Progress in Anesthesiology

THEORY AND APPLICATION OF HYPERBARIC OXYGEN THERAPY

Glen M. Atlas, M.D., M.Sc.
Fellow in Pain Management
Department of Anesthesiology
State University of New York
Health Science Center at Syracuse
Syracuse, New York

and

Enrico M. Camporesi, M.D.
Chairman
Department of Anesthesiology
State University of New York
Health Science Center at Syracuse
Syracuse, New York

Objectives

Review basic oxygen transport.
Understand hyperbaric oxygenation (HBO).
Present mathematical models of oxygen diffusion.
Understand the administration of HBO therapy.
Review the pharmacology of HBO therapy.
Understand the application of HBO therapy in clinical medicine.

Introduction

Hyperbaric oxygen therapy (HBO) entails the exposure of the whole body to increased atmospheric pressure, usually between 2 and 3 atmospheres, while breathing pure oxygen or O_2-enriched gas mixtures. The exposures are usually provided inside pressure-resistant hyperbaric chambers. Modern HBO therapy is based on precise physiologic principles. The goal of this chapter is to supply a rationale for the indications and limitations of hyperbaric oxygen therapy.

The physiologic principles of normal oxygen transport and diffusion at 1 atmosphere can be extended to understand the rational basis of oxygen transport under hyperbaric conditions and the clinical use of hyperbaric medicine. A variety of disease states are amenable to either primary or adjuvant HBO therapy. These include: intravascular gas, or bubble-mediated diseases, toxicosis, acute and chronic infections, as well as acute and chronic ischemic processes. The availability of low-cost monoplace chambers has made hyperbaric therapy accessible and affordable in many clinical settings. Thus, hyperbaric oxygenation will continue to be a growing area of medical research and practice.

Alveolar and Tissue Gases at Different Pressures

Under normal barometric conditions at sea level, air is inhaled into the lungs where it mixes with the normally present water vapor and alveolar gases. The oxygen transport chain thus begins with a pressure gradient that continues from the lungs to the cells. If one ignores trace atmospheric gases, the alveolar partial pressure of oxygen (P_AO_2) can be calculated from the alveolar gas equation:

$$P_AO_2 = (P_b - P_{H_2O}) \bullet F_IO_2 - P_ACO_2 \bullet \left(F_ICO_2 - \frac{(1 - F_IO_2)}{R}\right)$$

Where P_b is atmospheric barometric pressure (normally 760 mmHg at sea level). Alveolar CO_2 partial pressure (P_ACO_2) can be assumed equal to arterial (P_aCO_2) as carbon dioxide readily diffuses through the lung parenchyma. R represents the respiratory quotient, i.e., the ratio of CO_2 produced to O_2 consumed in moles, or volume of gas evolved, at standard conditions (STPD). A typical healthy 70 kg adult male produces 200 ml • min^{-1} of CO_2 and requires 250 ml • min^{-1} of oxygen. R is then expressed as a dimensionless ratio:

$$R = \frac{CO_2 \text{ Production}}{O_2 \text{ Consumption}} = \frac{200 \text{ ml} \bullet \text{min}^{-1}}{250 \text{ ml} \bullet \text{min}^{-1}} = 0.8$$

F_IO_2 and F_ICO_2 are the fractional concentrations of inspired oxygen and carbon dioxide respectively. Assuming that the subject is not rebreathing any expired gas, F_ICO_2 can be assumed to be zero. P_{H_2O} accounts for the water vapor pressure within the lung and is normally 47 mmHg at the normal body temperature of 37°C. This value is not altered significantly when P_b increases to 3 atm absolute. $PaCO_2$ is usually controlled around 40 mmHg over the range of 1 to 3 atm absolute. The alveolar gas equation can therefore be simplified to:

$$P_AO_2 = P_b - 47 \bullet F_IO_2 - \left(\frac{P_aCO_2}{0.8}\right)$$

Based on the above formula, the normal alveolar partial pressure of oxygen at sea level can be calculated as approximately 100 mmHg. The same formula can also be applied to environments where P_b is increased to values larger than 1 atmosphere absolute, or hyperbaric environments. Thus, at 3 atm absolute, P_AO_2 will be approximately 2183 mmHg. Effects not taken into account by this formula are atelectasis, intracardiac right-to-left shunts, and arterial-venous shunts. These tend to decrease P_aO_2. Any ventilation-to-perfusion mismatch will also tend to decrease arterial oxygenation. A normal decline of P_aO_2 with aging is also commonly observed. This relationship has been usefully modelled, in the supine position and in mmHg, as:[2]

$$PaO_2 = 100 - (0.3 \bullet \text{age in years})$$

The next step in oxygen transport, from the pulmonary capillary to the peripheral cell, is mainly dependent upon circulation. Under normobaric conditions, oxygen transport within the circulatory beds depends upon the reversible binding of hemoglobin with oxygen. This effect is represented by the oxygen-hemoglobin dissociation curve (Figure 1). Typically, a rightward shift in this curve is associated with an increase in the delivery of oxygen at the tissue level. This is observed with increases in temperature, 2,3 DPG (2,3 diphosphoglycerate) content within the red blood cell, and by a decrease in pH.[3] Alkalosis, hypothermia, and decreases in 2,3 DPG are associated with a leftward shift in the dissociation curve. This shift tends to decrease oxygen delivery at the tissue level.

