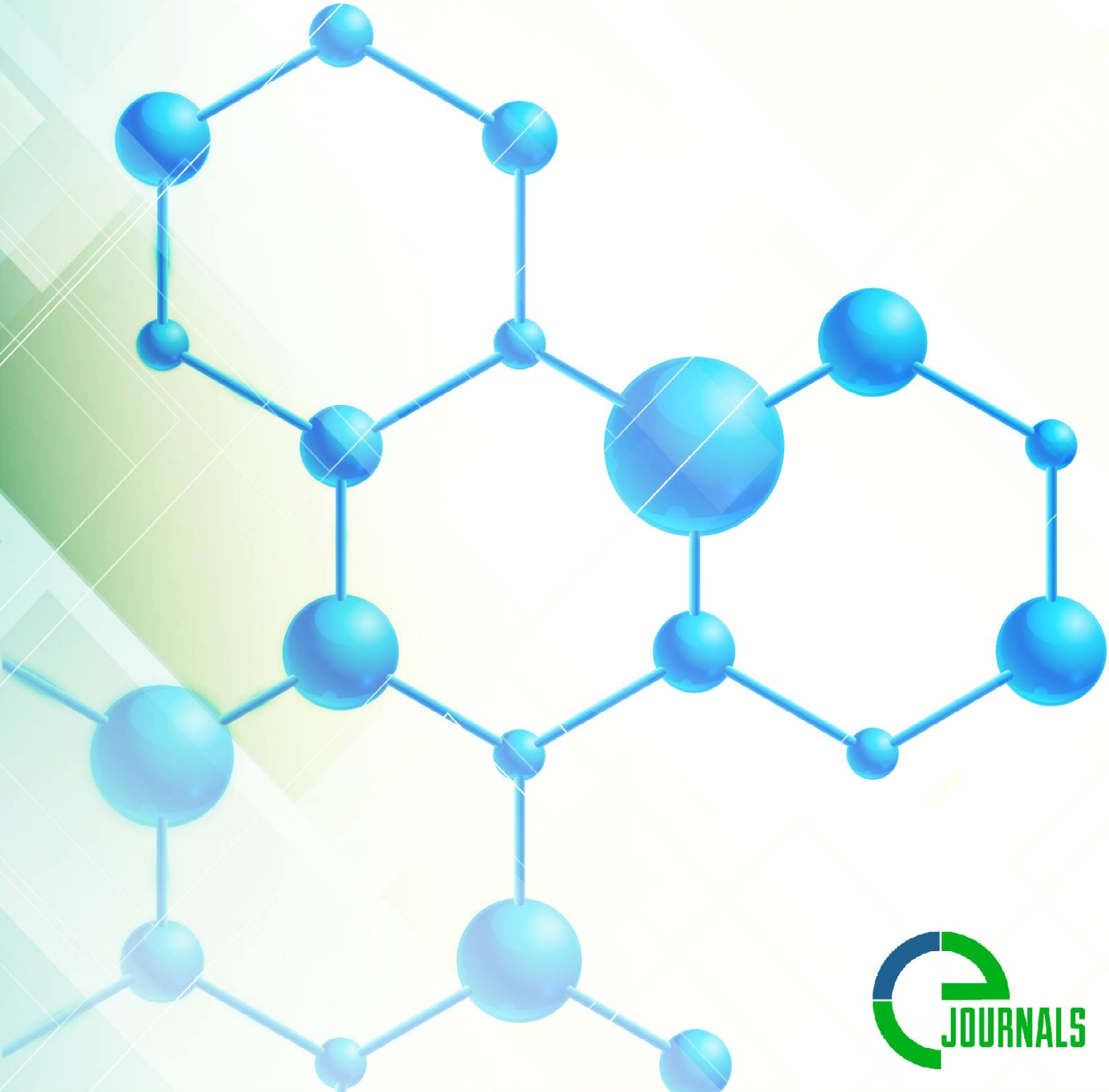
EUROPEAN JOURNAL OF

MOLECULAR MEDICINE



European Journal of Molecular medicine
Volume 1, Issue 1, March 2021

Internet address: http://ejournals.id/index.php/EJMM/issue/archive
E-mail: info@ejournals.id
Published by ejournals PVT LTD
Issued Bimonthly
DOI prefix: 10.52325
Potsdamer Straße 170, 10784 Berlin, Germany

Requirements for the authors.

