# Probing the causes of MS

BY JOAN AREHART-TREICHEL

## Scientists work on several fronts to combat this baffling disease

Thirteen years ago at the age of 25, Carol F. started to realize that something was terribly wrong with her body. When she got out of the car she fell, and when she danced she could no longer keep time with the music. She was diagnosed as having multiple sclerosis, a central nervous system disease that afflicts a quarter-million Americans. The cause or causes are unknown and there is no treatment other than steroid hormones to shorten and ease attacks.

For many patients, multiple sclerosis is mild and does not interfere much with their lives. But for others, such as Carol, the disease is rapidly progressive, leading to severe disabilities within a few years. For instance, after Carol was found to have MS, she started using a cane, but it soon could not prevent her from falling. She switched to a walker, but, as the months went by, couldn't stand, even with its help. Two years ago she became confined to a wheelchair; six months ago her arms and hands became so weak that she could no longer hold a pencil. Today she depends totally on her husband and children to dress and feed her and to move her to and from her wheelchair, the bed and the toilet. In the years to come her condition may become even worse, leading perhaps to loss of bladder control, and to partial blindness or deterioration in her thinking, memory or emotions. One of the things that keeps her going is hope — hope that "before I die medical scientists will find a cure for my disease."

Is this going to happen? Maybe. Or maybe not. But what *can* be said for sure is that medical researchers believe they are closer than they have ever been to identifying the cause or causes of multiple sclerosis and to finding some way to stop the disease.

Research suggests that MS results from a viral infection that precipitates autoimmune disease, in which the body's own immune defenses attack myelin, a fatty sheath that insulates nerve fibers in the brain and spinal cord. Other MS research results involve oligodendrocytes, the cells that make myelin around brain and spinal cord nerves.

Advances in immunology may prove important in understanding and treating MS. The identification of T cells is one major advance. It has been found that the levels of suppressor T cells, which check the action of killer T cells in destroying antigens in the blood, decrease in the blood of MS patients experiencing attacks. This finding may be "of major importance," says Byron H. Waksman, director of Research Programs at the National Multiple Sclerosis Society in New York. In related research, reported by Joel Oger of the University of Chicago at the 12th World Congress of Neurology in Kyoto, Japan last September, spinal fluid levels of helper T cells, which assist killer T cells and help form antibodies, were found to increase in MS patients.

Howard Weiner of Harvard Medical School is using such findings as a basis for possible treatments. He is currently conducting a pilot study to see whether removal of T cells from the blood might help MS patients. For the past three years Weiner and his colleagues have also been trying three different forms of treatment on 60 patients with chronically progressive MS. One group of patients has received the drug cyclophosphamide, an immune system suppressant. Another group has received a synthetic form of adrenocorticotropic hormone (ACTH), one of the steroid hormones given to shorten and ease attacks of the disease. The third treatment involves removal of antibodies from the blood, a technique that has helped patients with the autoimmune disease myasthenia gravis.

The outcome of this trial should become apparent later this year, Weiner told SCIENCE NEWS. He says he also hopes soon to begin, with the help of investigators at four other centers, a double-blind trial to determine whether antibody removal is an effective MS treatment. "We know a lot more about the altered immune features of multiple sclerosis now than five years ago, there's no question about it," Weiner says, "so I am hopeful there will be something in these immunotherapies that will help patients."

In other research involving the immune system's role in MS, J.G. McLeod and colleagues of the University of Sydney gave the white blood cell substance transfer factor to 30 MS patients for two years, giving another 30 patients a control. Although previous research results involving the use of transfer factor to treat MS were disappointing (SN: 5/13/78, p. 311), McLeod and his team found that transfer factor slowed the progress of MS, provided the disease was not in a severe stage at the start of treatment and provided that the patients first received transfer factor for a number of months.

Other researchers are concentrating on the evidence that a viral infection may cause the decrease in T cell levels. Ashley T. Hause of the University of California at San Francisco has found that some MS patients have persistent measles virus in their brains. According to Barry R. Bloom and colleagues of Albert Einstein College of Medicine in the Bronx, interferon, which appears in the blood in reponse to viral infections, seems to be deficient in MS patients. Bloom's work was reported in the May 1981 NEUROLOGY.

