Modern Pulse Corticosteroid Therapy in Patients with Multiple Sclerosis: Adverse Events and Clinical and Pharmacological Measures to Eliminate Them

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Abstract. Pulse therapy with methylprednisolone remains the standard treatment for exacerbations of multiple sclerosis. The appointment of corticosteroids can cause several undesirable phenomena and complications, one of which is the development of steroid myopathy and pronounced general weakness. To reduce the expressiveness of these violations, metacartin was used. The study included 57 patients with a reliable diagnosis of multiple sclerosis at the stage of exacerbation of the pathological process. There were 32 (56.14%) patients with the relapsing-remitting course of multiple sclerosis, and 25 (43.85%) with the secondary-progressive course. All patients were randomly divided into two groups: I – 33 (80.83%) patients who underwent a course of pulse therapy with methylprednisolone followed by the introduction of metacartin, and II – 24 (19.17%) patients who received only pulse therapy with methylprednisolone therapy. Group I included 23 patients with relapsing-remitting course and 10 patients with secondary-progressive course multiple sclerosis. 15 patients with relapsing-remitting course and 9 patients with secondary-progressive course multiple sclerosis was included in the II group. The study showed the effectiveness of combination of pulse-therapy with methylprednisolone and the metacartin, the prescription of which reliably reduced the severity of "muscular" symptoms when pulse therapy was prescribed.

Keywords: multiple sclerosis, pulse therapy, corticosteroids, methylprednisolone, metacartin, steroid myopathy, side effects.

Introduction. Despite significant progress in the clinical evaluation of multiple sclerosis, thanks to the widespread availability of magnetic resonance imaging of the brain and spine, our

understanding of the underlying etiology of the disease remains limited. Complete control of the disease and repair of damaged myelin are key challenges for current and future researchers [1, 2].

There are no specific tests for multiple sclerosis; the doctor makes the diagnosis based on a combination of medical history, physical examination, magnetic resonance imaging, and spinal tap results. The diagnosis of multiple sclerosis also involves ruling out other diseases that can cause similar symptoms. This is known as differential diagnosis (Fig. 1) [3].

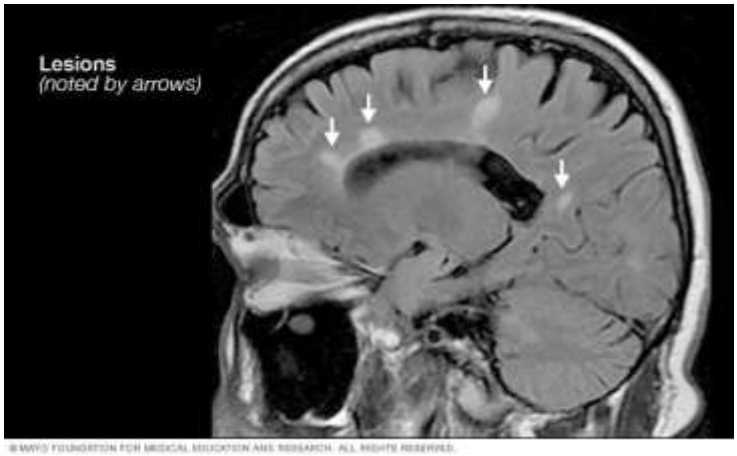

Fig. 1. Magnetic Resonance Imaging of the brain: white matter lesions associated with multiple sclerosis [3].

The strategic goal of treating multiple sclerosis is to slow down the progression of the patient's disability, reduce the severity of the disease, and provide the patient with a relatively healthy and long-term lifestyle. The main directions of pathogenetic pharmacotherapy of the multiple sclerosis are [4-10]:

- treatment of exacerbations and periods of a sharp increase in disease activity;
- prevention of exacerbations and progression of disability.

The main components of the therapeutic strategy of multiple sclerosis are exacerbation therapy and disease-modifying pharmacotherapy [11]. The direction of disease-modifying therapy of multiple sclerosis is developing very actively at present. Not so long ago, doctors had in their arsenal only medicines of the interferon group and glatiramer acetate. The modern arsenal includes many medicines of the monoclonal antibody group, highly active chemotherapeutic agents, Bruton's tyrosine kinase inhibitors, other clinical and pharmacological, classification and legal, nomenclature and legal groups [12-18].

The purpose of the study was to conduct an identification of undesirable phenomena and application of clinical-pharmacological measures to eliminate them during the use of modern pulse therapy of corticosteroids in patients with multiple sclerosis to improve their health status and life expectancy.

Material and methods. Based on the department of autoimmune and degenerative diseases of the nervous system, Center of Multiple Sclerosis, P.V. Voloshyn Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine studied 57 patients with multiple sclerosis were examined and treated.

The research of the article is a fragment of research works of P.V. Voloshyn Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine on the topic of "To study mechanisms of inheritance of multiple sclerosis in persons born from parents with this disease (state registration number 0121U111900, implementation period 2022-2024).

Results and discussion. Specialists of the P.V. Voloshyn Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine in 2024 prepared “Clinical guideline based on evidence – Multiple sclerosis in adults and children” for clinical practice and improving the level of the system of legal relations “doctor-patient-pharmacist” [19]. This is a continuation of the work begun by professor Voloshyn P.V. The publication of the action algorithm

“Clinical recommendations for providing medical care to patients with neurological, mental and behavioral disorders” is intended for a wide range specialists: general practitioners – family doctors, neurologists, neuropathologists, psychiatrists, narcologists, researchers, teachers of medical institutions of higher education and institutions of postgraduate education of doctors [20, 21].

At the same time, clinicians are actively investigating the possibilities of cell therapy for multiple sclerosis [22-24].

The tactics of treating patients during exacerbations of multiple sclerosis have not undergone significant changes. However, doctors have conducted quite a few clinical studies during treatment on the effectiveness and safety of the use of corticosteroids (prednisolone, adrenocorticotropic hormone, triamcinolone, methylprednisolone) and various routes of their administration. It turned out that the most optimal in terms of the ratio of effectiveness and safety is the intravenous route of methylprednisolone administration in the form of pulse therapy [6, 25].

It is important that back in 1976 Cathcart E.S., Idelson B.A., Scheinberg M.A., Couser W.G. reported the positive effect of infusions of ultra-high doses of methylprednisolone in patients with lupus glomerulonephritis and rapid deterioration of kidney function [26].

Since then, the concept of pulse pharmacotherapy has begun to take shape. Pulse pharmacotherapy involves intermittent administration of medicines to enhance the therapeutic effect and reduce the risk of side effects. Plasmapheresis is also used in therapy. Immunoglobulins are prescribed more often in combination with pulse therapy with corticosteroids [11]. Therefore, the standard treatment for exacerbation of multiple sclerosis is the appointment of pulse therapy with methylprednisolone at a dose of 1000-2000 mg from 3 to 7-10 consecutive days.

