Current indications for hyperbaric oxygen therapy

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ALTHOUGH THE APPLICATION OF COMPRESSED GAS in medicine had its origins centuries ago, it is only in the last 40 years that good science has existed to support some of its current applications. A lack of soundly constructed scientific research, overenthusiastic reactions to isolated cases, public pressure and financial issues have all contributed to the scepticism which has influenced the acceptance of hyperbaric oxygen therapy into mainstream medicine.

This review provides a brief outline of the history, physiological basis, current indications and side effects of hyperbaric oxygen (HBO) therapy.

History

Hyperbaric air

The concept of using respirable gases at raised ambient pressures in the treatment of illnesses dates back three centuries. In 1662 hyperbaric air was used by Henshaw, a British clergyman, for the treatment of "affections of the lung".[1] However, on considering the apparatus used at the time, it seems likely that the reported benefits were a placebo effect.[2]

In 1834 Junod, in France, built a chamber to treat pulmonary conditions at pressures between 2 and 4 atmospheres absolute (ATA). Over the next one hundred years "pneumatic centres" were established in various European cities and in the USA. Hyperbaric air was used to treat a wide variety of ailments, including lung infections, cardiac disease, carcinomas, diabetes, and dementia, and was used as an aid to surgery, providing "deeper anaesthesia and less cyanosis".[3] By the 19th century "hyperbaric centres" had begun to develop a reputation in competition with "health spas".[4]

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Synopsis

- Hyperbaric oxygen (HBO) therapy has a long history, but there is a lack of scientific evidence for some of its past applications.
- The Undersea and Hyperbaric Medical Association has published guidelines for the clinical indications and appropriate use of HBO therapy.
- HBO therapy greatly increases the oxygen concentration in plasma, reducing the need for haemoglobin in blood oxygen transport.
- HBO has bacteriostatic or bactericidal effects, and has positive effects on the physiology of tissue rendered ischaemic by trauma or infection.
- The main conditions for which HBO therapy is indicated are decompression sickness, air or gas embolism, carbon monoxide poisoning and gas gangrene.
- HBO may be indicated for the treatment of crush injury, compartment syndrome, delayed radiation injury, exceptional blood loss, compromised skin grafts and flaps, necrotising soft tissue infections, intracranial abscess, actinomycosis and thermal burns.

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Orval J Cunningham, a professor of anaesthesia at the University of Kansas in the early 1900s, is regarded as being the last exponent of compressed air therapy.[2,5] His observations that people with heart disease and other circulatory disorders did poorly at altitude and improved at sea level formed the basis for his use of hyperbaric air.[6] In 1918 he successfully treated sufferers of the Spanish flu epidemic with hyperbaric air. He went on to build the largest ever-constructed hyperbaric chamber (Box 1). In 1930 the American Medical Association forced him to close the centre due to his refusal or inability to provide any scientific evidence for his treatments.[7] In 1937 his "steel ball hospital" in Cleveland was sold for scrap metal.

Hyperbaric oxygen

Oxygen was discovered in 1775 by an English scientist, Joseph Priestley, who called it "dephlogisticated air".[4] However, shortly after its discovery, reports of toxic effects of HBO on the central nervous system and lungs[8,9] were enough to prevent its formal application under pressure until 1937, when it

was first used in the treatment of decompression illness by Behnke and Shaw.

The application of HBO in clinical medicine really began with separate work done by Churchill-Davidson and Boerema in 1955 and 1956. Churchill-Davidson, in the UK, used it to enhance the radiosensitivity of tumours.[10] Ite Boerema, Professor of Surgery at the University of Amsterdam, successfully used it in cardiac surgery to prolong the time allowed for cross-clamping of the major vessels.[11]

In 1961 W H Brummelkamp et al. (also at the University of Amsterdam) published work on the use of HBO in the treatment of anaerobic infections (clostridial gas gangrene).[12] In 1962 Smith and Sharp reported success in the treatment of carbon monoxide poisoning with HBO in Glasgow, Scotland.[13]

Throughout the 1960s, enthusiasm for the use of HBO grew, as it had a dramatic impact in the areas of cardiac surgery, carbon monoxide poisoning and gas gangrene. Many chambers were established across North America and Eurasia. As the number of chambers and excitement for the treatment grew, many centres began to treat a wide range of ailments with HBO on the basis of very little scientific evidence or rationale. Often it was used to treat conditions that failed to respond to conventional therapies, such as senility, stroke, arthritis, and emphysema.

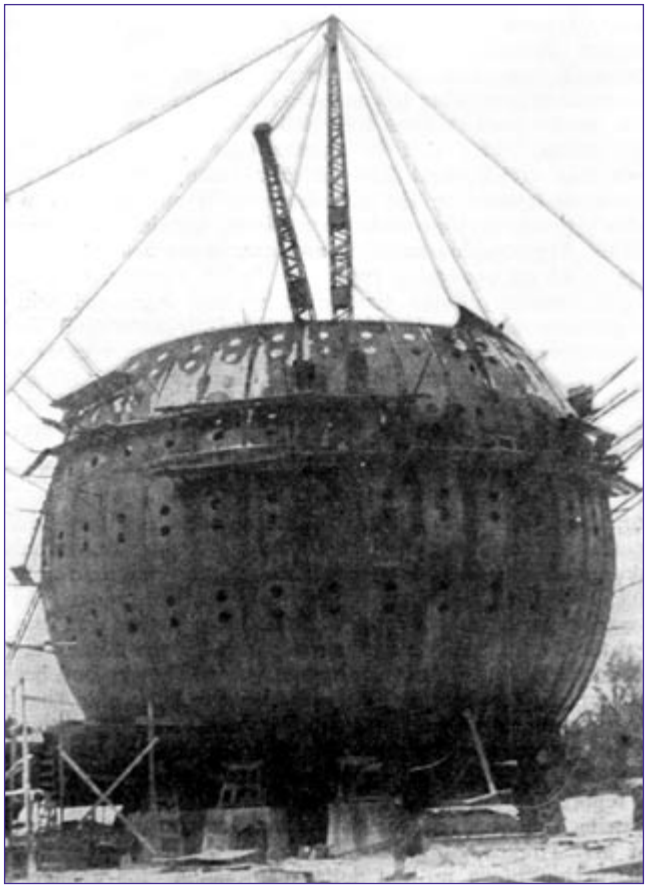
In the early 1970s huge progress was made in the development of cardiopulmonary bypass equipment and hence the requirement to perform cardiac surgery under hyperbaric conditions declined. Cardiac surgeons had been some of the most energetic promoters of the use of HBO. As these early pioneers left the field of hyperbaric medicine so did much of the enthusiasm for extensive and high quality research.