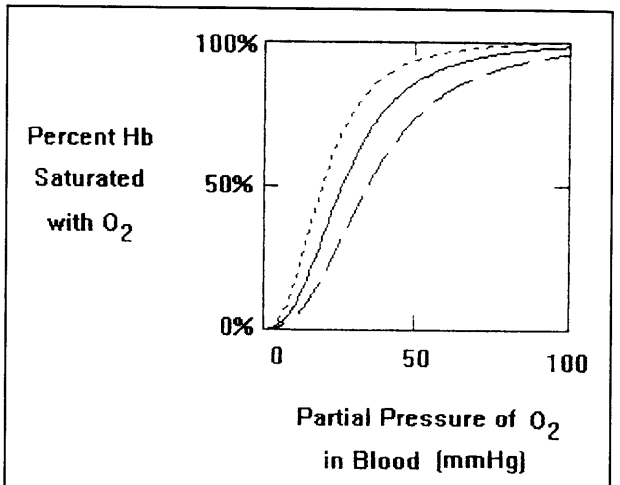


Figure 1. The oxyhemoglobin dissociation curve. The solid line represents normal conditions whereas the dotted line indicates a leftward shift and the dashed line a rightward shift. Left and right shifts are associated with lower and higher P_{50} values, respectively.

The degree of right or left shift in the oxygen-hemoglobin dissociation curve is defined by determining the P_aO_2 at which the hemoglobin is 50% saturated with oxygen and is known as P_{50}. As P_{50} increases, the affinity of hemoglobin for oxygen will decrease.[3,4] Saturation of hemoglobin with oxygen (SaO_2), can be empirically modelled using the Hill equation:

$$SaO_2 = \frac{(P_aO_2)^n}{(P_aO_2)^n + (P_{50})^n}$$

The dimensionless constant **n** takes on a value of approximately 2.73 while P_{50} is normally about 26.6 mmHg. As noted previously, P_{50} varies with pH, 2,3 DPG, and temperature but is unaffected by atmospheric pressures of 1 to 3 atm absolute. Each molecule of normal adult hemoglobin can reversibly bind up to four molecules of oxygen. Each gram of hemoglobin, when maximally saturated, can carry approximately

1.34 ml of oxygen. At one atmosphere pressure, only a small quantity of oxygen is normally dissolved in the plasma. Quantitatively, this relationship can be represented as:

$$CaO_2 = \underbrace{1.34 \bullet Hb \bullet (SaO_2)}_{\text{Bound to Hb}} + \underbrace{(.0031) \bullet P_aO_2}_{\text{Dissolved in plasma}}$$

where CaO_2 is the total oxygen carrying capacity of the blood and is measured in ml of gaseous O_2 per deciliter of blood (ml • dL^{-1}). While the dissolved fraction of oxygen is small at normal environmental pressure, it is this component that ultimately is responsible for establishing a diffusion gradient between the blood and the tissues. The O_2 dissolved in plasma also increases linearly with total environmental pressure. Once the hemoglobin is 100% saturated, any further increases in oxygen carrying capacity can only be achieved by increasing the amount of dissolved O_2.[5] This is represented graphically in Figure 2.

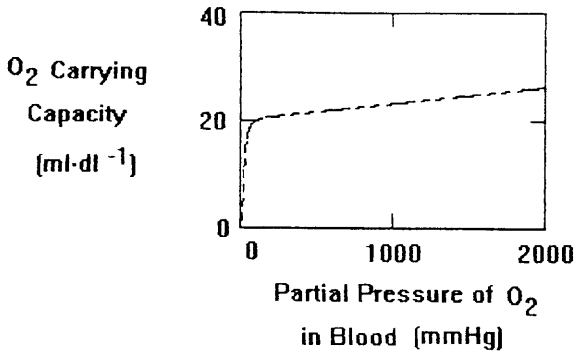


Figure 2. An increase in oxygen carrying capacity occurs with an increasing partial pressure of oxygen.

The coefficient of **.0031** is derived from Henry's law which states that the partial pressure of a gas and its resulting concentration, dissolved in liquid, are directly proportional:

Concentration α (partial pressure)

Hyperbaric oxygen can thus increase the oxygen carrying capacity of the blood significantly by increasing the amount of dissolved oxygen. Table 1 summarizes the relationship between atmospheric pressure, alveolar partial pressure, and the resulting arterial oxygenation.[6,7,8] As shown in this table, breathing 100% oxygen causes arterial P_aO_2 to increase from about 600 mmHg at 1 atm absolute, to approximately 1864 mmHg at 3 atm absolute.

At the tissue level, the diffusion of oxygen from the peripheral capillary can be represented using the Krogh model.[9] This relationship is based on an assumption of a radial diffusion of oxygen out of the capillary. Figure 3 demonstrates this overall increase in the diffusion distance as a function of increasing partial pressure of oxygen. The greatest limitation to tissue oxygenation appears to be intercapillary distance. The Krogh equation (and other models of O_2 diffusion[10]) has greatly aided understanding of oxygen delivery within tissue:

$$P_{O_2}(cap) = \left[\frac{V_{O_2}}{2 \bullet K}\right] \bullet \left[R_O^2 \bullet \ln\left(\frac{R_O}{r_c}\right) - \frac{R_O^2 - r_c^2}{2}\right]$$

where $P_{O_2}(cap)$ is about 40 mmHg at the venous end of the capillary, V_{O_2} is the rate of oxygen consumption which, for muscle, is approximately 10^{-3} ml O_2 ml of

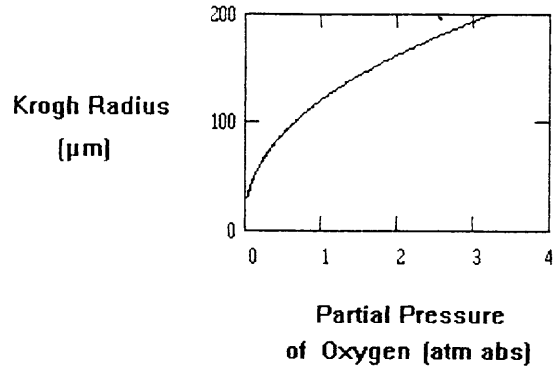


Figure 3. The radius of the Krogh cylinder increases with increasing partial pressure of oxygen. Thus, a greater margin of tissue will be adequately oxygenated under conditions of hyperoxia.

TABLE 1

Alveolar and arterial response to respiratory gas composition and pressure.

