

## Long-term hyperbaric oxygenation retards progression in multiple sclerosis patients

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### Abstract

**Objective:** To evaluate the effect of prolonged courses of hyperbaric oxygen treatment (HBO<sub>2</sub>T) on the progressive deterioration of multiple sclerosis (MS) patients.

**Design:** Prospective study of the disability of 703 MS patients first treated five or more years previously.

**Setting:** The MS National Therapy Centres in the UK and Ireland.

**Results:** Of the 117 patients who had attended regularly and without interruption for 5 to 15 years, the Kurtzke value (KDS) had not increased by more than 1 point. One hundred and four of 1384 patients (11%) first treated 17 or more years previously were still attending for regular treatment.

About 300 treatments in 10+ years (about once a fortnight) were required to appreciably retard the progression of disability of Relapsing/Remitting patients, while more than 500 treatments (say, once a week) were more effective.

**Conclusions:** The response to treatment is better in patients with less advanced disease and is related to the frequency and continuity of treatment. Treatment should therefore be started as soon as the condition is diagnosed and before irreversible lesions have become established.

### Key Words

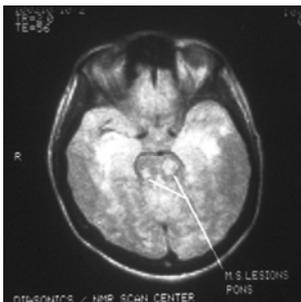
Multiple Sclerosis, blood brain barrier, hyperbaric oxygenation

It is generally accepted that focal breakdown of the blood brain barrier is the initial event in the formation of MS lesions.<sup>1</sup> This is followed by inflammation, local damage to myelin, nerve fibres and sometimes neurones.

Magnetic resonance spectroscopy has shown the presence of lactate, indicating a failure of oxygen delivery.<sup>2</sup> The presence of focal oedema and inflam-

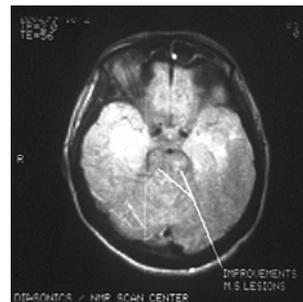
mation, with increased diffusion distances for oxygen, provides a sound rationale for the use of oxygen under increased pressure.

Post mortem studies have shown the presence of barrier damage and focal oedema in chronic MS lesions and magnetic resonance imaging has demonstrated the reduction of oedema *in vivo* (Figures 1 a & b).



**Fig 1a:** Magnetic resonance image of a patient with MS showing two large MS lesions in the pons

(Illustrations courtesy of Dr. Richard Neubauer and Dr. Robert Kagan, MRI Scan Center, Fort Lauderdale, Florida).



**Fig 1b:** Image after oxygen treatment showing improvement in the lesions.

(Illustrations courtesy of Dr. Richard Neubauer and Dr. Robert Kagan, MRI Scan Center, Fort Lauderdale, Florida).

† Deceased on 1st of November 2005

Neubauer *et al*<sup>3</sup> reported that one or more lesions disappeared in 11 of 35 patients (31.4%) after 1 hour of HBO<sub>2</sub>T (hyperbaric oxygen treatment). Short-term controlled trials have shown that a course of HBO<sub>2</sub>T benefits many multiple sclerosis patients. Fischer *et al*,<sup>4</sup> in New York University, performed the first randomised, placebo-controlled, double blind trial. Improvement in balance and bladder function were found in 12 of 17 patients ( $P < 0.0001$ ). Those patients with a less severe form of the disease had a more favourable and long lasting response. After a year with no further treatment, the treated group showed a positive change ( $P < 0.0008$ ).

Barnes *et al*<sup>5</sup> found overall benefit in their treated group ( $P < 0.03$ ) and a year later there was less deterioration in cerebellar function ( $P < 0.03$ ). They called for further studies.

Two other controlled studies have reported sustained benefit with follow-on treatment. Oriani *et al*<sup>6</sup> used patients with a low Kurtzke disability score<sup>7</sup> and compared 22 controls with 22 patients treated each week for a year. They detected an appreciable difference in outcome ( $P < 0.01$ ).

Pallotta *et al*<sup>8</sup> followed 22 patients for 8 years. All received an initial course of 20 treatments and 11 were treated thereafter with 2 sessions every 20 days (Figure 2).

