Baromedicine Today — Rational Uses of Hyperbaric Oxygen Therapy

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Compressed air, and more recently hyperbaric oxygen, have been used and misused in medical treatment for more than 300 years. Advances in physiology have led to rational protocols for hyperbaric oxygen use.

Hyperbaric oxygen will enhance wound healing by fibroblast and capillary proliferation, suppress infection, reduce edema, reverse CNS damage from carbon monoxide and cyanide poisoning, and reduce clostridial alpha toxins.

Monoplace and multiplace chambers are used for treatment during which EKG and oxygen tissue monitoring, as well as hemodynamic and respiratory support, can be continued. Iatrogenic air embolism and diving decompression sickness demand immediate treatment.

Investigative uses of adjunct therapy for several other clinical problems include treatment of MS, acute spinal cord injuries, and acute MI. Specific indications agreed on by the Undersea and Hyperbaric Medicine Society are recognized by most third-party payers including Medicare, Champus, and HMSA. Hyperbaric medicine remains a fertile area for basic physiologic investigation and outcomes research.

Hyperbaric oxygen therapy is a relatively new treatment concept based on diving physiology and the unique effects of oxygen breathed at increased pressure.

Boyle first saw decompression sickness in 1671 in a decompressed viper writhing in a bell jar. Bends were described in 1841 by caisson workers who walked in a contorted way from bubble pain in their joints. More vicious forms of decompression sickness—cerebral and pulmonary air embolism—can result from an iatrogenic accident masquerading as a stroke following cardiovascular surgery and minor invasions such as placement of lines and arterial catheters.[1,2]

Rapid pressurization of patients injured by intravascular air from any source is usually critical to survival, depending on the volume of introduced gas and its final destination, particularly the brain circulation. The risk of cerebral air embolism in both divers and hospital patients is increased by the 25% to 30% incidence of potentially patent foramen ovale through which air passes to the arterial system and brain.[3]

Other situations, primarily CO poisoning, smoke inhalation, gas gangrene, necrotizing infections and crush injuries respond favorably to hyperbaric oxygen; not because of pressure alone, but because of other arcane results of increased oxygen tension in perfused tissues, such as antibacterial effects, stimulation of angiogenesis, and suppression of the reperfusion syndrome.[4-9]

Hyperbaric medicine is defined by the Undersea and Hyperbaric Medical Society (UHMS) as "a therapeutic technique using air or other gas mixtures at greater–than–atmospheric pressure for short intervals, over days or months, to treat various disease states." World War II research led to the wider use of 100% oxygen in decompression sickness—from this work, other physiologic effects of hyperbaric oxygen were found that have led to the presently accepted uses approved by the UHMS and most third-party payers. [10, 11]

Despite 5 international hyperbaric conferences, support of the New York Academy of Sciences, and rigorous annual UHMS committee reports, charlatanism has been a problem, now offset by peer–reviewed articles in specialty journals.

Hyperbaric Medicine in Hawaii

Hawaii, as a sports–diving area and the locale of U.S. Navy submarine work during and since WWII, has been prominent in decompression and therapeutic hyperbaric research.

After 1962, physicians and basic faculty members of the Department of Physiology, University of Hawaii John A. Burns School of Medicine, (Hong S, Lin Y, Strauss D, Yount D, Beckman E, Lally D, Hayashi E) developed in vitro decompression models in gelatin to refine decompression protocols. In April 1983 a facility (HTC) was developed by the State of Hawaii at Kewalo Basin for treatment of bends patients and also accepted cases requiring hyperbaric oxygen for other indications. HTC serves the diving community and has continued diving research. It plans expansion to a local hospital setting; however, at present, HTC is treating approximately 100 divers a year for accidents, and approximately 20 other patients who receive hyperbaric oxygen therapy.

Diving Accidents and Deaths

Causes of diving deaths in Hawaii were analyzed by C. Edmonds (UHMS meeting, October 1992, Fairfield, Calif.) in a paper entitled "Diving Deaths in Paradise." Causes were similar to those in Australia and New Zealand:

During training	15%
During black coral dives	12%
Drowning (usually fatigue)	61%

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Barotrauma	15%
Cardiac deaths	9%
Decompression sickness	5%

Human factors such as lack of judgment and preparation contributed to 44% of the deaths, equipment problems, 40% and sea conditions, 56%. In the U.S. as a whole Diver's Alert Network (DAN), which analyses most sports-diving accidents, reports an overall diving accident rate of 0.2%, based on 80,000 dives. In 1989, 32% of all injured divers were using dive computers, 68% theoretically were using dive tables, probably poorly if at all. Despite excellent local opportunities for training, many Hawaiian sports divers largely ignore decompression limits in a macho style that invites bends and in the long-term, osteonecrosis. Compounding this problem is the prevalence of yo-yo diving—multiple dives daily with very short surface breaks; neither dive tables nor computers are designed to manage more than 2 or 3 dives a day. Nor does any present computer or table address the cumulative gas load of many successive days of multiple dives, often as many as 6 or more daily. Like gravity, the fundamental gas laws cannot be ignored.

