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Key Inforbits

- Multiple Sclerosis – Just the Facts
- Types of MS
- History of MS
- Diagnosing MS
- Is there a cure?
- Which treatment is best?

Multiple Sclerosis Awareness Week is March 2nd – 8th

Multiple Sclerosis – An Introduction

Multiple sclerosis (MS) is a chronic, unpredictable disease of the central nervous system. The name refers to two characteristics of the disease: the numerous affected areas of the brain and spinal cord and plaques or sclerosed areas which are a hallmark of the disease.[1] MS affects over 400,000 Americans and there are 200 new cases diagnosed each week.[2] Women are more than twice as likely as men to be afflicted by MS and it occurs more commonly in people of northern European ancestry.[2] Most people are diagnosed between the ages of 20 and 50.[2] The disease prevalence seems to increase with distance from the equator and the prevalence of MS in the United States seems to be higher above the 37th parallel or roughly the southern border of Kansas.[1] MS is not considered fatal and most people afflicted with MS live a normal span, but they do experience increased difficulties and limitations.

1. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells, BG, Posey LM. Pharmacotherapy: A Pathophysiologic approach. 7th ed. NY: McGraw-Hill Medical, 2008: pg 913-926.
2. MS: Just the Facts [homepage on the internet] National Multiple Sclerosis Society; [cited 2009 Feb 4] Available from: http://www.nationalmssociety.org/about-multiple-sclerosis/what-is-ms/index.aspx .

Did you know there are different types of MS?[1]

MS progresses differently from person to person and the different courses that are outlined below will vary greatly.

- **Relapsing-Remitting MS**
  People with this type of MS experience clearly defined attacks of worsening neurologic function. These flare-ups are usually followed by partial or complete recovery periods, during which no disease progression occurs. Approximately 85% of people are initially diagnosed with relapsing-remitting MS.
- **Primary-Progressive MS**
  This disease course is characterized by slowly worsening neurologic function from the beginning and there are no distinct relapses or remissions. The rate of progression may vary over time, with occasional plateaus and temporary minor improvements. Approximately 10% of people are diagnosed with primary-progressive MS.

- **Secondary-Progressive MS**
  Following an initial period of relapsing-remitting MS, many people develop a secondary-progressive disease course in which the disease worsens more steadily. Before disease-modifying medications, approximately 50% of people with relapsing-remitting MS developed this form of the disease within 10 years.

- **Progressive-Relapsing MS**
  In this relatively rare course of MS (5%), people experience steadily worsening disease from the beginning, but with clear attacks of worsening neurologic function along the way.

1. MS: Just the Facts [homepage on the internet] National Multiple Sclerosis Society; [cited 2009 Feb 4] Available from: http://www.nationalmssociety.org/about-multiple-sclerosis/what-is-ms/index.aspx .

History 101 – Multiple Sclerosis[1]

The following is a timeline of important discoveries and events and their impact on how MS is treated:

- 1838 – autopsies reveal what today is recognized as MS
- 1868 – Jean-Martin Charcot found the characteristic plaques of MS during an autopsy of a woman he had examined who had tremors and slurred speech
- 1916 – Dr. James Dawson performs microscopic examination of brains from patients who had died with MS and noted damage to the myelin
- 1925 – Edgar Douglas Adrian studied the role of myelin in nerve conduction
- 1935 – Dr. Thomas Rivers demonstrated MS was due to nerve-tissue damage and not viruses, by injecting myelin into virus-free animals and inducing their immune system to attack their own myelin thereby producing MS-like symptoms
- 1946 – Sylvia Lawry, an ordinary citizen, forms the National MS Society to promote contacts among neurologists and to raise money
- 1960 – Dr. George Schumacher draws up standard guidelines for MS diagnosis
- 1978 – CAT scans performed on people with MS
- 1979 – first study of beta-interferons for MS treatment began
- Early 1980's – the macrophage is identified as the cause of actual damage to the myelin
- 1988 – sequential MRI scans show that MS is a progressive disease
- 1990's – demonstrated that there is a genetic determinant for MS, but there is no single "MS gene"
- 1993 – introduction of beta-interferon 1-b (Betaseron)
- 2008 – there are now six treatment options in the treatment of MS

More has been accomplished in the last decade in the treatment of MS than in the previous century. The average life span of a person with MS in 1900 was five years, now a person with MS can expect to have a normal life span given the new advances in treatment.

