

**SOME ASPECTS OF BIOLOGICAL PROPERTIES AND PHYSIOLOGICAL ACTIVITY
OF THE CEREBROSPINAL FLUID AND ITS SIGNIFICANCE IN THE BODY****Bogomolets National Medical University (Kyiv, Ukraine)**

Анотація: *Порушення органів і систем організму можуть призвести до змін складу і властивостей спинномозкової рідини. Деякі з них обумовлені безпосереднім впливом патологічного процесу на нервову систему, інші – опосередковано. Вони тісно пов'язані з метаболічними і гормональними порушеннями в організмі, що впливає на трофічні і захисні функції нервової системи. Останні викликані загальними порушеннями серцево-судинної системи, що веде до порушення циркуляції спинномозкової рідини. У разі інфекційних процесів за межами нервової системи зміни складу спинномозкової рідини можна розглядати як рефлекс, який ініціює захисні адаптивні процеси в нервовій системі. У разі значної інтоксикації враховується можливість істотного порушення функцій нервової системи (зниження її резистентності), що може вплинути на обмін речовин, проникнення токсинів і дисфункції як в центральній, так і периферичній нервовій системі. Всі порушення функцій нервової системи відображаються на змінах складу спинномозкової рідини. Це свідчить про важливість її детального вивчення як за наявності запальних процесів в організмі, так і у здорових людей.*

Ключові слова: *спинномозкова рідина, судинні сплетення, цистерни, підпаутинний простір, біологічно активні речовини, електроліти.*

Abstract: *The disorders of the body organs and organ systems may lead to the changes of composition and properties of the cerebrospinal fluid. Some of them are stipulated for the direct influence of the pathology onto the nervous system, others- indirectly. They are closely related to the metabolic and hormonal disorders in the body, which affect trophic and protective functions of nervous system. The last ones are caused by general circulatory disorders of the cardio-vascular system, which impair circulation of the cerebrospinal fluid. In case of infections outside the nervous system, the cerebrospinal fluid composition changes may be considered as a reflex which initiated protective adaptive processes of nervous system. In case of large intoxication one should consider possibility of crucial impairment of the nervous system function (its decreased resistance), which may affect the metabolism, penetration of toxins and disorganization of healthy functioning of both central and peripheral nervous systems. All disorders in functions of the nervous system components are reflected in the cerebrospinal fluid composition alterations. This evidences about the importance of its detailed study in healthy and unhealthy humans.*

Key words: *cerebrospinal fluid, choroid plexus, cisterns, subarachnoid space neurons, biologically active substances, electrolytes.*

Connection of the publication with planned research works.

The work is a fragment is the SRW «Morphological features of rats under conditions of experimental exogenous influence» (state registration number 0122U000491).

Introduction.

The cerebrospinal fluid is represented with the choroid plexuses, located in the cerebral ventricles. Its main part is produced by the choroid plexuses of the cerebrum, presumably by the plexus epithelium. By its origin the last one is a differentiated organ, formed from the epithelium covering brain cavities, the plexus epithelium deriving from the dermal epithelium. So, the choroid plexuses are similar with the glands originating from the epithelium of a different type.

The aim of the study.

To analyze modern literature data on the physiological significance of the cerebrospinal fluid in the body, with particular attention to its role in the neuro-endocrine and immune systems integration.

Main part.

The cerebrospinal fluid production should be considered as a secretion process, the cerebrospinal fluid itself considered as a secretion of the plexuses. The process is particularly unique, without any similar processes no-

ticed in other glands, as well as the secreted substance. Its unique character is stipulated for the peculiarities of the organ, being washed by the cerebrospinal fluid, and its significance for the organ vital activity [1].