In June 1989, a hyperbaric center was opened at Straub Clinic and Hospital and at present it accepts only patients requiring treatment for problems other than diving accidents. Since opening, more than 200 patients have received treatment courses averaging 30 ninety–minute compressions at 2 to 3 atmospheres of oxygen over 30 days. Indications for treatment were:

Preparation for plastic procedure	21%
Necrotizing soft tissue infection	15%
Peripheral arterial insufficiency, acute	15%
Diabetic foot ulcers	15%
Radionecrosis (bone or soft tissue)	12%
Other	21%

Because of the very high incidence of diabetes and its vascular complications among Hawaiians (nearly 5 times the rate for Caucasians) leading to refractory osteomyelitis and limb loss, a retrospective and prospective study of outcomes with and without adjunctive use of hyperbaric oxygen in refractory osteomyelitis has begun with Straub Foundation support.

Recent wider understanding and acceptance by Hawaii physicians of hyperbaric medicine following residency and CME training at baromedicine centers has greatly increased inpatient and outpatient referrals to Hawaii's 2 hyperbaric treatment sites.

Physiology and Clinical Applications

When breathing air under normal conditions, 98.4% of the available oxygen is bound to hemoglobin. The remaining portion is dissolved in plasma. Because hemoglobin is 97% saturated by inspired air, changing to a breathing source of straight oxygen changes hemoglobin-delivered oxygen by only 3%. The remaining oxygen will be dissolved in the plasma. For each additional atmosphere of pressure, the amount of additional oxygen dissolved in plasma is 2.3 vol%. Thus at about 3 ATA (3 atmospheres, absolute pressure, the maximum working pressure for most HBO treatment) more than 6 vol% is carried in the plasma. Because the tissue requirement for oxygen is roughly 5 vol%, enough oxygen is carried in the plasma alone to fully support life. Normal peripheral tissue oxygen tensions measured through the skin approximate 40 mm Hg; at treatment levels, this can be raised to over 2200 mm Hg, with remarkable local tissue effects.

Fibroblastic proliferation, collagen production, and neovascularization with resulting growth of granulation tissue occur in the presence of intermittent tissue hyperoxygenation. Under oxygen pressure, the diffusion distance of oxygen increases 2 to 3 times, which assists in the delivery of oxygen to hypoxic areas in healing wounds, enhancing the various elements of healing, particularly angiogenesis, of great interest in radiation necrosis of bone and soft tissues.

Months or years after radiation for malignancy, a few patients develop disabling clinical disease of soft tissue or necrotic bone that can be progressive, painful, and potentially fatal due to tissue breakdown and loss of protective barriers.[12,13,14] Even patients who do not develop such overt clinical disease can have radiation tissue damage which can be progressive and could develop later into overt disease with increased risk of infection, wound dehiscence, tissue loss, and graft loss when surgeries are required in irradiated tissues.[15,16,17,18]

The pathophysiology includes endarteritis, inflammation, fibrosis, and hypoxia—clinical states include radiated bowel syndrome, radiation mucositis, soft tissue radionecrosis, and laryngeal radionecrosis. Compromised tissues invite secondary infections, gangrenous bowel, cellulitis, fascitis, and hemorrhagic cystitis. Hyperbaric oxygen has been successful in management of the cystitis and other soft tissue problems involving infection and restoration of adequate vascularity.[19,20,21] Case management includes both pre– and post–operative treatment.

