

Smith Seminars  
Online Continuing Education  
AARC-Approved for 2 CRCE  
Hyperbaric Oxygen Therapy

Objectives

1. Recall key events in the history of the evolution of hyperbaric medicine
2. Compare of different types of hyperbaric oxygen therapy chambers
3. List the effects of hyperbaric oxygen treatments, oxygen toxicity, organs affected by barotrauma, and contraindications of hyperbaric oxygen therapy
4. Know the clinical application of hyperbaric oxygen therapy and treatment protocol guidelines

The use of increased atmosphere pressure for medical therapy has intrigued many physicians, scientists, and lay persons for hundreds of years. Vague accounts of increased atmosphere pressures used on humans date to the fifth century BC. Henshaw, a British clergyman, built the first sealed chamber, termed the Domicilium, in 1662. This chamber compressed air (21% oxygen) for numerous ailments such as inflammation, scurvy, arthritis, and rickets but likely had too little compression to do any physical good.

Following Priestley's discovery of oxygen in the late 1700s, Beddoes developed a pneumatic laboratory enriched with oxygen to treat chronic conditions such as leprosy. In the early 1930s, the Junod reported improvement in patients with cardiorespiratory disorders when treated in 2 atm of pressure in a copper compression chamber. These early reports spawned the creation of a number of "pneumatic institutes" in Europe. These chambers were able to treat up to 10 people at once and reached pressures of 2 or more atm. Compression therapy became the "in vogue" spas of the day. Pneumatic spas came to North America in 1860, with the first compression chamber built in Oshawa, Ontario, Canada.

The French surgeon Fontaine built a mobile compressorized operating suite in 1879. Patients reportedly had better outcomes because of improved oxygenation and decreased postoperative vomiting and cyanosis. Easier reduction of hernias was noted. Corning introduced the therapeutic compression chamber to the US in 1891 to treat nervous and mental afflictions. This chamber was the first operated by electric power.

Orville Cunningham noted 25 years later that patients with certain cardiovascular disorders improved when moved from high altitudes to sea-level altitudes. He discovered this during the Spanish flu epidemic in 1918, which resulted in more than 500,000 deaths. Many of these victims died in a cyanotic state. Under the care of Dr Cunningham, a rather sick resident physician was treated in the compression chamber and recovered completely. Cunningham subsequently built an 88-ft long and 10-ft wide chamber to treat numerous patients, with remarkable success. The credibility of the compression chamber was reinforced during treatment of flu patients. One night when the chamber's power accidentally was shut off, all patients died. At the time, the interpretation credited hyperbaric therapy with keeping the patients alive. When the compression stopped, these

patients died. However, the deaths were likely the result of rapid ascent from the compression rather than the secondary effects of the Spanish flu.

In 1928, Mr. Timkin, an appreciative patient whose uremic state was resolved after receiving hyperbaric therapies, constructed for Cunningham an enormous 60-ft tall, 6-story hyperbaric hospital that looked like a steel sphere. Conditions such as hypertension, diabetes, syphilis, and cancer were treated here until 1930, when the local medical society closed the hyperbaric hospital for lack of scientific evidence or merit. After 1930, much of the medical or scientific community did not look favorably upon the use of hyperbaric medicine.

Supplemental use of oxygen increased with availability after this time. The military soon had an increased interest in underwater activities, and this promoted the use of oxygen and hyperbaric medicine for diving and decompression sickness. Hyperbaric medicine treatments had sound physiologic principles based on known physics of mixed gas when treating decompression sickness.

A flurry of interest in therapeutic hyperbaric medicine was fostered by Dr I. Boerema, who, while in Amsterdam in 1956, reported hyperbaric oxygen (HBO) as an aid in cardiopulmonary surgery, particularly for congenital conditions such as tetralogy of Fallot, transposition of great vessels, and pulmonic stenosis. A colleague of Boerema's, W. H. Brummelkamp, also interested in hyperbaric medicine, discovered in 1959 (and subsequently published in 1961) that anaerobic infections were inhibited by hyperbaric therapy. Meanwhile, Boerema had published an article, "Life without blood," a report of fatally anemic pigs treated successfully with volume expansion and pressurized hyperoxygenation. Boerema often is credited as the father of modern-day hyperbaric medicine.

In 1962, Smith and Sharp reported the enormous benefits of HBO in carbon monoxide poisoning. International interest thus was rekindled, and HBO therapy was thrust into the modern era. Hyperbaric units subsequently were built at Duke University, New York Mount Sinai Hospital, Presbyterian Hospital and Edgeworth Hospital in Chicago, Good Samaritan in Los Angeles, St. Barnaby Hospital in New Jersey, Harvard Children's Hospital, and St. Luke's Hospital in Milwaukee. Further chambers were installed in numerous international sites.

The benefits of hyperbaric medicine subsequently were observed for split-thickness skin graft acceptance, flap survival and salvage, wound re-epithelization, and acute thermal burns. These studies lent credibility to the therapeutic employment of HBO therapy. This fostered the establishment of organized scientific congresses and societies such as the International Congress on Hyperbaric Oxygen and the Undersea Medical Society. Unfortunately, as the availability of hyperbaric medicine chambers increased, the indiscriminate and inappropriate use of the chamber for a variety of medical conditions by practitioners searching for a "cure-all" therapy resulted in a backlash from the scientific society, once again tarnishing the credibility of hyperbaric medicine. As a

result, by the late 1970s, the Undersea Medical Society had formulated guidelines for the use of hyperbaric therapy.