By the late 1970s there was growing concern in the USA by both hyperbaric and general physicians that HBO was being applied indiscriminately, that there was a lack of scientific progress in the field and that there was no regulatory body. These concerns led the Undersea Medical Society (UMS), which had been originally formed in 1967 by US Navy medical officers with an interest in Diving and Submarine Medicine, to form an ad hoc Committee on Hyperbaric Oxygenation.[2] This committee has become the internationally recognised authority on accepted indications for HBO. It regularly updates and publishes its list of accepted indications and discriminates between those conditions that are approved for treatment and those that are supported by sound scientific theory but are still requiring research. The UMS is now known as the UHMS (Undersea and Hyperbaric Medical Society).

Internationally, there is some variation between centres in the lists of conditions that are accepted as being appropriate for HBO therapy. Some conditions are undeniably appropriate for HBO therapy, but others are accepted for treatment in the setting of controlled clinical trials or on the merits of the individual case.

The lack of sound scientific evidence of the efficacy of HBO has bred uncertainty in the wider medical community regarding its legitimacy. HBO therapy has been described as "a therapy in search of diseases".[14] However, in the last three decades a greater understanding of the mechanisms of action of HBO has developed through clinical experience, animal studies and clinical trials.

1 Hyperbaric hubris



Five stories high and 64 feet in diameter, this gigantic hyperbaric chamber in Cleveland, Ohio, was commissioned by Dr Orval Cunningham in partnership with a businessman who anticipated healthy profits from the treatment of diabetes and other diseases. Shown here under construction in 1928 (a photograph published in *JAMA* and newspaper publicity of the day),[7] the chamber was scrapped two years later.

Mechanisms of action

The clinical benefits of hyperbaric oxygen can be explained theoretically by the mechanical effects of pressure and the physics of gas laws, the physiological and biochemical effects of hyperoxia, and also through the reversal of local hypoxia in target tissues.

At sea level the dissolved oxygen concentration in plasma is 3 mL/L.[15,16] At rest normally perfused tissue requires about 60 mL of oxygen per litre of blood. At 3 ATA the dissolved oxygen concentration rises to about 60 mL/L,[16] sufficient to

supply the tissue oxygen requirement without resort to the oxygen carried by haemoglobin.[2] Hence, the benefits of HBO are obvious in pathologies involving haemoglobin, such as carbon monoxide poisoning and severe anaemia (including patients who refuse transfusions on religious grounds).

Box 2 lists the effects of high partial pressures of oxygen on various organs, tissues and biochemical reactions. The effects are multiple and often complex. Some are described briefly below. They assume varying degrees of importance depending on the disease processes involved and their application in some specific indications is discussed later.

HBO therapy exerts both direct and indirect effects against bacteria. Direct bactericidal and bacteriostatic effects occur through the generation of oxygen free radicals. These free radicals oxidise proteins and membrane lipids, damage DNA and inhibit metabolic functions essential for the growth of organisms. The susceptibility of anaerobes to HBO is enhanced by their lack of adequate antioxidant defences. Facultative anaerobes are able to resist the toxic effects of oxygen exposure by increasing their synthesis of antioxidant enzymes.[17]

The indirect effect of hyperbaric oxygen in bacterial killing is through improving leucocyte function and is regarded as being more significant than the direct bactericidal and bacteriostatic effects.[18,2] Neutrophils require oxygen as a substrate for microbial killing, after phagocytosis occurs. Hypoxia reduces this function. Significant reductions in the killing capacity of leucocytes occur when tissue Po_2 falls below 30 mmHg.[19] Infected and traumatised tissues often have a partial pressure of oxygen below this, making them much more susceptible to infection due to the decrease in neutrophil activity.[2] Hyperoxia and HBO also influence the activity of some antibiotics, enhancing the effectiveness of some and inhibiting others.[2]

The formation of collagen matrix, and hence angioneogenesis and wound healing, is highly dependent on the presence of adequate amounts of oxygen.[30-32] Wound healing is a complex process and involves the interaction of many cell types and biochemical mediators. HBO increases tissue oxygenation and amplifies the oxygen gradient along the periphery of ischaemic wounds. This oxygen gradient has been demonstrated to be an important stimulus to angioneogenesis and wound healing.[34] Healing is both faster and stronger in hypoxic wounds when treated with HBO.[30] Intermittent increases in tissue oxygen tensions have been shown to optimise fibroblast proliferation and stimulate angioneogenesis.[33,34] HBO given at 2.5 ATA for 3 sessions of 2 hours was shown to produce an increase in the bursting strength and to stimulate angiogenesis in the early stages of healing of incisions in rats.[35] In animal models, it has also been demonstrated that the quantity and size of blood vessels in skin flaps was significantly increased when treated with HBO.[36]

Reperfusion injury contributes to the worsening of crush injuries, compartment syndromes and the failure of skin flaps, grafts and reattachment procedures. Neutrophils have been implicated as a major contributor in this pathological process.[37] By adhering to the walls of ischaemic tissue they release proteases and produce free radicals, which leads to pathological vasoconstriction and extensive tissue destruction.[38] Various mechanisms have been thought to be responsible for the benefit of HBO therapy in reperfusion injury. These include HBO's effect of promoting the generation of scavengers to detoxify tissue from radicals, preventing lipid peroxidation of cell membranes,[39] and promoting the sequestration of leucocytes in the lungs, thereby preventing their accumulation in the injured tissue.[40] Hyperbaric oxygen inhibits neutrophil adherence and post-ischaemic vasoconstriction in ischaemic rat tissue.[37,40]

Hyperoxia has been shown to decrease blood flow in limbs[41] and the cerebral circulation[42] in man. HBO in man also decreases cardiac output by 24%–35% and increases afterload by 30%–60%.[43] Studies in rats have demonstrated that HBO decreases blood flow to myocardium, kidney, brain and splanchnic areas.[44,45]

These changes in haemodynamics and reduced blood flow to organs do not, however, compromise the oxygenation of healthy tissues, as this is compensated for by an increase in the oxygen dissolved in plasma.[2,46] Hypoxic and diseased tissue has been shown not to demonstrate this same vasoconstrictive