In the presence of bacterial infection the phagocytic leukocyte is an important defense. Although the ingestion of bacteria can be an anaerobic function, effective killing requires oxygen as a substrate. Increased levels of molecular oxygen are converted by the leukocyte into high energy radicals (the superoxide free radical, hydrogen peroxide, and the hydroxyl radical), all toxic to bacteria.[22] Since active infection in a rabbit tibia by *Staphylococcus aureus* has been shown by Mader[23] to reduce tissue oxygen levels to half that necessary for leukocytic function, and addition of oxygen by hyperbaric pressure effectively restores the killing action, a rationale exists for *adjunct* use of hyperbaric oxygen in refractory infections of bone, and in overwhelming soft tissue infections. The combination of adequate debridement, antibiotics, and hyperbaric treatment are most effective in preventing recurrence. The dramatic effect of hyperbaric oxygen on clostridial and other anaerobic infections is well established clinically, although the exact mechanism of suppression of alpha toxins is not understood.[24]

Another interesting effect of increased oxygen tension is a 20% to 50% reduction of blood flow, primarily through arterial vasoconstriction, without reduction in oxygen availability because of the greatly increased amount of oxygen carried in

solution.[25] This vasoconstriction is reported to be of clinical value in reducing edema, tissue loss, and scarring in burn patients,[26] and prompt reduction of compartment pressures in compartment syndrome.[27]

Recent interest in the reperfusion syndrome has ranged across many tissues, including brain, heart, and skeletal muscle. In vivo histologic and chemical studies by Zamboni[28] show that in rat muscle, ischemia causes "sticking and rolling" of neutrophils on venule walls accompanied by the release of thromboxane and other vasoactive substances into the interstitium, causing vasoconstriction of adjacent arterioles and further ischemia. This process appears to be related to superoxide production by the neutrophils and action can be blocked by high oxygen tensions.

In the experimental model, exposure to hyperbaric oxygen within 12 hours of reperfusion altered the usual free–radical pathway to produce harmless hyperperoxyl radicals that react with lipid radicals to form nonradical products, probably reducing lipid peroxidation.[29] Further clinical trials of the use of hyperbaric oxygen to reverse the baleful microvascular events that accompany reperfusion are necessary. Present interest centers around CVA, cord injuries, crush injury, compartment syndrome, and acute MI.

In unpublished data, Youngblood and others[30] report prompt relief of migraine headache and its associated symptoms in more than 90% of patients within minutes after compression, probably on the basis of vasoconstriction. Cerebral edema of various origins has been considered an indication for hyperbaric oxygen therapy, but current clinical information does not support this use.

In carbon monoxide and cyanide poisoning, past teaching has stressed the importance of loss of oxygen transport by hemoglobin linkage, leading to CNS anoxia, collapse, and death. Recent research indicates the loss of oxygen transport is of little significance compared with the direct effect of CO or CN on CNS cells, which primarily impairs mitochondrial cytochrome by binding to cytochrome c oxidase.[33] Also, lipid peroxidation damage occurs; both insults are reversible by use of hyperbaric oxygen, but not with the use of oxygen at ambient pressure.[32]

If CO poisoning is suspected, carboxyhemoglobin determinations are of little use, since low levels can be found in patients with already serious brain damage from direct CO/cytochrome c oxidase binding. High carboxyhemoglobin levels are simply confirmatory of CO exposure and are not even of much prognostic use. Careful clinical evaluation, particularly of cognitive and neurologic function, is essential to making an accurate diagnosis of CO poisoning and selecting a choice of therapy. If there is any doubt about the degree of CO or CN exposure, hyperbaric oxygen treatment is essential in reducing the very real risks of late sequelae that often result in permanent cognitive or psychiatric disorders.

Although hyperbaric oxygen does not in any way replace conventional management, several researchers have found it to be an important adjunctive measure in treatment of thermal burns. Its beneficial effects were discovered accidentally when Wada in Japan used hyperbaric oxygen in treating burned coal miners for associated CO poisoning. The burns of the treated miners healed faster than the burns of the untreated miners. Since then, a growing body of research has shown hyperbaric oxygen to be effective in treatment of thermal injuries.[34,35,36,37]

Beneficial effects include: Reduction in fluid requirements during the initial resuscitation phase, a reduction in edema formation, improvement in the microcirculation, and faster epithelization and neovascularization. Fibrinolysis is activated, leading to earlier capillary patency. Perfusion is improved, with less fluid loss, and conversion of second- to third-degree burns appears to be lessened. Because of the earlier epithelization and neovascularization, grafting is possible sooner.

Treating 138 patients with adjunctive hyperbaric oxygen, Hart reported a reduction of mortality of nearly 30% when compared with an untreated control group. Accelerated wound healing occurred and fluid requirements were reduced nearly 35% during the initial resuscitative period. In this study, mean healing time for the treated group was 19 days and 44 days for the untreated group. Cianci reported reduction in the length of hospital stays averaging 43 days compared to 73 days for those not treated, and a reduction by nearly half of necessary surgical procedures.

