Multiple sclerosis treatment

There are three groups of treatment for the disease:

1. Treatments during the acute phase of the disease and its relapses:

A. Corticosteroids - anti-inflammatory drugs
Steroids are given during an attack of the disease in order to stop it, improve clinical symptoms and hasten recovery. These include oral prednisone and methyl-prednisolone ( Solumdrol ) which is given intravenously.
Steroids have a quick impact and sometimes striking results on the symptoms of the disease. However, there are side effects that may occur as a result of steroid therapy, including accelerated heart rate, increased blood pressure and blood sugar values, hot flashes, sleep problems, swelling and osteoporosis. Taking steroids may also affect mood. There are those who feel a sense of “mood elevation”. However there may also be a decrease in mood and irritability. These side effects are usually temporary, but may be more significant in cases where the patient is taking large doses of steroids for long periods of months or years.

B. Plasmapheresis
Plasmapheresis is the treatment that involves " mechanical " cleaning / filtering of the blood from antibodies that target/attack the myelin. This treatment, similar to steroids, is not a unique treatment for MS but also for other inflammatory diseases. Plasmapheresis is performed by a device similar to a dialysis machine. The patient is inserted an intravenous catheter that removes and returns the blood after passing it to the machine. Every treatment lasts about two hours. Plasmapheresis may lead to impressive improvement in some patients, especially those with unique characteristics of MS (such as patients with Myelitis - inflammation in the spinal cord and those who have not responded adequately to steroids). There are very few side-effects associated with this treatment, including occasional changes in blood pressure and blood viscosity.

2. Preventive and chronic treatments:

A. Medications that “balance” the immune system (immune modulation)
These drugs are given chronically to prevent relapses and delay the progression of the disease. Are these drugs can lower an average of 30 to 50 % the number of MS-relapses and inhibit the progression of the disease. However, not all patients respond equally to these therapies.
Preparations of this group include COPAXONE and 3 types of interferon ( AVONEX, REBIF and BETAFERON), TYSABRI, GILENYA, TECFIDERA and more.
Copaxone ( Teva ) - This medication consists of 4 amino acids, and its structure bears resemblance to the myelin proteins. The drug is administered by subcutaneous injection once a day and because of the similarity to myelin it causes a decrease in the autoimmune response against the myelin. There are almost no side effects, except occasional “flashes” and mild redness and swelling at the injection site or allergic reactions.
Avonex ( Biogen ) - it is injected intramuscularly once a week. Possible side effects include mainly flu-like symptoms ( fever, muscle aches ).
Rebif ( Serono ) - is administered by subcutaneous injection three times a week. Possible side effects include mainly flu-like symptoms ( fever, muscle pain ), liver dysfunction and redness and swelling at the injection site.
Betaferon ( Bayer ) - is injected subcutaneously every other day. Possible side effects include mainly flu-like symptoms ( fever, muscle pain ), liver dysfunction and redness and swelling at the injection site.
All interferons side effects usually persist up to 24 hours of injection, and decrease as the body gets used to the drug and can be significantly reduced by altering the timing of injection ( injection in the afternoon) and by administration of paracetamol after the injection.
Avonex, Betaferon and Rebif - are very similar in their chemical composition; they are all different types of beta interferon (a natural hormone that exists in our bodies and its role is to suppress /
stop inflammation), with minor differences in the composition and the quantity of amount of the active ingredient in each of them.

**Tysabri** (Biogen) - is a drug that belongs to a new class of therapies that affect the immune system and reduce inflammation. This group of drugs are defined as monoclonal antibodies, i.e. antibodies synthesized in order to attack specific proteins on the surface of inflammatory white cells. In this way, the suppression of the immune system is not generalised but more specific. There are several drugs in this group in addition to Tysabri, and include RITUXIMAB, and ALEMTUZUMAB. Meanwhile, only Tysabri was approved in most countries as a treatment for MS. Tysabri binds to a protein (on the surface of lymphocytes), which is responsible for the migration of cells into the central nervous system. Thus, although there are inflammatory cells in the blood, they do not enter the central nervous system and therefore they cannot cause damage to the myelin. Along with the great effectiveness of Tysabri in multiple sclerosis, this drug may also cause various and even dangerous, side effects, and especially/specifically an acute viral infection called PML, which can be sometimes fatal. So far, the risk of such infection after Tysabri-treatment has been estimated to approximately - 1/1000 treated patients. Therefore, treatment with Tysabri is intended only for cases in which disease activity is particularly high, and which have failed on first-line treatments (interferons and COPAXONE). Recently, there is a special blood test that can help to estimate the risk of PML in Tysabri-treated patients, the anti-JC virus antibody test. Antibody negative patients are at lower risk and can be treated for longer time periods with Tysabri.

**Fingolimod** (Gilenya) - Fingolimod, is a novel immunomodulating treatment for MS intended for patients with extensive forms of disease. The drug is administered orally at a dose of 0.5 mg. Gilenya belongs to a new class of drugs that affect the lymphocyte trafficking. It "locks" the lymphocytes outside the lymph nodes and prevents from them to reach the brain, reducing thus the risk for CNS inflammation and demyelination. No serious side effects were reported from the use of this drug. Common conditions include changes in heart rate and blood pressure after the first dose (requiring therefore a close follow up for few hours during the first day of treatment), and edema of the inner eye in a very small percentage of patients. These effects are reversible.