2 Some physiological and biochemical effects of hyperoxia

- Suppression of alpha-toxin production by *Clostridium perfringens*[20]
- Bactericidal for *Clostridium perfringens* in vitro[21,22] and in vivo (mice).[23] (Bactericidal for others, but mostly only at pressures and durations of oxygen exposure greater than are safe to be used in clinical practice.)[2]
- Bacteriostatic for some species of *Escherichia* and *Pseudomonas*,[24-26] and also for a range of enteric bacteria (*Salmonella, Shigella and Proteus*).[27]
- Improved leucocyte killing activity.[19,28,29]
- Promotion of fibroblast proliferation, collagen formation and angioneogenesis in problem wounds, flaps and irradiated tissues.[30-36]
- Reduced falls in adenosine triphosphate (ATP) and phosphocreatinine levels in burns and post-ischaemic tissue.
- Decreased white cell adherence to capillary walls.
- Vasoconstriction in normal blood vessels.
- Decreased post-traumatic tissue oedema.
- Reduced half-life of carboxyhaemoglobin, improved dissociation of carbon monoxide from cytochrome-c oxidase and prevention of neuronal injury in carbon monoxide poisoning.
- Decreased lipid peroxidation.

reaction,[2] and in fact blood flow in the microcirculation of ischaemic tissue has been found to be significantly improved by HBO.[40,47] With HBO, vasoconstriction does not reduce local tissue oxygenation but does reduce posttraumatic tissue oedema.

In experimental models, HBO reduced oedema formation by about 20% and necrosis by 50% in injured muscle.[48] Nylander et al. showed a significant reduction in postischaemic oedema with HBO in rats.[49] This anti-oedema benefit of HBO contributes to its benefit in the treatment of crush injuries, compartment syndrome and burns.[50]

ATP production is vital for the maintenance of cell membranes and the transport of ions and molecules across cell membranes. In burn injury and ischaemic injury, the production of ATP falls, as its production is highly dependent on oxygen. HBO has been shown to reduce the fall in ATP after ischaemia and reduce the lactate accumulation in ischaemic tissue.[51-53]

Lipid peroxidation is believed to be one of the main processes involved in neuronal damage following ischaemic–hypoxic injury and exposures to drugs and poisons.[2] Thom, in his study of rats and CO poisoning, concluded that HBO exposure over 2 ATA prevented lipid peroxidation.[53]

Indications

Box 3 lists the currently accepted indications for the use of HBO. The clinical evidence supporting some of these indications is described below. For a more comprehensive examination of others, I recommend Kindwall[2] and the UHMS committee report[55] as further references.

Decompression illness and arterial gas embolism

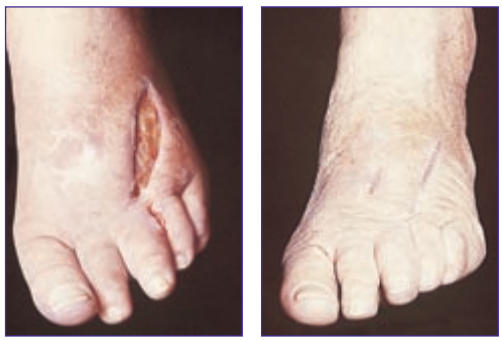
Decompression illness and arterial gas embolism occur when bubbles form in blood vessels and tissues. Largely a disease of divers, decompression illness or arterial gas embolism can also occur in persons exposed to altitude, iatrogenically and through other miscellaneous causes (eg, aircrew and parachute training in hypobaric chambers, mechanical ventilation, central venous catheterisation, cardiothoracic surgery and vaginal insufflation in pregnant women during orogenital sex).[56-58] Other factors which are known to predispose individuals to decompression illness include dehydration and hangovers, recent injury, heavy physical exercise at depth and cold exposure. These are thought to contribute through influences on gas uptake and elimination.

Bubbles deform tissues and obstruct blood vessels and also exert biochemical effects at the blood–gas interface, leading to alterations in haemostasis, endothelial damage and activation of leucocytes.[59,60] Patients can present with symptoms ranging from rash to paraesthesia, joint pain, paralysis, seizures and coma.

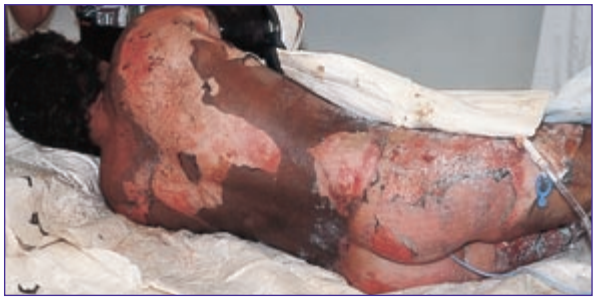
The laws of Boyle, Henry and Dalton explain some of the pathology of this bubble formation and the benefits of HBO in its treatment. In simple terms, with exposure to increasing pressures the amount of nitrogen dissolved in tissues increases in accordance with Henry's law. Rapid ascents in

3 Indications for hyperbaric oxygen therapy approved by the Undersea and Hyperbaric Medical Society[55]

1 Air or gas embolism
2 Carbon monoxide poisoning and smoke inhalation; carbon monoxide poisoning complicated by cyanide poisoning
3 Clostridial myositis and myonecrosis (gas gangrene)
4 Crush injury, compartment syndrome, and other acute traumatic ischaemias
5 Decompression sickness
6 Enhancement of healing in selected problem wounds
7 Exceptional blood loss (anaemia)
8 Intracranial abscess, actinomycosis
9 Necrotising soft tissue infections
10 Osteomyelitis (refractory)
11 Delayed radiation injury (soft tissue and bony necrosis)
12 Skin grafts and flaps (compromised)
13 Thermal burns



Problem wound:
(Left) chronic infection, 8 months of discharging sinus. Nocardia brasiliensis *cultured. No improvement with surgical debridement and high dose antibiotic therapy.*
(Right) Complete resolution of wound with 19 HBO treatments (1 hour at 18 m pressure [1.8 bar] with 30 minute ascent to surface pressure).



Severe burns treated with HBO.

diving and hypobaric exposures cause the partial pressure of nitrogen dissolved in solution to exceed the ambient pressure. This causes it to bubble in the blood and tissues.

