2 Chatak NR, Hirano A, Lijtmaer H, Zimmerman HM. *Arch Neurol*. 1974; 30: 484

3 Poser CM *Arch Neurol*. 1980; 37: 471

4 James PB. *Lancet*. 1982; ii: 380

5 Sears ES, Tindall RSA, Zarnow H. *Arch Neurol*. 1978; 35: 426

6 Schumacher GA. Reported in *Med Tribune*. 1983; 24: 4

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AN OPEN LETTER TO ALL BAROMEDICAL PHYSICIANS

Richard A Neubauer

I am concerned about the current worldwide explosion in the treatment of multiple sclerosis (MS) with hyperbaric oxygen (HBO). My concern is specifically about certain of the protocols being used for treatment.

At Ocean Medical Centre in Florida, we began our work with HBO for MS in 1973. The first publication of our studies was in 1978.[1] The original data provoked enough interest to lead to the funding of two animal studies.[2,3] A well-documented human trial was later performed by Fischer et al at New York University.[4]

In addition to these controlled research studies, there have been clinical studies involving up to 2,000 patients worldwide, to date. Following the publication of the results from the first 250 MS patients at Ocean Medical Centre,[5] I presented a report on the similarity of results between 500 MS patients and 100 MS patients treated in Italy, at the 5th Congresso Nazionale della Societa Italiana di Medicini Subacquea e Iperbaric in October 1982.[6] At the 8th Annual Conference on Clinical Applications of HBO in Anaheim, California in June 1983, I presented an international survey of reports on the HBO treatment of 1740 MS patients.[7] This was followed in September 1983 by an update and compilation of further controlled and/or longitudinal studies either underway or in the planning stages, presented at the First European Conference on Hyperbaric Medicine.[8] Many other reports have been published.[9,14,17,18]

One overwhelming fact stands out in these studies: All report encouraging results. Yet I receive several telephone calls and letters each week from MS patients regarding the deterioration they are experiencing with HBO. Rarely do I hear from their physicians.

Why is this? Especially in view of the extensive positive published reports. I believe that it is because these patients are being treated at a fixed pressure of 2 ATA (and occasionally higher), usually in a monoplace chamber.

For some reason, the fixed pressure protocol has been adopted at most centres which have started to treat MS with HBO since Fischer's publication. There is no concern about treatment differences between monoplace or multi-station chambers. The differences in the effect on the PaO_2 should be obvious to any baromedical physician (eg. Fischer's PaO_2 levels varied widely even with a fixed 2 ATA protocol in this multistation chamber). In the monoplace chamber, the PaO_2 is directly related to the pressure being used.

There is a scientific basis for the use of a variable, low-pressure protocol. My development of this approach was not entirely empirical. Research by reputable scientists, including Holbach, Wassman et al[14] and Kelly et al[15] clearly indicates that low and variable pressures are preferable in chronic neurological diseases.

This variable, low-pressure protocol has been widely used both in research and in clinical treatment. At Ocean Medical Centre we have treated over 700 MS patients with it. None have deteriorated due to pressure. The work of Fischer, et al[4] also lends support to this protocol. Their results showed that better clinical improvement occurred in patients having PaO_2 levels equalling those in a monoplace chamber at 1.4 - 1.6 ATA. Careful reading of that report would lead any physician to adjust the 2 ATA protocol downward, especially when using a monoplace chamber.

Additionally, the article recently published by Golovkin[16] in the USSR showed that MS patients exposed to pressures over 2 ATA for 20 minutes deteriorated rapidly. He now treats at 1.7 ATA in a multi-station chamber. Similar experience by Pallotta[17] and others in Italy led to the adoption of reduced depths. Davidson and James in Scotland,[11] using a multi-station chamber, changed from the Fischer protocol of fixed pressures to a lower beginning pressure protocol with improved results. Pressure is particularly critical to MS patients with abnormal nervous tissue, especially when optic neuritis is present.

There are three types of MS patients:

1) Newly diagnosed with early symptomology.
2) Stable chronic progressive.
3) Chronic progressive in exacerbation (relapsing/ remitting).

The variable pressure protocol starting at 1.5 ATA and ranging to 2 ATA is well established as effective in stable chronic progressive MS patients (type 2). Most of the published data on MS and HBO deals with type 2 patients. Invariably, HBO treatment leads to encouraging results when appropriate follow-up HBO treatments are given. Long-term longitudinal studies indicate that these patients secure alteration of the course of the disease.

Fewer early cases have been treated with HBO. They invariably respond, as they do with any other modality that is used. Further study is needed in this area. Such patients would have to have a longer follow-up period and more patients would be needed to differentiate between actual alteration of the disease and a placebo effect. James' comparison of decompression illness and MS led to his conclusion that all newly diagnosed MS patients should have HBO with the same priority as in decompression illness. (See his article in "Pressure Points", 13(5): 7-8, 1983 which appears on page 16).

