Genetics

The genes a person inherits help determine whether that person is at increased risk for developing MS. While there is evidence from studies that this genetic component exists, it appears to be only one factor among several that determine who gets MS. Most likely, an individual's genetic blueprint ultimately determines if that individual will be susceptible to a triggering factor in the environment, which in turn initiates the autoimmune process that leads to the development of MS.

What Population Studies Show

Epidemiologic surveys have determined that an individual's risk of developing MS increases several-fold if a close family member has MS. While the average person in the United States has about 1 chance in 750 of developing MS, the risk for a person who has a parent with MS increases to about 1 in 40. MS. Thus, the risk increases significantly for a person whose parent has MS, but still remains relatively low.

These risk estimates, however, are oversimplifications that can easily be misinterpreted. We now know, for example, that risk estimates can vary greatly depending upon the structure of a person's family. In families in which MS occurs in many relatives, the risks for any given individual are significantly higher than they are for an individual who has no family members with MS. Risk for MS is also affected in part by a person's ethnic background and other factors that haven't yet been clearly identified.

How do we know that genes are not the only factor in determining who gets MS? The identical twin of a person with MS has a 1 in 4 chance of developing the disease. The fact that identical twins of people with MS—who share all the same genes—don't always get MS, and that more than 80% of people with MS do not have a first-degree relative with MS, demonstrates conclusively that MS is not directly inherited and that factors other than genetics must be involved.

New Techniques Help Pinpoint Genetic Factors

In the past few years, scientists have developed a set of tools that give them the ability to pinpoint the genetic factors that make a person susceptible to MS. These tools are the methods of molecular genetics—techniques used to isolate and determine the chemical structure of genes.

In the 1980s, scientists began to apply the tools of molecular genetics to human diseases caused by defects in single genes.This work led to major advances in understanding diseases such as Duchenne muscular dystrophy and cystic fibrosis. The situation for diseases such as multiple sclerosis is more complicated. Scientists now believe that a person is susceptible to multiple sclerosis only if he or she inherits an unlucky combination of numerous genes.

Advances in molecular genetics and the identification of large families in which several members have MS—“multiplex” MS families—have facilitated scientists’ efforts to uncover MS susceptibility genes. Since 1991, the National MS Society has supported an international project searching for these genes. The research teams have the challenging task of finding an unknown number of genes that confer susceptibility to MS. This requires searching the 3.2 billion DNA bases that form the code of the 30,000 to 40,000 genes that make up the human genome.

Scientists Are Searching for ‘DNA Markers’

Many multiplex families from throughout the world have agreed to participate in these studies. The researchers are looking for patterns of genetic material that are consistently inherited by people with MS. These recognizable patterns are called “DNA markers.” To do this, scientists probe the DNA of white blood cells from multiplex families searching for identifiable patterns or markers in the DNA code inherited in common by the individuals with the disease but absent in their healthy relatives.

When one of these markers is identified, scientists focus on that area, seeking additional markers closer to that gene. Eventually the location of that gene can be identified. This process of moving closer to the gene until it is identified has to be repeated for each of the marker regions from the multiplex families. By 1996, as many as 20 locations that may contain genes contributing to MS were identified, but no single gene was shown to have a major influence on susceptibility to MS. Research will likely find that other, as yet unidentified genes, contribute to MS.

After the location of each susceptibility gene is identified, the role that the gene plays in the immune system and neurologic aspects of people with MS will have to be determined. Because the immune system is so involved in MS, many scientists think at least some of the susceptibility genes are related to the immune system. Already there have been reports linking some immune system genes to MS.

How This Research Could Help People With MS

Finding the genes responsible for susceptibility to MS may lead to the development of new and more effective ways to treat the disease. Such research could also uncover the basic cause of the disease and help predict the course of the disease in an individual. This would make it easier for physicians to tailor therapies and provide information to help people make life decisions.

Another possible benefit may be the early diagnosis of people in families where one or more member already has MS. Many physicians believe that the earlier MS is diagnosed and treatment begun, the better the outcome will be.

See also…

Sourcebook

- Epidemiology
- Etiology (Cause of MS)
- Research

Society Web Resources

- Brochure: Genetics: The Basic Facts
  www.nationalmssociety.org/Genetics
- Targeted Research
  www.nationalmssociety.org/Targeted

Book

Murray TJ. *Multiple Sclerosis: The History of a Disease*. New York: Demos Medical Publishing, 2005.
—Ch. 11 Searching for the Cause of MS

The National Multiple Sclerosis Society is proud to be a source of information about multiple sclerosis. Our comments are based on professional advice, published experience, and expert opinion, but do not represent individual therapeutic recommendations or prescription. For specific information and advice, consult your personal physician.

To contact your chapter, call **1-800-FIGHT-MS** (1-800-344-4867) or visit the National MS Society web site: www.nationalmssociety.org.

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