

Clinical review

ABC of oxygen **Hyperbaric oxygen therapy**

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Over the past 40 years hyperbaric oxygen therapy has been recommended and used in a wide variety of medical conditions, often without adequate scientific validation of efficacy or safety. Consequently a high degree of medical scepticism has developed regarding its use. The Undersea and Hyperbaric Medical Society approves use of hyperbaric oxygen for a few conditions for which there is thought to be reasonable scientific evidence or well validated clinical experience. In these conditions early referral is essential.

Hyperbaric oxygen has been shown ineffective in diseases such as multiple sclerosis and dementia, but it continues to be used despite the risks of the treatment. For conditions where its use remains unproved—for example, rheumatoid arthritis, cirrhosis, and gastroduodenal ulcer—hyperbaric oxygen should be used only in the context of well controlled clinical trials.

Biochemical and physiological effects

At sea level the plasma oxygen concentration is 3 ml/l. Tissues at rest require about 60 ml of oxygen per litre of blood flow (assuming normal perfusion) to maintain normal cellular metabolism, although requirements vary between tissues. At a pressure of 3 atmospheres (304 kPa) dissolved oxygen approaches 60 ml/l of plasma, which is almost sufficient to supply the resting total oxygen requirement of many tissues without a contribution from oxygen bound to haemoglobin. This has advantages in situations such as carbon monoxide poisoning or in severe anaemia where difficult crossmatching or religious belief prevents blood transfusion.

Oxygen at 300 kPa increases oxygen tension in arterial blood to nearly 270 kPa and in tissue to about 53 kPa. This improves the cellular oxygen supply by raising the tissue-cellular diffusion gradient. The hyperoxia has potential benefits including improved angiogenesis. The formation of collagen matrix is essential for angiogenesis and is inhibited by hypoxia. In irradiated tissue hyperbaric oxygen is more effective than normobaric oxygen at raising tissue partial pressure of oxygen and promoting angiogenesis and wound healing. The healing process may also be helped in non-irradiated tissues with compromised perfusion, but this requires further validation.

The value of hyperbaric oxygen therapy in decompression illness and arterial gas embolism depends on the physical properties of gases. The volume of a gas in an enclosed space is inversely proportional to the pressure exerted on it (Boyle's law). At 300 kPa bubble volume is reduced by about two thirds. Any intravascular bubbles causing obstruction move to smaller vessels, which reduces extravascular tissue damage. Dissolution of the gas bubble is enhanced by replacing the inert gas in the bubble with oxygen, which is then rapidly metabolised by the tissues.

Availability and administration

Multiplace chambers are available in a few NHS hospitals (Aberdeen, Craigavon, Newcastle upon Tyne), Royal Navy centres, private units, police diving units, professional diver training schools, and sites associated with the North Sea oil industry. The United States has over 250 facilities.

Therapeutic uses of hyperbaric oxygen

Strong scientific evidence

Main treatment

Decompression sickness
Arterial gas embolism
Severe carbon monoxide poisoning and smoke inhalation

Adjunctive treatment

Prevention and treatment of osteoradionecrosis
Improved skin graft and flap healing
Clostridial myonecrosis

Suggestive scientific evidence

Adjunctive treatment

Refractory osteomyelitis
Radiation induced injury
Acute traumatic ischaemic injury
Prolonged failure of wound healing
Exceptional anaemia from blood loss

Cellular and biochemical benefits of hyperbaric oxygen

- Promotes angiogenesis and wound healing
- Kills certain anaerobes
- Prevents growth of species such as *Pseudomonas*
- Prevents production of clostridial alpha toxin
- Restores neutrophil mediated bacterial killing in previously hypoxic tissues
- Reduces leucocyte adhesion in reperfusion injury, preventing release of proteases and free radicals which cause vasoconstriction and cellular damage



Coronal section of magnetic resonance image showing brain lesions in diver with decompression illness

Advice on the nearest suitable UK unit and help to coordinate the management can be obtained from the Institute of Naval Medicine, Gosport (24 hour emergency number 0831 151523, daytime inquiries 01705 768026)

Often early treatment is essential for maximum benefit. This poses appreciable practical problems as severely ill patients may have to be transported long distances and may require intensive medical support, including mechanical ventilation, between treatment sessions. It is important to discuss the potential benefits and risks for each patient with the regional hyperbaric oxygen facilities.