Barometric Pressure	1 atm abs (sea level)	1 atm abs (sea level)	2 atm abs	3 atm abs
Inspired gas	air	oxygen	oxygen	oxygen
Arterial P_aO_2 (mmHg)	98	600	1218	1864
Arterial oxygen content (ml 100 ml)	19.3	21.3	23.4	25.5
Venous P_vO_2 (mmHg)	39	48	68	360
Venous oxygen content (ml 100 ml)	14.3	16.3	18.4	20.5
Dissolved O_2 content (ml 100 ml)	0.32	1.7	3.7	5.6

(Modified from Nunn[6] and Saltzman[7]).

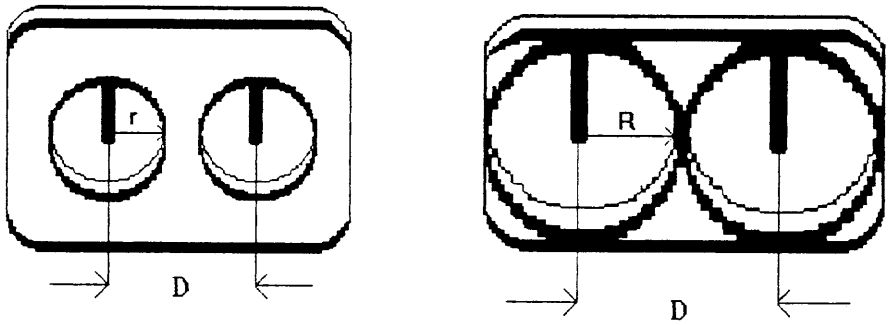


Figure 4. Each of these diagrams represents a set of two capillaries within a section of tissue. The two capillaries on the left each has a Krogh radius of r whereas those on the right have a larger Krogh radius of R. Note how a larger Krogh radius leads to a greater margin of adequately oxygenated tissue. The distance D, between the capillaries, is the same in each diagram. Situations, such as this, may arise when edema causes intercapillary distance to increase.

tissue^{-1} • sec^{-1}. The radius of the capillary r_c is assumed to be 3μm. K is Krogh's diffusion coefficient, which is the product of the solubility and diffusion constants for oxygen and is approximately 22.8 μ^2 • sec^{-1} • ml O_2 • ml tissue^{-1} • atm^{-1}. R_0 represents the diffusion distance or "Krogh radius."

Thus, the intercapillary distance must be equal to or less than twice the Krogh radius to prevent tissue hypoxia. This is illustrated in Figure 4. Specifically, if each capillary is able to oxygenate a radius of R_0, then the maximum distance between capillaries should not exceed $2R_0$. At 1 atm absolute in air, PO_2 will fall from about 100 mmHg at the arterial end of the capillary to 34 mmHg at the venous end. Under normobaric conditions, breathing air, the arterial end of a capillary will adequately oxygenate a radius of approximately 51 μm whereas the venous end of a capillary will adequately oxygenate a radius of approximately 33 μm. Hyperbaric oxygenation to 3 atm absolute increases the arterial and venous partial pressures of oxygen to approximately 2000 and 100 mmHg respectively. With 100% oxygen at 3 atm absolute, the arterial radius will increase to about 200 μm and the venous radius will also expand to approximately 50 μm. This theoretical increase in diffusion distance is shown in Figure 3. Figure 4 illustrates the increased amount of tissue oxygenated under hyperbaric conditions; provided, however, that the same constant number of capillaries remain perfused. This assumption may not be valid.

Blum has shown how the oxygen concentration gradient falls monotonically along the longitudinal axis of a capillary.[7] This principle can be modelled by the cone-like shape of the volume of tissue comprising the Krogh cylinder and is illustrated in Figure 5. Middleman has described that the longitudinal diffusion of oxygen is small and can be neglected relative to axial diffusion.[12]

Clearly there are conditions not taken into account with the Krogh model. Capillary beds within a given tissue segment may open or close and perfusion to a particular region may be altered because of this. Furthermore, the Krogh model does not consider the geometric distribution of capillaries within tissue. In addition, oxygen consumption may not be constant and may vary depending on O_2 supply as well as metabolic demands. Despite these shortcomings, the Krogh equation has generated considerable insight into the understanding of the interrelationship between capillary diameter, oxygen consumption, oxygen partial pressures, and resulting O_2 diffusion.

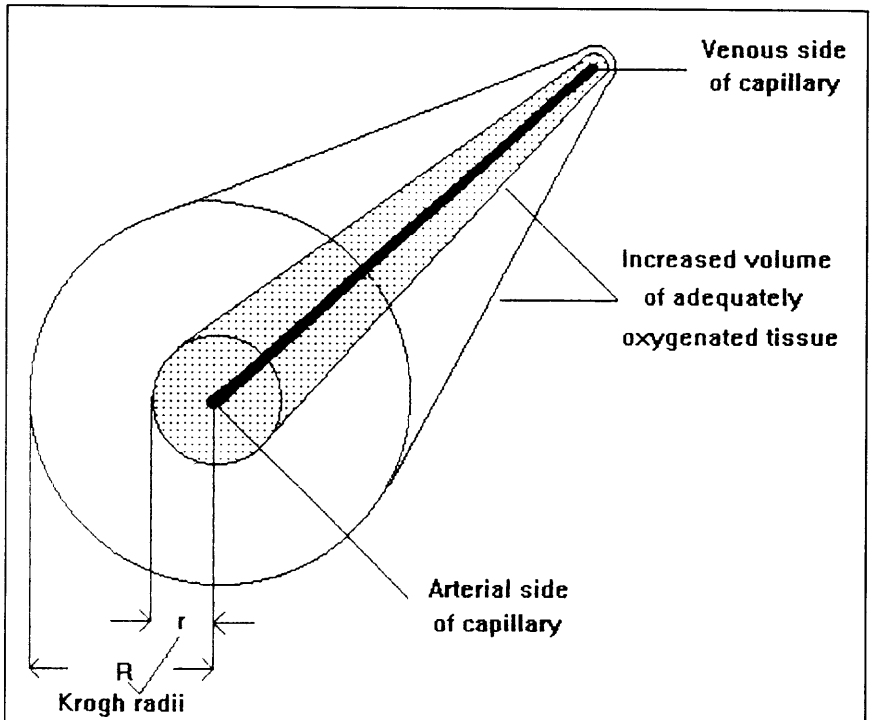


Figure 5. Diagram illustrating the relative increase in the volume of tissue which is adequately oxygenated by an increased partial pressure of oxygen. The thin black cylinder represents a capillary. The two cones, with base radii r and R, represent the normal and increased oxygenated tissue volumes, respectively.

