

UNDERSTANDING MULTIPLE SCLEROSIS

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INTRODUCTION

The term multiple sclerosis (MS) has been heard often in recent years, yet many people still do not understand even the basic aspects of the disease. Laypersons sometimes confuse multiple sclerosis with similar-sounding diseases, such as muscular dystrophy or arteriosclerosis. MS is very different from either of those diseases. Multiple Sclerosis is a chronic autoimmune disease affecting the central nervous systems (CNS).

In the United States, approximately 400,000 people have MS;¹ 200 people are diagnosed with the disease each week. Globally, it is estimated that approximately 2.5 million people have MS.

A person is not born with the disease, nor can a person “catch” MS from someone else. However, there is a good chance that you know, or will eventually know, someone who has MS because it can affect anyone.

MS is an extremely unpredictable disease. Perhaps it is the unpredictability of MS that makes the disease so frightening. It can be terrifying to someone recently diagnosed, family members of that person, and others who wonder whether they will also develop MS.

Many people associate MS with wheelchairs. People have seen MS-stricken celebrities like Richard Pryor, Annette Funicello, and David “Squiggy” Lander speaking out from their wheelchairs. Teri Garr announced on the Larry King show that she has had MS for 19 years, but it took several years for doctors to make the correct diagnosis.² She walks with a limp and wears a leg brace to correct for an MS consequence known as *footdrop*.

It is true that for some patients MS can be a disabling disease and that the most severe types are the most visible. However, there are different types of MS; with some being less severe and disabling. The degree of MS severity is also unpredictable. It is common to hear an MS sufferer refer to the disease as “my MS.” The disease becomes very personal because those with MS know

that their symptoms may be quite different from those of someone else who has the same disease type.

This article will attempt to shed light on the disease. It will describe what multiple sclerosis is, in addition to what it is not. It will discuss the symptoms of the disease, how a diagnosis is made, the role that imaging plays in the diagnosis, and the treatments that are available today.

Multiple sclerosis has been referred to as *disseminated sclerosis* in Britain and as *sclerose en plaques* in France.³ Both names emphasize the essential feature of MS, which is scattered plaques throughout the central nervous system. The French word *plaque* loosely translates to mean flat surface and is used interchangeably with the word *lesion* when describing the disease.⁴ The flat surface refers to the appearance of a lesion after it has been cross-sectioned. The term *multiple sclerosis* began as American terminology. Now this name (or its abbreviation [*MS*]) is the accepted term worldwide for all patients suffering from the disease. This change is primarily due to the influence of the National Multiple Sclerosis Society in America.

BRAIN AND SPINAL CORD INVOLVEMENT

MS is a chronic autoimmune disease affecting the central nervous system (CNS). *Myelin*, the protective (i.e., insulating) fatty substance covering the nerve fibers is attacked and destroyed by certain types of white blood cells that mistake the myelin for a foreign substance. These so called *demyelinated* areas—known as plaques (or lesions)—show up distinctively with magnetic resonance imaging (MRI).

There tend to be multiple lesions located in the white matter of the spinal cord and/or the brain. The diameter of a lesion lies somewhere between several centimeters to less than 1 millimeter.³ They are easily distinguished visually from the white matter because of their pink-gray color, which is caused by the loss of myelin.

Over time, the lesions are infiltrated by cells known as *macrophages*. Additionally, star-shaped cells called *astrocytes* located in and around the lesions increase in quantity and grow in size.³ A more thorough description of the autoimmune response will appear later in this article.

One school of thought is that the origin of MS might be traced back to a viral infection which occurred during

childhood (i.e., some type of retrovirus). However, researchers still cannot find any evidence of a virus in the tissues of MS patients.³ Nevertheless, research continues in this area in hopes of new discoveries.

A more plausible school of thought at present, one that is widely accepted in the medical world, is that MS is an autoimmune disease. Because of the burgeoning information we now have about how the body's immune system works, it is known that certain viruses (and bacteria too) can carry proteins that cause them to resemble functional tissue cells. This "trickery" triggers an immune system response because the immune system can't distinguish the "good" cells from the "bad cells," so it destroys both by attacking myelin. The destruction of myelin interrupts transmission of nerve impulses, resulting in neurologic problems. The particular nerves that are affected determine a patient's symptoms and also explain why symptom severity varies greatly among MS patients.

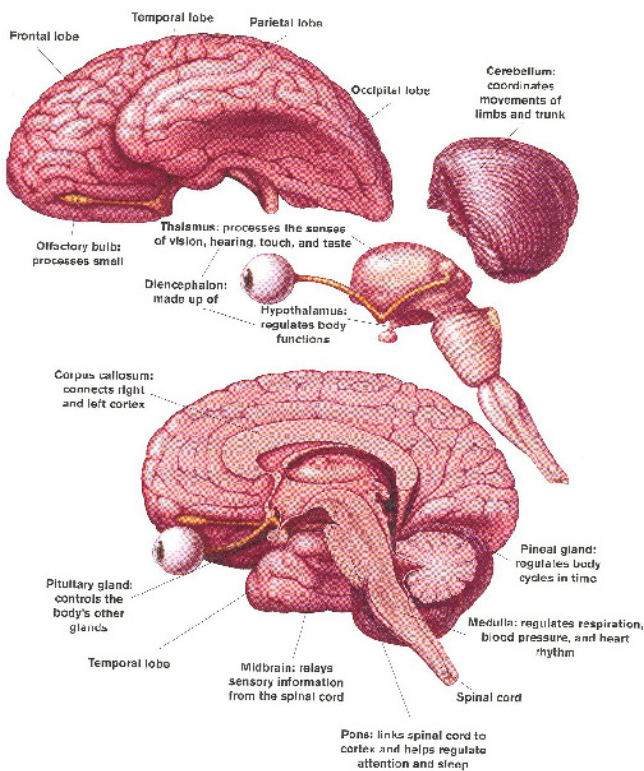


FIGURE 1. The CNS serves as the body's communication center. Reprinted with permission from *The Dana Guide to Brain Health*, Simon & Schuster.

CNS REVIEW

To understand MS and its impact on the body, it is important to review the components of the central nervous system. The CNS consists of the spinal cord and the brain that connect together at the base of the skull. As shown in Figure 1, the CNS functions as a commu-

nication center. In the brain, the cerebrum is responsible for initiating movement and thoughts, and the cerebellum coordinates movement and smooth muscle activity and also handles balance. The brainstem, whose nerves control eye movement and other vital functions, is located above the spinal cord and beneath the cerebrum and cerebellum.

The spinal cord works as a message carrier system, delivering information between the brain centers and various parts of the body. It is composed of gray matter in its central region, and is surrounded by white matter. There are four sections of the cord. The first section, beginning at the base of the brain, having eight segments, is the *cervical cord*. It joins with the *thoracic cord*, which has 12 segments. The *lumbar cord* begins at the base of the thoracic cord, and lastly the *sacral cord* connects to the lumbar cord. The sacral and lumbar cords each have five segments. Within each cord are the dorsal and ventral horns. The *sensory neurons*, or nerve cells, are contained in the dorsal horn. They are the receivers of sensory information coming from the body's surface. The *motor neurons* are contained within the ventral horn, and they are the senders of information to the skeletal muscles.

