What is Multiple Sclerosis?

Multiple Sclerosis (MS) is a disease of the central nervous system (including the brain and spinal cord) in which the nerves degenerate.

- A disease of the central nervous system (brain and spinal cord) in which the nerves degenerate
- Patients with Multiple Sclerosis have inflammation which causes the myelin to disappear
- **Myelin, which provides a covering or insulation for nerves, improves the conduction of impulses along the nerves**
  - **What is Myelin?**
  - The insulation for the nerves.
  - Important for maintaining the “health” of the nerves
  - MS causes the Myelin to disappear
  - Consequently the electrical impulses that travel along the nerves decelerate

**Summary:**

Patients with MS have inflammation, which causes the myelin to disappear, causing permanent nerve damage. Due to inflammation and deterioration of the myelin, the nerves themselves are damaged. As the MS progresses, the patient experiences a progressive interference with functions that are controlled by the central nervous system.

Some **symptoms** of MS include, but not limited to:

- Visual disturbances
- Limb weakness
- Muscle spasms
- Loss of sensation, speech impediment, tremors, or dizziness
- Depression
- Manic depressions
- Paranoia
- Uncontrollable urge to laugh or weep
- Vision
- Speech
- Walking
- Writing
- Memory
**Whom does MS affect?**

Approximately 350,000 people in the United States have MS. The norm is to be diagnosed with MS between the ages of 20 to 50 years of age, although there have been cases of children and the elderly population diagnosed. Women are twice as likely to be diagnosed with MS than men. MS is twice as likely to occur in Caucasians than any other group.

What is the etiology or the cause of Multiple Sclerosis? The cause of Multiple Sclerosis is still unknown. Many researchers have focused in the past 20 years on disorders of the immune system and genetics for explanations.

One Theory is described below:

- The immune system is the body's defender and is highly organized and regulated.
- If triggered by an aggressor or foreign object, the immune system mounts a defensive action which identifies and attacks the invader and then withdraws.
- This process depends upon rapid communication among the immune cells and the production of cells that can destroy the intruder.
- In Multiple Sclerosis, researchers suspect that a foreign agent, such as a virus, alters the immune system so that it perceives myelin as an intruder and attacks it.

Autoimmunity is when our normally protective immune system is directed against the body's own tissues, it is called an autoimmune response. Multiple Sclerosis is believed to be a disease of autoimmunity. While some of the myelin may be repaired after the assault, some of the nerves are stripped of their myelin causing demyelination.

One of the most common symptoms of Multiple Sclerosis is spasms. What is a muscle spasm?

A muscle spasm is an involuntary contraction of a muscle.

**Characteristics:**

- A spasm or a cramp is an involuntary contraction of a muscle.
- Usually occurs suddenly, resolves quickly, and can be painful.
- Different from a muscle twitch (a muscle twitch or fasciculation is uncontrolled fine movement of a small segment of a larger muscle).
Types of Muscles

- Muscles are complex structures that cause movement in the body.
- There are three types of muscles in the body:
  - Cardiac muscle (heart)
  - Skeletal muscle (Moves external parts)
  - Smooth muscle (stomach, intestine)
- Skeletal muscles are anchored to bone, directly or by a tendon. When the muscles contract, the associated structure moves.

Is Multiple Sclerosis inherited?

- Although the role is unclear, genetics does play a role in multiple sclerosis.
- The chance increases in families where a first degree relative has the disease.
  - Thus, a brother or sister, parent, or a child of a person with MS stands a one percent to three percent chance of developing MS.
- The general population has less than a one percent chance of developing multiple sclerosis.
- An identical twin runs nearly a 30% chance of acquiring MS, whereas a non-identical twin has only a 4% chance of acquiring MS.
- These statistics suggest that there is a genetic factor.
Types of Multiple Sclerosis

- Relapsing – Remitting (RR) MS
- Primary – Progressive (PP) MS
- Secondary – Progressive (SP) MS
- Progressive – Relapsing (PR) MS
- Malignant or Fulminant MS