In addition to the increase in blood oxygen carrying capacity and diffusion distance afforded by HBO, the hyperbaric environment allows for compression of pathologic air or gas emboli. Gas bubbles, which form from either iatrogenic causes or by too rapid a decompression, such as an ascent during diving, can be reduced in size significantly by hyperbaric pressure. This relationship can be quantitated by Boyle's law:

Pressure • volume = constant

Since air consists of a mixture of approximately 79% nitrogen and 21% oxygen, breathing 100% O_2 allows for a maximum diffusion gradient for nitrogen from air emboli. The oxygen which will diffuse into the intravascular bubbles will be eventually metabolized.

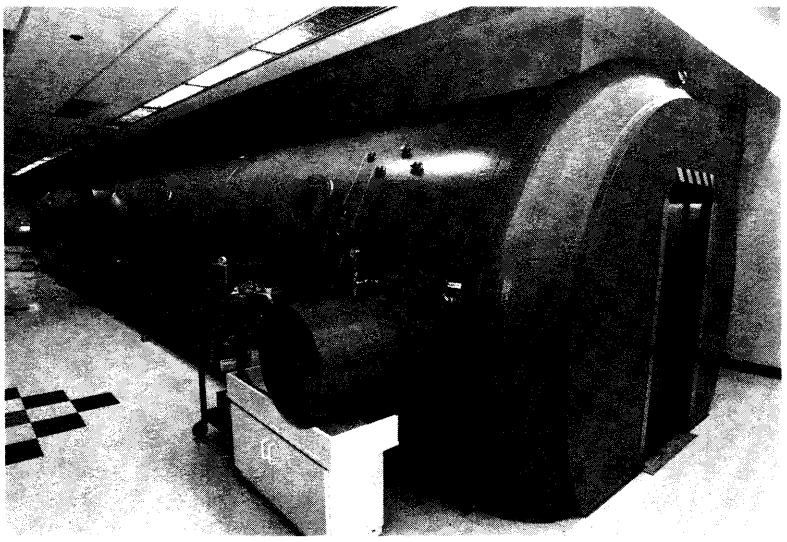
In the hyperbaric environment, gas density rises in direct proportion to gas pressure and the work of breathing consequently increases. Maximum expiratory flow and maximum voluntary ventilation are reduced. These factors must be considered in compensating for gas-flow devices, such as ventilators, used within hyperbaric environments.

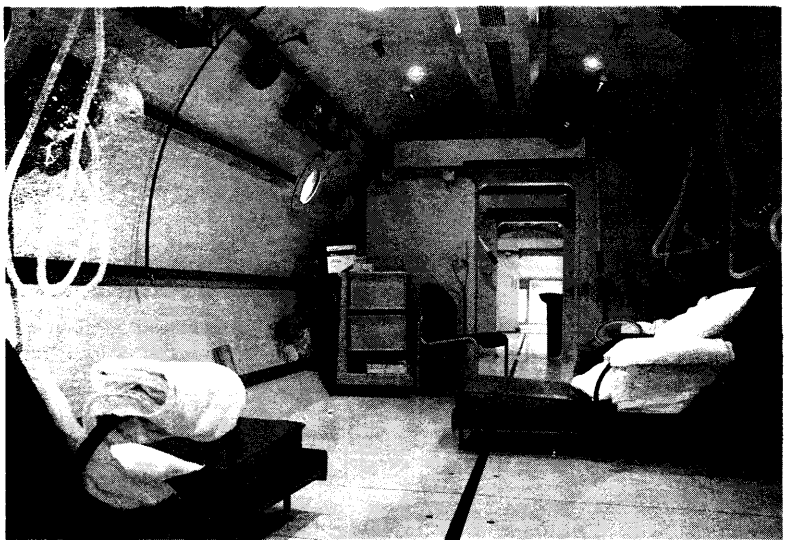
Finally, afferent carotid chemoreceptor sensitivity appears to be reduced by the elevated O_2 pressure in the hyperbaric environment. This results in a small elevation of CO_2 in the CNS and consequently a fall in CNS pH.[13] In addition, venous hemoglobin liberates approximately 0.4 mmoles of CO_2 when it is fully saturated with oxygen. This further reduces pH and must be compensated by a net increase in respiratory drive and ventilation.

Administration Of Hyperbaric Oxygen

Hyperbaric oxygen can be practically administered with either monoplace or multiplace chambers. As shown in Figures 6A and 6B, multiplace chambers have a capacity to expose several patients and attendant staff simultaneously. Most therapeutic support equipment, such as ventilators, intravascular catheters, and intravenous fluids can be maintained with relative ease by the attending staff. Physicians and nurses, compressed within the multiplace chamber with the patients, can continue to provide appropriate care and direct hands-on management. Compressed air is commonly utilized for these multiplace facilities, usually with a maximum pressure range of up to six atm absolute. The patients may breathe O_2-enriched gas mixtures or 100% oxygen via a face mask or through an endotracheal tube. Patients can receive 100% O_2 limited to a maximum partial pressure of 3 atm absolute. Higher total oxygen pressure is rapidly toxic and is never utilized. Transfer of materials into and out of the chamber may be done via pressure interlocks. This greatly facilitates long-term care and comfort. Multiplace chambers are costly to maintain and to operate and may carry the drawback that decompression time is often accrued by attending staff while breathing compressed air.

