DOI: https://doi.org/10.30841/2786-7323.3.2024.316658
UDC: 616.832-004.2-006: [616.62-008.22:616.34-008.1:616.69:618.17]-02:616.83]-036.1-08-035

# Pelvic disorders in patients with multiple sclerosis in the presence of comorbidity

***N. K. Svyrydova, G. M. Chupryna, V. G. Sereda***
**Interregional Academy of Personnel Management, Kyiv**

**The prevalence and features of pelvic disorders in patients with multiple sclerosis with comorbidity were investigated. In total, 216 patients with various forms of the disease were examined. Clinical and demographic data, paraclinical characteristics, significance of nervous system dysfunction and disability, degree of pelvic dysfunction, severity of pain, severity of fatigue, severity of depression, severity of cognitive disorders, indicators of quality of life were analyzed.**
**During the clinical examination, the body mass index, the presence or absence of comorbid diseases and their duration were clinically determined, laboratory, instrumental studies and examinations by other specialists were used (ophthalmologist, therapist, cardiologist, rheumatologist, urologist, dentist).**
**When conducting a study of patients with multiple sclerosis of the general sample, symptoms associated with a violation of pyramidal functions were registered in 191 patients (88.4%), symptoms caused by a violation of cerebellar functions – in 178 patients (82.4%), symptoms caused by a violation of the functions of the trunk of the brain and cranial nerves – in 161 patients (74.5%), symptoms associated with impaired sensitivity functions – in 169 patients (78.2%), symptoms due to pelvic disorders – in 187 patients (87.0%), symptoms, caused by impaired visual functions – in 116 patients (53.7%), symptoms associated with impaired cerebral (mental) functions – in 184 patients (85.2%).**
**Pelvic organ dysfunction in patients with multiple sclerosis were most clearly correlated with the duration of the disease, level of disability, female sex, level of fatigue and indicators of quality of life. In the group of patients with multiple sclerosis with comorbid pathology, there is a significant prevalence of symptoms of pelvic organ dysfunction and combined forms of pelvic organ dysfunction.**
***Keywords:*** *multiple sclerosis, pelvic disorders, comorbidity.*

## Тазові розлади у хворих на розсіяний склероз за наявності коморбідності

***Н. К. Свиридова, Г. М. Чуприна, В. Г. Середа***

У дослідженні вивчали поширення й особливості тазових розладів у хворих на розсіяний склероз за умов коморбідності. Було досліджено 216 пацієнтів з різними формами захворювання. Аналізувались клініко-демографічні дані, параклінічні характеристики, значущість порушення функцій нервової системи та інвалідності, ступінь порушення тазових функцій, вираженості болю, тяжкості втоми, тяжкості депресії, вираженість когнітивних розладів, показники якості життя.
Під час клінічного обстеження оцінювали індекс маси тіла, визначали клінічну наявність або відсутність коморбідних захворювань, їх тривалість, використовували лабораторні (клінічні аналізи сечі і крові, біохімічні аналізи), інструментальні (ультразвукові, рентгенологічні) обстеження та огляд інших спеціалістів (офтальмолога, терапевта, кардіолога, ревматолога, уролога, стоматолога).
При проведенні дослідження хворих на розсіяний склероз загальної вибірки зареєстровано: симптоми, пов'язані з порушенням пірамідних функцій – у 191 пацієнта (88,4%); симптоми, обумовлені порушенням мозочкових функцій – у 178 пацієнтів (82,4%); симптоми, спричинені порушенням функцій стовбура мозку і черепних нервів – у 161 пацієнта (74,5%); симптоми, пов'язані з порушенням функцій чутливості – у 169 пацієнтів (78,2%); симптоми, зумовлені тазовими розладами – у 187 пацієнтів (87,0%); симптоми, зумовлені порушенням зорових функцій – у 116 пацієнтів (53,7%); симптоми, пов'язані з порушенням церебральних (психічних) функцій – у 184 пацієнтів (85,2%).
Найбільш чітко розлади функцій тазових органів у хворих на розсіяний склероз корелювали з тривалістю захворювання, рівнем інвалідності, жіночою статтю, рівнем втоми та показниками якості життя. У групі хворих на розсіяний склероз з коморбідною патологією спостерігається достовірне превалювання симптомів розладів і поєднаних форм розладів функцій тазових органів.
***Ключові слова:*** *розсіяний склероз, тазові розлади, коморбідність.*

The clinical features of multiple sclerosis have been known since the 19th century thanks to the works of Zh. M. Charcot and his school [1, 2]. This disease affects about 3,000,000 people in the world and about 20,000 in Ukraine, that is, it remains relevant even today [3]. Its pathognomonic signs are not any specific neurological symptom (there may be 685 of them with this pathology) [3], but "dispersion in space" (diffuse nature of the location of demyelination foci, significant variability in their number and size) and "dispersion in time" (a significant number of exacerbations of different nature caused by foci of different age).

However, it is known that certain symptoms or syndromes have been put forward by different scientists as pathognomonic: taking into account the significant prevalence of pelvic disorders in multiple sclerosis, Scheinberg puts forward a triad of symptoms sufficient to diagnose "multiple sclerosis" in 30-year-old men: urinary incontinence, constipation, impotence [1–4].

Pelvic organ dysfunction, which in modern neurology usually include the urinary bladder, intestines and sexual problems, are presented according to modern research in 34–96% of patients with multiple sclerosis [4–8], and quite often researchers talk about the hypodiagnosis of this problem [7–9]. Pelvic organ dysfunction in multiple sclerosis are poorly tolerated even under the conditions of a minor duration of the disease, their degree of expression directly correlates with the term of multiple sclerosis [4–6], and leads (especially combined forms of pelvic organ dysfunction) to a noticeable decrease in the quality of life [10].

Due to "scattering in space", pelvic organ disorders in multiple sclerosis can have signs of te central or peripheral type, depending on the level and depth of the demyelinating lesion [11, 12].

Clinical symptoms of pelvic organ dysfunction, limiting communicative functions, can cause a significant deterioration in the mental comfort of patients with multiple sclerosis and are no less significant cause of disability than limb paresis and movement coordination disorders [4–7]. Urgent urges to urinate with accompanying urinary incontinence, the most common in multiple sclerosis, are the reason that many patients are literally chained to their homes due to uncertainty about the reach of the toilet. Pelvic organ dysfunction is also the basis of secondary inflammation of the urinary tract and kidneys, as a result of which chronic renal failure, hydronephrosis, and urosepsis develop, which are among the main causes of death in patients with multiple sclerosis [4–7].