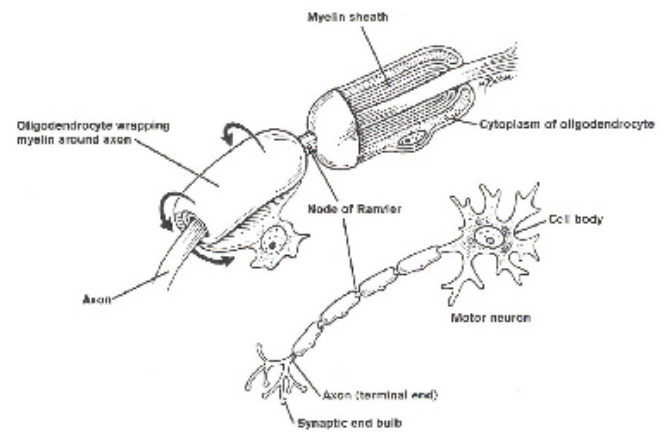


FIGURE 2. Myelin is the white fatty insulation around the axon that helps move the electrical impulses more efficiently.

The brain parts and the spinal cord are able to perform these functions because of electrical activity that they generate. This electrical activity regulates and stimulates activity in various parts of the body. In a healthy person, electrical nerve impulses can flow swiftly through their pathways, with little or no loss of information, because the conduction system is well insulated by myelin. When describing myelin, it is often compared with the covering of an electrical cord, which protects the wires within it; however, myelin is much more specialized (Figure 2). Besides its insulating quality, myelin also acts as the facilitator and expediter of electrical signals, transporting them efficiently and quickly. The electrical signals enter and exit at the nodes of Ranvier, where the myelin sheath

narrows and the axon is exposed. The axon can carry electrical signals over distances of 0.1 mm to 3.0 m. These electrical signals, also called *action potentials*, are conducted from the initial segment of the axon and down the axon at a speed of 1 to 100 m per second.⁵

The formation of myelin in the brain and spinal cord begins while the fetus is still in the womb and continues during childhood. The process of creating myelin is done by a group of specialized *glial cells* called *oligodendrocytes*. During the eighth month of pregnancy, the brain of the fetus begins to protect itself by producing the myelin sheath. The myelin wraps itself around the axon, layer upon layer.

DEMYELINATION

In a healthy person, electrical signals are sent and received rapidly—they leap from one node of Ranvier to the next. In a process referred to as *demyelination*, MS damages this conduction method by destroying the myelin sheath. When the nerve impulses become blocked, there is no longer efficient communication between the brain and other parts of the body.

Sometimes, the impulses may function properly under normal conditions but become blocked during times when the body is stressed, as with exercise or fever. In experiments, a temperature increase of only 0.5°C (< 1°F) can block transmission.⁶

McAlpine studied the onset of MS in 219 patients; symptoms were found to develop either suddenly or gradually.³ In this patient group, fully developed symptoms varied as follows: 20% within a matter of minutes; 20% within a few hours; 30% within a day to several days; 20% over a few weeks to a few months; and 10% over months to years.

When symptoms appear rapidly, they are referred to as an attack. Remission in MS does not mean that all symptoms have disappeared; it means that the patient has returned to the baseline that existed before the last exacerbation. These remission times may last for weeks, months, years, or forever. Symptoms may then recur and after a variable period of time reside once again for another period of remission.

An *exacerbation* essentially is the same as an attack; these words are often used interchangeably. Exacerbation refers to a sudden worsening of an MS symptom (or symptoms) or the appearance of new symptoms one month after the previous exacerbation; an exacerbation lasts for at least 24 hours.⁷ When symptoms have occurred before and then reappear, they are referred to as a *relapse*. A relapse ends when the person recovers.

EPIDEMIOLOGY

There are several methods for evaluating the suspected causes of MS. Certain statistics point to genetic predisposition, whereas other statistics suggest environmental factors or, as previously mentioned, possibly a viral infec-

tion. The cause may also be a combination of these factors.⁸ Many studies have been done to determine a person's susceptibility to developing multiple sclerosis, and heredity does influence how susceptible a person is to develop MS.

GENETIC FACTORS

There does seem to be a connection between MS and a person's family history. Many studies have shown that genetics plays at least a partial role in a person's susceptibility to MS. An individual has a greater risk of developing MS if a family member already has the disease. Approximately 10% to 20% of people with MS have pre-existing MS in their extended families.⁹ An average person living in the United States has a 1 in 1000 risk of developing MS.^{8,10} A person living in the United States that has a parent or sibling with MS has a 1 in 100 risk of developing the disease.

Generally speaking, women have a higher probability of developing MS. If a parent has MS:

- * A daughter has a 4:100 (4%) chance of getting MS⁹
- * A son has a 2:100 (2%) chance of getting MS³

A person who has a first-degree relative with MS has a slightly less than 5% risk of acquiring the disease.¹¹ That same person who has a first-degree relative with MS has a 20 to 40 times greater risk than an individual from the general public.¹¹ However, 80% of MS patients *do not have* a first-degree relative with MS.¹⁰

Women are two to three times more likely to develop the disease than men.^{3,6} In identical twins, if one twin already has MS, the other twin has a 1 in 3 chance of developing the disease.¹⁰ MS research on twins has been carefully studied. There is a greater risk of both twins acquiring MS if they are monozygotic.⁶ One study revealed that the susceptibility rate between monozygotic and dizygotic twins is approximately 6 to 1 (31% to 5%, respectively).¹¹ In one study, 12 of 35 pairs of monozygotic twins were diagnosed, whereas only 2 of 49 pairs of dizygotic twins were diagnosed.⁹

Another key fact that points to a genetic cause is that in populations where there is a high concentration of the HLA-DR2 allele, there is also a high prevalence and incidence rate of MS. Prevalence here relates to the number of individuals who were already diagnosed with MS prior to the start of the study, and incidence indicates the number of newly-diagnosed cases that occurred during the study. The HLA-DR2 allele is believed to be a marker for an MS susceptibility gene, perhaps even an immune response gene.^{8,9,11} A person who has the DR2 marker has an increased risk of acquiring MS by a factor of 3 to 5.⁹

The prevalence and incidence rate of MS in certain parts of the world and among certain populations is quite interesting. Studies show the rate is lower for some populations, and higher for others. Researchers believe that

due to genetic makeup and gene-pool mixtures (or lack thereof), there is both a racial resistance to MS and a racial susceptibility.

MS is rare among North American Indian tribes.⁶ The Inuit population of Canada has practically no history of MS. Prevalence of this disease among Canadian Inuits is only 5% of that of other Canadians living in the same area.⁶ The prevalence rate of MS in the general Canadian population is 30 to 80 per 100,000.³

The prevalence rate of MS in equatorial regions is less than 1 per 100,000.³ MS also occurs less frequently in Africa, the Orient, continental South America, and India.⁶ In the southern United States and southern Europe, the prevalence rate for MS is 6 to 14 per 100,000.³ In Michigan, Minnesota, and Wisconsin, much higher rates of MS have been found.⁶ Researchers believe this is due to the greater number of people of Scandinavian descent living in those three states. MS is common among Caucasians and less common among blacks.^{6,10} The disease is also more common among people with a northern European ancestry.^{6,12}

These statistics suggest a genetic connection, specifically a racial susceptibility in northern European—particularly Nordic—populations. Research has shown that Scandinavian gene pools have high numbers of the HLA-DR2 allele, which increases susceptibility to MS.⁶ This information adds credence to the notion of MS as an autoimmune disease, because autoimmune diseases appear to be at least partly due to a genetic predisposition. That is, people who become afflicted with MS appear to have inherited a certain set of genetic factors that increased their susceptibility to the disease. For 10% to 20% of people with MS, the disease is found in extended family members, which is a higher rate than would be expected by chance.⁹

