MULTIPLE SCLEROSIS—A DIFFICULT DISEASE
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Multiple sclerosis is a difficult disease to write about. The jury's still out on the cause, the cure, even the definition of what multiple sclerosis is.

MS is not a disease of old people. According to recent estimates, the average age of onset is between 20 to 50. Children as young as 2 have been diagnosed with MS. It is progressive, degenerative, irreversible, and incurable. Nearly 1 out of every 750 people in the US – around 400,000 people – has multiple sclerosis (MS), according to the National Multiple Sclerosis Society. This figure is 50% higher than that estimated by a similarly large literature review published in 1982. MS is on the rise, and treatments are few.

MS is a disease in which lesions, also called plaques, form in the central nervous system, causing disablility. This disability may take many forms: pain, numbness, fatigue, muscle weakness, vision problems, memory loss, bladder dysfunction, depression and so on. The lesions--hard, scarred patches--are the result of injury to the myelin sheath around the axons of the nerve cells. *Sclerosis* is scarring; *multiple* lesions must be present for the disease to be defined as MS.

MS is characterized by abrupt onset of symptoms. Various clinical courses have been described for MS, leading some doctors to speculate that MS is really several different diseases. Most people with MS display a pattern of relapses and remissions, often with increasing disability. Others are chronic progressive (symptoms get steadily worse); still others, chronic static (symptoms do not get either worse or better). Uncertainty as to the progression of the disease is one of the factors contributing to depression in people with MS.

MS was long thought to be an autoimmune disease, in which the body, through its immune system, launches a defensive attack against its own tissues, triggering inflammation. However, new research points to a *vascular* mechanism (one having to do with the blood vessels). All the immune markers investigated in MS have also been found in stroke patients and at the same levels. (Stroke, of course, is blockage or rupture of blood vessels to the brain.)

It is now accepted that MS is characterized by dysfunction of, and damage to, the blood-brain barrier (BBB). The BBB is the tightly-packed formation of endothelial cells on the walls of the capillaries in the brain. Whereas in other parts of the body many substances can pass through the gaps in the endothelial cells, in the brain only a few types of substances can cross the BBB. The BBB protects the brain from many chemicals which flow through the body, and from infections.

In MS, white blood cells called T lymphocytes destroy the myelin. It has been supposed that a malfunctioning autoimmune system was the cause of T cells attacking these protective sheaths. However, we can see that if the BBB is broken down, allowing the white blood cells to enter the brain and cause damage, it is really a *vascular* and not an

autoimmune mechanism operating.

Breakdown of the barrier results in edema (swelling) and associated effects (reperfusion injury, for example). It seems logical that treatments for conditions with similar pathogenesis, like traumatic brain injury, might also be effective for MS. The wide range of symptoms and the relapsing/remitting nature of the disease, however, make the design of an acceptable study difficult.

The earliest reports of HBOT used to treat MS are from the 1970s. Boschetty and Cernoch (1970) administered HBO at 2ATA twice a day to 26 patients over 10 to 20 days in Czechoslovakia. 15 patients reported improvement of their symptoms. However, as the improvement was of limited duration, the researchers concluded that HBOT had no value and did no follow-up studies.

In 1978, Dr. Richard A. Neubauer serendipitously discovered a beneficial effect from HBOT on a patient with a diagnosis of both MS and osteomyelitis. The patient was being treated for the osteomyelitis (a conventional use of HBOT), but the MS symptoms were also abating with each treatment. He published his findings and continued treating MS patients. At the end of two years he had followed the progress of 262 patients. Neubauer concluded that, although HBOT was not a cure for MS, it favorably altered the natural history of the disease. Patients who received the therapy did not progress as far or as rapidly as those who did not have therapy. He also concluded that proper dose was essential (1.5-1.75 ATA), and that occasional followup treatments were necessary. These conclusions go a long way to explain why the Boschetty and Cernoch study was ineffective: the pressure was too high, and the treatment period too short. Dr. Neubauer was a practicing physician, not a researcher equipped to do clinical trials. He simply continued to treat his MS patients, as well as those with a wide range of other diagnoses.

The first randomized, placebo-controlled double-blind study of HBOT for MS was conducted in 1983 by Fischer *et al*. They administered 2 ATA for 90 minutes, once a day, five days a week for four weeks. 12 of 17 patients receiving HBOT reported improvement, as compared to only 1 in 20 in the control group. Despite the rather high pressure, the limited number of treatments, and the lack of continuation therapy, 12 of 17 patients receiving the treatments improved, as compared with only 1 in 20 of the placebo-treated patients.

The Fischer study was not well received in the American medical community. It attracted more attention worldwide, however, notably in the UK. Favorable results of a longitudinal study in Scotland led to the opening of many treatment centers throughout the UK. Since 1982 over 14,000 patients have been treated in these centers without significant incident and with favorable results.

Over 700 of these patients were followed in a 14-year study. About 70% reported improvement of two or more symptoms after 20 daily treatments. Periodic assessments were made, confirming the hypothesis that improvements are maintained by continued

treatment. Response was better in patients with less advanced disease. The biggest improvement was shown to be in bladder function.

More studies are urgently needed on HBOT and MS. Chronic drug treatment, the current standard of care, is expensive and does not cure MS or even alleviate all symptoms. The long-term efficacy and possible adverse effects of many of these drugs is unknown, whereas HBOT has virtually no side effects. Started at the onset of symptoms, HBOT may prevent the development of new lesions in many patients. This opportunity should be available to all people with MS.