Neurotrophic factors and steroid hormones interact in the processes of regulation of various neuronal processes, such as the growth of neurites, differentiation and neuroprotection. The use of testosterone for therapeutic purposes protects motor neurons from atrophy caused by the death of adjacent motor neurons.

There are studies that androgens greatly contribute to the reorganization of the neural chains of the spinal cord of adults, in particular, are crucial for maintaining the organization of synaptic inputs of spinal motor neurons. Androgens provide neuroprotection of CNS neurons due to the lack of growth factors in apoptosis. Androgens can affect the turnover of a cytoskeleton matrix responsible for the structure of the axon. Testosterone has a neuroprotective effect in nerve fibers and the testosterone deficiency can lead to various forms of degeneration of the nerves, which may ultimately result in even anatomical changes. Neuroprotective effects are manifested at the physiological concentration of the hormone and due to the interaction with the receptors of androgens. Some data suggest that neuroprotection of androgens may be mediated by the mitigation of oxidative stress. Thus, directly through membrane or nuclear receptors, or indirectly by metabolic effects, androgens affect all the links in the somatic reflex arc. However, very few studies show the peculiarities of their functioning, in vivo, and electrophysiological studies have almost not been conducted, which provides the basis for further searches for answers to questions about the influence of male sex hormones on the nervous system.

Key words: testosterone, androgens, receptors, nervous system, neuron, axon.

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MULTIPLE SCLEROSIS: SOME ASPECTS ON PATHOGENESIS AND MORPHOLOGY

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Multiple sclerosis (MS) is a chronic, progressive demyelinating disease of the central nervous system.

It affects mostly young people of working age with the peak incidence at the age of 20-40 years. MS is more often observed in women and manifests 1-2 years earlier than in men [1]. The publications report that the incidence of MS is progressively growing from year to year, especially in economically developed countries. The prevalence of this disease depends on the geographic latitude, designating three zones of morbidity risk: high risk zone (more than 50 cases per 100 000 people), moderate risk zone (10-50 cases per 100 000 people) and low risk zone (less than 10 cases per 100 000 people). Notably, Ukraine is located on the border of the high and moderate risk zones, and the morbidity rate in Ukraine is rapidly growing. Progression of MS leads to early disability and death [2,3,4]. All these facts confirm the relevance of the problem and necessity for its comprehensive study.

Currently, the etiology of multiple sclerosis is unknown and considered as the multifactorial disease. Genetic and immunological factors, viral infection and influence of exogenous factors play the crucial role.

Genetic susceptibility to multiple sclerosis is confirmed by numerous findings of genealogical, twin and population studies. This provision is proved by the fact that the risk for MS development in monozygotic twins is 7 times higher than in dizygotic ones [2]. However, the index of MS concordance in monozygotic twins is accounted for only 25-30% that does not fit the framework of the monogenic model of inheritance and can be explained by the polygenic inheritance and genetic polymorphism, as well as the influence of external factors. This is also confirmed by the study of the MS morbidity in migrants, the rate of which is dependent on the variety of medical and social factors, though its growth in migration from region with low risk to region of the high risk is self-evident [5].

It has been established that intoxication and diet are considered the most possible external factors. Recently, the impact of insolation and associated vitamin D deficiency [6,7], as the main factor of geographical dissemination, smoking [7,8] and ecological characteristics of the habitat of patients [4,9,10] have been the issue for discussion.

Viral hypothesis for the development of multiple sclerosis appears to be of main importance, since high IgG concentration to many viruses has been found in the cerebrospinal fluid and blood of more than 90% of patients with MS. Indirect evidence that MS is caused by viruses is the relation of several viruses with demyelinating encephalopathy in people and induced demyelination in experimental animals infected with viruses. However, none of the viruses were isolated from the brain of patients with multiple sclerosis [11].

