SILENT PROGRESSION

Reveal invisible symptoms of **multiple sclerosis progression** in time

Discover the possibilities of overall disease management

Contents

SM Treatment Centers

2nd department of Neurology
(University Hospital in Bratislava – Kramáre)

1st department of Neurology
(University Hospital in Bratislava – Old town)

Department of Neurology
(University Hospital in Bratislava – Ružinov)

Department of Neurology
(St. Michal's Hospital in Bratislava)

Department of Neurology
(J.A. Reiman University Hospital in Prešov)

Department of Neurology
(University Hospital in Martin)

Department of Neurology
(Louis Pasteur University Hospital in Košice)

Department of Neurology
(University Hospital in Nitra)

Department of Neurology
(University Hospital in Trnava)

2nd department of Neurology
(University Hospital in Banská Bystrica)

Department of Neurology
(Central Military Hospital in Ružomberok)

Department of Neurology
(University Hospital in Trenčín)

Department of Child Neurology
(National Institute of Children's diseases, Department of Pediatrics, Medical Faculty, Comenius University in Bratislava)

Dear friends,

I'm sure you'll agree with me if I say that the most expensive treatment is the treatment of an uneducated patient.

This idea is also the main reason why we published this educational brochure with the distinctive title "Silent progression of multiple sclerosis'. Educated people understand the challenges of their MS, cooperate better with the medical doctor and other health professionals and have much bigger chance of keeping their MS under control and having the highest quality of life possible.

This educational brochure brings people with MS several new perspectives on MS, better understanding of management and current treatment options. No less important part of it is about the need of social support and meeting other people with MS.

We have prepared an educational brochure for you on the occasion of the 30th anniversary of the establishment of Slovak multiple sclerosis association in collaboration with health proffesionals from workplaces, where people with MS are treated.

Jarmila Fajnorová
President of the Slovak MS Association

MULTIPLE SCLEROSIS - WHY DOES IT OCCUR AND WHAT CAUSES IT?

Assoc. prof. Jarmila Szilásiová, MD, PhD.
Department of Neurology (Louis Pasteur University Hospital in Košice)

Multiple sclerosis (MS) is a chronic disease affecting the brain and the spinal cord (central nervous system – CNS), causing an inflammatory process. MS cannot be completely and definitively cured, but in the last 20 years, many new effective drugs have been developed and introduced as a treatment, which enables people to have a good quality of life.

The exact cause of MS is still unclear. However, the autoimmune mechanism is considered to be one of the causing agents. It means that immune system damages its own tissues, especially the protective conductive sheath of the nerve cells, present in the brain and the spinal cord - myelin, but also the nerve cells (neurons) and their branches, that conduct a nerve signal (axons). MS is one of the most debilitating neurological non-traumatic diseases of young adults in our geographical area.

MS most often begins between the ages of 20 and 40, and it is not uncommon for MS to appear in 15-year-olds, or after the age of 50. The occurrence in women compared to men is in a ratio of 2:1. The incidence of MS in Slovakia is moderately high; the prevalence is approximately 100-150 cases per 100,000 people.

The disease is not hereditary, but the incidence of MS in several members of one family can be in 3-10%, the risk of developing MS in a child whose parent has MS is 2-5%.

Several factors are involved in the development of the disease, including certain genetic predispositions as well as external, or environmental, factors, including recurrent viral and bacterial infections, obesity, cigarette smoking, low levels of vitamin D with the lack of sun exposure and altered composition of gut microbiota (nutritional factor).

All of these factors lead to an abnormal response of the immune system, especially immune cells called T and B lymphocytes. In a healthy individual, these cells have protective function. Inflammation occurs in the brain and the spinal cord in multiple small areas. Sites of inflammation contain many immune cells, where the myelin is damaged or destroyed. This phenomenon is called demyelination. Damaged fibres can no longer conduct nerve signal through a neural pathway fast enough, or the signal

transmission stops completely. A change in the structure of the nerve cell coating, with the destruction of myelin, is followed by the formation of a scar at this site (gliosis) and if the fibre, without the myelin sheath, is exposed for a longer period of time, it ruptures, which is called the loss of the axon.

Axon loss is permanent, as axons don't have the ability to regenerate or repair. We call this a process of neurodegeneration. In addition to the neurons themselves, as a result of inflammation, damage occurs in other important cells – oligodendrocytes. Normally, oligodendrocytes form a myelin sheath around the neurons. Permanently damaged fibres are replaced by scars (gliosis), also called „sclerotic plaques". The historical name of the disease „Sclérose en plaques" comes from the name of the plaques. These plaques are spread in the brain and the spinal cord. There are different degrees of inflammation, demyelination, or axonal loss in each person. The size of the lesions can range from a few millimetres (5-9 mm) to a few centimetres, exceptionally over 3 cm. Apart from the brain, inflammation is often formed in the cervical, less often thoracic spinal cord.

The loss of myelin, as well as axons, leads to a loss of the brain and spinal cord volume - this process is called atrophication. Brain atrophy is also observed in healthy people, and the decrease in brain volume is induced by age-related changes, but atrophy in people with MS is accelerated. In people with MS, an annual loss of the brain tissue was found ranging from 0.6 to 1.0%, compared to natural aging, where there is a decrease in the brain volume of about 0.2-0.4% per year. Apart from the white brain matter, which is made up of nerve fibres, the disease also affects the grey brain matter, which is made up of the bodies of the brain's neuronal cell bodies in the cerebral cortex.

What is a relapse?

MS is very variable in its clinical manifestation and course, and each person with MS develops a combination of various symptoms. After the first manifestation, in most cases, new events of worsening or worsening of already existing symptoms occurs. These events are called relapses, and they alternate with the periods when the symptoms completely disappear or become less serious – these periods are called remissions. The duration of remission varies, is unpredictable and can last for weeks, months or years. Worsening of the clinical symptoms is usually accompanied by the formation of new lesions in the brain or the spinal cord. Relapses can cause permanent neurological as well as psychological symptoms. If the disease is not treated, at least one relapse per year may occur and the person's condition can worsen permanently. Especially in young people, at the beginning of the disease, symptoms last for several days to weeks and improve relatively well, even disappear completely. Later, however, there is always present a permanent loss of a specific neurological function, as a result of a relapse, or a permanent neurological deficit. This deficit also called disability, which, after several years of illness, can lead to a loss of employment, need for assistance in walking (e.g. mallet, crutches, walking apparatus, wheelchair), or need for assistance in daily activities.

Subtypes of the disease, symptoms of the disease

MS can be divided into three subtypes (also called clinical forms, or the MS phenotypes). Most people begin with a relapsing course of MS (RMS) – MS begins this way in approximately 85% of all people. Relapses alternate with the periods of stabilisation. The relapse is an appearance of new or wor-

sening of older symptoms lasting more than 24 hours, and these conditions are not caused by another disease, e.g. infection, fever, etc. People with MS, who have more relapses during the first two years of the disease, and/or the time between the first and second relapse is short, have a prognosis of a more severe disease course. Approximately 50% people with MS do not fully recover after a relapse. The first MS relapse is called Clinically Isolated Syndrome (CIS). If people won't start treatment on time, then it's possible they experience another relapse in the next 2 - 5 years.

MS and its first event (CIS) typically manifests itself as an:

• impaired vision, as a result of the inflammation occurring in the optic nerve (optic neuritis). It manifests as a foggy or blurred vision in one eye,

• impaired perception of sensory stimuli (touch - tingling, numbness, perception of heat, cold, pain, perception of position or movement of the limb and torso). It's caused by an inflammatory lesion, or more lesions, in the cervical, less often thoracic or lumbar spinal cord, and is called partial transverse myelitis. Altered sensitivity is often accompanied by impaired lower urinary tract control, e.g. the person is unable to urinate completely, or feels a frequent urge to urinate, or has incontinence.

• impaired balance, coordination of movements, speech, or double vision – these are the symptoms of brainstem cerebellar syndrome. People experience dizziness, double vision, numbness in a part of the face, mouth, or tongue, loss of balance when standing and walking, feeling as if „drunk", hand and leg dexterity are also impaired.

These three symptom groups are among the most common symptoms at the beginning of MS, they can occur alone or combined together. Rarely, MS can also start with paralysis, clumsiness (paresis) of half of the body (right or left, called hemiparesis), stretching of the torso or limbs to an atypical position (dystonia), twitching in the facial muscles (facial hemispasm). MS is often accompanied by mood disorders, such as depression or anxiety, excessive fatigue, feeling of electrification in the body when flexing the neck (Lhermitte's sign), painful cramps and tension in the legs, feeling of a locking „hoop" around the waist (or MS hug), sleep disorders. Symptoms such as hearing loss, epileptic seizures, swallowing disorders, tremors, or head tremors are rare.

Relatively common symptom is a cognitive dysfunction. Symptoms tend to be mild, but affect 40 to 70% of people at all stages of the disease, even during the first manifestation of the disease. It mainly affects attention, memory (working, short-term), learning, preservation and reproduction of information, or abstract thinking. People complain of a slight slowdown in thinking, poorer expression of words. The symptoms of MS are very variable and none of them are typical only for MS, they also occur in other diseases of the brain and the spinal cord, such as stroke, virus infection, migraine etc.

The secondary progressive MS (SPMS) is a continuation of the relapsing MS. This is a permanent deterioration and increase of the disability. It is observed in 50-80% of people with RMS about 7-15 years after the disease onset. After the initial alternation of relapses and remissions, chronic progression occurs despite treatment – gradual permanent deterioration with or without the indicated relapses.