The manuscript authors must provide reliable results of the work done, as well as an objective judgment on the significance of the study. The data underlying the work should be presented accurately, without errors. The work should contain enough details and bibliographic references for possible reproduction. False or knowingly erroneous statements are perceived as unethical behavior and unacceptable.

Authors should make sure that the original work is submitted and, if other authors' works or claims are used, provide appropriate bibliographic references or citations. Plagiarism can exist in many forms - from representing someone else's work as copyright to copying or paraphrasing significant parts of another's work without attribution, as well as claiming one's rights to the results of another's research. Plagiarism in all forms constitutes unethical acts and is unacceptable. Responsibility for plagiarism is entirely on the shoulders of the authors.

Significant errors in published works. If the author detects significant errors or inaccuracies in the publication, the author must inform the editor of the journal or the publisher about this and interact with them in order to remove the publication as soon as possible or correct errors. If the editor or publisher has received information from a third party that the publication contains significant errors, the author must withdraw the work or correct the errors as soon as possible.

OPEN ACCESS

Copyright © 2021 by ejournals PVT LTD

CHIEF EDITOR

Serikuly Zhandos
PhD, Associate Professor, RWTH Aachen University, *Aachen, Germany*

EDITORIAL BOARD

Bob Anderson
ImmusanT, *USA*

Marco Bruno
Erasmus Medical Center,
The Netherlands

Antoni Castells
Hospital Clinic
Barcelona, Spain

Giacomo Caio
University of Ferrara, *Italy*

Michael Farthing
St George's Hospital Medical School, *UK*

Carmelo Scarpignato
University of Parma,
Italy

Geriatric Medicine

Ian Cameron
The University of Sydney,
Australia

Sutthichai Jitapunkul
Chulalongkorn University,
Thailand

Juulia Jylhävä
Karolinska Institute, *Sweden*

Kenneth Rockwood
Dalhousie University,
Canada

CONTENT

MORPHOLOGICAL FEATURES OF ISCHEMIC AND HEMORRHAGIC BRAIN STROKES

Kamalova M.I., Islamov SH.E.
Samarkand State Medical Institute, Republic of Uzbekistan

Abstract. The article is devoted to pathomorphological features of ischemic and hemorrhagic brain strokes. The aim of the research was to establish morphological peculiarities of brain stroke development in the basins of carotid, vertebral-basilar and both arterial systems. The analysis of 50 cases of tanatological study in which acute cerebral blood circulation disorder was diagnosed was carried out.

It has been established that changes in the microcirculatory channel vessels during a hemorrhagic stroke are caused by hypoxia and ischemia of the brain, its swelling, and a sharp violation of vascular permeability. Such changes are local and widespread, can be divided into acute, which occurred during a stroke, and chronic, which developed before the stroke. Pathomorphological changes cover all structural and functional levels of the arterial system of the brain, the most important of which are the vessels of the microcirculatory channel.

Keywords: acute cerebral circulation disorder, brain, ischemic stroke, hemorrhagic stroke, pathomorphological features.