Notwithstanding the important or even critical role of various microorganisms, only Epstein-Barr virus stands out as a consistent and strong risk factor among the infectious agents that can be related to MS. The comparison of the risk for MS in infected and uninfected people has shown that the possible onset of multiple sclerosis is 10 times higher in young people with HIV infection, whereas it is 20 times higher in people with mononucleosis in the past history. The presence of antigenic mimicry between the main myelin protein and Epstein-Barr virus pan-peptide has been found [12,13]. The role of other pathogens, namely, Human herpes virus 6 [14], Chlamydia pneumoniae [15], chicken pox, rubella, measles and others can be also considered [16,17]. In addition, some researchers believe the presence of inflammatory infiltrates in the brain plaques and tissue to be a strong evidence of the infectious nature of multiple sclerosis [18].

Currently, no etiological theory and unambiguous consensus on the pathogenesis of lesions in multiple sclerosis exists. Apparently, no single view on the mechanism of the onset and development of this disease is given.

Immunologists consider multiple sclerosis as an autoimmune disease when the specific T-lymphocytes that are myelin antigens activate the inflammatory response in the central nervous system, which eventually leads to demyelination and subsequent damage to the axons. Such a view on the pathogenesis of multiple sclerosis comes up from the analysis of the animal model of experimental autoimmune encephalomyelitis [19]. Unfortunately, this oversimplified view reproduces the incomplete picture of the pathogenesis of multiple sclerosis, urging the experts to conduct further searches in different directions.

Currently, the studies of the role of genetic disorders are at the forefront in the development of multiple sclerosis. This is substantiated by more frequent detection of A3, B7, DW2, DR2 antigens in patients with MS as compared with healthy people. It is hypothesized that the occurrence of certain combination of tissue histocompatibility antigents in single chromosome and gene of susceptibility to MS is crucial in the onset of the disease [20].

Consequently, the interaction of environmental factors and genetically determined susceptibility results in the initiation of immunopathological processes that are the triggering mechanism of pathogenesis of multiple sclerosis.

Currently, the pathogenesis of MS is seen as a phased process, involving the initial inflammatory phase, which is accompanied by demyelination, and the neurodegenerative phase [21,22].

T-cells with various functional differentiation and corresponding regulatory interactions are crucial in the development of immunopathological reactions. Activation of inactive CD4 + T-cells occurs at the initial stage in the interaction of autoantigen, bound with II class molecules of the major histocompatibility complex on the antigen-presenting cells with the appropriate receptor. Subsequently, proliferation and differentiation of T-lymphocytes into effector T-helper (Th) of two types, namely, pro-inflammatory Th1 and anti-inflammatory Th2, occurs, depending on the exposure to the antigen, cytokine profile of the adjacent tissues and co-stimulation [23]. The secretion of pro-inflammatory cytokines promotes activation of B-lymphocytes, monocytes and other T-cells, which enhances the immune response [24].

Activated CD4 + T-cells, involving chemokines, adhesion molecules and proteases, penetrate through the blood-brain barrier. In the central nervous system the macrophages and microglia ensure reactivation of the T-cells, which secrete proinflammatory cytokines (interferon-γ, tumor necrosis factor-α (TNF-α), lymphotoxin, etc.), potentiating the inflammatory response and enhancing the violation of permeability of blood-brain barrier [25].

Furthermore, hormonal factor plays an important role in the development and progression of immunopathological processes in MS, which can also explain a clear gender dimorphism of this disease. The debut of multiple sclerosis in women occurs at the age of 20 years, when the level of estradiol stabilizes, and in men the peak incidence is observed at the age of 25-30 years, which coincides with the period of maximal secretion of testosterone with its gradual decrease with age [26,27]. It has been found that lowering of the level of estrogen and testosterone is associated with increased activity of pro-inflammatory cytokines. It is confirmed by hyperproduction of interleukins (IL), IL1, IL6, IL8 and TNF-α and supported by IL2. The recovery of the level of steroid hormones leads to activation of anti-inflammatory cytokines. Noteworthy, the estriol suppresses the activity of IL2 and TNF-α, in men it increases the level of anti-inflammatory cytokine IL5, which is not observed in women. Androgens also trigger immunological cascade in response to the load by the main myelin protein, reducing the production of IL2 and TNF-α [28]. Consequently, gonadal hormones have a clear immunomodulatory action and are crucial in the pathogenesis of multiple sclerosis.

