

Considering Your Options:

Choosing an MS Therapy



A DVD program and information booklet from



Considering Your Options:

Choosing an MS Therapy

If your doctor has recommended that you start a disease-modifying therapy to treat your MS, the enclosed video program will explain why treatment may be your best option.

The full-length video examines the benefits and challenges of starting therapy and features a candid conversation with leading MS experts:



Dr. T. Jock Murray

Professor Emeritus
Founder,
Dalhousie MS Research Unit
Halifax, Nova Scotia

Colleen Harris

Nurse Practitioner
University of Calgary MS clinic
Calgary, Alberta

Dr. Daniel Selchen

Chief of Neurology
St. Michael's Hospital
Consultant, MS clinic
Toronto, Ontario

Lynn McEwan

Advanced Practice Nurse
London Health Sciences Centre
MS clinic
London, Ontario

Hosted by Aprile Royal, RN MEd, Assistant Vice President, Medical Information and Education for the MS Society of Canada. The program also features Dr. Paul O'Connor, Director of the MS clinic, St. Michael's Hospital, Professor of Neurology, University of Toronto, and National Scientific and Clinical Advisor to the MS Society of Canada.

■ Considering Your Options

If you are a person living with multiple sclerosis, you and your doctor may have discussed starting treatment with a disease-modifying therapy to control your disease.

For many years, there were no effective treatments for MS and we are indeed fortunate that there are now five medications from which to choose. But having a choice is always challenging. How are the medications different? What effects will they have, and what side effects? How do you select the best therapy for your individual circumstances?

Considering Your Options: *Choosing an MS Therapy* was developed by the MS Society of Canada to address these very issues. During the program you'll meet Krista, a young woman who decided to start treatment a year ago; and Janet, a remarkable woman who has continued on therapy for 11 years. There is also a lively discussion among MS experts, who will answer many of the questions you may have about treatment.

This booklet provides a summary of the information contained in the video program and addresses some of the issues and concerns you may have about starting therapy.

The MS Society of Canada does not recommend or endorse any specific medication for MS. But our hope is that the information in this program will help you make a more informed decision when faced with the treatment options available to you.



Aprile Royal, RN MEd

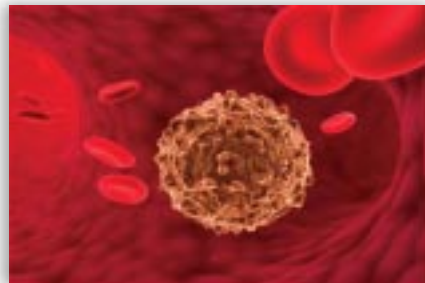
Assistant Vice President
Medical Information and Education
MS Society of Canada

■ What is MS?

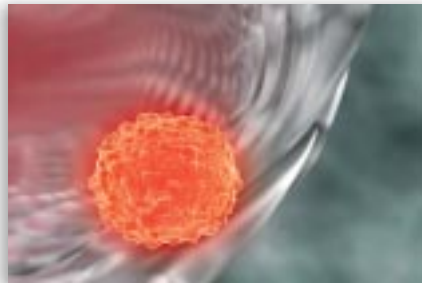
Multiple sclerosis is believed to be a disorder of the immune system. Normally, the immune response protects the body by attacking foreign invaders, such as bacteria and viruses. But in MS, this attack is directed against the body's own tissues. This is called an autoimmune response (*auto* means *self*), and MS is believed to be an *autoimmune disorder*.

A T cell's journey in MS

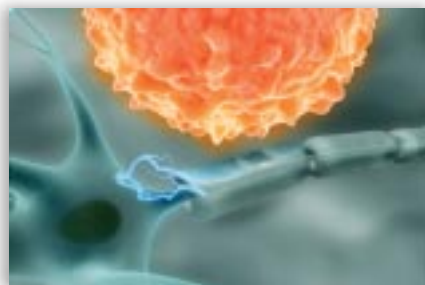
1. *T cells become activated and migrate to the blood-brain barrier (BBB), which normally prevents harmful substances from entering the central nervous system (CNS).*



2. *Activated T cells adhere to the BBB, then infiltrate the CNS.*



3. *In the CNS, activated T cells attack the myelin that protects nerve fibres.*



Two of the hallmarks of an immune response are inflammation and swelling. For example, these are normally seen when your immune system reacts to a mosquito bite or a bee sting — the skin becomes inflamed and swollen. A similar process occurs in MS. The immune system becomes activated, although the trigger for this immune flare-up isn't known. As part of this process, cells of the immune system (called T cells) migrate into the central nervous system (CNS, i.e. the brain and spinal cord). Once inside the CNS, these activated T cells cause inflammation and swelling in the brain and spinal cord.