In clinical conditions, methylprednisolone has a variety of effects on the patient's immune system [27, 28]:

- slows down the activation and proliferation of T-lymphocytes;
- affects their apoptosis both in the peripheral blood and in the brain parenchyma;
- reduces the formation of antibodies, but its most important effect in multiple sclerosis is the reduction of the permeability of the blood-brain barrier.

This effect on the immune system is achieved by influencing adhesion molecules and reducing the level of matrix metalloproteinases [29].

As is known, disruption of the blood-brain barrier in connection with inflammatory changes in the central nervous system is one of the first stages of the formation of new foci of demyelination. Relative stabilization of the blood-brain barrier persists for several weeks after pharmacotherapy of corticosteroids [28, 30].

Some authors consider it advisable to prescribe a course of oral prednisolone or methylprednisolone after pulse therapy according to the pharmaceutical correction scheme [31-34].

Corticosteroids have a complex and multifaceted effect on the functions of the body. They affect carbohydrate, protein, fat, water-electrolyte metabolism, play an important role in the regulation of the activity of the cardiovascular system, kidneys, skeletal muscles, nervous system and other organs and tissues [6, 11, 32, 35, 36].

When prescribing corticosteroids in any regimen, side effects may develop from various organs and systems, which is observed in more than 50% of patients [37, 38]. Many side effects after corticosteroids are dose-dependent. They often develop with prolonged use of low or medium doses, but nevertheless, they often develop in patients with multiple sclerosis when using high doses in short courses according to the pulse therapy regimen [6, 37, 38]. Special attention when using pulse therapy is required for patients with comorbid pathology.

Side effects can be divided into two groups:

- Group 1 – development directly when taking corticosteroids;
- Group 2 – undesirable effects when canceling corticosteroids, especially with their prolonged use – the so-called "withdrawal syndrome".

Group 1 includes the phenomena of exogenous hypercorticism (electrolyte disorders, fluid retention in the body, arterial hypertension, hyperglycemia and glycosuria, increased susceptibility to infections, gastritis, exacerbation of peptic ulcer disease, osteoporosis, myopathy, mental

disorders, cataracts, glaucoma, growth retardation in children, development of Cushingoid syndrome with redistribution of adipose tissue, striae, ecchymoses, acne and hirsutism). The spectrum of symptoms of exogenous hypercorticism differs little from endogenous Itsenko-Cushing's syndrome [39].

However, in endogenous Itsenko-Cushing's syndrome, benign increased intracranial pressure, glaucoma, posterior subcapsular cataracts, pancreatitis, and aseptic bone necrosis, which are characteristic of long-term use of large doses of corticosteroids, are practically absent. At the same time, in Itsenko-Cushing's syndrome, arterial hypertension, acne, menstrual irregularities, hirsutism and virilization in women, impotence in men, striae and purpura are more common. Weight gain, mental disorders, edema, and impaired wound healing are characteristic of both forms of the syndromes. These differences are associated with the fact that in Itsenko-Cushing's syndrome, the synthesis of adrenocorticotropic hormone occurs. In iatrogenic hypercorticism, the synthesis of this hormone is suppressed (the secretion of androgens and mineralocorticoids does not increase) [20, 25, 35, 38].

For the initial stages of pharmacotherapy with corticosteroids, the development of insomnia, emotional lability, increased appetite, and weight gain is almost inevitable. In the presence of risk factors, comorbid pathology, arterial hypertension, hyperglycemia often occur, up to the development of type I or II diabetes [32, 37, 38, 40, 41].

Complications of gastric or duodenal ulcers in patients with a history of ulcers are very dangerous [42]. Expected when using high doses for a long time is the development of a "Cushingoid" appearance, suppression of the hypothalamic-pituitary-adrenal axis, susceptibility to infectious diseases, osteonecrosis, myopathy, poor wound healing [37, 38].

Adverse events that develop late and are probably due to dose accumulation: osteoporosis, cataracts, atherosclerosis, growth retardation in children, fatty hepatosis. Among the rare and unpredictable side effects are: psychosis, benign pseudotumor cerebri, glaucoma, epidural lipomatosis, pancreatitis.

Frequent side effects after pharmacotherapy of corticosteroids are leukocytosis, hypokalemia. These undesirable effects are transient in nature and, as a rule, do not pose a threat to the patient's health [32, 35, 37, 43-46].

The likelihood of developing side effects increases when prescribing long-acting corticosteroids (triamcinolone, betameson, dexamethasone) compared to drugs with a shorter half-life (prednisolone, methylprednisolone, hydrocortisone) [32, 35].

Most side effects are dose-dependent. Therefore, the appointment of medicines even with a short effect in large doses significantly increases the frequency of their development. The duration of pharmacotherapy, as well as the dose, is of decisive importance in the development of side effects [35].

The risk of side effects associated with long-term use of corticosteroids can be reduced by rational use of sparing dosing regimens and careful monitoring of expected side effects. The development of side effects often depends not only on the dose and duration of treatment, but also on the individual characteristics of the patient, his genetic and constitutional predisposition. Often side effects develop in patients who already have relevant diseases or are predisposed to their development [37, 38].

Hyperglycemia

Is associated with a decrease in tissue sensitivity to insulin and the action of corticosteroids. Although pharmacotherapy of corticosteroids can complicate glycemic control in patients with type I or II diabetes mellitus and provoke hyperglycemia in patients predisposed to this. The appearance of glucosuria does not prevent the continuation of corticosteroids. Just as the presence of diabetes mellitus is not a contraindication for conducting corticosteroids pharmacotherapy [40, 47].

Disturbances of water and electrolyte metabolism

Manifested by hypokalemia, hypocalcemia, sodium, and water retention. Fluid retention and hyperchloremic alkalosis are rarely observed in patients receiving synthetic corticosteroids. Even less often when taking corticosteroids with low mineralocorticoid activity [47].

Arterial hypertension

Can be observed in patients receiving corticosteroids for a long time and in high doses. The mechanism of hypertensive action of corticosteroids is not well understood. Arterial hypertension is probably due to the ability of corticosteroids to increase the expression of adrenergic receptors of the vascular wall [45, 47]. Significant hypertension is likely during pulse therapy. For its treatment, calcium antagonists, potassium-sparing diuretics, and angiotensin II receptor antagonists can be used [45, 46].

Ulcerogenic effect

Gastric or duodenal ulcer is an infrequent but very serious complication of corticosteroid therapy. The mechanism of the ulcerogenic effect of corticosteroids is associated with increased secretion of hydrochloric acid, decreased mucus synthesis and inhibition of epithelial regeneration.

Ulcer formation may manifest as epigastric pain and dyspepsia, but often occurs asymptomatically, manifesting as bleeding or perforation [37, 42].