The specific pathomorphological changes in multiple sclerosis are caused by activation of immunological reactions, including macrophages, B-lymphocytes with production of antibodies, which leads to the myelin sheath damage. In the development of demyelination, antibodies activate the cascade of complement system with subsequent destruction of myelin and induction of macrophage reaction, inducing phagocytosis of damaged myelin areas [29]. Immunoinflammatory alterations and demyelination of the nerve fibers is accompanied by damage to the axons already at the early stages of the disease. The death of axons is considered a key link in the development of neurological symptoms and transformation of the remitting course into the secondary progressive one with the steady rise of the rate of invalidization [30].

Immunopathological reaction in MS leads not only to the destruction of myelin, but also to the development of vascular inflammatory and proliferative processes of the derivatives of mesenchyme and glia with subsequent formation of the multiple sclerosis plaques.

Macroscopically, no specific changes are revealed during the external examination of the brain and spinal cord in multiple sclerosis, though, sometimes, the edema and thickening of pia mater is noted. The mass of the brain can be reduced. Convolutions of brain are narrowed; sulci between them are broad and deep, indicating about growing atrophic processes. Ependyma is usually smooth, shiny, in some cases is tuberous, due to the subependimal gliosis [31].

In section, the brain and spinal cord is characterized by the presence of foci, heterogeneous in size and form that differ from normal tissue by color and texture. Fresh foci have a soft pink texture. Inactive, “old” plaque is gray with a pinkish or yellowish tinge has clear contours and dense on palpation. The dimensions of the plaques range from a few millimeters to a few centimeters; large conglomerates can be formed with the progression of the disease. Generally, plaques are located in the white matter and can rarely spread on the gray matter (cortex and subcortical nuclei). In the spinal cord and medulla oblongata the plaques are localized on the periphery and are wedge-shaped. In the cerebellum the plaques are located in the white matter near the dentate nuclei. Therefore, localization of the plaques is variable, but most often they are found paraventricularly in the sub-

ependymal portions, surrounding the lateral ventricles, in the thalami [32]. The life-time development of epileptiform or demented syndromes can be explained by the localization of the plaques in the area of the cortex of cerebrum. The following clinicomorphological forms of the disease can be distinguished, depending on the localization of the plaques in the CNS: spinal, cerebral, cerebrospinal, cerebellar, stem and optical [2].

Histologically, three types of the plaques are distinguished depending on the stage of morphogenesis: the acute plaques (active foci of demyelination), chronic (inactive foci) and chronic foci with signs of activation [31,32,33,34].

The acute active plaques are formed as a result of the acute perivascular inflammation and manifested by the destruction of myelin and brain tissue edema. Weigert stained micro-specimens of the brain have shown multiple foci of demyelination. First, the myelin sheaths swell and change their tinctorial properties; their contours are crenated and thickening along the fibers are marked. Subsequently, fragmentation and disintegration of the myelin sheaths occurs. The products of myelin disintegration are absorbed by the microglia cells, transforming into granular globules; the macrophages with foamy cytoplasm are also detected. The products of myelin degradation in the cytoplasm of the macrophages are the markers of acute demyelination. The zone of infiltration by lymphocytes and plasmacytes appears on the plaque's periphery. Such infiltrates can be found in the centre of the plaque if the blood vessel runs along its center. Usually, T-lymphocytes-suppressors and T-lymphocytes-helpers dominate around the blood vessels and on the periphery of demyelination areas, respectively. Astrocytes with thickened processes are found in the perifocal zone and scarce oligodendrocytes are found in the demyelination area.

