

KNOWLEDGE UPDATE ON THE SYMPTOMATIC TREATMENT OF MULTIPLE SCLEROSIS



MS Multiple Sclerosis Society of Canada
Quebec Division

GUIDE FOR GENERAL PRACTITIONERS



INTRODUCTION

This brochure has been developed for general practitioners who would like information on how to treat the signs (symptomatic treatment) of multiple sclerosis. In 2005, an earlier brochure concerning the epidemiology and diagnosis of this disease was published by the Multiple Sclerosis Society of Canada, Quebec Division.

MS may begin with the relapsing-remitting form (attacks and remissions); from 85% to 90% of patients, or with the primary-progressive form (from 10% to 15%). The average frequency of attacks is one every two years, and their average duration is six weeks. Approximately 40% of attacks leave after-effects. The relapsing-remitting form develops into the secondary-progressive form approximately 15 years after the first attack in about 50% of patients. At that point, the disease progresses fairly gradually and may or may not be accompanied by attacks.

Treatments can be prescribed to slow down the development of the relapsing-remitting form and the secondary-progressive form with attacks, to treat an acute attack, or to alleviate symptoms. In the progressive forms (without attacks), only the treatment of symptoms is possible today.

A multiple sclerosis attack is defined by the appearance of a new symptom or the aggravation of an old symptom corresponding to an attack on the brain's white matter, which is objectively demonstrable with a neurological exam and lasts for a minimum of 48 hours. Attacks that compromise daily activities (change in vision, walking problems, vertigo, etc.) can be treated with methylprednisolone (Solu-Medrol®), at a dose of 1000 mg I.V. per day for a period of three to five days. This treatment generally makes it possible to shorten an attack without, however, reducing the risk of after-effects.

Treatments that can change the course of MS have been available since the 1990s. They include beta interferons (Betaseron®, Avonex® and Rebif®) and glatiramer acetate (Copaxone®). These drugs decrease the number of attacks by 30% to 35%. A fifth treatment, natalizumab (Tysabri™), has been available since October 2006 for people who do not respond to the first four treatments. These substances, which do not treat MS symptoms, will not be discussed in this document.

The goal of this publication is to help general practitioners to assess and treat a number of multiple sclerosis symptoms. Both drugs and non-drug treatments can be prescribed by a family doctor. They often improve patients' quality of life considerably. The following symptoms, which are widespread in MS, will be described in detail below: pain; spasticity; bladder, bowel and sexual problems; fatigue; depression; and cognitive problems. Unfortunately, some symptoms such as paresthesia, ataxia, diplopia, tremor and nystagmus are not very or not at all treatable. They will not be discussed here. This publication was prepared by neurologists and nurses who specialize in MS and was reviewed by a general practitioner.

PAIN IN MULTIPLE SCLEROSIS¹

Pain is frequent in multiple sclerosis. Approximately 40% of patients present with it during the course of their disease.² Pain can have many causes, some of which are specific to the disease, and others secondary to the physical limitations it gives rise to. A clinical diagnosis requires the physician not only to have a good knowledge of the different kinds of pain, but also to do a good physical examination of the patient so that he or she can accurately identify the nature of the pain and recommend appropriate treatment.

References:

- 1- Chatel, M., M. Lantérini-Minet and C. Lebrun-Frenay. "Les douleurs dans la sclérose en plaques". *Revue Neurologique*, Paris, 2001, vol. 157, no. 8-9, pp. 1072–1078.
- 2- Paty, D.W. and G.C. Ebers. *Multiple Sclerosis*. Philadelphia, FA Davis, 1997, pp. 135–191.

PAIN IN THE EARLY STAGES OF THE DISEASE

Although it is uncommon at the onset of the disease, pain may occur during an attack. In that case, its presentation will tend to be paroxysmal. The best-known kinds of pain are trigeminal neuralgia, Lhermitte's sign, intercostal neuralgia and tonic seizure.

A - Trigeminal neuralgia

Trigeminal neuralgia is characterized by strong, paroxysmal pain that lasts for several seconds, is located in the jaw, and reappears several times a day. Unlike the idiopathic form, it may be bilateral and may be associated with sensory deficits in the territory of the fifth cranial nerve. It generally lasts no more than a few weeks, just like a multiple sclerosis attack, but it can also be chronic. It is usually caused by the presence of a plaque where the sensory fibres of the fifth cranial nerve enter the brainstem.