Introduction. At present, high frequency of strokes can be caused by the lack of an effective primary and secondary prevention system for stroke, as well as their over diagnosis. Clarification of this issue is associated with a detailed study of risk factors, the course and prevention of stroke in our country. Comparatively little studied remains the question of the implementation of secondary prevention of ischemic stroke in our country, especially with its different subtypes, which makes relevant further research in this direction [10]. There are three main types of stroke: ischemic stroke, cerebral stroke and subarachnoid hemorrhage. Intracerebral hemorrhage and (not in all classifications) non-traumatic subraumatic hemorrhage are classified as hemorrhagic insult. According to international multicenter studies, the ratio of ischemic to hemorrhagic strokes is 4:1-5:1 on average (80-85% and 15-20%) [6,11,18]. According to practical medicine, the most common ischemic type of stroke, which is of high medical and social significance due to its leading position in the structure of morbidity, disability and mortality in many countries. According to pathological and anatomical studies, heart attacks with clinical manifestations were characterized by a great variety of magnitude and localization [5]. Stroke incidence in the Russian Federation is one of the highest in the world, reaching almost 5 cases per 1000 people per year, with the share of ischemic strokes accounting for up to 87% of all strokes (20). Only 8-10% of strokes end in complete restoration of impaired function, while most surviving patients have a marked neurological deficit, often resulting in severe disability (14). Stroke fatality in different countries is 1.3-1.8 per 1000 people per year, increasing 1.5 times with repeated stroke. In recent decades, the idea of pathogenetic subtypes of strokes and criteria for their diagnosis has been formed, and certain difficulties arise in tanatological practice [16]. Usually, ischemic strokes of the cerebral hemispheres in case of cerebral circulation disorders in the pool of the internal carotid artery are 2-5 times more frequent than in the pool of the vertebrobasilar system, especially in the cortical subcortical branches of the middle cerebral artery. The problem of determining the age of cerebral stroke is particularly relevant in forensic practice, where sudden death occurs on the scene in the absence of anamnesis, investigation and other data on the circumstances of the case. Therefore, the identification of characteristic morphological changes in brain stroke, as well as the creation of a classification of stroke on the basis of this representation are extremely important tools for the choice of tactics for their treatment and secondary prevention, the definition of short- and long-term prognosis, standardization in clinical and epidemiological studies.

Research materials and methods. As a material, a retrospective analysis of 20 reports of forensic examinations conducted at the Tanatological Department of the Samarkand Regional Branch of the Republican Scientific and Practical Center for Forensic Medical Examination and 28 protocols of pathological and anatomical examination of the subdivisions of the Republican Pathological Anatomical Center in the period 2019-2020 was carried out. Generally accepted research methods were applied, i.e. macro- and microscopic study of the brain and its arterial system was conducted at all structural and functional levels, including the main arteries of the head - internal carotid and vertebral arteries, intracranial arteries - vessels of the williesian circle and their branches, as well as intra cerebral arteries and vessels of the microcirculatory channel (ICR). The study of the brain determined the size and localization of intracerebral hematomas, the presence of a blood rupture into the ventricular system, the severity of cerebral edema, dislocation and compression of its trunk.

. Visible brain changes (small hemorrhages, perivascular edema, white spongiform state) were taken into account. Microscopic examination of the brain was carried out in the histological preparations encased in paraffin. Which were stained with hematoxylin and eosin, according to the methods of Van Gijson (determination of collagen fibers and myocytes in vessels), Weigert (determination of elastic fibers in vessels). Particular attention was paid to the microcirculatory vessels within the hematoma, in the perifocal zone, as well as at a distance from the hematoma.

