HYPERBARIC OXYGEN TREATMENT

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INTRODUCTION

The application of air under pressure in an effort to treat certain respiratory disease dates back to 1662. An English physician named Henshaw constructed a small spherical chamber capable of hyperbaric conditions. Although there was little or no understanding of the theory involved, patients with a variety of medical complaints seemed to have benefitted. Word of the treatment spread across Europe and a few other chambers were built. The medicinal uses of oxygen were first reported by Beddoes in 1794, and the first article about using oxygen under pressure as an adjunct to conventional therapy was written by Fontaine in 1879. The use of hyperbaric oxygen has waxed and waned since those times.

Hyperbaric oxygen treatment (HBO) is that in which a patient breathes 100% oxygen in a treatment chamber at a pressure greater than sea level pressure, (i.e. >1 atmosphere absolute). Treatment can be carried out in mono- or multi-place chambers. In a mono-place chamber a single person breathes pressurised 100% oxygen. In a multi-place chamber the patients breathe 100% oxygen via a mask whilst the chamber is pressurised with compressed air. In many countries hyperbaric oxygen therapy is established as the primary treatment of many conditions such as decompression sickness, air embolism, carbon monoxide poisoning and gas gangrene. In Japan approximately 65 chambers are being commissioned every year and over 400 are in use at present. In America it has become mandatory to treat carbon monoxide poisoning with hyperbaric oxygen to avoid the possibility of litigation at a later date.

OXYGEN TRANSPORT

The final transport of oxygen to tissue is dependant upon the amount dissolved in the plasma, not unlike drug delivery to tissue. At sea level inspired air containing 21% oxygen produces only 0.3ml of oxygen per 100ml of saturated blood. Most of this is transported chemically combined with haemoglobin. However it is only the oxygen dissolved in plasma that is available for transfer into the tissues. This exerts a partial pressure of between 90 and 100mmHg. By breathing 100% oxygen at 1 ATA (760mmHg) there is an almost five fold increase in the partial pressure of oxygen to about 500mmHg.

The deficit (760-500mmHg) is because of water vapour and carbon dioxide in the alveoli and a mismatch in ventilation and perfusion that exists even in normal lungs. There is about 1.5ml of oxygen dissolved per 100ml of blood at 760mmHg. Doubling the atmospheric pressure (as in a chamber) will double this figure. At this pressure, dissolved oxygen will supply the vast majority of the body’s demand so that the haemoglobin remains fully saturated.

Although the additional volume of oxygen carried at 2 ATA is only about 15% the partial pressure exerted by the dissolved oxygen is in excess of 1000mmHg. There is, therefore, a tenfold increase in the driving pressure of oxygen into the tissues. This partial pressure will not exist at the tissue cellular level because of a ‘loss’ of pressure across the various diffusion gradients from capillary cells to intercellular fluid and then to tissue cell.

Body tissues auto-regulate to control the amount of oxygen passing through so that venous oxygen tensions are little altered compared to breathing room air. Cardiac output falls by approximately 20% at 2 ATA by a reduction in heart rate, stroke volume remaining constant.

The only tissue unable to auto-regulate is lung parenchyma because it is directly exposed to added oxygen. It is, therefore, the lungs that first show signs of oxygen toxicity. After about six hours at 2 ATA, subternal discomfort is experienced which disappears rapidly on breathing room air. Most hyperbaric therapeutic regimes limit the treatment times to a maximum of two hours at 2 ATA and this exposure is without toxic side effects.

INDICATIONS FOR HYPERBARIC OXYGEN

The eminent physiologist J.S. Haldane said “It may be argued that such measures as the administration of oxygen are at best only palliative and are of no real use, since they do not remove the cause of the pathological condition. As a physiologist, I cannot for one moment agree with this reasoning. The living body is no machine, but an organism constantly tending to revert to the normal and the respite afforded by such measures as the temporary administration of oxygen is not wasted, but utilised for recuperation.

The mistake is often made of not grasping the serious, widespread, and lasting effects caused by the want of oxygen...”

And on another occasion: “A lack of oxygen does not simply involve stoppage of the engine, but also the total ruin of what we took to be machinery.”
MECHANISM OF ACTION OF HBO

**Direct oxygenation**
HBO provides immediate support for poorly perfused tissues. This interim measure maintains tissue viability until a new blood supply develops or vascular surgery can establish adequate blood supply.