Various interpretations of the mechanism of myelin destruction in the foci of multiple sclerosis have been proposed. Some researchers believe that the monocytes only absorb fragments of the myelin sheath, which was already disintegrated under the influence of other factors. The other ones argue that monocytes are directly involved in destruction of myelin. Clathrin-coated depressions, adjacent to the myelin sheath are found in the membrane of macrophages. Hypothetically, it in this area that Fc-dependent interaction between the antibody and the receptor occurs that leads to opsonization of the myelin by the monocytes. It has been also shown that macrophages penetrate directly into the myelin sheath, causing the formation of vesicles inside the myelin.

Chronic inactive plaque has clear borders and characterized by the increased amount of astrocytes, absence of active destruction of the myelin, decreased amount of oligodendrocytes and axonal degeneration. Lymphoplasmacytic infiltrates disappear and signs of perivascular sclerosis appear. In some cases, in the area of the plaque the processes of remyelination can be developed, resulted in the recovery of conductivity of some axons. The source of oligodendrocytes, which are responsible for remyelination, can be the mature cells that survived in the focus of lesion, or cells that migrated from the adjacent area, or young oligodendrocytes formed from the cells-predecessors. It is hypothesized that the degree of destruction of mature oligodendrocytes determines the potential of remyelination in the focus. Compared with normal axons, remyelinized axons have thinner myelin sheath with truncated myelin segments and dilated nodes of Ranvier.

Chronic active plaques appear on the stage of acute exacerbation of the disease and are characterized by the occurrence of circumferential chronic inactive plaque of the macrophages due to progressive disintegration of the myelin, as well as T-lymphocytes and reactive astrocytes. The first signs of damage to axons occur in these plaques in the form of swelling and fragmentation of the axial cylinders.

Apparently, the axonal changes only partially correlated with the processes of demyelination. Their close relationships with the prominence of the inflammatory process are markedly expressed [35]. Morphological study of foci of demyelination indicates about heterogeneous changes in MS, enabling to distinguish the main groups of pathological changes: T-cells, macrophage- and antibody-mediated demyelination; distal oligodendrogliopathy and apoptosis of oligodendrocytes, which mechanisms are unknown [29]. Notably, single mechanism of demyelination is specific for single patient. It is assumed that only one pathogenetic mechanism exists that is based on genetic determinant [36].

Demyelination is found not only in multiple sclerosis, but also in other pathological conditions and diseases that must be considered for differentiated microscopic diagnosis of lesions of the central nervous system. Myelin-oligodendrocytic complex is sensitive to the action of multiple factors, namely, metabolic, infectious, inflammatory and ischemic. Consequently, demyelination is possible in multiple diseases. A common feature of demyelinating diseases is the destruction of the myelin sheath in relative preservation of axons and other supporting elements.

Three types of demyelination can be distinguished according to the origin and mechanism of development [37].

The first type of demyelination is characterized by the primary damage to oligodendrocytes, known as myelin-forming cells, which are sensitive to hypoxia, toxins, viruses (the inclusion of the virus genome in the cell genome with impaired myelin formation). Possibly, the primary damage to oligodendrocytes is caused by the metabolic processes disorder that occurs in affection of the endocrine glands, liver, gastrointestinal tract.

The second type of demyelination is characterized by disintegration of the myelin with preservation of oligodendrocytes. It occurs in sensitization and development of immediate hypersensitivity reactions to the myelin and products of its disintegration. Autoimmune process, which is specific not only for multiple sclerosis, but also for the vaccine, serum, parainfectious, paraneoplastic processes in the nervous system, is developed. Such mechanism of demyelination is specific for experimental allergic encephalomyelitis and polyneuritis.

The third kind of demyelination is characterized by the destruction of the myelin with the simultaneous death of oligodendrocytes, marked by the intensity and rate of the development of pathological process: hyperimmune reaction with release of the pro-inflammatory cytokines (TNF-α, interferon), the development of acidosis, accumulation of toxic factors.