To achieve maximum benefits, treatment of burns must be started within 24 hours of injury, preferably sooner. Complex life support can be maintained in the chamber.

The treatment of decompression sickness or bends in its many forms is of course a fundamental use of hyperbaric air, or preferably, oxygen. Bends treatment has a long history of trial and error leading to the many treatment protocols known as tables developed by their various users worldwide. Recent changes in treatment of decompression sickness have moved toward the use of 100% oxygen at up to 3 atmospheres of pressure, rather than the older routines using air or prepared inert gas-oxygen mixtures starting at 5 or 6 atmospheres of pressure. Various routines are still under investigation since much of the pathophysiology of decompression sickness remains unclear at the tissue and molecular level.[38]

Equipment

Hyperbaric therapy is given either in a monoplace or multiplace chamber. The commonly used monoplace Sechrist chamber is a double-walled acrylic cylinder into which the patient is placed on a movable stretcher, rolled inside on rails from a mating transport gurney, Fig 1. Special ports in the chamber door allow respirator operation, EKG, hemodynamic monitoring, tissue oxygen monitoring, and intravenous infusions. Controls for chamber operation are on the unit, allowing the operator close contact and communication with the patient, important in allaying anxiety and pressure–change problems. Most treatment protocols for use in this type of chamber use 100% oxygen at 2 to 3 atmospheres of pressure, with *air breaks* during longer routines.

Multiplace chambers are large walk-in installations accommodating many patients, often with their attendants, Fig 2. Chamber pressure usually is provided by air, with single gases

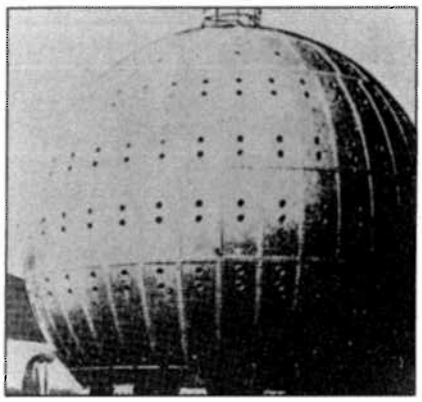

Fig 1.—Cunningham's 5 story, 60 room hyperbaric chamber in Cleveland, Ohio.

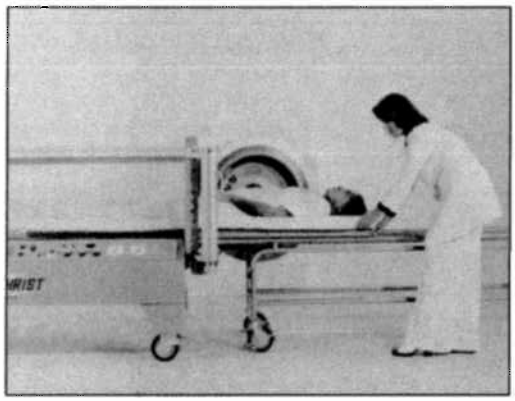

Fig 2.—Monoplace acrylic chamer with access gurney.

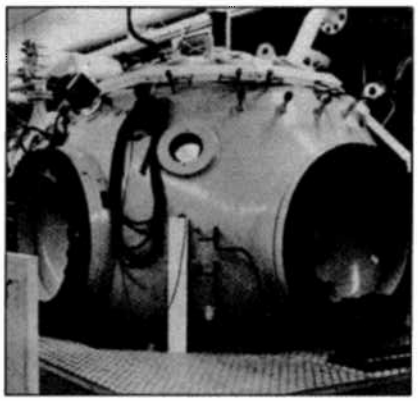

Fig 3.—Multiplace chamber with air locks allowing entry and exit of attendants during treatment.

or gas mixtures tailored to patient needs given by mask or hood within the chamber. Most of the indications for hyperbaric therapy can be met in either type of chamber and each has its advantages.

Transportable chambers now are available that can be pressurized in transit and carried in a small plane or vehicle, Fig 3. These chambers often allow space for an inside attendant, have air lock provisions, and can be linked to a larger chamber.

Because of the urgency of immediate repressurization of bends patients and the risks of transporting them in only partially pressurized airplane cabins, Hawaii's need for dependably staffed chambers on other islands or pressurized, transportable equipment for air ambulance use is clear.

