This study of patients with long-standing multiple sclerosis was completed well before the introduction of Copaxone and the beta Interferons. NICE had recommended that these ‘disease-modifying’ drugs should not be prescribed as they did not offer sufficient benefit to patients based in view of their considerable cost. However, following intensive lobbying by the UK MS Society, the MS Trust and the Association of British Neurologists the government allowed the drugs to be prescribed provided the results were assessed on a two yearly basis. This was known as the ‘Risk-Sharing Scheme’ in which the cost of the drugs would be reduced if less than the expected benefit was shown.

Because there was academic disagreement about methods of assessment of patients with multiple sclerosis several years were lost and an assessment of the drugs effects were not available until 2009. The outcomes of patients receiving the drugs over 2 years were compared to historical controls. It was conclusively shown that patients were worse than if they had not received any treatment.

This 2 year study of hyperbaric oxygen treatment in 128 patients was refused publication in the 1990s because editors deemed the use of a comparison with historical controls inadmissible. Since this trial was undertaken more MS Therapy Centres have opened and another long-term study following a cohort of 703 has finally been published in the International Journal of Neuroprotection and Neuroregeneration (2005;2:45-48). It showed dramatic benefit from continuing hyperbaric oxygen treatment for up to 15 years after an initial course of 20 sessions.

The science supporting the use of hyperbaric oxygen treatment has increased dramatically with the discovery that changes in cellular oxygen levels control over 300 genes. This control extends to inflammation, the key feature of multiple sclerosis. A course of oxygen treatment has also been shown to increase the number of stem cells in the circulation eight-fold. Time does not change the results detailed in the following paper and oxygen remains the only agent proven to benefit patients with chronic multiple sclerosis.

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2010
LONG-TERM HYPERBARIC OXYGEN THERAPY
FOR MULTIPLE SCLEROSIS PATIENTS

Two Year Results in 128 Patients

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Although concluding, in their preliminary report, that hyperbaric oxygen was unlikely to be of benefit in the management of multiple sclerosis, the Newcastle group have now called for further trials. As several other controlled trials have demonstrated short-term benefit in a number of functions and longer-term improvement in bladder function, a 2 year study of hyperbaric oxygen has been undertaken in 128 patients. All the patients received an initial course of twenty sessions at 1.5-2.0 ATA. Two groups, including both progressive and stable patients, have been studied, with and without maintenance therapy. Although patients were not randomised to these groups, many of those who reported initial benefit were unable to continue and other patients, who had no initial benefit, actually continued treatment. Although long-term benefit was found mainly in bladder function, patients who continued with the therapy showed a greater tendency to stability in other functions, when compared to the non-maintenance group. Even in the progressive group at the end of two years, 70% of patients maintaining therapy had either stabilised, or shown small improvements, and only 30% had deteriorated. A recent American study of a very similar group of patients over two years, has shown that the expected rate of deterioration would be 95%. The conclusion from this study is that patients can be recommended to use oxygen therapy, because it has been shown to be of value to the majority of sufferers, especially in the control of bladder dysfunction and in the stabilisation of the disease. The evidence argues for the use of hyperbaric oxygen at time of the first symptoms, when magnetic resonance imaging indicates that multiple areas are already affected in the majority of patients.
Introduction

The suggestion that the extra oxygen made available under hyperbaric conditions (HBO) may help multiple sclerosis patients has provoked considerable controversy in the U.K., despite the fact that it has not been suggested that it is a cure for the disease. The first A.R.M.S. centre to use hyperbaric oxygen was established in Dundee in August 1982, by a group of patients who had personal experience of the treatment. They had participated in a small study,\(^1\) based on the work of Dr. Richard Neubauer,\(^2\) which had been confirmed by a meticulous double-blind controlled trial, first presented in Los Angeles in June 1982 and subsequently published in the New England Journal of Medicine.\(^3\)

This trial, by Fischer et al, at the New York University Medical Center, was funded by the U.S. National Multiple Sclerosis Society, after successful studies of hyperbaric oxygen therapy in an animal model used in multiple sclerosis research.\(^4\) It remains the only trial in which patients have been matched in pairs and then randomly assigned to either the treatment or the control group. Fischer et al recommended that future studies should concentrate on patients with acute attacks and longer-term studies of chronic patients, to determine the value of oxygen in the management of the disease. Generally, their recommendations have not been followed and subsequent trials have concentrated on more seriously disabled patients, who are not likely to improve significantly from any therapy.

