

The Retreat of Multiple Sclerosis

For the first time, medical treatment has been shown to halt disease progression or even to produce improvement in multiple sclerosis patients

By JOAN AREHART-TREICHEL

Two treatments have halted disease progression or have even reduced disability in some patients with multiple sclerosis, a central nervous system disease that afflicts a quarter-million Americans. Until now, only the steroid hormone ACTH has been shown to have any impact on the disorder, and even it was found to only shorten acute disease attacks.

One of the treatments is the immunosuppressant drug cyclophosphamide combined with ACTH. The other is hyperbaric oxygen -- the breathing of pure oxygen under pressure in a special chamber called a hyperbaric chamber. Study results with both regimens were reported in the Jan. 27 *NEW ENGLAND JOURNAL OF MEDICINE*—the former by Howard L. Weiner of Harvard Medical School in Boston and colleagues, and the latter by Boguslav H. Fischer and co-workers at New York University Medical Center in New York City.

Although the cause of multiple sclerosis is unknown, growing evidence suggests that it is an autoimmune disease related in some way to infection with a virus, perhaps a measles virus (ESN: 1/30/82, p. 76). Weiner and his team performed a clinical trial to see whether cyclophosphamide or removal of antibodies from the blood might counter multiple sclerosis. Cyclophosphamide is known to suppress the immune system and might dampen an autoimmune response, and antibody removal has benefited patients with the autoimmune disease myasthenia gravis. They decided to include only patients with rapidly progressive, unrelenting disease in their trial. One reason was that this type of multiple sclerosis is more devastating than the stable kind, where disease progresses more slowly, or than the relapsing-remitting variety where disease strikes acutely then subsides. Another reason was that this kind of multiple sclerosis rarely lets up spontaneously, as does the relapsing-remitting sort, and thus it would be easier to measure the impact of treatment on it than on the latter.

The researchers placed 58 such patients into one of three treatment groups. Twenty

received 25 units of ACTH—the standard dose used to treat multiple sclerosis—by injection into the vein or muscle daily for 21 consecutive days. Then 20 patients received large doses of cyclophosphamide (80 to 100 milligrams per kilogram of body weight) plus ACTH daily by intravenous injection for 10 to 14 consecutive days. Finally, 18 patients were given four or five antibody removal treatments over a two-week period plus ACTH as given to the other two groups plus low doses of cyclophosphamide (2 mg per kg of body weight) daily by mouth for eight consecutive weeks. ACTH was given to maximize any treatment response. Oral cyclophosphamide was included as part of the third group's treatment because prior studies had suggested that antibody exchange needs immunosuppression to achieve a beneficial effect. Each of the regimens was given over the time period considered the most effective for it.

During a one-year follow-up period, 16 out of 20 patients who received large doses of cyclophosphamide plus ACTH showed no disease progression or even less neurologic disability than before. Some, for example, were able to walk independently after requiring canes or crutches or even after being confined to a wheelchair. In contrast, nine out of 18 patients who got the antibody exchange, low-dose cyclophosphamide plus ACTH demonstrated no disease progression or improvement, while only 4 out of 20 patients who got ACTH alone did so. Thus, "high-dose cyclophosphamide plus ACTH was most effective in halting progression of the disease," Weiner and his team conclude.

The study by Fischer and colleagues was also based on growing evidence that multiple sclerosis may be an autoimmune disease and that suppression of the immune system might counter multiple sclerosis. But the treatment they decided to test was hyperbaric oxygen, since past evidence had indicated that it is immunosuppressive. Also, anecdotal reports had implied that it can benefit multiple sclerosis patients.

They focused their study on patients who had already suffered extensive damage and who at the time of the study were

in either a progressive or stable disease state. Twenty served as a placebo group and received 10 percent oxygen and 90 percent nitrogen — a gas mixture resembling normal air—under a pressure of two atmospheres in a hyperbaric chamber once daily, for a total of 20 exposures. Seventeen served as an experimental group and received pure oxygen at a pressure of two atmospheres in a hyperbaric chamber once daily, for a total of 20 exposures. At the end of the treatment course, there was increased mobility, restoration of bladder control, sharper vision, better coordination and other signs of lessened neurologic disability in 12 of 17 patients treated with hyperbaric oxygen, but in only 1 of 20 who had gotten a placebo. What's more, improvement lasted throughout the year of follow up in 5 of the 12 patients. "This study indicates an apparent beneficial effect of hyperbaric oxygen treatment on multiple sclerosis," Fischer and his co-workers conclude.

Although high-dose cyclophosphamide plus ACTH, as well as hyperbaric oxygen therapy, may eventually prove to be of great benefit to a number of multiple sclerosis victims, it is too early for physicians to offer them as routine treatments, say Weiner and Fischer, as well as other multiple sclerosis authorities. They note that 11 of the 16 patients whose disease progression was halted or who improved one year after getting high-dose cyclophosphamide plus ACTH have since experienced recurrent disease, and whether they will respond to a second course of treatment remains to be determined. In addition, the long-term safety of the two regimens needs to be carefully evaluated because cyclophosphamide and hyperbaric oxygen appear to be capable of exerting serious side effects — for instance, bladder cancer in the case of the former or transient blindness in the case of the latter. Finally, as Robert Slater, chief of Medical Programs for the National Multiple Sclerosis Society in New York City, points out, hyperbaric oxygen is expensive — about \$100 a treatment — and until its value as a multiple sclerosis therapy is further documented, we don't think insurance companies should provide reimbursement for its use."