What Causes MS? Pursuing Genetic and Environmental Answers to Stop and End MS

Ending MS means no one will ever get this disease again. Progress has been made identifying some factors that may combine to increase a person’s chances of developing MS, such as specific genes, infections, and lifestyle factors, although none of these factors is a single cause of the disease. It is clear that not everyone who has been exposed to these factors will develop MS, and that not everyone who has MS has been exposed to these factors. These clues provide insights that may lead to ways to prevent the disease, and are also helping to identify new approaches to stopping disease activity. We need to find what triggers MS, and what may protect against it. Here’s how:

- Aggressively pursue studies to identify all genetic variations that increase susceptibility to MS.
- Better understand all of the factors in the environment or lifestyle that influence risk for MS.
- Identify possible infectious triggers for MS, such as viruses or bacteria.

Identifying all genes
Research suggests that MS occurs in individuals and in families whose genes make them susceptible, and that many genes contribute to MS susceptibility. Pinpointing and understanding “MS genes” is important because it will provide key information regarding the cause of the disease and therefore how to prevent it, and genes that are associated with MS may be targets for the development of new therapies.

The International MS Genetics Consortium (IMSGC) was launched with early funding from the National MS Society, and brings together MS genetics researchers from 15 countries. Through studies that involved over 100,000 people, the IMSGC has identified 200 genetic variations related to MS, and has begun to identify the specific immune cells and proteins involved. These teams could not have accomplished this massive task if not for this international collaboration. Now the challenge remains to interpret how these genes contribute to MS development.

Who gets MS?
Pursuing the question of “who gets MS” has uncovered several promising areas. Research of populations to study disease patterns, including variations in geography, demographics, socioeconomic status, genetics, environmental risk factors, and exposure to infectious agents, is called “epidemiology.” These studies provide vital information about relationships among these factors, so that we can better understand who gets MS and why, identify and explain areas with high or low rates of the disease, and assist in planning for health care and other services.
Epidemiologic studies have given us some important clues:
- The disease affects more than twice as many women as men, leading to research to understand gender differences and treatment trials of gender hormones.
- MS is more prevalent in temperate regions of the world than in the tropics. As a result, researchers have suspected a link between the disease and sun exposure, or the vitamin D that sun exposure produces, and are increasingly pointing to low levels of vitamin D as a risk factor for developing MS. This research has led to clinical trials to determine if vitamin D supplements can reduce MS disease activity.
Substantial evidence links smoking to an increased chance of MS development and progression. No single virus or bacterium has been proved to cause MS. However, studies have suggested an association with several viruses, most notably the Epstein-Barr virus (EBV, which causes mononucleosis).

We Are Funding Progress
Accelerated research breakthroughs will change lives and end MS forever. The National MS Society is committed to driving research progress into the causes of MS by making strategic investments in the following areas:

- **Taking the next steps in gene studies**
  - **Interpreting genetic variations** identified by the IMSGC: Duke University and Yale researchers are using new technologies to identify MS risk genes that are important in particular types of immune cells, and uncover the exact pathways by which MS develops.
  - **Predicting MS risk**: Harvard researchers are developing an individualized risk prediction tool that incorporates the latest knowledge in MS genetics and may be able to predict a person’s risk for developing MS.
  - **Focusing on ethnic groups** with varying levels of susceptibility to MS may help to understand the clinical differences between these groups. A nationwide team of researchers screened for known gene variants in more than 1,000 African Americans with MS, showing significant differences that may help sort out why MS is often more severe for African Americans. Researchers in Miami are also amassing such information on Hispanics/Latinos with MS.

- **Moving environmental studies forward**
  - **The interaction of genes and environmental factors**: The Network of Pediatric MS Centers is studying children with early relapsing-remitting MS to determine environmental and genetic risk factors that make children susceptible to developing MS. So far, we have learned that low vitamin D status is associated with relapses only if a specific immune gene is present.
  - **The MS Microbiome Consortium**: Accumulating research suggests that gut bacteria are critical in the establishment and maintenance of immune balance by the molecules they release, and this balance may be askew in MS. This collaboration is comparing gut bacteria of people with relapsing and progressive MS. Findings may lead to the development of novel probiotic approaches to treating MS.
  - **Vitamin D trial**: Investigators at several centers nationwide are recruiting 172 people with relapsing-remitting MS to compare the effectiveness of the current recommended amount of vitamin D supplementation versus high dose vitamin D supplementation at reducing MS disease activity, when added to standard therapy.
  - **Pinpointing triggers**: Researchers at Cornell University Medical College in New York City are investigating if a toxin derived from a particular type of bacteria can induce the types of changes seen in early MS damage. University of Illinois at Chicago researchers are devising a method to detect the presence of viruses (any virus) in newly forming MS lesions, in hopes of identifying the cause of MS and preventing its development.