Researchers conducting wound-healing studies continued to try to take advantage of the angiogenic properties of increasing oxygen gradients resulting from hyperbaric therapy. Foot wounds from diabetes, radiation ulcers, and other ischemic wounds have been manipulated and successfully treated with HBO. Prospective blinded randomized trials and well-executed laboratory studies continue to further define the role of hyperbaric therapy in medical therapeutics.

In 1989, in recognition of advances in hyperbaric treatments, the American Board of Medical Specialists approved a certification of added competency in Undersea Medicine. The National Board of Hyperbaric Medicine Technology gave its first certification to hyperbaric technicians in 1991. In 1986, the Undersea Medical Society changed its name to the Undersea and Hyperbaric Medical Society.

### Comparison of Types of Hyperbaric Oxygen Therapy Chambers

#### Monoplace chambers

##### Advantages

- Relatively low purchase price
- Requires little space and relatively minor facility renovations
- Modest program capitalization
- Treatment protocol specific to patient and/or condition
- Modest staffing requirements
- Patient does not wear mask/hood/head tent for oxygen delivery
- Relatively mobile chamber for possible relocation
- No risk of iatrogenic decompression sickness in patient or staff
- Add-on capability for ease of program expansion

##### Disadvantages

- Patient isolated during treatment
- Inability to suction patient
- Limited pressure capability (3 ATA)
- Pure oxygen environment; associated fire hazard
- Inability to use certain diagnostic and/or therapeutic equipment (transcutaneous oxygen assessment now available [radiometer - transcutaneous monitor -3])
- Increased risk of complications from pneumothorax and/or tension pneumothorax and arterial air embolism developing during decompression

#### Multiplace chambers

##### Advantages

- Greater working pressure
- Constant patient attendance
- Ability to use a variety of electrically generated signals during therapy
- Attendants able to enter and exit during therapy

Ability to manage complications such as pneumothorax without releasing pressure  
Ability to conduct intensive care activities during treatment

#### Disadvantages

Higher capitalization requirements  
Major space requirements; basement and/or ground floor level limitations  
Higher operating costs  
Larger and experienced staffing requirements  
Risk of decompression sickness in internal personnel  
All patients on same protocol  
Uncertain oxygen delivery tension at patient with face mask  
Severe maxillofacial and/or head and neck involvement possibly making effective delivery of oxygen difficult  
Facility fire-associated decompression requirements  
Significant equipment maintenance and system upkeep requirements

#### Effects of Hyperbaric Treatments on Cardiovascular System

Heart rate - Decreased  
Contractility - No effect  
Stroke volume - No effect  
Cardiac output - Decreased  
Blood pressure - Possible minimal increase  
Systemic vascular resistance - Afterload increases, arterial vasoconstriction

#### Primary Effects of Hyperbaric Oxygen

Hyperoxygenation: Greater oxygen carrying capacity, increased oxygen diffusion in tissue fluid, diffusion distance proportional to the square root of dissolved oxygen  
Clinical Uses: Severe blood loss anemia (unable to carry oxygen), crush injury, compartment syndrome graft, and flap salvage (decreased perfusion), edema (increased diffusion barrier)  
Decrease gas bubble size: Boyle law - Gas volume inversely proportional to pressure.  
Hyperbaric diffusion gradient favors gas leaving the bubble and oxygen moving in, metabolizing oxygen in the bubble.  
Law of Laplace-- The law of Laplace gives the relation between pressure within the lumen of a hollow organ and the stress in the wall.  
Bubbles unstable as they decrease in size.  
Clinical Uses: Decompression sickness, air embolus syndrome

#### Secondary Effects of Hyperbaric Medicine

Vasoconstriction: Decreased inflow into tissues, decreased edema  
Clinical Uses: Crush injuries, acute burns, compartment syndrome  
Angiogenesis: Increased oxygen gradient between wound and surrounding environment. Increased fibroblast proliferation leading to increased collagen deposition and increased fibronectin, which aids in neovascularization.  
Clinical Uses: Graft and flap salvage, osteoradionecrosis, radiation endarteritis obliterans, and chronic wounds

Fibroblast proliferation: Oxygen-dependent proliferation  
Clinical Uses: Chronic wounds, radiation-induced injury  
Leukocyte oxidative killing: Increased oxygen free radicals.  
Anaerobes lack superoxide dismutase to control oxygen free radicals.  
Clinical Uses: Necrotizing soft-tissue infections, chronic osteomyelitis  
Toxin inhibition: Decreased clostridial alpha toxins  
Clinical Uses: Clostridial gas gangrene, decreased cardio toxins  
Antibiotic synergy: Fluoroquinolones, amphotericin B, and aminoglycosides - Use oxygen to transport across cell membranes  
Clinical Uses: Sepsis, necrotizing infections