Inflammation and swelling in the CNS cause damage to myelin, the protective insulation that covers nerve fibres. These nerve fibres act like “wires” for the body's electrical signals. When an electrical cord is damaged, it can cause a short circuit or a loss of power. A similar process occurs in MS. When the myelin “insulation” is damaged, the electrical signals travelling along the nerves can be interrupted. The “short circuits” are experienced as MS symptoms, such as:

- Tingling
- Numbness
- Pain
- Muscle weakness.



Magnetic resonance imaging (MRI) allows doctors to see inflammation in the central nervous system. Areas of inflammation are called lesions or plaques and are characteristic of MS.

■ Why Treat MS?

An MS relapse is an indication that there is inflammation in the brain and/or spinal cord. However, the number of relapses you have doesn't give a true picture of disease activity. Inflammation is an ongoing process and only 1 in 10 inflammatory episodes will be felt as an MS relapse.

As inflammation flares and subsides, your body has time to recover from some of the damage that has been caused. That may be why MS symptoms can disappear completely in between relapses. Unfortunately, over the lifetime course of MS, your body isn't able to keep up with all the repair work that is needed. As a result, there is a steady accumulation of myelin damage, and a progressive loss of nerve fibres.

Even a healthy brain will accumulate nerve damage because of aging, but this process is much more rapid in MS. Initially, the brain can compensate for some of the damage, just as a stronger leg will carry the burden for a weaker leg. But this capacity is limited, and over the long course of MS, the brain uses up its reserves. Once nerve damage reaches the "tipping point", permanent and irreversible nerve deficits will appear.

The key to preserving nerve function and preventing permanent disability is to slow down the disease process before the tipping point is reached.

“ *It's important that people select treatment early. The reason initially is to reduce evidence of activity of the disease. Not just to reduce relapses but evidence of the activity that we see on the MRI. We know that activity is occurring even when very little seems to be happening. But the hope is that treating people early will reduce long-term disability.* ”

Dr. Jock Murray



How Do MS Medications Work?

The process that leads to nervous system damage in MS can be summarized as a series of steps:

- Step 1.** Specialized cells of the immune system, called T cells, become activated.
- Step 2.** Activated T cells in the blood stream adhere to the blood-brain barrier (BBB). The BBB is a layer of tightly-packed cells that acts as a filter, preventing many substances from entering the central nervous system (CNS).
- Step 3.** The BBB filter is more porous in MS, so activated T cells are able to enter the CNS.
- Step 4.** Inside the CNS, activated T cells cause inflammation and damage to myelin and nerve fibres.

An important end goal of MS therapy is to prevent or lessen the damage being done to myelin and nerve fibres. This can be achieved by targeting the activated T cells — either by preventing them from entering the CNS or by making their effects less harmful.

There are three different types of medication for MS: the beta-interferons, glatiramer acetate, and natalizumab. All of these therapies alter, or modulate, the immune response but do so by different mechanisms.

Beta-interferons – Avonex, Betaseron and Rebif

Interferons are proteins that occur naturally in the body and are normally produced by immune cells to “interfere” with foreign invaders, such as viruses, bacteria or parasites. Interferons can also be synthesized in a laboratory for use as medications to treat a variety of diseases. In MS, the type used is called beta-interferon, of which there are two subtypes: beta-interferon-1a (Avonex, Rebif); and beta-interferon-1b (Betaseron).

Beta-interferons have a number of beneficial effects on the MS disease process. One effect seen in MS is to strengthen the blood-brain barrier (BBB). As mentioned previously, the BBB filters out harmful substances so they don't enter the CNS. But in MS, the BBB becomes more porous, allowing activated T cells to gain access to the brain and spinal cord.

Beta-interferons reinforce the barrier (Step 3 above), so fewer activated T cells can enter the CNS and cause myelin damage.