**Di-methyl Fumarate (BG12)** (TECFIDERA). A novel immunomodulatory drug that has shown high efficacy in preventing MS relapses and has an innovative mechanism of action that prevents oxidation and nerve damage. TECFIDERA is given orally and may be accompanied by flashing phenomena, pain and side gastrointestinal side effects.

**Teriflunomide** (AUBAGIO): A new generation immunosuppressive drug (similar in action to azathioprine but also with immunomodulatory properties). Was shown to suppress the relapse rate by around 30 % (similar action to interferons) and is recently registered for relapsing form of MS. Side effects may include alopecia, infections and liver enzymes elevation.

**B. Drugs that suppress the immune system (Cytotoxic/immunosuppressive)**

Such drugs are used in patients with a chronic progressive course, in order to suppress inflammation by lowering the number of white cells in the immune system (and consequently, delay the progression of the disease). These drugs can be beneficial in selected patients and their action is not specific. Because of the weakening of the body's immune defence there is a greater risk for infections.

Medications of this group that are in use for MS, include:

**Azathioprine, methotrexate and cyclosporine** - which are oral medications. These are relatively mild treatments among the immunosuppressants.

**Cyclophosphamide** - can be given orally or intravenously. It represents one of the most effective immunosuppressive treatments and is primarily intended for situations of a highly active and progressive disease.
Mithoxanthrone (NOVANTRONE)- is administered intravenously once a month to once every 3 months, and has been proven as an effective immunosuppressive treatment of multiple sclerosis. However, prolonged treatment may cause a decrease in cardiac function and is associated with a high risk cancer of the blood.

Teriflunomide - (AUBAGIO) may also be considered as a “soft” immunosuppressive medication. This group treatments are actually a kind of low-dose chemotherapy. A good monitoring of blood counts and liver function can prevent many of the side effects, which sometimes include acute infections, liver enzymes elevation, gastrointestinal effects, alopecia and risk for cancer.

C. New and future treatments:
Aelmtuzumab (Lentrada)
This is a new monoclonal antibody that blocks all the mature lymphocytes and induces a repopulation (rebuilding) of the whole immune system. The drug has been recently introduced as a third line therapy for MS. It has shown impressive efficacy, including the possibility of improvement in disability in approximately half of the treated patients, but it is also associated with risks of side effects (infections, thyroid disease, and a low risk for inflammatory autoimmune thrombocytopenia and nephritis).
There is a also a new generation of immunomodulatory drugs, that are currently at the very advanced stages of clinical trials with encouraging results. This group includes LAQUINIMOD, RITUXIMAB/OCRELIZUMAB, and more.

Stem cells:
During the recent years there has been remarkable progress in the use of stem cells as a possible treatment for MS (and other inflammatory and degenerative neurological diseases). Our Center is one of the world leaders in the study of treatment with stem cells and their application to clinical practice. We recently completed at Hadassah, a pilot safety trial with autologous stem cells in MS patients, with encouraging findings.
Stem cells are a type of cells characterized by their ability to differentiate into cells of all tissue types. Their role is to build every part of your body during fetal life. The stem cell has the ability to differentiate into any cell type of the body, including also cells of the nervous system such as the cells that produce myelin. Recently, stem cells could be isolated also from many tissues of the body and especially the bone marrow, during the adult life.
In our trials we used stem cells taken from the patient’s bone marrow and therefore there was no need for a “donor” and no risk of rejection of the transplanted cells.
Our current and future steps in the field of stem cell therapeutic application, include a new trial to examine the clinical efficacy of the stem-cells treatment in MS and the documentation of possible improvement of neurological disability and of rebuilding of the myelin.
It is important to underline that at this stage, any stem cell treatments are still considered experimental, and provided only in the framework of a clinical trial.

3. Symptomatic treatments
In addition to treatments that affect inflammation and disease mechanisms, there are a variety of treatments that help / improve the various symptoms of the disease:
A. Medications for control of the sphincters, such as NOVITROPAN, DETRUSITOL, and others.
B. Drugs that reduce spasticity (muscle stiffness), such as BACLOSYL (given orally but also with a special pump directly into the spinal fluid), CLONEX, TIZANIDINE.
C. Medications for neuralgic pains, such as DANTOIN, TEGRETOOL, ELATROL, LYRICA, SYMBALTA, medical cannabis and others.
D. Antidepressant drugs, such as PROZAC, CIPRALEX and many others.
E. Drugs against fatigue such as PK-MERZ, and PROVIGIL.
F. Muscle-strengthening drugs: FAMPYRA, which is a novel drug with a good impact on the ability to walk in about a third of the treated MS patients.

Rehabilitation
Our Center works closely with the Department of Rehabilitation at Hadassah, including rehabilitation services in Ein Kerem hospital and the Rehabilitation department at Mount Scopus. As part of the rehabilitation there is now in a unique MS rehabilitation program, performed by a
multidisciplinary rehabilitation team specialised in the treatment of multiple sclerosis. This Program includes physical therapy, device therapy robotic walking (LOKOMAT), improving handling and balance, hydrotherapy pool and exercise room. Additionally, patients receive occupational therapy, speech therapy, and group therapy and are evaluated by a social worker and by a psychologist.