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# Assessing the Effectiveness of Hyperbaric Oxygen Therapy in Treating Disease

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# Assessing the Effectiveness of Hyperbaric Oxygen Therapy in Treating Disease

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## Abstract

Since it has been possible to venture into the deep ocean, it has been science that has determined how far we could delve. As our technology and understanding of the deep oceans grew, so did our ability to deal with the challenges of going underwater. These advancements in understanding have not only allowed us explore the oceans that cover 70% of our planet, but have also enabled us to attempt to treat some previously untreatable diseases on dry land. Much is unknown about the physiological consequences of going underwater on our bodies, but the applications of many things we do understand are becoming apparent. We review the literature in relation to hyperbaric oxygen therapy.

## Introduction

Since it has been possible to venture into the deep ocean, it has been science that has determined how far we could delve. As our technology and understanding of the deep oceans grew, so did our ability to deal with the challenges of going underwater. These advancements in understanding have not only allowed us explore the oceans that cover 70% of our planet, but have also enabled us to attempt to treat some previously untreatable diseases on dry land. Much is unknown about the physiological consequences of going underwater on our bodies, but the applications of many things we do understand are becoming apparent.

Perhaps the most useful application of underwater medicine has been the invention of hyperbaric medicine. The process works by supplying oxygen to a patient at a much higher atmospheric pressure than usual. It is usually delivered in a pressurised chamber that has been designed to comfortably house a human for a length of time in order to saturate their body with oxygen. The first documented use for medical purposes was in 1662 by the Clergyman Henshaw; he developed an airtight room called a 'domicilium' where the room's pressure and climatic conditions could be changed using a pair of bellows. Without any particular scientific knowledge supporting its use, he used his

Hyperbaric Chamber to attempt to treat a variety of diseases, and thus Hyperbaric Medicine was born.

Modern day methods have improved drastically and countless people have claimed that Hyperbaric Oxygen Therapy (HBOT) has been beneficial to them in a variety of ways; however many people remain sceptical about the science behind these claims. I will be reviewing the research conducted with respect to treating these diseases using HBOT and assessing whether this is a useful treatment for the disease.

Claims for the efficacy of HBOT treating diseases are numerous, they include treating: conditions which affect the amount of oxygen that can be held in the blood (anaemia, carbon monoxide poisoning); degenerative organ diseases such as cardiovascular (heart ischaemia) or neurodegenerative diseases (multiple sclerosis) and also developmental diseases such as autism. I will focus on the diseases which I feel demonstrate the varying degree of efficacy that HBOT has in treating disease. I will divide the report into 3 three main sections: diseases which have significant evidence that they can be effectively treated using HBOT; diseases which have inconclusive evidence that they can be effectively treated using HBOT and diseases which have little or no evidence that they can be effectively treated using HBOT.

## Background Science

Henry's law states that the amount of gas dissolved in a liquid is proportional to the partial pressure of that gas in contact with the liquid; meaning that at pressure, tissue oxygenation is maximised.

At hyperbaric pressures, this causes 220 times the partial pressure of oxygen to be available in the breathable air (102 mmHg at normal at normobaric conditions but 22193 mmHg at 100% oxygen at 3 ATA (Jain, 1999)). This subsequently causes a vast 6.3% increase of oxygen dissolved in solution, according to Tintinalli J E et al (2010 ch e18.1), meaning it can reach areas which are usually poorly vascularised and thus poorly supplied with oxygen. In addition to this the delivery of oxygen can be independent of haemoglobin, which makes it particularly relevant in diseases which cause the body's red blood cells to be compromised e.g. anaemia or carbon monoxide poisoning.

This is all explained by Boyle's law (pressure and volume have an inversely proportional relationship with any given mass of gas in a closed system) because the volume of gas decreases with increasing pressure; in a Hyperbaric Oxygen Chamber this means that there are more molecules of oxygen per cubic metre than there would be at normobaric conditions. Subsequently once the subject breathes in; there will be more molecules of oxygen in solution inside them when they are in a Hyperbaric Oxygen Chamber than if they were in normal atmospheric conditions.