Monoplace chambers (Figure 7) allow for administration of hyperbaric oxygen to a single patient. These are far less costly to set up than multiplace chambers and can utilize a hospital's existing oxygen supply. A typical monoplace chamber is a cylinder, usually 2 to 3 feet in diameter, with acrylic walls to allow better inspection of the patient and to minimize claustrophobia. Oxygen then flows into the chamber at a rate





Figures 6A and 6B. Multiplace hyperbaric chambers allow for treatment of several patients simultaneously. Attendant staff can also provide immediate hands-on care from directly within the chamber. ***Photographs courtesy of Roy A.M. Myers, M.D., University of Maryland Medical Center.***

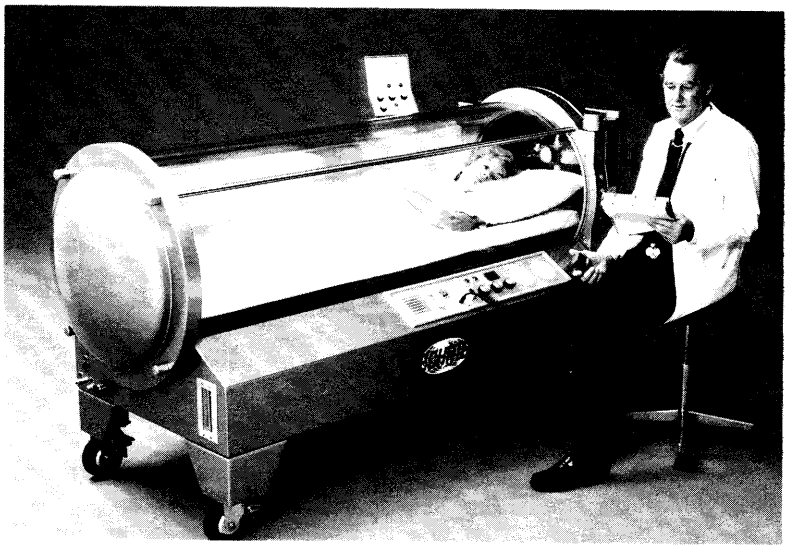


Figure 7. A monoplace chamber is an economical means of providing hyperbaric therapy while utilizing a hospital's existing O_2 supply. ***Photograph courtesy of Sechrist Industries, Inc.***

of 200 - 400 liter • minute^{-1} and an environment of 100% O_2 is rapidly created. Hyperbaric-compatible IV pumps and ventilators are available which can be located external to the monoplace chamber. Automated non-invasive blood pressure monitoring has also been developed for use within a hyperbaric environment. Monitoring of electrocardiograms (ECG) can be done. In addition, intra-arterial blood pressure and blood gas monitoring, with periodic sampling through the pressurized wall, is possible with experienced personnel. Thus, even critically-ill patients may receive hyperbaric oxygen without compromising physiologic monitoring. Unfortunately, very few hyperbaric units, and especially few monoplace chambers, have significant experience in caring for critically-ill patients.

It is important to remember that the pressure changes within the chamber must be taken into account when using external pressure-sensitive equipment, such as IV pumps and ventilators. Incorrect settings could lead to an over or under dosing of medications and or fluids. Similarly, a ventilated patient may receive an inappropriate tidal volume. Airway pressure must be constantly monitored.

Physiologic and Toxic Responses to Hyperbaric Oxygen

During hyperbaric oxygenation, systemic blood pressure tends to remain normal or will slightly increase.[14] This apparently results from a generalized vasoconstriction that is observed during hyperoxia in normal tissues. Peripheral vascular resistance is thus raised. Reflexly, cardiac output decreases by 10% to 20% which results from both a reduction in heart rate and stroke volume. Despite the apparent rise in afterload, myocardial oxygen consumption is decreased as much as 11% at 3 atm absolute. This probably offsets the coronary vasoconstrictive effects of hyperoxia.[15]

Oxygen toxicity in both the normobaric and hyperbaric environments has been well documented. Currently this pathology is believed to be mediated by the generation of oxygen free radicals.[16] Clinically, oxygen toxicity may present as pulmonary and/or central nervous system pathology. Pulmonary manifestations of oxygen toxicity can range from a mild reversible tracheal irritation to pulmonary edema and frank pulmonary endothelial necrosis. Complications of oxygen diffusion happen late in the course of pulmonary toxicity and can be quantitated as a widening of the alveolar:arterial oxygen tension gradient. Decreases in thoracic compliance and vital capacity have also been observed. Neurological effects of hyperbaric oxygen are rare. However, neurological aspects of oxygen toxicity can be manifested as twitching of the perioral muscles, anxiety, or behavioral changes. Vertigo, syncope, and seizures can occur without prodromes.

To reduce the risk of oxygen toxicity during hyperbaric therapy, air can be administered intermittently for periods of 5 to 10 minutes for every 20 or 30 minutes of O_2 breathing. This is easier to accomplish in multiplace chambers, but recent provision of compressed air lines, inside monoplace chambers, has permitted extension of "air breaks" also within the monoplace environment. Free radical scavenger agents, such as vitamin E, may be helpful in preventing acute toxic effects.

Barotrauma from rapid compression can result in rupture of the tympanic membranes, as well as trauma to the paranasal sinuses. Patients generally can swallow or yawn to equilibrate middle ear pressure with that of the hyperbaric chamber. Those who are unconscious or unable to adequately do this may need bilateral tympanotomies and insertion of pressure equalization (PE) tubes. Rapid decompression after hyperbaric oxygenation can also cause clinically significant barotrauma, such as a pneumothorax or air embolism. In clinical practice this is very dangerous, but extremely rare.