GEOGRAPHIC (ENVIRONMENTAL) FACTORS

John Kurtzke developed a scale to determine the prevalence rate of multiple sclerosis.⁶ He used this scale to chart the prevalence of MS in various regions of the world. Areas where there were less than 5 cases of MS per 100,000 people were considered to be low-prevalence areas. Intermediate prevalence was defined as 5 to 30 cases per 100,000 people, and high prevalence was defined as 30 or more cases per 100,000.¹¹ Northern Europe, southern Australia, and the middle of North America have the highest prevalence, although the prevalence and incidence rate in southern Europe is increasing.¹¹

The distribution of MS in the United States follows a fairly horizontal gradient, with a higher incidence of MS in states above the 37th parallel, which stretches from Santa Cruz, California to across the northern border of Arizona and all the way to the northern border of North Carolina.¹⁰ The prevalence rate for MS in this area is 110 to 140 cases per 100,000.¹⁰ Below the 37th parallel, the prevalence rate drops to 57 to 78 cases per 100,000.¹⁰

The highest prevalence rates are in the Midwest, and the lowest prevalence rates occur in the Mississippi delta area.⁶ In general, the frequency of MS decreases in latitudes closer to the equator.¹⁰

Much information has been gathered by many researchers to identify geographical areas with higher prevalence and incidence rates of MS. However, the results are only as complete as the research itself, and comparing results can be difficult because the survey methodologies are not the same. But despite this, it is acknowledged that certain distribution patterns of MS do exist in various parts of the world.

There is a low prevalence rate of MS in the Orient, the Arabian peninsula, Africa, continental South America, and India.⁶ Southern Scandinavia has a higher prevalence rate than Northern Scandinavia.⁶ The Shetland Islands, Orkney (just north of Great Britain), and northeast Scotland have a higher prevalence rate than all other parts of the United Kingdom.⁶

MS is common in parts of Italy, such as Sardinia, but not in Greece; and it is common in Sicily but not in nearby Malta.⁶ Northern Germany has a higher prevalence rate compared to France, Spain, and the eastern Mediterranean countries.⁶

The distribution rates of MS have increased in some parts of the world; the explanation seems to be a combination of environmental factors coupled with a genetic admixture of different populations as people migrate into and out of countries. Migration patterns have been studied quite thoroughly.⁶ The role of migration in the acquisition of MS points to the involvement of environmental factors. For example, in the West Indies, MS is a rare disease.⁴ Studies of people who moved from the West Indies to Great Britain as adults show that for them, MS is still rare, but for their children born in Great Britain, MS is as common as the rest of the population.⁴

The aforementioned facts make a sound case for environmental factors playing a role in the development of MS, and exposure to them, it seems, must occur during childhood years. Susceptibility to MS seems to hinge on where a person lives during the early years of life. Studies have been done on families with children who moved from northern Europe (i.e., a high-risk area) to Hawaii and Israel (i.e., low-risk areas).⁴ MS was found to be more prevalent in the adults than in the children.⁴

Although the specific environmental factors that contribute to the susceptibility to MS are not yet known, it is recognized that where you live and when you live there have enormous impact on the occurrence of MS. People who move during adolescence will retain the risk factor of their original homeland, whereas those who move before adolescence will assume the risk factor of their new geographic area. Youths between the ages of 5 and 15 years seem to be the most vulnerable.^{4,9}

VIRAL ETIOLOGY

Much speculation about the cause of MS points to a virus—in particular a *retrovirus*. The idea of a virus as the initiator of MS is plausible, considering that MS resembles the behavior of a retrovirus, in that it is encountered in childhood but remains dormant until adulthood.³ Studies have not yet been able to substantiate this idea and researchers are continuing to pursue the possibility. If exposure to a virus is the cause, researchers must also identify the triggering mechanism that actually activates the MS.

An autoimmune response may be that triggering mechanism. Researchers have looked for similarities between MS and other autoimmune diseases, such as autoimmune-mediated encephalomyelitis and other demyelinating diseases like Guillain-Barré syndrome. Viral diseases that occur in childhood (e.g., rubella) could cause T lymphocytes to autoimmunize against *myelin basic protein (MBP)*. In this scenario, T lymphocytes are fooled into recognizing the myelin sheath as a viral structure. The existence of “copycat antigens” between a virus and myelin in the CNS is believed to be the causative mechanism in other diseases (e.g., rheumatic fever). In studies of cerebrospinal fluid (CSF) from MS patients, antibodies to MBP were found, the levels of which increase (as do the T cells that are reactive to MBP) with MS activity. These findings lend credibility to the viral origin school of thought.³ More information about how the immune system works (or fails to work properly) and how this information relates to understanding MS is presented later in the Autoimmune Disease section.

DIAGNOSIS

Typically, the onset of MS occurs between the ages of 15 and 45. In the early years, the disease may go unnoticed and undiagnosed. After the first episode, the patient typically recovers completely or at least partially. A latency period of one to 10 years is common following the initial, minor symptom. Following this latency period symptoms may recur, either a return of the initial symptoms or the emergence of new, more characteristic symptoms.

A general rule in diagnosing MS is a history of relapse and remission involving two or more attacks that are a month or more apart; each time the symptoms last for more than 24 hours. A more definitive diagnosis includes evidence of two or more discrete CNS lesions, usually seen by MRI, that alter the patient’s neurologic function.

DISEASE COURSE

Because the disease course follows patterns, it was necessary to develop category levels to serve as generalized prognosis guidelines. Much terminology has been coined to describe the various courses of MS: *relapsing-remitting*, *chronically progressive*, *primary progressive*, *secondary progressive*, *transitional-progressive*, *relapsing-progressive*, *progressive-relapsing*, *progressive-cumulative*, *acute progressive*, and *malignant progressive*.¹³ The number of names was overwhelming, and the similarity among some of the names was confusing.

As a result, two prognosis charts have been developed from observational data. The categories in these two charts are distinguished by type of symptoms, symptom severity, frequency of attacks, and prognosis. The first prognosis chart contains four levels. As is apparent from the category descriptions, some MS patients experience little or no disabilities, whereas others suffer lifetime disabilities.

PROGNOSIS CHART 1^{2,3}

1. RELAPSING-REMITTING MS (RRMS)

This is the most common type of MS. Most RRMS patients experience their first symptoms between 20 to 40 years of age. Approximately 85% of MS patients start out with the RRMS course.

These patients will experience total or partial recovery after attacks. New lesions (as shown by MRI) may or may not form during periods of remission. Patients may need use of a cane but rarely progress to needing a wheelchair. They live a life span equivalent to the population at large. Some cases of RRMS will develop into the next level, secondary-progressive MS.

2. SECONDARY-PROGRESSIVE MS (SPMS)

Thirty percent of MS patients are initially diagnosed as having SPMS. However, this course usually begins as RRMS; relapsing-remitting episodes which become steadily progressive. Fifty percent of the eighty-five percent of patients who began with RRMS will develop SPMS within 10 years; 90% will develop SPMS within 25 years. Neurologic symptoms get progressively worse after years of relapses and remissions.

3. PRIMARY-PROGRESSIVE MS (PPMS)

There is no remission with this course; it is progressive from the beginning. Gradual disability develops, but there are no acute attacks. Ten percent of MS patients are initially diagnosed with PPMS. This course usually occurs in people over 40 years of age.

