recorded effect is in septic shock); transfusions of hyperimmune plasma; extracorporeal hemosorption, which provides a combination of detoxifying and immunological effects.
  3. Cytokine therapy (the goal is to correct the key link in the pathogenesis of sepsis and cytokine imbalance; the drug of choice is rancoleukin, the indications are the fact of sepsis, the dosage and frequency are determined by the nature and individual severity of immunodeficiency).
  4. Metabolic support of the immune system: enteral and parenteral nutritional support; systemic antihypoxia (hyperbaric oxygenation, indirect electrochemical oxidation of blood with sodium hypochlorite); systemic antioxidant.

The above immunometabolic complex is a powerful means of pathogenetic therapy, which not only complements, but also optimizes standard etiotropic antibiotic therapy, which is aimed only at passive eradication of pathogens.

When studying the problems of traumatic illness, little attention is paid to the integration of psychosomatic and physiological approaches, which makes it possible to answer a significant part of the questions posed, and instead molecular and cellular mechanisms that do not express emotions are studied. Chronic stress load is one of the main factors in the progression of the most common somatic diseases, which certainly worsens the course of traumatic illness. Undoubtedly, in order to prevent this, it is necessary to apply improved approaches to the problem of the influence of stress factors, which would cover a complex of preventive, therapeutic and rehabilitation measures, taking into account the impact of chronic stress on the development of metabolic disorders.

Stress, both psycho-emotional and physiological, causes a wave-like activation of free radical oxidation in the blood and tissues, in the brain tissues in particular. A short-term oxidative rise is observed already in the first minutes of stress, then it decreases and disappears, due to the reactive activation of antioxidant systems, and a secondary rise occurs at the 2-4th week of severe chronic stress and is characterized by exhaustion phenomena. In the limbic-reticular structures of the brain, local blood flow slows down and structural damage occurs in the hippocampus, hypothalamus and cerebral cortex. Under the influence of



intense and prolonged stress, the anxiety response, the resistance phase and the exhaustion phase quickly replace each other. Numerous chemical processes necessary for the body to adapt to new conditions of existence lead to the formation of a certain amount of insoluble toxins, which provoke a loss of tissue elasticity, which means a slowdown in all regenerative processes. The degree of resistance of the body to the action of a stress factor is determined by the functional state of the hypothalamic-pituitary-adrenal system. The activation of this system provides adaptive restructuring in the body and acts as an indicator of the manifestation of a stress reaction. With age, the level of its activity decreases and, accordingly, the adaptive capabilities of the body decrease. With emotional stress, the neurochemical properties of neurons are restructured, the sensitivity of membrane receptors to neurotransmitters and neuropeptides decreases, as a result of which postsynaptic processes slow down. As a result of the above changes, stagnant arousal is formed in the emotional zones of the brain, which leads to functional disorders. It has been established that disorders in the hypothalamolimbic-reticular structures of the brain form a general nonspecific reaction, subsequently spreading to the cortex of the cerebral hemispheres and further to peripheral organs through the autonomic nervous system, providing adaptive restructuring in the body. This is what triggers pathogenetic factors that are responsible for the next chain of pathophysiological disorders, in chronic stress, which directly affect the course of traumatic illness [29,30-32].

## CONCLUSIONS

Chronic stress is an important factor that affects the clinical course of traumatic illness through the development of neuropsychiatric disorders due to the impact of stressful events on brain and body functions. The impact of stress occurs in several dimensions simultaneously (anatomy, electrophysiology, behavior, social interaction). Thus, chronic stress promotes the development of inflammatory processes, slows down healing and increases the risk of infectious complications, through an imbalance of the nervous, immune and humoral systems of the body. In this regard, the treatment of such patients should be comprehensive, including not only pathogenetic eradication of pathogens, but also immunocorrection, hormone control and psychological support. The introduction of a therapeutic complex of immunotherapy of traumatic disease with a pronounced stress component, with the possible development of severe complications, will make it possible to improve the results of treatment and rehabilitation of patients with traumatic illness.