Such findings are also leading to possible treatments. Lawrence Jacobs of the State University of New York School of Medicine and co-workers reported, in the Nov. 27, 1981 SCIENCE, results of a study in which they injected interferon into the spinal fluid of 10 MS patients for six months. The researchers found that the patients experienced a reduction in flare-ups at the end of six months. In related work, Hillel Panitch of the University of

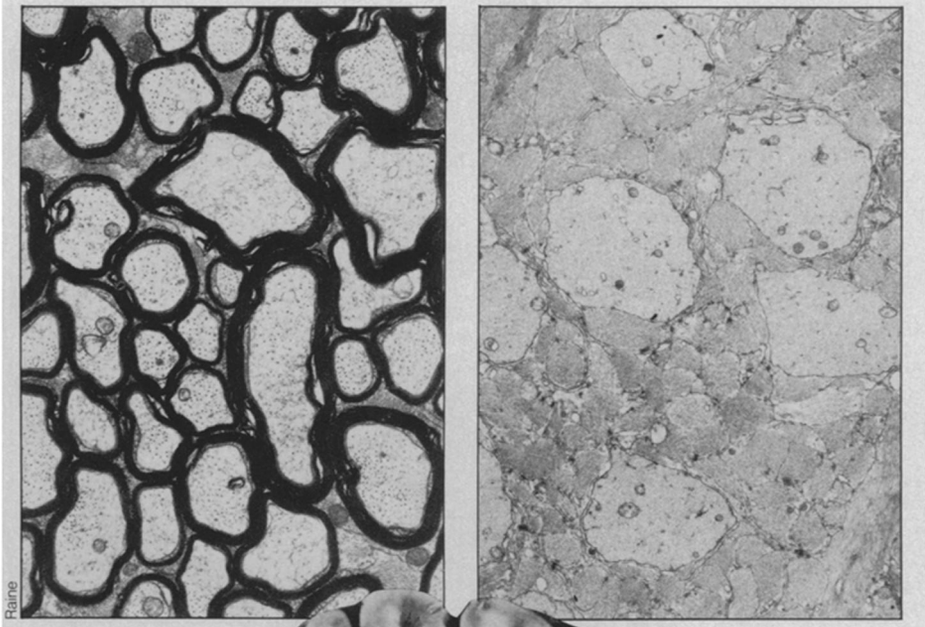
California at San Francisco, Thomas Merigan of Stanford University and Robert Knobler of the Scripps Clinic and Research Foundation have injected 24 MS patients with interferon in a double-blind crossover protocol. This means that each patient will get, for the duration of the study, both interferon and a placebo, thus serving as their own controls. Neither the patients nor the physicians caring for them will know when they are receiving interferon and when they are receiving a placebo. So far the study has been underway two years and has another year to go. Panitch told SCIENCE NEWS, "Our patients were picked because of their frequency of multiple sclerosis attacks — between two and four a year — and since the study started, some of them have stopped having attacks whereas others still are. This suggests to me something is going on. I don't know if the patients on interferon are the ones who have ceased having attacks, but I certainly hope so."

In addition to the research being done with human MS victims the experimental production in laboratory animals of chronic relapsing experimental allergic encephomyelitis, an MS-like disease, has led to promising findings. Cedric S. Raine of the Albert Einstein College of Medicine announced at the 12th World Congress of Neurology that he and his colleagues successfully stopped progression of the disease by injecting animals with two constituents of myelin, myelin basic protein and a glycolipid. "If results still look good another year from now," Raine told SCIENCE NEWS, "we shall consider using the two substances together in a trial on multiple sclerosis patients."

The finding that oligodendrocytes disappear in areas of the brain and spinal cord damaged by MS has prompted research on how they function. Such research has been aided by the perfection of a technique whereby these cells can be precisely identified in tissue samples grown in tissue culture. Further study of oligodendrocyte deficiency may link it to the deficiency of suppressor T cells, a link that, according to Barry G.W. Arnason of the University of Chicago, "would be a powerful clue as to what is going on in the disease."