B - LHERMITTE'S SIGN

Lhermitte's sign is a feeling like an electric shock emanating from the cervical spinal column and radiating either out to the extremities or along the dorso-lumbar spine. It is triggered by a neck flexion and is associated with the presence of a lesion in the posterior region of the cervical spinal cord.

C - Intercostal neuralgia

Intercostal neuralgia is a more continuous presentation of trigeminal neuralgia. The pain is intense; simply touching the skin of the painful area, which is located along a thoracic or abdominal intercostal region, becomes intolerable. The pain generally lasts for a few weeks only, like an attack; it is much less common than trigeminal neuralgia or Lhermitte's sign.

D - Tonic seizure

Tonic seizure is very rare and may go unnoticed if it is not suspected. It is characterized by short dystonic contractions (torsions) affecting an extremity (hand or foot). A tonic seizure may be accompanied by pain. Like trigeminal neuralgia, the pain may recur several times a day and may last for several weeks.

All of these kinds of pain are of limited duration; they also generally respond well to medication. Carbamazepine is generally the first choice for paroxysmal pain. Gabapentin and lamotrigine can also be used, singly or in association.

Table 1 – Treatments for acute pain

Symptoms	Name	Dosage	Side-effects
Trigeminal neuralgia, Lhermitte's sign, intercostal pain, tonic seizure	Carbamazepine (Tegretol®)	100 mg t.i.d. to 200 mg q.i.d.	Somnolence, headaches, loss of balance, diplopia, dry mouth, blurred vision, vertigo, dizziness, clumsiness, nausea, stomach aches.
Trigeminal neuralgia, intercostal pain	Gabapentin (Neurontin™)	100 mg HS to 1,200 mg t.i.d.	Somnolence, dizziness, vertigo, ataxia, fatigue.
Trigeminal neuralgia, intercostal pain	Lamotrigine (Lamictal®)	50-200 mg b.i.d.	Dizziness, headaches, diplopia, somnolence, ataxia, nausea, asthenia.
Refractory trigeminal neuralgia	Thermocoagulation, microvascular decompression, radiosurgery		Possible complications: hypoesthesia in the territory of the nerve.

Table 1 – continued

Symptoms	Name	Dosage	Side-effects
Tonic seizure	Baclofen (Lioresal®)	10 mg t.i.d. to 20 mg q.i.d.	Weakness, somnolence, dizziness, fatigue, nausea.
Tonic seizure	Clonazepam (Rivotril®)	0,5 mg to 1,0 mg t.i.d.	Dry mouth, nausea, vomiting, constipation, blurred vision, numbness of the fingers, depression, apathy, nervousness, urinary retention.
Lhermitte's sign	Amytriptyline (Elavil®*)	10-75 mg HS	Dry mouth, somnolence, fatigue, vision problems, constipation, urinary retention, dizziness and nausea.

*In Canada, the generic drug replaces the original product.

Another kind of pain is eye pain associated with optic neuritis. In the first days of an acute visual attack causing a loss of vision because of inflammation of the optic nerve, patients often complain, within the first days, of retro-ocular pain, which is aggravated by eye movements. This pain is generally of short duration and clears up spontaneously. It can be alleviated with a regular painkiller.

PAIN IN THE ADVANCED FORMS OF MULTIPLE SCLEROSIS

In the advanced forms of the disease, the acute pain described above may present. In addition, one may observe other kinds of pain that are associated with a range of pathophysiological mechanisms.

A - Neuropathic pain

Neuropathic pain can be a major cause of disability and a source of great psychological distress for some patients. It may also be present at the beginning of the disease. This kind of pain feels severe and constant and is sometimes described as a burning or pulling feeling or a cramp. It may be associated with a dysesthetic feeling, that is, intolerance of simple skin contact in the pain zone. This type of pain generally radiates out from a body part: a limb, a hemicorpus or the two lower limbs. It is generally chronic and may last for a long time, so it represents a major challenge for clinicians working with people who have multiple sclerosis. It often requires the kind of multidisciplinary approach offered in pain clinics.

Pharmacological treatment of neuropathic pain may start with a simple painkiller, namely acetaminophen, aspirin or non-steroidal anti-inflammatories. When this basic approach is inadequate, the use of a drug that can modify pain perception, such as amitriptyline, gabapentin, lamotrigine or pregabalin is indicated. If these approaches fail, the use of narcotics or cannabis derivatives may be contemplated.