The first disease to be effectively treated with HBOT was decompression sickness ('The Bends'). This disease occurs when a person, usually a diver or an unpressurised aircraft pilot, undergoes rapid changes in pressure. This causes dissolved gases found in solution in the body (usually nitrogen) to come out of solution and form bubbles. These bubbles can then cause a variety of symptoms ranging from intense pain in the joints and nausea and vomiting to much more severe symptoms such as seizures and amnesia and in the most severe scenarios, death. Immediate treatment with HBOT can effectively re-compress the air in the body back into solution, alleviating the problems.

It is worth mentioning that there are some risks involved with undergoing HBOT, principally oxygen toxicity; symptoms of which include: dizziness, confusion, nausea, pulmonary oedema and even damage to the eye. This can be avoided by taking regular 'break' periods where the subject will breathe in normal atmospheric oxygen opposed to 100% oxygen to prevent oxygen building to dangerous levels in their body.

Unfortunately, the pressure of the chamber, as well as the optimum duration for treatment for diseases other than decompression sickness are not universally agreed on, so it may be that there will be varying methods of administering HBOT in the studies I research.

## Methods

Whilst reviewing the research available on each disease, I will try to establish whether this research is reliable, bias free and relevant to the entire population of people being treated. I will do this by giving weighting to each type of study I have included in this report via the widely used 'Hierarchy of Evidence' method. I have found however that HBOT is only regularly used in a select few individuals or in very few

specific scenarios and thus, often the 'Gold Standard' research method is not applicable. In light of this I will have my own style of comparing the study designs inspired by the systems available at present. I will also try to ensure that the authors of the paper are not obviously linked with any vested interests such as funding from organisations supporting the use of Hyperbaric Medicine to treat a particular disease in order to reduce bias. I will also exclude any studies which are purely based on anecdotal evidence and I will also exclude any studies which show the results as being not statistically significant.

Study Design	Rating
1) Systematic reviews and meta-analyses	Gold (N/A in this report)
2) Randomised controlled trials	High
3) Cohort studies	Medium
4) Case-control studies	
5) Cross sectional surveys	Low
6) Case reports	
Fig 1 (Table on how studies will be ranked; adapted from: <i>BMJ</i> 1997;315:243 (Greenhalgh, 1997))	

## Evidence that HBOT can Treat Disease

As mentioned previously, decompression sickness was the first disease to be effectively treated using HBOT. The evidence for its use are so well proven and tested that it is now the Gold standard treatment for decompression sickness and used by large medical organisation globally, such as the NHS. I will therefore not scrutinise the evidence for its use in this report. Instead I will focus on possibilities for using HBOT to treat other diseases asides from decompression sickness.

The use of HBOT has some other obvious possible applications. With the example of gas gangrene ("Clostridial myonecrosis") this is evident. Clostridial myonecrosis is an infection caused by the Clostridium perfringens bacteria which causes gas to be produced in tissues, resulting in myonecrosis and sepsis. This form of gangrene is very serious and can cause a rapid deterioration in the patient's condition. Clostridium perfringens is an anaerobic bacterium that can penetrate deeply into a person's tissues; something which made it hard to treat in the past. Nowadays excision along with a course of strong antibiotics can usually cure the infection. However it has been found that it is beneficial to use HBOT in conjunction with these treatments to fully cure any infections, prevent any regrowth and lower the mortality rates.

In a controlled study performed in rats, it was found

that once infected with *Clostridium perfringens* intramuscularly, if left untreated, the mortality was 100%. If the rats were treated with surgery alone, the mortality fell to 38%. However if the rats were treated with surgery and HBOT, their mortality dropped to just 13% (Hirn, 1993). This evidence shows that there is a dramatic decrease in mortality in rats which have been given the HBOT combined with surgery compared to surgery alone.