### Signs and Symptoms of Oxygen Toxicity

#### Central Nervous System

Nausea and vomiting  
Seizures  
Sweating  
Pallor  
Muscle twitching  
Anxiety and/or respiratory changes  
Visual changes  
Tinnitus  
Hallucinations  
Vertigo  
Hiccups  
Decreased level of consciousness

#### Pulmonary

Dry cough  
Substernal chest pain  
Bronchitis  
Shortness of breath  
Pulmonary edema  
Pulmonary fibrosis

### Contraindications to Hyperbaric Oxygen

Claustrophobia due to anxiety  
Pneumothorax caused by a gas emboli, pneumomediastinum, pneumoperitoneum, tension (pneumothorax), or subcutaneous emphysema.  
History of spontaneous pneumothorax, due to increased lung blebs.  
Chronic obstructive pulmonary disease because of increased oxygen intolerance and increased risk of seizures.  
Pneumocystis carinii pneumonia - fetal teratogen  
Seizure disorders due to barotrauma to the sinuses, ears, or lungs.  
Pregnancy - may be required in pregnancy in situations of carbon monoxide poisoning, cerebral gas embolus, decompression sickness, or clostridial myonecrosis.  
Upper respiratory infection may cause hemolysis.

Hyperthermia  
 Hereditary spherocytosis  
 Optic neuritis – increased optic nerve pathology  
 Malignant tumors - increased vascularity for tumors  
 Acidosis - Decreased threshold for oxygen seizures

Drugs

cis-platinum - Decreased wound healing  
 Doxorubicin - Increased free oxygen radicals  
 Bleomycin - Pulmonary fibrosis leading to pneumothorax  
 Steroids - Decreased threshold for oxygen seizure  
 Alcohol - Dehydration (increased risk of decompression sickness)  
 Aromatic hydrocarbons - Spontaneous combustion  
 Disulfiram - Inhibits superoxide dismutase  
 Nicotine - Decreased seizure threshold

Organs Affected by Barotrauma

Sinuses, congestion and/or occlusion with pain and/or bloody discharge  
 Middle ear, eustachian tube occluded, failure to equalize pressure within middle ear space, leading to edema, rupture, or retraction of tympanic membrane, hemorrhage.  
 External ear, wax build-up or ear plugs occlude canal with pain and/or bleeding.  
 Inner ear, oval or round window rupture, with ataxia, vertigo, tinnitus, and/or hearing loss.  
 GI tract, gas in bowels and distention on ascent, with vomiting, nausea, flatulence, and/or colicky pain.  
 Teeth, infected or restored teeth (may harbor gas) with tooth pain with possible implosion or explosion.  
 Gas embolus, emergent decompression with blocked glottis (extremely rare), sudden decreased level of consciousness; hemiplegia, and/or blown pupil.

Teed Scale – Middle-Ear Barotrauma of Descent

Grade 0	Symptoms without signs
Grade I	Injection of the tympanic membrane, especially along the handle of the malleus
Grade II	Injection plus slight hemorrhage within the substance of the tympanic membrane
Grade III	Gross hemorrhage within the substance of the tympanic membrane
Grade IV	Free blood in the middle ear as evidenced by blueness and bulging
Grade V	Perforation of the tympanic membrane

### Clinical Application of Hyperbaric Oxygen

Primary Therapy	Adjunctive Therapy
Carbon monoxide poisoning	Radiation tissue damage
Cerebral arterial gas embolus	Osteoradionecrosis prophylaxis
Decompression sickness	Acute ischemia and/or crush injuries
Osteoradionecrosis	Necrotizing infections
Clostridial gas gangrene	Acute exceptional blood loss
	Acute thermal burns
	Compromised skin grafts or flaps
	Selected problem wounds
	Refractory osteomyelitis

### Treatment Protocol Guidelines

Dosage	Indications
2.0 ATA* oxygen X 90 min	Wound healing Compromised skin grafts and/or flaps Thermal burns, Osteomyelitis Crush injury and/or compartment syndrome Mucormycosis
2.0 ATA oxygen X 90 min with 10 min air break (high seizure risk)	Wound healing Compromised skin graft and/or flaps Thermal burns, Osteomyelitis Crush injury and/or compartment syndrome Mucormycosis
2.5 ATA oxygen X 90 min	Nonclostridial gas gangrene, Necrotizing infections, Osteomyelitis ( <i>Escherichia coli</i> or <i>Pseudomonas</i> species isolated) Late radiation tissue injury (osteoradionecrosis, soft tissue radionecrosis)
3.0 ATA oxygen X 90 min	Carbon monoxide poisoning Clostridial gas gangrene

\*ATA = atmosphere absolute: a unit of absolute pressure (barometric pressure) expressed in atm.

### Physical Basis for Hyperbaric Medicine

Delivery of hyperbaric pressures generally is accepted through one of two different chambers. Monoplace chambers house one individual placed in the supine position. Current chambers have an acrylic shell, which allows the patient to observe his or her surroundings. Communication devices located within the chamber allow direct conversation between the patient and the hyperbaric medicine technician or physician. Conversely, multiplace chambers can accommodate 2-10 patients. Gas is piped directly from its source to the chamber. Humidification and heat exchange gases are present in all modern chambers.