**Vasoconstriction**
Hyperbaric oxygen is a potent vasoconstrictor. However the reduction in blood flow caused is exceeded by the oxygen's ability to dissolve in the blood stream and diffuse into tissue fluids. The latter is particularly valuable in thermal burns and crush injury when there is significant vascular damage. Vaso-constriction reduces blood flow and the intracapillary hydrostatic pressure. This results in a reduction in tissue extracellular water and hence oedema.

**Superoxide Free Radical formation**
This has been shown to enhance white cell phagocytosis and the killing of bacteria, part of the rationale behind the use of hyperbaric oxygen in chronic osteomyelitis.

**Neovascularization**
The delayed and beneficial effect of hyperbaric oxygen some 7-14 days after therapy is the formation of new blood vessels and new collagen. This enhances the acceptance of skin grafts and flaps especially in compromised tissues such as radiation necrosis, infection, ischaemic lesions and diabetic ulcers. The induction of osteoneogenesis at a hypoxic fracture site may be of value in the management of non-healing fractures.

Hyperoxygenation increases the amount of physically dissolved oxygen in the fluids of plasma and tissue and is directly proportional to the partial pressure of inhaled oxygen. At 3 ATA there is a fifteen fold increase in dissolved oxygen, sufficient to meet the basal metabolic oxygen requirements without haemoglobin borne oxygen. Hyper-oxygenation also helps to drive oxygen across partial barriers such as the intracellular and interstitial oedema associated with many disease and trauma events.

Hyperbaric oxygen causes vasoconstriction by a direct action of an increased partial pressure of oxygen upon the blood vessels, reducing blood flow by about 20%. This vasoconstrictive effect may seem to be undesirable but the net effect is maintenance of tissue oxygenation, reduced capillary blood pressure, and a decrease in transudation of fluid into the interstitial space.

**CLINICAL USES OF HBO**

**Wound healing**
Why does breathing a high concentration of oxygen for only one or two hours a day influence the recovery of hypoxic tissues? Healing is oxygen dependent and it is reasonable to assume that damaged tissues have impaired oxygen delivery. Trauma disrupts capillary blood flow and causes oedema, increasing the distance oxygen has to travel from capillary to tissue cell. In inflammation, the unit volume of blood flow may be increased many fold but because of the invasion of oxygen demanding inflammatory cells into an oedematous region there is likely to be a central anoxic area. Not only does this threaten cell viability but it also reduces the activity of macrophages and denies the oxygen necessary for the killing of micro-organisms by the intracellular liberation of oxygen (O₂) free radicals. Oxygen reduces permeability and resolves oedema for longer than the time spent breathing it at high pressure. This is analogous to intermittent drug administration. Interest in the pathology of O₂ free radicals has grown dramatically over the last decade and pulmonary oxygen toxicity is widely recognised as a complication of increasing the inspired oxygen. However oxygen deficiency initiates the generation of intermediate metabolic products that cause the formation of O₂ free radicals. Therefore, the faster the relief of hypoxia the less tissue damage there is from free radical formation.

<table>
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<tr>
<th>Reaction</th>
<th>Effect</th>
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<tr>
<td>Reduces size of gas emboli</td>
<td>Replaces air emboli with oxygen which is easily removed</td>
</tr>
<tr>
<td>Displaces carbon monoxide from haemoglobin</td>
<td>Displaces carbon monoxide from mitochondrial cytochrome oxidase</td>
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<tr>
<td>Antagonises lipid peroxidation by improving oxygen delivery to cells</td>
<td>Reduces cerebral oedema</td>
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<tr>
<td>Improves oxygen carriage in cyanide poisoning (cyanide antidote is sodium nitrate which forms methaemoglobin reduces oxygen transport)</td>
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Fig. 1 - HBO: rationale for its use

**Osteomyelitis**
Apart from the vascular effects of hypoxia, there are other important forces at work. Hypoxia interferes with several cellular functions. The proliferation of fibroblasts and the production of collagen to support capillary angiogenesis are impaired. Although leucocytes migrate into relatively ischaemic and hypoxic tissue, oxidative killing of bacteria by the leucocyte is impaired by hypoxia.

Elevation of the oxygen tension in the wound to a normal or above normal level enhances the bactericidal potential of the leucocytes.

The standard treatment of osteomyelitis includes surgical debridement of devitalized tissues with administration of antibiotics. Treatment failures are attributed to a combination of factors: persistent necrotic infected debris, inadequate antibiotic levels at the primary site, failure to obliterate surgical dead space, oedema and hypoxia. Hyperbaric oxygen is helpful in minimizing oedema and hypoxia.

