Being There:

MS Clinical Trials as Seen by Some Volunteers

by Gary Sullivan photos by Charles Harris

North Carolinian Brian Cole would seem an unlikely participant in a clinical trial of an experimental MS drug. A business development manager for a software company, Cole, who was diagnosed in 1995, had been taking Avonex for a decade. He attributed the relative mildness of his disease to the drug. But in August 2007, he signed up for a 1,292-participant, double-blind, head-to-head trial comparing two different doses of fingolimod against Avonex in people with relapsing-remitting MS. (Fingolimod is one of more than a dozen oral therapies in trials today: See "In the Pipeline: MS Pills" on page 24.)

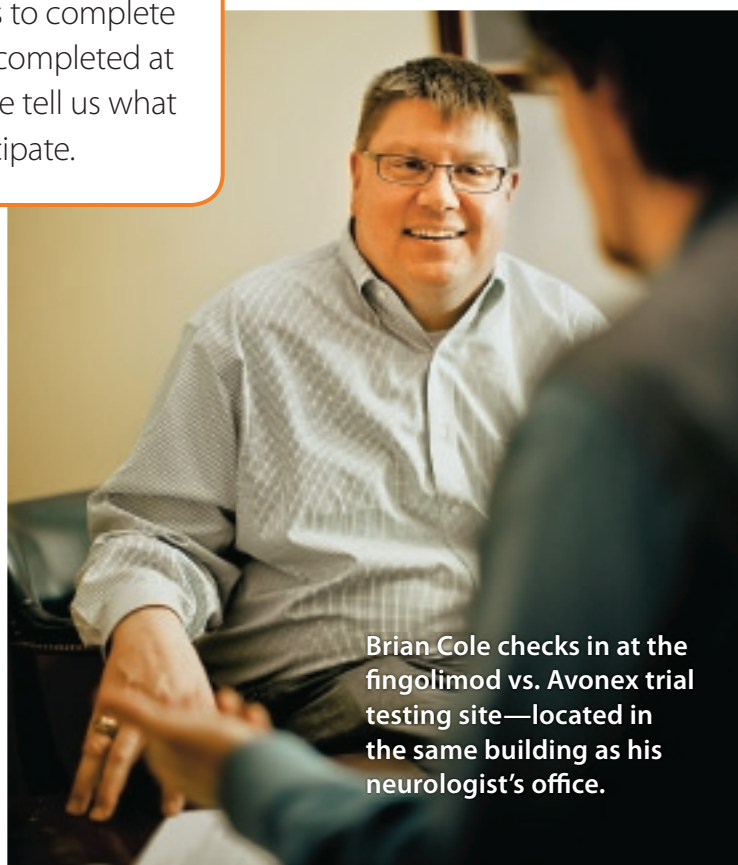
As the number of clinical trials for MS agents increases, it becomes urgent to find willing and qualified participants. Without plenty of volunteers, trials might take extra years to complete or may not be completed at all. Three people tell us what it's like to participate.

Mary Ellen Wittenberg,[1] a grammar school teacher living in urban Texas, woke up one day late last year unable to see out of her left eye. An MRI showed signs of possible MS. Now diagnosed with CIS, or clinically isolated syndrome, and a chance of MS in her future, Wittenberg discussed options with her neurologist. A double-blind, placebo-controlled phase III trial for teriflunomide, an oral medication used to treat rheumatoid arthritis, had just been launched. Wittenberg signed up.

Lori Heney, a preschool teacher in suburban Massachusetts, was diagnosed 18 years ago. She had been on Betaseron for more than seven years and her exacerbations, which had occurred infrequently, were getting stronger. Heney and her doctor discussed other treatment options. One—taking steroids once a month—seemed overwhelming. Another—joining a double-blind, placebo-controlled trial for fingolimod—sounded more intriguing.