It should be noted that pelvic organ dysfunction in multiple sclerosis can most often be primary in nature and be associated with the main pathological process (they are most clearly correlated with foci of demyelination in the area of the brain stem and along the pyramidal tracts) [11, 12], but also its nature and the degree of severity may be due to comorbid pathology (sometimes premorbid), and in addition, it may be aggravated by such manifestations of multiple sclerosis as fatigue, depression, paresis of limbs and the limitation of the ability to move caused by them, or spasticity, pain, side effects of drugs and others psychological, emotional, social factors [4].

Symptomatic medical treatment with the aim of normalizing the function of the urinary bladder in multiple sclerosis is used most often and consists of prescribing of anticholinergic (antimuscarinic) drugs as first-line drugs in the case of urinary incontinence: oxybutyn, fesoterodine, propantheline bromide, propiverine hydrochloride, tolterodine, trospium chloride, solifenacin succinate; as the second choice drugs – darifenacin, as well as muscle relaxants baclofenum and tizanidinum [4,7]. In the case of nocturia, the tricyclic antidepressant imipramine hydrochloride is effective [6,7], and in case of urinary retention, alpha-adrenergic blockers doxazosin, alfuzosin, prazosin, terazosin, as well as myoreactants, cannabinoids, desmopressin [6, 7].

In order to normalize intestinal function in multiple sclerosis in the case of constipation, which often bothers patients, a diet with a high fiber content, sufficient fluid intake (1.5–2 liters of water, broth, tea per day), and sufficient physical activity are recommended first of all [6]. As laxatives, it is advisable not to use those drugs that have a powerful action that stimulates intestinal peristalsis (castor oil, correctol, bisacodyl), but to prescribe those drugs that have a softening stool effect (vaseline oil, hronulak, portalac) and saline or osmotic (magnesium sulfate, lactulose, Karlovy Vary salt) laxatives. In the case of diarrhea, which, although less common in multiple sclerosis than constipation (it can be the result of increased reflex activity of the intestine caused by demyelinating damage, the influence of comorbid diseases of the gastrointestinal tract, taking some medications, and unbalanced nutrition), it is nevertheless possible.

To determine the prevalence of pelvic organ dysfunction in patients with multiple sclerosis and to find out the peculiarities of their course in the aspect of comorbidity; to find relationships between indicators of pelvic organ dysfunction in patients with multiple sclerosis in terms of comorbidity and degree of disability (Expanded Disability Status Scale, EDSS), manifestations of fatigue according to the Fatigue Severity Scale (FSS), pain according to the Visual Analogue Scale (VAS), level of depression according to the Depression of Beck II Scale (BDI-II) and cognitive function disorders according to the Mini-Mental-State-Examinations (MMSE), and indicators of quality of life were determined according to the SF-36.

## MATERIAL AND METHODS

216 patients (75 men and 141 women) aged 21 to 62 years (average 39.9±9.7) with a diagnosis of multiple sclerosis according to the McDonald criteria (2005) [11], (2010) [12] with different forms of course (remitting and progressive) were examined with a degree of disability from 1 to 5.5 points according to the EDSS with and without concomitant diseases. The comparison group consisted of 157 people (70 men and 87 women), including 34 patients with the consequences of acute diffuse encephalomyelitis, as well as 123 practically healthy people, whose average age was 38.5±6.2 and 35.3±10.1 years, respectively. The research protocol was approved by the local ethics committee (ethics committee of the Shupyk National Healthcare University of Ukraine, protocol of the KE No. 9 dated October 1, 2012).

Due to the fact that the study was conducted in the period from 2007 to 2016, all patients were evaluated according to the McDonald criteria 2005 (for patients with multiple sclerosis who were included in the study in 2007–2010) and 2010 (for patients with multiple sclerosis who were included in the study in 2011–2016), later criteria for the diagnosis of multiple sclerosis, in particular McDonald criteria 2017, were not used.

The clinical condition of the patients was described in accordance with the Functional System scale (FS scale), and degree of severity of neurological deficit – based on research data on the Expanded Disability Status Scale (EDSS) [13].

For the convenience in summarising the symptoms of multiple sclerosis and adequately assessing the picture of the disease, the scale of lesions of the leading functional systems, proposed by J. Kurtzke [13], was used, which contains 7 sections for the assessment:

1) pyramidal functions;
2) cerebellar functions;
3) functions of the brain stem and cranial nerves;
4) sensitivity functions;
5) bowel and bladder functions;
6) visual functions;
7) cerebral (mental) functions.

Each section displays a conditional classification of violations of the function of each system in points, from

*Table 1*

**Pelvic function study according to the FS-5 scale by J. Kurtzke**

| Functional System | Assessment of the degree of impaired functions in points | | | |
|---|---|---|---|---|
| | 0 | 1 | 2 | 3 |
| FS-5 Pelvic function | Norm | Mild hesitancy when urinating, urges or retention of urine | Moderately expressed hesitancy during urination, imperative urges, constipation or retention of urine, or rarely urinary incontinence (periodic self-catheterization, manual compression to improve bladder evacuation or manual manipulations to empty the intestine) | Frequent urinary incontinence |

less pronounced to more pronounced. The number of points is estimated for each scale separately (from FS-1 to FS-7). The use of this scale allows not only to obtain an in-depth clinical characteristic, but also to conduct dynamic monitoring of the course of the disease in patients with multiple sclerosis [4, 13].

We determined the level of disability (EDSS) [13], revealed the presence or absence of pelvic organ dysfunction during the examination, as well as in the anamnesis, before and after the diagnosis of multiple sclerosis, and clarified their nature. When the determination was made the degree of violations (FS-5) (pelvic functions) as a reference point for pathological changes, we took imperative urges to urinate, and the maximum score was set taking into account the most gross violations of the function of either the bladder or the intestines (disorders of sexual functions are not included in the FS-5) (table 1).

A point assessment of the severity of sexual function disorders in patients with multiple sclerosis was carried out according to the following scale: absence – 0 points, minimal or slightly expressed sexual function disorders – 1 point, moderate – 2 points, pronounced sexual function disorders – 3 points [14].