In accordance with Boyle's law, increasing the ambient pressure reduces the size of the bubble and also changes its shape. Recompression to 3 ATA reduces the length of cylindrical bubbles by two-thirds. As 100% oxygen is breathed, the inert gas within the bubble is gradually exchanged with oxygen which can be metabolised, further reducing bubble size. As the size of the bubble decreases, the surface tension forces eventually exceed the pressures within the bubble and it collapses. In addition to the mechanical benefits of HBO therapy, it may also aid in counteracting the interaction of the bubble with vessel endothelium, and platelet and leucocyte activation.[61,62]

Extensive clinical experiences over the last 50 years and some clinical trials have established HBO therapy as the mainstay of treatment for decompression illness and arterial gas embolism.[63] Series published by Kizer and Green in the 1980s show that recompression to between 3 and 6 ATA is the most reliable and effective treatment for decompression illness.[64,65] Extensive studies by the US Navy,[2] and clinical trials such as those by Guyatt et al[66] and McLeod et al,[67] have also demonstrated its efficacy.

Carbon monoxide poisoning

Carbon monoxide is the product of the incomplete combustion of hydrocarbons. Carbon monoxide is a normal product of the catabolism of haemoglobin and a level of 1%–3% can be detected in normal people.[68] Blood carboxyhaemoglobin (COHb) levels can reach 10%–15% in smokers.[69] Sources of exogenous carbon monoxide that cause poisoning include motor vehicle exhausts; the burning of charcoal, wood, kerosene and gas; and methylene chloride, a paint stripper which when absorbed into the body is metabolised by the liver to produce carbon monoxide.[70,71]

Carbon monoxide toxicity is the result of both tissue hypoxia and its interference with cellular metabolism. Carbon monoxide binds to haemoglobin with an affinity 200 to 250 times greater than oxygen.[72] The resulting decrease in arterial oxygen content and the shift of the oxygen–haemoglobin dissociation curve to the left[73] explains the acute hypoxic symptoms seen in carbon monoxide poisoning (Box 4). However, the delayed neurological sequelae (Box 5) cannot be accounted for by this process alone and research suggests that carbon monoxide is also toxic through its intracellular uptake. In rats it has been shown to cause lipid peroxidation, leading to reversible demyelinisation of central nervous system lipids,[74] and to cause mitochondrial dysfunction by binding to cytochrome oxidase.[75] Platelets and vascular endothelial cells have also been shown to release free radicals when damaged by carbon monoxide exposure.[76]

HBO has a dramatic effect on the half-life of carboxyhaemoglobin, shortening it to less than 30 minutes, compared with 4–6 hours when breathing room air.[78] However, it is unlikely that this effect is entirely responsible for the clinical benefit of HBO, as levels of carboxyhaemoglobin do not correlate well with the clinical picture. Other studies in animals have shown that HBO accelerates the dissociation of carbon monoxide from cytochrome oxidase and induces a more rapid return to the normal energy state of cells,[75] reduces brain lipid peroxidation,[79] inhibits white cell adhesion in brain injury from carbon monoxide poisoning,[80] and prevents intracranial hypertension in carbon monoxide poisoned rats.[81]

It is not known whether these laboratory benefits of HBO correlate directly with improvements in the outcome of patients treated with HBO, as few clinical trials have been reported and those in the literature are often technically flawed and have results which are conflicting.[70,71,82,83] One of the central questions debated is whether HBO has any benefit over normobaric oxygen in the treatment of carbon monoxide poisoning.[84] Despite the controversy that exists, and on the basis of decades of clinical experience and some of the published evidence, HBO therapy is still recommended by most experts in the field and especially when certain clinical indications exist (Box 6). The decision to use hyperbaric oxygen should be made early, as it has been demonstrated that efficacy may decrease with delay, especially beyond six hours.[85]

4 Acute clinical manifestations of carbon monoxide poisoning

Dizziness	Ataxia
Headache	Tachycardia
Nausea	Tachypnoea
Vomiting	Coma
Confusion	Myocardial ischaemia
Blurred vision	Myonecrosis
Muscle cramps	Seizures
Abdominal pain	Dysrhythmias

Adapted from Tomaszewski,[70] Ernst and Zibrak,[71] and Meyers and Thom.[77]

5 Delayed neurological sequelae following carbon monoxide poisoning

Chronic headaches	Neurological deficits
Cognitive deficits	Movement disorders
Personality disorders	Parkinson's disease
Aphasia	Psychosis
Apraxia	Gait disturbances
Cortical blindness	

Adapted from Tomaszewski,[70] Ernst and Zibrak,[71] and Meyers and Thom.[77]

Necrotising infections

Clostridial myonecrosis (gas gangrene) is an anaerobic infection that occurs when clostridial spores germinate within the hypoxic environment of devitalised tissue. These organisms then produce toxins that are vasoactive and liquefactive, resulting in rapid and extensive tissue destruction. Contamination of traumatic wounds is the most common cause but it can follow a variety of major and minor medical procedures.[86]

HBO has become an accepted adjunct to the treatment of clostridial myonecrosis, despite a lack of randomised controlled clinical trials to support its use. Over 100 case reports and citations exist in the medical literature to support its use in this disease,[86] beginning with Brummelkamp et al in 1961,[12] who reported a benefit when HBO was used alone. Several clinical series reports were later published which showed the benefit of using surgery, antibiotics and HBO adjunctively.[86,87]

DeMello et al, in a study using dogs, showed that using surgery, antibiotics or HBO alone was not as effective as combining them.[88] Surgeons experienced in the field describe the clinical benefits of HBO in aiding demarcation of healthy from devitalised tissue (allowing for more conservative surgical procedures) and in reducing the systemic toxicity (allowing patients to better tolerate surgical procedures).[46,61]

Necrotising fasciitis is a progressive, generally rapidly spreading, inflammatory process located in the deep fascia, with secondary necrosis of subcutaneous tissues and skin. Haemolytic streptococci are thought to play a central role but other aerobes and anaerobes have been implicated. Mortality rates range from 30%–75%. Progressive bacterial gangrene is generally a slowly advancing infectious process involving the epidermis, dermis, subcutaneous tissue and hair follicles, but never the deep fascia. Bacterial synergism plays an important role but the cause can be anaerobic, aerobic or mixed.[89]

Because of the clinical similarities of these two conditions with clostridial myonecrosis, the treatment regimens advocated have also involved the use of HBO as an adjunct to surgery and antibiotics. Clinical evidence of its efficacy in these settings is mainly limited to reports of small case series and there are no randomised controlled clinical trials. In the treatment of Fournier's gangrene, Paty and Smith demonstrated that mortality and morbidity increase if one of the three modalities is excluded.[90] Eltorai et al reported no deaths among nine patients in whom HBO was added to the standard therapy.[91] Korhonen et al demonstrated in their retrospective clinical study that HBO reduced systemic toxicity, prevented extension of the necrotising infection, increased demarcation and reduced mortality.[92]