Consequently, the main diagnostic criterion of MS is not only the existence of foci of demyelination, but also the formation of the fibrous-cellular gliosis at the certain stages. Gliosis is one of the specific morphological manifestations of MS, which is characterized by the decreased amount of oligodendrocytes in the plaques in the increased percentage of composition of astrocytes, whereas their absolute amount is decreasing [31]. Some authors consider the definition of "gliosis" to be incorrect which is characterized by the reduction of the amount of glia cells and the increase in the number of glial fibers in the form of the fibrous isomorphic matrix [38, 39].

In conclusion, edema, inflammation, re- and demyelination, gliosis, damage to axons is observed in the development of multiple sclerosis. Demyelination and death of axons lead to atrophy of the brain and spinal cord. Morphologically, the nature and progress of the pathological process, developed in multiple sclerosis, is heterogeneous. It is known that autoimmune responses in MS, manifested by the foci of demyelination, are involved in the pathogenesis of other diseases of the nervous system (inflammatory, vascular, etc.). In addition, the cause of the myelin disintegration can be a chronic hypoxia and metabolic disorders. They are crucial in the differentiated diagnosis of the disease. Multifactorial nature of multiple sclerosis to a certain extent reflects heterogeneity of the demyelinating process.

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ДЕЯКІ АСПЕКТИ ПАТОГЕНЕЗУ ТА МОРФОЛОГІЇ РОЗСІЯНОГО СКЛЕРОЗУ

Филенко Б. М., Ройко Н. В., Проскурня С. А., Совгиря С. М., Винник Н. І.

Резюме. Сучасна імунологія розглядає розсіяний склероз як аутоімунне захворювання.

Макроскопічно під час зовнішнього огляду головного та спинного мозку при розсіяному склерозі характерних змін не відмічають, інколи виявляють набряк і потовщення м'яких мозкових оболонок. Гістологічно, в залежності від стадії морфогенезу, розрізняють три типи бляшок: гострі бляшки (активні осередки демієлінізації), хронічні (неактивні осередки) і хронічні вогнища з ознаками активізації. Гострі активні бляшки формуються внаслідок гострого периваскулярного запалення і проявляються руйнуванням мієліну, набряком тканини мозку. Хронічна неактивна бляшка чітко окреслена, характеризується збільшенням кількості астроцитів, відсутністю активної деструкції мієліну, зменшенням кількості олігодендроцитів, аксональною дегенерацією. З'являються ознаки периваскулярного склерозу. Хронічні активні бляшки характеризуються появою по периферії хронічної неактивної бляшки макрофагів, внаслідок прогресуючого розпаду мієліну, а також Т-лімфоцитів і реактивних астроцитів.

Таким чином, при розвитку розсіяного склерозу спостерігаються такі процеси, як набряк, запалення, де- і ремієлінізація, гліоз, ураження аксонів. Демієлінізація і загибель аксонів призводять до атрофії головного і спинного мозку.

Ключові слова: розсіяний склероз, патогенез, морфологія.

НЕКОТОРЫЕ АСПЕКТЫ ПАТОГЕНЕЗА И МОРФОЛОГИИ РАССЕЯННОГО СКЛЕРОЗА

Филенко Б. Н., Ройко Н. В., Проскурня С. А., Совгиря С. Н., Винник Н. И.

Резюме. Современная иммунология рассматривает рассеянный склероз как аутоиммунное заболевание.

Макроскопически при внешнем осмотре головного и спинного мозга при рассеянном склерозе характерных изменений не отмечают, иногда обнаруживают отек и утолщение мягких мозговых оболочек. Гистологически, в зависимости от стадии морфогенеза, различают три типа бляшек: острые бляшки (активные очаги демиелинизации), хронические (неактивные очаги) и хронические очаги с признаками активизации. Острые активные бляшки формируются вследствие острого периваскулярного воспаления и проявляются разрушением миелина, отеком ткани мозга. Хроническая неактивная бляшка четко очерчена, характеризуется увеличением количества астроцитов, отсутствием активной деструкции миелина, уменьшением количества олигодендроцитов, аксональной дегенерацией. Появляются признаки периваскулярного склероза. Хронические активные бляшки характеризуются появлением по периферии хронической неактивной бляшки макрофагов, вследствие прогрессирующего распада миелина, а также Т-лимфоцитов и реактивных астроцитов.