The patient having chronic progressive MS with acute exacerbation presents a less clear picture than the above. My results in the treatment of such patients has not been as rewarding as those of McGehee in Houston, Texas or Pallotta in Italy. Recently James courageously treated a chronic progressive patient with an acute exacerbation including optic neuritis in a multi-station chamber using pressures up to 2.75 ATA. The pressure was cautiously titrated upward only after failure at a lower pressure. A dramatic result ensued. This experience warrants further cautious study. It does not indicate that all MS patients should be treated with such high pressures; deterioration is frequently seen in stable chronic progressive patients at 2 ATA or higher. This stage of the disease may require an entirely different protocol.

Understandably, research scientists find it difficult to use a variable pressure protocol in controlled studies. For them, I would suggest that better results might be attained with a steady pressure of 1.5 ATA throughout, rather than 2 ATA or higher, with particular reference to the monoplace chamber. In the monoplace chamber PaO_2 levels are identical with treatment at any given pressure. Only in the multi-station chambers used for research are PaO_2 measurements desirable.

There is one final concern related to the length of the initial series and follow-up treatments. The original Ocean Medical Centre protocol for MS called for 10 treatments in the initial series. This was raised to 20 when we observed that in patients who had longer initial series, results often did not appear until near 20 treatments. As many as 80 treatments have been given in the initial series in refractory patients.

Regression is predictable after the initial series when appropriate follow-up exposures are not given. It is remarkable that in Fischer's oxygen patients, who had only the initial series of 20 treatments, statistically less deterioration was noted at the end of a year. It seems unreasonable to me to withhold this treatment from research subjects. This is also not the appropriate way to utilize the published protocol.

As George Schumacher MD, noted in May of 1979 at the University of Vermont: In the treatment of multiple sclerosis "the only dependable evidence of beneficial therapeutic effect is stabilization, that is, no further worsening in the clinical status thenceforward .... Longitudinal comparisons over time of each patient's pre- and post-treatment status would provide the essential data". Results to date using the low, variable pressure HBO protocol are promising.

REFERENCES

1 Neubauer RA. Treatment of multiple sclerosis with monoplace HBO. J Fla *Med Assn*. 1978; 65: 101

2 Warren J et al. Oxygen immunosuppression: modification of experimental allergic encephalomyelitis in rodents *J Immunol*. 1978; 121: 315-320

3 Prockup LD, Grasso RJ. Ameliorating effects of HBO on experimental allergic encephalomyelitis. *Brain Res.* 1977: 221-225

4 Fischer BH et al. HBO treatment of MS a randomized placebo-controlled double-blind study. *N Eng J Med*. 1983; 308: 181-2

5 Neubauer RA. Exposure of MS patients to HBO 15 to 2 ATA. *J Fla Med Assn*. 1980; 67: 498-504

6 Neubauer RA. Keynote Address HBO in neurologic disorders. V Congr Naz Soc Ital Med Subac Iperbar. *III Ruin Com Mediter Med Subac Iperbar*. *Montecatini Terme*, 21-24 0ctobre 1982

7 Neubauer RA. Hyperbaric oxygen as treatment for multiple sclerosis. A comparison of 3 groups totalling 600 patients. *Seventh Ann Conf Clin Appl HBO*. Anaheim CA; June 1982

8 Neubauer RA. A summary of worldwide experience in the treatment of multiple sclerosis with hyperbaric oxygen. In: *(Program and Abstracts) First Europ Conf Hyperbar Med*. 7-9 September 1983. Amsterdam, The Netherlands; 36

9 Boschetty V, Cernoch J. Use of HBO in various neurologic diseases (preliminary report). *Bratisi Lek Listy*. 1970; 52: 298-301

10 Baixe JH. Bilan de onze anees d'activite en medicine hyperbare. *Medicine aeronautiaque et spatiale Medicine subaquatique et hyperbare*. 1978; Tome XIVV: n65

11 Zannini et al. 40 cases of MS treated with HBO therapy. *Min Med*. 1982; 3(42): 293-945

12 Editorial. Treatment of Multiple Sclerosis. *Lancet*. 1983; 308: 181-6

13 James PB. Oxygen for MS (Letter). *Lancet*. 1983; 1: 1161-62

14 Hammond ES, Ibarra EL. Evoked potentials after HBO treatment of MS *N Eng J Med.* 1983; 309(4): 241-242

15 Holbach KH, Wassmann H, Caroli E. Cerebral energy metabolism in patients with brain lesions at normo and hyperbaric oxygen pressures *J Neurol*. 1977; 217: 1730

16 Kelly KL, Lassiter K, Vongsuivut A et al. Effects of HBO and tissue oxygen studies in experimental paraplegia. *J Neurol*. 1972; 36: 425-429

18 Golovkin VI et al. HBO as immunity stimulator in disseminated sclerosis. *Sovetskay Med*. 1982; 12: 70-75

19 Pallotta R. Hyperbaric therapy of multiple sclerosis. *Min Med*. 1982; 73(42): 2947-2954

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ANZICS
ROCKHAMPTON MEETING OCTOBER 1983

We are grateful to the Queensland Regional Committee of the Australian and New Zealand Intensive Care Society for permission to publish papers which were presented at their inaugural annual meeting here in Rockhampton. The guest speakers were Dr Struan K Sutherland of the Commonwealth Serum Laboratories and Dr John Knight of SPUMS. Transcripts of the papers given at the second session on envenomation and the second session on underwater medicine appear below.

