

AU InforMed

Volume 11 Number 3 (Issue 262)

Friday, March 1, 2013

Guest Editors: Abby Lynn Adams and Michael Morgan, Pharm.D. Candidates 2013, Wesley T. Lindsey, Pharm.D.



Key Inforbits

- Background Information on MS
- Different Types of MS
- Diagnosing MS
- Treatments Available for MS
- Potential Treatments in the Future

MULTIPLE SCLEROSIS AWARENESS WEEK: MARCH 11-17

Background Information^{1,2}

Multiple Sclerosis (MS) is an autoimmune disease that involves an attack on the central nervous system (CNS). **Myelin**, which is a substance that surrounds and protects the nerve fibers, is damaged which leads to the formation of scar tissue, or sclerosis. It is a disease that affects more women than men (about a 2:1 ratio), and about 1 in every 200 women are diagnosed with the disease. In general, the prevalence of MS increases the further one goes from the equator. In the United States, there is a higher prevalence in states above the **37th parallel**, and about 10,000 new cases of MS are diagnosed each year.

Four Different Courses of MS^{2,3}

No two individuals will have exactly the same experience when it comes to their MS course so the courses (below) may vary from person to person.

1. Relapsing-Remitting MS

This course is described as having clearly defined attacks of worsening neurologic function followed by partial or complete recovery periods (remissions). About 85% of patients are initially diagnosed with this course.

2. Primary-Progressive MS

This course is characterized by slowly worsening neurologic function from the onset of the disease with no distinct period of remission. There is no time-table for the rate of progression, so this typically varies from person to person. About 10% of patients are initially diagnosed with this course of the disease, and it is most commonly diagnosed in individuals who are older than 50 at the time of diagnosis.

3. Secondary-Progressive MS

This course of the disease follows an initial period of relapsing-remitting MS. After this initial period, the disease begins to worsen steadily, with or without periods of remission. Once again, the time-table to conversion varies from person to person, but an average time frame is 20-25 years after diagnosis. With the treatment options currently available, it is not currently known whether or not treatment affects transition.



Image taken from: <http://www.health.harvard.edu/newsweek/time-for-more-vitamin-d.htm>

4. Progressive-Relapsing MS

This is the rarest course of the disease with about 5% of patients initially diagnosed. In this disease course, patients experience steadily worsening disease from the onset. The disease progressively worsens with attacks along the way. This differs from primary-progressive due to the presence of distinct attacks; in primary progressive there is an absence of distinct attacks.

Diagnosis^{1,3-4}

The diagnosis for MS is typically between the ages of 15-45 years old. There is no specific test to diagnose MS, however, there are a variety of techniques that are used to aid in diagnosis. These techniques include the following:

- **Magnetic Resonance Imaging (MRI)**
 - Reveals areas of damage in the CNS caused by MS plaques.
 - This is the preferred imaging technique, and it is more sensitive than computed tomography (CT) scans.
- **Cerebrospinal Fluid Analysis (CSF)**
 - Used to determine the levels of IgG in an individual's CNS.
 - Individuals with MS have an increased synthesis of IgG in the CNS whereas serum IgG levels are normal.
 - IgG separates into small bands, called **oligoclonal bands** in electrophoretic studies; 5 or more of these bands are present in 90-95% of patients with MS.
- **Evoked Potentials**
 - Electrical activity is produced by the stimulation of certain nerve pathways, and this test is used to measure that activity
 - This test helps establish areas of demyelination, however this test is considered less sensitive and specific compared to MRI and CSF analysis.

As more information has become available about MS, the clinical guidelines have evolved as well. In the 2005 guidelines by the International Panel on the Diagnosis of MS, also known as the **McDonald Criteria**, a diagnosis of MS could only be made if an individual “had an appearance of a new lesion on a scan compared to a baseline scan at least 30 days after the onset of the initial clinical event.”⁵ The McDonald Criteria was revised in 2010 and now allows for the use of MRI to fulfill the criteria of a diagnosis when a new lesion is discovered regardless of timing. The McDonald criteria also states that CSF findings can aid in the diagnosis and help evaluate alternative diagnoses. With primary-progressive MS, the McDonald Criteria states that a diagnosis can be made “when there is continuous progression of neurological symptoms during a one year period with characteristic MRI and CSF findings.”

Treatment:

The treatment of MS is subdivided into 3 categories which include:¹

- **Symptomatic Treatment:** helps maintain a patient's quality of life
 - The following symptoms may benefit from pharmacologic management: spasticity, tremor, bowel and bladder symptoms, depression, sexual dysfunction, and fatigue
- **Treatment of Acute Attacks**
 - IV injection of high-dose corticosteroids is recommended with methylprednisolone (dose of 500-1,000 mg/day for 3-10 days per American Academy of Neurology) being the preferred agent
- **Disease-modifying Treatment**
 - These are taken for long term treatment with the aim to reduce relapse rates, lessen severity, and to slow progression of disability and cognitive decline

Treatment is highly variable and differs for patients based on disease severity, cost, side effect profiles, and patient and prescriber preference. Unfortunately, there is no cure for MS.