Relapsing – Remitting MS

- Most common type
- Patients experience a series of attacks followed by complete or partial disappearance of symptoms (remission) until another attack occurs (relapse)
- The time between relapses may be weeks or decades

Primary – Progressive MS

- A continuous disease process
- This presents in patients with a gradual decline in a person’s physical abilities from the outset
- This type of MS does not experience any periods of remission

Secondary – Progressive MS

- Occurs in patients who have Relapsing – Remitting MS
- The patients enter a phase when the relapses are rare, but more disabilities accumulate
- About 50 % of RR – MS individuals will develop SP – MS within ten years

Progressive – Relapsing MS

- Characterized by a steady decline in abilities accompanied by sporadic attacks
- Usually cases that are mild and can be recognized only in retrospect after many years

Malignant or Fulminant MS

- Extremely rare
- Can sometimes be fatal
- Very fast progression
How is MS diagnosed?

- Due to the broad range and subtleties of symptoms, multiple sclerosis may not be diagnosed for months to years after the onset of symptoms.
- Physicians, particularly neurologists, take detailed histories and perform complete physical and neurological examinations

Ways to Diagnose

- MRI (magnetic resonance imaging) scans with intravenous gadolinium helps to identify, describe, and in some instances, date the lesions in the brain (plaques)
- An electro-physiological test, evoked potentials, examines the impulses traveling through the nerves to determine if the impulses are moving normally or too slowly
- Finally examining the cerebro-spinal fluid that surrounds the brain and spinal cord may identify abnormal chemicals (antibodies) or cells that suggest the presence of multiple sclerosis.

The goals of treatment

- Improving the speed of recovery from attacks (treatment with steroid drugs)
- Reducing the number of attacks or the number of MRI lesions
- Attempting to slow the progression of the disease (treatment with disease modifying drugs or DMD’s)
- Relief from complications due to the loss of function of affected organs (treatment with drugs aimed at specific symptoms)
Disease Modifying Drugs (DMD)

- Most neurologists will consider DMSs once the diagnoses of relapsing remitting multiple sclerosis is established
- Many neurologists will begin treatment at the time of the first MS attack, since the clinical trials have suggested that patients in whom treatment is delayed may not benefit as much as those who are treated early

Glatiramer acetate (Copaxone)

- Disease Modifying Drug
- Approved for reducing the frequency of relapses in RR-MS.
- A synthetic (man made) amino acid mixture that resemble a protein component of myelin
- It is thought to be the immune system reaction against myelin in MS may be blocked or diminished by glatiramer acetate

Copaxone Side Effects

- A reaction occurring immediately after the injection is common, affecting one out of 10 patients
- The reaction may involve
  - Flushing
  - Chest pain or tightness
  - Palpitations
  - Anxiety
  - Shortness of Breath
  - Tightness in the throat
  - Hives

Natalizumab (Tysabri)

- FDA approved for treating relapsing MS
- Used to treat patients with relapsing forms of MS to delay the progression of physical disabilities and reduce the frequency of clinical relapses
- A monoclonal antibody against VLA-4 (a molecule required for immune cells to adhere to other cells, and penetrate into the brain)
• Administered monthly via intravenous infusion

**Tysabri Side Effects**

• Progressive Multifocal Leukoencephalopathy (PML) can occur from Tysabri
• PML a viral infection of the brain that usually leads to death or severe disability
• Patients are required to sign up for this treatment under a controlled drug distribution program
• Generally only recommended for patients who have had an inadequate response to, or are unable to tolerate an alternate MS therapy

**Mitoxantrone (Novantrone)**

• FDA approved for the treatment of multiple sclerosis
• Used for reducing neurologic disability and/or frequency of clinical relapses in patients with SP-MS, RR-MS, or worsening RR-MS. This therapy is not used in the treatment of PP-MS
• Usually used for more advanced or worsening cases of multiple sclerosis
• A limited amount that can be administered

**Novantrone Side Effects**

• A chemotherapy drug that carries the risk of serious cardiac side effects or cancer (leukemia)
• Cardiac monitoring prior to each dose and yearly following last dose of mitoxantrone also is necessary