The process of the production of the cerebrospinal fluid by the choroid plexuses isn't restricted only by the physical-chemical processes. Rich innervation of the plexus and presence of the receptor structures in it evidence about the reflex nature of the cerebrospinal fluid production, which is regulated by the central nervous system, changing according to the qualitative and quantitative influence of the interior and exterior media. The cerebrospinal pressure changes represent special stimuli of the plexus receptors. Increased pressure in the ventricles inhibits its production, while the decreased pressure intensifies it. The vascular pressure changes affect plexus functioning: venous congestion leads to the increase of the cerebral volume and causes decrease of the cerebrospinal fluid production. Its chemical composition changes may be caused by local metabolic processes and pathological conditions in the ventricles. The composition is regulated by the plexus activity and sorption function of the ependyma. Under pathological conditions (inflammation, intoxication) some changes due to increased activity occur in the plexus: reticulation and vacuolization of the

cells with their swelling; abrupt increase in number of the epithelial cells is noted as well [2, 3].

The reflex which provides for the plexus unconditioned functioning, withdraws in the subcortical structures of the cerebrum, though it depends whether this is a single regulatory center or a complex one, closely related to other reflexes (vascular ones). This unconditioned reflex during life of the human provides basis for the conditioned reflexes which regulate activity of the plexus under interior (chemical and physiological) and the exterior changes which may affect human's mental health. These changes indirectly affect the choroid plexus, thus influencing the vessels, respiration and directly affecting the plexus epithelium [4].

As the plexuses produce the cerebrospinal fluid, it leaves the ventricles: they contain approximately 30-50 ml of the fluid, totally producing 600ml a day. Some portion of the fluid flows by channels along the cerebral gyri on the cerebral convex surface [5, 6]. This is so called external fluid, located between the external surface of the cerebrum with the spinal cord and their bony framework. The exterior spinal fluid serves as a hydraulics which may protect it from injuries and stress. The cerebral metabolites leave the exterior spinal fluid into the veins [7].

The cerebrospinal fluid within the cerebrum circulates in some interacting cavities or cisterns. All the cisterns together make up a system – the fluid axis of the cerebrum which is composed of two lateral cisterns in cerebral hemispheres, one in the central cerebrum and between the cerebellum and medulla oblongata, and central canal of the spinal cord which terminates between the 3rd and 4th lumbar vertebrae in a small extended cavity, the terminal cistern. The cranial pia matter doesn't participate in production of the cerebrospinal fluid, but regulates its composition by excretion and absorption, with the barrier function being the basic one. The products of the meninges (perivascular lymph) quite often penetrate the subarachnoid space. The subarachnoid space fluid is mixed with the fluid produced in the cerebrum and neural sheaths of peripheral nerves. So, the cerebrospinal fluid in the ventricles is represented as is. The fluid of the subarachnoid spaces, mixed in its composition, is produced primarily from the ventricular fluid, mixed with the metabolites of the meninges, cerebral parenchyma and peripheral nerves. This stipulates for difference in composition of the ventricular and subarachnoid fluid, reflected in impairment of the cerebral meningeal regulation function. The cerebrospinal fluid in subarachnoid space makes oscillate and jerking motions which cause the fluid mix. These motions insignificantly depend on the standard pulse and respiratory effects regulating the cerebrospinal fluid pressure: body or body parts motions, body movement in environment and factors affecting respiration and pulse are of primary importance. Functional load of the cerebrum and psychogenic factors are somewhat important in the alterations of the cerebrospinal fluid pressure and its motion in the subarachnoid space [7, 8]. Except for the oscillation and jerking motions, the cerebrospinal fluid within the subarachnoid space is continuously moving forward, from the production region to the spot where it leaves the subarachnoid space. The direction of this motion depends on its absorption spot. Clarification on the cerebrospinal fluid leakage spot is closely related to the direction of the current. The speed of the cerebrospinal fluid restoration is a derivative from

its excretion and subarachnoid space leakage speed, which isn't a static one. Depending on the day period, this speed in different time periods may be slowed or accelerated, due to the workload affecting central nervous, muscular and other body organ systems. Under pathological circumstances the speed of the cerebrospinal fluid flow may alter even more (usually increasing). The basic spots of its leakage from the subarachnoid space in an adult are the arachnoid granulations and villi: the intrasinus, intralacunar and subdural ones. The arachnoid granulations represent with the arachnoid villi located along the cerebral sinuses. They don't protrude the sinus walls but come through the hard meninges and directly attach to the venous sinus endothelium. In children the cerebrospinal fluid is removed by means of the arachnoid granulations rudiments – microvilli and tubercles. While penetrating through the arachnoid matter, the cerebrospinal fluid reaches blood of the sinuses and lacunae, directly or through the dura matter gaps. In spinal cord it travels to the epidural space veins and into the lymph vessels of the space.