Reversible visual changes may occur with extended oxygen use. Typically this is observed as an increasing myopia. Retrolental fibroplasia has been reported in neonates and premature infants receiving over 50% oxygen at sea level or 1 atm absolute. This can result in blindness.[17] Calustrophobia can also occur as a result

of the limited space available within a hyperbaric chamber. This can be usually treated with mild sedation when necessary. Because 100% oxygen can support violent combustion, there is a great potential for fire within these enclosed chambers. Practically, this restricts the use of all electrical equipment within hyperbaric environments. It is mandatory to utilize careful preventive measures to avoid this disastrous complication.

Mechanisms of Action of Hyperbaric Oxygen

Empirical experience has shown favorable clinical results with the use of hyperbaric oxygenation in a variety of diseases and syndromes. An official review of clinical benefits derived from HBO is provided periodically by the Hyperbaric Oxygen Committee of the Undersea and Hyperbaric Medical Society. This is an international organization of physicians, scientists and practitioners involved in a range of studies and observations of patients exposed to increased environmental pressure. Table 2 shows the most common syndromes with improved outcome following HBO.

TABLE 2

Clinical Conditions Responding To Hyperbaric Oxygen Therapy

1. **Gas Bubble-Mediated Diseases:**
   - Air or gas embolism (acute)
   - Decompression sickness
   - Altitude decompression sickness
2. **Toxicosis:**
   - Carbon monoxide poisoning
   - Cyanide poisoning
   - Hydrogen sulfide poisoning
3. **Acute Infections:**
   - Clostridial myonecrosis (gas gangrene)
   - Necrotizing infections
4. **Chronic Infections:**
   - Refractory Osteomyelitis
5. **Acute Ischemic Processes:**
   - Crush injury
   - Compartment syndrome
6. **Chronic Ischemic Processes:**
   - Selected nonhealing wounds
   - Radiation necrosis
   - Skin graft preparation
   - Burns
7. **Exceptional Blood Loss-Anemia**

The heterogeneity of diseases treated by HBO exemplifies the diversity of action of hyperbaric oxygen in various syndromes. Four different mechanisms can be identified:

1. Increase in total barometric pressure.
2. Direct increase in oxygen partial pressure in arterial blood, interstitial fluids, and tissues.
3. Increase in oxygen content of arterial blood.
4. Reactive biological phenomena caused by intermittent exposure to increased oxygen pressure.

The first three mechanisms produce different oxygen transport regimens in specific syndromes. As an example, in acute arterial gas embolism it is postulated that symptoms are caused by sudden vascular obstruction in a terminal arteriole or in a capillary, by a gaseous bolus. In this case, rapid compression from 3 to 5 atm absolute may decrease the volume of the obstructing bubble and will favor resumption of critical blood flow to the affected area. This has been demonstrated by the very rapid resolution of major neurological symptoms, such as paraplegia resulting from decompression syndrome, after rapid recompression in a hyperbaric chamber. A different mechanism of action is operative when HBO is utilized to alleviate symptoms of extensive acute anemia, such as after a catastrophic hemorrhage in patients refusing blood transfusion, or when temporary difficulties in cross-matching of blood make red cell replacement difficult or impossible. In this case, HBO from 2.5 to 3 atm absolute and 100% oxygen breathing will acutely provide a sufficient increase in oxygen content in arterial blood. This will alleviate the resultant tachycardia and metabolic acidosis and allows time to facilitate an essential transfusion. A still different mechanism of action, an increase in oxygen partial pressure in arterial blood, is operative when an acutely comatose patient with carbon monoxide intoxication is treated with 2.8 atm absolute and 100% O_2 and awakens within minutes. The large increase in O_2 gradient from blood to tissue may explain the improved elimination of carbon monoxide from the body. This is the reason for the decreased half-life of carboxyhemoglobin when switching from air to oxygen at 1 atm absolute. An even greater reduction in the half-life of carboxyhemoglobin will occur with oxygen administered at 3 atm absolute.

Finally, the last mechanism of reactive mediator activation is invoked to explain the stimulation of endothelial bed development in chronic non-healing wounds. This occurs when the wound is exposed to periodic increases and decreases in PO_2.

Accepted Conditions For Hyperbaric Therapy

In this section, the rationale and clinical basis for the therapeutic use of hyperbaric oxygen will be examined in greater detail. Table 2 outlines indications currently recommended by the Hyperbaric Oxygen Therapy Committee Report of the Undersea and Hyperbaric Medical Society.[18] This report is reviewed every 2-3 years on the basis of scientific evidence and constitutes the most complete document published in the field.

Air And Gas Embolism

The entry of air or gas into the intravascular space often occurs without recognition. It can happen as a

consequence of iatrogenic processes, traumatic injuries, or may be a result of accidental rapid decompression.[19] A large number of procedures may lead to iatrogenic gas emboli: complications of head, neck or thoracic surgery, cardiopulmonary bypass,[20] penetrating chest injury,[21] needle or catheter placement, renal dialysis, obstetric or gynecologic manipulation, as well as urologic procedures.[22] The pathologic mechanism of intravascular air bubbles involves mechanical obstruction of blood flow to the regions where they are dispersed, a secondary activation of hemostatic mechanisms, and platelet aggregation.[23]

Manifestations of gas emboli are varied depending on the size of the bubbles, volume of gas entrained, rapidity of the event, position of the patient at the time of the event, and whether gas is located within an artery or vein.[24] Intra-arterial gas emboli usually present with symptoms involving the central nervous system or the myocardium. Common presentations include: dizziness, nausea, sensory or motor deficits, visual disturbances, coma, and seizures.[25] Myocardial manifestations of ischemia, such as chest pain and ECG changes, may occur. Venous air emboli may present with pulmonary symptoms such as chest pain, cough, dyspnea, and hemodynamic instability. In both cases mortality and morbidity are significant. Diagnostic confirmation of air emboli may be difficult unless air entry is actually observed, a characteristic "millwheel murmur" is present on cardiac auscultation, or air is found on aspiration from a central line. New Doppler and neuro-imaging modalities add to the diagnostic armamentarium. A recent study found that magnetic resonance imaging is more sensitive in detecting focal cerebral ischemia due to air embolism, than conventional computerized tomographic scanning.[26]