B - Pain secondary to complications of the disease

Other kinds of pain are associated with the complications that the disease can trigger. Musculoskeletal pain is frequent in patients who have a physical disability. Those who use a cane or a walker may develop pain in the hips, knees or shoulders, whereas wheelchair-bound patients may experience backaches because of poor positioning. Patients with motor disorders may develop spasticity, which can be painful. In the latter case, the use of baclofen, tizanidine or dantrolene (if this drug is used, its hepatotoxicity must be closely monitored) may be justified. (See Table 3 – Treatments for spasticity, on page 9.)

Table 2 – Treatments for pain in the advanced stages of multiple sclerosis

Name	Dosage	Side-effects
Carbamazepine (Tegretol®)	from 100 mg t.i.d. to 200 mg q.i.d.	Somnolence, headaches, loss of balance, diplopia, dry mouth, blurred vision, vertigo, dizziness, clumsiness, nausea, stomach aches.
Gabapentin (Neurontin®)	from 100 mg HS to 1,200 mg t.i.d.	Somnolence, dizziness, vertigo, ataxia, fatigue.
Lamotrigine (Lamictal®)	50-200 mg b.i.d.	Dizziness, headaches, diplopia, somnolence, ataxia, nausea, asthenia.
Amitriptyline (Elavil®)*	10-75 mg HS	Dry mouth, somnolence, fatigue, blurred vision, constipation, urinary retention, weight gain, dizziness and nausea.
Baclofen (Lioresal®)	from 10 mg t.i.d. to 20 mg q.i.d.	Weakness, somnolence, dizziness, fatigue, nausea.
Pregabalin (Lyrica®)	from 50 mg HS to 200 mg t.i.d.	Dizziness, somnolence, peripheral edema, dry mouth.
Clonazepam (Rivotril®)	from 0,5 mg t.i.d. to 1,0 mg t.i.d.	Dry mouth, nausea, vomiting, constipation, blurred vision, numbness of the fingers, depression, apathy, confusion, urinary retention, ataxia.

*In Canada, the generic drug replaces the original product.

SPASTICITY IN THE EARLY STAGES OF THE DISEASE

Spasticity is muscular hypertonia that results from a lesion to the central motor pathways, either in the cerebral hemispheres, the brainstem or the spinal cord. During the course of MS, from 50% to 75% of patients will be affected by it. At the pathophysiological level, spasticity essentially represents a hyperactive tendon reflex. Spasticity, hyperreflexia, clonus, and the Babinski sign are manifestations of pyramidal syndrome.

Initially, in MS, spasticity is manifested as stiff, unstable walking. In the relapsing-remitting form, it generally occurs several weeks or months after an attack that involves the central motor pathways, from which the patient has not completely recovered.

In the primary-progressive form of MS, spinal cord lesions are common from the onset of the disease and spasticity is often evident at the time of the first clinical evaluation. It sets in insidiously, often without any significant associated weakness.

Spasticity is often harmful to ambulatory patients whose muscles remain fairly strong; in such cases, it must be treated. Muscle stretching represents the basic treatment for spasticity. Early in the development of spasticity, stretching is often intended to maintain muscle flexibility; later, it helps to prevent contractures. In the beginning, this muscle stretching, which patients can learn to do by themselves in physiotherapy, may be all that is needed to make walking easier. Aerobic exercise and relaxation are recommended. However, these non-pharmaceutical treatments may prove inadequate, and recourse to an antispasmodic drug may become necessary.

Baclofen, the first intention medication, is introduced at a dosage of 5 mg, three times a day (see Table 3). In the beginning, a dose of 10 mg per day is often effective. If not, the dosage may be increased to as much as 20 mg, four times a day. If this drug is ineffective, poorly tolerated or associated with increased muscle weakness, tizanidine (from 4 mg to 8 mg, three times a day) may be introduced gradually, either singly or in association with baclofen.

The administration of 5 mg of Valium may be beneficial for patients who present nocturnal symptoms or who have another indication for this drug. Dantrolene is

reserved for bedridden patients, given the significant muscle weakness that it induces. The hepatotoxicity of this drug must be closely monitored.

Table 3 – Treatments for spasticity

Name	Initial dose	Usual maintenance dose	Maximum dose	Side-effects
Baclofen (Lioresal®)	5 mg t.i.d.	10 mg t.i.d. or q.i.d.	20 mg q.i.d.	Dry mouth, somnolence, dizziness.
Tizanidine* (Zanaflex®)	2 mg t.i.d.	4 mg t.i.d.	8-12 mg t.i.d.	Dry mouth somnolence, asthenia.
Diazepam (Valium®)	5 mg HS	5-10 mg HS	5 mg t.i.d.	Somnolence, dizziness.
Dantrolene (Dantrium®)	25 mg die	100 b.i.d.	100 q.i.d.	Somnolence, weakness, hepatotoxicity, dizziness.