Other case series of necrotising fasciitis have demonstrated mortality rates of 12.5%–20% in patients treated with a combination of surgery, antibiotics and HBO.[93,94] Mader[95] and Riseman[96] reported significantly reduced mortality rates in groups treated with HBO compared with groups not treated with HBO. While prompt and aggressive surgical debridement remains the cornerstone of treatment, it is accepted that best results are obtained with the combination of surgery, antibiotics and HBO.[89]

Radiation-induced tissue injury / radionecrosis

When malignant tissue is irradiated, some degree of damage to normal tissue is unavoidable. The initial pathological process is a progressive, obliterative endarteritis. This eventually results in hypocellular, hypovascular and hypoxic tissue, which is more prone to breakdown when subsequently wounded or damaged. Radionecrosis can develop spontaneously in these tissues if the radiation dose has been high enough. HBO exerts its benefits in this disease through promoting angiogenesis and fibroplasia.

The effectiveness of HBO in radiation tissue injury has been validated through a series of randomised, prospective studies. Work done by Marx et al was instrumental in establishing the benefits of HBO via angiogenesis and fibroplasia.[97-100] In these and other studies, Marx et al demonstrated satisfactory surgical outcomes in over 90% of patients undergoing reconstructive and other surgical procedures on irradiated and radionecrotic tissue when treated with HBO before and after surgery. These results have been corroborated by others.[101-103]

6 Suggested indications for HBO in patients with carbon monoxide poisoning

- Coma
- Any period of unconsciousness
- Seizures
- Focal neurological deficits
- Carboxyhaemoglobin level >25% of haemoglobin level (or >15% in pregnancy)
- Cardiac ischaemia or arrhythmia
- Persistent neurological dysfunction after initial treatment with normobaric 100% oxygen for 2–4 hours.

Adapted from Tomaszewski,[70] Ernst and Zibrak,[71] and Meyers and Thom.[77]

Contraindications

Contraindications to hyperbaric oxygen therapy are listed in Box 7. When considering contraindications, the potential benefit should be weighed against the patient's condition and the potential side effects of treatment. The only absolute contraindication is untreated tension pneumothorax.

For a discussion of contraindications, Kindwall[104] is suggested as a reference.

Adverse effects

Adverse effects of HBO therapy can be thought of in two groups — those related to the effects of pressure on enclosed gas spaces and those related to the toxic effects of oxygen. Middle ear barotrauma is the most common complication of HBO therapy, with an incidence of about 2%.[105] Some patients require elective myringotomy or tympanostomy insertion. However, careful instruction in the autoinflation technique is usually enough to prevent middle ear barotrauma.

Inner ear barotrauma is a very rare occurrence, usually only occurring in the setting of a forced Valsalva manoeuvre. In an unconscious patient, tympanic membrane rupture would occur before the round or oval windows rupture. Inner ear barotrauma can result in permanent hearing loss, tinnitus and vertigo.

Sinus squeeze is the second most common complication of HBO therapy and causes pain on compression when the openings to various sinuses are blocked in the setting of a respiratory tract infection or rhinitis.[105] Treatment with decongestants can allow the HBO therapy to continue.

Air embolism and pneumothorax are very rare complications of HBO therapy. If they do occur, it is usually in patients with severe pre-existing lung disease.

Tooth pain can occur during compression or decompression and this typically follows dental work that has created an air space under a dental filling.

Reversible myopia is also observed in some patients undergoing HBO therapy. Its exact mechanism is unknown but is thought to be due to changes in the shape of the lens. Cataract formation has only been documented in patients receiving in excess of 100 treatments.[106]

Neurological oxygen toxicity lowers seizure thresholds, precipitating generalised seizures that are self-limiting once oxygen therapy is ceased and cause no permanent damage. It is a rare complication of HBO therapy, with a quoted incidence as low as 1.3 per 10 000 treatments.[105]

Pulmonary oxygen toxicity can occur in patients exposed to 100% oxygen at 1 ATA for prolonged periods. It is quicker to develop in patients receiving HBO therapy as well as high concentrations of oxygen between treatments. Symptoms are not produced in patients exposed to daily treatments within the limits of accepted treatment protocols.[55] Symptoms include retrosternal chest discomfort, chest tightness, dyspnoea and cough. These patients may also show significant reversible reductions in their forced vital capacity.[104]

Decompression illness as a result of HBO is highly unlikely in patients unless given air for prolonged periods of time. However, the risk for attendants who breathe chamber air is greater. The Royal Adelaide Hospital reported only two cases of decompression illness in chamber attendants from 3900 treatments between 1985 and 1991.[107] The risk of decompression illness in these subjects was minimised by administering 100% oxygen to attendants for the ascent to aid in the elimination of nitrogen from their tissues, and by limiting the number of dives in the chamber to one a day for each attendant. These safety practices are adopted by many hyperbaric units.

Fire is by far the most common fatal complication of hyperbaric oxygen therapy. Over the last 20 years (with millions of compressions worldwide) there have been 52 deaths reported, most due to inadequate fire precautions.[108]

7 Contraindications for HBO

Absolute

- Untreated tension pneumothorax

Relative

- Upper respiratory tract infection
- Emphysema with carbon dioxide retention
- Asymptomatic pulmonary lesions seen on chest x-ray
- History of thoracic or ear surgery
- Uncontrolled hyperthermia
- Pregnancy
- Claustrophobia
- Seizure disorder.

Conclusions

As with most areas of medicine, in hyperbaric medicine there is a constant struggle to balance enthusiasm for progress in the field with the need to apply it on the basis of established evidence. Consideration must be given to both the benefits and the risks of a therapy when contemplating its application in any clinical situation. Although HBO therapy is not without side effects, most specialists in the field consider the risk profile for patients acceptable when treating the conditions for which HBO is clearly indicated.