The frequency of relapses decreased dramatically in

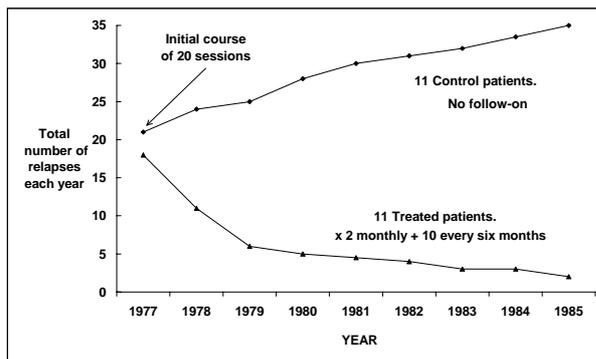


Fig. 2 Incidence of relapses in 22 patients with and without regular HBO<sub>2</sub>T, followed for 8 years by Pallotta *et al*.<sup>8</sup>

the prolonged treatment group.

**Methods**

Since 1982, over 15,000 MS patients have received treatment by the MS National Therapy Centres, run by a UK Charity. They use single lock, multiplace chambers and are distributed throughout the UK and Ireland (Figure 3).

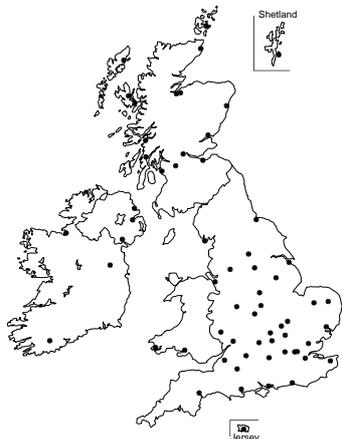


Fig. 3 The location of the MS National Therapy Centres

Involvement by physicians has been restricted to data collection and advice. The records provide a unique opportunity to evaluate the effectiveness of long-lasting courses of HBO<sub>2</sub>T.

Seven hundred and three patients were followed up for 10 – 14 years since first receiving a course of treatment. They breathed oxygen from an oronasal mask in a chamber filled with air. In an initial course, five daily treatments of one hour were given at 1.5 atm abs. If two or more symptoms improved, a course of twenty treatments was completed at this pressure. Otherwise the pressure was raised in weekly increments of 0.25 atm abs until a response was obtained or five treatments at 2.0 atm abs had no effect. Thereafter the patients were invited to return for a 'follow-on' treatment on a weekly basis, or failing that, as often as they felt the need or found it possible.

The bladder improvements observed in other studies were confirmed (Table 1).

	Before Initial course	After Initial course	Improvement
Frequency	$\bar{x}$	$\bar{x}$	
Night time	1232 2.4	651 1.2	47%
Daytime	3873 7.4	2960 5.7	24%

Assessments were made between two and four years, and again between six and eight years after the initial course. A third survey was conducted between ten and fourteen years. By now 126 had died (8% were over 60 years old when first treated), 99 had become 'lost to follow-up', 29 had suffered injuries that affected their KDS value and 2 had had their original diagnosis revised; 447 therefore remained for analysis.

**Results**

The records provide a unique opportunity to evaluate the effectiveness of long-lasting courses of HBO<sub>2</sub>T for MS.

Thirty-eight of the patients who had received less than 10 follow-on treatments had deteriorated by a mean of 2.0 on the KDS. Twenty-five patients receiving more than 400 treatments had only deteriorated by 1.0 point. An analysis reveals that about 300 treatments in 10+ years (about once a fortnight) are required to delay progression of Relapsing/Remitting patients, while more than 500 treatments (say, once a week) are more effective. After 10 years, 23% of the 447 patients remaining eligible for study had not deteriorated and 7% had improved. As might be expected, those with a low Kurtzke score do well. (Figure 4).

Long-term controlled studies are impractical in a multicentre setting as patients do not comply with the protocol. However it is possible to compare groups of patients who have received different treatment regimes (Figure 5).

## Long-term hyperbaric oxygenation retards progression of multiple sclerosis

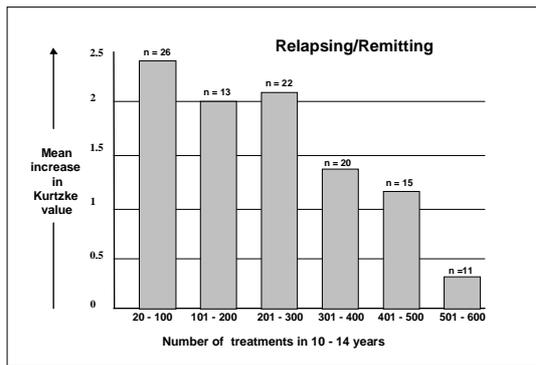


Fig. 4 The increase in Kurtzke value in patients with Relapsing/Remitting MS related to the number of treatments over 10-14 years

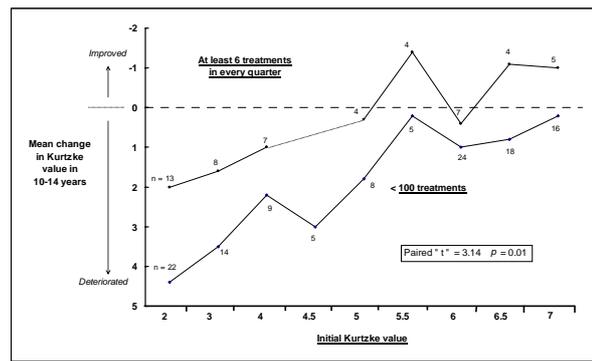


Fig. 5. Patients who received at least 6 treatments in every quarter compared with those receiving less than 100 in 10-14 years.