The results of the research and their discussion. All were diagnosed with acute cerebral blood circulation disorder (ACBD) by ischemic and hemorrhagic types. Among them 36 men (75.0%) aged 20 to 72 years, 12 women (25.0%) aged 33 to 65 years. In all cases, massive intracerebral haemorrhages were detected, located in 64% of cases in the hemispheres of the brain: lateral - 53%, medial - 15%, mixed - 32%. The volume of hemorrhagic foci exceeded 40 cm?. In 16% of observations quite large hemorrhages were found in the brainstem and cerebellar hemispheres. In most cases, blood has spread to the ventricular system, accompanied by swelling, dislocation and compression of the brain stem, often causing death. Many observations revealed previously transferred NMK in the form of posthemorrhagic cysts of various sizes (67%), localized mainly in brain regions, symmetrical fresh hematoma, significant longevity single lacunar infarcts (LI), as well as organized and organized multi ple LI (lacunar state of the brain), which in more than a third of cases were combined with organized foci of hemorrhage [4]. Organized ischemia and lacunar foci were most often located in the basal nuclei and white matter of both brain hemispheres, sometimes in the thalamus, brain bridge, and cerebellar hemispheres. The microscopic examination of all sectioned cases revealed changes in the intracerebral arteries, which are typical for hypertensive angiopathy and cause major brain haemorrhages: plasma impregnation of arterial walls and hemorrhage in them with stenosis and lumen lining, focal or total fibrinoid necrosis with formation of miliary aneurysm, as well as primary (isolated) necrosis of middle arterial muscle cells with vascular rupture.

The hemorrhages were found to have occurred against the background of small-focus and diffuse changes in brain matter characteristic of hypertensive encephalopathy and caused by severe arterial and CDM pathology of the brain - small-focus perivascular hemorrhages, foci of perivascular edema, brain tissue necrosis in the perivascular region, periventricular white matter edema [19]. In chronic changes, fibrosis and thickening of the walls of capillaries and other microvessels with narrowing, emptying and obliteration of their lumen were revealed. Active proliferation of cell wall elements of many microvessels with the formation of convolutions - microvascular formations with multiple lumen, which are a sign of adaptive changes of the ICR, which developed in the ischemically hypoxic state of the brain due to the reduction of blood flow through the arteries, which underwent severe destructive changes with concomitant stenosis and obliteration, was also revealed.

The above chronic changes of the ICR were found in the cortex and white matter of hemispheres and cerebellum, basal nuclei, thalamus, various parts of the brain stem, including nuclei of cranial nerves and reticular formation. Leukostasis was detected in small vessels and leukodiasis. The walls of a number of microvessels located near the hemorrhage were necrotized. On the first day, at a considerable distance from the hematoma, a sharply pronounced edema of the brain substance was detected, giving it a spongiform structure, full-blooded PCR, arteries and veins, stasis and thrombosis in capillaries, perivascular hemorrhages with erythrocyte proliferation along white matter fibers. Blood that penetrated the perivascular spaces from the hematoma was found in them at quite large distances from the hematoma up to the subarachnoid space.