The cerebrospinal fluid functions as a mediator between blood and neurons. The neurons are extremely sensitive cells which immediately respond onto the slightest changes of the environment: sometimes even one millionth of a gram of the substance is sufficient to excite it. So, the composition and properties of the cerebrospinal fluid must be balanced so that the cells wouldn't be too much excited or inhibited. Constancy of the composition and properties of the cerebrospinal fluid make up a predisposing condition for functioning of the brain at whole and each neuron separately [9].

The cerebrospinal fluid provides neurons with various nutrients, while neurons release metabolic wastes in it. The cerebrospinal fluid is also supplied through blood vessels with the substances which provide for interaction of cerebral cells: hormones, metabolites and mediators. The performed analysis established presence of endorphins, protein-like substances with anesthetic effect, in it. Their concentration increases in situations when the body needs to neutralize negative effect of pain stimuli. The research data show that they serve many functions: endorphins, like other protein compounds, control all information which reaches the cerebrum, defining in this way the emotional response of a human, his behavior, memory and intellectual characteristics [10, 11].

As a humoral medium which contains many biologically active substances, the cerebrospinal fluid is a unique one. High liquor concentration of some hormones produced by the epiphysis and hypophysis is explained for prolonged presence of biologically active substances in it, unlike in the blood, and their retrograde transport by the portal vessels until medial increase, and then diffuse transport to the third ventricle. The studies have established prolonged half-disintegration period, and a more significant activity of biologically active substances in the cerebrospinal fluid, compared to the blood serum. E.g., the oxytocin half-destruction in the cerebrospinal fluid period lasts for 35 minutes, while in the blood it makes up a few minutes, which is related to the low content of oxytocinase in the cerebrospinal fluid. This evidences about the long-lasting action of biologically active substances on the receptors and neurons [12].

So, the presence of biologically active substances in the cerebrospinal fluid suggests that it serves as an aux-

iliary connector canal to the neurons, as the medial-central position of its internal system provides for sufficiently quick exchange between it and the regulatory cerebral centers.

Central system position provides for equal opportunities of contact between the substances of the cerebrospinal fluid and the right and left hemisphere cells as well as joint function conditions. Being closely connected to the cerebrum, it reflects its functional condition and its changes (the cerebrospinal fluid of a healthy and ill person significantly differ by the composition). This property is successfully used for diagnostics of some diseases. The altered external appearance of the cerebrospinal fluid, its clouding, presence of pathologically changed cells, disordered metabolism products and blood debris may aid in diagnosing the central nervous system disorders [13].

So, the functions of the cerebrospinal fluid may be defined as follows:

1. Mechanical protection from external mechanical factors.
2. By changing the pressure it regulates production and absorption processes as well as the blood supply of the cerebrum.
3. It supports and regulates the osmotic equilibrium of nerve elements.
4. It serves as a nutritious medium for the nervous system.
5. Removing the metabolites of central nervous system and other pathological products outside the subarachnoid space.
6. Protective properties – lytic, bactericidal, as an area of antibodies accumulation.

The cerebrospinal fluid physiology can't be related to only one of the recalled paragraphs, being quite complex, with all components similarly valuable. The least significant is the mechanical protection from external factors. Sometimes, in case of the head injuries, the cerebrospinal fluid doesn't protect the cerebrum, but causes brain injury. In case of small changes of the cerebral volume due to the pulse rate, respiration and venous congestion, caused by body movements, walking or jumping, the cerebrospinal fluid serves a protective function. Another function which is closely related to the mechanical protection is regulatory function due to its own pressure and

the circulatory pressure, as the pressure changes may arise with the above mentioned motions. Disordered regulatory function, as for its own pressure or cerebral blood supply, always creates either permanent or pathological condition, expressed in increase of the intracranial pressure [14]. The most influential are the cerebrospinal fluid functions related to central nervous system: its nutrition and protection. Here the cerebrospinal fluid is physiologically related to the mesenchyma formations, performing their functions (metabolism and protection) through regulatory influence of the central nervous system. By its composition the cerebrospinal fluid can't be considered as a nutritious medium. It is poor in colloids and rich in crystalloids, being the fluid, necessary for regulation and balancing all disorders in the osmotic (salt) equilibrium of nervous system elements, which provide for support and protection. Though, this is not all that provides for its significance of the electrolyte medium. Its electrolyte ratio, constancy of the ratio and quick concentration shifts provide for the conditions, necessary for excitement and the excitement conduction [15].