Therefore, all patients receiving corticosteroids, regardless of the presence of a history of ulcer, should be prescribed gastroprotectors (H2-histamine receptor blockers, proton pump inhibitors, antacids, etc.).

Psychiatric disorders

Mild psychoemotional disorders (nervousness, anxiety, mild euphoria, mood swings, insomnia) are often observed from the very beginning of corticosteroid pharmacotherapy [43]. The development of severe psychoses of the manic-depressive or schizophrenic spectrum is rare. Suicidal tendencies are not excluded. It has been shown that a predisposition to mental disorders does not increase the risk of these AEs and vice versa, the absence of a history of mental disorders does not exclude the possibility of psychosis during corticosteroid pharmacotherapy [43, 44].

Infectious complications

The immunosuppressive effect of corticosteroids (suppression of neutrophil and monocyte activity, cellular immunological reactions, lymphopenia) leads to increased susceptibility to infectious diseases and the risk of reactivation of latent diseases such as chickenpox, herpes zoster, mycoses, tuberculosis. Patients with underlying immune disorders are more susceptible to infectious complications. As a rule, due to the anti-inflammatory effect of corticosteroids, infections are asymptomatic and tend to generalize. In the presence of an infectious process, corticosteroids pharmacotherapy can be carried out only in case of absolute necessity and with the parallel appointment of adequate antibacterial, antiviral, and antifungal pharmacotherapy [41, 48-51].

Among the undesirable phenomena there are also changes in the blood, osteoporosis, and aseptic bone necrosis, decreased synthesis of adrenal hormones and sex hormones, withdrawal syndrome. Careful monitoring of the patient receiving corticosteroids pharmacotherapy allows to avoid most side effects [32, 35].

General weakness and fatigue

General weakness, fatigue, and rapid fatigue are among the most common complaints in patients with multiple sclerosis and often do not depend on the inflammatory activity of the pathological process. Even in the absence of paresis, general fatigue and weakness can significantly affect the patient's motor function. It is not for nothing that the Expanded Disability Status Scale for multiple sclerosis included an assessment of general motor function, which supplemented the scale from the functional side. If during the examination the patient does not objectify paresis, but there are complaints about a reduction in walking distance, inability to perform the previous amount of work, etc., this certainly affects the score on the functions of the system scale.

Fatigue is a subjective symptom; it is quite difficult to objectify and measure it. Patients describe fatigue as “a feeling of inability to start or continue any voluntary movement”, “a feeling of increased fatigue that occurs when performing certain actions”, “lack of sufficient motivation when performing objective actions”. Fatigue is a phenomenon that consists of both a physical component (muscle fatigue when performing work) and certain mental processes (feelings, experiences).

In multiple sclerosis, a complex pathophysiological cascade of immune-mediated inflammatory processes occurs in the nervous system, due to which both morphological and immunobiological changes occur, which in turn lead to neurodegeneration. Damage to myelin leads to a slowdown in impulse transmission and more rapid energy depletion of the neuron. Damage to the gray matter, especially the motor cortex, affects the planning and reproduction of motor acts. Damage to neurons of the cingulate gyrus, insula, and amygdala interfere with the maintenance of antrib, excitatory motivation for action. Also, due to the presence of a chronic inflammatory process, several changes occur in the mediator and neurotransmitter system of the brain. All these changes prevent the development of neuroplastic processes in the patient's nervous system and, consequently, its adaptation to lesions [52].

The presence of chronic inflammation leads to a decrease in the level of dopamine, noradrenaline, and serotonin, which are very important in creating motivation, arousal to action and mood [44].

It should also be considered that patients receiving high doses of corticosteroids may develop myopathic syndrome. The mechanism of its development is associated with the negative effect of corticosteroids on protein and mineral metabolism. Quite often, after pulse therapy with corticosteroids, the patient develops general weakness, the severity of which increases precisely during corticosteroids [6, 32, 35].

This phenomenon often reduces the expected positive effect of pulse therapy. Myopathy develops soon after the start of therapy and can be quite severe, limiting the movement of patients. The process can even spread to the respiratory muscles (intercostal muscles, diaphragm), contributing to the development of respiratory failure. The development of severe myopathy is considered an indication for the cessation of corticosteroids pharmacotherapy. Recovery occurs slowly and may be incomplete. Medicines of potassium and anabolic steroids are used for treatment [53].

The question of the occurrence of myopathic syndrome and asthenia during pulse therapy in patients with multiple sclerosis arises.

The diagnosis was established according to the criteria of McDonald W. et al. [54, 55]:

- of 57 patients with multiple sclerosis, there were 22 men (38.59%), 35 women (61.40%);
- patients with relapsing-remitting course of multiple sclerosis were 32 (56.14%) people, with secondary-progressive course – 25 (43.85%) people;
- the average age of the patients was 38.96±10.15 years;
- average duration of the disease – 12.16±8.15 years;
- clinical and tomographic activity of the disease was observed in all patients.

All patients were shown pulse pharmacotherapy with corticosteroids (Fig. 2):

- neurological symptoms were dominated by lesions:
  - pyramidal system (98.71%);
  - cerebellar system (87.52%);
- lesions of other functional systems (FS) in patients were as follows:
  - trunk – in 61.64%;
  - pelvic organs – in 66.87%;
  - sensory – in 45.17%;
  - optical – in 36.03%:
- disorders from the cerebral system were represented mainly by symptoms of fatigue (does not affect the total disability score), which were noted in 74.35% of patients.