The application of HBO depends on the physical properties of gases under pressure, specifically, oxygen at pressure greater than 1 atm. Oxygen is essential in a variety of enzymatic, biochemical, and physiologic interactions that promote normal cellular respiration and tissue function. Mono-oxygenase, intradioxygenase, and interdioxygenase are specific enzymes that recruit oxygen as a cofactor to perform required biologic processes. Collagen deposition and synthesis depend on an oxygen-dependent prolyl-hydroxylase hydroxylation of proline. Angiogenesis and epithelization also are oxygen dependent.

Under normal conditions, 97.5% of oxygen is carried in the bloodstream bound to hemoglobin. The remaining 2.5% is dissolved in plasma. Oxygen is combined with hemoglobin in the bloodstream, with each gram of hemoglobin combined with 1.34 cm<sup>3</sup> of oxygen. This represents a physiologic maximum. Under normal conditions at sea level, the arterial hemoglobin saturation is 97%, and the venous hemoglobin saturation is 70%. The oxygen content can be calculated with the following equation:  
Oxygen Content = 1.34 mL of O<sub>2</sub>/g of Hb X g of Hb/100 cm<sup>3</sup> X Percent Saturation  
Above 200 mL of mercury of pressure, the oxygen dissolved in plasma significantly increases. This is calculated with the Henry law:

Dissolved Oxygen (vol %) = 0.0031 (mL O<sub>2</sub>/100 cm<sup>3</sup>/mm Hg) X PaO<sub>2</sub>

The total oxygen content of blood under hyperbaric conditions is equal to the oxygen content calculation plus the dissolved oxygen content. The average metabolic consumption of oxygen by the human body at sea level is 6.6 cm<sup>3</sup>/100 cm<sup>3</sup> of blood.

Under hyperbaric conditions of 3 atm while breathing 100% oxygen, the total dissolved oxygen content delivered is in excess of this metabolic requirement, meaning that oxygen can be supplied under these conditions even in the absence of hemoglobin.

Carbon dioxide, the byproduct of cellular respiration, is carried in the blood as bicarbonate (75%), as carboxy hemoglobin (20%), and dissolved in plasma (5%). Through the Haldane effect, the saturation of hemoglobin with carbon dioxide depends on deoxygenation. As oxygen is released from hemoglobin, carbon dioxide may combine.

Under conditions in which the hemoglobin remains saturated, such as in hyperbaric medicine, the PaCO<sub>2</sub> therefore may rise. Unless the normal respiratory compensatory conditions are present to exhale the extra carbon dioxide, the patient may develop significant carbon dioxide retention, as may be observed with chronic obstructive pulmonary disease. This can be exacerbated by an increase in the work of breathing fostered by hyperbaric treatments. The work of breathing is dependent on pressure and volume, and it becomes greater as hyperbaric pressure increases. Patients who already are compromised with increased airway pressures may be subject to respiratory failure.

Decreased cardiac output is a direct result of decreased heart rate (cardiac output = stroke volume X heart rate). Cardiac output may be compromised further in patients with congestive heart failure in whom the preload is high. An increase in the systemic vascular resistance increases the after load, which can worsen congestive heart failure.

#### Mechanism of Action in Hyperbaric Medicine

The mechanism of action of hyperbaric treatments is attributed to the immediate direct physical affects of oxygen and other gases under pressure and to the delayed secondary physiologic and biochemical effects that are set into motion with each hyperbaric treatment. Benefits of hyperbaric treatment often use both the primary and secondary mechanisms to promote the desired effect. Charles law states that if a volume of gas is kept constant, the temperature varies with the pressure. Together, Charles and Boyle laws are known as the general gas law, expressed as  $D1V1/T1 = P2V2//T2$ . Henry law states that "at a constant temperature, the amount of a gas that will dissolve in a liquid is proportional to the partial pressure of the gas."

Each of the physical laws directly governs the principles of hyperbaric medicine through hyperoxygenation bubble size change and the myriad secondary effects noted above. These principles account for the clinical application in the adjunctive therapies below.

#### Oxygen Toxicity

Elemental oxygen is required to maintain cellular respiration and to allow for normal cellular protein production. Hyperbaric medicine is considered extremely safe under appropriate supervision and utility. Toxic effects of oxygen are observed at extremely high doses over prolonged periods. HBO treatment increases the relative dose of oxygen; thus susceptible patients need to be recognized and modifications made to prevent the manifestations of oxygen toxicity. Damaging or toxic effects of oxygen therapy likely are related to the unbridled formation and release of reactive oxygen species, such as superoxide, hydroxyl radical, and hydrogen peroxide. Superoxide dismutase, catalase, glutathione, and glutathione reductase keep the formation of these radicals in check until the oxygen load overwhelms the enzymes, leading to the detrimental affects on cell membranes, proteins, and enzymes. Other antioxidants used by the body include vitamins C and E, selenium, and glutathione.