4. PROGRESSIVE-RELAPSING MS (PRMS)

This course is rare; only 5% of those with MS have this type. It is progressive from the beginning, with superimposed acute attacks.

The second prognosis chart is similar, offering up an additional level of benign sensory MS. The naming conventions and descriptions used in Prognosis Chart 2 are slightly different from those used in Prognosis Chart 1. In research papers, the authors' preferences seem to dictate which nomenclature is used, so it is helpful to be aware that both charts exist.

PROGNOSIS CHART 2³⁷

1. BENIGN SENSORY MS
The patient experiences feelings of numbness, dizziness, and/or pain, but the disease is not confirmed by examination.
2. BENIGN RELAPSING/REMITTING MS (EQUATES TO RRMS)
On average, patients suffer one new clinical attack every 6 to 12 months that results in little or no permanent disability.
3. CHRONIC RELAPSING/PROGRESSIVE MS (EQUATES TO SPMS)
Patients experience relapses and a gradual worsening of symptoms.
4. CHRONIC PROGRESSIVE MS (EQUATES TO PPMS)
The patient's symptoms progressively worsen after each attack.
4. ACUTE PROGRESSIVE MS (EQUATES TO PRMS)
The patient's symptoms rapidly and progressively worsen.

A patient diagnosed with a benign case of MS will be treated much less aggressively than a patient classified as progressive.

Statistics show that 50% of the 85% of patients starting out with the RRMS type will convert to SPMS at some point.¹⁵ Eventually, the time between attacks and recovery shortens and symptoms that were noticed only during attacks become ever-present. The disease continues to worsen whether or not attacks occur (Figure 3). With SPMS, half the patients will remain ambulatory, and the other half will require assistance and have a greater risk of eventually needing a wheelchair permanently.

The PPMS form is more severe (Figure 4). Patients in this category do not recover. Their MS worsen over time. There may be periods when attacks stop and then start up again, or stop altogether. For some patients, the disease progressively worsens without remission. Regardless of which path PPMS takes, the patient with PPMS does not recover.

Figure 5 illustrates the features of RRMS. With this form of MS, symptoms can come and go. RRMS can be benign, or it can progress to SPMS.

A clinical examination alone may not provide enough information for a doctor to make the diagnosis of MS. Fortunately, doctors have several other methods (discussed next) to help make a correct diagnosis.

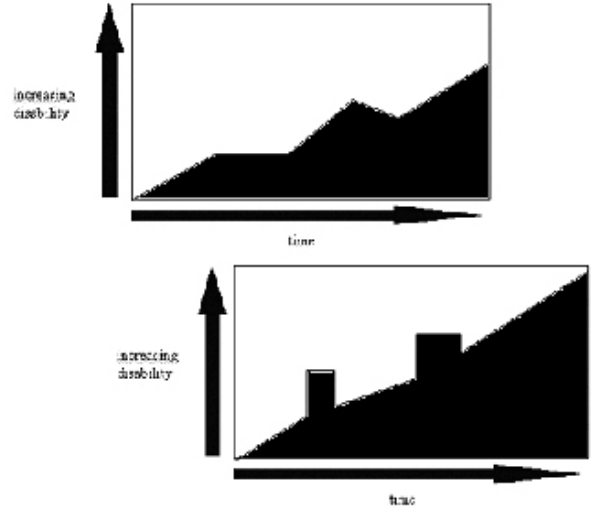


FIGURE 3. Patterns of Secondary-Progressive MS

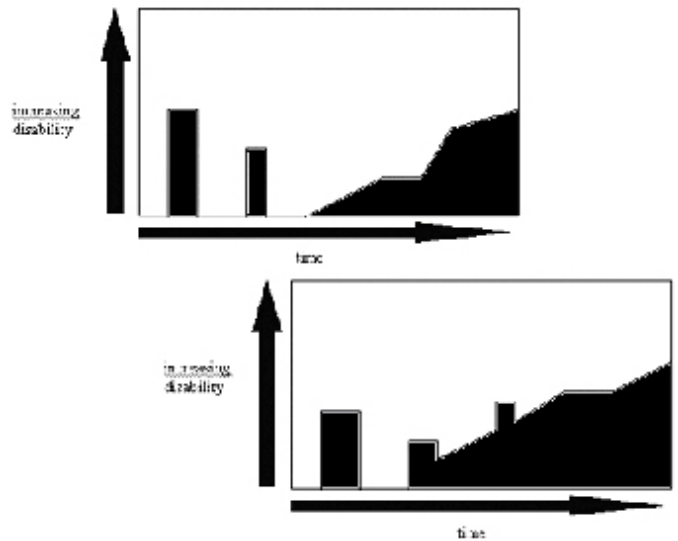


FIGURE 4. Patterns of Primary-Progressive MS

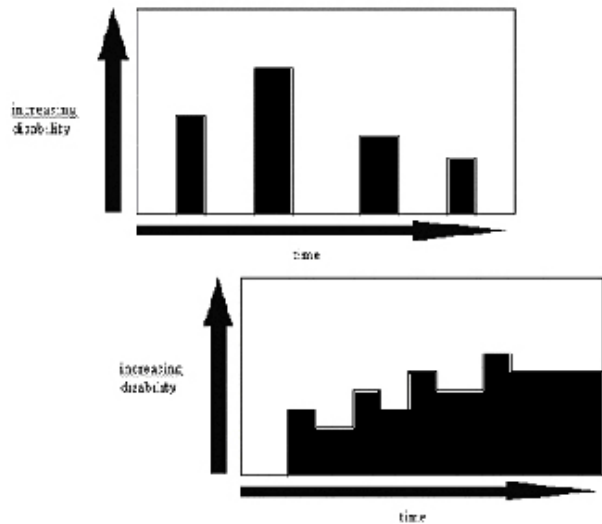


FIGURE 5. Patterns of Relapsing-Remitting MS

TESTING CEREBROSPINAL FLUID

A lumbar puncture is sometimes used as a test for MS. A needle is inserted between two of the vertebrae in the lower back, and fluid is withdrawn. However, today this procedure is not done as frequently since MRI produces more reliable results. Also, this procedure is more uncomfortable for the patient and there is always the risk of headaches or leakage of spinal fluid from the puncture site.

The CSF in MS patients shows higher concentrations of antibodies. Also, the CSF has other characteristics in MS patients. During an exacerbation, the CSF displays high concentrations of MBP, and lower concentrations are present during remission periods.⁶ Through electrophoresis, different types of protein in the CSF are displayed according to their molecular weight. With this method, the globulin protein in approximately 90% of MS patients will display one or more types of protein that are not normally present.⁴ On blotting paper, these globulin protein types appear as bands—*oligoclonal bands*. However, because MS is not the only disease with lesions that destroy myelin, measuring the MBP merely indicates the probability of MS. That is, the presence of oligoclonal bands is a laboratory predictor that suggests MS and thus aids in the diagnosis.

TESTING EVOKED RESPONSES

The *evoked response test* is a technique that records the electrical potentials evoked by sensory stimulation to the central nervous system. Electrodes are applied to the patient's scalp and neck, and then the person is subjected to various stimuli: light, sound, and electrical current. The recording device is triggered by the response to the stimulus. A long period between the stimulus and the brain's response indicates that the electrical impulses are blocked. The evoked response test can detect lesions in the brain and spinal cord.