Acute changes of the ICR, which were observed in a number of cases of particularly severe hemorrhagic stroke with the development of extensive hematomas and blood rupture into the ventricles, also included the phenomena characteristic of the syndrome of disseminated intravascular blood clotting: widespread microvascular thrombosis with clot fragmentation, pre-thrombotic state in vestigial clusters of fibrin threads in veins, thromboemboles in the lumen of the latter, as well as pericapillary, periarterial and perivenular hemorrhages [2]At the same time it has been established that ICR takes an active part at different stages of hematoma organization: from edema and organization of necrosis of the surrounding brain tissue in the initial stage, to reabsorption of red blood cells in the second stage and formation of gliomezodermal scar around the pseudocyst in the final stage. Ischemic strokes were also divided into acute (up to 3 days) and subacute (4-6 days) strokes. Fresh strokes were macroscopically characterized by the following: respectively, the focus of colliquation necrosis revealed a well-defined hemorrhagic component in the form of a dark red hemorrhage under the soft cerebral membranes and into the cerebral cortex, the demarcation line (perifocal zone) is not determined. In microscopic examination - signs of cerebral substance edema with the appearance of multiple honeycomb (hole) cavities along the perimeter of strokes, further signs of ischemic strokes in the form of migration of blood cells (neutrophils, monocytes, etc.) through the wall of vessels [3, 8, 9]. During the day, when examined in the focus of ischemic strokes and the adjacent soft envelopes, stagnation of blood vessels, cyanosis, swelling and other signs of aseptic inflammation are observed. At the same time, the consistency of the brain, as well as the structure of the furrows and curves have not been changed. Brain tissue in the section has a clearly distinguishable boundary between layers (cortex and white matter) [21]. Over time, the focus was clearer and pale. There is no demarcation line. The stroke area has a slightly bluish hue, usual consistency, or is slightly soft to the touch, without sharp borders, and passes into the surrounding brain tissue. After a day of macroscopic aseptic inflammation has indistinct outlines with blurred borders. The cortex is pale grey with a pink or red hue (due to the hemorrhagic component). The white substance in the pathological focus is lighter than the surrounding undamaged tissue (due to ischemic emptying of microcirculatory channel vessels and swelling of the stroke zone). On the 2nd-3rd day, the swelling in the soft membranes and brain matter is significantly pronounced (especially in the border zone) and reaches its maximum. The line of demarcation in the stroke zone was not visually detected or indistinctly expressed. Only at palpation the borders of the pathological focus can be determined by the difference in consistency between the flabby area of the heart attack and the unchanged elastic (springing) surrounding tissues. Sometimes on the 3rd day the edge of the necrosis zone on the peri phery of the stroke may swell up visually above the surface of the slice (edematous border zone). Slight softening of the brain substance and visual absence of a demarcation line are important macroscopic criteria for stroke in the acute stage of development, with a limitation period of up to 3 days [1].In amicroscopic examination on the peri phery of the focal point of ischemic stroke, cerebral edema in the form of enlarged perivascular spaces was detected in the first 24 hours; in the border zone there is a distinct increase in the vascular network due to hyperemia of the reserve capillaries. The marginal position of segmental leukocytes, plasma diapaedesis, neutrophils and erythrocytes in the stroke zone through the dilated vascular wall was noted. There is a gradual increase in the number of drainage forms of oligodendroglyocytes, i.e., macroglia cells with a large volume of cytoplasm and eccentrically located nuclei [7]. The characteristic irreversible ischemic changes of neurons (tigerolysis, reduction of volume and eosinophilia of cytoplasm, as well as its vacuumization, blurring of nuclear membrane, turbidity of nucleoplasm, etc.) were detected. A day later, ring-shaped perivascular hemorrhages (microscopic equivalents of the hemorrhagic component) were detected around the vessels of the soft membranes and in grey matter. Some red blood cells are poorly coloured by leaching. With increasing hemolysis of erythrocytes, a blood pigment appears, which looks like small grains of dark brown color. In the border zone, swelling of brain tissue is quickly detected, which reaches its maximum by the 3rd day. Characteristically, the oedema with the accumulation of drainage forms of glia becomes so intense that gray and white brain matter during microscopic examination becomes honeycomb (holey, porous), reminiscent of bee honeycomb. Hole (honeycomb) character of the brain substance (visible only in histological examination) is an important differential-diagnostic criterion for ischemic stroke [13]. In later terms (duration about 4-6 days) the organization of stroke is noted, and it is typical that simultaneously with collictional necrosis and resorption of ischemic stroke zone there is a gradual increase of proliferation processes. The formation of a stale hemorrhagic component was observed (i.e. various combinations of shades of green, yellow and brown appear in the stroke area due to neutrophilic autolysis of the blood pigment).The examination reveals moist necrosis and tissue resorption,