Multioccupancy chambers are required for critically ill patients who require an attendant within the chamber and are usually used for acute problems. Monoplace chambers can be used to treat patients with chronic medical conditions. Hyperbaric oxygen is inhaled through masks, tight fitting hoods, or endotracheal tubes.

Inside the chambers pressure is usually increased to about 250-280 kPa, equivalent to a depth of 15-18 m of water. The duration of treatment varies from 45 to 300 min and patients may receive up to 40 sessions. Appropriate monitoring is essential during treatment, and facilities for resuscitation and immediate mechanical ventilation should be available.

Dangers of hyperbaric oxygen

The potential risks and risk-benefit ratio of hyperbaric oxygen have often been underemphasised in therapeutic trials. The side effects are often mild and reversible but can be severe and life threatening. In general, if pressures do not exceed 300 kPa and the length of treatment is less than 120 minutes, hyperbaric oxygen therapy is safe. Overall, severe central nervous system symptoms occur in 1-2% of treated patients, symptomatic reversible barotrauma in 15-20%, pulmonary symptoms in 15-20%, and reversible optic symptoms in up to 20% of patients.

Reversible myopia, due to oxygen toxicity on the lens, is the commonest side effect and can last for weeks or months. Epileptic fits are rare and usually cause no permanent damage. A suggested carcinogenic effect of hyperbaric oxygen has not been substantiated in extensive studies.

Pneumothoraces must be adequately drained before treatment with hyperbaric oxygen. Pulmonary oxygen toxicity with chest tightness, cough, and reversible falls in pulmonary function may occur with repeated treatment, particularly in patients exposed to high oxygen levels before treatment. Oxygen toxicity can be prevented in most tissues by using air in the chamber for 5 minutes every 30 minutes. This allows antioxidants to deal with free oxygen radicals formed during the hyperoxic period.

Therapeutic uses

Decompression sickness and arterial gas embolism

When divers surface too rapidly the partial pressure of nitrogen dissolved in the tissues may exceed the ambient atmospheric pressure sufficiently to form gas bubbles in the blood and the tissues. Although less common, rapid ascent to over 5500 m can result in high altitude decompression sickness.

Decompression sickness may produce mild problems such as rash or joint pain or be more serious with paralysis, confusion, convulsions, and ultimately death secondary to blockage of vital blood vessels. Hyperbaric oxygen is the main treatment, and its efficacy has been validated by extensive clinical experience and scientific studies. Recompression rapidly alleviates the symptoms, and tables are available to determine safe periods for subsequent decompression. Treatment should be started as soon as possible and given in sessions of 2-5 hours until the symptoms have resolved.

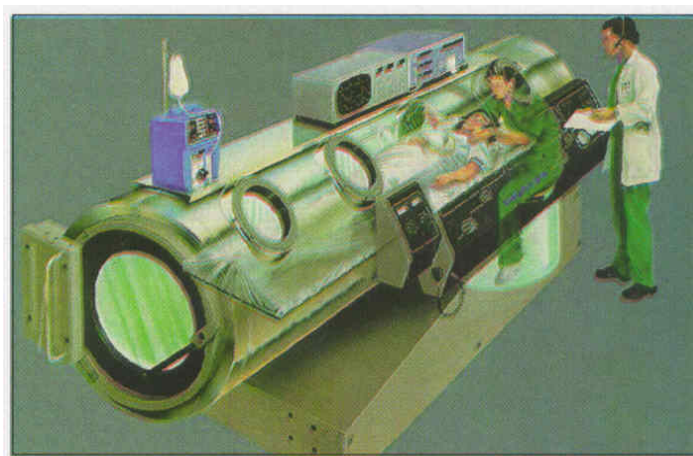
Comparison of monoplace and multiplace hyperbaric oxygen chambers

Monoplace

- Claustrophobic environment; limited access to patient
- Whole chamber contains hyperbaric oxygen, increasing fire risk
- Lower cost
- Portable