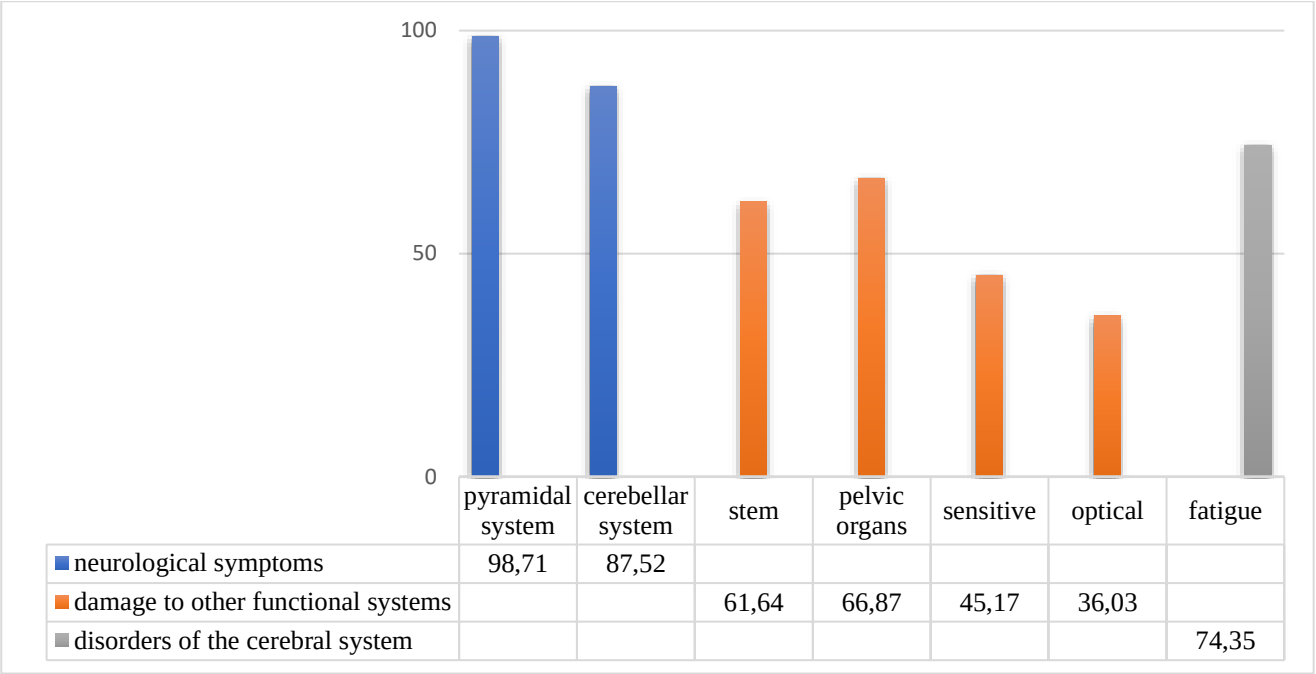

Fig. 2. Percentage of symptoms of the lesion during pulse therapy with corticosteroids.

The distribution of patients by gender and type of disease course is presented in Table 3.

Table 1. Distribution of patients by gender and type of disease course.

Gender	Type of course of multiple sclerosis	
	Relapsing-remitting course (n=32) %	Secondary-progressive course (n=25) %
Male	38,85	36,73
Female	59,15	63,27

All patients underwent pulse pharmacotherapy with methylprednisolone at a dosage of 1000 mg 5 to 7 times in a row according to the standard method.

To prevent "muscular" symptoms that often occur against the background of pulse therapy with corticosteroids, authors used L-carnitine (metacartin). Carnitine is a natural component of cells in which it plays:

- a fundamental role in the processes of synthesis and transport of energy;
- is the only indispensable factor for the process of penetration of long-chain fatty acids into mitochondria and their participation in β-oxidation;
- controls the transport of energy produced by mitochondria into the cytoplasm by modulating the enzyme adenine nucleotide translocase.

Considering the above data, we suggested the possibility of reducing the phenomena of asthenia and elements of myopathic syndrome in patients with multiple sclerosis by using levocarnitine (metacartin). Medicine levocarnitine (metacartin) was administered at 2000 mg per day, intravenously slowly for 10 days, the first 5 days, combining the introduction of pulse pharmacotherapy with methylprednisolone.

In accordance with the purpose of the study, all patients were randomly divided into two groups:

I – 33 (80.83%) patients who underwent a course of pulse therapy with methylprednisolone followed by the introduction of metacartin. Group I included 23 patients with relapsing-remitting course and 10 patients with secondary-progressive course of multiple sclerosis.

II – 24 (19.17%) patients who received only pulse therapy with methylprednisolone. Group II included 15 patients with relapsing-remitting course and 9 patients with secondary-progressive course of multiple sclerosis.

Patients of both groups I and II continued to receive a course of disease-modifying therapy.

Among patients of group I of multiple sclerosis, the average score on the Expanded Disability Status Scale was 3.55±0.53, after complex therapy 2.57±0.42 ($p<0.05$). The greatest positive dynamics was achieved by reducing the pyramidal system score – 3.78±0.47 before complex therapy, 3.16±0.38 ($p<0.05$) after the course of treatment. The cerebellar Functions of the System (3.16±0.39 before complex therapy and 2.46±0.26 after complex therapy ($p<0.03$)) was also sensitive to complex therapy.

It is noteworthy that the walking distance in patients of group I multiple sclerosis after complex therapy increased significantly to 3243.38±337.59 ($p<0.05$) and the need for assistance in moving decreased to 0.48±0.1 ($p<0.05$).

In patients of group II, there was also an improvement in the Functions of the System and Expanded Disability Status Scale [56] scales, mainly due to the pyramidal and cerebellar Functions of the System. Positive dynamics were also observed in the walking distance indicator. However, it should be noted that, unlike group I, there were no significant changes in the cerebral Functions of the System. On the contrary, we observed a slight increase in the score due to the general fatigue indicator.

Table 2. Expanded Disability Status Scale and Functions of the System indicators in patients of groups I and II with relapsing-remitting course of multiple sclerosis.

Functions of the System	**Study groups**			
	I group		**II group**	
	Before complex therapy (n=23)	After complex therapy (n=23)	Before complex therapy (n=15)	After complex therapy (n=15)
Optical	1,43±0,21	1,43±0,16	1,26±0,16	1,26±0,11
Brainstem	1,60±0,24	1,48±0,19	1,61±0,20	1,54±0,18
Pyramid	3,78±0,47	3,16±0,38*	3,62±0,43	3,34±0,36
Cerebellar	3,16±0,39	2,46±0,26*	3,04±0,36	2,76±0,32
Sensory	1,20±0,16	0,87±0,11	1,10±0,12	0,91±0,23
Pelvic organs	1,39±0,18	1,27±0,13	1,61±0,22	1,45±0,28
Cerebral	1,67±0,25	1,54±0,21	1,70±0,24	1,87±0,32
Walking distance (m)	2876,62±228,00	3243,38±337,59*	2769,57±351,31	2998,87±290,17
Need for assistance	0,72±0,12	0,48±0,1*	0,69±0,08	0,7±0,1
Expanded Disability Status Scale	3,55±0,53	2,57±0,42*	3,52±0,58	2,99±0,65

Notes:

* significant differences between assessments before and after therapy, $p<0.05$

- data given in the format: arithmetic mean ± standard deviation of the arithmetic mean (M±σ)

We observed a similar dynamic of indicators on the Functions of the System and Expanded Disability Status Scale scales in patients with secondary-progressive course. However, it should be noted that the response to pulse therapy in general in patients with secondary-progressive course of multiple sclerosis was much worse compared to the group of relapsing-remitting course of multiple sclerosis.

The most sensitive to complex therapy were also the “motor” Functions of the System – pyramidal (4.32±0.47 before therapy and 3.75±0.41 after, $p<0.05$) and cerebellar (3.75±0.41 before and 3.29±0.38 after).

It is impossible not to pay attention to the significant difference in cerebral Functions of the System in patients of group I according to the results of therapy (2.74±0.31 before complex therapy; 2.11±0.24 after the course of treatment, $p<0.05$).