During the clinical and somatic examination, the body mass index was calculated according to the Quetelet formula, the presence or absence of comorbid diseases and their duration were determined clinically, laboratory (clinical urine and blood tests, biochemical tests), instrumental studies and examination by other specialists were used (ophthalmologist, therapist, cardiologist, rheumatologist, urologist, dentist) [14–16].

A neuropsychological study was also conducted: manifestations of fatigue according Fatigue Severity Scale (FSS), pain according to the Visual Analogue Scale (VAS), level of depression according to the Depression of Beck II Scale (BDI-II), cognitive function disorders according to the Mini-Mental-State-Examinations (MMSE) and indicators of quality of life were determined according to the SF-36.

Multiple sclerosis patients with pelvic organ dysfunction were treated with acupuncture methods as part of complex therapy, and its results were analyzed.

## RESULTS AND DISCUSSION

All 216 patients with multiple sclerosis examined by us with different forms of the course, depending on the presence or absence of comorbid pathology, were divided into 2 groups: without any concomitant disease (group I – 109 patients); one or more concomitant diseases (group II – 107 patients).

The group II consisted of 107 patients with multiple sclerosis, who at the time of examination had a clinically significant comorbid pathology, the data of which were revealed through a detailed survey of patients during an objective examination and analysis of medical documentation. At the same time, in group II, 40 (18.5%) patients with multiple sclerosis had one comorbid pathology, 27 (12.5%) – two comorbid pathologies, 21 (9.7%) – three comorbid pathologies, and 19 (8.8%) – four or more comorbid pathologies.

The average age in the study group was 39.9±9.7 years, minimum – 21 years, maximum – 62 years. The gender ratio (female/male) was approximately 7/4 (141/75), which confirms the data of modern researchers about the predominance of women among patients with multiple sclerosis [4]. Regarding the marital status of patients with multiple sclerosis, married people prevailed in the study group – 60.7% (131/85).

In 96 (44.4%) patients with relapsing course of multiple sclerosis, the stage of exacerbation of the disease of various degrees of severity was registered, and in 43 (19.9%) patients – the stage of remission. Among patients with a progressive course of multiple sclerosis, 54 (25.0%) had a gradual increase in symptoms of neurological deficit with slow dynamics, and in 23 (10.7%) – symptoms of neurological deficit increased constantly, at a faster pace.

During the initial examination, all patients with multiple sclerosis had complaints of varying intensity. 157 (72.7%) patients with diffuse symptoms complained of general malaise of varying severity. It was found that among the general clinical manifestations in the vast majority of patients with multiple sclerosis of both groups, both in the premorbid period and after the diagnosis of multiple sclerosis, there were complaints from the digestive organs: decreased appetite (67.1%), frequent belching air (20.8%), periodic spasmodic pains in the epigastrium (22.2%) or in the right hypochondrium (16.2%), a feeling of heaviness and discomfort in the costal and subcostal area on the right (21.8%), a tendency to flatulence and irregular stool (22.7%). Then, the presence of diseases of the digestive system was diagnosed in only 28 patients (13.0%), who were included in the group with gastroenterological comorbid pathology. This indicates hypodiagnosis of diseases of the digestive system in patients with multiple sclerosis.

When determining the body mass index according to the formula of A. Ketele [14, 15], it was found that with an average body mass index of 24.15±5.15 kg/m$^2$, which corresponds to the norm, there is excess body weight (25.0 < body mass index > 30.0) and obesity of the first degree (30.0 < body mass index >35.0) in 86 (39.8%) patients with multiple sclerosis. General clinical and demographic characteristics of patients with multiple sclerosis are shown in table 2.

*Table 2*

**General clinical and demographic characteristics of patients with multiple sclerosis**

| No. | Indicator | A general group of examined patients with multiple sclerosis, n=216 |
|---|---|---|
| 1. | Average age, years (mean ± standard deviation) | 39.9±9.7 |
| 2. | Average age of onset of multiple sclerosis, years (mean ± standard deviation) | 28.7±7.6 |
| 3. | Duration of the disease, years (mean ± standard deviation) | 6.4±3.5 |
| 4. | Gender ratio (women / men, %) | 62.3/37.7 |
| 5. | Marital status (married, %) | 60.7 |
| 6. | Degree of disability for the EDSS scale. %<br>light<br>average<br>severe<br>group average, points (mean ± standard deviation): | <br>46.8<br>53.2<br>–<br>3.8±1.3 |
| Type of course of multiple sclerosis | | |
| 7. | Remitting, %<br>Including:<br>Relapsing-remitting multiple sclerosis<br>Relapsing-progressive multiple sclerosis | 64.4<br><br>42.6<br>21.8 |
| 8. | Progressive, %<br>Including:<br>Primary progressive multiple sclerosis<br>Secondary progressive multiple sclerosis | 33.6<br><br>20.8<br>12.8 |

*Table 3*

**Analysis of clinical and demographic data of patients with multiple sclerosis in the aspect of division into clinical groups (comorbidity)**

| No. | Indicator | A general group of examined patients with multiple sclerosis, n=216 | |
|---|---|---|---|
| | | I group, n=109 | II group, n=107 |
| 1. | Average age, years (mean ± standard deviation) | 36.9±9.3 | 42.3±10.4 * |
| 2. | Average age of onset of multiple sclerosis, years (mean ± standard deviation) | 28.4±7.3 | 29.1±7.9 |
| 3. | Duration of the disease, years (mean ± standard deviation) | 5.3±1.9 | 7.4±2.0 * |
| 4. | Gender ratio (women/men, %) | 66.1/33.9 | 64.5/35.5 |
| 5. | Marital status (married, %) | 57.8 | 63.5 * |
| 6. | Degree of disability for the EDSS scale, %<br>light<br>average<br>severe<br>group average, points (mean ± standard deviation): | <br>51.4*<br>48.6<br>–<br>3.4±1.2 | <br>42.1%<br>57.9%*<br>–<br>4.3±1.4* |
| Type of course of multiple sclerosis | | | |
| 7. | Remitting, %<br>Including:<br>Relapsing-remitting multiple sclerosis<br>Relapsing-progressive multiple sclerosis | 34.3*<br><br>24.5*<br>9.7 | 30.1<br><br>18.1<br>12.0 |
| 8. | Progressive, %<br>Including:<br>Primary progressive multiple sclerosis<br>Secondary progressive multiple sclerosis | 16.2<br><br>8.3<br>7.9 | 19.4*<br><br>12.5*<br>6.9 |

*Note.* * – Level of significance of differences in indicators when comparing groups I and II, p<0.05.