Glatiramer acetate – Copaxone

The immune system produces many types of T cell, including T helper cells (Th), which help to regulate the immune response. When a Th cell detects a foreign protein (such as bacteria, bee venom, etc.), some Th cells will respond by promoting inflammation (called Th1 cells), while others will respond by reducing inflammation (called Th2 cells). Having cells that promote inflammation and others that reduce inflammation enables the body to fine-tune the immune response according to the body's needs at the time.

Glatiramer acetate (Copaxone) is a synthetic mixture of amino acids, the building blocks of proteins. As a protein, glatiramer acetate is detected by the immune system. But instead of the immune system responding with Th1 and Th2 cells, the medication shifts the response in favour of Th2. So a higher proportion of the Th cells will be Th2, i.e anti-inflammatory.

When these Th2 cells enter the CNS, they cause less inflammation and damage than the inflammatory Th1 cells (Step 4 above). This means that during an MS flare-up, people taking glatiramer acetate will experience less tissue damage in the brain and spinal cord.



Natalizumab – Tysabri

As part of the immune response, the body produces a variety of antibodies, each of which is targeted to a certain type of protein. When scientists identify a type of protein that is involved in a disease process, they can target that protein by synthesizing a specific type of antibody.

As mentioned previously, before an activated T cell can enter the CNS, it must first stick to the blood-brain barrier. To stick to the BBB, T cells use a type of “glue”, called an adhesion molecule. This adhesion molecule (called alpha-4 integrin) is a protein, so it can be targeted by a synthetic antibody.

Natalizumab (Tysabri) is synthetic antibody (called a monoclonal antibody) that specifically binds to alpha-4 integrin. By blocking this adhesion molecule, natalizumab prevents activated T cells from sticking to the BBB (Step 2 above). This means that fewer activated T cells are able to squeeze through the BBB and cause tissue damage inside the CNS.

What Can I Expect From My MS Medication?

One immediate benefit of an MS medication may be fewer relapses. This doesn't mean that you'll have no relapses. Many people with relapsing-remitting MS have just one or two relapses per year on average, so a beneficial effect on relapses may not be noticeable. We're aware when an MS relapse occurs, but we're not aware of the relapse that has been prevented.

It's also important to realize that if you do have a relapse, this doesn't mean that your medication isn't working. Attacks can still occur while on therapy. But the hope is that the inflammatory relapses that do occur will cause less nerve damage.

The effect of treatment on relapses is important, but this benefit is not the goal of therapy. The real intent of these *disease-modifying drugs* is to modify the MS disease process itself.

Medications can be used to treat an acute condition (such as a headache), or a chronic problem (such as high blood pressure). This is an important distinction because a chronic medication often won't have any perceived benefits right away — but it's still important to stay on therapy.

“ *We have to make very clear to patients that what we're trying to do with therapy is to prevent them from getting worse — to prevent the disease from progressing. A lot of patients will not be completely relapse-free on medication, and that that doesn't necessarily mean that the medication isn't working. The management of expectations is exceedingly important because if people start treatment with the wrong conception of what treatment is going to do for them, they're at very high risk for dropping out of therapy.* **”**

Dr. Dan Selchen



Disease-modifying drugs should be thought of as a chronic therapy. In MS, you aren't aware of CNS inflammation until you have a relapse. Similarly, you will not be aware of how treatment is reducing inflammation and nerve damage on a day-to-day basis. But the hope is that you will prevent — or at least limit — some of the nerve damage that typically accumulates in people living with MS. The further hope is that preventing nerve damage in the short term will mean that you will not worsen and develop disability in 15 or 20 years from now.

When starting any treatment, it's important to have realistic expectations of what the medication will and won't do. MS medications won't relieve any symptoms you may be having. They won't make you feel better. In fact, you may feel a little worse — at least in the short term — because of the medication's side effects. The same is true of other preventive therapies such as blood pressure medications: the goal when lowering blood pressure is not to feel better but to prevent a heart attack or stroke in the future.

Starting an MS medication can be challenging. But it's important to realize that with each injection, you are “sticking it” to the disease. The needle is your best weapon in your personal battle with MS.

“*I think it's a very positive time once they've made the decision to start therapy. They can now control their disease. They can do something about it — follow this wellness approach to stay as well as possible for as long as possible.*”

Colleen Harris



What Medication Side Effects Should I Expect?

