

First Phase Tested Safety

Fleming's Worm Egg Research Entering Second Phase

By Amanda Gasper

Not many people would think about drinking worm eggs. But that's what five MS patients did during the initial phase of a study to evaluate the safety of digesting worm eggs to regulate the immune response in MS.

Dr. John Fleming is leading the study. The next phase of his research will again test the use of worm eggs as a treatment for MS, but will involve more patients and last longer.

Dr. Fleming is a professor of neurology at the University of Wisconsin School of Medicine and Public Health and the director of the Multiple Sclerosis Clinic at the University of Wisconsin Hospital and Clinics. His interest in MS started in the '70s when he was a research fellow for the National Multiple Sclerosis Society. Raised in Hawaii, Dr. Fleming has resided in Wisconsin for the past 20 years.

This study, called Helminth-Induced Immunomodulation Therapy (HINT), offers an alternative approach to treatment of MS. It is funded by a \$567,110 grant from the National MS Society and is looking at the use of parasitic worms that live inside a host, called a helminth, to treat the symptoms of MS.

Hygiene Hypothesis

The theory driving the study is called "the hygiene hypothesis." This hypothesis suggests that developed



A technician looks at worm eggs through a microscope at OvaMed, the German biotech company that supplies the eggs used in Dr. Fleming's study. Photo provided by OvaMed, Hamburg, Germany.

countries, such as the United States, have higher incidences of allergies and autoimmune diseases, because there is little or no exposure to parasites and other infections.

"In the developing world where they have many helminths and other infections, they just don't get multiple sclerosis," Dr. Fleming said. "But in developed countries; where kids are vaccinated, we take antibiotics all the time and the water is super clean; we have higher

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- Dr. Fleming

incidences of autoimmunity.” And that means higher incidences of MS.

“Hygiene sanitation is a good thing,” added Dr. Fleming. “We don't want epidemics like cholera.” But the environment has changed faster than our genetics, said Dr. Fleming. The immune system was accustomed to exposure to parasites. Without them, the immune system sometimes attacks the human body instead.

“Helminths and other kinds of natural infections learn how to modulate the host,” said Dr. Fleming. “For their own survival, they produce substances that reduce the intensity of the immune response. And similarly, the host realizes these are big multi-cellular organisms. The body won't launch a massive immune attack on them, or it'll harm its own tissues by causing too much inflammation.” This “immunological truce,” as Dr. Fleming calls it, is seen in the body's response to parasitic infection. It pushes the immune system towards a less inflammatory response.

And this is where the worms come in.

Dr. Fleming believes the worms can potentially redirect the body's immune system away from the inflammatory response that happens in MS. “We're basically using the helminth as a probiotic to change the immune system to help people with MS,” Dr. Fleming said. Probiotics are living organisms that benefit the health of the host. They can be found

in food products such as yogurt, cottage cheese, sauerkraut and many pickles.

Five Patients Drank Worm Eggs

In Dr. Fleming's HINT1 study, five recently diagnosed relapsing-remitting MS patients, with no previous treatment, drank worm eggs – or more specifically, *Trichuris suis* eggs, which are pig whip worms. They did this every two weeks for three months, 2,500 eggs at a time.

Many might wonder how drinking worm eggs from pigs could be safe for humans. The eggs come from disease-free pigs that are grown in a clean environment at a biotech company, Dr. Fleming said. He further explained: "Because it's not a human pathogen, it doesn't cause disease in people. The idea is a little bit like using cow pox to help human small pox. If you gave anything from a human, like attenuated small pox (a less harmful, but still living, version of small pox), you always have the danger that it's going to revert (to being harmful)."

Previously, researchers at the University of Iowa showed that *T. suis* was safe to ingest and reduced symptoms in patients with Crohn's, an inflammatory bowel disease.

Dr. Fleming added, "It's not like you're drinking a glass of earthworms on a reality show. We give it as microscopic little ova, or eggs, in a sports drink. Essentially, Gatorade."

Kristen, a patient who participated in the study, said this about the worm egg cocktail: "The first time, I wasn't sure what it would be like. I was a little grossed out, but it was super easy to do. I liked that it was something natural."

And how does it taste?

"It was a little salty," Kristen said.

According to Dr. Fleming, after the eggs are ingested, the larvae hatch in the small intestine. By the time they travel to the large intestine, they are a fraction of an inch. This is where they are destroyed by the immune system, he said.