The rationale for the use of hyperbaric oxygen therapy in gas embolism is based upon rapidly increasing ambient pressure to decrease bubble size and improve blood flow to the affected area. Ventilation with 100% oxygen induces the largest possible gradient for the inert gas (usually nitrogen when air is aspirated) within the bubble to be reabsorbed. Vasoconstriction, due to high tissue oxygen tension, may contribute to reduce the volume of cerebral edema. Increased tissue oxygen tension will improve the survival of marginally viable and ischemic areas.[27-29] Numerous cases of successful hyperbaric oxygen therapy for air emboli have been reported.[24,25,29,30]

The treatment of choice for air or gas emboli is compression in a hyperbaric chamber. This should be instituted as close to the time of insult as possible. However, clinical improvement has been documented after a delay of 7 hours[24] and up to 42 hours.[31] Therefore, a delay in referral does not preclude successful hyperbaric therapy. Different regimens exist which vary from administering oxygen at 2.8 atm absolute, to using compressed air or Nitrox (50% oxygen combined with 50% nitrogen) at 6.0 atm absolute. The United States Navy dive Table 6 can be utilized as well.[32] Treatments may be repeated until there is no further clinical improvement.

Decompression Sickness

Decompression sickness (DCS) is a clinical syndrome presenting with a large variety of manifestations. It occurs when an inert gas (usually nitrogen) that is dissolved in bodily tissues is released from physical solution during decompression. This is the cause of pathologic bubble formation.

Decompression sickness may present in a great variety of ways. A high index of suspicion and the history of recent compression at elevated environmental pressure play an important diagnostic role. Correct diagnosis is vital. Without proper treatment, permanent neurologic deficits may result in previously healthy individuals. The most common symptom (in over 90% of cases) is deep, dull pain occurring in any joint ("bends" or Type I DCS). The central nervous system is affected in approximately 25% of cases of decompression sickness, with a predominance of spinal cord involvement (Type II DCS). Dizziness, nausea, behavioral changes, visual disturbances, seizures and coma are among the most common presentations. Presence of motor and sensory deficits, paraplegia, bowel or bladder incontinence, and loss of sexual function usually indicate spinal cord involvement. Symptoms attributable to the peripheral nervous system occur in approximately 22% of sport divers presenting with decompression sickness. These manifest as low back pain, paresthesia, weakness or proprioceptive deficits.[33] Pulmonary involvement ("the chokes") is rare and presents usually after a major intravascular gas load, with chest pain, dyspnea, nonproductive cough, and cyanosis. Decompression sickness shock is a serious complication characterized by a generalized transcapillary plasma leakage. DCS shock may result in hypovolemia, cardiovascular collapse, or pulmonary edema.

Predisposing factors leading to decompression sickness include: cramped position during or after decompression, recent strain or sprain of a muscle or joint, and hard exercise during or after decompression. Hyperthermia, recent alcohol consumption, age over 40 years, and hypercarbia also may contribute. In addition, Moon et al.[34] showed that out of 23 divers with serious decompression sickness, there was an increased incidence (39%) of patent foramen ovale, compared to an incidence of 5% in 176 normal volunteers. They hypothesize that a patent foramen ovale may allow otherwise innocuous venous gas bubbles to enter the arterial circulation and produce symptoms.

The definitive treatment for decompressive disease

is recompression in a hyperbaric chamber. Often, patients must be transported some distance to the nearest hyperbaric facility. They should be kept as close to sea level as possible during transport by using pressurized or low-flying aircraft (maximum altitude 1000 feet). To hasten the elimination of nitrogen from the tissues 100% oxygen, via tight-fitting face mask or endotracheal tube, should be used in the time period prior to hyperbaric treatment. Resuscitation with intravenous crystalloids or colloid must be used to maintain tissue perfusion. This may also aid in the elimination of nitrogen. Steroids may be used whenever central nervous system or spinal cord edema is presumed although it may take several hours for these to have an effect. Steroids have been shown to increase the risk of oxygen toxicity in animals, but this has not proven to be clinically significant in humans.

Specific hyperbaric treatments vary according to clinical case but US Navy Table 6 is most commonly used. Multiple treatments may be given until there is no further symptomatic improvement. The sooner the patient is recompressed, the better the results, particularly in labyrinthine decompression sickness. However, treatment may still be effective after a delay of several days.[35]

Altitude decompression sickness is similar to diving decompression sickness in its mechanism and clinical manifestation. Return to sea level and oxygen breathing are usually sufficient to treat mild cases. Compression to hyperbaric pressures may be needed in more serious circumstances. Davis et al.[36] reported complete resolution of symptoms in 143 out of 145 cases of altitude decompression sickness when treated with recompression at 2.8 atm absolute.

Toxicosis: Carbon Monoxide Poisoning

Carbon monoxide poisoning is common, often accidental, and may present with nonspecific, generalized symptoms. It occurs predominantly during cold weather, as sources of carbon monoxide include malfunctioning heaters, industrial furnaces, motor vehicle exhaust and smoke inhalation from accidental fires. Neurologic and cardiovascular involvement are common and patients may present acutely with nausea, vomiting, hypotension, headache, syncope, vasomotor collapse, behavioral abnormalities, seizures, or coma. The classic "cherry-red" lips are rarely seen on admission to the emergency department. Acutely, carboxyhemoglobin (HbCO) levels are elevated in blood and may range from 10-20% in asymptomatic patients to 50-60% in comatose patients. However, HbCO measurements performed hours after exposure do not correlate with clinical findings, presumably because part of the toxic effects may be attributed to intracellular poisoning. Norkool and Kirkpatrick[37] showed, in a large series of patients, that the mean carboxyhemoglobin level in survivors (29.3%) was not significantly different from those who died (30.8%). In addition, Myers et al.[38] found that psychometric testing may be necessary to demonstrate subtle neuropsychiatric abnormalities. The duration of exposure, activity during that period, and interval between exposure and assessment are also factors in judging the severity of intoxication.[39]

Subacute neurologic sequelae have been described.[38] Out of 213 patients treated for carbon monoxide poisoning, none of those treated with hyperbaric oxygenation suffered clinically significant sequelae. However, 12.1% of those not treated with hyperbaric oxygenation developed subacute neurologic deficits. Symptoms such as headache, memory loss, abnormal psychometric testing and personality change have developed up to 21 days after initial exposure, and have been treated successfully with hyperbaric oxygen therapy.