1. The History of MS [homepage on the internet] National Multiple Sclerosis Society; [cited 2009 Feb 4] Available from: http://www.nationalmssociety.org/research/how-far-weve-come/index.aspx .

The Mechanism behind MS

In MS, the myelin coating surrounding the nerves is destroyed and signals cannot be transmitted as efficiently in the central nervous system.[1] It has been shown that myelinated nerves conduct impulses at 70 m/s as compared to 1 m/s in unmyelinated nerves.[2] This interruption of nerve impulses results in the symptoms associated with MS. There is substantial evidence to suggest that this is caused by an autoimmune response against myelin and oligodendrocytes, the cells that make myelin. The actual mediators of the myelin destruction and events that trigger it are still unclear. While there is no single gene responsible for MS, there does seem to be a genetic susceptibility to MS. The average US citizen has a 1 in 750 chance of developing MS, but a person with a direct relative having MS carries a higher chance of developing MS (ranges from one in 40 to one in 100).[2]

1. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells, BG, Posey LM. Pharmacotherapy: A Pathophysiologic approach. 7th ed. NY: McGraw-Hill Medical, 2008: pg 913-926.
2. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, eds. Harrison's Principles of Internal Medicine. 16th ed. NY: McGraw-Hill Medical, 2005: pg 2461-2471.

Diagnosing MS[1,2]

Diagnosing MS continues to be difficult for physicians due to the intermittent symptoms and the fact that there is no one test that can be used to confirm MS. To diagnoses MS, the physician must rely on medical history including symptoms and signs of MS along with various tests such as MRI, evoked potentials, and spinal fluid analysis.

- Symptoms – these vary greatly from person to person and include reduced or abnormal sensations, vision changes, clumsiness, weakness, sudden loss of bladder control. These symptoms are usually random and will disappear for a period of time.
- Signs – common signs that a physician looks for include altered reflexes, evidence of weakness in the arms or legs, altered eye movements and abnormal responses of the pupils, impaired coordination, and changes in speech patterns.
- Tests - common tests include an MRI to look for lesions or plaques, evoked potentials to determine if there is a slowing of messages to the brain, and cerebrospinal fluid is tested for antibodies.

In order to make a diagnosis of MS, the physician must:

1. Find evidence of damage in at least two separate areas of the central nervous system (CNS), which includes the brain, spinal cord and optic nerves AND
2. Find evidence that the damage occurred at least one month apart AND
3. Rule out all other possible diagnoses

1. Diagnosis of MS [homepage on the internet] National Multiple Sclerosis Society; [cited 2009 Feb 5] Available from: http://www.nationalmssociety.org/about-multiple-sclerosis/diagnosing-ms/index.aspx .
2. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells, BG, Posey LM. Pharmacotherapy: A Pathophysiologic approach. 7th ed. NY: McGraw-Hill Medical, 2008: pg 913-926.

Treating MS – Is there hope?