Таким образом, при развитии рассеянного склероза наблюдаются такие процессы, как отек, воспаление, де- и ремиелинизация, глиоз, поражение аксонов. Демиелинизация и гибель аксонов приводят к атрофии головного и спинного мозга.

Ключевые слова: рассеянный склероз, патогенез, морфология.

MULTIPLE SCLEROSIS: SOME ASPECTS ON PATHOGENESIS AND MORPHOLOGY

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Abstract. Multiple sclerosis (MS) is a chronic, progressive demyelinating disease of the central nervous system.

Currently, the etiology of multiple sclerosis is unknown and considered as the multifactorial disease. Genetic and immunological factors, viral infection and influence of exogenous factors play the crucial role.

Genetic susceptibility to multiple sclerosis is confirmed by numerous findings of genealogical, twin and population studies. It has been established that intoxication and diet are considered the most possible external factors. Recently, the impact of insolation and associated vitamin D deficiency, as the main factor of geographical dissemination, smoking and ecological characteristics of the habitat of patients have been the issue for discussion.

Viral hypothesis for the development of multiple sclerosis appears to be of main importance, since high IgG concentration to many viruses has been found in the cerebrospinal fluid and blood of more than 90% of patients with MS.

Currently, no etiological theory and unambiguous consensus on the pathogenesis of lesions in multiple sclerosis exists. Apparently, no single view on the mechanism of the onset and development of this disease is given.

Immunologists consider multiple sclerosis as an autoimmune disease when the specific T-lymphocytes that are myelin antigens activate the inflammatory response in the central nervous system, which eventually leads to demyelination and subsequent damage to the axons.

Currently, the studies of the role of genetic disorders are at the forefront in the development of multiple sclerosis. This is substantiated by more frequent detection of A3, B7, DW2, DR2 antigens in patients with MS as compared with healthy people. It is hypothesized that the occurrence of certain combination of tissue histocompatibility antigents in single chromosome and gene of susceptibility to MS is crucial in the onset of the disease.

Currently, the pathogenesis of MS is seen as a phased process, involving the initial inflammatory phase, which is accompanied by demyelination, and the neurodegenerative phase.

The specific pathomorphological changes in multiple sclerosis are caused by activation of immunological reactions, including macrophages, B-lymphocytes with production of antibodies, which leads to the myelin sheath damage. Immunopathological reaction in MS leads not only to the destruction of myelin, but also to the development of vascular inflammatory and proliferative processes of the derivatives of mesenchyme and glia with subsequent formation of the multiple sclerosis plaques.

Macroscopically, no specific changes are revealed during the external examination of the brain and spinal cord in multiple sclerosis, though, sometimes, the edema and thickening of pia mater is noted. The mass of the brain can be reduced. Convolutions of brain are narrowed; sulci between them are broad and deep, indicating about growing atrophic processes. Ependyma is usually smooth, shiny, in some cases is tuberous, due to the subependimal gliosis.

Histologically, three types of the plaques are distinguished depending on the stage of morphogenesis: the acute plaques (active foci of demyelination), chronic (inactive foci) and chronic foci with signs of activation.

Edema, inflammation, re- and demyelination, gliosis, damage to axons is observed in the development of multiple sclerosis. Demyelination and death of axons lead to atrophy of the brain and spinal cord. Morphologically, the nature and progress of the pathological process, developed in multiple sclerosis, is heterogeneous. It is known that autoimmune responses in MS, manifested by the foci of demyelination, are involved in the pathogenesis of other diseases of the nervous system (inflammatory, vascular, etc.). In addition, the cause of the myelin disintegration can be a chronic hypoxia and metabolic disorders. They are crucial in the differentiated diagnosis of the disease. Multifactorial nature of multiple sclerosis to a certain extent reflects heterogeneity of the demyelinating process.