so the brain becomes flabby. Characteristic of the presence of signs of stale hemorrhagic component (change in blood pigment color) in the brain membranes, cortex and white matter of the brain. In this case, the soft membranes are mainly in the course of blood vessels intensively impregnated with products of hemoglobin decomposition (hemosiderin). First, they have a slightly greenish or greenish-yellow color, and then a rusty hue with coloring of the affected tissues of varying intensity from dark brown to light yellow [15]. Necrotized bark has a rusty appearance with a variety of shades of colors and their combinations (green, brown, yellow). In a number of observations, the stale hemorrhagic component spread from the cortex to the subject white matter. In such cases, in the white matter adjoining the cortex, the width of the zone of imbination by the decaying blood pigments is usually about 0.3-0.5 cm. This is due to the lesions of the short cortical medullary arteries and arterioles, which supply blood to the bark and the adjoining arched (associative) fibres of white matter. With the progression of the pathological process (with major strokes) stroke zone extends to the pool of cortical and medullary arteries of medium length. At that time, the stale hemorrhagic component also captured the middle parts of the white matter, which was rarely observed. Sometimes there were cases of isolated damage to the white matter of the brain only, then the so-called white (gray) heart attacks are formed, ie without the hemorrhagic component. In exceptional cases, white (grey) heart attacks may also occur in the cerebral cortex [16].

In microscopic examination - the organization of stroke in the early stage (4-6 days) is manifested by increasing the number of drainage forms of oligodendrogliocytes and reactive changes in astrocytes along the edge of the boundary zone. The perforated (honeycomb) character of the affected tissue is preserved and small vascular gaps begin to form. In general, the phenomena of cerebral edema decrease and make up an area no wider than 0.2-0.4 cm in the border zone on the periphery of stroke.Cotoval nature of brain substance and the degree of oedema in the perifocal zone are important microscopic differential-diagnostic signs of heart attacks with the limitation period of 4-6 days [12]. Vascular proliferation with mitosis in endothelial cells and sclerosis sites has been noted. In the demarcation zone, except for reserve capillaries, proliferation of newly formed capillaries is observed. Single macrophages are detected along the vessels in the boundary zone. In the focus of stroke, the vascular pattern is generally preserved. Only in some places a peculiar "amputation" of microvessels is observed, in which case fresh small-point or focal hemorrhages may appear, visible histologically [17].

Conclusion. As a result of the morphological studies carried out, differential diagnostic features of hemodynamic strokes have been established and, at the same time, some features of their implementation have been noted. In particular, changes in the vessels of the ICR during hemorrhagic stroke are caused by hypoxia and ischemia of the brain, its swelling, sharp disturbance of the blood vessels permeability. These changes are local and widespread, can be divided into acute, which occurred during a stroke, and chronic, which developed before the stroke. In the initial period of stroke development (2-3 days) the picture of the expressed fresh hemorrhagic component in the form of dark red is characteristic.

hemorrhages (subarachnoidal and foci in the brain tissue adjacent to the soft cerebral membranes). In typical cases, in the acute stage of stroke, the hemorrhage is located only in the cerebral cortex (especially in its surface layers adjacent to the soft membranes), less often the hemorrhagic component captures not only the cortex but also the white matter of the brain.

Conclusions. In the later stages of stroke (the period of the organising stroke) a heart attack lasting about 4-6 days) there is a stale hemorrhagic component with spreading from the cortex to the white matter of the brain (in the area of stroke there are different combinations of shades of green, yellow and brown colors due to neutrophilic autolysis of the pigment of blood). The revealed feature of color scale of not fresh hemorrhagic component as a differential-diagnostic criterion to distinguish the stages of strokes, it is necessary to apply in conjunction with other macroscopic criteria (flabby brain consistency and the emergence of demarcation lines). Also to clarify the stage of brain stroke development it is necessary to perform histological examination (presence of signs of neutrophil and macrophage autolysis development). Thus change of hemorrhagic component character with occurrence of fine point or focal fresh hemorrhages in a stroke focus should be considered at interpretation of results on determination of duration of strokes formation. Pathomorphological changes cover all structural and functional levels of the arterial system of the brain, the most important of which is the ICR vessels.

References

1.Anttila J.E., Whitaker K.W., Wires E.S., Harvey B.K., Airavaara M. Role of microglia in ischemic focal stroke and recovery: focus on toll-like receptors. //Prog. Neuropsychopharmacol. Biol. Psychiatry. - 2016. - №79(Pt A), - P.3-14.