The primary-progressive form (PPMS) of the disease affects about 10% of all people with MS, and from the beginning, there is a steadily growing neurological deficit with no apparent relapses and no remission.

All types of MS can be further subdivided into active or inactive form. The active form means that the person with MS has a clinical relapse or disease activity showed on magnetic resonance imaging (MRI). The activity is manifested by the presence of new lesions found on MRI scans or lesions, which are highlighted after the administration of the gadolinium. The term disease progression refers to an increase in disability over a certain period of time.

Prognosis

The prognosis of further development of the disease is very individual for each person. Important factors are – disease activity, number and severity of individual relapses during the first years from the disease onset, nature of initial symptoms, age, and sex. Lesions in the brain and spinal cord found on MRI scans are also important for the prognosis. Their number, location, activity after administration of the gadolinium – assessed during the first relapse. Relatively favourable prognostic factor is female gender, disease onset before the age of 40, initial relapsing-remitting course, complete recovery after the first relapse if the disease started with visual or sensory disturbances, and a low number of relapses during the first years of the disease.

Diagnostic process

The diagnostic process comprises of taking a medical history, observation of clinical symptoms, interpreting findings of different relevant examinations, and the exclusion of other possible diagnoses. It follows internationally valid diagnostic criteria, currently the most recent McDonald criteria from 2010 were revised in 2017. There is no single specific test that clearly confirms or excludes MS.
A thorough and detailed medical history and the various clinical symptoms indicates the variable character of the lesions and clinical symptoms in the brain and spinal cord in time and space. When diagnosing MS, it's necessary to exclude all diseases that are manifested by symptoms similar to MS. This needs to be done via various examination methods. Sometimes the diagnostic process is longer because the symptoms may mimic other diseases, such as toothache, panic attack, tetany, spine or joint disease etc. In particular, diseases of the sensory system in young people are often incorrectly evaluated as spinal cord injuries, anxiety disorders, or stress. Dizziness, excessive fatigue, or cognitive impairment are also underestimated symptoms.

Magnetic resonance imaging

If MS is suspected, based on the medical history and the presence of specific symptoms, magnetic resonance imaging (MRI) is indicated.
MRI of the brain and the spinal cord is a method that allows us to see lesions with altered signals, which are lesions of demyelination, and also allows us to see the type of lesions where a loss of axons is recorded. We evaluate their number, placement, localisation in the brain and the spinal cord, size, and activity after administration of the gadolinium on several scans (image 1).

On the T2 weighted image, the lesions appear as highlighted, the hypersignal plaques, hyperintensive, and the lesions with axonal losses appear hyposignal, called „black holes," appearing on the T1 weighted image. Lesions on MRI scans must be distinguished from other similar lesions, which can be a result of e. g. brain infections, damage (blockage) of small cerebral vessels (vascular lesions), diabetes, high blood pressure, diseases of the bloodstream, and others.

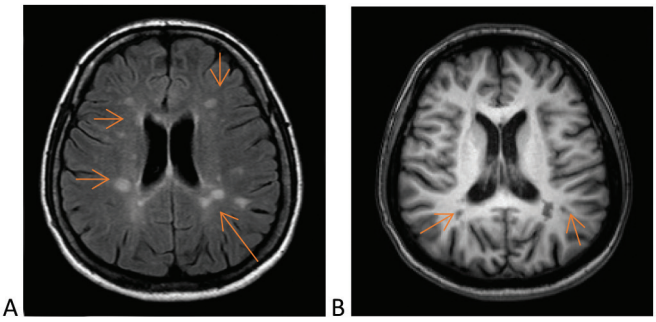


Image 1. MRI of the brain. A / Image of multiple hypersignal lesions (T2 weighted image) in both cerebral hemispheres. B / Image with hyposignal lesions (T1 weighted image).

(Archive of the Department of Neurology, Faculty of Medicine, PJŠU and LPUH Košice, and the Department of Radiodiagnostics and Examination Methods, Faculty of Medicine, PJŠU and LPUH Košice).

Examination of the cerebrospinal fluid

Examination of the cerebrospinal fluid, taken by lumbar puncture (we take a small amount of the liquid), is necessary to distinguish MS from other diseases. In the cerebrospinal fluid of the people with MS, it's possible to confirm the presence of oligoclonal antibody bands by the isoelectric focusing bands of antibodies (IgG), which are formed by B cells directly in the brain and spinal cord. The presence of oligoclonal antibody bands is typical for MS and is common in 95-97% of patients.

Evoked potentials

Other examination methods, such as evoked potentials, are also used in the diagnostic process. They detect a slowdown of the nerve signal in specific neural pathways, a change in the brainwaves, a decrease in the amplitude of the brainwaves, which supports the consideration of damage to the myelin or whole axons of the specific neural pathways. A typical finding on the visual evoked potentials (VEP) is an extension of the P100 wave latency and suggests a demyelinating type of damage to the optic pathway, especially the optic nerve. Prolongation of P100 wave latency in VEP is present in up to 70-90% of people with MS.

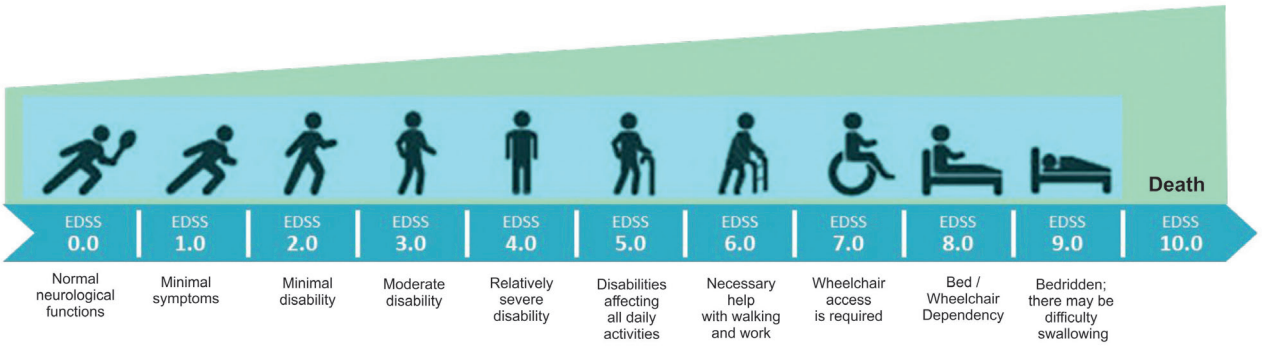
SILENT PROGRESSION OF MULTIPLE SCLEROSIS - HOW WE UNDERSTAND IT?

Slavomíra Kováčová, MD
Department of Neurology (University Hospital in Nitra)

It is very important for neurologists to be able to assess the rate of progression of multiple sclerosis (MS) in real time and compare the current condition with the patient‘s condition in the past. On the basis of such a comprehensive examination, they can say whether the patient ,s condition has worsened or improved and whether the disability is permanent.

Progression in clinical practice is most often assessed by the EDSS (Expanded Disability Status Scale). (Fig 1)

Figure 1: EDSS scale



To determine the degree of EDSS, the physician must examine and evaluate 7 areas of the patient‘s health. That includes the assessment of:

- visual function (symptoms may include visual impairment, blurred vision or vision field loss)
- motor functions (symptoms may include impaired mobility, stiffness, limb weakness)
- cerebellar function (symptoms may include problems with balance, tremor)
- brainstem function (symptoms may include double vision, problems with speech or swallowing)
- sensory (symptoms may include abnormal skin sensation like tingling, numbness or pain)
- bowel and bladder functions (frequency and/or urgency or urination, incontinence, inability to empty the bladder completely)
- cerebral functions (problems with thinking and memory)

Motor functions and especially the lower limbs mobility play an important role in this scale.

A patient who is not able to walk more than 500 meters has a score of 4 and a patient who is confined to a wheelchair has EDSS score 7.

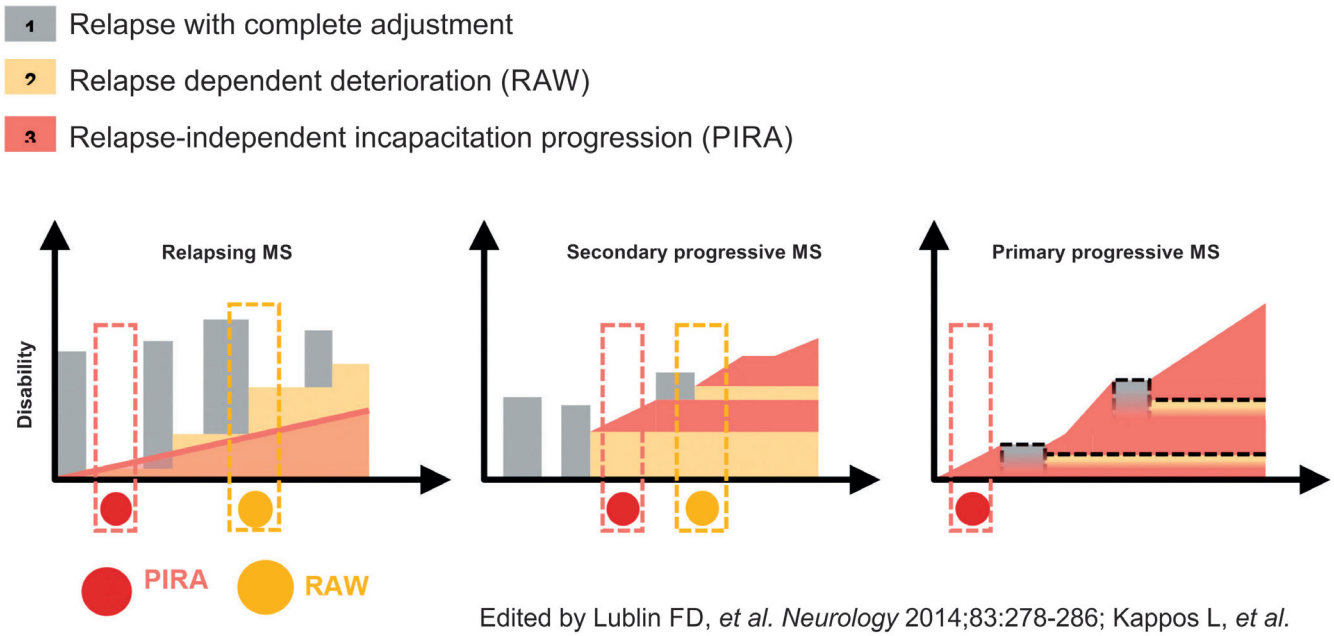
What types of progression do we recognize?