Lavoisier first observed the detrimental effects of hyperoxygenation in 1789. In 1878, Paul Bert demonstrated that HBO induced seizures. This became known as the "Paul Bert effect" or oxygen-induced seizures. This neurologic effect may be related to the free

radical-induced peroxidation of neurons and glial cells upon interaction with iron. Alternatively, a decrease in the GABA levels induced by hyperbaric pressures and increased oxygen may be important in seizure induction.

In 1899, Lorraine Smith reported the pathologic effects of increased oxygen tension on the respiratory system. The Lorraine Smith effect became known as a clinical syndrome of decreased vital capacity, sternal chest pain, and patchy atelectasis.

There is a wide variety of manifestations of oxygen toxicity. These effects may occur at any point in the treatment regimen. A distinct correlation between the number of treatments and oxygen toxicity is not apparent, but rather the duration of the treatments (i.e., >2 h) and the patient's susceptibility appear to be related to toxicity. The patient's susceptibility is an ill-defined variable, but a number of conditions may make certain individuals poor candidates for hyperbaric therapy.

The most important factor that may decrease the potential predisposition to oxygen toxicity is intermittent exposure to room air. Give susceptible patients "air breaks" at some point during the treatment. During this time, the patient is breathing room air that is piped into the chamber. A 10-minute air break may be all that is required to prevent the symptoms of oxygen toxicity. Other potential counteractive measures to decrease oxygen toxicity include inducing hypothermia or administering vitamin E, disulfiram, glutathione, phenobarbital, diazepam, or adrenergic blockers.

Decompress patients who develop oxygen toxicity. During a seizure, initiate decompression following the tonic phase of the seizure, as the patient is holding his or her breath. During the chronic phase, the patient is breathing. While in the chamber, the patient can be cooled and allowed to breathe room air. Correct any metabolic conditions (e.g., acidosis). The administration of diazepam or phenobarbital may be required if the seizure persists. Oxygen toxicity seizures usually last only 1-2 minutes. Closely observe the patient for the next 4-6 hours.

Such oxygen-induced seizures do not require a neurologic assessment unless other confounding medical conditions have indicated a thorough workup. Oxygen toxicity seizures occur in approximately 1 in 10,000 exposures. If intravenous (IV) access is available in either a monoplace or multiplace chamber, diazepam or phenobarbital can be administered via this route. Slowly decompress patients in monoplace chambers without IV access. The hyperbaric attendant must be observant that the patient is not air trapping to avoid pulmonary barotrauma.

For excellent patient education resources, visit eMedicine's Environmental Exposures and Injuries Center and Poisoning Center. Also, see eMedicine's patient education articles The Bends - Decompression Syndromes and Carbon Monoxide Poisoning.

#### Potential Complications

Other potential complications of hyperbaric treatments relate to direct barotrauma. Because of the properties of gases, any gas-containing organ or cavity within the body

may be subject to barotrauma. This represents injury related to gas expansion in closed spaces.

The most common barotrauma is middle ear injury. The Teed scale denotes a graduated injury of the middle ear tympanic membrane. Grade 0 and 1 require only improved ear pressure equalization maneuvers (e.g., Frenzel maneuver, Valsalva maneuver). Perform the Frenzel maneuver by raising the pressure in the oral pharynx, pinching the nostrils, and closing the glottis. This opens the eustachian tubes. The Valsalva maneuver forces respiratory air into the oropharynx while closing the nose and mouth.

Grade II Teed scale ear injuries require topical decongestants as well as ear decompression maneuvers, since the patient is symptomatic. Grade III injuries often occur while patients are in the ascending phase of the treatment. A more central decongestant may be required. Teed scale grades IV and V require definitive evaluation by otolaryngology. Myringotomy tubes often are required in patients with significant middle ear symptoms.

Occasionally, patients may experience reversible myopia that presumably is related to retrolental oxygen effects.

Treat intrachamber emergencies (e.g., cardiac respiratory arrest) with immediate decompression and standard resuscitation measures. A pneumothorax obtained during treatment should alert the attendant to assemble a team required for chest tube insertion and possible resuscitation. The patient then may be decompressed rapidly.

Fires also may arise in a chamber, since oxygen readily fosters combustion. This is an extremely rare, although disastrous, consequence of something igniting within the chamber. Begin rapid decompression and resuscitation after stopping the oxygen.

Patients with diabetes mellitus deserve special mention. Hyperbaric therapies may affect glucose uptake and metabolism. The vasoconstricting effects of hyperbaric therapy also may impair the subcutaneous absorption of insulin, rendering the patient hypoglycemic.

Other medications also may have detrimental affects when administered in conjunction with hyperbaric therapy, as may pertinent medical history and conditions specific to individual patients. Perform a full history and physical examination prior to hyperbaric treatments so that the absolute and relative contraindications can be recognized and appropriately handled.

#### Hyperbaric Medicine in Clinical Practice

Clinical applications of hyperbaric medicine take advantage of the primary and secondary properties of pressurized oxygen therapy. The Undersea and Hyperbaric Medical Society recognized conditions that have definitive and adjunctive benefit from hyperbaric therapy.

## Carbon Monoxide Poisoning

Smoke inhalation injuries are common in house fires and other fire and/or smoke situations in closed spaces. Carbon monoxide, found in smoke, is the leading cause of poisoning deaths in the US. Carbon monoxide is a colorless, odorless, tasteless, and nonirritating gas that has a 210-fold greater affinity for hemoglobin than oxygen.