References

1. Simpson A. Compressed air as a therapeutic agent in the treatment of consumption, asthma, chronic bronchitis and other diseases. Edinburgh: Sutherland and Knox, 1857.
2. Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing Company, 1995.
3. Fontaine JA. Emploi chirurgical de l'air comprime. *Union Med* 1879; 28: 445.
4. Corning JL. The use of compressed air in conjunction with medical solutions in the treatment of nervous and mental affections, being a new system of cerebrospinal therapeutics. *Med Record* 1891; 40: 225.
5. Jain KK. Textbook of hyperbaric medicine. Toronto: Hogrefe & Huber, 1990.
6. Cunningham OJ. Oxygen therapy by means of compressed air. *Anesth Anal* 1927; 6: 64.
7. American Medical Association Bureau of Investigation. The Cunningham "tank treatment". The alleged value of compressed air in the treatment of diabetes mellitus, pernicious anaemia and carcinoma. *JAMA* 1928; 90: 1494-1496.
8. Bert P. La pression barométrique. *Recherches de physiologie expérimentelle* 1878: 579. Translated by Hitchcock MS, Hitchcock FA as: Barometric pressure. Bethesda, Md: Undersea Medical Society, 1978.

9. Lorrain-Smith J. The pathological effects due to increase of oxygen tension in the air breathed. *J Physiol* 1889; 24: 19-35.
10. Churchill-Davidson I, Sanger C, Thomlinson RH. High-pressure oxygen and radiotherapy. *Lancet* 1955; 1: 1091-1095.
11. Boerema I, Knoll JA, Meijne NG, et al. High atmospheric pressure as an aid to cardiac surgery. *Arch Chir Neerl* 1956; 8: 193-211.
12. Brummelkamp WH, Hogenijk J, Boerema I. Treatment of anaerobic infections (clostridial myositis) by drenching the tissue with oxygen under high atmospheric pressure. *Surgery* 1961; 49: 299-302.
13. Smith G, Sharp GR. Treatment of coal gas poisoning with oxygen at two atmospheres pressure. *Lancet* 1962; 1: 816-819.
14. Gabb G, Robin ED. Hyperbaric oxygen — a therapy in search of diseases. *Chest* 1987; 92: 1074-1082.
15. Boerema I, Meyne NG, Brummelkamp WK, et al. Life without blood: a study of the influence of high atmospheric pressure and hypothermia on dilution of blood. *J Cardiovasc Surg* 1960; 1: 133-146.
16. Lambertsen CJ, Kough RH, Cooper DY, et al. Oxygen toxicity: effects in man of oxygen inhalation at 1 and 3.5 atmospheres upon blood gas transport, cerebral circulation and cerebral metabolism. *J Appl Physiol* 1953; 5: 471-486.
17. Gregory EM, Fridorich I. Induction of superoxide dismutase by molecular oxygen. *J Bacteriol* 1973; 114: 543-548.
18. Adams KR, Roberts RM, Mader JT. In vitro killing of *Clostridium perfringens* by oxygen with and without polymorphonuclear leucocytes [abstract]. *Undersea Biomed Res* 1990; 17 Suppl: 123.
19. Hohn DC, MacKay RD, Halliday B, Hunt TK. The effect of oxygen tension on the microbial function of leucocytes in wounds and in vitro. *Surg Forum* 1976; 27: 18-20.
20. van Unnik AJM. Inhibition of toxin production in *Clostridium perfringens* in vitro by hyperbaric oxygen. *Antonie Van Leeuwenhoek* 1965; 31: 181-186.
21. Tally FP, Stewart PR, Suter VL, Rosenblatt JE. Oxygen tolerance of fresh clinical anaerobic bacteria. *J Clin Microbiol* 1975; 1: 161-164.
22. Hill GB, Osterhaut S. Experimental effects of hyperbaric oxygen on selected clostridial species. I. In-vitro studies. *J Infect Dis* 1972; 125: 17-25.
23. Hill GB, Osterhaut S. Experimental effects of HBO on selected clostridial species II. In vivo studies in mice. *J Infect Dis* 1972; 125: 26-35.
24. Boehme DE, Vincent K, Brown OR. Oxygen and toxicity inhibition of amino acid biosynthesis. *Nature (Lond)* 1976; 262: 418-420.
25. Brown OR. Reversible inhibition of respiration of *E. coli* by hyperoxia. *Microbios* 1972; 5: 7-16.
26. Muhrich KH, Park MK, Myers RAM, Marzella L. Hyperoxia and the antimicrobial susceptibility of *Esherischia coli* and *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1989; 33: 1526-1530.
27. Bornside GH, Paleman LM, Ordong AA. Inhibition of pathogenic enteric bacteria by hyperbaric oxygen: enhanced antibacterial activity in the absence of carbon dioxide. *Antimicrob Agents Chemother* 1975; 7: 682-687.
28. Babior BM. Oxygen-dependent microbial killing by phagocytes. *N Engl J Med* 1978; 298: 659-668.
29. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic: the effect of inspired oxygen on infection. *Arch Surg* 1984; 119: 199-204.
30. Hunt TK. The physiology of wound healing. *Ann Emerg Med* 1988; 17: 1265-1273.
31. Prockop DJ, Kivirikko KI, Tuderman L, Guzman NA. The biosynthesis of collagen and its disorders. *N Engl J Med* 1979; 301: 13-23, 77-85.