What happens in the body during an inflammatory attack (relapse)? Depending on which part of brain or spinal cord is affected, new neurological symptoms will appear or the previous ones will get worse. During the relapse EDSS may increase,

Then the EDSS increases, but this condition is not irreversible and the symptoms subside completely or partially within a few months and the patient‘s condition stabilizes. If the patient‘s condition returns to the original level, we speak of a complete recovery from relapse. If the symptoms persist after relapse, we are talking about a partial recovery from relapse. In this case, **progression in the patient is related to relapse activity** (RAW – relapse associated worsening).

However, in multiple sclerosis, we also know the increase in progression, which is not related to the activity of relapses. We often observe a worsening of the symptoms of the disease, even in the early stages and with a low degree of disability. We call this progression **PIRA** (Progression Independent of Relapse Activity) (Fig. 2). We could also call this progression „silent“ progression, as the symptoms of the disease slowly worsen. The patient himself is often unaware of this slow change, and even the doctor may not detect it during a routine neurological examination.

Figure 2: Progression dependent and independent of Relapse Activity



Edited by Lublin FD, *et al. Neurology* 2014;83:278-286; Kappos L, *et al.* ECTRIMS 2018 (P547); Kappos L, *et al. Mult Scler* 2018;24:963-973.

PIRA is probably associated with chronic inflammation and direct involvement of nerve cells in the gray matter (the part of the brain where nerve cells are located). It has been found that clusters of immune cells, mainly B and T lymphocytes form meningeal aggregates mimicking the lymph nodes in the body. These, so-called lymphoid follicular structures are co-responsible for the presence of chronic inflammation and subsequent progression of MS, as well as for cognitive impairment.

Can we detect „silent" progression?

The EDSS scale is not very suitable for detecting the so-called silent progression. However, there are other, more sensitive tests that should be performed.

The first of these is the T25FWT (Timed 25-Foot Walk Test), a 25-foot walk speed test in which the patient is asked to walk a specified distance (about 8 meters back and forth) while the staff measure time. (Fig. 3). If the change in walking speed is more than 20% compared to the previous performance, it is considered as significant worsening.

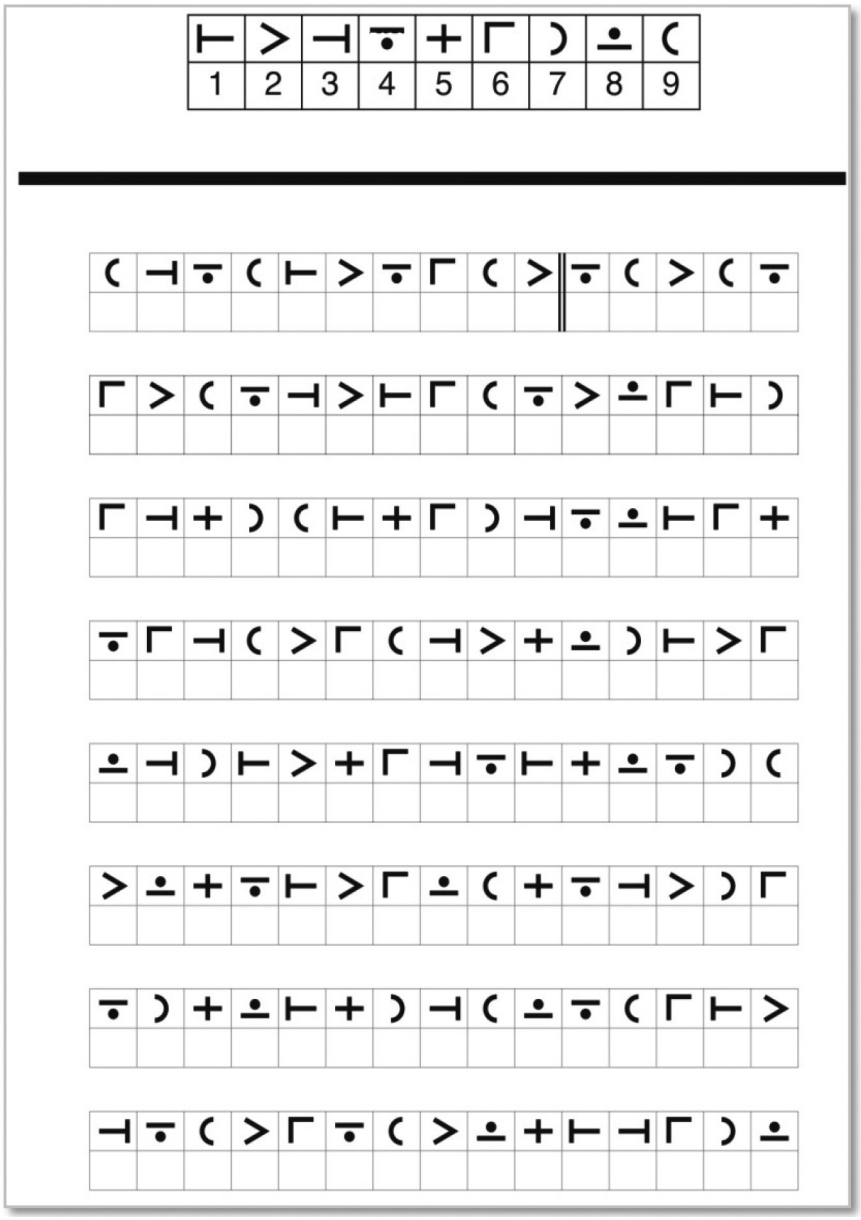
Figure 3: T25FWT

The second test focuses on upper limb function. It is called 9HPT (9-Hole Peg Test). The patient removes the pegs from the bowl with his right and left hand and inserts them into 9 holrs and back (Fig. 4). Of course, also with the assistance of staff who measure time. A change in time that is more than 20% is considered significant.

Figure 4: 9-HPT

The last test that can help to detect silent progression is the cognitive function test, SDMT (Symbol Digit Modalities Test), a test of assigning numbers to characters (Fig. 5). This test is especially recommended as a screening method for monitoring od cognitive disorders in MS. If the change in the test is more than 10% compared to the previous performance, the complex neuropsychological examination should be done.

Figure 5: SDMT



Using these three simple tests with EDSS can increase the sensitivity of progression detection. In practice, this means that if a neurologist detects a worsening of results in these tests and registers progression despite a stable EDSS, he may consider more intensive patient monitoring and possibly a change in treatment.

In order to detect the silent progression in MS, these tests should be performed at least once a year on each patient (if he or she is able to perform the test).

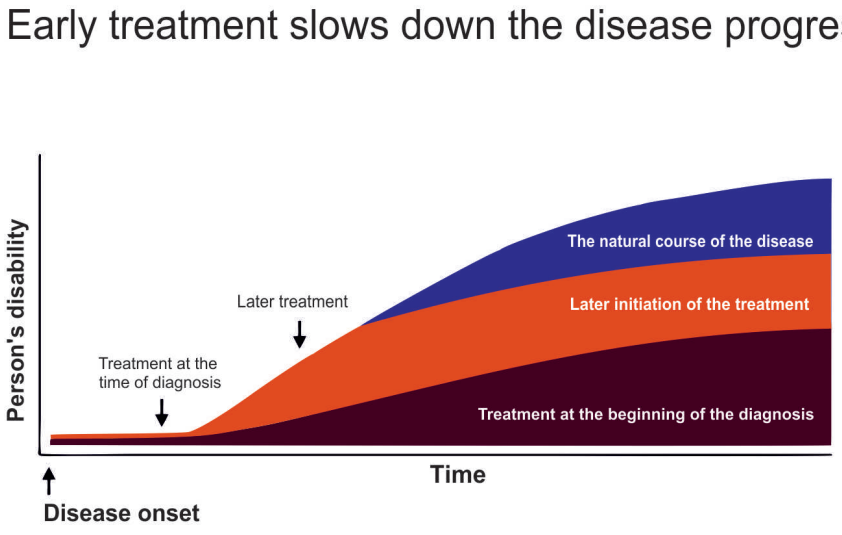
Nowadays, the development of digital technologies allows us to use different devices – such as smartphones. These devices can monitor the patient‘s condition and his progression for 24 hours. There are ongoing clinical trials of applications that can significantly help patients and physicians to identify changes during MS.