Multiplace

- More room; assistant can enter to deal with acute problems such as pneumothorax
- Hyperbaric oxygen via tight fitting mask—chamber gas can be air (reduced fire risk)
- Risk of cross infection when used for ulcers etc



Monoplace hyperbaric chamber

Risks of hyperbaric oxygen

Fire hazard

Most common fatal complication

General features

- Claustrophobia
- Reversible myopia
- Fatigue
- Headache
- Vomiting

Barotrauma

- Ear damage
- Sinus damage
- Ruptured middle ear
- Lung damage

Oxygen toxicity

- Brain
 - Convulsions
 - Psychological
- Lung
 - Pulmonary oedema, haemorrhage
 - Pulmonary toxicity
 - Respiratory failure (may be irreversible when due to pulmonary fibrosis)

Decompression illness

- Decompression sickness
- Pneumothorax
- Gas emboli

Air may also enter the circulation during placement of arterial and venous catheters, cardiothoracic surgery, haemodialysis, or mechanical ventilation. Although no formal trials support the use of hyperbaric oxygen in air embolism, the well established physical properties of gases and extensive clinical experience justify its use as the primary treatment. Treatment should begin immediately at pressures of 250-300 kPa for 2-5 hours. Benefit is reported when hyperbaric oxygen therapy begins several hours after the onset of air embolism but further trials are required to establish the delay after which hyperbaric oxygen is no longer of value.

Carbon monoxide poisoning

Carbon monoxide poisoning is an important cause of death from poisoning, particularly in the United States. Carbon monoxide binds to haemoglobin with an affinity 240 times that of oxygen. This reduces the oxygen carrying capacity of the blood. Unoccupied haemoglobin binding sites have an increased affinity for oxygen, further reducing the availability of oxygen to the tissues. In addition, carbon monoxide binds to the large pool of myoglobin increasing tissue hypoxia. Hyperbaric oxygen provides an alternative source of tissue oxygenation through oxygen dissolved in the plasma. It also facilitates dissociation of carbon monoxide from the haemoglobin and myoglobin; the carboxyhaemoglobin half life is 240-320 min breathing air, 80-100 min breathing 100% oxygen, and about 20 min with hyperbaric oxygen. In addition, hyperbaric oxygen dissociates carbon monoxide from cytochrome c oxidase, improving electron transport and cellular energy state.

Controlled studies comparing hyperbaric oxygen and normobaric 100% oxygen in the acute and delayed effects of carbon monoxide poisoning have produced conflicting results, although some benefit was seen in patients who experienced loss of consciousness or neurological abnormality.

If carbon monoxide poisoning results in unconsciousness, convulsions, neurological impairment (including abnormal gait or mental state test results) or severe metabolic acidosis the case should be discussed with the nearest regional centre. A single session of hyperbaric oxygen therapy will usually reverse the acute, potentially life threatening effects of carbon monoxide poisoning, but additional treatments may be needed to reduce the delayed neuropsychological sequelae. Patients with less severe poisoning should be treated with 100% oxygen.

Necrotising infections and osteomyelitis

The primary treatment of myonecrosis and gas gangrene of soft tissues resulting from clostridial infection and alpha toxin production is surgical debridement and antibiotics. However, experimental evidence and clinical experience suggest that adjunctive treatment with hyperbaric oxygen improves systemic illness and decreases tissue loss by demarcating the border between devitalised and healthy tissue. This reduces the extent of surgical amputation or debridement. Controlled trials of hyperbaric oxygen and normobaric 100% oxygen are not available. In necrotising fasciitis (rapidly progressive skin infection without muscle disease) retrospective studies suggest that hyperbaric oxygen is beneficial in combination with surgical debridement but prospective controlled trials are lacking.

Hyperbaric oxygen is also claimed to be helpful in refractory osteomyelitis. Animal experiments show improved healing of osteomyelitis compared with no treatment, but the effect is no better than that with antibiotics alone and the two treatments have no synergistic effect. Uncontrolled trials of surgery and antibiotics combined with hyperbaric oxygen in refractory osteomyelitis have reported success rates of as high as 85%, but controlled trials are needed.