## REFERENCES

1. Yajing Sun, Uanyuan Qu, Jianwei Zhu. The Relationship Between Inflammation and Post-traumatic Stress Disorder. *Front. Psychiatry*. 2021 doi:10.3389/fpsyt.2021.707543. DOI
2. Du J, Diao H, Zhou X et al. Posttraumatic stress disorder: a psychiatric disorder requiring urgent attention. *Med Rev (Berl)*. 2022;2(3):219-43. doi: 10.1515/mr-2022-0012. DOI
3. Tsybalyuk VI et al. Vohnepalni poranennia miakyykh tkanyn (dosvid antyterorystychnoi operatsii/operatsii obiednanykh syl). [Soft tissue gunshot wounds (counter-terrorist operation/joint force operation experience).] Kharkiv: Collegium. 2020, p.400. (Ukrainian)
4. Du J, Diao H, Zhou X et al. Posttraumatic stress disorder: a psychiatric disorder requiring urgent attention. *Med Rev (Berl)*. 2022;2(3):219-43. doi: 10.1515/mr-2022-0012. DOI
5. Nechitaylo IS, Myloslavskaya OV. Psykholohichniy dystres naselennia Ukrainy pid chas viiny. Tezy dopovidei uchasnykiv mizhnarodnoho psykholohichnoho forumu «Osobystist, Suspilstvo, Viina». [Psychological distress of the population of Ukraine during the war. In: Abstracts of the reports of the participants of the international psychological forum «Personality, Society, War»]. Kharkiv: KhNUiA. 2022. p. 85-7. (Ukrainian)
6. Baraboy VA, Reznikov AG. Fiziologhiia, biokhimiia i psykholohiia stresu [Physiology, biochemistry and psychology of stress]. Kiev: Interservice. 2013, p.314. (Ukrainian)
7. Lamotte G, Shouman K, Benarroch EE. Stress and central autonomic network. *Auton Neurosci*. 2021;235:102870. doi: 10.1016/j.autneu.2021.102870. DOI
8. Frankova IO. Zhyttia na mezhi: sotsialnyi stres, travma ta psykhopatologhiia: ohliad materialiv konhresu 29-ho Yevropeiskoho koledzhu neiropsykhofarmakologhii [Living on the edge: social stress, trauma and psychopathology] 29th Congress of the European College of Neuropsychopharmacology. 2017;2(1):e020115. doi: 10.26766/PMGPV211.15. (Ukrainian) DOI
9. Kornatsky VM, Mikhal'chuk VM, Dyachenko LO. Vplyv stresu na rozvytok i perebih zakhvoryuvan' [The effects of stress on the development and course of diseases]. *Svit medytsyny ta biolohiyi*. 2017;1(59):194-202. (Ukrainian)
10. Desborough JP. The stress response to trauma and surgery. *Brit. J. Anaesth*. 2000;1(85):109-17. doi: 10.1093/bja/85.1.109. DOI
11. Vinogradov VV. Stress i patologiia [Stress and pathology]. RUE «Publishing House». 2007, p.352. (Ukrainian)
12. Gozhenko AI. Teoriia bolezni [Disease theory]. Odessa: Fenix. 2017, p.142. (Ukrainian)
13. Oitzl MS, Champagne DL, van der Veen R, de Kloet ER. Brain development under stress: hypotheses of glucocorticoid actions revisited. *Neurosci Biobehav Rev*. 2010;34(6):853-66. doi: 10.1016/j.neubiorev.2009.07.006. DOI
14. Hryshko YuM. Suchasnyy pohlyad na problemu metabolichnoho syndromu [Modern view on the problem of metabolic syndrome]. *Aktual'ni problemy transportnoyi medytsyny*. 2018;3(53):37-46. (Ukrainian)
15. Baraboy VA, Reznikov OG. Fiziologhiia, biokhimiia i psykholohiia stresu [Physiology, biochemistry and psychology of stress]. Kiev: Interservis. 2013, p.314. (Ukrainian)
16. Ebrecht M, Hextall J, Kirtley L-G et al. Perceived stress and cortisol levels predict speed of wound healing in healthy male adults. *Psychoneuroendocrinology*. 2004;29(6): 798-809. doi:10.1016/S0306-4530(03)00144-6. DOI
17. Saxbe DE. A field (researcher's) guide to cortisol: tracking HPA axis functioning in everyday life. *Health Psychol Rev*. 2008;2(2):163-90. doi:10.1080/17437190802530812. DOI
18. Anderson RM. A role for Dicer in aging and stress survival. *Cell Metabolism*. 2012; 3(16): 285-6.
19. Mori MA et al. Role of microRNA processing in adipose tissue in stress defense and longevity. *Cell Metabolism*. 2012;3(16):336-47. doi: 10.1016/j.cmet.2012.07.017. DOI
20. Rabasa C, Dickson SL. Impact of stress on metabolism and energy balance. *Current Opinion in Behavioral Sciences*. 2016;9:71-7. doi:10.1016/j.cobeha.2016.01.011. DOI
21. Kovalenko VM. Rol' emotsiynoho stresu u vynykenni arterial'noyi hipertenziyi: fakty i nevyrisheni pytannia [The Role of Emotional Stress in Arterial Hypertension: Facts and Unresolved Issues]. *Science and Practice. International Medical Journal*. 2014;1(2):116-27. (Ukrainian)
22. Hryshko YuM. Zahal'nyy adaptatsiynnyy syndrom ta yoho metabolichne zabezpechennia [General adaptive syndrome and its metabolic support]. *Visnyk Mors'koyi Medytsyny*. 2019;1(55):29-40. (Ukrainian)
23. Weinmann M. Stress-induced hormonal alterations. *Crit. Care Clin*. 2001;1(17):33-49. doi:10.1016/S0749-0704(05)70148-2. DOI
24. Mishchenko IV. Reaktsiyyi perekysnoho okysnennia lipidiv i hemostazu u riznykh tkanynakh pry hostromu emotsiyno-bol'ovomu stresy [Reactions of lipid peroxidation and haemostasis in various tissues in acute emotional-pain stress]. *Fiziolohichniy zhurnal*. 2002;6(48): 66-9. (Ukrainian)
25. Boyarchuk OD. Biokhimiia stresu [Biochemistry of stress]. Lugansk View of «LNU n. Taras Shevchenko». 2013, p.177. (Ukrainian)
26. Peters S, Slattery DA, Uschold-Schmidt N et al. Dose-dependent effects of chronic central infusion of oxytocin on anxiety, oxytocin receptor binding and stress-related parameters in mice. *Psychoneuroendocrinology*. 2014;42:225-236. doi: 10.1016/j.psyneuen.2014.01.021.