TREATMENT OF MULTIPLE SCLEROSIS – WHAT ARE THE CURRENT OPTIONS?

Darina Slezáková, MD, PhD.
II. Department of Neurology, (University Hospital in Bratislava – Kramáre)

As a long term effect of the disease, most people with multiple sclerosis (MS) progress to significant and irreversible physical and psychological disability. The degree of disability can progress from relatively mild to severe in just a few years. Neuropsychological symptoms (such as fatigue, memory impairment, difficulties with maintaining focus, anxiety, depression, etc.) can also occur. Even if it appears to be a mild form of the disease, due to a very high interindividual variability of the disease course, any delay in the treatment initiation or reluctance to make necessary changes is risky and incorrect, as today's medical guidelines state. Early effective treatment is the only prevention of the disability progression (Image 1). Even though we are still unable to cure MS, trying to maintain the inflammatory process under control and halting the process of the nerve tissue destruction can protect endangered nerve tissue in the long term.

Image 1. Prognosis of a person with MS depending on the time factor of treatment initiation



Modified by Trapp et al. Curr Opin Neurol. 1999;12:295; Trapp et al. Neuroscientist. 1999;5:48; Trapp et al. N Engl J Med. 1998;338:278; Jeffery. J Neurol Sci. 2002;197:1; Cohen et al. J Neuroimmunol. 1999;98:29.

What is the ideal treatment for a person with MS?

Acute treatment of an MS relapse consists of the corticosteroid treatment (methylprednisone), another long-term option, disease modifying treatment (DMT), already falls within the competence of specialised workplaces for the treatment of MS.
DMT is designed to reduce the disease activity (number of relapses) and slow its progression. The goal of the treatment is the NEDA concept („no evidence of disease activity“, Image 2), which means there's no disease activity recorded – no relapses, no disability worsening, or new inflammatory lesions on MRI.

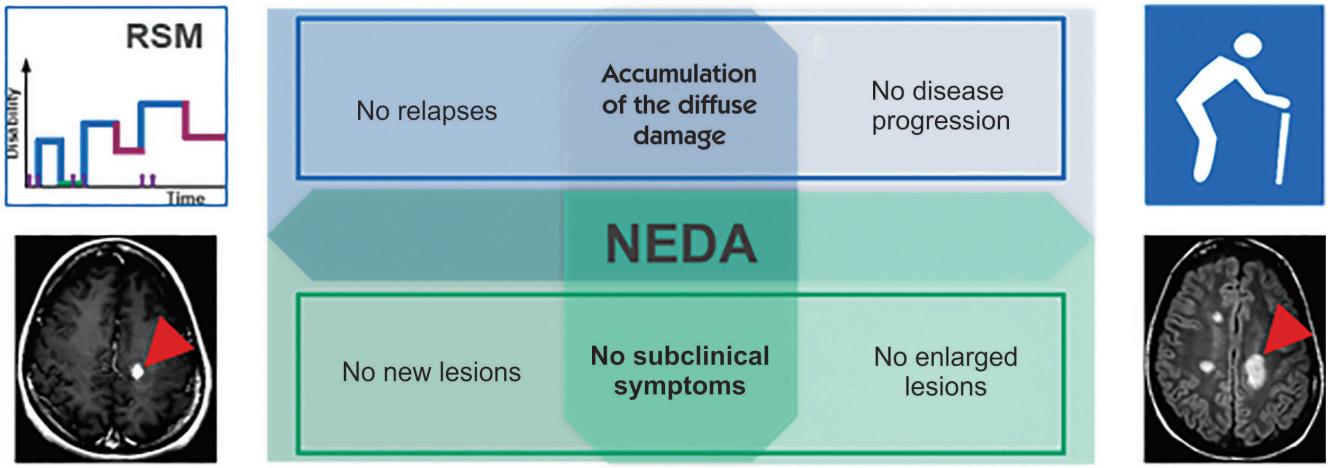


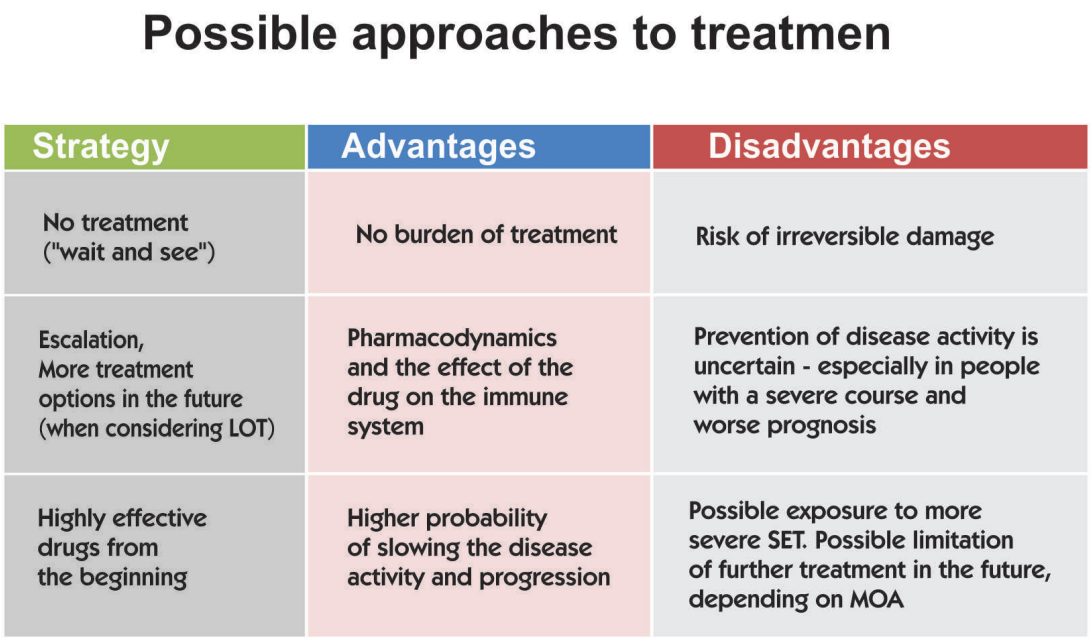
Image 2. NEDA concept

There are several lines where DMTs are included. Their use in Slovakia is subjected to the so-called indication restrictions, which are regulated by the Ministry of Health of the Slovakia.

First line DMTs include interferons beta-1b, glatiramer acetate, teriflunomide, and (more or less) dimethyl fumarate. If the disease course is expected to be mild, we start with the first line DMTs (efficacy approximately 30%, higher safety). If the person does not have a good response to the current treatment, no time should be wasted and the treatment should be escalated, or changed to a DMT with higher efficacy (Image 3).

Second line DMTs (50-80% efficacy) include natalizumab, ocrelizumab, alemtuzumab, cladribine, and fingolimod. In certain cases, it's more appropriate to start the treatment with this line of DMTs, because if the person has unfavourable prognosis, there is a risk of rapid disease progression if we start with the first line DMT.

Image 3. Current approach to the treatment of a person with MS



Unfavourable clinical prognostic factors for evaluating person's initial treatment include:

a) Residual symptoms after a relapse (new symptoms, as a result of a relapse, that didn't improve after the corticosteroid treatment),

b) short interval between relapses and higher frequency of relapses in the first years of the disease,

c) high initial EDSS and high EDSS in the first 5 years of the disease (disability or incapacity of the person),

d) progressive course of the disease,

e) age 40 or more years at the disease onset,

f) men with MS,

g) when the first relapse is accompanied by difficulties with urinating, severe movement disorders, cerebellar symptoms, or involvement of several neurological areas at the same time,

h) presence of the brainstem and spinal cord lesions at the initial MRI.

While monitoring the effect of treatment itself on achieving remission (stabilisation) of the disease, it's necessary to monitor not only the clinical condition, but also the disease activity showed on MRI scans, which means change in structure or appearance of new lesions in the brain and/or spinal cord. MRI is an important indicator subclinical disease activity and, in case of a significant increase in the number of lesions or their activity, a change in treatment is indicated. Even if people are feeling well and haven't experienced worsening of their condition, and therefore don't understand why the treatment should be changed. Disease activity, which we can detect by an MRI, clearly precedes the clinical manifestation of the disease progression (or relapse), and therefore a change in treatment is significant prevention of the disability progression, which may increase with each subsequent relapse.

At this time, it's possible to use an MRI to monitor the loss of the brain volume, or brain atrophy, which is another indicator of the treatment effectiveness and is manifested by worsening of

memory impairment, often overlapping with fatigue or depression. In clinical follow-up, the rate of relapses is related to the disability progression and the rate of remission (stabilisation) is prognostically significant in the long term. Change of treatment is indicated in people with a severe relapse whose clinical condition haven't improved within 6 months. This is because most of the relapses are resolved within 3 months after their onset in people in an early-stage of MS, and in 10% of people within 6-12 months after the onset of relapse.

Regular monitoring of the person on disease-modifying treatment (DMT)

There's one important thing we need to know about DMT – depending on the type of the DMT, it affects the immune system, e.g. some DMTs with the desired mechanism of action cause a significant decrease in some white blood cells.