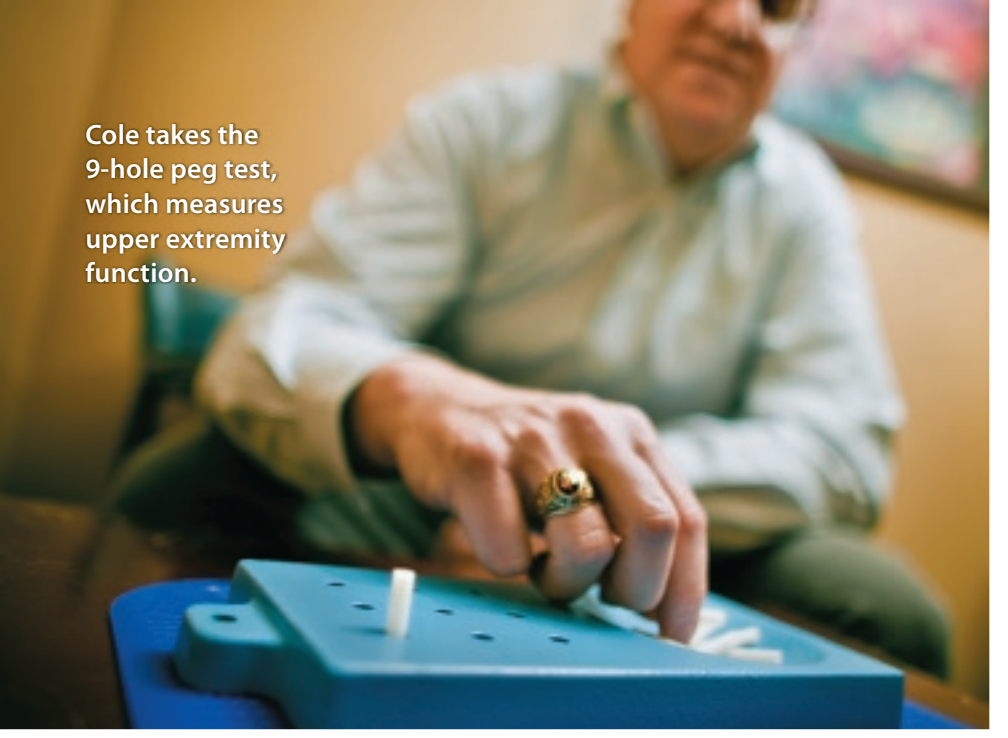
The bottleneck

According to a 2008 **Momentum** article by John Richert, MD ("New treatments await—if they can be tested," Fall 2008), there are some 136



Brian Cole checks in at the fingolimod vs. Avonex trial testing site—located in the same building as his neurologist's office.

[1]Not her real name.



Cole takes the 9-hole peg test, which measures upper extremity function.

ongoing clinical trials for MS drugs. Dr. Richert, who is executive vice president for the Society's Research and Clinical Programs, estimates that these trials will need more than 35,000 volunteers.

"Investigators have strict criteria by which they determine who may enroll in a study. Some studies require that participants have never taken a disease-modifying agent … a hard group of people to find." Dr. Richert also notes that people may be reluctant to forego proven medication in a trial in which the control group only receives a placebo. (See "In the Know: Drug Trial Basics," page 25.)

Some researchers are calling this a "bottleneck problem" as trials, especially phase III trials that require hundreds of participants, take longer than expected.

Making the decision

Brian Cole's neurologist has an office at Raleigh Neurology Associates, PA, a testing site for a number of trials, and the subject had come up before. "But this was the first trial that really made sense for me," Cole said.

Participants in the Avonex vs. fingolimod trial would take both injections and pills, but one of the two pills would be a dummy placebo. No one would know which. Cole was already taking Avonex, and dreamed of one day being able to take an oral medication. "Let's face it," he said. "There's nothing natural about injecting yourself. I never got used to it.

"I met with the study coordinator," he explained, "who told me that, after the first 'blind' year of not knowing which drug I was getting, everyone who opted to continue would be getting fingolimod."

Unlike Cole, Wittenberg and Heney signed up for placebo-control trials. They would not know if they were getting a real drug until the end of their participation.

"Two years of not knowing, and then I can opt to be on the drug," Heney told **Momentum**. "My husband and daughter were concerned that I might not be getting any treatment. But I always have the option of dropping out of the trial and getting on something else. My doctor and I agreed to consider it if I have another attack."

Wittenberg joined a trial testing two different doses of teriflunomide vs. placebo. "My neurologist can't tell me yet if I have MS for sure, or if I do, which form of the disease I have. But I'm closely monitored while in the trial, and receiving regular MRIs. By the end of this study, we'll know a lot more about my own personal situation—as well as whether or not the drug they are testing works." Wittenberg's husband supported her decision. He often accompanies her when she comes in to the clinic.

Cole's wife and friends also felt he was doing the right thing, but his mother was worried.

"She had seen the positive impact that Avonex had had on me and thought that I might be risking a year of taking something that didn't work as well for me. I understood her point of view. But it was a

Next, the trial staff will evaluate the time Cole needs to walk 25 feet.

risk I was willing to take, especially considering the positive results of earlier fingolimod trials."

Participation ins and outs

For the first several months, Cole visited Raleigh Neurology every two weeks, where he picked up his medication and underwent tests. Later, his visits were reduced to once every six months.

"I got several MRIs, regular pulmonary exams, and eye pressure tests," he said. (The side effects of fingolimod include possible heightened eye pressure.)

"I was still injecting myself once a week and also taking a pill every day. I didn't know if my pill was the real one."

Heney made the 45-minute trip to her clinic in Boston every two weeks at first, then once a month. "Now it's once every three months," she said. The drive into Boston is the worst part, she admitted. "I don't mind taking the time off work, even though the trial doesn't compensate me—I've got plenty of vacation and sick days. But I hate driving." Heney's husband usually goes with her. When he is unable to take off work, her mother drives her.