The preliminary report of a study in Newcastle-upon-Tyne, published in 1985,\(^5\) found statistically significant improvement in bladder and bowel function in the patients treated with hyperbaric oxygen and an overall difference between the oxygen group and the controls.\(^6\) Nevertheless, the authors concluded that; “hyperbaric oxygen is unlikely to have a role in the management of a patient with multiple sclerosis,” although they admitted that they were “not in a position to comment on the possibility that hyperbaric oxygen may halt the progression of the disease.” Unfortunately, their results were widely publicised through the news agency Associated Press as disproving the New York University study. Although Fischer et al had found the same improvement in bladder function, other findings were more positive than the Newcastle study. The discrepancy in the results needs an explanation. From discussions with Professor Fischer (personal communication, P.B. James), the most likely reason is that, in the New York trial, the patients were examined on the day the chamber sessions were completed, rather than at varying times over the following weeks. Experience in A.R.M.S. centres indicates that, with the possible exception of bladder control, benefits are soon lost if oxygen therapy is not maintained. However variation in the results of clinical trials is common and not limited to multiple sclerosis studies. In a trial of the use of aspirin in the prevention of heart attacks, an American study,\(^7\) involving 22,071 physicians, was terminated, because the results were so positive in demonstrating the reduction of deaths, that it was felt to be unethical not to advise the control group of doctors taking the placebo to also take aspirin. The results have, nevertheless, been contested by physicians in the U.K.

Another trial in the U.K., again reported as negative by the authors,\(^8\) has also shown positive results, especially in bladder function, by using measurements of bladder volume, (cystometry), confirming a similar study in the U.S.A.\(^9\) Some sensory functions also improved to a level that was statistically significant in the oxygen group. An A.R.M.S. double-blind study,\(^10\) conducted at the Central Middlesex Hospital, reported that chronic stable patients did not appear to benefit at the single pressure used (1.5 ATA), but did find significant benefit in patients with relapsing/remitting disease. This highlights the “Catch 22” of treatment in multiple sclerosis. If improvements are found during treatment in patients with fluctuating symptoms, then it is difficult to determine whether or not they represent “spontaneous” remission. However, patients with long-term, stable, disabilities are unlikely to respond to any treatment. This problem has been overcome, in the short-term trials, by using patients, who are not given treatment, as a control group. In this study, the great majority of the patients have been suffering from chronic disease and Kurtzke has observed that remission only occurs in about 7% of patients when a symptom has been present for over two years.\(^11\)

The Newcastle group have now published the final report of their hyperbaric oxygen study,\(^12\) and state that the improvement in bladder function was maintained without continuation therapy (top-ups) for six months. It is also admitted that there was less deterioration in cerebellar function (balance and co-ordination) in the oxygen group, when compared to the controls, at the end of a year. They have now called for further studies to confirm their observations, clearly disregarding the fact that their results confirm those of Fischer et al,\(^3\) in New York. Another double-blind trial in Italy has now been published, providing further confirmation over a one year period.\(^13\) It remains to be seen if the harm caused by the publicity given to the premature conclusions of the Newcastle group can be undone.
Many physicians cannot think of a reason why sessions of hyperbaric oxygen should be of value in the management of multiple sclerosis. However, Dr. Byron Waksman, Director of Research in the US National MS Society, has pointed out that oxygen is of benefit in suppressing inflammation and it has also been shown to be an effective immunosuppressive agent. It is universally recognised that the areas of damage that lead to the formation of plaques in MS are associated with leaking veins, inflammation and oedema. Recent research has shown that oxygen deficiency may be present, even when blood flow is increased in inflammation.

The unique property of the additional oxygen supplied under hyperbaric conditions is to reduce blood flow, but paradoxically increase the availability of oxygen to the tissues. Vasoconstriction, that is reducing the diameter of a blood vessel, also reduces its permeability. This is clearly a most useful effect, especially in the treatment of the early symptoms. The degree of vasoconstriction induced by oxygen varies considerably from patient to patient, which may account for variations in their response to different chamber pressures. The level of oxygen in the areas affected in multiple sclerosis is critical to the production of remission. This study is to determine if the level of remission in chronic patients can be improved, over a two year period, by the additional oxygen available under hyperbaric conditions.