"The worm doesn't penetrate the gut walls," Dr. Fleming said. "You never have to worry about it going into tissue, liver, lungs or something like that. It just kind of slithers along."

Participants Received Frequent MRIs

Patients were monitored during the study with MRI scans to look at the number of new lesions that developed before, during and after the ingestion of worm eggs. According to Dr. Fleming, "An MRI scan is much more sensitive than clinical measures. The average patient will have maybe one attack in a year in MS, but 10 MRI events. To date, the MRI findings are encouraging, but larger and longer studies will be required before any definite conclusions are possible."

Kristen, who is newly diagnosed with MS, said participating in the study was reassuring.

"I had to do a lot of MRIs," she said. "It helped me track what was going on with my disease."

The MRIs also helped Dr. Fleming keep track of the patients' safety by making sure the treatment didn't make their MS worse. Kristen added, "Dr. Fleming was wonderful, checking in to make sure you were

feeling alright. I wasn't ever concerned."

Kristen said she participated in the trial because she was hoping that it would help advance research. "It's promising," she said.

The next step is a study with 18 patients, called HINT2, that will last 18 months.

"Another question for the future is, do we want to be using the whole worm or do we isolate the molecule



Dr. Fleming's patients drank 2,500 microscopic eggs in a tablespoon of a sports drink-like fluid from bottles such as these. Photo provided by OvaMed, Hamburg, Germany.

which is active in the worm and use it in pill form,” Dr. Fleming said. “The pill is probably the ultimate goal, but you have to start somewhere. We are starting with the crude preparation, but we don’t want to stop there.”

Research also doesn’t stop at relapsing-remitting MS. Dr. Fleming said, “Most new treatments for MS start with relapsing-remitting patients. They are the most active, so it’s easiest to see if something has an effect. Many times, if something seems to have an effect in relapsing-remitting MS, then you go on to look at secondary progressive.”



Dr. Fleming’s research may benefit other autoimmune diseases, in addition to MS.

Dr. Fleming added that it might not stop with MS. If this type of treatment works for one autoimmune disease, such as Crohn’s, and if it were to work on a second autoimmune disease, like MS, could it work for others?

But for now, Dr. Fleming has “cautious optimism, with the emphasis on caution,” he said.

Amanda Gasper is a recent graduate of the University of Wisconsin-Madison where she studied Life Sciences Communication. She is a part-time copywriter for the Wisconsin Chapter.

Participants Sought for Second Phase of Dr. Fleming’s Worm Egg Study

Dr. Fleming seeks 18 individuals to participate in the second phase of his HINT study. The main criteria for participation are: Newly diagnosed with MS or have experienced first attack of an MS-like disease (such as optic neuritis). No prior treatment with MS drugs. Willingness to participate in an experimental oral treatment. For information contact:

- University of Wisconsin site: Namita Azad, 608-265-8765, nazad@clinicaltrials.wisc.edu
- Marshfield Clinic site: Carol Beck, 800-782-8581 ext. 93144; Beck.Carol@mcrf.mfldclin.edu

Dr. Fleming Says Hypothesis Merits Study

MS Society’s CCSVI Research Awards to be Announced in June

Recent reports have called attention to the idea that CCSVI, a reported abnormality in blood drainage from the brain and spinal cord, may contribute to nervous system damage in MS. Dr. Paulo Zamboni from the University of Ferrara in Italy, conducted a pilot study (published in April 2009), and suggested that a larger, better-controlled evaluation of the possible impact of CCSVI on MS be undertaken. The National MS Society subsequently issued a request for proposals and in June will announce its funding decisions for CCSVI-related research.

Weighing in on the possible connection between CCSVI and MS, Dr. John Fleming, professor of neurology at the University of Wisconsin School of Medicine and Public Health and the Director of the Multiple Sclerosis

Clinic at the University of Wisconsin Hospital and Clinics said, “CCSVI is an interesting hypothesis that needs to be followed up on.”

“We are very enthusiastic about the research,” continued Dr. Fleming, “but clinical treatment right now is premature. We don’t even know if it’s safe. This is experimental, so should only be done under an ethics board-approved experimental study, both in terms of diagnosis and treatment. Understandably, people are anxious. This might be a breakthrough and they feel like they can’t wait, but it’s the best way to do it.”

To learn more about CCSVI and the National MS Society’s research initiative, go to nationalMSSociety.org.