All medications have the potential to cause side effects. The following is a list of some of the more common side effects that may occur with a disease-modifying therapy.

Beta-interferons

Side effects that may occur with a beta-interferon include:

- **Flu-like symptoms**, such as muscle aches and pains, which can make you feel as if you are coming down with the flu. These can occur at any time during therapy but are most often experienced in the first few months after starting treatment. Flu-like effects generally diminish over time as your body adjusts to the medication. Taking a non-prescription pain medication (such as Aspirin or ibuprofen) before or after your injection can relieve these symptoms.
- **Injection site reactions**. These may include redness, itching or swelling at the site of injection. They occur because your body is reacting to the needle penetrating the skin. Applying hot or cold compresses before or after the injection can minimize this effect. It is also important not to inject the same part of the body too often since this will irritate and damage the skin.

Beta-interferons have the potential to cause serious liver injury (e.g. hepatitis), although this is very rare. There is also the chance of treatment producing too great an effect on the immune system, which could increase the likelihood of infection. So during beta-interferon treatment, you will be required to have periodic blood tests to monitor your blood cell count and to ensure that your liver is functioning normally.

Other symptoms can occur and should be reported to your doctor. For example, early studies of the beta-interferons suggested that there may be an increased risk of depression with treatment, although it's important to know that MS itself can be associated with depression. Symptoms of depression may include depressed mood, anxiety, weight gain/loss and sleep difficulties. Talk to your family doctor or neurologist if you are experiencing any mood changes.



Glatiramer acetate

The most common side effects with glatiramer acetate include:

- **Injection site reactions.** These may include redness, itching or swelling at the site of injection. They occur because your body is reacting to the needle penetrating the skin. Applying hot or cold compresses before or after the injection can minimize this effect. It is also important not to inject the same part of the body too often since this will irritate and damage the skin.
- **Post-injection reactions.** Symptoms may include breathlessness, chest pain and anxiety. This can feel as if you are having a heart attack or an anxiety attack. The cause is unknown. Symptoms typically improve within 15 minutes and do not have any lasting effect.
- **Lipoatrophy** (denting or pitting of the skin) can occur over the longer term. This is caused by a loss of fatty tissue under the skin. Regularly injecting different sites will help to minimize this effect.

“ *The discomfort and the skin reactions are sometimes an issue for patients. However, we can teach them strategies to help manage these. And they often master it and learn how to inject comfortably at the right time of the day when they have time to do it correctly.* ”

Colleen Harris

Natalizumab

Unlike the other MS medications, natalizumab is not self-injected. It is administered by a doctor or nurse in a specialized infusion centre. Side effects are most common during or immediately after the infusion, and a health professional will monitor you for any untoward effects. Later effects may also occur and should be reported to your doctor.

The most common side effects seen with natalizumab can include:

- **Hypersensitivity reactions**, such as rash, hives, itching or flushing. In extreme cases, hypersensitivity reaction can also include rigors, a drop in blood pressure, difficulty breathing and chest pain.
- **Infusion-related reactions**, such as headache, dizziness or fatigue, can also occur, usually within the first two hours after the infusion.
- **Increased risk of infections** (e.g. urinary tract infection, pneumonia). If you feel you are developing an infection, report it to your family doctor or neurologist immediately.

A Note of Caution

Natalizumab (Tysabri) is generally not the first choice when selecting an MS medication. This is because natalizumab has been associated with an increased risk of a condition called PML (progressive multifocal leukoencephalopathy), which can cause severe disability or death. This side effect is very rare. The only reported cases in MS occurred when natalizumab was used in combination with another disease-modifying drug.

Although the risk of PML is very low, it is a very serious complication. So natalizumab is generally used only after a person has not responded to another disease-modifying drug, or if they cannot tolerate the side effects of a beta-interferon or glatiramer acetate.





How Do I Choose the Right Medication for Me?

Before you choose to take a disease-modifying drug for your MS, it's important to do a bit of homework. Your doctor and MS clinic nurse can talk to you about the different options available to you. The MS Society of Canada can also provide you with detailed regulatory information for each of the disease-modifying medications. Some people find it helpful to talk to others who are living with MS. You can contact other people with MS either through the MS Society, your local MS support group, or through the growing online community of chat rooms and websites for people affected by MS.