Carboxyhemoglobin produces a leftward shift of the oxygen dissociation curve, making oxygen less available to the tissues (Haldane effect). The half-life of carboxyhemoglobin at room air, 100% oxygen, and 3 ATA 100% oxygen is 320, 90, and 23 minutes, respectively. This indicates HBO treatment for patients with carbon monoxide poisoning.

Clinically, a wide variety of signs and symptoms may be noticed in patients with carbon monoxide poisoning. Cardiac dysrhythmias, visual impairments, memory loss, decreased level of consciousness, motor and sensory loss, cognitive dysfunction, and dysphagia may be identified in carbon monoxide-intoxicated patients. Lab tests drawn at the time of insult can reveal a markedly increased carboxyhemoglobin level and a mild metabolic anion gap acidosis. Late neuropsychiatric symptoms may develop 2-3 weeks after exposure. The duration and severity of these changes vary, but they may last months.

Hyperbaric treatment of carbon monoxide poisoning, attempts to accelerate the release and subsequent elimination of carbon monoxide from hemoglobin, hyperoxygenate tissues, antagonize brain lipid peroxidation (potential cerebral sequela of carbon monoxide), reactivate cellular enzymes and proteins, and decrease cerebral edema and neuropsychiatric sequelae.

Indications for hyperbaric treatment of carbon monoxide poisoning include comatose patients, patients with ischemic changes on ECG, those with abnormal psychological and neurologic tests, those with carboxyhemoglobin levels greater than 40%, symptomatic pregnant patients or those with carboxyhemoglobin level greater than 15%, and patients who are symptomatic after 4 hours of 100% oxygen treatment.

## Decompression Sickness

Naval investigations and experiments have increased understanding and treatment of severe decompression sickness ("bends"). During decompression or resurfacing, gases within the vasculature and other tissues come out of solution and expand to promote a mechanical and proinflammatory reaction. The gas bubbles disrupt vascular endothelium and nerve tissue, cause middle ear and cochlear dysfunction, foster edema via vascular and lymphatic occlusion, and promote ischemia by blocking vessels. Proinflammatory cytokines are released from neutrophils, platelets, and endothelial cells while the complement and coagulation cascade systems are activated. The CNS and other tissues develop microhemorrhages.

Patients present clinically with joint and/or muscle pain, pruritus, edema, and mottled skin. More severe and ominous symptoms include upper lumbar cord and CNS dysfunction, cardiac dysrhythmias, respiratory embarrassment, and severe abdominal pain.

Onset of symptoms usually occurs within the first 30 minutes postdive but can take up to 12 hours. HBO attempts to reduce the bubble size until the inert gas is eliminated while tissues are hyperoxygenated.

#### Clostridial Gas Gangrene

Clostridial gas gangrene is a life-threatening and/or limb-threatening infection that mandates emergent surgical intervention. Only use HBO in conjunction with surgery. Hyperbaric medicine works by a number of mechanisms to decrease the production of the alpha toxin released from clostridium, limit bacterial replication, and oxygenate tissues. Perform treatments immediately following surgery and continue them at least twice daily until evidence of the toxin hemolysis subsides.

#### Radiation Injury

Radiation injury alters the normal tissue physiology and anatomy. Marx observed the triad of hypocellularity, hypovascularity, and hypoxia in tissues subjected to radiotherapy. A progressive tissue fibrosis and capillary loss are associated with the endarteritis obliterans related to the sensitivity of cell lines (e.g., endothelial cells, fibroblasts, muscle, nerve cells). The resulting tissue insult may manifest as nonhealing ulcers, pigmentary skin changes, tissue induration, loss of elasticity, and local erythema and tenderness. Bone may progress to an avascular necrosis. The central avascular region of ulcers and osteoradionecrosis is rendered hypoxic, and the surrounding tissues have greater oxygen content.

Hyperbaric treatment promotes angiogenesis and hyperoxygenation to the radiated affected tissues. Increasing the oxygen content to the surrounding tissues markedly increases the overall oxygen gradient between these tissues and the central hypoxic area. The increased oxygen gradient is the essential catalytic factor for angiogenesis. Multiple hyperbaric treatments are required to significantly increase the capillary density in the affected tissues. Prophylactic hyperbaric medicine is recommended by the National Cancer Institute for procedures (e.g., tooth extraction) that are performed on irradiated mandibles.

#### Chronic Nonhealing Wounds

The rationale for treatment of chronic nonhealing wounds with hyperbaric therapy uses the known secondary mechanism of action. Oxygen is required for angiogenesis (which is fostered by the increased oxygen gradient), collagen deposition, re-epithelialization, cellular respiration, and oxidative killing of bacteria. Decreased edema noted following hyperbaric treatment allows better diffusion of oxygen and nutrients through tissues while also relieving pressure on surrounding vessels and structures. In this light, HBO has been used for treating foot ulcers in patients with diabetes, venous and arterial insufficiencies, burn wounds, crush injuries, marginal flaps, and skin grafts. Before initiating hyperbaric treatment, optimize the patient's overall medical status, facilitate nursing care of the patient, and address local wound care and dressing.