FDA Approved Disease Modifying Therapies for Multiple Sclerosis ^{1,6,7}			
	Name	Type	Administration
Self-Injected	Avonex[®]	Interferon beta-1a	30 mcg intramuscular injection every week
	Betaseron[®]	Interferon beta-1b	250 mcg subcutaneous injection every other day
	Extavia[®]	Interferon beta-1b	250 mcg subcutaneous injection every other day
	Rebif[®]	Interferon beta-1a	44 mcg subcutaneous injection 3 times weekly
	Comments for Interferon beta-1a/1b:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing forms of MS • Common side effects: flu-like symptoms and injection site reactions • Check CBC and liver function test at 1,3, and 6 months, then periodically 		
	Copaxone[®]	Glatiramer acetate; Synthetic chain of four amino acids.	20 mg subcutaneous injection once daily
	Comments for Copaxone[®]:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing forms of MS • Post injection site reaction may occur within minutes after injection that includes: flushing, chest pain, palpitations, anxiety, shortness of breath, throat constriction and hives • Common side effect: injection site reactions 		
Infused	Novantrone[®]	Mitoxantrone; Antineoplastic agent	IV infusion once every 3 months (2-3 years max)
	Comments for Novantrone[®]:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing and secondary progressive forms of MS • Patients may only be on therapy for 2-3 years due to risk of heart damage and leukemia • Need regular testing for cardiotoxicity, liver function, and white blood cells 		
	Tysabri[®]	Natalizumab; Humanized monoclonal antibody	IV infusion every 4 weeks
	Comments for Tysabri[®]:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing forms of MS • Common side effects: headache, fatigue, pneumonia, infections, joint and abdominal pain • Uncommon but serious side effect is progressive multifocal leukoencephopathy, PML. Risk is higher for patients who have John Cunningham (JC) virus antibodies (in an immunocompromised patient, JC virus could reactivate and cause PML), patients who have been on immunosuppressive therapy previously, and those on Tysabri[®] two or more years • Patients should be JC virus tested every six months and therapy should be discontinued if positive 		
Oral	Aubagio[®]	Teriflunomide; Immunomodulator	7 mg or 14 mg tablet by mouth once daily
	Comments for Aubagio[®]:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing forms of MS • FDA approved September 2012 • Common side effects: diarrhea, hair thinning, mild increase in hepatic enzymes, headache, and paresthesia • Can cause severe liver injury and liver function should regularly be tested • Carries a high risk of birth defects and patients should avoid pregnancy while on drug therapy 		
	Gilenya[™]	Fingolimod; S1P- receptor modulator	0.5 mg capsule by mouth once daily
	Comments for Gilenya[™]:		
	<ul style="list-style-type: none"> • Treatment of remitting-relapsing forms of MS • FDA approved September 2010 • After first dose, a 6 hour monitoring period is advised due to possible decreased heart rate, abnormally slow heart rhythm, mild reduction in FEV-1 • Side effects: reversible increase of liver enzymes, mild blood pressure increase, macular edema, and increase in herpes infections 		

*Table adapted from: Multiple Sclerosis Association of America: <http://mymsaa.org/about-ms/treatments/long-term/>

“In the Pipeline” Therapies:^{6,8-9}

For many years, treatment options for MS consisted primarily of the beta interferons and glatiramer acetate (**Copaxone**[®]). With the addition of the two new oral agents as well as JC virus antibody testing for **natalizumab** making it more of a first line treatment option in JC virus negative patients, options for therapies have expanded. The next most likely agent to receive FDA approval is **dimethyl fumarate or BG-12**. This drug is given orally and has shown anti-inflammatory and neuroprotective properties. It has a favorable safety profile and adverse events include flushing and gastrointestinal problems such as nausea, diarrhea and upper abdominal pain. In addition to BG-12 another oral agent **laquinimod** is being studied. Laquinimod is an immunomodulatory agent. The exact mechanism of action is unknown, but in animals, it showed decreased inflammation, demyelination, and axonal injury. This agent could be used in combinations. **Alemtuzumab, daclizumab, and ocrelizumab** are three separate agents being investigated. They are all humanized monoclonal antibodies given IV and are immunosuppressive.

HELPFUL LINKS

- National MS Society: <http://www.nationalmssociety.org/>
- MS Association of America: <http://www.mymsaa.org/>

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The last “dose” ...

*"A pessimist sees the difficulty in every opportunity;
an optimist sees the opportunity in every difficulty."*

~ Winston Churchill [British statesman, 1874 – 1965]

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