A search of the records has revealed 1384 patients who were first treated 17 or more years previously and 104 (11%) are still attending for regular treatment. Table 2 gives the details of 117 patients who have attended regularly without interruption for 5 to 17 years. Between 5 and 15 years the Kurtzke value of Relapsing/Remitting patients has not increased by more than one point.

The Therapy Centres have now been providing hyperbaric treatment for twenty two years without a serious incident. This has established that low pressure facilities can play an important part in the care of MS patients. The treatment has been shown to be practicable, cost-effective and very safe. After 10 or more

years 38% of the final group of 447 patients were still attending regularly. The cost of each treatment in this charity setting is about £10 so that the benefit may be obtained for less than £300 (US \$ 450) a year. The earlier treatment is started in the disease the better. Many patients continue to attend as their symptoms, particularly frequency of micturition, are only controlled by regular attendance. Some arrange their holidays so as to be near a Centre. Others having difficulty reaching a Centre become so dependent on regular treatment that they install simple mono-place chambers in their own homes. The social and economic advantages to be gained from such a regime are obvious.

Table 2 Details of 117 patients who have attended regularly for 5 - 17 years

No of patients	MS Type	Average difference in Kurtzke value	Attended For	Average no of treatments
13	Relapsing / Remitting	0.6	5 - 10 years	351
19	Chronic Progressive	1		323
2	Chronic Static	0.75		248
17	Relapsing / Remitting	1	10 - 15 years	464
24	Chronic Progressive	0.8		523
8	Chronic Static	0.5		488
12	Relapsing / Remitting	0	> 14 years	466
16	Chronic Progressive	1		494
6	Chronic Static	2		664
117				

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that is highly relevant for our understanding of the disease in several aspects. The conclusions are sound and the results of this investigation will be very helpful for the better treatment and effective patient care in the field.

**Reviewer 1**

The paper by Perrins and James evaluate the effect of prolonged courses of hyperbaric oxygen treatment (HBO<sub>2</sub>T) on the progressive deterioration of multiple sclerosis (MS) in relatively large number of patients. The study is well designed and addresses an important and clinically very relevant issue not well addressed before. The study is well conducted and designed to cover long-term follow-up and outcome

Anonymous

**Reviewer 2**

The study is well designed and addresses very important issue. The findings could be of general interest and provide new insight in patient care. The authors should be commended on their achievement.

Anonymous



**Obituary**

David JD Perrins MD FRCS  
1924 -2005.



Born into the Worcestershire Perrins family in 1924, David Perrins entered Cambridge in 1943 to read medicine and rowed for the University in the 1946 Boat Race. He became a House Surgeon in St Thomas's in 1950 and then joined the Royal Navy to complete his National Service at a time when senior naval doctors were involved in hyperbaric medicine.

On returning to civilian practice he trained in surgery gaining experience in the use of hyperbaric oxygen treatment when the field was rapidly evolving. His seminal publications, many in the Lancet, on the use of this treatment in a variety of conditions, including skin grafting, burns, chronic osteomyelitis and diabetic ulceration are still widely quoted. He completed his MD thesis in 1972 on the use of adjunctive hyperbaric oxygen treatment in plastic surgery. Less successful was ten years spent at the Churchill Hospital in Oxford on the use of oxygen as a radiosensitiser. Promising in vitro studies did not lead to equivalent success in patients. He moved to Stockholm for two years working with Dr Per Oluf Barr studying the use of hyperbaric oxygen treatment to avoid amputation in patients with diabetic peripheral vascular disease.

On returning to the UK, Dr Perrins became involved with the MS National Multiple Sclerosis Therapy centres. The charity had been formed by sufferers following controlled studies indicating that hyperbaric oxygen therapy could relieve many of the symptoms of multiple sclerosis and slow progression of the disease. The paper in this journal, which confirms the beneficial effect of this treatment on the course of the disease in a large cohort of chronic patients, is a tribute to his meticulous attention to detail in the analysis of data collected over many years.

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Professor of Hyperbaric Medicine