When analyzing the difference between groups I and II by age, gender characteristics, duration of multiple sclerosis and type of its course (table 3), gender differences were insignificant (p>0.05), while differences in age and clinical features of the disease were established, which emphasized deeper manifestations of multiple sclerosis in patients of the group II.

A fairly high frequency of body weight deficiency (body mass index <18.5) in 14 (6.5%) patients of the group II compared to 5 (2.3%) patients of the group I in the formation of which a certain role is played by physical overloads that took place in the premorbid period in 26 (12.0%) patients in group II compared to 16 (7.4%) patients in group I.

Thus, patients with multiple sclerosis of the group II were older and had a longer duration of multiple sclerosis than patients of the group I, which correlates with the data of other

researchers on the increase in the frequency of comorbid pathology as the course of multiple sclerosis progresses [17].

To a greater extent, the factors mentioned above, which were associated with the formation of comorbid pathology in patients with multiple sclerosis, were observed in women.

On the other hand, such factors as the lack of a full night's sleep – 93 (44.0%) in the general study group, which occurred in 52 (24.1%) patients of the group II compared to 41 (19.0%) patients of the group I, as well as smoking, which occurred in 69 (31.9%) patients with multiple sclerosis, were more characteristic of men.

It was also noted that patients with multiple sclerosis in the premorbid period were almost completely absent from short-term daytime sleep: 182 (84.3%) in the general study group, while the difference between groups I and II of patients with multiple sclerosis was significant: 85 (39.4%) patients and 97 (44.9%) patients, respectively, ($p<0.05$), which can indicate the probable influence of this factor on the pathological mechanism of the development of multiple sclerosis (due to a decrease in stress resistance and neuroplasticity of brain mechanisms) [4].

Among the patients of the group II, 42, (19.4%; $p<0.05$) patients had progressive multiple sclerosis and 27, (12.5%; $p<0.05$) patients had primary progressive multiple sclerosis; similarly, relapsing-progressive multiple sclerosis was observed in the group II significantly more often than in the group I – 53 (24,5%; $p<0.05$) and 35, (16.2%; 18, 8,3%; 21, 9.7%) respectively, and relapsing-remitting multiple sclerosis was significantly more common among patients of the group I – 53, (24.5%; $p<0.01$), than among patients of the group II – 39 (18.1%; $p<0.05$). Analysis of clinical and demographic data of patients with multiple sclerosis in the aspect of division into clinical groups is presented in table 3.

Thus, it can be seen that relatively benign forms of the course of multiple sclerosis are more common in the group II, and relatively benign forms are less common, as well as more pronounced disability according to the EDSS scale.

The average FS-5 score in the study group was 1.3±0.24 (the group I – 1.2±0.19; the group II – 1.4±0.27). At the same time, according to FS-5 data, the following were recorded: 0 points – 41 patients (the group I – 24; the group II – 17), 1 point – 85 patients (the group I – 46; the group II – 39), 2 points – 73 patients (the group I – 32; the group – 41); 3 points – 17 patients (the group I – 7; the group – 10).

Presence of pelvic disorders according to FS-5 – 158 patients (73.2%). The group I – 68 (31.5%) patients, the group II – 90 (46.7%; $p<0.05$) patients.

In total, 187 (87.0%) patients with multiple sclerosis had pelvic disorders, including their complaints and history. The group I – 91 patients (42.1%), the group II – 96 patients (44.4%; $p<0.05$).

With regard to sexual dysfunctions, the most frequent complaints in the study group were a decrease in libido (25.5%), erectile dysfunction and premature ejaculation in men (20.0%), impaired vaginal hydration (17.0%), and decreased intensity of orgasm (13.5%) in women, on the other hand, 4.7% of patients of both sexes noted an increase in libido.

The presence of sexual disorders in patients with multiple sclerosis in general, was observed in 69 patients (31.9%). The group I – 30 (13.9%) patients, the group II – 39 (18.1%; $p<0.05$) patients.

Data on pelvic disorders in patients with multiple sclerosis are shown in table 4.

Presence of sexual disorders, points, in general, was 0.6±0.1. It was higher in the group II than in the group I, but it did not reach statistical significance ($p>0.05$).

At the same time, mono-forms of pelvic disorders (bladder, bowel or sexual dysfunction) were observed in 53 (24.5%) patients (the group II – 23 (10.7%) patients, and the group I – 30 (13.9%) patients). Combined forms of pelvic disorders were observed in 134 (62,0%) patients: simultaneous damage to two of these three systems – in 106 (49.1%) patients in general, (the group II – 85 (39.4%) patients, and the group I – 17 (7.9%) patients), dysfunction of all three systems – in 32 (17.1%) patients (the group II – 21 (9.7%) patients, and the group I – 11 (5.1%) patients).

Mono-forms of pelvic disorders were observed significantly more often among patients with multiple sclerosis in the group I – 30 (13.9%; $p<0.05$), and combined forms of pelvic disorders were observed in total among patients of the group II – 106 (49.1%; $p<0.05$).

Multiple sclerosis is a paradoxical disease. Its essence is a multifocal lesion mainly of the central nervous system, and

*Table 4*

**Rating of pelvic organ dysfunction in patients with multiple sclerosis in the aspect of division into clinical groups (comorbidity)**

| No. | Indicator | A general group of examined patients with multiple sclerosis (n = 216) | |
|---|---|---|---|
| | | I group (n = 109) | II group (n =107) |
| 1. | FS-5 rating, points (mean ± standard deviation) | 1.2±0.19 | 1.4±0.27 |
| 2. | Presence of pelvic disorders according to FS-5, abs./% | 68/1.5%) | 90/46.7%* |
| 3. | The presence of pelvic disorders in patients with multiple sclerosis in general (abs/%) | 91/42.1% | 96/44.4%* |
| 4. | Presence of sexual disorders (abs/%) | 30/13.9% | 39/18.1%* |
| 5. | Presence of sexual disorders, points (mean ± standard deviation) | 0.5±0.1 | 0.7±0.1 |
| 6. | Mono-forms of pelvic disorders (abs/%) | 30 (13.9% )* | 23 (10.7%) |
| 7. | Combined forms of pelvic disorders (abs/%)<br>Including:<br>Simultaneous damage to two of these three systems (abs/%)<br>Dysfunction of all three systems (abs/%) | 28 (13.0%)<br><br>17 (7.9%)<br>11 (5.1%) | 106 (49.1%)*<br><br>85 (39.4%)*<br>21 (9.7%)* |