The process of demyelination causes a slowing down of electrical nervous conduction.^{4,8} The main evoked visual response that normally occurs at 100 milliseconds from the time of the stimulus slows to 150 milliseconds (or longer) during an attack of *optic neuritis* (a common symptom of MS).⁴ After the attack, the conduction rate remains slowed indefinitely. Because of this phenomenon, doctors can detect demyelination even when symptoms are absent. This test is a reasonable detector for MS; many studies have demonstrated the reliability of the evoked response test. Some studies report that 80% of patients with clinical-definite MS and 60% of patients with possible MS have abnormal visual-evoked responses.³ The percentages drop a little with somatosensory stimulation 69% (clinical-definite MS) and 51% (possible MS) will have abnormal evoked responses with this type of stimulation.³ The percentages decline even further with brainstem auditory stimulation: 47% and 20%, respectively.³

CT SCANNING

Computed tomography (CT) scanning can also detect lesions. More lesions will be found if the patient is experiencing an acute exacerbation and if the CT scan is performed using double the typical dose of iodinated contrast media (as compared to a routine brain study). The contrast-enhanced scans are even more sensitive if they are acquired one hour after the patient has been injected with the contrast material.³ Following its intravenous administration the iodinated contrast material will accumulate in the damaged areas of the brain.⁴

MRI

MRI is the most commonly used tool today to detect scarring. This technique will often show several more lesions than a doctor can predict by clinical examination. Injecting gadolinium (a heavy metal contrast media) can make the lesions even more visible on MRI, particularly during an acute exacerbation. This process uses a powerful magnetic field that causes the hydrogen atoms inside the organ (in this case, the brain or spinal cord) to align themselves to the field. Then a burst of radiofrequency (RF) waves pass through the organ and disturb the alignment. When the waves are turned off, the spinning atoms realign again to the magnetic field and send off RF waves that are recorded. The MRI technique is more sensitive than CT scanning in the identification of plaques and is thus a more reliable test for detecting MS lesions. The hydrogen atoms in the brain are mostly in water molecules; if the water content is abnormally high, the MRI gives off increased signal. This increased signal will show up on the image as a lesion or as fluid replacing normal tissue that has been lost because of chronic demyelination. MRI makes it simpler to detect MS and will also demonstrate and help to differentiate other lesions. However, this imaging procedure cannot be used as the sole tool in diagnosing MS because other diseases can also produce abnormal MRI findings.

MRI, combined with clinical examination, provides physicians with more confidence in diagnosing MS. MRI plays an important diagnostic role because CNS lesions are very well seen with this imaging procedure. In fact, because some intracranial lesions are asymptomatic, they may go undetected unless MRI is utilized.

DISABILITY SCALES

When patients learn that they have MS, their most common concern is about disease outcome. Will their prognosis be favorable? As a medical professional, common sense dictates that it is usually best to err on the optimistic side with newly diagnosed patients. However, if and when the disease progresses, a patient should be made aware of what to expect. Various prognostic indicator scales have been developed.

A classification system was defined and expanded by John Kurtzke in 1961 and 1983, respectively.⁶ The first system is a 10-point disability scale system (DSS) that is still the most commonly used in research trials. The expanded disability scale system, or EDSS (Table 1), further extends the DDS by taking points 1 through 9 of the 10-point scale and dividing them into half points. The expanded scale was designed to measure only the *mobility* of MS patients, not the other effects of MS.

Since 1983, other scales have been created to determine and rate the severity of a patient’s disability; one such example is *Hauser’s ambulation index*.⁶ This scale is based on the EDSS, but it is generally thought to be overly complex and needs more validation.

Some researchers in the field have speculated about using a scoring system based on neurologic examination rather than mobility scales. At first thought, this approach seems to be the most practical way of providing a sensitive and reproducible measure of MS severity. However, neurologic examination has not proven to be a useful way to evaluate MS. Studies have shown that the standard neurologic examination score yields highly variable results among examiners.⁶ The intraobserver variability were significant enough to illustrate that such a scoring system has inherent problems. Sometimes scores from the same examiner differed, even when there was no change in the patient’s symptoms. A neurologic scoring system that provides reliable and reproducible results may be forthcoming, but to date one does not exist.

Despite the lack of a reliable neurologic evaluation tool, the DSS or EDSS is helpful as an indicator. These scales are still widely used in clinical trials. One example is a study that was done on 1844 patients (1562 had relapsing-remitting, and 282 had one of the progressive forms of MS).⁴⁵ The researchers conducting this study were looking at the length of time it takes for a patient, at the onset of MS, to reach different levels on the DSS scale. The median time (across all 1844 patients) from the onset of MS to a DSS of 4 took 8.4 years. The median time from onset to a DSS of 6 took 20.1 years. The median time from onset to a DSS of 7 took 29.9 years. As expected, the median interval from onset of MS to reaching each of these DSS scores took much longer for the relapsing-remitting patients than for those who had a progressive form of MS. Patients with relapsing-remitting MS have a better prognosis than patients with other forms of MS.

TABLE 1—Expanded Disability Scale⁶

Grade	Description
0	Normal neurologic examination (all grade 0 in functional systems [FS]; cerebral grade 1 acceptable)
1.0	No disability, minimal signs in 1 FS (i.e., grade 1 excluding cerebral grade 1)
1.5	No disability, minimal signs in > 1 FS (> 1 grade 1 excluding cerebral grade 1)
2	Minimal disability in 1 FS (1 FS grade 2, others 0 or 1)
2.5	Minimal disability in 2 FS (2 FS grade 2, others 0 or 1)
3.0	Moderate disability in 1 FS (1 FS grade 3, others 0 or 1), or mild disability in 3–4 FS (3–4 FS grade 2, others 0 or 1), though fully ambulatory
3.5	Fully ambulatory but with moderate disability in 1 FS (1 FS grade 3) and 1–2 FS grade 2; or FS grade 3; or 5 FS grade 2 (others 0 or 1)
4.0	Fully ambulatory without aid, self-sufficient, up and about for approximately 12 hours a day despite relatively severe disability consisting of 1 FS grade 4 (others 0 or 1), or combinations of lesser grades exceeding limits of previous steps; able to walk without aid or rest for approximately 500 m
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability, usually consisting of 1 FS grade 4 (others 0 or 1) or combination of lesser grades exceeding limits of previous steps; able to walk without aid or rest for approximately 300 m
5.0	Ambulatory without aid or rest for approximately 200 m; disability severe enough to impair full daily activities (e.g., work full day without special provisions); (usual FS equivalents are 1 grade 5 alone, others 0 or 1; or combination of lesser grades exceeding specifications for step 4.0)
5.5	Ambulatory without aid or rest for approximately 100 m, disability severe enough to preclude full daily activities (usual FS equivalents are 1 grade 5 alone, others 0 or 1; or combination of lesser grades usually exceeding those for step 4.0).
6.0	Intermittent or unilateral constant assistance (i.e., cane, crutch, or brace) required to walk approximately 100 m with or without resting; (usual FS equivalents are combinations with >2 FS grade 3+)
6.5	Constant bilateral assistance (i.e., canes, crutches, or braces) required to walk approximately 20 m without resting; (usual FS equivalents are combinations with >2 FS grade 3+)
7.0	Unable to walk beyond 5 m even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day; (usual FS equivalents are combinations >1 FS grade 4+; very rarely, pyramidal grade 5 alone)
7.5	Unable to take more than a few steps; restricted to wheelchair, may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair; (usual FS equivalents are combinations with >1 FS grade 4+)
8.0	Essentially restricted to bed or wheelchair, or perambulated in wheelchair but may be out of bed much of the day; retains many self-care functions; generally has effective use of arms; (usual FS equivalents are combinations, generally 4+ in several systems)
8.5	Essentially restricted to bed much of the day; has some effective use of arm(s); retains some self-care functions; (usual FS equivalents are combinations, generally 4+ in several systems)
9.0	Helpless, bedridden patient; can communicate and eat; (usual FS equivalents are combinations, mostly grade 4+)
9.5	Totally helpless, bedridden patient; unable to communicate effectively or eat/swallow; (usual FS equivalents are combinations, almost all grade 4+)
10.0	Death due to multiple sclerosis