Methods

A total of 147 patients received 20 sessions of hyperbaric oxygen therapy in the Glasgow A.R.M.S. centre, between February and August 1984. All but four had been confirmed to be suffering from multiple sclerosis by neurologists. The four patients not suffering from multiple sclerosis were excluded from the study. Five patients were also excluded, because they could not be contacted for assessment beyond 6 months. Two patients died within the first 12 months, from recognised complications associated with multiple sclerosis and a further 3 patients were admitted to hospital and could not be assessed. Four patients refused assessments. It has, therefore, only been possible to include results from 128 patients evaluated over two years. The patients excluded were not exceptional in disease type, or response to treatment.

In summary, 128 patients of the 147 originally treated were admitted to the study. Nineteen patients were not included for the reasons given, but 13 patients, not assessed at 12 months, were successfully followed up at 24 months.

The average age of the 44 male patients was 47.8 years, with a range of 24 to 69 years and their average disease duration was 15 years, with a range of 2 to 43 years. For the 84 female patients, the average age was 49.7 years, with a range from 24 to 69 years. Their average disease duration was 16.0 years, with a range of 3 to 38 years. (Figures 7 and 8) The patients followed the ascending pressure protocol employed in A.R.M.S. centres, in which six sessions are completed at low pressure (1.5 ATA), followed, if there is no improvement, by six at an intermediate pressure, (1.75 ATA) and finally, again if there is no response, by the remainder of the twenty sessions at 2 ATA. All patients, therefore, received an initial course of twenty, one hour, sessions. The pressure found to be the most beneficial was used by the patients for their continuation treatment. A detailed disease history was obtained for each patient, with particular attention being paid to the year prior to treatment. From the nature of the disease during this period, the patient was classified as progressive, or stable. To be described as progressive, the patient must have experienced continuous worsening of symptoms, or chronic symptoms with relapses. The numbers in each category were:

Progressive 92; Stable 36

If potential treatments for multiple sclerosis are to be studied for an effect over a long period, then it is necessary to be able to make a reasonably certain prediction of the course of the disease, at least for groups of patients. The patient classification used for the two years of the study proved to be surprisingly accurate in this study, when the results at two years are examined. (Tables 2-4) To avoid any confusion from the effect of treatment, only the results for patients who did not maintain therapy were reviewed. For both bladder and communicating, the Progressive and Stable patients displayed courses that were significantly different (p<0.05) and consistent with the prognoses implied by the terms. There is increasing acceptance, internationally, that a high degree of predictability does apply for chronic patients. Two recently published two-year investigations, of Cyclophosphamide and Copolymer 1, have embodied the idea of predictability and the prevention of deterioration.
Assessments

The lack of reliable measurements of the neurological and physical condition of patients, for use before and after a therapy under test, makes the evaluation of any treatment for MS very difficult. Not only is there no diagnostic test for the disease, there are no objective measures of disease activity. A conventional neurological examination is carried out in order to try to measure the patient’s condition, and the results may be combined to arrive at a rating on a scale, such as the one devised by Kurtzke, to give an overall picture of the patient’s disabilities. These assessments are, however, often subject to considerable variation, unless there is advanced disability. Any examination of a patient is also conducted at a single point in time. Unfortunately, MS is notorious for producing day-to-day variations and, even within one day, some patients can vary dramatically, provoked, for example, even by a hot bath. Neurological assessment is also very imprecise. In an effort to overcome this problem, and also to make the study more meaningful, the patients in this study were assessed on an Activity of Daily Living basis. The results relate to the ability of the patient to lead an independent life, recognizing the views of Roper et al., who noted that "a growing number of writers and practitioners now consider that the health status of the individual is dependent on his ability to adapt and cope with the challenges he meets during life". These writers identified twelve essential Activities of Daily Living (ADLs) which, in this study, have been reduced to eight, to provide a broad description of the patient’s capabilities. They were recorded in a structured way, to make the data collection as objective as possible, to allow assessments of changes in individual patients and comparisons to be made between patients.