If we compare the data of groups I and II of secondary-progressive course of multiple sclerosis with each other after complex therapy (2.11±0.24 in group I and 2.53±0.32 in group II). It is also possible to note better indicators in terms of walking distance and need for assistance according to the results of complex therapy in patients of group I.

Table 3. Indicators of Expanded Disability Status Scale and Functions of the System in patients of group I and II of secondary-progressive course of multiple sclerosis.

Functions of the System	Study groups			
	I group		II group	
	Before complex therapy (n=10)	After complex therapy (n=10)	Before complex therapy (n=9)	After complex therapy (n=9)
Optical	2,54±0,32	2,33±0,16	2,67±0,16	2,77±0,11
Brainstem	2,17±0,24	1,98±0,19	2,47±0,20	2,13±0,18
Pyramid	4,32±0,47	3,75±0,41*	4,46±0,43	4,18±0,36
Cerebellar	3,75±0,41	3,29±0,38	3,84±0,36	3,51±0,42
Sensory	2,13±0,16	2,06±0,11	2,11±0,12	2,09±0,23
Pelvic organs	2,29±0,18	2,11±0,13	2,25±0,22	2,15±0,28
Cerebral	2,74±0,31	2,11±0,24*	2,71±0,24	2,53±0,32
Walking distance (m)	1694,43±228,00	1909,73±276,59	1754,57±351,31	1795,87±290,17
Need for assistance	0,78±0,12	0,54±0,1	0,81±0,08	0,74±0,1
Expanded Disability Status Scale	5,23±0,53	4,81±0,51	5,11±0,58	4,99±0,65

Notes:
* significant differences between assessments before and after rehabilitation, $p<0.05$
- data presented in the format: arithmetic mean ± standard deviation of the arithmetic mean (M±σ)

According to the data obtained, under the influence of the complex therapy, positive dynamics in the Functions of the System and Expanded Disability Status Scale indicators were determined in patients with all types of multiple sclerosis. However, more pronounced dynamics were noted in patients with relapsing-remitting course of multiple sclerosis.

Thus, the maximum decrease in the indicators of the pyramidal and cerebellar systems was determined in the relapsing-remitting course of multiple sclerosis (0.62±0.12 and 0.70±0.1 points). In patients with secondary-progressive course of multiple sclerosis, these indicators had slightly lower dynamics (0.57±0.11 and 0.46±0.1 points).

The improvement of walking distance under the influence of complex therapy was determined in all types of multiple sclerosis. At the same time, the maximum improvement was demonstrated by patients with relapsing-remitting course of multiple sclerosis (-366.76±32.11 m), somewhat lower dynamics were detected in secondary-progressive course of multiple sclerosis (-215.3±29.3 m).

A similar trend was determined by the total score of the Expanded Disability Status Scale: the greatest dynamics, i.e. improvement of indicators, were detected in patients with relapsing-remitting course of multiple sclerosis (dynamics indicator – d Expanded Disability Status Scale = 0.98±0.16 points), less pronounced dynamics were observed in secondary-progressive course of multiple sclerosis (d Expanded Disability Status Scale =0.42±0.09 points).

The Expanded Disability Status Scale reflects the neurological status of the patient to a greater extent, while the assessment of the patient's functional conditions is very important. For this purpose, we used the Multiple Sclerosis Functional Composite test battery, which includes a 25-foot walk test (about 7.5 m) – 25 Functions of the System, a test for assessing hand coordination and motor skills – 9-peg test (9 HPT), and an audio test - Paced Auditory Serial Addition Test [57, 58].

Table 4. Multiple Sclerosis Functional Composite indicators in patients of groups I and II with relapsing-remitting course of multiple sclerosis.

Tests	Study groups			
	I group		II group	
	Before complex therapy (n=23)	After complex therapy (n=23)	Before complex therapy (n=15)	After complex therapy (n=15)

25 Functions of the System	6,21±0,72	4,63±0,56*	6,11±0,68	5,33±0,11
9 HPT	24,35±1,74	21,56±1,39*	23,87±1,62	22,91±1,48
Paced Auditory Serial Addition Test	37,51±4,56	41,87±3,71	35,69±4,8	37,75±4,35
* significant differences between assessments before and after rehabilitation, p<0.05 - data presented in the format: arithmetic mean ± standard deviation of the arithmetic mean (M±σ)				

When evaluating the data obtained in patients with relapsing-remitting course of multiple sclerosis, it is possible to note a significant improvement in motor functions in patients of group I according to the 25-foot walking test (6.21±0.21 before complex therapy and 4.63±0.16 after complex therapy) and the 9-peg test (24.35±0.24 – before complex therapy, 21.56±0.19 – after complex therapy). According to the audio test parameter Paced Auditory Serial Addition Test, an improvement in the indicators according to the results of treatment at the trend level was also found in patients of group I, probably due to a decrease in the level of asthenia.

Table 5. Multiple Sclerosis Functional Composite indicators in patients of group I and II with secondary-progressive course of multiple sclerosis.

Tests	**Study groups**			
	I group		**II group**	
	Before complex therapy (n=10)	After complex therapy (n=10)	Before complex therapy (n=9)	After complex therapy (n=9)
25 Functions of the System	7,34±0,81	6,51±0,73	7,23±0,96	7,11±0,9
9 HPT	27,21±3,44	25,63±3,12	28,12±4,20	27,42±3,68
Paced Auditory Serial Addition Test	30,21±4,16	34,31±3,81	31,13±4,4	33,51±4,65
* significant differences between assessments before and after rehabilitation, p<0.05 - data presented in the format: arithmetic mean ± standard deviation of the arithmetic mean (M±σ)				

In patients with secondary-progressive course of multiple sclerosis, there was also a more positive dynamics in the indicators of 25 Functions of the System and 9 HPT tests in patients of group I compared to group II. Despite the positive dynamics obtained in the indicators of the Paced Auditory Serial Addition Test before and after the therapy, no significant difference was determined between groups I and II.

In the presence of activity of the pathological process in multiple sclerosis, the most appropriate tactic remains pulse therapy with methylprednisolone. The study confirmed the existing data that pulse therapy provides a more significant result in relapsing-remitting course of multiple sclerosis compared to the secondary-progressive course. In which the severity of degenerative changes is much greater, and the ability to adapt, respectively, is lower. The appointment of corticosteroids pharmacotherapy may be accompanied by various side effects. Careful collection of anamnestic data and timely appointment of adequate accompanying therapy significantly minimizes the risk of their development. The occurrence of general weakness, phenomena of myopathic syndrome during pulse therapy can significantly worsen the expected result. There are many medicines of vasoactive, neuroprotective action, which are offered to reduce general asthenia. As a medicine of choice that can prevent the development of "muscular" motor side effects, metacartin is well tolerated, reduces the phenomena of asthenia, muscle fatigue and improves the general condition of the patient.