**Interferon’s for RR-MS**

• Used to manage Multiple Sclerosis
• A medication that alters the immune system
• Interferon beta – 1b (Betaseron) was the first interferon approved in the U.S. to manage RR-MS in 1993
• Avonex (Interferon beta-1a) FDA approved in 1993 for RR-MS (delivered intramuscular)
• Subcutaneous Interferon beta-1a (Rebif) was approved in the U.S. in 2002

**How they work**

• All interferons have the ability to regulate the immune system and play an important role in protecting against intruders including viruses.
• Each interferon functions differently, but the Beta Interferon’s have been found to be useful in managing multiple sclerosis

• Overall most patients treated with interferon’s experience fewer relapses or a longer interval between relapses

Interferon Side Effects

• Most common side effect is a flu-like symptom that includes: fever, tiredness, weakness, chills, and muscle aches (these symptoms tend to occur less frequently as therapy continues)

• Injection site reactions

• Changes in blood cell counts

• Abnormalities in liver function tests

( http://www.webmd.com/multiple-sclerosis/guide/ms-drug-therapy)

How are the physical manifestations treated?

• There are numerous medications used to manage complications associated with multiple sclerosis

• The following table lists common complications, examples of drug and non-drug therapies and comments about complications and/or management
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Drugs</th>
<th>Non-Drug Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty walking</td>
<td>Ampyra</td>
<td>Ampyra was FDA approved in 2010 to improve walking in pts with MS</td>
</tr>
<tr>
<td>Muscle spasticity</td>
<td>Lioresal, Zanaflex, Valium, Klonopin, Dantrium</td>
<td>Physical therapy may also provide benefit. Most drugs are PO some are given via intrathecal route</td>
</tr>
<tr>
<td>Weakness</td>
<td>none</td>
<td>Physical therapy and exercise are used primarily. Foot braces, canes and walkers also benefit</td>
</tr>
<tr>
<td>Eye problems</td>
<td>Solu-Medrol</td>
<td>Solu-Medrol is given during an acute attack sometimes followed by corticosteroid by mouth</td>
</tr>
<tr>
<td>Fatigue and or emotional outbursts</td>
<td>Anti-depressants (amantadine), Symmetral for fatigue, Provigil for fatigue</td>
<td>Decrease or avoid physical activity and heat exposure. Amitriptyline is used for sudden laughing/weeping</td>
</tr>
<tr>
<td>Pain</td>
<td>Aspirin, Ibuprofen, Acetaminophen, Anti-consultants’, Anti-depressants</td>
<td>Aspirin, NSAIDS are used for muscle and back pain. Anti-consultants’ (tegretol, or Neurontin) are used for face/limp pain Anti-depressants are used for prickling, intense, tingling, and burning pain</td>
</tr>
<tr>
<td>Bladder dysfunction</td>
<td>Antibiotics, Vitamin C, Ditropan</td>
<td>Antibiotics to manage infections, Vitamin C and cranberry juice to prevent infections, Bladder dysfunction is treated with Ditropan</td>
</tr>
<tr>
<td>Condition</td>
<td>Treatment Options</td>
<td>Notes</td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Constipation</td>
<td>Increase fluids and fiber</td>
<td></td>
</tr>
<tr>
<td>Sexual Dysfunction</td>
<td>Viagra, Cialis, Levitra, Vaginal Gels</td>
<td>Males: erectile dysfunction drugs, Females: vaginal gels</td>
</tr>
<tr>
<td>Tremors</td>
<td></td>
<td>Often resistant to treatment. Sometimes drugs, or surgery are used if tremors are severe</td>
</tr>
</tbody>
</table>

**MS at a glance**

- Multiple Sclerosis is a disease which progressively injures the nerves of the brain and spinal cord
- Injury to the nerves in multiple sclerosis may be reflected by alterations of virtually any sensory or motor (muscular) function in the body
- The cause of Multiple Sclerosis is unknown, but it has become widely accepted that genetic, immunological, and environmental factors play a role
- The selection of drug/therapy should be made after the patient with MS has been properly informed of drug efficacy, in particular FDA approved uses, administration routes, risk of adverse effects, and methods to enhance tolerability and compliance