The patient's nutritional status is extremely important for wound healing. Proteins, cofactors, essential fatty acids, and proper calorie intake must be optimized for the collagen deposition, angiogenesis, epithelialization, and ground substance to facilitate wound healing. The cardiopulmonary and endocrine systems should be primed to allow

adequate perfusion. Hyperbaric treatment is not a substitute for appropriate limb revascularization. For adjunctive therapeutic value of HBO to have effect, correct peripheral vascular disease as much as possible via the vascular surgery service.

Similarly, local wound management with appropriate debridement, irrigation, infection control, and daily dressing changes is required to aid in healing. Patient positioning and pressure relief with special beds, orthosis, or splints may be necessary to optimize the local wound milieu. Advise patients to stop smoking, since nicotine adversely affects the wound's vascularity and increases potential complications of hyperbaric treatments. The general approach to these problem wounds is therefore multidisciplinary.

#### Foot Wounds of Patients with Diabetes

Foot wounds of patients with diabetes offer a particularly difficult problem. These patients often have an impaired immune system, predisposing them to infections. Blood supply to the wounds is hindered by large and small disease. The red blood cells are sticky and nonpliable, which leads to capillary occlusion and distal ischemia. Neuropathies render the foot insensate and impair motor function. This impaired motor function flattens the foot so that the metatarsal heads become prominent and promote further susceptibility to ulceration via pressure.

Use of hyperbaric therapy in foot wounds of patients with diabetes engenders much controversy. Many early reports were anecdotal and fraught with confounding information that did not support or justify hyperbaric treatment. Recently, a number of randomized prospective studies demonstrated the benefit of hyperbaric therapy in healing foot wounds of patients with diabetes. Other retrospective studies demonstrated similar results.

Problem wounds are just that, difficult problems that have not responded to other treatment modalities. HBO may offer added fuel to the overall armamentarium in the treatment of chronic wounds.

#### Reperfusion Injuries

The benefits of hyperbaric treatment on ischemic insults, ischemia reperfusion injuries, and crush injuries also have been subject to controversy. These injuries result from the reperfusion that follows an extended period of ischemia. Oxygen free radicals rise, thromboxane A<sub>2</sub> and adhesion molecules are activated, platelet aggregation occurs, and vascular vasoconstriction activity is increased. The endothelium is damaged, which promotes vascular leakage, edema, and thrombosis. Tissue necrosis ensues, and the activation of white blood cells is pivotal to the reperfusion injury. Using hyperbaric treatment that may increase oxygen free radicals to benefit the reperfusion injury seems paradoxical. Zamboni et al demonstrated that HBO promotes hyperoxygenation and vasoconstriction to decrease edema and neurovascularization and inhibits neutrophil activation, preventing margination, rolling, and accumulation of white cells. Neutrophils therefore are not permitted to produce detrimental oxygen free radicals.

As further work in hyperbaric physiology progresses, further well-organized prospective randomized studies should help identify the appropriate therapeutic benefits of HBO.

### Transcutaneous Oxygen

Assessment of the perfusion and oxygenation in and around a particular wound is another important aspect of general wound care that needs to be addressed. Transcutaneous oxygen has emerged as an easy yet reliable noninvasive means of measuring local oxygenation relative to a standard area on the body. Transcutaneous oxygen measurements attempt to measure the local ramifications of macrovascular and microvascular disruption. Transcutaneous oxygen is affected by local factors such as improper electrode placements, cellulitis, edema, and increased skin thickness.

Systematically, ventilation and cardiac output, limb macroperfusion, and the patient's hemoglobin may influence the results of transcutaneous oxygen measurements. The vasoconstrictive effects of smoking also may interfere with transcutaneous oxygen levels. The normal lower extremity transcutaneous oxygen measurement should be approximately 50 mm Hg. Minor physiologic variations may occur in the same individual. A standard control on the trunk of the patient (usually the second intercostal space) is used in conjunction with the local wound and surrounding tissue transcutaneous oxygen mapping. Obtain at least 4 sites at equal distances around the ulcer.

A hyperoxic challenge (100% oxygen for 20 min) normally increases the transcutaneous oxygen reading to greater than 300 mm Hg. Generally, responses less than 50 mm Hg require a vascular workup, and HBO likely is of little benefit. Patients with intermediate responses may benefit from hyperbaric treatments. An appropriate candidate for hyperbaric treatment is a patient who has local ischemia but responds to the oxygen challenge. Confirm a response to the hyperbaric treatment by further transcutaneous oxygen testing after 14-20 hyperbaric treatments.

Hyperbaric medicine has a definite role in treating certain conditions. Its use in the future depends on continued enthusiasm, research, and practice based on sound principles. The future of HBO therapy depends on continued sound, scientific, and clinical studies.

Wound healing centers may harbor most hyperbaric chambers. Reimbursement issues for physicians and hospitals also may alter practices traumatically; for the physician and hospital to be paid, present guidelines urge for physicians to be present throughout the hyperbaric treatment. In 2000, more than 300 hyperbaric chambers were operating in the US.