*Note.* * – Level of significance of differences in indicators of pelvic disorders in comparison between groups I and II, $p<0.05$.

it often happens that several of its functions are affected at once, including the functions of the pelvic organs [4, 14, 18]. It can have a mild course, or it can have serious consequences, quickly lead to disability and end in death. The cause of death from multiple sclerosis is cardiovascular disease (including, as a result of comorbid diseases) cancer, fulminant pneumonia (since patients with multiple sclerosis have a lack of motor activity due to paresis, the central regulation of the lungs is disturbed due to numerous foci of demyelination in the brain and spinal cord, and immune disorders occur), septicemia, the cause of which is often the pelvic organ dysfunction, in particular, urosepsis with untimely bladder catheterization in case of urinary retention [3, 14]. When multiple sclerosis ends fatally, it has 10 points on the EDSS scale [13, 14, 19].

Death is often preceded by some comorbid disease, of which there can be many in multiple sclerosis - because this pathology is long-lasting, so to speak "for a lifetime" [14, 19].

Previous studies have characterized study groups of patients with mild to moderate impairment according to the EDSS scale [14, 18, 20]. According to the assessment of the research data on the EDSS scale, a mild degree of persistent neurological deficit (0–2.5 points) occurred in 101 (46.8%) patients with multiple sclerosis; the average degree of persistent neurological deficit (3.0–5.5 points) – occurred in 115 (53.2%) patients with multiple sclerosis.

Among the frequent complaints of a somatic nature, the oral cavity problems should be noted, which occurred in 105 (48.6%) patients with multiple sclerosis due to dental problems, and in 83 (38.4%) patients with multiple sclerosis due to periodontal problems [21].

As described earlier, 146 (67.6%) patients complained of decreased muscle strength in the legs, 43 (19.9%) patients complained of decreased muscle strength in the arms, 109 (50.5%) patients said about impaired gait and balance – 119 (55.1%) patients – about impaired coordination of movements in the limbs, – 107 (49.5%), complaints for trembling hands – 103 (47.7%) patients, for double vision – 39 (18.1%), for blurred vision or its misting – 63 (29.2%), for dizziness or vertigo – 51 (23.6%), for noise in the head – 64 (29.6%), for numbness in the legs – 123 (56.9%), numbness in the hands – 51 (23.6%), pain of various nature – 138 (63.9%), and pelvic disorders – 163 (75.5% ) [18, 20].

As previously reported, sleep disorders were among the common complaints in patients with multiple sclerosis – 132 (61.1%) patients had the following symptoms: insomnia (difficulty falling asleep, frequent night or early morning awakenings) – 116 (53.7%) patients; hypersomnias (increased duration of night sleep or daytime sleepiness, attacks of an irresistible desire to sleep with falling asleep during the day) – 90 (41.7%) patients; parasomnias (motor and behavioral disturbances occurring during sleep) – 38 (17.6%) patients [22, 23].

It should be noted that emotional lability and sleep disturbances most often bothered patients with complaints from the gastrointestinal tract and were most pronounced in patients with gastroenterological comorbidity [22, 23].

When analyzing complaints, as shown in previous works, researchers found that 4 leading neurological syndromes were most regularly detected in patients with multiple sclerosis in the study group: pyramidal syndrome – 184 (85.2%), cerebrasthenic syndrome – 176 (81.5%), pelvic disorders – 187 (87.0), sensitive disorders – 149 (69.0%) [18, 20].

Hormonal disorders, in particular related to disorders of sex hormones (increased testosterone levels), were observed in 14.0% of patients with multiple sclerosis (in women). 6.7% of women associated the onset of their disease with pregnancy and childbirth, after which the first signs of multiple sclerosis were observed [4].

Violations of the psycho-emotional sphere in the examined patients with multiple sclerosis were represented mainly by complaints of a neurotic and affective nature. Among the neurosis-like manifestations, asthenic complaints prevailed: general weakness – 129 (59.7%) patients, increased fatigue – 137 (63.4%) patients, decreased vital energy – 184 (85.2%) patients; among affective manifestations there were depressive complaints: low mood – 117 (54.2%) patients, (50.5%), loss of interest in life – 53 (24.5%) patients, sadness – 126 (58.3%) patients [14, 23].

Violations of emotional control in the form of lability of affects and frequent mood changes were noted in 98 (45.4%) of the examined patients with multiple sclerosis, while euphoria was observed in the examined patients with multiple sclerosis much less often and less intensely than depressive manifestations, and was noted in 36 (16.7%) patients (mostly women), which confirms the data of other authors about the low frequency of euphoria in the early stages of the disease. Pronounced euphoria with underestimation of the severity of her condition occurred only in one patient with prevalence in the clinic of coordination disorders and subcortical dementia. Also, relatively infrequently, cognitive disorders were also presented: in the form of complaints about decreased memory – 54 (25.0%) and decreased concentration of attention – 86 (39.8%) [14, 23].

During description the examination of patients with multiple sclerosis of the general sample, symptoms associated with a violation of pyramidal functions were registered in 191 (88.4%) patients, symptoms caused by a violation of cerebellar functions - in 178 (82.4%) patients, symptoms caused by a violation of the functions of the brain stem and cranial nerves – in 161 (74.5%) patients, symptoms associated with impaired sensitivity functions [19] – in 169 (78.2%) patients, symptoms caused by pelvic disorders – in 187 (87.0%) patients, symptoms caused by violation of visual functions – in 116 (53.7%) patients, symptoms related to violation of cerebral (mental) functions – in 184 (85.2%) patients [18, 20].

Clinical examination, described in previous works, it was found that at the time of the examination, the most frequent complaints in terms of bladder function disorders in the study group were complaints of imperative urges to urinate (47.2%), nocturia (40.7%), periodic incontinence (23.6%) and urinary retention (21.7%); complaints about change in color and smell of urine (20.8%), feeling of incomplete emptying of the bladder (19.4%), sluggish stream of urine (15.3%), difficult (13.4%), painful (12.5%), and frequent (10.7%) urination, pain in the lower back (18.5%) and lower abdomen (10.2%) [4, 14].