Therefore, depending on the type of DMT, we regularly monitor blood test results, especially complete blood count, in every person with MS who's treated. Liver and kidney tests or laboratory tests of thyroid function are equally important. Frequent laboratory tests (monthly or every 3 months) are effective prevention and are able to detect side effects of treatment that can be resolved effectively (e. g. dose reduction or change of treatment, haematological and endocrinological treatment, liver protection, treatment of urinary tract infections and more). At workplaces for the treatment of MS, we are able to regularly test people with MS and also detect potential risks, e. g. presence and level of JC (John Cunningham) virus during treatment with natalizumab, which at a specified duration of treatment may cause a severe devastating brain infection (progressive multifocal leukoencephalopathy, or PML). Managing and monitoring possible side effects of the treatment is, as a process, very well designed and therefore concerns about side effects as a reason for refusing treatment with a clear benefit to the person with MS are not justified. To put it bluntly, the person with MS can „safely become disabled" or accept the risk of possible side effects and live a good life with the maximum possible deceleration of the disease progression.

Therefore, people's knowledge is very important factor when making decision about the treatment, as well as people's interest and responsibility, when it comes to cooperation in the treatment, monitoring their condition at home, as well as for regular check-ups with their doctor.

Without good person-doctor cooperation, a person cannot be stabilised and satisfied

Any treatment of a chronic disease, such as MS, depends mostly on a cooperation, or a person's adherence to the treatment. Research clearly confirms that fewer relapses, hospitalisations, not to mention a lower degree of the disability, are observed in people with a high degree of adherence to the treatment. A person who's treatment is well-managed adheres to the treatment regimen, has a significantly higher chance of staying stable, which clearly increases quality of life.

What are the current treatment options?

Therapeutic options consist not only of the classic first-line injection treatment. Since the launch of interferon beta-1b in 1993, the range of therapeutic options has been expanding persistently and rapidly.

First line injectable therapy, which includes **interferons beta-1b and glatiramer acetate**, is safe but less effective standard. It's designated for people with low disease activity. Side effects such

as flu-like symptoms and changes in some laboratory parameters (e. g. increased liver parameters) during the treatment with interferons beta-1b, or skin reactions with both injectable preparations can be well managed, which is a knowledge based on many years of experience. In person is treated with interferons beta-1b, the activity of the MxA protein is controlled. This protein is produced by the action of interferon beta-1b and therefore its reduction means insufficient effect of this treatment and a possible risk of a relapse.

Glatiramer acetate is suitable DMT for women planning pregnancy, as it's safe to take during pregnancy, or for people with more severe disorder of the immune system, thyroid disease, liver disease. It's administered 3 times a week subcutaneously, with the risk of lipodystrophy (adipose tissue disorder) with the long-term application, but without flu-like symptoms. Occasionally, there may be a post-injection reaction (chest tightness, shortness of breath, similar to a panic attack), which, however, is not a manifestation of an allergy reaction, isn't a life-threatening condition and it resolves itself spontaneously.

The emergence of a peroral treatment in Slovakia a couple of years ago offered the possibility to manage person's adherence to treatment more effectively, especially because of no unpleasant skin reactions or fear of injections.

Teriflunomide is given as a tablet, taken once a day. It has similar efficacy in suppressing disease activity as injectables and is very well tolerated. Some people report gastrointestinal (GIT) problems (digestive tract problems) and hair loss during the first months of treatment, which usually is not a reason to stop the treatment. As a part of laboratory tests, it's necessary to monitor blood parameters, especially liver parameters, regularly every 3 months, because they tend to worsen temporarily. The DMT damages the foetus during pregnancy, therefore strict use of contraceptives is required. However, this DMT can be quickly eliminated from the body using a special substance – cholestyramine.

Dimethyl fumarate is taken twice a day as a capsule. Its effectiveness is somewhere between the first and second line treatments. Ideal situation is when we start to treat a newly diagnosed person with this DMT when the disease activity is moderate. The most common side effects are redness (30%) and GIT problems (40%), which occur mostly during the first month of treatment, but usually tend to get better later. Liver enzymes increase temporarily during the first months of the treatment. During the treatment with dimethyl fumarate, it's important to regularly monitor white blood cells count every 3 months to prevent potentially serious infection complications. A significantly low white blood cells count lasting more than 6 months is a reason to discontinue the treatment, especially because of a risk of a serious brain infection, the progressive multifocal leukoencephalopathy (PML) - see for more information on PML in natalizumab.

Natalizumab and fingolimod are among the first available second-line drugs for people with high disease activity.

Natalizumab is a biological treatment that is administered once in a 4 - 6 weeks intravenously (IV). It's well tolerated. More frequent herpes infections were observed in some people. The threat is an occurrence of the aforementioned serious brain infection PML (progressive multifocal leukoencephalopathy), which can be fatal or can be completely disabling for the person. Therefore, people should be monitored regularly for the presence of the JC virus in their blood, based on well-

defined criteria. The predisposition for this disease is in particular a previous immunosuppressive treatment causing a suppression of the immune system. PML may also occur during the treatment with fingolimod.

Fingolimod is taken once a day as a tablet. It‘s very well tolerated. During the treatment with this DMT, as in the case of biological treatment, more frequent herpes infections were observed, which is usually not the reason for a change of treatment, if the person’s health condition is good and stabilised. When taking the first dose of fingolimod, a 6-hour follow-up of each person is required to monitor the ECG and blood pressure for possible bradycardia (decrease of the heart rate). Laboratory parameters should be monitored every 3 months, especially white blood cells count and liver function. People undergo preventive eye and skin examinations.

Alemtuzumab is a biological DMT that is given in 2-3 cycles of IV administration during a few days, each time once a year. In case of this treatment, premedication should be given to the person before infusion to suppress infusion reactions occurring during the administration of an infusion or other potential treatment adverse events (e. g. herpes infections). This DMT requires thorough monitoring of laboratory parameters each month during 4 years from the last cycle of the treatment. In particular, blood count, thyroid and kidney functions are monitored because of the possible damage, and with such frequent monitoring, the detection of possible side effects is very successful and can be resolved quickly.

Strokes, recently reported in the United States, can be particularly dangerous, so there’s a need to be even more careful in choosing the right person, considering various comorbidities.

Newer second-line DMTs for the treatment of MS that have come into use in recent years include ocrelizumab and cladribine.

Ocrelizumab is biological treatment with a very convenient dosage (every 6 months). It‘s the first treatment targeted at B lymphocytes and, to this date, the only treatment that can treat, not only relapsing, but also a primary progressive form of MS. With ocrelizumab, premedication should be given to each person before infusion to suppress possible negative infusion reactions. Prior to treatment with ocrelizumab, it is important to screen for the presence of HBV (hepatitis B virus), which could reactivate during treatment and cause hepatitis B.

Cladribine is taken as a tablet, depending on the person’s weight, for 2 weeks in 2 years of treatment, but the effect should last for up to 4 years (long-term data on the treatment efficacy are not yet available). Cladribine treatment requires more frequent monitoring of blood count, especially count of the white blood cells, and liver function tests, including the exclusion of active hepatitis. Tuberculosis should be ruled out in people before treatment with cladribine.

And what about people with primary or secondary progressive MS?

It‘s necessary to talk to the people with MS about the fact that in the late stages of MS, brain repair mechanisms are worn-out and when the progressive phase of the disease is reached, when the death of the nerve cells occurs, it’s too late and the effect of the DMT is practically non-existent. There are currently more than 30 studies where people with secondary progressive disease (SPMS)

are included and 21 possible treatment strategies. In these studies, the sample consists of 35 to 1949 people.

In people in early stages of the progressive disease course presenting with the signs of the disease activity (relapse), we have 2 options:

1. Change the treatment within the specific line of the DMTs (so-called lateral switch) and monitor the disease intensively.
2. Escalate the treatment in case of a high disease activity or a rapid progression.

In people without the evidence of the disease activity, with a high EDSS score, long disease duration, and the presence of a brain atrophy without active lesions, which can be found on an MRI, it's appropriate to discontinue the treatment and focus on the symptom treatment. Often people themselves, worried about stopping the treatment, confirm that they don't feel any different, plus their quality of life has improved, e. g. they may not tolerate painful injections or flu-like symptoms after discontinuation of interferons. There's a need to be careful while indicating a treatment to these people, especially with second-line DMTs where the risk (severe disability itself is a predisposition to diseases of internal organs) outweighs efficacy. A new DMT for the treatment of SPMS is currently expected. Preliminary positive results in a clinical trial were recorded for another approximately 5 treatment options.

People with a primary progressive course of MS (PPMS), where effective treatment wasn't available, can be treated with ocrelizumab in Slovakia, although currently only as an exception of a health insurance company.

What to add at the end?

The continuously expanding spectrum of the treatment for MS, while closely monitoring the effect of the DMTs on the person's condition and occurrence of the side effects, clearly provides us with the opportunity to improve quality of life and prolong a life without inconvenient disability. Early and person-centred treatment strategy reduces the progression of the disability in such a devastating disease as MS definitely is.

MONITORING OF THE MS TREATMENT – WHAT EXAMINATIONS ARE NECESSARY?

Anna Cvengrošová, MD
Department of Neurology (J. A. Reiman University Hospital in Prešov)

Monitoring of the MS treatment – what examinations are necessary?