Some of the issues you may want to consider when choosing a medication are:

- **Effectiveness:** The five MS medications have been studied extensively in clinical trials. All have been shown to be effective in reducing the frequency of relapses and CNS inflammation.
- **Safety:** Long-term studies — involving people on treatment for 15 years or more — have indicated that the beta-interferons and glatiramer acetate appear to be safe. As mentioned previously, there is a small risk of severe side effects with natalizumab. This medication has not been available for as long as the others so the long-term effects are not known.
- **Side effect profile:** In reading through the possible side effects of each medication, you may decide that there are some side effects that you want to avoid because of your lifestyle or personal preference. It's important to note, however, that no one knows how you will react to a medication before you try it. Once you start therapy, keep your doctor informed of any unpleasant effects you're experiencing. If you find that your first choice is just too difficult to keep taking, you can always switch to another one of the medications. It's more important to stay on one of the therapies rather than stay with the same therapy.

- **Frequency of injections:** As we see in Table 1, MS medications must be taken at different intervals — from once a day for Copaxone, to once a week for Avonex, and once a month for Tysabri. This difference will be an important factor to some people. For example, if you travel frequently for extended periods, you may want less frequent injections. Others like to incorporate their injection into their daily routine. What works best will depend on your lifestyle and personal choice. Self-injection is like joining a gym: if it doesn't suit your lifestyle, it won't become part of your regular routine. So choose what works for you.

“If somebody has side effects on one treatment and they're not doing very well on it, I wouldn't rule out that treatment for you. One person's experience may not be your experience. You need to find a treatment that's best for you.”

Krista



Table 1. MS Medications in Canada

Type of medication	How it is administered	Frequency of injections
Beta-interferon <ul style="list-style-type: none"> • Avonex • Betaseron • Rebif 	<ul style="list-style-type: none"> • Intramuscular • Subcutaneous • Subcutaneous 	<ul style="list-style-type: none"> • 1 time per week • 1 time every 2 days • 3 times per week
<ul style="list-style-type: none"> • Glatiramer acetate (Copaxone) • Natalizumab (Tysabri) 	<ul style="list-style-type: none"> • Subcutaneous • Intravenous infusion 	<ul style="list-style-type: none"> • 1 time per day • 1 time every 4 weeks

*Intramuscular = into the muscle. Subcutaneous = under the skin.
Intravenous infusion = slow drip into a vein (in a clinic or hospital).*





■ Some Common Questions About Starting Therapy

“Why do MS medications have to be injected?”

All of the MS medications are proteins, and many protein-based drugs (such as insulin) are quickly destroyed by stomach acid if they are ingested. So all of the MS medications must be injected into the body (which bypasses the stomach) to be effective. A number of treatments are currently being developed as oral medications (pills or capsules), but these aren't available yet.

“Is self-injection difficult?”

Self-injection is a technique that needs to be learned so it is performed properly and safely. An MS nurse will be there to instruct you when you start therapy. The drugs' manufacturers also provide help lines and will be able to provide some helpful tips. Most people are able to master self-injection very quickly — within two or three sessions with a nurse.

To make injections easier, Avonex, Copaxone and Rebif are available as a pre-filled syringe, which means that it's ready to inject. You won't have to mix the medication yourself. Betaseron comes with a syringe that is pre-filled with a diluent (diluting agent) that you must mix with the drug (which is a powder). Tysabri is administered by a health professional in a specialized setting.

The three beta-interferons and glatiramer acetate also come with an auto-injector device, which positions the needle correctly. You just have to push a button. (The auto-injector also hides the needle in case you're a little squeamish.)

“ *I was one of the worst people when I was told that I was going to have to have an injection because I’m afraid of needles. And at first it kind of took over my life. If I had to have an injection it would wreck my day. But I’ve been injecting for 11 years now and one thing that really helped me was that I learned meditation. I learned to accept things as they are.* **”**

Janet



“Is there anything I can do to make the injections less painful?”

Some people find that applying a cold compress before injecting helps to numb the site and makes things less painful. A bag of frozen vegetables wrapped in a towel should do the trick. A warm (not hot) compress can also be helpful.

Another tip is to take a non-prescription pain reliever (such as Aspirin or ibuprofen) about an hour before injecting.