### Chronic Stroke Rehabilitation

With the injury to the brain, blood vessels are damaged or destroyed. The tissue that surrounds the area of outright necrosis has had its circulation compromised and may be only receiving a fraction of the blood flow and oxygen that it needs for optimum health. Thus a disruption in structure creates immediately a change (decrease) in function. This decrease in function remains for months or years and the neurons in these areas are said to be in hibernation or sleeping. Hyperbaric oxygen treatment, when given daily, stimulates a process called angiogenesis or the formation of new blood vessels. New blood vessels form in the vicinity of the damaged tissues as a result of certain chemical signals (e.g. angiogenin) that are produced by the newly re-energized neurons, endothelial cells and macrophages and are then secreted into the surrounding tissues.

These signals stimulate new blood vessels which slowly reconnect to the damaged tissues and within 60 days of daily treatments, the sleeping neurons wake up and resume their normal functions as the proper structures return back in place. The hyperbaric oxygen induced blood vessel repair results in a permanent structural change in the blood vessels that re-supply the previously damaged and nonfunctioning nerve tissue which was occurring due to diminished and inadequate blood flow. These new blood vessels improve the blood flow and oxygen delivery to the damaged brain tissues and this results in permanent improvements in the stroke and traumatically brain injured person.

Clinically, what you see is the return to life of a previously paralyzed and useless limb or limbs, improvement in swallowing, speech, thinking (cognition), memory, etc. Quite obviously not all of the disabilities disappear since there was a central core of dead tissue that cannot be revived. However, after the two months of therapy, these people may continue to improve for at least two years after their treatment with hyperbaric oxygen especially if they continue with physical therapy. This all occurs in patients who may have not seen any improvement in their conditions for years after their stroke even with the use of any and all other therapies indicating that the brain's milieu intérieur has been altered for the better since the neurons are able to slowly re-establish their lost connections in ways not possible before hyperbaric oxygen.

Outcome in stroke may be predicted to some degree by the volume of tissue affected. Comparative functional volume obtained by single photon emission computerized tomography (SPECT) often indicates a larger region of recoverable tissue than CT. This functional volume of the infarct size can be demonstrated to decrease after one to several hyperbaric oxygen treatments and this increase in blood flow to the area of infarction that occurs as a result of hyperbaric oxygen can serve as a clinical test to determine if there is salvageable neurons still present in the penumbra. Presumably, if the test (SPECT first, then HBO then repeat SPECT) is positive, the person should receive benefit from the use of a series of hyperbaric oxygen treatments because of the revitalization of the ischemic penumbral tissues.

Since the literature and clinical experience predicts that between 80 to 90 percent of stroke victims will be helped by hyperbaric oxygen, perhaps the SPECT scan may be missing some other fundamental mechanism by which hyperbaric oxygen is helping these people improve. For example, when rat's forebrains are made ischemic for 10 minutes and then after 1, 2, 3 weeks and 3 months their cerebral glucose utilization is measured, generalized reductions in glucose utilization is found throughout the majority of gray matter indicating that widespread alterations of functional activity prevail in postischemic brains beyond the selectively vulnerable regions. Following acute, localized lesions of the central nervous system, arising from any cause, there are immediate depressions of neuronal synaptic functions in other areas of the central nervous system remote from the lesion. These remote effects result from deafferentation, a phenomenon known as diaschisis.

After an interval of time, which will vary directly with the severity of the lesion, functional recovery may occur to some degree due to synaptic reactivation of neurons.

This is favorably influenced by rehabilitation. Diaschisis most commonly manifests itself by such neurological signs as impaired consciousness or cognitive impairments including dementia, dyspraxias, dystaxias, dysphasias, incoordination and sensory neglect. The nature of diaschisis has been demonstrated by widespread depressions of local cerebral blood flow and metabolism extending far beyond the anatomical lesion. Development of diaschisis is enhanced by latent circulatory disorders in both the affected and unaffected areas of the brain. Recovery of function is associated with recovery of local perfusion and metabolism.

More recently PET scans have shown that diaschisis does not independently add to the clinical deficit in human cerebral infarction but represents part of the damage done by the stroke. Diaschisis is a functional phenomenon that correlates with both stroke severity and infarct hypoperfusion volume.

In a PET scan study of 31 patients with infarcts involving the frontal sensorimotor cortex, 23 had persistent diaschisis up to 5 years after onset while the remaining 8 had the diaschisis recover without recovery of oxygen metabolism in the infarcted area. This implies that tissue in the ischemic penumbra did recover and this is what allowed for recovery of the diaschisis.

Thus if functionless ischemic penumbral tissue can be made to function again, a corresponding amount of the areas of diaschisis will be returned to normal with normal blood flow and function returning.

A number of studies showed that vasoconstriction and reduced cerebral blood flow do not produce any clinically observable effects in a healthy adult when pressures of 1.5 to 2 ATA are used. The effects of HBO are more pronounced in hypoxic/ischemic states of the brain. HBO reduces cerebral edema and improves the function of neurons rendered inactive by ischemia/hypoxia. The improvement of brain function is reflected by the improved electrical activity of the brain.

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