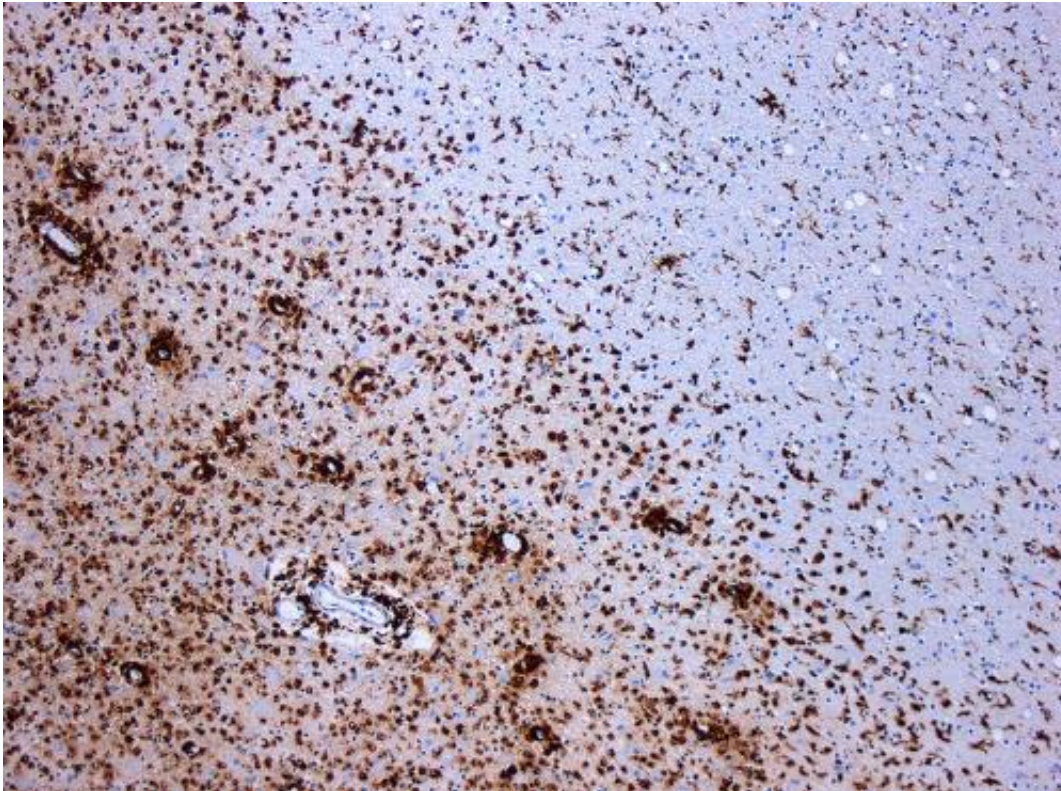


Predicting who will develop multiple sclerosis

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Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: [CC BY-SA 3.0](#) Marvin 101/Wikipedia

A team of investigators at Brigham and Women's Hospital (BWH) and the National Institute of Neurological Disorders and Stroke (NINDS) has launched a study of individuals at risk for multiple sclerosis (MS). By focusing on first-degree family members of MS patients, the research

team seeks to better understand the sequence of events that leads some people to develop the disease. Their work also sets the stage for developing and testing interventions with which to block the onset of MS. The research team introduces the Genes and Environment in Multiple Sclerosis (GEMS) project, a large prospective natural history study, in a publication in the *Annals of Neurology*.

"Early detection of MS means the possibility of earlier treatment, which could delay the accumulation of disability," said co-senior author Phil De Jager, MD, PhD, who directs the Program in Translational NeuroPsychiatric Genomics at the Ann Romney Center for Neurologic Diseases at BWH. "Our long-term goal is to map out the sequence of events leading from health to disease, in order to be able to identify and intervene early in individuals at high-risk of MS."

The GEMS study leverages the outreach efforts of patient advocacy groups such as the National Multiple Sclerosis Society, social media tools such as Facebook and electronic communication to recruit first-degree relatives (parent, sibling or child) of people who have been diagnosed with MS. More than 2,600 family members have been recruited from across the U.S. Family members can interact with the study via its Facebook page where updates on the project and MS-related news are shared. The study, which will ultimately enroll 5,000 first-degree relatives, will continue for the next 20 years.

"This first report from the GEMS study is important because it shows that we can recruit the large number of family members that is necessary to perform a well-powered study of MS risk factors," said lead author Zongqi Xia, PhD, of BWH's Ann Romney Center for Neurologic Diseases.

Upon enrollment in the study, participants completed a web-based questionnaire about their medical history, family history, environmental

exposures and more. Participants also submitted a saliva sample for DNA extraction.

"Since the disease likely starts many years before the first symptom appears, we do not yet understand how genetic and environmental risk factors come together to trigger MS," said co-senior author Daniel Reich, MD, PhD, of the Division of Neuroimmunology and Neurovirology at the NINDS. "When a patient comes to see a neurologist for the first time, the process of brain inflammation is well underway, since many lesions have few or no symptoms."

Although first-degree relatives are 20 to 40 times more likely to develop MS than the general population, their risk is still low: the researchers estimate that of 10,000 first-degree relatives, only about 62 will be diagnosed with MS over five years. Having a means to predict who is most at risk for developing MS not only means opportunity for early intervention, but also makes clinical trials for new treatments more feasible since the incidence of MS is low in the general population.

In their preliminary analysis, the research team tested a method to calculate an individual's risk of MS, and identified a subset of family members that may have a higher risk of developing MS than the average family member. Although not yet clinically deployable, this risk score could help design long-term studies of higher-risk individuals.

"This report is an important first step. We do not yet have a tool that we can use clinically to predict MS. To develop such tools further, and to develop a platform for testing strategies to prevent the disease altogether, we are expanding GEMS into a larger collaborative study that will accelerate the progress of discovery and bring together a community of investigators to overcome this important challenge," says De Jager. "Overall, the risk of MS remains very small for most [family members](#). The most effective therapies for MS will ultimately be those that prevent

its onset, as halting inflammation and disease progression are much more difficult once the disease has become established."

More information: Zongqi Xia et al. GEMS Project: A Platform to Investigate Multiple Sclerosis Risk, *Annals of Neurology* (2015). [DOI: 10.1002/ana.24560](https://doi.org/10.1002/ana.24560)

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