“There are some patients who come in who are very adamant that they cannot do it. So you find the means to help them with it. But a majority of people, even though they say they don’t like needles — and I think we’re all in that category — are really able to do it and they surprise themselves that they’re able to do it.”

Lynn McEwan



“Are there resources to help me?”

All across Canada there are thousands of people living with MS and many resources available to help you. Your best introduction to what is available is the MS Society of Canada. The Society will provide you with information about MS and can put you in touch with your local chapter and support groups in your area. The MS Society’s contact information is listed in the back of this booklet.

For more information about a specific medication, you can contact the drug’s manufacturer. The contact information is also listed in the back of this booklet.



“How long will I need to receive treatment?”

MS is a chronic illness so you will need life-long treatment. It’s important to note that none of the MS therapies is a cure. But if taken regularly as prescribed by your doctor, your medication will help keep your disease under control and may help to prevent disability in the future.

“Should I become pregnant while taking an MS medication?”

It is best to avoid taking any medication during pregnancy — and this applies to MS treatments as well. If you are a woman taking a disease-modifying drug, it is strongly advised that you use an effective method of birth control to prevent pregnancy.

Doctors generally advise women to stop taking their medication a few months before they plan to become pregnant. The frequency of MS relapses often diminishes during pregnancy, probably because of the effect of hormonal changes on your immune system. However, the risk of having a relapse increases immediately after childbirth. To re-gain control of your disease, it’s best to re-start your medication after giving birth. But to avoid exposing the baby to your medication, you will be advised not to breastfeed while taking an MS medication.

These issues will need to be discussed in detail with your doctor so you can devise a plan that works best for the health of you and your baby.



“Is there anything else I can do for my MS?”

While you must take care of your MS, you must also take care of yourself. MS doesn't exempt you from any of the other medical problems that can affect us. So it's important that treatment is incorporated into a healthy lifestyle that includes a sensible, well-balanced diet and regular exercise.

“ There is a tendency to think that a drug is the treatment for a disease — but it's just one of the components of treatment. Treatment is a broad idea that involves the person's general health — things like an appropriate diet, exercise, their personal life, how they make decisions about their relationships, communications, support systems, having professionals that you rely on. Patients should understand that they're really in control of their life and their treatment. Drugs are part of it. But the over-reliance on medications to answer everything tends to result in disappointment. ”

Dr. Jock Murray



■ A View to the Future

If you and your doctor have decided that starting treatment now is your best option, it's important to take some time to think about how you will incorporate therapy into your daily life. The best treatment will be the one that you can continue taking in the many years that lie ahead of you.

Despite all of the many uncertainties of living with MS, starting treatment enables you to take control of the situation. As you look to the future, you can be reassured that you are doing everything you can to fight your illness.

MS therapy has changed dramatically in the past 15 years with the introduction of medications that modify the course of the disease. The next 15 years should be equally exciting. Ongoing research, our current medications and new drugs that are now being developed promise a very bright future for people living with MS.

■ Contact Information

Multiple Sclerosis Society of Canada

175 Bloor St. E.

Suite 700, North Tower

Toronto ON M4W 3R8

Telephone (toll-free in Canada): 1-800-268-7582

Fax: (416) 922-7538

www.mssociety.ca

Drug manufacturers

- Bayer Healthcare (Betaseron): 1-800-977-2770
- Biogen Idec Canada (Avonex, Tysabri): 1-888-456-2263
- EMD Serono (Rebif). English: 1-888-677-3243; French: 1-877-777-3243
- Teva Neuroscience (Copaxone): 1-800-283-0034



Produced by



on behalf of



Multiple Sclerosis Society of Canada
Call toll-free in Canada 1-800-268-7582
Email: info@mssociety.ca
Web site: www.mssociety.ca

© Multiple Sclerosis Society of Canada 2008. All rights reserved.
None of the contents may be reproduced in any form without prior
written permission of the Multiple Sclerosis Society of Canada.

The opinions expressed do not necessarily reflect the opinions or recommendations
of the sponsor. Consult full prescribing information before initiating any medication
described herein.

Printed in Canada

Supported through
an unrestricted
educational grant from







Multiple Sclerosis Society of Canada
Call toll-free in Canada 1-800-268-7582
Email: info@mssociety.ca
Web site: www.mssociety.ca