The eight ADLs assessed were:

- Maintaining a safe environment
- Communicating
- Eating/drinking
- Eliminating
- Mobilizing
- Personal cleansing / Dressing
- Work/ Leisure
- Sleeping

For each, a seven point scale was devised, with a score of 1 representing normal and complete independence, ranging to 7, describing complete loss of function and total dependence. A full description for each point on the ADL scales ensured consistency between the interviewing assessors, who were qualified and experienced senior nurses. This allowed a numerical score to be compiled, describing the status of each patient at any time. It is beyond the scope of this paper to present or discuss the detailed ADL results, but it was seen that bladder and mobility problems appeared relatively early in the disease and affected 90 - 95% of the patients. In contrast, speech disturbance affected less than a third of the patients. It was clear that, as would be predicted, the greater the degree of dysfunction the less often patients described improvement after treatment. For example, patients with total bladder dysfunction (scores 6-7) never reported improvement. Most of the patients who improved had scores between two and four.

Patients were assessed immediately prior to the initial course of treatment and at one month after its completion. Further assessments were carried out at six, twelve, and twenty four months. At each assessment, the nurses were aware of the results of the previous assessment in order to provide them with a baseline for comparison with current findings. This has been criticised, because it has been suggested that the interviewer is likely to be influenced and to influence the patient from the previous record. However, without this reminder, patients can both exaggerate and minimise changes in their condition. It is, of course, certainly true that patients undertaking their own therapy do not want to appear to be wasting their time and indeed the time of others, but, even allowing for these factors, patients recognise that it is necessary to be as candid as possible. Certainly, the distortion introduced by the need many patients feel to please physicians is absent from this study and although the environment of the centre is supportive, it does not rate alongside a hospital as a high technology unit.

During the follow up period, patients were encouraged to maintain weekly treatment, but the regime actually followed was left to the individual. On average, the treatment frequency was about once every two weeks in the continuation group. Patients were not included in the continuation group if the intervals between sessions exceeded five weeks and, for this second group, the average treatment frequency was once a year.
Although data, over the two year period of the study, was gathered on eight different Activities of Daily Living (ADLs), detailed analysis has been carried out on only three, together with a combination of these to provide a measure of overall status. The three ADLs, Eliminating (bladder function), Mobilizing (mainly walking ability) and Communicating (speech) were chosen to describe different neurological functions.

Bladder function is complex and uses long nerve pathways involving the brain, the spinal cord and the autonomic nervous system. The vulnerability is illustrated by the very large percentage of MS patients with bladder disturbances. For example, of the 92 progressive patients, 91 had disturbance of bladder function.

Mobilizing is dependent on efficient conduction of motor nerve impulses from the brain down the spinal cord, but also other more complex functions, which allow the brain to sense where the legs are in space and co-ordinate the relative power given to the different sets of muscles. Balance too is critical, which again involves several senses. The large number of MS patients with walking difficulty testifies to the complexity and the vulnerability of the functions involved. Finally, muscles and joints, which are not used, deteriorate and physiotherapy is essential to maximise neurological improvement and restore function. The importance of physiotherapy for multiple sclerosis patients has been demonstrated in an A.R.M.S. study. Physiotherapy had not yet been organised at the Glasgow centre at the time this study was undertaken and less than 2% of the patients had physiotherapy.

The ability to communicate is one of the most important in determining the quality of life. That the speech function is less frequently affected in multiple sclerosis may simply illustrate that the long tracts of spinal cord are not involved in the co-ordination of the functions of the brain, vocal cords, mouth and tongue. However, the function of speech requires the activity of the brain stem and problems in this area indicate advanced disease.

Results

The results indicate the changes of one point or more on the seven point scale in the score determined before and at intervals after HBO therapy. Assessment results are shown in Tables 2-4 and as bar charts in Figures 1-6, at one month following first treatment, at one year, and at two years. Results are given for the Progressive and the Stable groups of patients, divided in each case between those who maintained HBO therapy for the period stated, and those who did not. Figures 1 to 6 give the data in bar chart form. Several patients could not be contacted at the 12 month assessment (+/- 1 month), but were available for assessment at 24 months. Records showed that those who maintained treatment, on the basis of an HBO session at least once every five weeks, averaged one treatment every 2.3 weeks in the first year and every 2.4 weeks in the second year. Those who did not maintain treatment averaged one treatment a year over the two-year follow-up period.