Rash due to decompression illness

Symptoms of carbon monoxide poisoning

- Loss of consciousness
- Neurological abnormalities
- Myocardial ischaemia
- Pulmonary oedema
- Metabolic acidosis
- Headache
- Nausea
- Delayed neuropsychological features (often permanent)

The clinical severity of carbon monoxide poisoning does not correlate well with carboxyhaemoglobin concentrations



Gas gangrene

Post radiation damage

Soft tissue radionecrosis and osteonecrosis after surgery on irradiated mandibles are reduced by hyperbaric oxygen. In a controlled study comparing osteoradionecrosis at six months postoperatively, the incidence was 5% in patients receiving 30 preoperative hyperbaric oxygen treatments compared with 30% in patients who received only preoperative antibiotics. A similar improvement in wound healing after surgery has been shown in patients with irradiated tissue who receive preoperative hyperbaric oxygen therapy. Normobaric 100% oxygen does not seem to confer the same benefits. The higher partial pressures achieved with hyperbaric oxygen may stimulate new vessel growth and healing in damaged irradiated tissue which has lost the capacity for restorative cellular proliferation.

Skin grafts, flaps, and wound healing

In poorly vascularised tissue hyperbaric oxygen improves both graft and flap survival compared with routine postoperative surgical care alone. The effect of normobaric 100% oxygen was not examined in these studies. In the United States problem wounds are the commonest indication for a trial of adjunctive hyperbaric oxygen therapy and include diabetic and other small vessel ischaemic foot ulcers. Several studies have shown improved healing and a lower incidence of amputation with 4-30 sessions.

Other indications

Hyperbaric oxygen has been used successfully to treat haemorrhagic shock in patients who refuse blood on religious grounds or for whom suitable blood was not available. Similarly, there is evidence for benefit in acute traumatic ischaemic injuries including compartmental syndromes and crush injuries.

Conditions which do not benefit

Hyperbaric oxygen has been tried in numerous conditions and is often reported to be beneficial. However, in many of these situations the scientific evidence is flimsy and use should be restricted to randomised controlled trials. Hyperbaric oxygen has been clearly shown not to be beneficial in several diseases including multiple sclerosis and senility.

The suggestion that hyperbaric oxygen may be beneficial in multiple sclerosis arose from animal work suggesting that it improved experimental allergic encephalomyelitis and several uncontrolled studies suggesting disease remission in humans with multiple sclerosis. In 1983, a small controlled trial reported significant benefit, and large numbers of patients with multiple sclerosis were treated with hyperbaric oxygen. Since this initial trial at least 14 trials, of which eight are high quality randomised controlled studies, have been published. In the eight high quality studies the patients had chronic stable or chronic progressive multiple sclerosis, had at least 20 sessions of therapy for 90 minutes over four weeks, and were adequately assessed with evoked potentials and for functional and disability state. Only one study showed a benefit from hyperbaric oxygen.

No convincing evidence exists for using hyperbaric oxygen in thermal burns. In the only randomised controlled trial of hyperbaric oxygen and usual burn care the length of hospital stay, need for autografting, and mortality were virtually identical with both treatments.

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To prevent mandibular osteonecrosis after surgery on irradiated facial and neck tissue 30 preoperative 90 minute sessions and 10 postoperative sessions are recommended

Hyperbaric oxygen should be considered for problem wounds if the facility is readily available



Necrotic heel of diabetic patient before and after 14 weeks of hyperbaric oxygen therapy

Summary

- Lack of randomised controlled trials makes it difficult to assess the efficacy of hyperbaric oxygen in many diseases
- Side effects are usually mild but can be life threatening
- Clear evidence of benefit has been found in decompression sickness and a few other conditions
- Much work remains to be done to establish the timing, indications, and therapeutic regimens required to obtain the best clinical and cost effective results
- The cellular, biochemical, and physiological mechanisms by which hyperbaric oxygen achieves beneficial results are not fully established

The pictures of the hyperbaric chamber and necrotic heel of diabetic patient were downloaded from the internet with permission from Proteus Hyperbaric Systems. The picture of gas gangrene was downloaded with permission from St Joseph Medical Center, Fort Wayne, Indiana, USA

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