32. Hunt TK, Pai MP. The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet* 1972; 135: 561-567.
33. Silver IA. Local and systemic factors which affect the proliferation of fibroblasts. In: Kulonen E, Pikkarainen J, editors. The biology of fibroblast. Orlando, Fl: Academic Press, 1973: 507-520.
34. Knighton D, Silver I, Hunt TK. Regulation of wound healing angiogenesis: effect of oxygen gradients and inspired oxygen concentration. *Surgery* 1981; 90: 262-270.
35. Meltzer T, Meyers B. The effect of hyperbaric oxygen on the bursting strength and rate of vascularisation of skin wounds in the rat. *Am Surg* 1986; 52: 659-662.
36. Nemiroff PM, Lungu AL. The influence of hyperbaric oxygen and irradiation on vascularity in skin flaps. A controlled study. *Surg Forum* 1987; 38: 565-567.
37. Zamboni WA, Roth AG, Russell RC, et al. Morphologic analysis of the microcirculation during reperfusion of ischaemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg* 1993; 91: 1110-1123.
38. Weiss SJ. Tissue destruction by neutrophils. *N Engl J Med* 1989; 320: 365-376.
39. Thom SR. Antagonism of CO-mediated brain lipid peroxidation by hyperbaric oxygen. *Toxicol Appl Pharmacol* 1990; 105: 340-344.
40. Zamboni WA, Roth AC, Russell RC, et al. The effect of acute hyperbaric oxygen therapy on axial pattern skin flap survival when administered during and after total ischaemia. *J Reconstr Microsurg* 1989; 5: 343-347.
41. Bird AD, Telfer ABM. Effect of hyperbaric oxygen on limb circulation. *Lancet* 1965; 1: 355-356.
42. Ohta H, Yasui N, Suzuki E, et al. Measurement of cerebral blood flow under hyperbaric oxygenation in man — relationship between PaO_2 and cerebral blood flow. In: Kindwall E, editor. Proceedings of the Eighth International Congress on Hyperbaric Medicine. Flagstaff, Arizona: Best Publishing, 1987: 62-67.
43. Villanucci S, Di Marzio GE, Scholl M, et al. Cardiovascular changes induced by hyperbaric oxygen therapy. *Undersea Biomed Res* 1990; 17 Suppl 1: 117.
44. Risber J, Tyssebotn I. Hyperbaric exposure to a 5 ATA He-N2-O2 atmosphere affects the cardiac function and organ blood flow distribution in awake trained rats. *Undersea Biomed Res* 1986; 13: 77-90.
45. Hordnes C, Tyssebotn I. Effect of high ambient pressure and oxygen tension on organ blood flow in conscious trained rats. *Undersea Biomed Res* 1985; 12: 115-118.
46. Grim PS, Gottlieb LJ, Boddie A, Batson E. Hyperbaric oxygen therapy. *JAMA* 1990; 263: 2216-2220.
47. Sirsjo A, Lewis D. Improved bloodflow in post-ischaemic skeletal muscle after hyperbaric oxygen treatment. *Int J Microcirc Clin Exp* 1990; 1 Suppl 1: 156.
48. Strauss MB, Hargens AR, Gershuni DG, et al. Reduction of skeletal muscle necrosis using intermittent hyperbaric oxygen in model compartment syndrome. *J Bone Joint Surg* 1983; 65A: 656-662.
49. Nylander G, Lewis D, Lewis D, et al. Reduction of post-ischaemic oedema with hyperbaric oxygen. *Plast Reconstr Surg* 1985; 76: 596-601.
50. Wattel F, Mathieu D, Neviere R, Bocquillon N. Hyperbaric therapy: acute peripheral ischaemia and compartment syndromes: a role for hyperbaric oxygenation. *Anaesthesia* 1998; 53 Suppl 2: 63-80.
51. Nylander G, Nordstrom H, Lewis DH, Larsson J. Metabolic effects of hyperbaric oxygen in post-ischaemic muscle. *Plastic Reconstr Surg* 1987; 79: 91-97.
52. Szirsjo A, Larsson J, Haapaniemi T, et al. Reduction of necrosis and increased levels of adenosine triphosphate (ATP) and phosphocreatine (Pcr) in post-ischaemic skeletal muscle after hyperbaric oxygen treatment. *Int J Microcirc Clin Exp* 1990; 1 Suppl: 24.
53. Stewart RJ, Yamaguchi KT, Mason SW, et al. Tissue ATP levels in burn injured skin treated with hyperbaric oxygen. *Undersea Biomed Res* 1989; 16 Suppl: 53.
54. Thom SR. Carbon monoxide poisoning in a rat model: Physiological correlation with clinical events and the effects of HBO [abstract]. *Undersea Biomed Res* 1989; 16 Suppl: 51-52.
55. Undersea and Hyperbaric Medical Society. Hyperbaric oxygen therapy: a committee report. Maryland, 1996.
56. Murphy BP, Harford FJ, Cramer FS. Cerebral air embolism resulting from invasive medical procedures: treatment with hyperbaric oxygen. *Ann Surg* 1985; 201: 242-245.
57. Baskin SE, Wozniac RF. Hyperbaric oxygenation in the treatment of haemodialysis-associated air embolism. *N Engl J Med* 1975; 293: 184-185.
58. Fyke FE III, Kazmier FJ, Harms RW. Venous air embolism: life-threatening complication of orogenital sex during pregnancy. *Am J Med* 1985; 78: 333-336.