In general, each treatment is evaluated by the doctor from two perspectives. The first view focuses on the effectiveness of the treatment. Does the medicine have the desired effect? Is it sufficient for the patient, or are there other, more effective alternatives? The second view, no less important, is on safety. What side effects might the medicine have? Is the risk to the patient outweighed by the benefit the medicine brings? The ideal drug would have excellent efficacy and equally good safety and tolerability. However, we do not know of many such medicines and, as a rule, the doctor has to seek a balance between these two parameters. In sclerosis multiplex (SM), the situation is complicated by the disease itself. SM is unpredictable in terms of the course of the disease, the occurrence of symptoms and even their intensity. At the onset, we cannot tell how the disease will develop in the future. A patient with mild symptoms in the beginning may develop severe attacks in the later period. Patients with a primarily progressive form of the disease have a continuous worsening of their condition without periods of remission (stabilisation of the disease). Therefore, it is very important that the doctor assesses the patient‘s condition at regular intervals, with at least annual follow-up during the treatment of SM.

How is the effectiveness of the treatment evaluated?

In terms of treatment efficacy, it is necessary to evaluate the inflammatory activity of the disease and the progression of the patient‘s neurological deterioration (disability, disabling). The first rule is to start immunomodulatory therapy in time, within a short period of time after diagnosis. The second rule is regular monitoring of the disease status and changes in treatment if it does not work. In addition to neurological examination and other clinical examinations, annual assessment of disease activity by magnetic resonance imaging significantly helps in monitoring the disease. (MRI). The radiologist can assess at annual intervals whether the patient has acquired inflammatory lesions in the MR image, can count how many have been added, and can also assess whether there is significant atrophy (loss of brain tissue volume caused by the disease). Based on information from the patient and the neurological examination, the neurologist evaluates the number of attacks (relapses), the change from the previous year and the status of progression of incapacitation (disability) in the patient using the EDSS scale - the Expanded Functional Disability Status Scale. It is appropriate to complement some other clinical tests,

such as gait tests and upper limb function tests or cognitive function tests. The ideal goal of treatment is to achieve a state with no evidence of disease activity, called NEDA (No Evidence of Disease Activity). In practice, this means that any sign of activity or deterioration may be a reason to change treatment. Currently, the doctor and the patient have to work together to choose from a wide range of effective medicines and more will be added.

How is the safety of treatment evaluated?

In terms of the safety of the treatment, the safety profile of the drug indicated to the patient must be taken into account. The safety profile of a medicinal product consists of all available information on the medicinal product from the clinical trial, such as the incidence of adverse reactions and the occurrence of serious adverse events, as well as any special treatment measures or required investigations that have established the marketing authorisation of the medicinal product. All this information is published in the so-called summary of product characteristics for the doctor, as well as in the package leaflet for the for the patient.

▼ This medicine is subject of further monitoring. This will allow new safety information to be obtained quickly. You can contribute by reporting any side effects if you experience. You can see such a label in the leaflets of many modern medicines. The inclusion of a medicine among medicines that are subject to further monitoring does not mean that the medicine is less safe than other medicines. It means that the medicine is monitored even more intensively than other medicines and is given special attention, for example, tis re-evaluated more frequently in the light of new information that this closer monitoring helps to gather. The aim of the information obtained in this way is to ensure that the medicine is as effective and safe as possible for patients who are already using it or will be treated with it in the future. The inverted black triangle with which these medicines are labelled is not a warning symbol but an information symbol.

Why are medicines monitored after registration?

A relatively small number of patients are enrolled in clinical trials for a limited time. Patients are carefully selected for clinical trials under controlled conditions and very closely monitored. Under real-life conditions, a larger and more diverse group of patients will take the medicine. They may have different diseases and may take different medicines. Some less common side effects effects may occur, only after long-term use of the medicine by a large number of people. Therefore tis extremely important that the safety of all medicines continues to be monitored until, in practice use. If certain important measures are necessary for the safety of the treatment, they are imposed by the regulatory authorities (in our case the European Medicines Agency – EMA and the State Institute for Drug Control – ŠUKL) as part of the registration of the medicinal product. This process is called a Risk Management Plan (RMP). The overall aim of risk management is to ensure that the benefits of a particular medicine outweigh its risks as far as possible for the individual patient as well as for the target population. This can be achieved by either increasing the benefits or reducing the risks of a particular medicine. Risk management plans may include the additional measures and investigations to be carried out by the doctor for a given treatment,

what information and related information booklets the patient must receive from the doctor, and also the doctor‘s obligation to obtain the patient‘s consent to the treatment – the patient agrees to a certain risk by signing of treatment with a given medicine.

Which DMT’s have risk management plans?

Medical products with a defined risk management plan (RMP)	**Medical products without a defined risk management plan (RMP)**
Teriflunomid	Interferons beta-1b
Fingolimod	Glatirameracetate
Natalizumab	Dimethylfumarate
Alemtuzumab	Ocrelizumab
Cladribin	

The tests that the doctor indicates vary from simple ones, such as a blood test to check for infection before giving the medicine, or a liver enzyme test at regular intervals, to more complex ones such as individualised monitoring of PML risk (progressive multifocal leukoencephalopathy) during natalizumab treatment. Depending on the distribution of patients in each risk level, patients may also be required to have MRI scans every 3 months. Simpler safety follow-ups include, for example, regular checks of liver function during teriflunomide treatment; conversely, one of the more burdensome is the commitment to regular monthly blood draws within 4 years of the last administration of alemtuzumab. In terms of teratogenicity (possible fetal harm), with cladribine, it is strongly recommended that patients use effective contraception during treatment and for at least 6 months after the last dose. When fingolimod tablet is first administered, monitoring of the patient for several hours is prescribed because of possible complications in the patient‘s heart rhythm. These are just a few examples to understand what all can be included in a risk management plan (RMP). It is important to stress once again that the physician has a duty to carefully inform the patient about the risk management plan, if one is established for the medicine. If a patient with such treatment, it is essential that these investigations, in terms of the patient‘s own safety to complete.

What to add in conclusion?

However, the success of the treatment depends largely on the patient himself. No medicine can work if it is not taken properly and regularly and the patient does not follow the advice of the doctor or nurse regarding the overall treatment regimen, including lifestyle. At the same time, the physician must be informed whether the patient has deteriorated in his/her SM condition, as well as about the side effects of the treatment. The patient must attend regular check-ups with his/her doctor. Mutual trust and cooperation between the patient, the neurologist and the nurse in the SM outpatient clinic is essential in the fight against multiple sclerosis.

MULTIPLE SCLEROSIS AND PREGNANCY

Miriam Fedičová, MD
Department of Neurology (Louis Pasteur University Hospital in Košice)

Multiple sclerosis (MS) affects women three times more often than men, especially during their reproductive period of life. For that reason, the often discussed topics are about the issue of pregnancy, parenthood, and heredity of MS.

In the second half of the 20th century, women with MS were advised not to become pregnant due to the risk of worsening the disease and in extreme cases even being disabled after childbirth. Abortion has sometimes been recommended. These facts were based on the lack of information about the effect of pregnancy during the course of this particular disease. At present, we do not discourage women with multiple sclerosis from planning a pregnancy.

A woman with MS can easily get pregnant and give birth to a healthy baby. MS is not considered an inherited disease, although genetic factors play a role in the development of the disease. There is a 98% chance that their child will not inherit MS. If both parents have MS, the risk of the disease increases up to 25%.

Pregnancy planning

Expectant mothers should plan their pregnancies more carefully due to their illness. It is most favorable to wait for the period of stabilization of the disease, it means at least 8-12 months from the last outbreak (attack).

Pregnancy and treatment

Some medicines used for MS treatment are not safe during pregnancy and need to be stopped before conceiving a child. In certain cases, we also have medicines available that patients with MS can take during pregnancy. Research has shown that pregnancy does not have a negative effect on the course of MS even in the long term. It is a period when sex hormones cause changes in the immune system, which is reflected in a reduced number of attacks of the disease. Many patients feel very well at that time and do not have relapses at all.

Childbirth and MS

Multiple sclerosis does not increase the risk of complications during pregnancy and does not have an adverse effect on the fetus, or premature birth, or miscarriage.

Women with multiple sclerosis can naturally direct childbirth unless there are other complications or a cesarean section. The decision is a matter for the obstetrician. Epidural or spinal anesthesia during childbirth is safe and is not accompanied by an increased risk of any other complications. The period of childbirth and the first three months after it are considered risky due to the hormonal imbalance in terms of the outbreak of disease activity.

Breastfeeding and MS

Breast-feeding is a condition in which the hormone prolactin is secreted in the mother‘s body, which has an adverse effect on multiple sclerosis and can lead to a relapse of the disease. In stabilized patients without attack or new changes in the control magnetic resonance imaging of the brain, it is recommended to stop breastfeeding within 4 months, no later than half a year after delivery. If a patient with MS was enrolled in a long-term treatment before pregnancy, this treatment should be continued after breastfeeding. With high disease activity, breastfeeding is not recommended and treatment for MS should be returned as soon as possible.

Infertility

In developed countries of the world, the infertility of women of childbearing age is estimated at 15%. It is important for a woman to know that multiple sclerosis does not affect fertility. If for some reason, a patient with MS cannot become naturally pregnant, she may seek the help of assisted reproduction. In general, it is recommended to undergo the procedure at the time of stabilization of the condition, not at the time of disease activity.