Patients in the non-maintenance group were asked why they did not return for treatment. For a few it was the cost of travel, but the main reasons were the failure of therapy to produce dramatic improvement and the effort required to reach the centre. These factors were often additive, in that the patient could not justify the cost and effort involved in relation to the level of benefit perceived. Although the stated aim of the therapy was to stabilise the disease, this proved less of a motivation than the hope of a cure. The obvious comment in a trial of this nature is that patients would simply self-select on the basis of whether or not they perceived benefit. This was the case, for some patients but, as the results show, by no means all, because many of the patients who perceived early benefit did not return and patients with no benefit continued. Indeed at two years there was little difference (Table 1) in the patterns of treatment maintenance between the patient groups, regardless of whether or not they had perceived initial benefit. Some patients who had stopped treatment discovered that they had, in fact, received benefit and returned to continue treatment. Table 1 summarises the experience of the maintenance and non-maintenance groups in relation to the perceived benefit at one month, one year and two years.

Bladder Function

The results are shown in Table 2 and Figure 1 for the Progressive Group. It is obvious that a significant number (42%) perceived immediate benefit. This continued to be the case at one year and, to a slightly lesser extent, at two years, for those who maintained treatment. By contrast, improvement was much less and deterioration much greater, at both one and two years in the group who did not maintain treatment. When subject to statistical analysis, the correlation between stabilization and continued treatment was highly significant. (p<0.03).
Surprisingly, 39% of the stable patients also reported improvement in bladder function at the end of the first month. The results for bladder function in the stable group are shown in Figure 2.

The immediate alleviation of the bladder dysfunction by hyperbaric oxygen therapy has been a frequent observation\(^{23,5,6,9}\) and objective urodynamic studies have generally confirmed the improvement in bladder function.\(^{24,5}\) This study has also found an immediate beneficial effect. The continuation of benefit over a two year period in this study has clearly been associated with the continued use of hyperbaric oxygen therapy. The consistency with which bladder benefit is reported subjectively and the objective confirmation must dismiss any contention that the effect is purely psychological. In the final report of the controlled trial by Barnes et al.\(^{12}\) they record that patients who had only had twenty sessions of HBO maintained their bladder improvement for six months, without further treatment.

For the Stable Group of patients, (Table 2, Figure 2) there is much less tendency to deteriorate with time, regardless of therapy maintenance. However, the improvement perceived is of the same order as in the Progressive Group, although the number of patients in the group is smaller. This difference in behaviour between groups is exactly what would be expected. The relationship between therapy maintenance and the prevention of deterioration with time should be most evident in a group of patients whose condition would be expected to deteriorate. The effect should be far less evident in those who would, in any case, be less likely to deteriorate. However it is of interest, that the levels of perceived improvement are similar in both groups. Bladder function involves less complex functions than, for example, walking and changes in bladder function can be noted more easily. Certainly, many patients report that they gauge their continuation treatment frequency by using the worsening of their bladder symptoms as a guide.

Mobilising

The results are shown in Table 3 and Figures 3 and 4. A relationship between continued treatment and stability in mobilisation is less evident than it is for bladder function, and, indeed, there is no statistically significant difference in benefit between the group continuing treatment and the group that did not. At one year in the Progressive Group there seems to be a greater tendency to deteriorate without treatment, but at two years there is no clear effect. For the Stable Group, the tendency to deteriorate at one year is less than that displayed by the Progressive Group. While this is what would be expected, there appears to be no difference at two years. At two years in the Stable Group, there is a suggestion that there is a greater tendency for deterioration in the patients not maintaining treatment.

The data obtained is consistent with the view expressed by Poser\(^{22}\) that "stability" in MS is only a relative term. If the complex function of mobilisation is more vulnerable to the disease process, then it is likely to be harder to control by any therapy. Bauer\(^{23}\) has also pointed out that improvement in neurological function may lead to the worsening of symptoms. For example, many patients use the stiffness of spasticity as support. Improvement of the spasticity reveals the underlying weakness. A patient may find that with actual neurological improvement, they may lose the ability to walk or even to stand.

The data in Table 3 suggests that the deterioration is slower in the Stable Group, at least over a twelve month period, but that by two years there is little difference between the Progressive and Stable groups. The only hint of an effect from HBO is an apparently greater tendency to deteriorate at one year in the Progressive Group and a greater level of perceived improvement at one year in the Progressive and Stable Groups for those maintaining treatment.

