

A gut reaction to MS



Exploring possible links between the gut, the immune system and MS

by Mary E. King

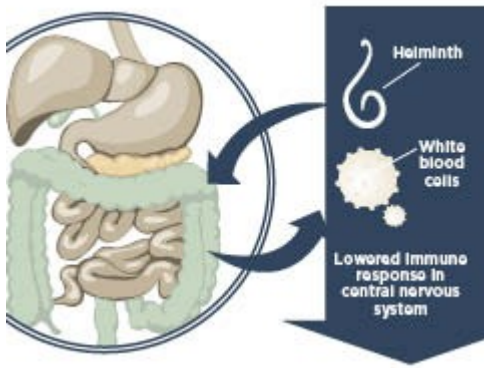
Biome defined

The word biome usually refers to a large geographical area with distinctive plant and animal species, such as the Arctic tundra or large freshwater lakes. The gut microbiome is a micro-version of a complex biome.

Scientists today are investigating the interaction between bacteria normally found in the gut and the gut's immune cells, and the potential influence of that interaction on the development of multiple sclerosis. An estimated 100 trillion "friendly" bacteria live in the gut. They assist in the digestion of food, and help prevent disease-causing bacteria that may be encountered in food or drink from making us sick. Harmless or possibly beneficial viruses, parasites and probably fungi also reside in the healthy human gut.

Collectively, these microorganisms are referred to as the gut microbiome. The members of the gut microbiome "talk" to immune cells in the gut, and the immune cells "talk back" by releasing specialized messenger molecules and subtypes of immune cells. These "discussions," researchers are learning, affect the entire immune system including, quite possibly, the immune attack in the central nervous system that is characteristic of MS.

Suppressing immune attacks



A clinical trial is underway at the University of Wisconsin-Madison to determine if the ingestion of helminths—tiny, parasitic worms—can suppress immune attacks going on elsewhere. As the body releases white blood cells to attack the helminth, it sets off a series of immune events that can regulate the immune system. It is hoped that this reaction can slow or stop the immune response against the brain in MS.

Scientists theorize that it might be possible to alter the gut microbiome in a way that slows or stops the immune reactions in MS. Or, they also theorize, differences in the types of organisms present in the gut could make some people either more or less susceptible to developing MS.

Interest in this frontier has intensified to the point that the National Institutes of Health has launched the [Human Microbiome Project](#) to begin mapping out variations found in people.

Three researchers who have received funding from the National MS Society are among those investigating the link between immune system and gut microbiome.

- Dr. Lloyd Kasper, professor of medicine and microbiology/immunology at the Geisel School of Medicine at Dartmouth in Hanover, N.H., is evaluating the effect of a specific molecule released by one type of gut bacteria that shows promise in preventing disease in a mouse model of MS.
- Dr. John Fleming, professor of neurology and MS director at the University of Wisconsin School of Medicine and Public Health in Madison, is conducting a trial testing whether a specific organism might alter the gut's immune system in a way that is beneficial to people with MS.
- Dr. Emmanuelle Waubant, professor of neurology and pediatrics, and director of the Regional Pediatric MS Center at the University of California, San Francisco, is analyzing profiles of gut bacteria in children with and without MS to see if she can identify differences in the gut microbiome that could explain MS onset in the context of specific environmental exposures.

Investigating a single molecule

Dr. Kasper is examining the effects of a molecule called polysaccharide A that is released by

a specific species of gut bacteria. (Polysaccharide A is referred to as “PSA,” but it has no relation to the other “PSA”—prostate specific antigen—that is the focus of a laboratory test used in prostate cancer screenings.) His project is underwritten by a grant to the Society from the Conrad N. Hilton Foundation.

Research began with two strains of mice that are susceptible to developing experimental autoimmune encephalitis (EAE), an MS-like disease. Previous research showed that if these mice are given oral antibiotics, which render their guts germ-free, they do not develop EAE. If the intestines of these germ-free mice are colonized with the intact microorganism *Bacteroides fragilis*, the mice continue to be resistant to EAE.