MANAGEMENT OF SPIDER BITE

Struan K Sutherland

I want to talk briefly about three spiders, the Red-back spider, Sydney Funnel-web spider and our Mystery spider, and to finally mention the Paralysis tick.

There are at least 2000 named species of spiders in Australia and perhaps 1000 unnamed. They all have poison glands except some of the little humped spiders. Even the Daddy-long-legs spiders have venom glands. Spiders are the most widely distributed venomous creatures in Australia and they show enormous variety. They are also one type of venomous creature that is found both inside houses and outside. This increases the opportunity for bites and stings.

RED-BACK SPIDER

The commonest reason for giving antivenom in Australia is the Red-back spider. This spider is found the length and breadth of this country and it is not just limited to outside toilets and back sheds. It is very common in the bush. Most people are bitten when they bring the spider into contact with their skin. This is a passive action such as when old clothing is picked up or gloves are used for the first time that day. It is the female which causes the harm, the male having fangs that are too small to penetrate human skin. It is closely related to the Black Widow spider in America. In most countries there are representatives of this spider which produce the syndrome called latrodectism. Per head of population we seem to get more cases of latrodectism than any other country in the world. Some countries like Italy have a little epidemic of the spiders every 10 years whereas we have it as a perennial problem.

The main toxin is alphalatrotoxin and it specifically acts at nerve endings. It releases transmitter substance and changes to nerves can be seen with the electron microscope. At the motor end plate this loss of transmitter substance produces a patchy sort of paralysis but most of the signs and symptoms are due to the effects on the autonomic nervous system where it releases catecholamines, to produce the classic syndrome. One can be bitten on the left hand and after a while there will be quite severe pains perhaps in the left foot and the right shoulder and arm will sweat profusely and then after a few more hours things will shift around. It is a strange disease.

First-Aid

In fact you really do not need any first-aid. The bite is moderately painful, it is like a mosquito sting at first but it then becomes quite painful over an hour or so. The venom works very slowly, so we do not recommend pressure immobilisation, you just take the spider and yourself safely to hospital.

Red-back Spider Antivenom

The antivenom has been available since 1956 and no-one has died since it became available. It is a very small volume antivenom and very rarely are there any reactions to it. Perhaps I should have mentioned this earlier but we do not believe in skin testing for any antivenom for sensitivity. It is quite unreliable and it wastes time.

THE SYDNEY FUNNEL-WEB SPIDER

A more interesting spider in some ways is the Funnel-web spider. It is unique to Australia and is the potentially most dangerous spider in the world. It is the only one which, for example, killed children in less than 90 minutes. Although bites and fatalities are rare, some three million people are at risk in the area around Sydney. The numbers of spiders are apparently increasing as people put in swimming pools and barbeques which produce more of the damp earth areas that the female spider likes. The male is the highly dangerous one. Without being sexist, this is the reverse of the normal situation in which the female spider is the more poisonous.

There are two very special features about the venom. One is that the venom affects mainly man and primates. The funnel-web venom will not kill rabbits, normal laboratory animals, mice, cats, dogs and so on. The other feature is that the venom has a specific action. Basically it attacks the outer covering of the nerves and causes spontaneous action potentials. It also disrupts some of the normal monitoring impulses coming down the nerve. The venom acts quite quickly and apart from hitting motor nerves, it attacks the autonomic nervous system releasing transmitter substance in a much more extensive fashion than with Red-back venom.

If someone is envenomed then within a few minutes they will get central effects such as nausea and headache. Muscle twitching can be extremely grotesque because everywhere the motor end-plates are firing off transmitter substance. Blood pressure can rise very dramatically perhaps up to 250 mm Hg systolic. The pulse rate of children can go over 200. Most patients develop generalised sweating.

Strangely enough it was not until 2 years ago that we finally determined why patients died. Dr Alan Duncan and Dr Jim Tibballs at the Royal Children's Hospital in Melbourne did a lot of work with CSL on monitored monkeys. The most important thing found was that sometimes when a monkey had received venom there would be a dramatic rise in the intracranial pressure which disturbed cerebral perfusion. It had the occasional effect of producing neurogenic pulmonary oedema so a monkey could have both impending brain death and pulmonary oedema. After looking back over the case histories we believe this is how many patients died. The unaided