As already reported, some patients noted that such complaints as imperative urges to urinate (7.9%), dysuric manifestations (10.6%), change in color (6.0%) and smell of urine (4.2%), lower back pain (8.8%) took place in them premorbidly, before the diagnosis of multiple sclerosis, sometimes (3.2%) several years before that [4].

As previously reported, in our opinion, in some cases it is associated with the monosymptomatic debut of multiple sclerosis, which was not diagnosed at the time (imperative

calls and change in urine color), and in others – with the development of premorbid multiple sclerosis (nephrological, neurological, and gynecological) pathology [4].

A small number of patients with multiple sclerosis (women) noted that the first signs of urination disorders (dysuria) appeared premorbidly after childbirth (5.6%). In total, we diagnosed 164 (75.9%) patients with multiple sclerosis of the study group with various degrees of bladder dysfunction [4].

A decrease in pain sensitivity in the anorectal zone (as well as in the S1-S5 segments in general), a decrease in "rectal sensation", pronounced lower paraparesis, and the presence of diarrhea correlated with intestinal function disorders in the aspect of incontinence in patients with multiple sclerosis. A small number of patients with multiple sclerosis (5.6%) noted that the first signs of bowel dysfunction occurred premorbidly, after abdominal surgery (appendectomy) or after childbirth [4].

As previously reported , during description laboratory tests of urine [14, 16], the vast majority (84.7%) of patients from the study group had general inflammatory signs (decrease in transparency, specific gravity, pH shift towards neutral and alkaline, mild increase in the number of leukocytes and erythrocytes, cylinders, protein, color change more often in the direction of green), which were more significantly expressed in patients with impaired bladder function.

Ultrasound examination of the bladder was performed in 47 patients with multiple sclerosis with moderate or clinically pronounced bladder dysfunction. It should be noted that the results of the examination showed an incomplete correspondence between the clinical symptoms and the data of the ultrasound examination of the bladder (clinical-instrumental dissociation): only 25 of 42 patients with multiple sclerosis, who reported a feeling of incomplete emptying of the bladder, had residual urine, while 7 patients who did not complain about the feeling of incomplete emptying of the bladder were found to have residual urine according to bladder ultrasound [4, 14].

As previously reported, an ultrasound examination of the kidneys was performed in 15 patients with multiple sclerosis of the group with documented nephrological comorbidity. The anatomical condition of the upper urinary tract, position and size, clarity and evenness of the contours of the kidneys, parenchyma thickness, the state of the calyx-pelvic system, the presence of concretions and formations were determined. An ultrasound examination of the kidneys revealed nephroptosis in 10 patients with multiple sclerosis, chronic pyelonephritis in 3, nephrolithiasis in 2, and ureteral stone in 1 patient. At the same time, it should be noted that the above pathology of the urinary system was found in 5 (5.2%) patients with two comorbid diseases, in 3 (2.1%) with three, and in 7 (7.3%) – with four or more comorbid diseases [4, 14].

Thus, the presence of inflammatory changes in laboratory urine tests, about which the authors write, as well as the phenomenon of clinical-instrumental dissociation that we discovered, indicates a possible underdiagnosis of urinary disorders in patients with multiple sclerosis, and gives grounds for recommending an ultrasound examination of the bladder for all multiple sclerosis patients with functional disorders pelvic organs [14].

When analyzing magnetic resonance imaging data of multiple sclerosis patients with disorders of the pelvic organs, it was found that foci of demyelination were most often found in the medial parts of the frontal lobes, brain stem, cerebellum, insula, midbrain, cervical and lumbar parts of the spinal cord [14].

Here we present a previously conducted correlation analysis by calculating the Pearson correlation coefficient, it was found that the presence and severity of pelvic organ dysfunction in patients with multiple sclerosis were most clearly correlated with the duration of the disease ($r=0.39$; $p<0.01$), the level of disability according to the EDSS scale ($r=0.35$; $p<0.05$), the level of fatigue (FSS) ($r=0.23$; $p<0.05$), due to direct correlations, and with indicators of quality of life (SF-36) ($r=-0.33$; $p<0.05$) due to inverse correlations (at the same time, the level of inverse correlations with levels of the quality of life was the highest in combined forms of pelvic organ dysfunction: ($r=-0.47$; $p<0.01$)[14].

In addition the analysis we described earlier: disorders of the brainstem functions (FS-3) ($r=0.27$; $p<0.05$) correlated with bladder dysfunction, mainly due to oculomotor symptoms; disorders of pyramidal functions (FS-1) ($r=0.25$; $p<0.05$), pain disorders (VAS) ($r=0.21$; $p<0.05$) correlated with bladder disorders; intestinal dysfunction correlated with cognitive disorders (MMSE) ($r=0.31$; $p<0.05$); disorders of sexual functions correlated with level of depression (BDI-II) ($r=0.38$; $p<0.05$), obesity (body mass index > 30 kg/m$^2$) ($r=0.32$; $p<0.05$)[4, 14].

But, on the other hand, reduced body weight, which often (according to our observations) [15] is a negative factor in the course of multiple sclerosis, correlated with persistent pelvic disorders that were poorly responsive for therapy (body mass index < 18.5 kg/m$^2$) ($r=0.24$; $p<0.05$) [4, 14].

Also, muscle spasticity and female gender were closely correlated with pelvic organ function disorders [14, 20].

Thus, in patients with multiple sclerosis with the presence of comorbidity, as shown earlier, where a significantly higher degree of disability ($p<0.05$), fatigue (FSS), depression (BDI-II), pain (VAS), cognitive disorders (MMSE), duration of the disease, a lower level of quality of life (SF-36), there is also a reliable prevalence of symptoms of pelvic organ dysfunction and combined forms of pelvic organ dysfunction [14].

Regarding the influence of various types of comorbidity on the development of symptoms of pelvic organ dysfunction in patients with multiple sclerosis, we found the closest correlations between bladder function disorders and nephrological comorbidity, lumbar pain syndromes; between intestinal function disorders and gastroenterological comorbidity and autoimmune comorbidity (especially diabetes and autoimmune thyroiditis); between sexual disorders and cephalgias and facial pain [4, 14].

The frequency of the most common symptoms of neurological deficits in patients with multiple sclerosis of the study group, investigated by us in previous works, in terms of the difference between the patients with multiple sclerosis without comorbidity and with comorbidity, is presented in table 5 [4, 14, 18].