*Exception drug (Quebec public drug insurance plan)

SPASTICITY IN THE ADVANCED STAGES OF THE DISEASE

Spasticity may appear late in the course of relapsing-remitting MS if the attacks in the early years have spared the central motor pathways. It especially affects the lower limbs, and particularly the quadriceps. Late in the disease, the thigh adductors are affected, resulting in a scissoring gait (thigh adduction), and making sphincter and sexual functions and perineal hygiene more complicated.

Sooner or later, spasticity may be associated with flexor or extensor spasms of the lower limbs. A spasm is the rapid contraction of a muscle group, followed by a slow relaxation. It may be spontaneous or triggered by movement, pain, urinary infection, urinary retention or constipation. The upper limbs are not affected by these spasms, which are not necessarily accompanied by pain. It should be noted that patients often use the word “spasm” to describe other symptoms than spasms and the word “shaking” to describe spasms, so it is important to ask patients to properly describe their symptoms.

A fundamental principle in handling spasticity is that treatment is not always desirable. At the phylogenetic level, spasticity probably represents an attempt by the central nervous system to compensate for muscle weakness. In fact, hypertonia allows a paraparetic patient to perform transfer pivots and even to walk a few steps with a walker. In these specific cases, it is important to avoid reducing the hypertonia, since it is having a beneficial effect.

Muscle stretching constitutes the basic treatment for spasticity at all stages of the disease, even the advanced ones when the stretching essentially aims to prevent contractures. In severely paretic patients who are confined to bed, the stretching must be done every day by another person, either a professional or a relative who has been given the necessary instructions. For patients who are living in long-term care facilities, physicians must often insist that this preventive care be administered, since if it is not done regularly, the stretching can soon become painful and ankylosis may set in. The triggering factors for spasms listed above should be sought out and treated. Antispasmodic medication, as described above, may be effective.

BLADDER AND BOWEL PROBLEMS

Botulinum toxin (Botox®) is reserved for people whose spasticity is restricted to one or two muscle groups. It is particularly useful in bedridden patients who have thigh adduction constraints, to facilitate hygiene. The injections are repeated every three or four months, on average.

An intrathecal baclofen pump and surgery (neurolysis and rhizotomy) are rarely necessary and require an extremely specialized assessment.

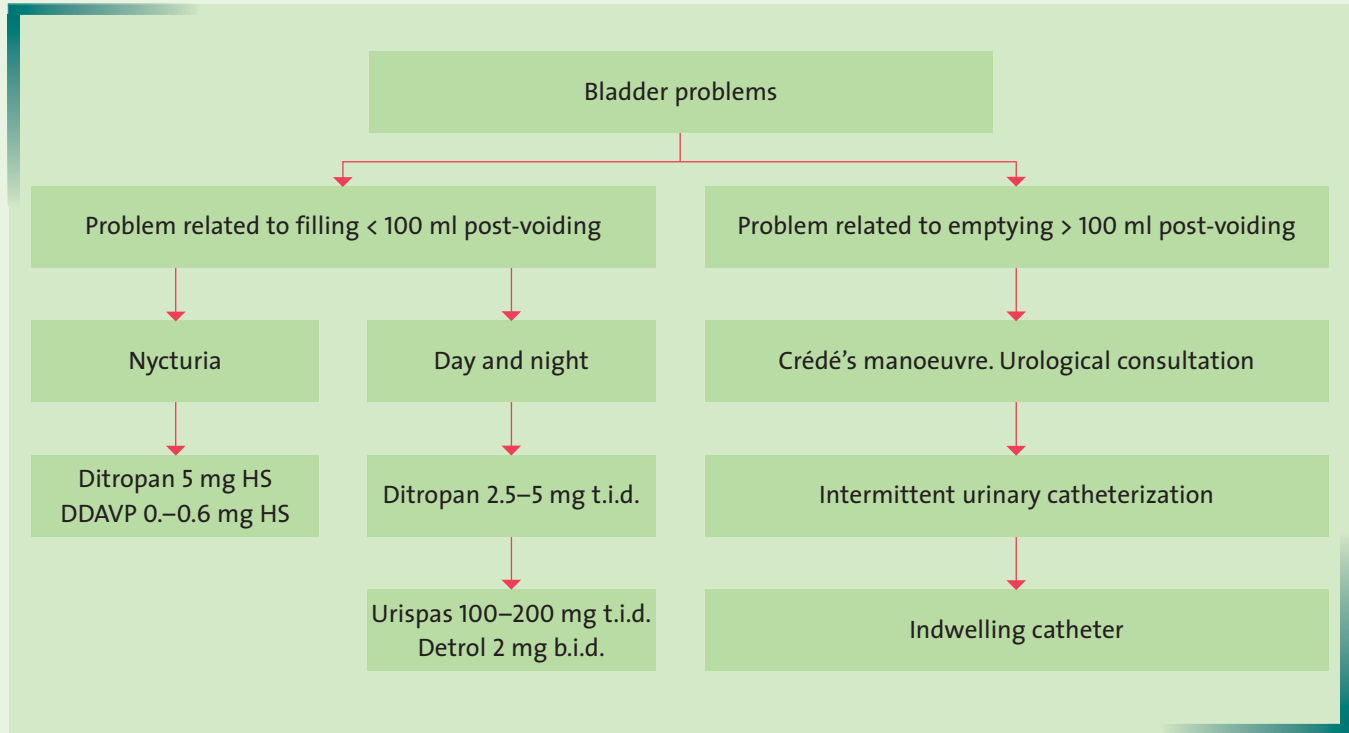
General reference:

Crayton, H., R.A. Heyman and H.S. Rossman. "A multimodal approach to managing the symptoms of multiple sclerosis". *Neurology*, 2004, vol. 63 (suppl. 5), pp. S12–S18.

Bladder and bowel problems are common in multiple sclerosis; in fact, 60% to 80% of people with this disease suffer from them. These symptoms are due to the deterioration of the myelin on the spinal cord.

There are two kinds of bladder problems: one related to filling (hypertonic bladder) and one related to emptying (atonic bladder). A hypertonic bladder is incapable of retaining a large volume of urine because of intermittent spastic contractions. These spasms cause urinary frequency, urinary urgency and incontinence. On the other hand, an atonic bladder, which is more common in the advanced stages of the disease, is characterized by an inability to begin urinating. In order to properly identify this problem, it is sometimes useful to do a urodynamic evaluation. However, if the patient is able to clearly describe the symptoms, it is easy to prescribe the appropriate medication.

People with MS usually complain of urinary urgency, nycturia, urinary retention and repeated urinary infections. The following flowchart clearly sums up the therapeutic options.



For problems related to retention, the two most frequently used drugs are Ditropan (oxybutynin) and Detrol (tolterodine). There is also a transdermal patch available under the name of Oxytrol (oxybutynin). These drugs favour urinary continence and reduce bladder spasms. Pelvic floor exercises will strengthen the muscles and improve the bladder's capacity to store urine.

For people who are unable to empty their bladder, intermittent catheterization is the solution. An indwelling catheter is a last resort, because of all the complications it can cause. In people for whom voiding is slow, double voiding can be recommended. For women, this means standing up for 2 or 3 minutes after urination, then sitting down again to continue urinating. For men, the opposite procedure applies: they should sit down for 2 or 3 minutes, then stand up again to continue urinating. This creates pressure on the bladder and allows for better evacuation. Some patients can use Cr  d  's method, which consists of pressing on the bladder with a fist. However, this method

must be used with caution since if the bladder is too full, there is a risk of reflux into the ureters and thus the possibility of pyelonephritis.

Note that aggravated neurological symptoms, such as increased difficulty walking, may conceal a urinary infection. People with multiple sclerosis may have an asymptomatic urinary infection. In order to avoid repeated urinary infections, it is important to do an analysis and take a urine culture to find out which antibiotic will be the most effective against the bacterium identified.

As for bowel problems, they take the form of constipation (present in about 36% to 51% of people with MS), which is defined as a maximum of two stools per week; urgent need to defecate; or fecal incontinence, which manifests as the involuntary voiding of stools. This kind of incontinence is present in 25% of people with MS,³ about once a week, and 51% of people with MS,⁴ less than once a month. Most people with constipation limit their consumption of liquids to avoid urinating too often, which aggravates the problem. Other factors that contribute to constipation include muscle weakness, certain medications, insufficient fibre and physical inactivity.

Certain emollient or laxative drugs may be needed to make elimination more regular. The most commonly used are docusate sodium (Colace®) and sennosides (Senokot®). The occasional use of glycerine suppositories may be recommended. Good mastery of bladder and bowel problems can improve the quality of life of people with multiple sclerosis.

References:

3- “Canadian MS Nursing Plan”, IntraMedical Health Services, 2000, p. 2–13.

4- Idem.