Key words: multiple sclerosis, pathogenesis, morphology.

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МЕДИКАМЕНТОЗНЕ ЛІКУВАННЯ РАКА ШЛУНКА

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Зв'язок публікації з плановими науково-дослідними роботами. Дана робота є фрагментом НДР «Дослідження ролі поліморфізму генів Toll-подібного рецептора 2(Arg753Gin) в прогнозуванні рецидивів та метастазів злоякісних новоутворень», № державної реєстрації 0114U004770.

Вступ. Рак шлунка (РШ) залишається одним з найпоширеніших онкологічних захворювань і займає четверте місце по частоті в структурі онкозахворюваності, а як причина смерті онкологічних хворих, знаходиться на другому місці і на його частку припадає понад 10% смертей. Щорічно в світі реєструється більше 750 тисяч випадків захворювання і близько 620 000 випадків смерті від РШ. Україна за рівнем захворюваності займає 8-9 місце в десятці країн з найбільш високою захворюваністю РШ – 24, 7 (чоловіки 42, 1, жінки – 16, 2), щорічно вперше діагностується близько 14 000 хворих, переважно в III-VI стадіях, тому однорічна летальність досягає 63% [1].

В США з числа хворих з локальною формою раку шлунка, виявленої при первинній діагностиці, у 45% протягом 5 років розвиваються метастази. Регіонарна форма у 85% пацієнтів прогресує і переходить в метастатичну фазу хвороби. У Великобританії серед пацієнтів з резектабельною пухлиною, які отримали доопераційну хіміотерапію, 5-річна виживаність становить 36%. Однак при поширених або метастатичних формах порога 5-річної виживаності досягають тільки 5-20% хворих. З числа щорічно діагностованих хворих в 85% випадків відразу або протягом 2-3 років хвороба переходить в метастатичний етап. При цьому необхідно зазначити, що медіана виживаності хворих на метастатичний рак шлунка, яких лікували симптоматично, обчислюється терміном на 3-4 місяці [2].

Хірургічне лікування є основним методом при раку шлунка. В даний час у світовій практиці накопичений величезний клінічний матеріал щодо застосування різних варіантів втручання при злоякісних пухлинах шлунка: розширені і супер розширені операції, а також розширені і супер розширені лімфодіссекції (ЛД) (D2, D3, D4) [2,3]. Аналіз результатів показав, що виконання подібних операцій дозволило поліпшити віддалені результати лікування практично при всіх стадіях захворювання [3]. З іншого боку, виникають сумніви в доцільності подальшого нарощування хірургічної агресивності при вирішенні цієї проблеми [4]. Хірургічний метод лікування практично досяг межі своїх можливостей, що відбивається на стабілізації показників виживання прооперованих пацієнтів протягом останнього десятиліття [3,4].

Агресивний перебіг раку шлунка, рання дисемінація вимагають розробки додаткових системних методів лікування, в першу чергу – ад'ювантної хіміотерапії (АХТ). На момент встановлення діагнозу, близько 46% хворих, вже мають III стадію захворювання, тобто відносяться до категорії пацієнтів підлягають в тому числі і медикаментозній терапії. Ад'ювантна хіміотерапія націлена на мікрометастази РШ, що залишилися після хірургічного видалення первинної пухлини. На даний момент не існує стандартів АХТ при РШ, так як результати міжнародних досліджень суперечливі [5,6]. Так, в Японії в ад'ювантному режимі позитивно зарекомендували себе похідні фторпіримідинів препарат S1, UFT [7]. Але ці результати виявилося неможливим екстраполювати на європейські країни і Америку. У ряді європейських і американських досліджень АХТ при РШ не привела до поліпшення виживаності, як безрецидивної [8], так і загальної [8,9,10,11,12,13]. Також немає