Life management during pregnancy

Expectant mothers with MS can support pregnancy without disease relapses with a proper diet, moderate exercise (with respect to pregnancy), and adequate rest. An important supplement that has a protective effect on the course of MS is vitamin D that may be used during pregnancy and even reduces the risk of developing MS in adults. Mothers with MS should not forget that there´s the family and their partner who happily help them so that they can fully devote themselves to the child and enjoy parenthood.

I, YOU, US WITH MULTIPLE SCLEROSIS

PhDr. Ján Grossmann
Department of Neurology (University Hospital in Martin)

„I don‘t want to belong to any association or self-help group!“ „Why would I go somewhere where I only see troublesome and difficult stories, it affects me badly, I myself have enough to do with the fact that I have an MS, and not to put up with the suffering of other people ...“.

Often than not, it is possible to hear patients and people who have MS having this kind of perspective. It is understandable, a portion of people with MS do not want to be in contact with other people who have MS at a certain time. Often, the fear is that I see what future holds for me and how will it turn out, then I am seeing all those difficult cases. They will ask things I don‘t want to find about just now. They may tap things I don‘t want to discuss just yet. At other times, it is rather the stance that „I am just fine and well, so for what will I need to meet with patients...“.

It is not easy to accept the illness

For some, it means accepting their own limitations, changing the way they have lived so far, or, rarely, beginning to live life to the fullest ... Well, these are often assumptions that are perceived as unchanging facts that my life, as I have known it so far, is over. The fact that I think that accepting a disease means losing life, giving up my own dreams, or the end of life that I know. These are thoughts and feelings (assumptions) that are understood as hard facts. (The difference between facts and thoughts is that facts are facts, thoughts are interpretations of facts). So, thoughts like „My life as I know it is over,“ „I‘ll end up in a wheelchair,“ are perceptions of the fact that I have multiple sclerosis (MS). The inner struggle with these kinds of thoughts draws on everyone who has to face an incurable disease. It is normal and natural for people to react to this new situation in this kind of way: I‘m terrified of it, I‘m afraid of what‘s to come.

MS does not only accompany single person, but the people around them

People who have been diagnosed with MS are going through a difficult period of time, which in various ways interferes with their normal functioning. It also affects a wider group of people, families

or partners, from parents to children, siblings, significant others, friends, acquaintances, and even neighbours. Our loved ones, as well as us, react to the fact that we have an MS. They may pity us, control us excessively, protect us inadequately, or deny the fact that we have an illness. They are worried about what awaits us, but they do not always communicate it to us adequately as well. The most difficult thing for people with MS is when our relatives treat us as a disabled person who can‘t do anything. Both men and women are very sensitive about whether their partner will leave when they find out about illnes. It is often women who perceive that their partners will leave for some else not affected by MS. And for these reasons, it‘s fine to have acquaintances, friend or friends who will help overcome the difficulties associated with MS.

When people with MS are informed about their diagnosis, they basically respond in three ways to this new situation. The first way is that they are trying to deal with a problem that has accompanied them for some time and the diagnosis confirms what they have been thinking for some time. The second way is that they are trying to control the emotions that evoked the announcement of the diagnosis, which came from the blue. Each of these ways of coping has its pitfalls. Firstly, that I need to keep in touch with their own emotions, and secondly, it is fine not to lose one´s head. When you try to focus on solving problems, it gives you a feeling of control and power over the disease. You can manage life more and control the manifestations of the disease. However, this can lead to over-reliance on one‘s own abilities and failure to seek help when you really need it. On the other hand, an excessive effort to manage one‘s own emotional health can lead to neglecting duties, procrastination, excessive support seeking and reassurance from loved ones or professionals. As mentioned earlier, over-fixation on one of the management strategies can bring more problems than it solves. For these reasons, it is worth considering getting to know other facets of the disease, whether it is getting more acquainted with the opinions and attitudes of other people or simply read stories from people with MS. It does not have to mean agreeing with every opinion and views, but rather reflecting on how my life situation resembles / does not resemble another person‘s experience. As the saying goes, He is a wise man who does not grieve for the things which he has not, but rejoices for those which he has. And there‘s a third way to respond to the discovery that I have MS, and that is to completely deny that something like this happened to me at all. I simply refuse to identify with as having MS. And this is also one of the management strategies, which turns out that in the short term, it is also appropriate to respond to it in this way. Simply put, I live on as if nothing had happened, I take the diagnosis as something that is only on paper and doesn‘t bother me that much. Even though I‘m tired, I can‘t see with one eye, I‘m pulling my leg behind me. Sooner or later, however, I will be confronted with reality, but until then I can live as „what the eye does not see, the heart does not bother ...“.

What does motivate people to meet when they have a problem or illness?

Is it (only) because they have a problem and are trying to overcome the problem together? Or is it because they need to meet people who have met a similar fate and do something to run out of time? There are many more reasons. Sometimes people need to leave their apartment for a while and just come up with other ideas, and with people who are experiencing something similar, they are nice and do not

always need to save the world.

It takes courage and probably inner strength to meet with people who have MS. Confront oneself with what I may be afraid of upon entering unknown territory. For one it is to see one‘s own fragility and vulnerability, for another to see a possible future, for another it is take pity from the others. Whatever worries and fears they are, they are justified and they are real. No one have to tell you of what you do or do not to worry about. It‘s okay to be afraid and be afraid of future. It is important to acknowledge and confirm to yourself that you are worried and afraid. In this respect, fear is a sign of coping and you and your body and soul are „struggling“ with a new situation, whether you realize it or not. However, people with MS may not experience fear more dramatically than it was outlined here. There are those who do not experience it in any way, either internally or externally, but there are people whose fear and horror engulfs (and rolls over) only when the topic of multiple sclerosis is brought up. In this regard, it is important that the people around you, who care about you do not put too much pressure on you and force you to do things that they think is best for you. After all, no one is saying that you have to go to self-help group meetings with people with MS. But it is a place where you can experience for yourself that you can live with MS, you can live well and you can live to the fullest. MS self-help groups and associations organize educational lectures and seminars, workshops and creative activities not only for those affected with MS but for significant others as well. Exercises are performed under the supervision of experts to improve physical condition. Last but not least, in self-help meetings with other patients with MS, we can learn a lot about the legal and social support, get tips on diet, nutritional supplements and recommendations for supportive treatment and physical activity. From experience it is known that many who had initial concerns from meeting with other patients were very pleased after did. Despite the initial fears the mutual understanding and acknowledgement from the patients and people with MS has unique effect for everyone. You will be able to see yourself with a unique story as well as the other MS patients. It gives bit of hope to see how the other have taken up with the illness. Despite all these hardships you might see that it may not be so terrible (even though it is difficult) to live with MS and still all the beautiful things around you.

A PERSON IS NEVER ALONE

Branislav Brežný, MD

People are social creatures. In the past, people were united in many different communities, whose members had the same goal. It is therefore a natural ability to socialise and be in multiple relationships in society.

Nowadays, it's the community that can become a tool for solving many (and not only) social problems in society. The community is characterized by elements such as: the same space and the same time, recognition of similar needs, values and goals, our identity, relative stability and relative autonomy. Cooperation between the members of the community themselves is also very important.

In the past, people with chronic diseases were members of the Association for the disabled people. The association had sections, depending on the type of disease – section for people with sensory impairment and section for people with heart diseases. For others, there was a section for people with the diseases of civilization. People with multiple sclerosis (MS) were included in the section for people with diseases of civilization. This section was a mixture of different diseases from different medical disciplines. These diseases were not related and each one of them had their individual needs. Therefore, about thirty years ago, a group of enthusiasts,people with MS, had met in the capital city of Slovakia, Bratislava. They established new and independent organisation associating patients with MS in Slovakia (Slovak MS Association, or SZSM). At that time, the Unie Roska had already been operating in the Czechia, associating patients with MS. Both MS associations are committed to the idea that all people are equal, regardless of race, religion, political or other beliefs, belonging to another ethnic group and regardless of the social situation in which they find themselves. In their actions, they condemn any manifestations of extremism and intolerance of ideas that would negatively affect society. They bring together patients with MS, their family members and friends of the association, who espoused the idea of mutual help. After all, the motto of SZSM is: We are here to help each other.

The SZSM is the umbrella MS organisation in Slovakia, but there are several small „MS clubs"which belong to the SZSM. The MS clubs are relatively autonomous civic associations, but they follow the rules and bylaws of SZSM. The MS clubs themselves create various activities for each year, which they plan by themselves, and follow the plan of these activities during the whole year.

The MS clubs are primarily focused on getting people with or affected by MS together.

That's done especially via club meetings. These meetings are held at least once a month. People usually have a discussion about the everyday life of club members, their needs and problems. They always try to talk about possible solutions for different issues, they are giving advice to each other on how to manage this disease, what might be helpful and what appears to be a dead end. They also talk about the latest trends in the treatment of MS, new laws and social regulations. These club meetings might also be a celebration of members' birthdays, where small snacks are served, just like in any other family. In addition to club meetings, creative workshops are also organised, so club members can demonstrate or work on their skills. There are also trips to nature, often associated with toasting or cooking some meal, or even trips to get to know our country. Many clubs also organise recreation in spa for their members. An inseparable part of the activity in some clubs is also physical activity, rehabilitation exercises under the guidance of trained trainers. However, this is tied to the possibility of visiting the gym, which is not always an option for each club.