Equipment for the non-invasive measurement of tissue oxygen levels has attracted recent interest. Calibrated electrodes connected to a readout unit are placed on the skin, allowing real–time determinations of oxygen perfusion (TcPO2) into questionable areas near wounds, grafts, or amputation sites, providing a fair indication of healing potential. Adjacent to ulcerations, for example, an oxygen level of less than 30 mm Hg that fails to rise promptly to several hundred mm at 2 ATA of oxygen portends treatment failure even with hyperbaric oxygen. Failure to heal is virtually certain, whereas a rapid rise to several hundred mm Hg appears to signify adequate healing potential with adjunct hyperbaric treatment, after which wounds usually remain healed for at least a reasonable time.[39] For the TcPO2 to be of significance, macrocirculation must be competent; measurement is then of the oxygen perfusion capability of the micro circulation, equally critical to wound healing. Further refinement of the predictive value of TcPO2 determinations at room air and under oxygen pressure will improve treatment decisions, both in plastic procedures and in the management of ulcerated feet and legs.

Barotrauma and Oxygen Toxicity

Hyperbaric therapy, involving Boyle's law (change of volume inversely with pressure) involves some constraints and cautions. Asthmatics, those with COPD, lung cysts or blebs, or with a history of lung collapse can develop pneumothorax on decompression. Similarly, patients with ear or sinus problems can encounter difficulties on compression or decompression; *needle myringotomies* are a simple solution for threatened eardrums.

➤ *Continued on page 119*

Table 1.— Investigational Indications

Nerve grafts.—Rats, controlled study, cut sciatic N., significant increase in neurone regrowth and 4 myelin production. (P=.0005)

Multiple sclerosis.—Patients, 37, 1 year controlled study, 12/17 showed improved mobility, balance, bladder function. 19/20 (controls with placebo[41] compression) deteriorated or not improved in 1 year.

Brain injury.—Patients, 99, contusion or intracranial hematoma, half treated with HBO, treated group, 33% recovery; control group, 6%[42] recovery.

Brown recluse spider bite.—Rabbits, controlled study. 58 ID injections of venom. Lesions produced: HBO treated, 1.7 cm[43], saline controls, 3.4 cm.

Fracture healing.—Rats, standardized femur fracture. HBO–treated animals healed in 3/4 of time of untreated controls.[44]

Pyoderma gangrenosum.—Patients, 6, 3 independent reports, after HBO, all patients healed with or without grafts.[45,46,47]

Retinal vein leakage.—Central retinal occlusion patients, 14, all improved vision with Cystoid macular edema HBO. No contols; all patients treated[48,49,50] as last resort for major visual loss.

MI.—Dog studies, LAD coronary a. occlusion, thrombolytics and HBO. 97% restoration of enzyme function, controls, 48%. Patients, 208, mortality reduced by half,[51,52] with use of HBO.

Migraine patients, 2 studies, 90% of patients[30,53] relieved within 1 hour of HBO treatment.

➤*(Continued from Page 115)*

For obtunded patients or for prolonged treatment courses in difficult situations, tympanotomy tubes often are placed.

Oxygen toxicity, even in ordinary bedside use, places limits on treatment times and pressures. Since maximum allowable exposures to oxygen are well known, safe time and pressure limits are followed. Toxicity usually manifests itself by nausea, chest discomfort, apprehension, and occasionally convulsions which are not fatal and cease on discontinuation of oxygen.

Summary

Currently, there are 12 firmly accepted indications for hyperbaric oxygen therapy that are agreed on by the UHMS. Reimbursement agreements exist with Medicare, Champus, and most third–party payers including Hawaii Medical Service Association (HMSA).

1. Air or gas embolism
2. CO poisoning and smoke inhalation CO complicated by CN poisoning
3. Gas gangrene
4. Crush injury, compartment syndrome, and other traumatic ischemias
5. Decompression sickness
6. Enhancement of healing in problem wounds
7. Exceptional blood loss (anemia)
8. Necrotizing soft tissue infections
9. Refractory osteomyelitis
10. Radiation tissue damage
11. Skin grafts and flaps (compromised)
12. Thermal burns

For investigational indications, see Table 1.

Hyperbaric oxygen therapy can be either an inpatient or outpatient procedure, depending on the acuity and severity of the clinical situation. Since hyperbaric treatment is adjunctive to other care, patients referred to hyperbaric facilities usually remain in the care of the referring physician.

In properly selected cases, adjunctive hyperbaric oxygen will improve treatment outcomes. Success depends on several factors, including the degree of impairment of tissue perfusion, associated systemic disorders, and the extent of tissue damage prior to initiating hyperbaric therapy. In acute problems such as CO poisoning, smoke inhalation, or trauma impairing tissue perfusion, early consultation is needed.

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