2.Brites D., Vaz, A.R. Microglia centered pathogenesis in ALS: insights in cell interconnectivity. // Front. Cell. Neurosci. - 2014. №8. - P.117.

3.Colonna M., Butovsky O. Microglia function in the central nervous system during health and neurodegeneration. // Annu. Rev. Immunol. - 2017. - №35 - P. 441-468.

4.Cooke R.A., Stewart B. Colour Atlas of Anatomical Pathology. - Churchill Livingstone. - 2004. - 300 p.

5.Donnan G. A., Fisher M., Macleod M., Davis S. M. Stroke (англ.) // The Lancet. - Elsevier, 2008. - May (vol. 371, no. 9624). - P. 1612-1623.

6.European Stroke Initiative recommendations for stroke management: update 2003 // Cerebrovasc. Dis. - 2003. - Vol. 16, - P.311-337.

7.Faustino J., Wang X., Johnson C.E., Klibanov A., Derugin N., Wendland M.F., et al. Microglial cells contribute to endogenous brain defenses after acute neonatal focal stroke. // J. Neurosci. - 2011. - №31. - P.12992-13001.

8.Fumagalli S., Perego C., Ortolano F., De Simoni M.G. CX3CR1 deficiency induces an early protective inflammatory environment in ischemic mice. // Glia. - 2013. - №61. P. 827-842.

9.Gelderblom M., Leypoldt F., Steinbach K., Behrens D.C., Choe U., Siler D.A., et al. Temporal and spatial dynamics of cerebral immune cell accumulation in stroke. / / Stroke. - 2009. №40. - P. 1849-1857.

10.Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015 (англ.) // The Lancet. - London, England: Elsevier, 2016-10-08. - Vol. 388, iss. 10053. - P. 1459-1544.

11.Goldstein L.B., Bushnell Ch.D., Adams R.J. et al. Guidelines for the Primary Prevention of Stroke: A Guideline for Healthcare Professionals From the American Heart Association // Stroke. - 2011. - Vol. 42. - P. 517-584.

12.Jack C.A., Ruffini F., Bar-Or A., Antel J.P. Microglia and multiple sclerosis.// J. Neurosci. Res. - 2005. - №81. - P.363-373.

13.Kriz J. Inflammation in ischemic brain injury: timing is important. // Crit. Rev. Neurobiol. - 2006. - №18. - P. 145-157.

14.Lloyd-Jones D., Adams R.J., Brown T.M. et al. Heart disease and stroke statistics - 2010 update: a report from the AHA // Circulation. - 2010. - Vol. 121. - P. 215-246.

15.Morrison H.W., Filosa J.A. A quantitative spatiotemporal analysis of microglia morphology during ischemic stroke and reperfusion. // J. Neuroinflammation. - 2013. №10. - P.4.

16.Oehmichen M., Roland N.Auer, Hans G?nter K?nig, Kurt A. Jellinger. Forensic

Neuropathology and Neurology . - Springer, 2005. - 660 p.

17.Streit W.J., Mrak R.E., Griffin W.S. Microglia and neuroinflammation: a pathological perspective. // J. Neuroinflammation. - 2004. - №1. P.14.

18.Towfighi A., Saver J. L. Stroke declines from third to fourth leading cause of death in the United States: historical perspective and challenges ahead (англ.) // Stroke journal.- Lippincott Williams & Wilkins., 2011.- August (vol.42, no.8).- P.2351-2355.

19.van Gijn J., Kerr R.S., Rinkel G.J. Subarachnoid haemorrhage (англ.) // The Lancet. - Elsevier, 2007. - Vol. 369, №9558. - P. 306-318.

20.WHO Disease and injury country estimates. World Health Organization (2009).

21.Wolf S.A., Boddeke H.W., Kettenmann H. Microglia in physiology and disease. / / Annu. Rev. Physiol. - 2017. - №79. - P. 619-643.