From which it can be seen that pyramidal function disorders were equally common in both groups, cerebellar disorders prevailed in patients with multiple sclerosis without comorbidity, while the functions of the brain stem and cranial nerves, sensitivities were more often disturbed in patients with multiple sclerosis with comorbidity, as well as disorders of visual and cerebral functions, pelvic disorders were more common in this group.

*Table 5*

**Analysis of the frequency of the most common symptoms of multiple sclerosis in the study group in terms of comorbidity**

| No. | Groups of symptoms associated with impaired functions: | Number of patients (abs., %) | | |
|---|---|---|---|---|
| | | I group, n=109 | II group, n=107 | Total, n=216 |
| 1. | Pyramidal | 97 (89.0%) | 95 (88.8%) | 192 (88.9%) |
| 2. | Cerebellar | 95 (87.2%) * | 83 (77.6%) | 178 (82.4%) |
| 3. | Brain stem | 79 (72.5%) | 93 (86.9%)* | 172 (79.6%) |
| 4. | Sensitivities | 67 (61.5%) | 76 (71.0%)* | 143 (66.2%) |
| 5. | Intestines and bladder | 68 (62.4%) | 90(84.1%) ** | 158 (73.1%) |
| 6. | Visual | 46 (42.2%) | 70 (65.4%) ** | 116 (53.7%) |
| 7. | Cerebral | 88 (80.7%) | 96 (89.7%)* | 184 (85.2%) |

*Note.* – The level of significance of the differences in indicators of nervous system dysfunction in the comparison between groups I and II, * – p<0.05; ** – p<0.01.

*Table 6*

**Analysis of severity of disorders in patients with multiple sclerosis in the aspect of comorbidity**

| No. | Type of violation | Number of patients (abs., %) | | |
|---|---|---|---|---|
| | | I group, n=109 | II group, n=107 | Total, n=216 |
| 1. | Score on the EDSS scale, points | 3.42±1.13* | 4.34±1.21 | 3.84±1.33 |
| 2. | Average score of functional systems, points | 9.44±0.7 | 9.96±0.8 | 9.74±0.8 |
| 3. | The average number of exacerbations of multiple sclerosis per year in the previous period | 0.46±0.71* | 0.54±0.75 | 0.50±0.77 |
| 4. | The average rate of progression of multiple sclerosis in the previous period | 0.33±0.1 * | 0.39±0.2 | 0.35±0.2 |
| 5. | Pyramidal disorders, points | 2.6±0.5 | 2.7±0.4 | 2.7±0.7 |
| 6. | Spasticity, points | 0.6±0.1 | 0.9±0.2* | 0.7±0.2 |
| 7. | Static-coordination disorders, points | 2.5±0.1* | 1.8±0.2 | 2.1±0.3 |
| 8. | Disorders of the function of cranial nerves, points | 1.5±0.2 | 1.9±0.3* | 1.7±0.3 |
| 9. | Sensitivity disorders, points | 1.3±0.3 | 1.4±0.4 | 1.3±0.4 |
| 10. | Sexual disorders, scores | 0.5±0.1 | 0.7±0.1 | 0.6±0.1 |
| 11. | Intestinal and bladder disorders, points | 1.2±0.19 | 1.4±0.27 | 1.3±0.24 |
| 12. | Disorders of visual functions, points | 0.8±0.2 | 1.4±0.3* | 1.1±0.3 |
| 13. | Neuropsychological disorders, points | 0.9±0.1 | 1.7±0.2* | 1.2±0.2 |

*Note.* * – The level of significance of the differences in the indicators of impaired functions of the nervous system in the comparison between groups I and II, p < 0.05.

The following were also determined: the average score of functional systems and each functional system separately, the average number of exacerbations of multiple sclerosis per year in the previous period, the average rate of progression of multiple sclerosis in the previous period, in the group of patients with multiple sclerosis

Analysis of severity of disorders in patients with multiple sclerosis in the aspect of comorbidity, carried out in previous works [18], is presented in table 6.

It shows that pelvic function dysfunctions: both intestinal and bladder disorders and sexual disorders are higher in patients with multiple sclerosis with comorbidity compared to patients with multiple sclerosis without comorbidity.

In addition to medication, we used, described by us earlier, effectively acupuncture methods [14, 24–26] to treat pelvic organ dysfunctions in patients with multiple sclerosis: classical acupuncture, scalp acupuncture, electroacupuncture, laser acupuncture, thermopuncture, microwave acupuncture, which allowed faster and efficiently control individual symptoms of pelvic organ dysfunctions, or reduce their severity. In addition, the use of acupuncture methods made it possible to achieve a positive result in patients with persistent manifestations of pelvic organ dysfunction.

## CONCLUSIONS

1. The average level of prevalence of pelvic organ dysfunction in the patients with multiple sclerosis studied by us is 87.0%.

2. In the group II (patients with multiple sclerosis with comorbid pathology), there is a significant prevalence of symptoms of pelvic organ dysfunction and combined forms of pelvic organ dysfunction in comparison with the group I (patients with multiple sclerosis without comorbid pathology).

3. Pelvic organ dysfunctions in patients with multiple sclerosis were most clearly correlated with the duration of the disease, the level of disability according to the EDSS scale, female sex, the severity of fatigue and decrease of indicators of quality of life.

4. The use of acupuncture methods in patients with multiple sclerosis makes it possible to more effectively treat manifestations of pelvic organ dysfunctions.

## Information about the authors

**Svyrydova Natalia K.** – doctor of medical sciences, professor, Interregional Academy of Personnel Management, Kyiv; tel.. (099) 285-69-98. *E-mail: natalia.svyrydova@gmail.com*

ORCID: 0000-0002-2166-5904

**Chupryna Gennadii M.** – doctor of medical sciences, associate professor, professor of the department of therapy and rehabilitation, Interregional Academy of Personnel Management, Kyiv; tel.: (067) 405-78-25. *E-mail: gen7chupryna@gmail.com*

ORCID: 0000-0003-1351-015X

**Sereda Vitaly G.** – candidate of medical sciences, department of general medical disciplines, Interregional Academy of Personnel Management, Kyiv; tel.: (067) 410-45-27. *E-mail: servit1967@gmail.com*

ORCID: 0000-0003-2498-0333

## Відомості про авторів

**Свиридова Наталія Костянтинівна** – д-р мед. наук, проф., Міжрегіональна академія управління персоналом, м. Київ; тел.: (099) 285-69-98. *E-mail: natalia.svyrydova@gmail.com*