Thus, modern pulse therapy with corticosteroids in patients with multiple sclerosis contributes to the improvement of their condition, by identifying side effects, conducting clinical and pharmacological measures to eliminate them.

Conclusions. Pulse therapy with methylprednisolone remains the standard of treatment for exacerbations of multiple sclerosis. At the same time, it is noted that the appointment of corticosteroids can cause several side effects, one of which is the development of steroid myopathy and severe general weakness. Metacartin was used to reduce the severity of these disorders. The study included 57 patients with a reliable diagnosis of multiple sclerosis at the stage of exacerbation of the pathological process. There were 32 (56.14%) patients with relapsing-remitting course of multiple sclerosis, 25 (43.85%) with secondary-progressive course. All patients were randomly divided into two groups: I – 33 (80.83%) patients who underwent a course of pulse therapy with methylprednisolone followed by the administration of metacartin, and II – 24 (19.17%) patients who received only pulse therapy with methylprednisolone. Group I included 23 patients with relapsing-remitting course and 10 patients with secondary-progressive course of multiple sclerosis. Group II included 15 patients with relapsing-remitting course and 9 patients with secondary-progressive course of multiple sclerosis. The study showed the effectiveness of the combination of pulse therapy with methylprednisolone and metacartin, the administration of which significantly reduced the severity of "muscular" symptoms when pulse therapy was administered.

Declaration of conflict interest. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The authors confirm that they are the authors of this work and have approved it for publication. The authors also certify that the obtained clinical data and research were conducted in compliance with the requirements of moral and ethical principles based on medical and pharmaceutical law, and in the absence of any commercial or financial relationships that could be interpreted as potential conflict of interest.

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Ethical approval. Ethical clearance was obtained from the administration of the P.V. Voloshyn Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine. Permission statement for conducting the experiments was received from the administration of the P.V. Voloshyn Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine. Before any data collection, the main purpose of the study was clearly explained to each department (concerned personnel).

Data availability statement. The datasets analyzed during the current study are available from the corresponding author on reasonable request.

References.

1. Olek M.J., Howard J. Treatment of acute exacerbations of multiple sclerosis in adults. *UpToDate.* 30.04.2024. URL: https://www.uptodate.com/contents/treatment-of-acute-exacerbations-of-multiple-sclerosis-in-adults/print
2. Dargahi N., Katsara M., Tselios T. et al. Multiple Sclerosis: Immunopathology and Treatment Update. *Brain. Sci.* 2017. Vol. 7. No.7. P.78. URL: https://doi.org/10.3390/brainsci7070078
3. Tobin O. Multiple sclerosis. Mayoclinic. 2024. URL: https://www.mayoclinic.org/diseases-conditions/multiple-sclerosis/diagnosis-treatment/drc-20350274
4. Voloshyna N., Nehreba T., Kirzhner V., et al. Clinical and mathematical analysis of differences for various types of course in sporadic and familial forms of multiple sclerosis. *International neurological journal*. 2021. Vol.16. No.4. P.26-32. DOI: https://doi.org/10.22141/2224-0713.16.4.2020.207347
5. Vasylovskyy V., Nehreba T., Voloshyna N. et al. Application of Glucocorticoids in Therapy of Multiple Sclerosis. *SSP Modern Pharmacy and Medicine*. 2024. Vol.4. No.2. P.1-14. DOI: https://doi.org/10.53933/sspmpm.v4i2.141
6. Voloshina N.P., Negreba T.V., Vasilovsky V.V. et al. Comparative effectiveness of hormonal pulse therapy in relapsing and secondary progressive types of multiple sclerosis with different prognosis (Communication II. Efficiency of hormonal pulse therapy at the onset and at the relapsing stage in relapsing and secondary progressive types of multiple sclerosis with different

prognosis). *International Neurological Journal.* 2018. No. 7 (101). P. 11-16.URL: http://www.mif-ua.com/archive/article/46247
7. Yamout B. et al. Disability outcomes of early cerebellar and brainstem symptoms in multiple sclerosis. *Multiple Sclerosis Journal*. 2020. Vol. 27. No 5. P. 755-766.
8. Thompson A.J. Multiple sclerosis. *The Lance*t. 2018. Vol.391. Is.10130. P.1622-1636. URL: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30481-1/abstract
9. Shapovalova V. The ICD-11 For the Twenty-First Century: The First View from The Organizational, Legal, Clinical and Pharmacological Aspects. *SSP Modern Pharmacy and Medicine*. 2022. Vol. 2. No 1. P. 1-13. DOI: https://doi.org/10.53933/sspmpm.v2i1.37
10. Ivanishyn-Hayduchok L., Shapovalova V., Shapovalov V. ICD-11: Organizational and Legal, Medical and Pharmaceutical, Social and Economic Issues of Implementation of the Program of State Guarantees of Medical Care in 2022 in Ukraine, Based on The Fundamental Principles of the European Union. *SSP Modern Pharmacy and Medicine*. 2022. Vol. 2. No 2. P. 1-14. DOI: https://doi.org/10.53933/sspmpm.v2i2.53
11. Voloshina N.P., Egorkina O.V. Strategies for the treatment of multiple sclerosis: efficacy and safety. *Ukr. med. journal.* 2012. No. 4. P. 32-37.URL: https://umj.com.ua/uk/publikatsia-38550-strategii-lecheniya-rasseyannogo-skleroza-effektivnost-i-bezopasnost
12. Shapovalova V. Multidisciplinary Case Studies of Neuro-Oncology Disorders: Administration, Clinical and Pharmacological, Organizational and Legal, Pharmaceutical Management. *SSP Modern Pharmacy and Medicine*. 2024. Vol.4. No.3. P.1-11. DOI: https://doi.org/10.53933/sspmpm.v4i3.151
13. Shapovalov V., Shapovalova V., Osyntseva A., et al. Multidisciplinary context of research of a new drug in infectious and inflammatory diseases. *Annals of Mechnikov's Institute*. 2024. No.3. P.3–9. DOI: https://doi.org/10.5281/zenodo.13820208
14. Shapovalova V. Post-Traumatic Stress Disorder: Administration, Clinical and Pharmacological, Organizational and Legal, Pharmaceutical Management, Recent Case Studies. *SSP Modern Pharmacy and Medicine*. 2024. Vol. 4. No 1. P. 1-8. DOI: https://doi.org/10.53933/sspmpm.v4i1.123
15. Shapovalova V. Administration, Marketing, Pharmacotherapy of Medicines in Neuro-Oncology. *SSP Modern Pharmacy and Medicine*. 2024. Vol. 4. No 4. P. 1-12. DOI: https://doi.org/10.53933/sspmpm.v4i4.161
16. Shapovalova V.A., Shapovalov V.V. The clinical efficacy of the combined drug agent Valcophen in children. *Likars'ka Sprava*. 01 Jan 1999. No 1. P. 124-126. URL: https://europepmc.org/article/med/10424023
17. Shapovalova V., Zbrozhek S., Shapovalov V. et al. Content analysis of pharmacies in Ukraine where extemporaneous medicines are manufactured. *Health of Society*. 2017. Vol. 6. No 3. P. 77-83. DOI: https://doi.org/10.22141/2306-2436.6.3.2017.12349838
18. Shapovalova V. Innovative approaches to medical and pharmaceutical care, pharmacotherapy, and availability of pharmaceutical supplies for Tuberculosis patients in wartime. *SSP Modern Pharmacy and Medicine*. 2025. Vol.5. No.1. P.1-17. URL: https://doi.org/10.53933/sspmpm.v5i1.170
19. Dubrov S.O., Negrych T.I., Voloshyna N.P. Evidence-based clinical guideline Multiple sclerosis in adults and children. State Enterprise "State Expert Center of the Ministry of Health of Ukraine". 2024. 310 p. URL: https://moz.gov.ua/uploads/ckeditor/%D0%93%D1%80%D0%BE%D0%BC%D0%B0%D0%B4%D1%81%D1%8C%D0%BA%D0%B5%20%D0%BE%D0%B1%D0%B3%D0%BE%D0%B2%D0%BE%D1%80%D0%B5%D0%BD%D0%BD%D1%8F/2024/02-2024/28-02-2024/2/024_02_09_%D0%9A%D0%9D_%D0%A0%D0%A1.pdf
20. Voloshin P.V., Linsky I.V., Maruta N.O. et al. Clinical recommendations for providing medical care to patients with neurological, mental and behavioral disorders. Kharkiv: Publisher Strokov D.V., 2021. 376 p. URL: https://cerebrolysin.com.ua/fileadmin/user_upload/materials/protocols/Clinical_guidelines-8-21.pdf