This effect can be attributed to the fact that the bacterium is anaerobic and therefore susceptible to death in exposure to oxygen. It was also found that the more (within the range set) exposures to hyperbaric oxygen delivered to mice infected with *Clostridia* bacteria; the higher the percentage of the mice survived the infection (Kaye, 1967).

However as these experiments were conducted on a small number of rats in a laboratory, drawing too much evidence from this alone does not constitute as solid scientific evidence and thus I will have to rank this as a medium standard of research (as per my ranking system in Fig 1). Nevertheless it is worth mentioning that due to the rarity of these cases and the severity of leaving this disease untreated, controlled, experimental data on patients who have had HBOT as an adjunctive treatment to surgery and antibiotics, against those have not had HBOT is unavailable. So this is the best research available at present.

Despite this, HBOT is being used to treat gas gangrene clinically. There are countless uncontrolled studies conducted by clinicians worldwide that have used HBOT as an adjunctive therapy and they have found it to be more effective in treating the disease than without HBOT. One such study conducted in Whipps Cross Hospital in London by Slack (1976 p. 326-327) was conducted over a period of 10 years and in the 80 patients with *Clostridial* infections he treated, there was 'often a detectable improvement' noticed once the first treatment of HBOT was given (Slack, 1976). Despite this representing a weak level of research, the sheer number of supportive studies seems to show that using HBOT to treat gas gangrene with has a significant efficacy.

Another disease which is perhaps an obvious candidate for treatment using HBOT is carbon monoxide poisoning. If carbon monoxide is binding to haemoglobin instead of oxygen, perhaps flooding the blood stream with oxygen will reverse this process?

There have been several randomised controlled trials (high rating) conducted on whether HBOT helps treat carbon monoxide poisoning. There was such a study conducted in the USA where patients with carbon

monoxide poisoning were assigned randomly in equal portions to one of 4 chambers: 3 with hyperbaric pressure and another with normobaric conditions acting as a control. Neurological tests were then conducted immediately after the sessions and in follow up tests which stretched up to 12 months after the first treatment. Results found that cognitive complications at 6 weeks were 21.1% less frequent in hyperbaric oxygen group than in the normobaric oxygen group (Weaver L K et al. 2002). The study was conducted via the 'intention to treat' method meaning that this is clinically relevant and these results clearly show the benefits of using HBOT to treat carbon monoxide poisoning. The only negative to this study is that it was stopped prematurely, which might have had an effect on the data.

Another study where 2 randomised controlled trials (High rating) were conducted shows slightly different results. The study included 179 patients in the trial A – all of whom has 'transient loss of consciousness' and 206 patients in the second trial (trial B) who all had initial coma. Both trials yielded differing results though. In trial A there was no significant evidence showing that HBOT improved the condition of the patient after 1 month as there was only a 2% increase in recovery rates in those getting the full hyperbaric treatment. In trial B however there was 21% increase in recovery rate in those treated fully with HBOT (Annane D et al. 2011). On the surface this seems to show that the use of HBOT to treat carbon monoxide poisoning doesn't produce a reliable, detectable benefit. However, looking more into the method of the study revealed some obvious flaws in their method of separating the groups. In trial A patients were split into 2 groups: those who received 6hrs of normobaric oxygen therapy (NBOT) and those who received 4hrs of NBOT followed by a session of HBOT. As well as this, in trial B, one group received 4hrs of NBOT and a session of HBOT whilst the other group received 4 hrs of NBOT but also 2 sessions of HBOT. As both groups in trial B were given HBOT there was no true control in this study and thus it difficult to draw significant conclusions from it. Asides from this there is also a lack of comparability between the 2 trials, which means it loses the possibility to solidify one hypothesis as being correct. Not only this, but the patients in trial A compared to trial B were in different medical states and we do not know how this could effect the results. So perhaps the results show that more than 1 session of HBOT is required to produce the desired effect?