Wittenberg makes her hour-long trek to her clinic every two weeks. She said the uncertainty about whether she's getting real medicine or placebo was less important to her than regular, free visits to the neurologist. "Since I don't even know at this point if I have MS, it's all sort of up in the air for me. The neurologist I'm seeing is very well-known locally, and a real professional. He had a lot to do with my decision to do this," she said.

Though Cole likes to describe himself as gung ho, there was a period when he started to question his participation.

"I began to experience an increase in clinical depression symptoms," Cole said. "I got the idea that the depression might mean I was on fingolimod and wondered what to do."[2] The nurse assigned to Cole suggested he begin taking a mild antidepressant. "That was nearly a deal-breaker," he said. "If I had to take another med on top of what I was already taking for MS, it might not be worth it."

A finger-touching test measures Cole's manual dexterity.

But after starting the antidepressant, Cole felt better. "Whatever MS med I was on now was working at least as well as what I had been taking before—I've only had a one relapse since the study began. And I am really looking forward to the day when I don't have to shoot myself up."

[2]Fingolimod has not been linked to depression.

Did you know?
Hidden benefits of clinical trials

As a general rule, people taking part in a clinical trial tend to do better than people not in a trial. They may be paying closer attention to their overall health due to the constant reminder of it and the increased medical attention they are getting. Participants are also more likely to adhere to their treatment regimen.

Last September, Cole completed the first, double-blinded portion of the trial. He opted to remain, which means he now receives fingolimod.

"That was one of the perks of this trial," he explained. "I keep getting it free of charge until the manufacturer, Novartis, decides to either abandon the study or fingolimod is approved by the FDA and available by prescription."

Life-changing experiences

Since starting her trial, Heney feels her life has gotten better. "Some of my symptoms—numb hands and tired legs—have improved," she said. "But for me, the best thing about this has been the level of medical care I've gotten. Before, I would only call the doctor when it was too late—in the middle of an exacerbation. Now I'm being monitored and monitoring myself."

Wittenberg agreed. "Since I've been in this trial, I've made changes in my environment to make it less stressful. I've also completely changed my diet. I cut out all dairy products, wheat and glutens, and I've lost a significant amount of weight. I feel a lot better—much stronger."

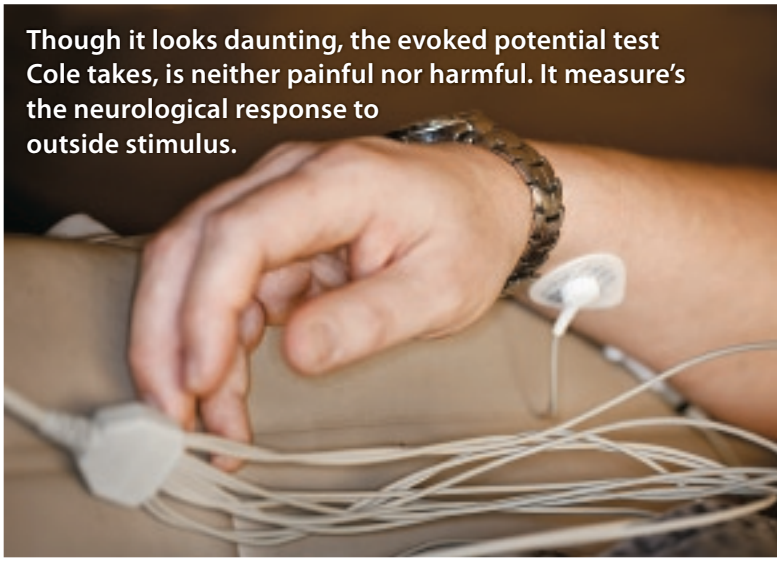
Cole said that the clinical trial has gotten him connected to the MS community in a way he hadn't been before.

"The first day, they kept me at the clinic to monitor me for any adverse reactions. I got to talking with people who were in other trials. So many of them were doing this because they couldn't afford meds any other way." It was the first time he'd spent time with others who also live with MS.

Cole reached out to the Eastern North Carolina Chapter and got involved with their Speakers Bureau. These days, Cole gives talks at chapter and community events ranging from the Jaycees to health fairs. "I do a lot of speaking for my job, so it seemed natural.

"I mostly talk to people who are newly diagnosed," he continued. "At that stage, when everything is so up in the air, it's important for people to see someone like me, someone 15 years into the disease, so they know they're not necessarily going to be in a wheelchair or out of a job."

Gary Sullivan is managing editor of **Momentum**.



Though it looks daunting, the evoked potential test Cole takes, is neither painful nor harmful. It measure's the neurological response to outside stimulus.