Table 4 – Treatments for bladder problems

Name	Dosage	Side-effects
Desmopressine (DDAVP®)	0.6 mg, 1 co po HS	Dry mouth, constipation, slight facial flushing, headaches, nausea, dizziness.
Tolterodine (Detrol®)	1 or 2 mg, 1 co po b.i.d.	Dry mouth, headaches, fatigue, vertigo or dizziness, abdominal pain, constipation, dyspepsia, diarrhea, urinary infection.
Tolterodine (Detrol LA®)	4 mg 1 co po HS	Dry mouth, constipation, vision problems, urinary retention, dry eyes.
Oxybutynin (Ditropan®)	2,5 or 5 mg 1 co po b.i.d. or t.i.d.	Dry mouth, somnolence, headaches, blurred vision, constipation, diarrhea, difficulty swallowing.
Oxybutynin (Ditropan XL®)	5 or 10 mg 1 co po HS	Dry mouth, headaches, constipation, diarrhea, urinary infections, dyspepsia, dizziness, pain, dry eyes.
Oxybutynin (Oxytrol®) Transdermal patch	36 mg - patch q. 3-4 days	Pruritis, erythema and blisters at the application site, dry mouth, diarrhea, dysuria.
Oxybutynine (Uromax®)	15 mg 1 co po HS	Dry mouth, headaches, dizziness, asthenia, abdominal pain, somnolence, vasodilatation, low back pain, syncope.
Flavoxate (Urispas®)	200 mg 1 co po t.i.d. or q.i.d.	Dry mouth, nausea, vomiting, nervousness, headaches, somnolence, increased eye pressure, hives and other skin problems, blurred vision.
Oxybutynin (controlled release) (Uromax®)	10 ou 15 mg 1 co HS	Dry mouth, headaches, dizziness, asthenia, abdominal pain, somnolence, vasodilatation, low back pain, syncope.

SEXUAL DYSFUNCTION

Sexual dysfunction is common in people with multiple sclerosis. Both sexes may experience a decline in libido, but it is more frequent in women. The causes are variable and may be organic. The decline in libido may also be related to a change in body image, depression or a change in the role of the sexual partner, who may become more of a “caregiver.” Some drugs such as antidepressants can also affect sexual desire. Dyspareunia, sensory problems, spasticity and urinary incontinence during intercourse or orgasm may also contribute to a decline in libido. Anorgasmia, due to a loss of sensitivity or vaginal dryness, may be both the cause and the consequence of low libido. Some products exist to treat vaginal dryness such as K-Y Jelly and Astroglyde. A prescription for hormones may be necessary to treat vaginal dryness and dyspareunia. In the case of a loss of sensitivity in the vagina or clitoris, the use of a vibrator may prove beneficial.

In men, the main causes of sexual dysfunction, other than the decline in libido, are erectile dysfunction and decreased penile sensitivity. When the other possible causes of erectile

dysfunction (diabetes, high blood pressure, heart disease, prostate problems, smoking, alcoholism, obesity, certain medications, and psychological problems) are ruled out, one can presume that this dysfunction is directly related to MS and is attributable to lesions of the spinal cord between D10 to L2 and S1 to S4.

Fortunately, there are now a number of medications to treat these problems. They have excellent efficacy in patients with multiple sclerosis. However, the RAMQ does not generally cover their cost, and private insurance companies only cover a portion of it.

Table 5 – Treatments for sexual dysfunction

Name	Dosage	Side-effects
Sildenafil (Viagra®)	50-100 mg po, from 45 to 60 minutes before sexual relations	Headaches, flushing, queasiness.
Tadalafil (Cialis®)	20 mg po, at least 1 hour before sexual relations	Headaches, dyspepsia, dorsalgia, myalgia, nasal congestion, flushing.
Vardenafil (Levitra®)	5-10 or 20 mg po, 30 to 60 minutes before sexual relations	Hot flush, headaches, nasal congestion, dyspepsia, dizziness, nausea.
Alprostadil (Caverject®)	1 inj. into corpus cavernosum, 15 minutes before sexual relations	In at least 1% of patients: pain in the penis after the injection or at the site of the injection, ecchymosis at the site of injection, penile edema, prolonged erection (4–6 hours), upper respiratory tract infections, flu-like symptoms, headaches, hypertension, etc.
Alprostadil (MUSE®)	125 µg, 250 µg, 500 µg, and 1,000 µg 1 trans-ureteral dose, 15 minutes before sexual relations	Pain in the penis, urethral burning sensation, slight bleeding or spotting from the urethra, testicular pain.