59. Francis TJR, Gorman DF. Pathogenesis of the decompression disorders. In: Bennett PB, Elliott DH, editors. The physiology and medicine of diving. 4th ed. Philadelphia: WB Saunders; 1993: 454-480.
60. Tanoue K, Mano Y, Kuroiwa K, et al. Consumption of platelets in decompression sickness of rabbits. *J Appl Physiol* 1987; 62: 1772-1779.
61. Tibbles PM, Edelsberg JS. Hyperbaric oxygen therapy. *N Engl J Med* 1996; 334: 1642-1648.
62. Kindwall EP. Gas embolism. In: Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing Company, 1995: 327-342.
63. Moon RE, Gorman DF. Treatment of decompression disorders. In: Bennett PB, Elliott DH, editors. The physiology and medicine of diving. 4th ed. Philadelphia: WB Saunders, 1993: 506-541.
64. Kizer KW. Delayed treatment of dysbarism : a retrospective review of 50 cases. *JAMA* 1982; 247: 2555-2558.
65. Green RD, Leitch DR. Twenty years of treating decompression sickness. *Aviat Space Environ Med* 1987; 58: 362-366.
66. Guyatt G, Sackett D, Taylor W, et al. Determining optimal therapy: randomised trials in individual patients. *N Engl J Med* 1986; 314: 889-892.
67. McLeod RS, Cohen Z, Taylor DW, Cullen JB. Single-patient randomised clinical trial. *Lancet* 1986; 1: 907-909.
68. Hausberg M, Somers VK. Neural circulatory responses to carbon monoxide in healthy humans. *Hypertension* 1997; 29: 1114-1118.
69. Hee J, Calais F, Momas I, et al. Smokers' behaviour and exposure according to cigarette yield and smoking experience. *Pharmacol Biochem Behav* 1995; 52: 195-203.
70. Tomaszewski C. Carbon monoxide poisoning — early awareness and intervention can save lives. *Postgrad Med* 1999; 105: 39-50.
71. Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med* 1998; 339: 1603-1608.
72. Rodkey FL, O'Neal JD, Collison HA, Uddin DE. Relative affinity of haemoglobin S and haemoglobin A for carbon monoxide and oxygen. *Clin Chem* 1974; 20: 83-84.
73. Roughton FJW, Darling RC. The effect of carbon monoxide on oxy-hemoglobin dissociation curve. *Am J Physiol* 1944; 141: 17-31.
74. Thom SR. Carbon monoxide-mediated brain lipid peroxidation in the rat. *J Appl Physiol* 1990; 68: 997-1003.
75. Brown SD, Piantadosi CA. Recovery of energy metabolism in rat brain after carbon monoxide hypoxia. *J Clin Invest* 1992; 89: 666-672.
76. Thom SR, Xu YA, Ischiropoulos H. Vascular endothelial cells generate peroxynitrate in response to carbon monoxide exposure. *Chem Res Toxicol* 1997; 10: 1023-1031.
77. Meyers RAM, Thom SR. Carbon monoxide and cyanide poisoning. In: Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing, 1995: 343-372.
78. Pace N, Strajman E, Walker E. Acceleration of carbon monoxide elimination in man by high pressure oxygen. *Science* 1950; 111: 652-654.
79. Thom SR. Antagonism of carbon monoxide-mediated brain lipid peroxidation by hyperbaric oxygen. *Toxicol Appl Pharmacol* 1990; 105: 340-344.
80. Thom SR. Functional inhibition of leucocyte B2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol* 1993; 123: 248-256.
81. Jiang J, Tysseborn I. Cerebrospinal fluid pressure changes after acute carbon monoxide poisoning and therapeutic effects of normobaric and hyperbaric oxygen in conscious rats. *Undersea Hyperbar Med* 1997; 24: 245-254.
82. Moon RE, DeLong E. Hyperbaric oxygen for carbon monoxide poisoning — are currently recommended regimens ineffective? [editorial]. *Med J Aust* 1999; 170: 197-199.
83. Olson KR, Seger D. Hyperbaric oxygen for carbon monoxide poisoning: Does it really work? [editorial]. *Ann Emerg Med* 1995; 25: 535-537.
84. Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust* 1999; 170: 302-210.
85. Hardy KR, Thom SR. Pathophysiology and treatment of carbon monoxide poisoning. *J Clin Toxicol* 1994; 32: 613-629.
86. Heimbach RD. Gas gangrene. In: Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing, 1995: 373-394.
87. Roding B, Groenveld PHA, Boerema I. Ten years of experience in the treatment of gas gangrene with hyperbaric oxygen. *Surg Gynecol Obstet* 1972; 134: 579-585.
88. DeMello FJ, Haglin JJ, Hitchcock CR. Comparative study of experimental *Clostridium perfringens* infection in dogs treated with antibiotic, surgery, and hyperbaric oxygen. *Surgery* 1973; 73: 936-941.
89. Bakker DJ. Selected aerobic and anaerobic soft tissue infections — diagnosis and the use of hyperbaric oxygen as an adjunct. In: Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing, 1995: 396-417.
90. Paty R, Smith AD. Gangrene and Fournier's gangrene. *Urol Clin North Am* 1992; 19: 149-162.
91. Eltorai IM, Hart GB, Strauss MB, et al. The role of hyperbaric oxygen in the management of Fournier's gangrene. *Int Surg* 1986; 71: 53-58.
92. Korhonen K, Hirn M, Niinikoski J. Hyperbaric oxygen in the treatment of Fournier's gangrene. *Eur J Surg* 1998; 164: 251-255.
93. Riegels-Nielsen P, Hesselfeldt-Nielsen J, Bang-Jensen E, Jacobsen E. Fournier's gangrene: Five patients treated with hyperbaric oxygen. *J Urol* 1984; 132: 918-920.
94. Bakker DJ. The use of hyperbaric oxygen in the treatment of certain infectious diseases especially gas gangrene and acute dermal gangrene. University of Amsterdam: Drukkerij Veenman BV. Wageningen, 1984: 74-90.
95. Mader J. Mixed anaerobic and aerobic soft issue infections. In: Davis JC, Hunt TK, editors. Problem wounds: the role of oxygen. New York: Elsevier, 1988: 153-172.
96. Riseman JA, Zamboni WA, Curtis A, et al. Hyperbaric oxygen therapy for necrotising fasciitis reduces mortality and the need for debridements. *Surg* 1990; 108: 847-850.
97. Marx RE, Ames JR. The use of hyperbaric oxygen in bony reconstruction of the irradiated and tissue deficient patient. *J Oral Maxillofac Surg* 1982; 40: 412-419.
98. Marx RE, Ehler WJ, Tayapongsak PT, Pierce LW. Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg* 1990; 160: 519-524.
99. Marx RE, Johnson RP, Kline SN. Prevention of osteoradionecrosis: A randomised prospective clinical trial of hyperbaric oxygen versus penicillin. *J Am Dent Assoc* 1985; 111: 49-54.
100. Marx RE, Johnson RP. Studies in the radiobiology of osteoradionecrosis and their clinical significance. *Oral Surg* 1987; 64: 379-390.
101. Farmer JC Jr, Sheldon DL, Angelillo JD, et al. Treatment of radiation-induced tissue injury by hyperbaric oxygen. *Ann Otol Rhinol Laryngol* 1978; 87: 707-715.
102. Davis JC, Dunn JM, Gates GA, Heimbach RD. Hyperbaric oxygen: a new adjunct in the management of radiation necrosis. *Arch Otolaryngol Head Neck Surg* 1979; 105: 58-61.
103. Kraut RA. Prophylactic hyperbaric oxygen to avoid osteoradionecrosis when extractions follow radiation necrosis. *Arch Otolaryngol Head Neck Surg* 1985; 7: 17-20.
104. Kindwall EP. Contraindications and side effects to hyperbaric oxygen treatment. In: Kindwall EP, editor. Hyperbaric medicine practice. Flagstaff, AZ: Best Publishing, 1995: 45-56.
105. Davis JC, Dunn JM, Heimbach RD. Hyperbaric medicine: patient selection, treatment procedures, and side effects. In: Davis JC, Hunt TK, editors. Problem wounds: the role of oxygen. New York: Elsevier Science, 1988: 233-235.
106. Palmquist BM, Phillipson B, Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. *Br J Ophthalmol* 1984; 68: 113-117.
107. Walker M, Capps R, Pirone C, Ramsay R. Doppler detection of circulating bubbles in attendants, decompressed on oxygen, following routine hyperbaric treatments. *SPUMS J* 1995; 25: 62-64.
108. Sheffield PJ, Desautels DA. Hyperbaric and hypobaric chamber fires: a 73 year analysis. *Undersea Hyperbar Med* 1997; 24: 153-164. ❑