Communicating

The results are shown in Table 4 and Figures 5 and 6. It should be noted that less than 40% of the patients studied had any speech difficulty. While there is a greater tendency to deteriorate among the Progressive Group than the Stable Group, over both one and two years, there seems to be no effect from HBO between those who maintained treatment and those who did not. Although many multiple sclerosis sufferers receiving HBO have described a greater mental alertness after treatment, and many carers have noted improvement in patients' speech, these results cannot be said to give supporting evidence. The stimulating and positive climate which prevails in ARMS Centres may be a significant factor which is, of course, a powerful argument for patients to continue attending, as stimulus and support are vital.
The overall results in the three ADLs at the end of two years, for both stable and progressive patients, with and without maintenance therapy, are shown in Table 5. The overall response to treatment at two years for the three activities of daily living are shown in Table 6.

Discussion

The purpose of this study was to follow a substantial number of multiple sclerosis patients over a significant period and assess whether or not hyperbaric oxygen could modify the course of the disease. It is necessary to be aware of the nature of the damage in the nervous system in MS in order to understand what can and cannot be expected from any therapy. Sclerosis means healing by the formation of scar tissue and is a universal response to injury. Unfortunately scars in the nervous system trap nerve fibres and may therefore produce disability. Recently, a technique, called Magnetic Resonance Imaging (M.R.I.), has become available, which can provide information about the living body in great detail. The technique has dramatically altered our understanding of nervous system disease. It has shown that the same appearances as seen in multiple sclerosis are very common in older people, especially those who have suffered a mild stroke. Also M.R.I. studies of patients, including children, with an attack typical of MS, but with only one symptom, have shown that most already have more than one area of the brain affected. The technique is also indicating that MS is much more common than currently recognised and affects at least 2% of the population in the U.K.

However, on present evidence, most of those affected will not develop obvious symptoms and be described as having the disease multiple sclerosis. Full remission is therefore much more common than is recognised, although as Kurtzke states, the level of remission depends upon the extent of the damage or sclerosis. Those patients who have only one area affected may correctly be described as suffering from monosclerosis. Although this term is not yet in use, it is clearly a sensible description of the condition.

It has been known for many years that the areas of damage found in MS surround blood-vessels in the nervous system and many eminent neurologists have emphasised the importance of this feature in therapy. It is also known that the blood vessels may heal, leaving a minimal amount of tissue damage and scarring, with no residual disability at all. The most crucial factor in this healing or remission is the local level of oxygen in the tissues. Although it is accepted that oxygen must be given to patients who are shocked and blue, restoring the correct level of oxygen in the blood cannot guarantee that all the tissues of the body have a normal level of oxygen. The object of oxygen therapy in MS should be to make more oxygen available to the areas affected to prevent or limit the extent of damage and secure the best remission.

For patients already affected by extensive scarring, that is scarring, the object of treatment is to stabilise the disease. Dr. George Schumacher, a former chairman of the International Federation of Multiple Sclerosis Societies, recognised this almost fifteen years ago.

"Far more realistic as an indicator of therapeutic effect than the lessening of symptoms or signs is the halting of progression of neurological deficit. The sole criterion of efficacy should be the prevention of downhill progression or recurrent exacerbations."

Whilst these criteria of efficacy are desirable, they are to some extent unrealistic. For example, a therapy which is successful in the treatment of a heart attack, may be unlikely to prevent another episode. Also the nervous system, like the rest of the body, ages and much of the spare capacity, needed to preserve function, is lost in the sclerosis, explaining the deterioration so often seen as patients enter middle age. This is particularly important, in view of the average age of the patients in this study being about 48 years. The ages of the patients are illustrated in Figure 7 and Figure 8 shows the disease durations from the onset of the first symptoms.

The timing of therapy aimed at the prevention of sclerosis is critical to success. Kurtzke has stated that remission is strongly related to the duration of the symptoms. Improvement rates are listed as, "86% for bouts of 0-7 days, 64% for 8-14 days and 38% for 15-31 days. For longer durations, up to one year, about 1 in 6 improved and only 7% for bouts in their second year." These observations are a clear indication of the value of hyperbaric oxygen therapy as shown by this study. It is therefore very important to put the findings
from this study into perspective for MS patients who are continuing to use HBO and for their relatives. The findings are, of course, just as relevant for those who have stopped HBO or indeed have never tried it.