Dr. Kasper’s group identified the molecule PSA as the critical component of the bacteria that is necessary for maintaining this resistance to EAE. They showed that if the intestines of the germ-free mice are colonized with *B. fragilis* that lacks the PSA molecule, the mice become susceptible to EAE again.

Now, Dr. Kasper is investigating how PSA affects immune system cells from healthy individuals and people with MS. The results of this research could open new pathways for stopping immune attacks in people with MS. While the initial results are promising, testing PSA as a drug in early human clinical trials is at least a year away.

The promise of this new approach is tempered by the history of drugs that have shown promise in the animal model, EAE. “There have been enough failed experiments moving from EAE into the clinic to know that if [a treatment] works in EAE, it is not necessarily going to work in human MS,” Dr. Kasper cautions.

More information on probiotics

The FDA has not approved any health claims for probiotics at this time; the research is still ongoing. Certain probiotics are being studied to see if they could be helpful in infant diarrhea, antibiotic-induced diarrhea and irritable bowel syndrome.

For more information, visit the [National Institute of Health website](#) for more information.

Studying a single organism

Dr. Fleming has taken a different approach, using the idea of probiotics. These “good” strains of microorganisms are thought to help maintain a healthy balance in the gut. Certain foods, such as yogurt, as well as some drinks and supplements contain live bacteria and introduce good microorganisms into the GI tract. Dr. Fleming’s research involves using a live organism, a tiny member of the worm family called a helminth, in a similar way, as a potential treatment for MS.

The research builds on the observation that the incidence of MS and other autoimmune

diseases has risen as sanitation and hygiene improve. Ingesting a safe microbe might change how the immune system responds in a way that reduces the risk of an autoimmune disease or slows its progress.

Dr. Fleming is lead investigator on a small clinical trial (with 10 to 20 people with relapsing-remitting MS) that is underway at the University of Wisconsin-Madison to test whether oral ingestion of helminth eggs can improve disease. Study volunteers ingest the innocuous eggs in a sports drink. The eggs hatch into larvae, which travel to the large intestine where they are killed during interaction with the gut immune system.

Dr. Fleming explains, "The gut and microorganisms at that site may be a key to how the whole immune system functions. For example, there may be complex [two-way] interactions between helminths and bacteria that may diminish autoimmune responses outside the gut, such as in the central nervous system."

Dr. Fleming's team is following the study participants for 10 months. They are using MRI and other tests to determine whether helminth ingestion shows any benefit. The hope is that altering the immune "conversation" in the gut will slow or stop the immune response against the brain in MS.

While the results so far are promising, the safety and efficacy of this treatment are unproven, so Dr. Fleming strongly advises that individuals not try this on their own. He expects to have some results from the study in 2014. Positive results could lead to larger clinical trials.

Investigating the entire microbiome

Dr. Waubant describes her approach to studying the gut-microbiome interaction by explaining, "Each of us has our own unique community of microorganisms in our guts, although we probably have a lot of the same types of microorganisms that, say, our close family members have." She and her team are studying the types and numbers of microorganisms in the gut microbiome, as well as in saliva and nasal samples from 100 children with MS and matched control subjects.

By comparing these children with and without MS, Dr. Waubant says, "We hope to see if there are big differences that suggest a role of specific [microorganisms] in triggering MS."

She will also be able to evaluate environmental factors' effect on the various microbiomes under study. Her focus is on children rather than adults with MS because, as she states, "If we think there have been changes in the composition of the gut microbiome that may contribute to the development of MS, [but we] wait too long to start looking into [it], we may see variations that are not relevant to how the disease was triggered."

This work could advance the understanding of MS and possibly its treatment or prevention. Still, Dr. Waubant states, "There is really much more work to be done to confirm exactly where it fits in our map of risk factors for MS and possible treatment algorithms."

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Learn more about the [Human Microbiome Project](#).