Money for the club activities can be obtained from the public collection, which takes place once a year in May, on the occasion of the "Sunflower Day", which is the name for the World MS Day in Slovakia. In addition, there is the possibility of obtaining funding from 2% of taxes that taxpayers can donate to the club. Membership fees in clubs are only symbolic and would not cover the annual budget of the club.

In addition to these basic activities in clubs, SZSM creates meetings on the national level of Slovak "MS-ers" and their families. It also organises an International Meeting of Patients with MS every two years, where the SZSM alternates with the Czech Unie Roska. In the spring, members of the SZSM participate in MARS (International exercise marathon for people with MS), which is attended mainly by "MS-ers" from the Czechia and Slovakia.

Every year in May, the SZSM develops activities on the occasion of the World MS Day – or the "Sunflower Day", through various activities throughout the territory of the Slovak Republic. This is mainly to make clubs and patients visible in the regions, and to raise awareness about MS, about the disease that affects about 8-10 thousand citizens in Slovakia, and to inform fellow citizens about the issues people with MS face in everyday life.

The variety of different disciplines, where people with MS compete, is called the International "Olympics of abilities". It's a tradition that this event is attended by national organisations, especially from Poland, Hungary and Czechia. We also had guests from Serbia and Norway. The "Olympics of abilities" offers more than 26 disciplines. This event is very popular – each year, more than 150 people attend this event.

Apart from these „social" activities, the SZSM makes nationwide reconditions for its members, which are aimed at acquiring and learning new skills. Every other year, it also organises these reconditions for wheelchair users and their family members.

In summer, the SZSM usually organises trips to Croatia and Italy, where people have a chance to relax and socialise with other people with or affected by MS. These trips are very popular and almost immediately booked. The advantage of these trips is that people with various disabilities

can (and are very welcome to) participate, and there's no reason to be ashamed of it in front of other people.

The SZSM also tries to educate its members, because the idea is that „the most expensive treatment is the treatment of an uneducated patient". The uneducated patient doesn't necessarily know the challenges of MS, treatment options and the possibility of helping himself and others. People with MS cannot orient themselves in the latest trends in the treatment of MS and many other areas. Many experts in the "field of MS" are a part of these events, including chief expert of the Ministry of Health of the Slovak Republic for neurology, and the lecturers are doctors from the MS ambulances, professors and associate professors of medical faculties. Seminars are held once a year for newly diagnosed patients with MS, also for children and adolescents with MS, and once a year there is a seminar for many other people with MS, young or old. The SZSM wants to make these educative events as accessible as possible, and educating its members is a very high priority for SZSM, so this events are free of charge for participants, mostly because people wouldn't be able to afford it. SZSM publishes its magazine, which is called „Hope". This magazine is published four times a year, it contains articles about the MS clubs, important information about social issues of citizens, informs about events in the association and in clubs at the national level. An integral part are also articles by doctors, which are related to MS, about the latest drugs and treatments.

The SZSM is cooperating with many patient civic associations. Together, they have an opportunity to negotiate with ministries, to comment on materials that are discussed in the government. Through the chief expert of the Ministry of Health of the Slovak Republic for neurology, the SZSM has an opportunity to consult many issues of its members and propose solutions to various, sometimes conflicting, situations.

The appreciation of SZSM's work is the recognition as a full member in international organisations, and participation in the activities of these organisations.

The work in the MS clubs is very important. Members of the SZSM gain new knowledge and new skills, which increases their self-confidence, they have an opportunity for self-realisation, the opportunity to make new friends. They have come to realise that many others have very similar fate, and they are not alone, because there are people they can rely on. Working in clubs is making them to come out of their apartment, opens up the possibility of learning new things, broadening the horizons of knowledge and experience. By working on themselves, their health can also be improved.

The SZSM and the MS clubs give their members a very unique opportunity to take back what MS has taken away from them. It's not their fault that they have MS and are struggling with an incurable, but manageable, neurological disease. People with MS need the help of the whole society, and the first step is a help of the SZSM and its MS clubs. We are one big family, the officials of the association and the clubs work pro bono, they work with love and passion for one another. That is why the motto of people with MS was adopted: Sursum corda!

Contact addresses of MS clubs in Slovakia

Banská Bystrica - Klub SM pri SZSM
Maroš Turiansky
Limbová 15, 974 09 Banská Bystrica
Kontakt: 0905 746 259
e-mail:m.turiansky@gmail.com

Bardejov - Klub SM pri SZSM
Anna Špíková
Lesnická 14
080 05 Prešov
Kontakt: 0917 572 581
e-mail: ankaspiková@gmail.com

Bratislava - Klub SM Dunaj
Dagmar Foltýnová
Osadná 2, 831 03 Bratislava
Kontakt: 0902 263 946
e-mail: v.krchniakova@gmail.com

Humenné - Klub SM pri SZSM
Ing. Ján Kohút
Dlhé nad Cirochou 265
067 82 Humenné
Kontakt: 0917 734 782, 057/762 44 02
e-mail: j.kohut54@gmail.com

Košice Klub SM pri SZSM
Marcela Zadáková
Karpatská 1
040 01 Košice
e-mail: smkeklub@gmail.com

Kysucké N. Mesto - Klub SM pri SZSM
Oľga Belková
ČSA 1306/21
024 04 Kysucké Nové Mesto
Kontakt: 0950 610 053, 0902 785 900
e-mail: knm.olga@gmail.com

Levice - Klub SM pri SZSM
Angela Wieslová
Agátová 33, 936 01 Šahy
Kontakt: 0902 742 887
e-mail: angela.wieslova@gmail.com

Liptovský Mikuláš - Klub SM pri SZSM
Ing. Iveta Janotková
Vavrišovo 127
032 42 Pribylina
Kontakt: 0905 550 259
e-mail: iveta2105@gmail.com

Lučenec - Klub SM pri SZSM
Ivana Gažová
Rúbanisko II/11
984 03 Lučenec
Kontakt: 0908 852 916
e-mail:gazova.ivana70@gmail.com

Kontaktná adresa predsedníčky
Sekcia deti ich rodičov a mládeže pri SZSM
Bianka Suchá
e-mail:bibka1sucha@gmail.com
Kontakt: 0949 182 020

Michalovce - Klub SM pri SZSM
Ing. Štefan Macík
072 54 Bajany 128
Kontakt: 0904 123 593
e-mail: pista82@azet.sk

Nitra - Klub SM
Anton Suchan
Novomeského 3/5, 949 11 Nitra
Kontakt: 0904 547 106
e-mail: suchan@ksmnr.sk
www.ksmnr.sk

Nové Zámky - Klub SM pri SZSM
Marta Révaiová
S. H. Vajanského 58
940 79 Nové Zámky
Kontakt: 0903 133 645
e-mail: mrevaiov@gmail.com

Piešťany - Klub SM pri SZSM
Daniela Valová
Štefánika 208, 922 03 Vrbové
Kontakt: 033/779 28 17, 0902 155 383
e-mail: danielavalova1303@gmail.com

Považská Bystrica - Klub SM pri SZSM
Daniel Kimlička
Štúrova 43 /21-9
017 01 Považská Bystrica
Kontakt: 0904 487 594
e-mail: klubsmpb@gmail.com
www.klubsmpb.blogspot.com

Partizánske - Klub SM pri SZSM
Anna Očenášová
Cigeľ 323
971 01 Prievidza
Kontakt: 0907 752 860
e-mail: annaocenasova11@gmail.com

Poprad - Klub SM pri SZSM
Jana Rusnáková
Levočská 1766/7
060 01 Kežmarok
Kontakt: 0908 026 283
e-mail: szsm.poprad@gmail.com
e-mail: janarusnakova68@gmail.com

Revúca - Klub SM pri SZSM
Lucia Belicová
I. Krasku 1122/9
050 01 Revúca
Kontakt: 0905 786 571
e-mail: lucinka05001@centrum.sk

Rimavská Sobota - Klub SM pri SZSM
Darina Kovácsová
Hlavná 5
980 01 Rimavské Janovce
Kontakt: 047/567 72 16, 0904 946 778
e-mail: darinkakovacsova@gmail.com

Ružomberok - Klub SM pri SZSM
Mgr. Mária Púchovská
Riadok 3
034 01 Ružomberok
Kontakt: 0908 576 973
e-mail: maria.puchovska@gmail.com

Trenčín - Klub SM pri SZSM
Jaroslava Michalechová
913 23 Dubodiel 373
Kontakt: 0918 039 510
e-mail: jamichalechova@gmail.com

Trnava - Klub SM
Bc. Miloš Žambokréthy
Vančurova 1, 917 01 Trnava
Kontakt: 0911 141 581, 0908 575 166
e-mail: klubsmtrnava@gmail.com
www.klubsmtrnava.webnode.sk

Vranov nad Topľou - Klub SM Slnečnica
Valéria Sivuličová
094 15 Zámutov 7
Kontakt: 0918 526 548, 0917 565 012
e-mail: valeriasivulicova@gmail.com
www.slnecnicasmk.org

Zvolen - Klub SM pri SZSM
Juraj Hanák
Jedľová1364/1
960 01 Zvolen
Kontakt: 0907 806171
e-mail: zvklubsm@gmail.com

Žilina - Klub SM pri SZSM
Mgr. Katarína Schűtzová
Hečkova 26, 010 01 Žilina
Kontakt: 0907 155 892
e-mail: zaklubsm@centrum.sk

This Educational brochure was created with the support of Roche

Scientific guarantee of this publication:
Assoc. prof. Jarmila Szilásiová, MD, PhD.