21. Shapovalova V.A., Sosin I.K., Butenko G.M. et al. Pharmaceutical law in narcology. Kharkov: “Fact”. 2004. 800 p.
22. Voloshina N.P., Vasylovsky V.V., Mikulinsky Yu.E. et al. Autotherapy with bone marrow stromal cells (MSCs) induced in the nerve in patients with chronic diseases of the CNS (multiple sclerosis, Parkinson's disease). *Ukrainian Neurosurgical Journal.* 2003. No. 3. P. 61-66. URL: https://theunj.org/article/view/107571/102525
23. Karussis D., Kassis I., Petrou P. Therapy with mesenchymal stem cell transplantation in multiple sclerosis is ready for prime time: YES. Multiple Sclerosis Journal. 2022. Vol. 28. Issue 9. P. 1324-1326. URL: https://pubmed.ncbi.nlm.nih.gov/35786042/
24. Voloshyn P.V., Vorobyeva T.M., Voloshina N.P. Neurobiological mechanisms of therapeutic effects of distant transplantation of embryonic nerve tissues in modeling multiple sclerosis. *Ukrainian Herald of Psychoneurology.* 2005. Volume 13. Issue. 1 (42). P. 5-9.
25. Sharrack B., Hughes R.C., Morris R.W. et al. The effect of oral and intravenosus methylprednisolone treatment on subsequent relapse rate in multiple sclerosis. *J. Neurol. Sci*. 2000. Vol. 173. Issue 1. P. 73-77. URL: https://www.jns-journal.com/action/showCitFormats?doi=10.1016%2FS0022-510X%2899%2900304-4&pii=S0022-510X%2899%2900304-4
26. Cathcart E.S., Idelson B.A., Scheinberg M.A. et al. Beneficial effects of methylprednisolone "pulse" therapy in diffuse proliferative lupus nephritis**.** *The Lancet*. 1976. Vol.307. Iss.7952. P.163-166. URL: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(76)91272-1/fulltext. URL: https://pubmed.ncbi.nlm.nih.gov/54681/
27. Leussink V.I., Jung S., Merschdorf U. et al. Therapy in Multiple Sclerosis Induces Apoptosis in Peripheral Blood Leukocytes. *Arch Neurol.* 2001. Vol. 58. Issue 1. P. 91-97. URL: https://jamanetwork.com/journals/jamaneurology/fullarticle/778382
28. Chernenko M.E. Albumin as an indicator of blood-brain barrier permeability in patients with multiple sclerosis. *International Medical Journal.* 2013. Vol. 19. No. 2 (74). P. 96-100.
29. Chernenko ME Matrix metalloproteinase-9 as an indicator of inflammatory process activity in patients with multiple sclerosis. *Tavrichesky Journal of Psychiatry.* 2012. Vol. 16. No. 4 (61). P. 96-100.
30. Negrich T.I,, Sorokin B.V. From generic diagnostics to effective therapy of multiple sclerosis. *International Neurological Journal.* 2012. No. 3. P. 152-158. URL: http://www.mif-ua.com/archive/article/29729
31. Schmidt J., Gold R., Schonroch L. et al. T-cell apoptosis in situ in experimental autoimmune encephalomyelitis following methylprednisolone pulse therapy. *Brain*. 2000. Vol. 123. Iss.7. P.1431-1441. DOI: https://doi.org/10.1093/brain/123.7.1431
32. Liu S., Liu X., Chen S. et al. Oral versus intravenous methylprednisolone for the treatment of multiple sclerosis relapses: A meta-analysis of randomized controlled trials. *PLoS ONE*. 2017. Vol.12. Iss.11. P.e0188644. DOI: https://doi.org/10.1371/journal.pone.0188644
33. Pyndus V., Shapovalov V. Study of Pharmaceutical Provision Under the Program of Medical Guarantees in Ukraine. *SSP Modern Pharmacy and Medicine*. 2024. Vol. 4. No. 3. P. 1-10. DOI: https://doi.org/10.53933/sspmpm.v4i3.155
34. Osyntseva A. Forensic and evidence pharmacy: features of medical, pharmacological and pharmaceutical correction. *Actual problem of medicine and pharmacy.* 2020. Vol. 1 No. 1-2. URL: Retrieved from https://apmplmi.com/index.php/apmp/article/view/19
35. Filipovic S.R., Drulovic J., Stojsavljevic N. et al. The effects of high-dose intravenous methylprednisolone on event-related potentials in patients with multiple sclerosis. *J. Neurol Sci.* 1997. Vol. 152. Issue 2. P. 147-153. URL: https://www.jns-journal.com/article/S0022-510X(97)00159-7/abstract
36. Gold R., Buttgereit F., Toyka K.V. Mechanism of action of glucocorticosteroid hormones: possible implications for therapy of neuroimmunological disorders. *J. Neuroimmunol.* 2001. Vol. 117. Issue 1. P. 1-8. URL: https://www.jni-journal.com/article/S0165-5728(01)00330-7/abstract