FATIGUE

Fatigue is known to be one of the most widespread symptoms among patients with multiple sclerosis. Some 80% of people with MS complain of fatigue. It is one of the worst MS symptoms for about 20% to 40% of patients, while 30% to 50% of patients experience fatigue more than any other symptom. According to the MS Council for Clinical Practice, fatigue is “a subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual or desired activities.”⁵

The exact cause of fatigue is still unknown. Certain hypotheses have been made, such as overactive inflammation resulting in the production of chemicals, and the distribution of plaques in the CNS, resulting in the inhibition of motor activity in the brain.

Certain factors may contribute to increasing fatigue, namely effort, stress, depression and infections. More obvious at the end of the day, it can be aggravated by heat and it interferes with physical activities, whether light or sustained, as well as with responsibilities at work, in society or at home. This symptom is often not well understood by

employers and sometimes not even by a patient’s family and friends or caregivers. In fact, fatigue is one of the main reasons why people with MS lose their jobs. And of course, a person who is suffering from fatigue may get the impression of having lost control over the disease. The more physical disabilities a person has, the more energy he or she has to expend to compensate for them. This kind of fatigue aggravates the motor disabilities.

Reference:

5- Multiple Sclerosis Council for Clinical Practice Guidelines (1998) – www.pva.org/prof/9811cpgs/fatigue

Table 6 – Characteristics of the three kinds of fatigue

Primary fatigue related to MS	Secondary fatigue related to MS	Secondary fatigue unrelated to MS
<ul style="list-style-type: none"> • Independent of the clinical form of MS • No relationship with the number of plaques on the MRI • Little relationship with the level of disability as measured by the EDSS* • Little relationship with depression • Aggravated by effort and heat • Increases during an attack 	<ul style="list-style-type: none"> • Reduced mobility • Side-effect of the following medications: <ul style="list-style-type: none"> - interferons - muscle relaxants (tizanidine, baclofen) - sedatives (clonazepam, Valium) - anticonvulsants (Tegretol, Neurontin) - antidepressants (Zoloft) • Disturbed sleep 	<ul style="list-style-type: none"> • Infections • Anxiety • Nutrition • Deconditioning (decrease in physical activity = decrease in cardiovascular capacity = increase in fatigue) • Depression

*EDSS: Expanded Disability Status Scale

Fatigue may be acute or chronic. Acute fatigue is related to an attack, an increase in the outside temperature or a fever, whereas chronic fatigue is persistent, that is, it is present for more than half of each day for more than six consecutive weeks.

Fatigue is a subjective symptom, which makes it difficult to assess. The first thing to do is to identify its origin and its nature. Giving the patient the right information will

make it possible to obtain the necessary data to treat any contributory factors. One might, for example, recommend the use of an air conditioner at home or at work (patients with MS may be able to deduct the cost of an air conditioner prescribed by a doctor from their income taxes) and controlled physical exercise, or one might help the patient to identify strategies to save energy. Fatigue can be reduced by rest, sleep and sexual activity.

DEPRESSION AND COGNITIVE DISORDERS

Certain drugs can mitigate the feeling of fatigue. However, their effectiveness varies greatly from one person to the next. The most commonly used drug is amantadine (Symmetrel, 100 mg, morning and noon), which is generally well tolerated. It reduces fatigue in about 30% of cases. If taken at the end of the day, it can cause sleep problems.

Other molecules such as fluoxetine (Prozac), sertraline (Zoloft) and dexamphetamine (Dexedrine) may also be prescribed.

In the case of acute fatigue, a few weeks' leave from work can be beneficial. However, for chronic fatigue, prolonged leave from work is rarely useful. If possible, it is preferable to opt for part-time work while attempting to gradually return to full-time work. Fatigue is one of the most disabling symptoms of MS and can sometimes cause permanent disability. A multidisciplinary therapeutic approach is often necessary.

Historically, multiple sclerosis has been considered to be a chronic disease that results in only physical limitations. Recently, it has become clear that depression is not only widespread among people with MS, but can develop at any stage of the disease. The frequency of depression in MS is significantly higher than in other chronic pathologies.⁶ Approximately 50% of people with MS⁷ experience an episode of depression by the age of 59, while only 12.9% of people with other chronic diseases will suffer from it. The severity of the depression is not linked to the extent of the physical limitations or the duration of the disease.