27. Neumann ID, Slattery DA. Oxytocin in general anxiety and social fear: a translational approach. *Biological Psychiatry*. 2016; 79(3):213-221. doi: 10.1016/j.biopsych.2015.06.004. 
28. Gozhenko AI. Funktsional'no-metabolichnyy kontynuum. [Functional-metabolic continuum]. *Zhurnal NAMN Ukrayiny*. 2016;1(22):3-8. (Ukrainian)
29. Gozhenko A, Hryshko Y. Khronichnyy stres ta yoho metabolichne zabezpechennya. [Chronic stress and its metabolic support]. Aktual'ni problemy suchasnoyi medytsyny: Visnyk Ukrayins'koyi medychnoyi stomatolohichnoyi akademiyi. 2019.19(4):123-129. doi:10.31718/2077-1096.19.4.123. (Ukrainian)
30. Gozhenko AI, Hryshko YuM, Hramatiuk SM. Rol' bilkovoho ta lipidnoho obminu v enerhetychnomu zabezpechenni orhanizmu. [The role of protein and lipid metabolism in the energy supply of the organism]. *Klinichna ta eksperymentalna patolohiia*. 2019;18(3):107-116. doi:10.24061/1727-4338.xviii.3.69.2019.18. (Ukrainian) 
31. Gozhenko AI, Hryshko YuM, Hramatiuk SM. Rol' systemnoho zapalennia v patohenezi metabolichnykh porushen. Chastyna I. Kontseptsiiia systemnoho zapalennia ta yoho patohenez. [The role of systemic inflammation in the pathogenesis of metabolic disorders. Part I. Concept of systemic inflammation and its pathogenesis.] *Visnyk morskoi medytsyny*. 2019;3(84):91-100. (Ukrainian)

*The work was carried out in the framework of research work 0124U002167 «Monitoring of traumatic disease against the background of chronic stress».*

## CONFLICT OF INTEREST

The Authors declare no conflict of interest

## CORRESPONDING AUTHOR

**Stepan S. Filip**

Uzhhorod National University

71 Minayska St, 88000 Uzhhorod, Ukraine

e-mail: filip.uz@i.ua

## ORCID AND CONTRIBUTIONSHIP

Stepan S. Filip: 0000-0002-6549-3892

Rudolf M. Slyvka: 0000-0002-0187-2711

Yuriy P. Skripinets: 0000-0002-9741-4175

Andriy M. Bratasyuk: 0000-0003-4390-2357

Antonina V. Varvaynets: 0000-0001-5859-1040

 – Work concept and design,  – Data collection and analysis,  – Responsibility for statistical analysis,  – Writing the article,  – Critical review,  – Final approval of the article

**RECEIVED:** 09.09.2024

**ACCEPTED:** 18.03.2025