While there is currently no cure for MS, great advances have been made in its treatment. Treatment of MS falls into two categories: treatment of acute attacks and disease-modifying therapies. There is currently no universally accepted treatment algorithm and treatment will vary among clinicians.[1]

- Treatment of acute attacks: Acute attacks last for several days to a few weeks and can be moderate or severe enough to affect a person's everyday activities. Acute attacks are typically treated with intravenous corticosteroids.[1]
- Disease-modifying therapies:[2,3] These drugs are taken on a long-term basis and their goal is to slow progression of the disease and prevent acute attacks. There are currently six different disease-modifying therapies available and the decision on when to initiate therapy and which one is best for a patient is highly individualized and one that should be made after a full discussion with their health-care provider.
  - Self-Injectable drugs:
    - Avonex® (interferon beta-1a) – 30 mcg once weekly
    - Betaseron® (interferon beta-1b) – 250 mcg every other day
    - Copaxone® (glatiramer acetate) – 20 mg every day
    - Rebif® (interferon beta-1a) – 44 mcg three times weekly
  - IV infusion
    - Tysabri® (natalizumab) – 300 mg every four weeks. NOTE: patients taking Tysabri® are at increased risk of progressive multifocal leukoencephalopathy (PML), a generally fatal brain disease which is caused by the common JC virus. The FDA announced that there were two new cases of PML reported in Europe.[4] No new cases have been seen in the US, where about 7,500 patients have received the drug for greater than one year and approximately 3,300 patients have received the drug for at least 1.5 years. In the U.S., Tysabri is available only to patients with relapsing multiple sclerosis or Crohn's disease enrolled in the risk minimization plan called the TOUCH Prescribing Program.[4]

- Novantrone® (mitoxantrone) – four times a year. NOTE that a patient can only have a lifetime cumulative dose of 140 mg/m^2 which is approximately 8-12 doses over 2-3 years.

- It is recommended that patients taking Avonex®, Betaseron®, Rebif®, or Tysabri® receive baseline liver function testing.[3]
- The most common side effects with these drugs include a flu-like reaction or injection site reactions.[3]
- It should be noted that these drugs will not cure MS and are very expensive with annual treatment costs as high as $25,000.[2]

1. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells, BG, Posey LM. Pharmacotherapy: A Pathophysiologic approach. 7th ed. NY: McGraw-Hill Medical, 2008: pg 913-926.
2. MS: Treatments [homepage on the internet] National Multiple Sclerosis Society; [cited 2009 Feb 4] Available from: http://www.nationalmssociety.org/about-multiple-sclerosis/treatments/index.aspx .
3. Lacy CF, Armstrong LL, Goldman MP, Lance LL, eds. Drug Information Handbook. 17th ed. Hudson, OH; Lexi-Comp, 2008.
4. Tysabri (nataluzimab) [homepage on the internet]. US Food and Drug Administration, August 25, 2008 [cited 10 Feb 2009]. Available from: http://www.fda.gov/medwatch/safety/2008/safety08.htm#Tysabri2 .

From the Medical Literature

A Comparison of the Disease-Modifying Therapies

It is difficult to determine which disease-modifying therapy is most effective because there are no head-to-head trials and cross-trial comparisons can be misleading because the patient populations are most likely quite different and the studies were conducted at different times. Additionally, if one of the agents being compared is used early in treatment compared with an agent used later in treatment, the bias will be substantial because it has been shown that early treatment is more effective. This study applied the number-needed-to-treat (NNT) and relative risk (RR) of therapy in cross-trial comparisons. Two conclusions were drawn from cross-trial comparisons between 14 trials: high dose interferon beta-1a or 1b subcutaneous injections were more effective than weekly interferon beta-1a injections and secondly, high dose interferon beta-1a or 1b subcutaneous injections were similar to glatiramer acetate.

1. Goodin DS. Disease-modifying therapy in multiple sclerosis: update and clinical implications. Neurology 2008;71(Suppl 3):S8-13.

For more information

- National MS Society: http://www.nationalmssociety.org/index.aspx
- National Institute of Neurologic Diseases and Stroke: http://www.ninds.nih.gov/disorders/multiple_sclerosis/multiple_sclerosis.htm
- MedLine Plus MS Interactive Tutorial: http://www.nlm.nih.gov/medlineplus/multiplesclerosis.html

The last "dose" …

Five frogs are sitting on a log. Four decide to jump off. How many are left?
Answer: five.

Why? Because there's a difference between deciding & doing.

- Old Irish Saying

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