References:

- 6- Even, C., Friedman, S., Dardennes, R., Zuber, M. et J.D. Guelfi. « Prévalence de la dépression dans la sclérose en plaques. Revue et méta-analyse », *Revue Neurologique*, Paris, 2004, vol. 160, no 10, p. 917-925.
- 6- Multiple Sclerosis Society of Canada, *Living Well with MS: Mind Matters* (MS Society of Canada Educational Series), IMAG, Westmount Quebec, 2004.
- 7- Sadovnic A.D., Remick R.A., Allen J., Swartz E., Yee I.M., Eisen K. and al « Depression and multiple sclerosis », *Neurology*, 1996, vol. 46, p. 628-632.

Depression amplifies multiple sclerosis symptoms and decreases quality of life. Given that it can affect the perception of other symptoms, depression may give patients the impression that their disease is getting worse, when in fact it is not.

The exact cause of depression in multiple sclerosis is not known, but the presence of certain factors can contribute to it. Psychosocial factors (separation, divorce or loss of employment) may trigger or exacerbate depression.

Feelings of loss are normal reactions at the time of diagnosis or when new symptoms appear. But unlike the grieving process that follows the loss of a loved one, the grieving process associated with MS generally fluctuates as a function of the symptoms and physical limitations that appear during the disease. Thus, every patient's reactions are unique. The most common ones are denial, anger, sadness and bargaining ("Maybe if I ate better, I would be cured"). Many patients feel real anxiety about what the future may hold for them. To reassure patients, it is important to remind them that most people with MS have a normal life expectancy and that, thanks to the

progress that has been made in recent years, in particular the development and release of new treatments, most of them will now be able to cope with the disease while maintaining a good quality of life.

The treatment of depression in MS is no different than in the general population. Both pharmacological and non-pharmacological approaches can be used. Physical exercise contributes to the maintenance of good physical and psychological health. More and more studies show that exercise has a positive impact on one's perception of one's overall health. Some people respond well to psychotherapy. On the pharmacological side, SSRIs are the drugs of choice. Citalopram (Celexa®), administered at a dose of 20 mg per day, is often effective and well tolerated. Tricyclic antidepressants (e.g., amitriptyline, at a dose of 10 to 75 mg at bedtime) may be useful, bearing in mind their effect on neuropathic pain, insomnia and urinary urgency.

One must be alert for depressive symptoms, especially since the suicide rate is 7.5 times higher in people with MS than in the general population, where it is 2% ⁷. So it is important to maintain good communications with the patient and promote openness about this often-taboo subject. Above all, do not hesitate to recommend a psychological consultation or make use of antidepressants, since successful treatment of depression may allow patients to keep their job and maintain their personal relationships, thereby improving their quality of life.

Cognitive disorders are frequent with MS, even in the first stages. During the course of the disease, they will affect 45% to 65% of patients. The functions most often affected are memory, attention and information processing. Typically, a person with MS and cognitive disorders complains of not being able to handle two things at once or to organize things properly. In addition, the cognitive deficit may significantly limit the patient's ability to concentrate.

Reference:

7- Sadovnic A.D., Remick R.A., Allen J., Swartz E., Yee I.M., Eisen K. et coll. « Depression and multiple sclerosis », *Neurology*, 1996, vol. 46, p. 628-632.

These cognitive problems have a negative impact on quality of life, work, sexuality and social activities.

A neuropsychological assessment should be performed if the patient mentions that cognitive disorders are causing difficulties at work. Cognitive rehabilitation offered by a neuropsychologist or occupational therapist should then be considered, bearing in mind the person's specific deficits.

In a two-year study, interferon beta-1a (Avonex®) slowed the development of cognitive problems. In addition, donepezil (Aricept®) has proven effective in reducing cognitive dysfunction during a small pilot study. A larger-scale study is under way.

CONCLUSION

The symptoms of multiple sclerosis can vary greatly from one person to another, and even in the same person over the course of the disease. Primary health care workers have a big role to play in maximizing the quality of life for their patients with multiple sclerosis.

Medical monitoring can make it possible to identify and treat certain disabling symptoms and thus help patients to better adapt to a disease with which they will have to deal for the rest of their lives.

OTHER PUBLICATIONS BY THE MULTIPLE SCLEROSIS SOCIETY OF CANADA

- Guide to MS Medications
- Living Well with MS: Managing Fatigue
- Understanding Bladder Dysfunction in MS
- Understanding Bowel Problems with MS
- Sexuality and MS
- Living for Today: Managing MS Pain
- Talking with Your MS Patients about Difficult Topics

You can obtain a complete list of publications by the Multiple Sclerosis Society of Canada, Quebec Division, by visiting the website at www.mssociety.ca/qc or calling 1-800-268-7582.

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To be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life.



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