Conclusions.

The disorders of the body organs and organ systems may lead to the changes of composition and properties of the cerebrospinal fluid. Some of them are stipulated for the direct influence of the pathology onto the nervous system, others- indirectly. They are closely related to the metabolic and hormonal disorders in the body, which affect trophic and protective functions of nervous system. The last ones are caused by general circulatory disorders of the cardio-vascular system, which impair circulation of the cerebrospinal fluid. In case of infections outside the nervous system, the cerebrospinal fluid composition changes may be considered as a reflex which initiated protective adaptive processes of nervous system. In case of large intoxication one should consider possibility of crucial impairment of the nervous system function (its decreased resistance), which may affect the metabolism, penetration of toxins and disorganization of healthy functioning of both central and peripheral nervous systems. All disorders in functions of the nervous system components are reflected in the cerebrospinal fluid composition alterations. This evidences about the importance of its detailed study in healthy and unhealthy humans.

References

1. Dean A. Cerebrospinal fluid analysis. Am. Fam. Physician. 2003;68:1103-8.
2. Bobryk II, Cherkasov VH. Suchasnyy aspekt funktsional'noyi anatomiyi tsentral'noyi nervovoyi systemy. Kyiv: NMU; 2001. 152 s. [in Ukrainian].
3. Bayle C. Analysis of tryptophan and tyrosine in cerebrospinal fluid by capillary electrophoresis and ball lens UV pulsed laser induced fluorescence detection. Journal of Chromatography. 2003;1013(1-2):123-130.
4. Carson MJ. CNS immune privilege: hiding in plain sight. Immunol Rev. 2006;213:48-65.
5. Baehr C. Choroid plexus epithelial monolayers a cell culture model from porcine brain. Cerebrospinal fluid research. 2006;3(13):1-14.
6. Torzewski M. Integrated cytology of cerebrospinal fluid. Berlin, Heidelberg: Springer-Verlag; 2008. 93 p.
7. Malakhov VO. Osnovy klinichnoyi likvorolohiyi. Sumy: SumDU; 2016. 352 s. [in Ukrainian].
8. Angelow S. Functional characterization of the active ascorbic acid transport into cerebrospinal fluid using primary cultured choroid plexus cells. Brain research. 2003;988(1-2):105-113.
9. Deisenhammer F. Guidelines on routine cerebrospinal fluid analysis. Report from an EFNS task force. European Journal of Neurology. 2006;13:913-922.
10. Celik O. Cerebrospinal fluid adrenomedullin levels in patients with preeclampsia. Acta Obstetrica Et Gynecologica Scandinavica. 2003;82(6):578-579.
11. Deane R. Brain capillary endothelium and choroid plexus epithelium regulate transport of transferrin bound and free iron into the rat brain. Journal of Neurochemistry. 2004;88:813-820.
12. Akefeldt A. Cerebrospinal fluid neuropeptide Y in Prader-Willi syndrome. Developmental Medicine and Child Neurology. 2001;43(4):286-287.
13. Stolyarov OI. Biokhimichnyy sklad ridyn orhanizmu ta yikh kliniko-diahnostychnye znachennya. Kyiv: Zdorov'ya; 2004. 192 s. [in Ukrainian].
14. Zakhariya KA. Poperedzhennya pomylok pry doslidzhenni spynnomozkovoyi ridyny. Laboratorna diahnostyka. 2011;4:35-43. [in Ukrainian].
15. Karelina I, Kasevych N M. Nevrolohiya. Kyiv: Medytsyna; 2014. 287 s. [in Ukrainian].