ORCID: 0000-0002-2166-5904

**Чуприна Геннадій Миколайович** – д-р мед. наук, доц., проф. кафедри терапії та реабілітації, Міжрегіональна академія управління персоналом, м. Київ; тел.: (067) 405-78-25. *E-mail: gen7chupryna@gmail.com*

ORCID: 0000-0003-1351-015X

**Середа Віталій Георгійович** – канд. мед. наук, завідувач, кафедра загальномедичних дисциплін, Міжрегіональна академія управління персоналом, м. Київ; тел.: (067) 410-45-27. *E-mail: servit1967@gmail.com*

ORCID: 0000-0003-2498-0333


## REFERENCES


1. Murray TJ. Multiple sclerosis: the history of a disease. New York: Demos; 2005. 248 p.
2. Chupryna G, Svyrydova N, Trufanov Y, Khanenko N, Cherednichenko T, Mykytei O, et al. Multiple sclerosis: treatment approaches in a historical perspective (clinical lecture, continued). East Eur J Neurol. 2016;10(4):4-10.
3. Chupryna GM. The use of reflexotherapy in the complex treatment of multiple sclerosis. In: Murashko NK, Morozova OG, Chupryna GM, editors. Reflexotherapy: national textbook. Kyiv: TOV SIKGRUP Ukraine; 2013, p. 281-300.
4. Chupryna G, Svyrydova N, Parnikoza T, Galusha A, Popov A. The course and approach to the treatment of pelvic organs disorders in patients with multiple sclerosis in the comorbidity. East Eur J Neurol. 2016;10(4):55-61.
5. Cordeau D, Courtois F. Sexual disorders in women with MS: assessment and management. Ann Phys Rehabil Med. 2014;57(5):337-47. doi: 10.1016/j.rehab. 2014.05.008.
6. DasGupta R, Fowler CJ. Bladder, bowel and sexual dysfunction in multiple sclerosis: management strategies. Drugs. 2003;63(2):153-66. doi: 10.2165/00003 495-200363020-00003.
7. Namey M, Halper J. Elimination Dysfunction in Multiple Sclerosis. Int J MS Care. 2012;14(1):1-26.
8. Murphy AM, Bethoux F, Stough D, Goldman HB. Prevalence of stress urinary incontinence in women with multiple sclerosis. Int Neurourol J. 2012;16(2):86-90. doi: 10.5213/inj.2012.16.2.86.
9. Dasgupta R, Wiseman OJ, Kanabar G, Fowler CJ, Mikol D. Efficacy of sildenafil in the treatment of female sexual dysfunction due to multiple sclerosis. J Urol. 2004;171(3):1189-93; doi: 10.1097/01.ju.0000113145.43174.24.
10. Chupryna G. Quality of life in patients with multiple sclerosis comorbidity aspect with SF-36. East Eur J Neurol. 2015;(6):50-5.
11. Polman CH, Reingold SC, Edan G, Filippi M, Hartung HP, Kappos L, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the «McDonald Criteria». Ann Neurol. 2005;58(6):840-6. doi: 10.1002/ana.20703.
12. Polman CH, Reingold SC, Banwell B, Clanet M, Cohen JA, Filippi M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011;69(2):292-302. doi: 10.1002/ana.22366.
13. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurol. 1983;33(11):1444-52. doi: 10.1212/wnl. 33.11.1444.
14. Chupryna GM. Multiple sclerosis: clinical and pathogenetic characteristics and therapeutic approaches taking into account comorbidity [dissertation]. Kyiv: Shupyk National Medical Academy of Postgraduate Education; 2017. 409 p.
15. Murashko NK, Chupryna GM. Analysis of comorbidity and lifestyle factors in patients with multiple sclerosis. Fam Med Eur Pract. 2013;49(5):85-7.
16. Chupryna GM. Evaluation of the data of laboratory studies in patients with multiple sclerosis in the aspect of comorbidity. Med Affair. 2019;1150(1-2):75-82.
17. Marrie RA, Horwitz RI, Cutter G, Tyry T, Vollmer T. Association between comorbidity and clinical characteristics of MS. Acta Neurol Scand. 2011;124(2):135-41. doi: 10.1111/j.1600-0404.2010.01436.x.
18. Chupryna GM, Svyrydova NK, Galusha AI. Clinical features of neurologic disturbances in patients with multiple sclerosis and acute acute disseminated encephalomielitis in the aspect of comorbidity. Fam Med Eur Pract. 2018;(1):86-90. doi: 10.30841/2307-5112.1.2018.135320.
19. Cutter GR, Zimmerman J, Salter AR, Knappertz V, Suarez G, Waterbor J, et al. Causes of death among persons with multiple sclerosis. Mult Scler Relat Disord. 2015;4(5):484-90. doi: 10.1016/j.msard.2015.07.008.
20. Chupryna G, Svyrydova N, Galusha A. Peculiarities of pyramidal and sensitive disorders in patients with multiple sclerosis under conditions of comorbidity. Fam Med Eur Pract. 2016;66(4):97-100.
21. Chupryna GN. Dental disorders in patients with multiple sclerosis: features of the course in terms of comorbidity, search for common pathophysiological mechanisms. East Eur J Neurol. 2015;(5):44-8.
22. Svyrydova NK, Chupryna GM. Pathogenesis, clinic, diagnosis, complex treatment of insomnia of various origins using reflexotherapy methods. East Eur J Neurol. 2016;2(1):26-35.
23. Chupryna G. Psychopathological disorders in patients with multiple sclerosis under conditions of comorbidity: prevalence and features of the course depending on the type of concomitant pathology. Fam Med Eur Pract. 2015;61(5):168-70.
24. Chupryna GM, Murashko NK. Approach to reflexotherapy in the complex treatment of patients with multiple sclerosis, taking into account comorbidity. Fam Med Eur Pract. 2013;(4):77-9.
25. Zhang T, Liu H, Liu Z, Wang L. Acupuncture for neurogenic bladder due to spinal cord injury: a systematic review protocol. BMJ Open. 2014;4(9):e006249. doi: 10.1136/bmjopen-2014-006249.
26. Karpatkin HI, Napolione D, Siminovich-Blok B. Acupuncture and multiple sclerosis: a review of the evidence. Evid Based Complement Alternat Med. 2014;2014:972935. doi: 10.1155/2014/972935.