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SYMPTOMS

The major culprit responsible for most MS symptoms is the failure of electrical impulse conduction. MS symptoms vary; typically, they come and go. In addition, MS affects each patient differently. It is incorrect to assume that a patient who is diagnosed as having a certain category of MS will exhibit the exact same set of symptoms as another patient who has been diagnosed with that same category.

The highly individual presentation of symptoms in MS patients can be explained by understanding how lesion may affect the CNS. The brain and spinal cord control movements and sensory information, but the precise location of the lesions determines which bodily functions will be affected. Even with that information, it is difficult to diagnose the severity. Usually, MS follows a “relapsing-remitting” pattern: symptoms flare up and then feel as though they’ve gone away. However, the disease is progressive due to the potential of continuing myelin damage even in the absence of symptoms.

Relapses and progressions are basic phenomena of MS. Relapses are clinical proof that a patient has acute inflammatory focal lesions involving the CNS. The presence of these lesions means that demyelination and axonal loss (loss of nerve impulses) has occurred or is occurring.¹⁶ Some MS patients will have only slight flare-ups, whereas others may become permanently disabled. Keeping this in mind, the following text contains information regarding possible symptoms that an MS patient may exhibit.

VISION PROBLEMS

The most common initial presentation of MS is a vision problem in one eye, which may occur as blurred vision, blind spots, difficulty clearly distinguishing red from other colors, or pain when moving the affected eye. It is rare that both eyes are affected at the same time. This condition is termed *demyelinating optic neuritis*, and it is caused by demyelination of the fatty covering of the optic nerves.⁸ This means that the optic nerve and the pathway for sending images between the retina and brain are affected (Figure 6). Most people recover from this initial attack, although some patients will have relapses of optic neuritis, which can ultimately lead to a total loss of vision. Fifty-five percent of individuals with MS will have an episode of optic neuritis.⁸ Some patients will experience only optic neuritis and no other symptom; it is uncertain whether this is a restricted type of MS or actually *post-infectious encephalomyelitis*.

In addition to the optic neuritis just described, some MS patients experience double vision when both eyes are open and none when either eye is covered. This double vision is caused by damage to the nerve fibers that coordinate eye movements; thus, in an MS patient, the eyes do not track together when focusing in on an image.

Nystagmus is a common MS symptom that affects vision. The eye movements are jerky and sometimes asynchronous. Nystagmus can affect eye movements in any direction. It is most often caused by lesions of the brainstem, although symmetrical horizontal gaze nystagmus is caused by lesions of the cerebellum (Figure 7).

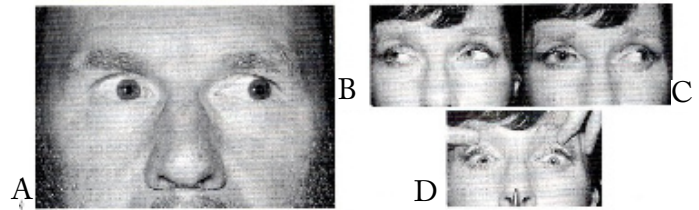


FIGURE 6. Internuclear Ophthalmoplegia (A) Unilateral, gaze to the left (normal); (B) Bilateral gaze to the right; (C) Bilateral gaze to the left; (D) Bilateral convergence (normal). Reprinted with permission from McAlpine's Multiple Sclerosis, Churchill Livingstone.

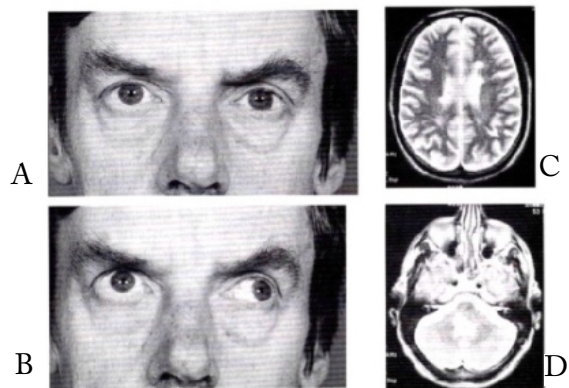


FIGURE 7. One-and-a-half Syndrome (A) Gaze to the right (absent); (B) Gaze to the left (abduction only). MRI View (C) Cerebral white matter abnormalities and the (D) Pontine lesion responsible for the eye movement disorder. Reprinted with permission from McAlpine's Multiple Sclerosis Churchill Livingstone.

IMBALANCE

The cerebellum is the main control center for balance. Demyelination damage to the cerebellum and its connections (i.e., ears, eyes, and nerves to the legs and arms) can cause MS patients to experience tremors of the head and limbs. Patients may also lose their balance when standing with both feet together or walking.

Some patients have weak muscles in their feet, which causes footdrop wherein the toes touch the ground before the heel. These patients risk falling down and injuring themselves. People with MS are known to suffer two to three times more physical injuries than people without MS.³ However, it is good news that roughly two thirds of those diagnosed with MS are still walking 20 years after disease onset.⁹

SPEECH PROBLEMS

Another possible symptom of MS is slurred (or scanned) speech. This is a frustrating condition because the MS patient is unable to speak clearly or control the flow of words.

SENSORY ABNORMALITIES

MS patients may also suffer sensory problems. Pain in the face, torso, or legs; tingling sensations; and paresthesias (feeling of needles and pins) are the most common sensory abnormalities. But some MS patients experience occasional feelings of cold, swelling, tightening, burning, or water running over the skin. Some patients (approximately 1%–2%) also suffer from trigeminal neuralgia, which is series of lightening-fast stabbing sensations occurring in the eye, temples, and cheek areas. Demyelinating plaques are sometimes found in the trigeminal nervous system.¹⁷

FATIGUE

This symptom is a frequent complaint of MS patients. In the most severe cases, the fatigue comes on suddenly. The patient may feel very tired or even fall asleep on the spot. This can happen at any time of the day or night.

BLADDER, BOWEL AND OTHER PROBLEMS

MS patients can also suffer bladder, and less commonly, bowel problems. Sexual dysfunction can occur, as can memory loss and mood swings. Depression affects more than half of MS patients.

AUTOIMMUNE DISEASE: REVIEW

As stated throughout this article, MS is thought to be a chronic autoimmune disease. To better understand this concept, a review of how the immune system functions is helpful. That is, knowing how this system operates will provide a better understanding of what happens when it does not function properly.

A healthy immune system works very hard to kill invaders. *Antibodies* are proteins produced by B lymphocytes (or B cells) in response to foreign substances entering the body. Bacteria, viruses, and parasites are *antigens*. B cells appear in the blood approximately 3 days after coming in contact with an antigen for the very first time. The B cells will search throughout the body, looking for that one particular antigen that caused the creation of the antibody. Antibodies then tag the invaders for destruction.