37. Schäcke H., Döcke W.D., Asadullah K. Mechanisms involved in the side effects of glucocorticoids. *Pharmacol. Ther*. 2002. Vol.96. Iss.1. P.23-43. DOI: https://doi.org/10.1016/S0163-7258(02)00297-8
38. Huscher D., Thiele K., Gromnica-Ihle E. et al. Dose-related patterns of glucocorticoid-induced side effects. *Ann. Rheum. Dis*. 2009. Vol. 68. Iss.7. P.1119-1124. URL: https://ard.eular.org/article/S0003-4967(24)21712-X/fulltext
39. Shevchuk O.M. Itsenko-Cushing's disease: symptoms, causes and treatment. Pharmacy we wish you health. 06.11.2024. URL: https://apteka.net.ua/articles/khvoroba-itsenko-kushynha-symptomy-prychyny-i-likuvannya
40. Hoes J.N., van der Goes M.C., van Raalte D.H. et al. Glucose tolerance, insulin sensitivity and β-cell function in patients with rheumatoid arthritis treated with or without low-to-medium dose glucocorticoids. *Ann. Rheum. Dis*. 2011. Vol.70. No.11. P.1887-94. URL: https://ard.eular.org/article/S0003-4967(24)19074-7/fulltext
41. Voloshina N.P., Vasilovsky V.V., Chernenko M.E. Influence of infectious factor on the state of the blood-brain barrier in patients with multiple sclerosis. *Ukrainian Bulletin of Psychoneurology*. 2013. Vol. 22. Issue. 1 (74). P. 5-6.URL: https://uvnpn.com.ua/
42. Piper J.M,. Ray W.A., Daugherty J.R. et al. Corticosteroid use and peptic ulcer disease: role of nonsteroidal anti-inflammatory drugs. *Ann. Intern. Med*. 1991. Vol. 114. No 9. P. 735-775. DOI: https://doi.org/10.7326/0003-4819-114-9-735
43. Brown E.S., Chandler P.A. Mood and Cognitive Changes During Systemic Corticosteroid Therapy. *Prim Care Companion J. Clin. Psychiatry*. 2001 Feb. Vol. 3. No 1. P. 17-21. URL: https://www.psychiatrist.com/pcc/mood-cognitive-changes-during-systemic-corticosteroid/
44. Stuart F.A., Segal T.Y., Keady S. Adverse psychological effects of corticosteroids in children and adolescents. *Arch. Dis. Child*. 2005 May. Vol. 90. Issue 5. P. 500-506. URL: https://adc.bmj.com/content/90/5/500
45. Panoulas V.F., Douglas K.M., Stavropoulos-Kalinoglou A. et al. Long-term exposure to medium-dose glucocorticoid therapy associates with hypertension in patients with rheumatoid arthritis. *Rheumatology (Oxford)*. 2008. Vol.47. Iss.1. P.72-77. DOI: https://doi.org/10.1093/rheumatology/kem311
46. Whitworth J.A. Mechanisms of glucocorticoid-induced hypertension. *Kidney Int*. 1987 May. Vol. 31. No 5. pp. 1213-1224. URL: https://pubmed.ncbi.nlm.nih.gov/3298796/
47. Hardman J.G. Limbird L.E., Gilman A.G. Goodman and Gilman's: The Pharmacological Basis of Therapeutics. *New York: Mcgraw-Hill (Tx); 9th edition*. 1996. P. 1475. URL: https://www.amazon.com/Goodman-Gilmans-Pharmacological-Basis-Therapeutics/dp/0070262667
48. Shapovalova V. Extemporaneous preparations in the pharmacotherapy of nervous system disorders: pharmaceutical management, marketing, analysis, application. *SSP Modern Pharmacy and Medicine*. 2023. Vol.3. No.4. P.1-7. URL: https://doi.org/10.53933/sspmpm.v3i4.111
49. Shapovalova V. Forensic and pharmaceutical risks in the organization of pharmacotherapy of covid, post-covid and long-covid disorders. COVID-19 and vaccination practice standards. *SSP Modern Pharmacy and Medicine*. 2022. Vol. 2. No. 4. P. 1–24. URL: https://doi.org/10.53933/sspmpm.v2i4.69.
50. Shapovalova V. Monkeypox virus – new challenges of modernity: experimental organizational and legal, clinical and pharmacological studies. *SSP Modern Pharmacy and Medicine*. 2022. Vol.2. N.3. P.1-15. URL: https://doi.org/10.53933/sspmpm.v2i3.54.
51. Shapovalova V. Pharmacotherapy of Depressive disorders in conditions of coronavirus disease: pharmacoeconomic experimental study. *SSP Modern Pharmacy and Medicine*. 2023. Vol.3. No.3. P.1-11. URL: https://doi.org/10.53933/sspmpm.v3i3.101
52. Chernenko M. E. The problem of neurogenesis in the context of therapy of neuroinflammatory/neurodegenerative processes. *International Medical Journal*. 2019. Vol. 25. No. 2 (98). P. 53-56.

53. Dalakas M.C. Current treatment of the inflammatory myopathies. *Curr. Opin. Rheumatol.* 1994. Vol.6. No.6. P.595-601. URL: https://journals.lww.com/co-rheumatology/abstract/1994/11000/current_treatment_of_the_inflammatory_myopathies.8.aspx
54. McDonald W.I., Compston A., Edan G., et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Annals. of neurology*. 2001. Vol.50. No.1. P.121-128. DOI: https://doi.org/10.1002/ana.20703
55. Wexler M. Guidelines for MS diagnosis: McDonald criteria. *Multiple Sclerosis News Today*. 13.04.2023. URL: https://multiplesclerosisnewstoday.com/ms-diagnosis-mcdonald-criteria/
56. Expanded Disability Status Scale (EDSS). *MS Trust*. 14.10.2024. URL: https://mstrust.org.uk/a-z/expanded-disability-status-scale-edss
57. Patzold T., Schwengelbeck M., Ossege L.M. et al. Changes of the MS Functional Composite and EDSS during and after treatment of relapses with methylprednisolone in patients with multiple sclerosis. *Acta Neurol. Scand.* 2002. Vol. 105. No 3. P. 164-172. DOI: https://doi.org/10.1034/j.1600-0404.2002.1o135.x
58. Arsoy E., Bulut N., Pamuk S. et al. The Multiple Sclerosis Functional Composite (MSFC) for Determining Disease Progression: A Methodological Study. *J. Mult. Scler. Res*. 2022. Vol.2. Iss.1. P. 5-12. URL: https://jmsres.com/jvi.aspx?pdir=jmsres&plng=eng&un=JMSRES-60352&look4=