These kind of limitations are quite common in these studies so until subsequent controlled studies are conducted we cannot be sure at present of the exact

benefit HBOT gives to CO poisoning patients. This is supported in a study conducted on the literature on HBOT treating CO poisoning (Buckley N A et al. 2011). Nonetheless, it is trusted well enough to administer it to some patients who present with this condition – especially when they are in a poor state. Despite this, realistically, normobaric oxygen therapy given to patients with the diseases is a much faster, easier, cheaper and more readily available method of treating them and this makes it unlikely for HBOT to replace the current treatment entirely at present.

## Inconclusive Evidence that HBOT can Treat Disease

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Moving away from curing medical emergencies, HBOT has potential for helping manage chronic diseases, for example multiple sclerosis (MS). MS is a degenerative disease which involves the demyelisation of axons in the CNS by action of the body's own immune system attacking the myelin which results in symptoms such as: muscle spasms and weakness; loss of sensation; urinary and bowel incontinence; lack of coordination and difficulty speaking. Currently there are no known cures for MS so we can only try to manage the symptoms. There have been numerous studies looking for new ways to manage this disease and one avenue that has begun to be explored is HBOT. Results have been mixed and as of yet inconclusive as to whether HBOT aids in the management of MS.

The rationale behind using HBOT to treat MS is that increased distances for diffusion are created when lesions arise, making it harder to transport oxygen to neurons and therefore increased oxygen concentrations in the blood and in solution would help counteract this. As well as this some argue that increased oxygen concentrations in solution would help in tissue repair of the myelin. Evidence has seemed to show that treatment with HBOT for 2 weeks caused increased oxygen levels in the area of the axons and made the myelin thicker, as compared to a control in rabbits (Vilela D S, Lazarini P R, Da Silva C F, 2008).

A randomised, double-blind, placebo-controlled trial (high rating) was conducted using 120 chronic sufferers of MS. They were separated into 2 groups: a HBOT group or a complete placebo group. The results were measured using the Kurtzke disability status (a specific method of measuring disability in MS), psychometric tests and measurements of lymphocyte sub-populations. Treatment with HBOT had no effect on the patients progressing up the Kurtzke disability

scale or on their psychometric test or lymphocyte sub-populations. However there was less cerebellar deterioration in HBOT than in the control group after 1 year (Barnes M P et al. 1987).

Another randomised, double-blind, placebo-controlled trial (High rating) conducted on 40 patients with chronic MS was divided into 2 groups: the treatment group received 100% oxygen whilst the control group received 10% oxygen but both were at 2 ATA for 90 minutes. There were improvements in the condition of 70.6% patients in the treatment group, whilst only 5% in the control group saw an improvement. After 1 year, 43% more patients experienced deterioration in their condition in the placebo group compared to the treatment group (Boguslav H et al. 1983).

As this shows there is a wide variety of study results available for the management of MS using HBOT. There are many studies which show that there is no benefit for MS sufferers using HBOT to manage their disease whereas many others say that there is a benefit. I think with such a chronic, degenerative disease like MS it is very difficult to categorically say there is no beneficial effect as each sufferer of the diseases is at a different stage in the disease and this means that comparing one group of patients in one study with another is almost impossible. The disease itself is not fully understood and until more studies with larger numbers of participants is carried out, a coherent conclusion cannot be reached.