Neurologists now accept that to carry out a study on the long-term effectiveness of any treatment, it is valid to compare patients who have continued treatment with those who have not. For example, neurological journals are prepared to publish studies of immuno-suppression carried out in this way.\textsuperscript{17,18} Inevitably this implies that the course of the disease can be predicted in chronic MS patients. In this study, a comparison of the groups in which the MS is Progressive and Stable has supported this patient classification. The recent study of cyclophosphamide and steroids in the U.S.A.\textsuperscript{17} has certainly dispelled any suggestion that the course of the disease in chronic progressive patients is unpredictable.

In their study, of 24 patients in the control group, 23 (95\%) were worse at the end of two years, contrasting with these results, where of 37 patients maintaining therapy only 11 (30\%) were worse over the same period. (Table 6)

There have been allegations that oxygen therapy produces benefit by the placebo effect. It is, of course, known that the stimulus of hope and belief can, through biochemical changes, modify the perception of pain by the brain. Clearly this effect is something to encourage, by maintaining hope and a positive attitude to the disease. It cannot and should not be denied that the creation of centres by the patients and their relatives has raised spirits, but, equally, it has been shown by controlled studies, that therapy is also playing an important part in stabilising the disease and the role of additional oxygen can certainly be defended scientifically, even for those whose claim that the disease is due to auto-immunity.\textsuperscript{4,5,10,14} The great majority of patients who attend for treatment in A.R.M.S. centres are suffering from advanced disease and have few illusions about therapeutic claims. The suggestion that the placebo effect is the sole reason for the remissions experienced by patients using hyperbaric oxygen in this study is simply not believable, but, in any case, has been disproved by the controlled studies cited.

The disease giving rise to multiple sclerosis is common and the natural history of the disease can be reliably predicted for a group of chronic patients and the results of hyperbaric oxygen therapy clearly differ from this experience. Patients are, of course, puzzled when one symptom, like bladder dysfunction improves, but others remain the same or even get worse. This is probably due to the different times the areas of damage have developed and also local variations in the blood supply. An interval as long as 56 years has been recorded between the two attacks required for the diagnosis of multiple sclerosis, in a patient who first presented with optic neuritis as a teenager. It is clear than an area damaged so long ago is unlikely to respond to therapy.

The safety of the treatment has been proven by the experience of about 1,000,000 sessions in 57 A.R.M.S. centres and the procedures used have been approved by the Health and Safety Executive. The International Federation of Multiple Sclerosis Societies has acknowledged that hyperbaric oxygen is safe for multiple sclerosis patients,\textsuperscript{29} in stark contrast to the dangers of many drugs which are still used, in the absence of scientific evidence of benefit.

Until research can lead to the prevention of the disease and eventually to its eradication, the provision of treatment facilities utilising hyperbaric oxygen, preferably in conjunction with physiotherapy and dietary advice, is both relevant and appropriate for multiple sclerosis. As the cost of an A.R.M.S. centre to support 200 patients a year with regular treatment sessions is in the region of £50,000, a cost per patient per annum of £250, (about the cost of a three-day stay in hospital) the therapy represents a worthwhile investment for sufferers. It is notable that oxygen supplementation for patients with chronic respiratory disease often costs over £5000 per annum. Regular treatment is likely to be of benefit to a significant proportion of chronic sufferers and there is no evidence of a harmful effect. It is vital that patients are encouraged to use hyperbaric oxygen therapy, as no other treatment has been shown to provide benefit in chronic sufferers and no other agent has the safety of oxygen. Now that the authors of the Newcastle study, who were responsible for much of the controversy about hyperbaric oxygen therapy for multiple sclerosis patients have modified their view, the Societies involved in the field of multiple sclerosis have a clear duty to make the facts known to the general public and work to establish the therapy even more widely in the U.K.
Conclusions

I. The course of multiple sclerosis can be reliably predicted in groups of patients with chronic disease, at least over a two year period, and this can be used in the evaluation of therapy.