Confirmation is important in evaluating the efficacy of new treatments for any disease, but especially in assessing the effectiveness of new therapies for an erratic disease like multiple sclerosis, where patients can experience short-term improvement just as easily from spontaneous remission as from treatment. Meanwhile, patients like Carol S. can be heartened by the words of Weiner, who has devoted a decade of his career to studying multiple sclerosis: "The last thing we want to do is raise false hopes among multiple sclerosis patients and thus cause them a lot of pain. But we *do* want them to know that we're working hard on finding something that can help them." □

*Although the cause of multiple sclerosis is unknown, it is characterized by damage to the nerve axons of the brain and spinal cord. Normal nerve axons (left) are surrounded by a fatty myelin sheath that insulates nerve fibers, but in persons with MS the axon is barren of myelin (right).*



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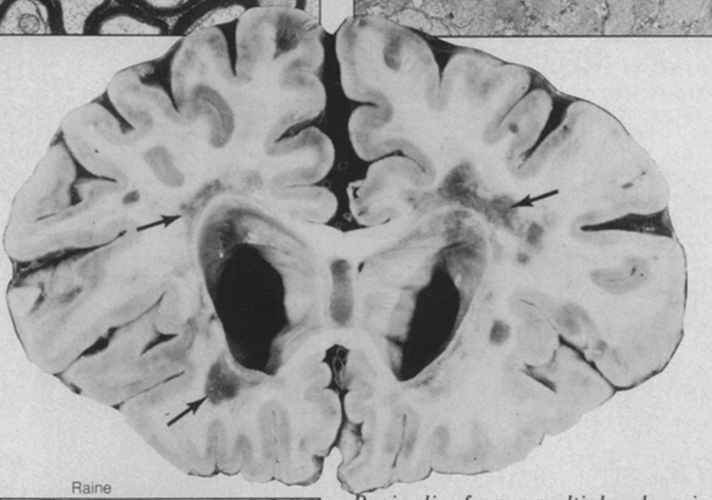

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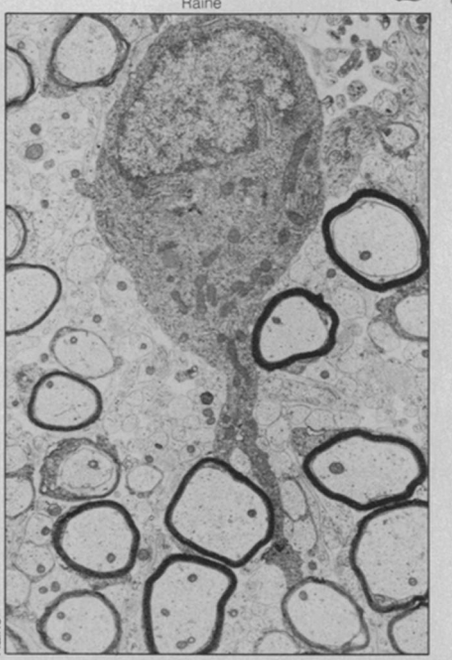
*Brain slice from a multiple sclerosis patient (above) shows where myelin around nerves has been lost. Instead, scar tissue forms that blocks communication from the brain to nerve terminals, leading to symptoms of the disease such as weakness and poor coordination.*



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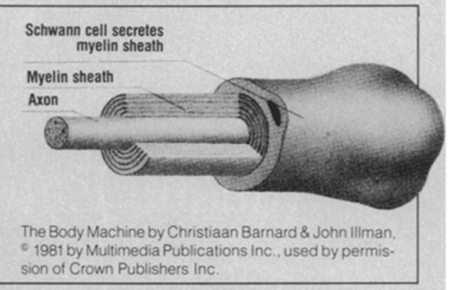


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*Oligodendrocytes (left), cells that make myelin around brain and spinal cord nerves, also disappear in areas damaged by MS. At the bottom of the oligodendrocyte are the cell processes going to the myelin sheaths around two axons (diagram above).*