## Evidence that HBOT cannot Treat Disease

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A different disorder which there is no cure for is autism. This genetic disorder causes problems with neural development which in turn interferes with the processing of information in the brain. It is not very well understood and there are a variety of different disorders that you can develop which are all classed as autism. At present there is no single treatment which can help alleviate all the symptoms of autism and the primary treatment for it is psychosocial therapy which gives children widely varying results. The number of reported cases of autism is rising quite dramatically so a more effective way to treat the disorder is something people are eagerly searching for. When viewing research on pioneering treatments for disorders, particularly those which are degenerative, chronic or congenital, one must exercise a particular sense of caution. This is as sufferers of the disorder and their families are very desperate to find a cure, and so too are the researchers – sometimes for the

prospect of becoming rich or famous and this can lead to misconduct; a view also expressed by Chris Chambers, a psychologist at Cardiff University in an article written for the Guardian newspaper (entitled 'False positives: fraud and misconduct are threatening scientific research'). To prevent this, I will try to corroborate any findings with as many supporting articles as possible.

HBOT was suggested as a possible treatment for autistic children as it was thought that the oxygen could reach parts of the brain to enhance their function. Subsequently a multicenter, randomised, double-blind, controlled trial (High rating) was conducted on 62 autistic children who were randomly allocated to a group of either hyperbaric or normobaric oxygen treatment. Results seemed to show positive results for the use of HBOT on autistic children as after 40hrs of therapy given on a 1 hr basis, it was found that the overall functioning, receptive language, social interaction and eye contact was improved' in 80% of children in the hyperbaric group, opposed to just 38% in the normobaric group (Rossignol D A et al. 2009). This research seems very promising however the way the children were assessed was using Physician and Parental 'Clinical Global Impression' which some say is subjective and therefore subject to bias. On the other hand, this is accepted by many as a good assessment of mental function and represents the best possible way of measuring the progress of the disease at present.

On the other hand, there have been various small scale case studies which have supported the use of HBOT in treating autism, such as a very small case study conducted on 7 autistic children in Thailand which showed a 75% improvement in the treatment group (Chungpaibulpatana J et al. 2008). However the numbers involved in these studies are far too small to hold any real bearing. This demonstrates the lack of hard scientific evidence to support the treatment of autism using HBOT.

## Stem Cell Mobilisation

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Recent studies on mice show that stem cells/progenitor cells could be recruited and stimulated to differentiate in response to HBOT (Milovanova T N et al. 2009). As we know stem cells have the potential to heal almost any tissue and HBOT could be a safe, easy, effective way to increase levels of stem cells in the body. If this can be proven to be effective in human trials, it could potential treat a very large number of diseases.

## Conclusion

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In conclusion, Hyperbaric Oxygen Therapy (HBOT) has a variety of potential applications – some diseases more effectively treated than others.

We know that decompression sickness is effectively treated using HBOT. There is significant evidence for the use of HBOT to treat many other diseases. I focussed on CO poisoning and gas gangrene and found that these have proved to respond well to HBOT.

There is inconclusive evidence for its use in several diseases however I have focussed on MS as it is a disease which currently has very few effective treatments for. I found research both supporting and rejecting the hypothesis that HBOT helps manage the symptoms of MS but until more conclusive research is conducted, we cannot be sure of the benefit it gives to sufferers.

On the other hand there are diseases which show very little evidence that HBOT is effective in their treatment, the disease I chose to research was autism as it is another example of a disease which has few treatments and no cures. The research showed some positive results but the number of studies conducted were too small to draw too much hope from. In general there was a lot more research showing that autistic children would not benefit from HBOT than that they would.

All in all, HBOT seems very useful for a select few diseases – especially if the diseases are a result of a tissue suffering hypoxia, which is something one might expect. From the reports and uncontrolled studies available it also seems to have more wide reaching benefits in treating diseases such as CVD and immune problems which are not entirely understood as of yet. It is important to point out that at the moment, the most cost-effective and efficient ways to treat these kinds of diseases is through conventional treatments and attempting to treat something as prevalent as CVD with HBOT is ambitious to say the least.

Ultimately, it is necessary for a standardised method of HBOT administration to be applied in a research setting. This will allow significant clinical trials to be undertaken, which will make it possible to prove whether or not it is wise to implement HBOT as a treatment for disease.

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