II. Hyperbaric oxygen therapy on a regular basis has a beneficial effect on the course of the disease. Many chronic patients, who would be expected to deteriorate, can be stabilised.

III. In this study, benefit was most evident in bladder function, which echoes the results of the controlled studies. This study has shown that if treatment is continued, the benefit is maintained. This is a finding of great importance, for proper bladder function is crucial to both quality of life and life expectancy.

IV. Although beneficial effects on walking ability were initially described by many patients, they were not maintained in most patients by HBO continued at the frequency used in this study. However, many patients did not deteriorate.

V. Early improvements in speech were described by patients and corroborated by relatives and friends. They were not maintained in most patients at the frequency of continuation treatment ("top-ups") used.

VI. Symptoms stable for over a year may show improvement. This applies particularly to bladder problems.

VII. The demonstration of modest improvements or reduced progression in many long-standing sufferers logically suggests that oxygen therapy should be used early in the disease, to induce the earliest and most complete remission and, hopefully, prevent later disability.

VIII. The treatment is safe. The results described were obtained by treatment administered by lay people within the community. No significant complications have been encountered. Over 57 centres have now been established by sufferers and their relatives within A.R.M.S. They represent a most important resource serving the needs of multiple sclerosis sufferers.

The overall conclusion of this work is that the additional oxygen provided under hyperbaric conditions can have a beneficial effect on bladder function and is capable of stabilising the disease in many patients suffering from multiple sclerosis. Patients must be encouraged to use hyperbaric oxygen regularly and it should be used as early as possible in the disease, to ensure the most complete remission and to minimise deterioration.

Acknowledgements

The authors are grateful for the funding provided by the Scottish Home and Health Department, the co-operation of the patients attending the Glasgow A.R.M.S. Centre, the help of the staff of the Maryhill centre and the encouragement of Mr. J. Simkins, Chairman of A.R.M.S.

References

Figure 2

BLADDER FUNCTION: STABLE GROUP

RELATIVE TO PRE-TREATMENT

<table>
<thead>
<tr>
<th>IMPROVED</th>
<th>SAME</th>
<th>WORSE</th>
</tr>
</thead>
</table>

ONE MONTH

No. OF PATIENTS 40

ONE YEAR

THERAPY MAINTAINED

THERAPY NOT MAINTAINED

TWO YEARS

THERAPY MAINTAINED

THERAPY NOT MAINTAINED

C Welton, Aug 1977, KEGP

Figure 2
Figure 3

MOBILIZING: PROGRESSIVE GROUP

RELATIVE TO PRE-TREATMENT

IMPROVED  SAME  WORSE

ONE MONTH

100
80
60
40
20
0

% PATIENTS

No. OF

40

ONE YEAR

100
80
60
40
20
0

% THERAPY MAINTAINED THERAPY NOT MAINTAINED

35
10
1

23
8

TWO YEARS

100
80
60
40
20
0

% THERAPY MAINTAINED THERAPY NOT MAINTAINED

19
10
3

20
7

Figure 3
Mobilizing: Stable Group

Relative to pre-treatment

Improved
Same
Worse

No. of patients: 40

One Month

One Year

Therapy maintained
Therapy not maintained

Two Years

Therapy maintained
Therapy not maintained
Figure 6

COMMUNICATING: STABLE GROUP

RELATIVE TO PRE-TREATMENT

IMPROVED  SAME  WORSE

ONE MONTH

%  

No. OF PATIENTS  40

ONE YEAR

THERAPY MAINTAINED  THERAPY NOT MAINTAINED

%  

THERAPY MAINTAINED  THERAPY NOT MAINTAINED

%  

C. Weller: Aug. 1987, A/102/P
Figure 7

PATIENT POPULATION - AGE DISTRIBUTION

FEMALE - 84 PATIENTS
MALE - 44 PATIENTS

PERCENTAGE %

PATIENT Nos.

0 6 19 36 25

AGE (YEARS)

15-24 25-34 35-44 45-54 > 54

Figure 7
Figure 8

PATIENT POPULATION - DISEASE DURATION

FEMALE - 84 PATIENTS
MALE - 44 PATIENTS

PATIENT Nos.

PERCENTAGE (%)

DURATION (YEARS)

1-4 5-9 10-14 16-19 20-24 >24

2 3 12 15 9 20 10 21 5 14 6 11