Necrotic bone and oedema provide a mechanical barrier through which oxygen may not be able to penetrate. In the patient with diabetes thickening of the capillary basement membrane and functional abnormalities of the vascular endothelium may further increase the distance for oxygen transfer.

The phagocytic leucocyte functions as the first line of defence against bacterial invasion. Although the ingestion of bacteria can be an anaerobic function, effective killing of the pathogen requires oxygen as substrate. When adequate levels of oxygen are present it is converted by the leucocyte into the high energy radicals that are toxic to bacteria. A minimal partial pressure of 30mmHg has been describe as necessary for active bacterial killing. Under normal air breathing
circumstances the partial pressure in bone is about 45mmHg. In the osteomyelitic bone the pressure falls to approximately 212mmHg, below the critical level for bacterial killing. In 100% oxygen at 2 ATA the partial pressure of oxygen in infected bone increases to 104mmHg and 321mmHg in normal bone. Hyperbaric oxygen helps in the eradication of bacteria in chronic osteomyelitis.

Cutaneous ulcers
Leg ulcers are a common problem of old age. Current estimates indicate that there are 600,000 people in this country suffering from chronic leg ulceration. Of these some 25% are refractory to current clinical management. It is calculated that each District Authority spends £4.875 million in the treatment of chronic ulcers.

It is generally accepted that hypoxia resulting from ischaemia and oedema is the major complicating factor retarding wound healing. Ischaemia causes profound changes in the microcirculation. The low amount of oxygen delivered to the tissue results in damage to the lining of the blood vessel so that fluid escapes and oedema is formed. The oedema causes compression of the capillary bed impairing local circulation, inducing hypoxia and further enhancing the ischemia. Much of the effort in healing or controlling leg ulcers is aimed at these underlying causes using compression bandages, elevation and dressing. Any deficiency in blood supply can be improved with pharmacological agents and surgical procedures. Despite this approximately 25% of the leg ulcer population suffer from long term chronic wounds not responding to standard management techniques.

Immunosuppression
In hypoxic conditions leukocyte activity is diminished thus compromising host defence mechanism. It has been shown that increasing the inspired oxygen fraction produces significant decrease in bacterial numbers. It is also clinically demonstrated that hyperbaric oxygen has a role in combating certain anaerobic infections acting directly against such organisms. Hyperbaric oxygen has a role in bacterial clearance and host defence.

HBO can have both a stimulator and depressant effect upon the immune system. Prolonged HBO 2 ATA for 5 hours stimulates the thymus and increases T lymphocyte production. At 5 ATA for 30 minutes oxygen toxicity reduces cellular production. In the main HBO stimulates lymphocyte production and improves the patient’s resistance to infection.

Haematological
The major function of the red blood cell is to transport haemoglobin which in turn carries oxygen from the lungs to the tissues. The normal RBC is deformable which allows it to traverse narrow capillaries. It must do this without stretching or rupturing the cell membrane. Hyperbaric oxygen increases the deformability of RBC and increases the RBC ability to traverse narrowed capillaries and improve tissue oxygenation. This effect occurs at HBO of 1 ATA and is associated with a drop in the haematocrit.

There are several changes in RBCs after exposure to HBO. There is a reduction in the haematocrit probably as a result of haemolysis. This haemolysis occurs because peroxidation of the phospholipid in the cellular membrane disrupts some RBCs.

HBO increases red blood cell sensitivity to hydrogen peroxide producing cells with an appearance similar to Vitamin E deficiency. The giving of vitamin E (which minimises the toxicity of hydrogen peroxide) may offer some protection against HBO haemolysis.

Reduced haematocrit
As already stated enough oxygen can be dissolved in plasma to support life. Animals have been kept alive in hyperbaric oxygen with virtually no haemoglobin, their complete recovery achieved with reinfusion of blood.

The average blood volume of a normal adult is 5000ml. After an acute haemorrhage plasma is replaced within 1-3 days, but a low concentration of red blood cell persists. In chronic blood loss (where a person cannot compensate) the haemoglobin falls to very low levels. The decrease in the viscosity of the blood lowers the resistance to flow in the peripheral vessels. The peripheral vessel may dilate further due to the hypoxia. The main impact is an increase in cardiac output and increased work load upon the heart. This may be sustainable at rest but during exercise increased oxygen demand may lead to extreme tissue hypoxia and acute cardiac failure. The conventional treatment consists of red blood cell replacement and correction of the cause.