In warding off antigens, the body's first line of defense is the *skin*, the physical barrier. Bacteria, viruses, and parasites have to get past the skin to do further battle. If the invader is successful in breaking through, it is met with

another defense mechanism, which is the *innate system*, a system armed with protective white blood cells.

T and B cells are made in the bone marrow, which is where *stem cells* reside. A stem cell divides to produce one daughter cell that is just like the mother cell, whereas the second daughter cell produced is slightly different. The second daughter cell will go on to become either a T or B cell. *Macrophages* are the “big defenders” (or more accurately, the “big eaters”). Bacteria and viruses send out chemical signals that attract macrophages, which devour the invaders. It is interesting to note that the term macrophage is derived from the Greek words *macro* (large) and *phage* (to eat).

As the macrophages devour the invaders, they too give off chemical signals that cause more blood to flow into the area. During the attack, they produce *cytokines*, which are proteins whose job it is to alert other macrophages and other blood cells that a battle is occurring. The cytokines call out to cells in nearby capillaries, telling them to exit the blood and join in the fight.

T cells mature in the thymus gland where they either become *T helper cells* or *T killer cells*. At the same time, they acquire the ability to recognize “self.” Distinguishing self from antigens is of great importance in the immune system response. With autoimmune disease, something goes haywire. At some point, the immune system no longer recognizes certain cells as self and begins to destroy them.

In MS, chronic inflammation causes destruction of the myelin sheath. The macrophages are probably the main cause of this inflammation. They and the other blood cells are beckoned to the scene by cytokines. MBP, which is the major component of the myelin sheath, is the target.

Why this happens is still a mystery. Many studies have been conducted regarding a link between MS and Epstein-Barr virus, which causes mononucleosis and other disorders. This virus is very common, and approximately 95% of adults in the United States have been exposed to it.¹⁸ The hypothesis is that a person who is genetically susceptible to MS at some point becomes infected by a virus such as Epstein-Barr, and in response to the infection, the body produces T cells that recognize proteins from the viruses.^{19,20}

Along the same lines, researchers are looking for a connection between MS and herpes viruses—specifically human herpes simplex 6 (HHS-6), which causes a disease called roseola. Roseola affects infants by producing a high fever for several days, followed by a body rash. Two thirds of MS sufferers have antibodies to HHS-6.²¹ However, this research has not been substantiated to date.

TREATMENT

Because approximately 200 people are diagnosed every week with MS, it's fortunate that they have treatment options. However, before 1996, very little medication therapy was available.²² Here's a brief synopsis of the medication choices now available for the MS patient.

FDA-APPROVED MEDICATIONS

There is no cure for MS, but there are medications that slow down the progression of the disease. These drugs work to suppress the immune system.

GLATIRAMER ACETATE AND INTERFERON- β (IFN- β)

IFN- β medications and glatiramer acetate are approved for treating MS; both agents reduce the frequency of relapses by one third. However, they are not effective in slowing down the progression of disability.¹⁶ In January 2003, one form of IFN- β was approved for treating individuals who have experienced only a single attack as long as their MRI's demonstrate lesions (or damaged areas) consistent with MS.²²

The interferons are made up of a group of proteins that the immune system normally produces in response to viral infections.²² These agents were thus named because of that feature, which is the ability to interfere with viral replication. Patients using interferons must undergo periodic liver function testing. They should begin treatment by having a baseline liver function evaluation and then be retested every three months.

Glatiramer acetate and the two forms of interferon- β forms (IFN- β -1a and IFN- β -1b) are categorized as *immunomodulators* (i.e., disease-modifying drugs) that are used to treat RRMS.²² Moving from one immunomodulator type to another is not known to produce negative effects. These drugs should be started as soon as possible once a definite diagnosis of RRMS is made. However, IFN- β -1b is the only immunomodulator drug used to treat SPMS. For women of childbearing age, there is an increased risk of miscarriage associated with interferon therapy.

Glatiramer acetate and the two forms of IFN- β are given by injection, and they can be self-administered.²² There are two forms of IFN- β -1a: one is injected into the muscle; the other is injected under the skin. Depending on the drug used, the frequency of injection varies: daily, every other day, three times per week, or once a week.

Mitoxantrone

There are fewer treatment options for the more severe types of MS. The Food and Drug Administration approved mitoxantrone in 2000, a chemotherapeutic agent administered by intravenous infusion for MS patients who meet certain criteria.²² This drug is classified as an

immunosuppressant because it suppresses the activity of T cells, B cells, and macrophages that attack the myelin sheath. This agent can be used to treat the following three MS types: (1) secondary progressive MS (changes from relapsing-remitting to progressive at a variable rate); (2) progressive-relapsing MS (gradual increase in disability from disease onset as well as acute relapses along the way); and (3) chronic relapsing-progressive MS (characterized by clinical attacks without complete remission, which results in a steplike worsening of disability).

Mitoxantrone is *not* FDA approved for treating PPMS. This agent is used to treat some SPMS patients who aren't responding to IFN- β -1b therapy. Studies have shown that mitoxantrone is effective in reducing the number of new lesions as detected by MRI. It also reduces the frequency of attacks and the progression rate of disability. However, the down side of using this drug is twofold. First, it can only be administered for a limited time to avoid side effects to the heart (*cardiotoxicity*). And second, like other medications of this type, it can also cause sterility.²²

Plasmapheresis

Plasmapheresis is the process wherein whole blood is drawn from a patient. The plasma portion is removed from the blood and replaced with a suitable medium. Then the blood (red and white cells) is transfused back into the patient. Basically, the process involves removing disease-causing antibodies from the plasma. This treatment is reserved for treating only MS patients who suffer from severe, acute attacks and do not respond to other treatments. Plasmapheresis has been used successfully to treat other autoimmune diseases such as Guillain-Barré syndrome and myasthenia gravis. However, its benefit in treating MS is uncertain.²²

EXPERIMENTAL DRUGS

Recently, a study was conducted with five MS patients who were given anti-myelin T-cell vaccinations.²³ The vaccine was created from CD4+ T lymphocytes that were isolated from the MS patients' CSF. Each patient was given three immunizations at two-month intervals. The results was the reactivity against MBP was low in all five patients. Other positive results were that (1) the patients showed decreased or stable values on the EDSS, (2) none of the five experienced a relapse during the treatment; and (3) the vaccine was tolerated well.

Another clinical study was performed by intravenously treating MS patients with *natalizumab*, which is an antibody against *integrin* (a cell adhesion receptor). The goal of this study was to reduce the formation of lesions.²⁴ The antibody was administered to the patients every 28 days for 6 months. In this study, 213 patients were selected who had either RRMS or SPMS. Seventy-one of the two hundred thirteen patients received a placebo. All remaining patients received natalizumab: 68 patients were given 3 mg/kg of body weight; 74 patients received

6 mg/kg of body weight. The mean number of lesions was less in the treated patients (0.7% in the 3-mg group and 1.1% in the 6-mg group) versus those patients who received placebo (9.6%). The number of patients who experienced relapses was also less in the treated group (13 in the 3-mg group and 14 in the 6-mg group) as compared to 27 in the placebo group. Also, the formation of lesions was reduced by 90% in both the 3- and 6-mg groups, which is better than the 50% to 80% reduction shown by using various forms of interferon- β (IFN- β) and the 30% reduction shown by using *glatiramer acetate*. However, adverse effects were experienced during treatment with natalizumab.²⁴

SUMMARY

In the United States, approximately 400,000 people have multiple sclerosis. Research continues in an attempt to understand how and why people acquire this disease. Some people, especially those of Nordic descent, seem especially susceptible to MS. Other races such as Inuits and Asians appear to be resistant. Certainly, genetic factors seem to be involved. However, geographic (environmental) factors are also implicated. Thus, the cause of MS is probably a combination of genetic and environmental factors. The disease is diagnosed by clinical examination over time along with the demonstration of demyelinating lesions (as seen on MRI) in the brain and spinal cord. There is no cure for MS, but several treatment options are available.

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UNDERSTANDING MULTIPLE SCLEROSIS POST TEST

Expires August 15, 2013 Approved for 2 ARRT Category A Credits

1. **MS affects approximately how many people in the United States?**
 - a. 70,000
 - b. 150,000
 - c. 400,000
 - d. 6 million
2. **A primary characteristic of MS is that**
 - a. it is unpredictable.
 - b. it affects only men.
 - c. symptoms are very specific to the disease, making diagnosis easy.
 - d. it is always severely disabling.
3. **When describing MS, the term plaque may be used interchangeably with**
 - a. tumor.
 - b. lesion.
 - c. mass.
 - d. growth.
4. **MS is a chronic autoimmune disease affecting the**
 - a. lymphatic system.
 - b. musculoskeletal system.
 - c. connective tissues.
 - d. central nervous system.
5. **Demyelinated areas are known as**
 - a. plaques.
 - b. astrocytes.
 - c. neurons.
 - d. axons.
6. **Myelin is the**
 - a. point of junction between two neurons in a neural pathway.
 - b. insulation around nerve fibers in the CNS.
 - c. branched protoplasmic process of a neuron.
 - d. part of the neuron responsible for protein synthesis.
7. **The cerebrum is responsible for**
 - a. balance.
 - b. smooth muscle activity.
 - c. initiating movement and thoughts.
 - d. respiration.
8. **How many segments compose the thoracic section of the spinal cord?**
 - a. 4
 - b. 8
 - c. 10
 - d. 12
9. **The sensory neurons are contained**
 - a. in the dorsal horn.
 - b. in the ventral horn.
 - c. exclusively in the first segment of the cervical cord.
 - d. in the thoracic cord only.
10. **The motor neurons are contained**
 - a. in the dorsal horn.
 - b. in the ventral horn.
 - c. exclusively in the first segment of the cervical cord.
 - d. in the thoracic cord only.
11. **A good analogy for myelin is a (an)**
 - a. computer processor.
 - b. fire hose.
 - c. piston.
 - d. electrical cord.
12. **Electrical signals enter and exit the myelin sheath at the**
 - a. choroid plexus.
 - b. nodes of Ranvier.
 - c. hilum.
 - d. foramen magnum.
13. **Electrical signals are also called**
 - a. action potentials.
 - b. auditory stimuli.
 - c. evoked responses.
 - d. encoded messages.
14. **The process of creating myelin is carried out by a group of special glial cells called**
 - a. oxyntic cells.
 - b. Reed-Sternberg cells.
 - c. Betz's cells.
 - d. oligodendrocytes.
15. **The study by McAlpine concluded that MS symptoms**
 - a. always develop within minutes.
 - b. always develop within a few hours.
 - c. most often develop over years.
 - d. can develop suddenly or gradually.
16. **Which of the following statements is TRUE concerning the risk of developing MS?**
 - a. Genetics doesn't play a role in the development of MS.
 - b. Women are two to three times more likely to have the disease than men.
 - c. If one identical twin has MS, the other twin has a 1 in 500 chance of also developing the disease.
 - d. Most patients with MS have a close relative that also has MS.
17. **In the United States, the highest prevalence rates for MS occur**
 - a. among the Inuit population in Alaska.
 - b. in the Mississippi delta area.
 - c. in the Midwest.
 - d. In the states that are closest to the equator, such as Florida and Hawaii.
18. **The most common type of MS is known as**
 - a. relapsing-remitting MS (RRMS).
 - b. secondary-progressive MS (SPMS).
 - c. primary-progressive MS (PPMS).
 - d. progressive-relapsing MS (PRMS).

19. **The most commonly used tool used to diagnose MS is**
- lumbar puncture.
 - the evoked response test.
 - CT.
 - MRI.
20. **The expanded disability scale developed by John Kurtzke is intended to**
- predict the course of MS in a specific patient.
 - provide a definitive diagnosis of MS.
 - measure the mobility of MS patients.
 - assess the mental capabilities of advanced MS patients.
21. **In an MS sufferer, the body function affected is determined by the**
- exact location of the lesions.
 - age at onset.
 - age that the patient reaches a 7 on the DSS scale.
 - category of MS.
22. **The most common first sign of MS is**
- footdrop.
 - vision problems in one eye.
 - slurred speech.
 - chest pain.
23. **Antibodies are**
- substances that act to inhibit blood clot formation.
 - substances that are foreign to the body.
 - proteins that are produced in response to any foreign, non-biologic substance in the body.
 - substances that opposes the action of globulin.
24. **Bacteria, viruses, and parasites are examples of**
- B lymphocytes.
 - antigens.
 - antibodies.
 - T-cells.
25. **The function of macrophages is to**
- destroy cells alien to the body.
 - produce new blood cells.
 - destroy old blood cells.
 - carry oxygen to all cells of the body.
26. **Autoimmune conditions occur when the body**
- cannot metabolize sugar efficiently.
 - cannot accurately distinguish between what is a normal substance and what is foreign to the body.
 - produces cells that divide abnormally.
 - fails to adequately absorb essential dietary factors such as vitamins or minerals.
27. **Epstein-Barr virus**
- is rare and occurs mainly in South Africa.
 - is rare in the United States, but prevalent in most other parts of the world.
 - causes mononucleosis and other disorders.
 - is not known to cause any diseases.
28. **Interferons are made up of**
- red blood cells.
 - lymphocytes.
 - antigens.
 - a group of proteins.
29. **Which of the following statements is TRUE concerning the treatment of MS?**
- A cure is possible if MS is diagnosed early and treatment started immediately.
 - There is no cure for MS, but there are medications that slow the progression of the disease.
 - Presently, there is no treatment for MS, and medications prescribed are focused on pain relief.
 - Treatment consists of drugs that boost the body's immune system.
30. **Relapsing-remitting MS is treated with**
- glatiramer acetate and the beta interferons.
 - bed rest and increased fluid intake.
 - antibiotics.
 - Tamoxifen.



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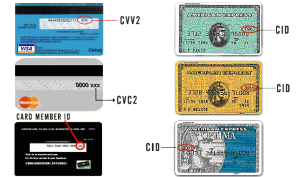
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1. a b c d	6. a b c d	11. a b c d	16. a b c d	21. a b c d	26. a b c d
2. a b c d	7. a b c d	12. a b c d	17. a b c d	22. a b c d	27. a b c d
3. a b c d	8. a b c d	13. a b c d	18. a b c d	23. a b c d	28. a b c d
4. a b c d	9. a b c d	14. a b c d	19. a b c d	24. a b c d	29. a b c d
5. a b c d	10. a b c d	15. a b c d	20. a b c d	25. a b c d	30. a b c d