Intermittent HBO therapy at 2 ATA for 60-90 minutes has been used successfully in the management of severely anaemic patients. Patients with haemoglobin as low as 2-3 g/100ml have survived. Other supportive measures include iv fluids, iron and vitamins.

Haemolysis syndromes
Haemolysis of red cells can occur for a variety of reasons, some hereditary, other acquired. Hyperbaric oxygen has been successfully used to limit sickling in sickle cell disease by stabilising the cell membrane.

In congenital spherocytosis the red blood cells are rigid and less deformable than usual. The use of HBO is a relative contraindication because of the increased risk of haemolysis. However it has been used with success in the treatment of leg ulcers in patients with spherocytosis. It is recommended that the haemoglobin, haematocrit and vitamin E levels be closely monitored and indeed vitamin E supplementation is given.

Transplantation
Human organ transplantation is being performed with increasing frequency. Finding suitable donors and then transporting organs are two main problems. Hyperbaric oxygen has proven benefits in organ preservation. It maintains tissue oxygenation by diffusion, depresses cell metabolism at higher pressures and reduces cell oedema. Hypothermia is still the mainstay of organ preservation but HBO offers some additional advantages.

Gas emboli
Carbon monoxide poisoning
Smoke inhalation
Cyanide poisoning (especially associated with carbon monoxide poisoning)
Gas gangrene
Glue sniffing

Fig. 2 – HBO: absolute indications
Crepitant anaerobic cellulitis
Progressive bacterial synergistic gangrene
Necrotising fascitis
Non-clostridial myonecrosis
Osteomyelitis (refractory)
Radiation tissue damage (Osteoradionecrosis)
Skin flaps/grafts (compromised)
Burns
Diabetic ulceration
Venous stasis ulceration
Arterial ischaemic ulceration
Anaemia (Acute haemorrhage where blood and blood products refused)

Air or gas embolism
Carbon monoxide poisoning and smoke inhalation
Clostridial myonecrosis (gas gangrene)
Crush injury, the compartment syndrome and other acute traumatic ischaemia
Decompression sickness
Enhancement of healing in selected wound problems
Exceptional anaemia resulting from blood loss
Necrotising soft tissue infections (of subcutaneous tissue, muscle or fascia)
Refractory tissue damage
Compromised skin grafts and flaps
Burns

Fig. 3 – HBO as an adjunct to conventional medical and surgical therapy

COMPLICATIONS
Clinical experience has indicated there to be three main untoward effects of hyperbaric oxygen therapy. These are cerebral oxygen toxicity manifesting itself in seizure behaviour, barotrauma to the middle ear of pulmonary bullae and anxiety due to confinement within the chamber. These effects are virtually eliminated by use of oxygen pressures below the threshold for seizure and subject examination to select out those at risk of barotrauma. The use of premedicant anti seizure drugs is limited to only a few centres, their need reduced by the adherence to strict treatment protocols.

HYPERBARIC FACILITIES
Around England, Scotland, Wales, Northern Ireland and the Isle of Man there are 21 registered hyperbaric oxygen chambers. There are many more privately owned chambers. A few of the major league football clubs have small hyperbaric oxygen chambers which are used to enhance healing as a result of sports injuries.

There are, however, only 6 medically sited hyperbaric oxygen chambers, which are at:
Peterborough District Hospital, Peterborough
Whipps Cross Hospital, London
Monsall Hospital, Manchester
Royal Victoria Hospital, Newcastle
Craigavon Area Hospital, Ireland
Galway Regional Hospital, Ireland.

In 1990 647 patients received hyperbaric oxygen therapy around Great Britain. One hundred and fifty nine were for decompression sickness and most were treated in the non medical chambers; 30% of the patients were treated for ulcers and 18% for carbon dioxide poisoning.

The Peterborough hyperbaric chamber based in the Intensive Care Unit of the Peterborough District Hospital has a local catchment population of 230,000 which is enough to support 2 mono-place chambers 9am-5pm, 5 days a week at an estimated charge of £75 per hour therapy. It attracts emergency referrals for cases of carbon monoxide poisoning and smoke inhalation from the east of England, between north London and the Scottish border.

The population of the north western region excluding north Manchester and Liverpool is approximately 2.63 million and slowly expanding.

SUMMARY
Hyperbaric oxygen is a clinically proven, research supported and cost effective therapy option in the management of a wide range of medical disorders. It should be used in conjunction with other tried and tested standard treatment regimes.

I believe that there are sufficient cases between local patients and out of district referrals to support a single mono-place hyperbaric oxygen chamber in the Intensive Care Unit of the Royal Lancaster Infirmary.

References