In 1895 Haldane demonstrated that the poisonous action of carbon monoxide was due to its combination with hemoglobin and that this effect could be reversed with oxygen administered at increased tensions.[40] The affinity of carbon monoxide for hemoglobin is over 200 times greater than the affinity of oxygen for hemoglobin.[41] Once carbon monoxide is bound, less hemoglobin is then available for oxygen transport and the oxygen dissociation curve of the remaining oxyhemoglobin is shifted to the left, resulting in functional tissue hypoxia. It has been discovered more recently that *in-vivo* intracellular binding of carbon monoxide to cytochrome oxidase a,a_3 may occur within mitochondria. In some cases intracellular binding may contribute to the pathophysiology of carbon monoxide poisoning. This may result in persistent disruption of intracellular respiration.[42]

Hyperbaric oxygen therapy increases the speed of dissociation of carboxyhemoglobin as the rate of carbon monoxide elimination is inversely related to the inspired oxygen partial pressure. Pace et al.[43] found that in healthy males, initial carboxyhemoglobin levels of 20 - 30% could be decreased from 249 minutes of breathing room air at 1 atm absolute, to 47 minutes of breathing 100% oxygen at 1 atm absolute, or to 22 minutes if breathing 100% oxygen at 2.5 atm absolute. Hyperbaric oxygen therapy also improves tissue oxygenation by increasing the amount of physically dissolved oxygen and by hastening the liberation of carbon monoxide from cytochromes.[42] Goulon et al.[44] demonstrated a decrease in mortality from 30% to 13.5% if hyperbaric oxygen therapy was administered within 6 hours of discovery, as compared to patients who received 100% oxygen at 1 atm absolute. They also found that those treated within 6 hours had a decreased incidence of long-term sequelae. These findings have been confirmed by Myers et al.[38] and Norkool and Kirkpatrick.[37]

Administration of hyperbaric oxygen for carbon monoxide intoxication during pregnancy has recently been reported by Van Hoesen et al.[45] They concluded that short hyperoxic exposures, attaned during hyperbaric therapy for carbon monoxide poisoning, should be tolerated by the fetus in all stages of pregnancy and may reduce the risk of death to the mother and deformity or death to the fetus.

Hyperbaric oxygen therapy is the treatment of choice in patients with carbon monoxide poisoning. Generally, patients with heavy exposure, as suggested by carboxyhemoglobin levels greater than 25%, should receive treatment. Patients with any residual neurologic symptoms, circulatory or respiratory collapse, or ischemic changes on ECG, ought to also receive treatment regardless of their carboxyhemoglobin levels. Patients should be given 100% oxygen via a tight-fitting face mask or endotracheal tube during transport and medically evaluated prior to hyperbaric therapy. Treatment is recommended at 2.5 to 3.0 atm absolute for up to 90 minutes depending on clinical status. Follow-up therapy may be administered within 12 to 24 hours after initial treatment in those patients presenting with severe manifestations of carbon monoxide poisoning or with residual symptoms.

Cyanide Intoxication

Most cyanide (CN) poisoning appears to be related to occupational exposure or may be associated with homicidal ingestion. Recently it has been shown that CN levels correlate with carbon monoxide levels in smoke inhalation victims.[46]

The mechanism of cyanide toxicity is thought to be through the inhibition of cytochrome oxidase which impairs intracellular respiration. The mainstays of treatment are sea level oxygen and chemical antidotes. The use of sodium nitrite enhances cyanmethemoglobin formation. Sodium thiosulfate treatment provides sulfur to hasten thiocyanate formation, which is less toxic than cyanide. Some animal studies have shown improvement with hyperbaric therapy, when used as an adjunct to chemical antidotes. Although case reports in humans have shown conflicting results,[47] good outcomes have been reported.[48,49]

Hydrogen Sulfide Poisoning

Hydrogen sulfide has the familiar "rotten egg" odor and is formed from the decomposition of organic matter containing sulfer. Hydrogen sulfide has been shown to have a toxic effect on cytochrome oxidase. For this reason, hyperbaric oxygenation has been suggested as adjunctive therapy when conventional treatment fails. Isolated case reports have documented improved outcome.[50,5

Acute Infections

Clostridial myonecrosis (gas gangrene) is characterized by a rapidly spreading muscle necrosis. The most commonly isolated organism is Clostridium perfringens as well as other clostridia species.[52] Although it is an anaerobe, it tolerates oxygen tensions up to 30 mmHg. C. perfingens is frequently found in the soil as well as the gastrointestinal tract. Its most significant pathological aspect is the ability to produce alpha-toxin. This exotoxin is an oxygen-stable lecithinase and results in progressive hemolysis, tissue liquefaction, and necrosis. Systemically, septic shock, hemolytic anemia, renal failure, as well as disseminated intravascular coagulation can result. Alpha-toxin can also lead to cardiac and neurological abnormalities. Patients at particular risk are those with diabetes and/or necrotizing infections, and injuries complicated by trauma, contamination, ischemia, compound fracture, or foreign bodies. These wounds are swollen, extremely painful, and often show an associated brown, sweet-smelling drainage. Gas within the soft tissues may be found on radiologic examination.

Anaerobic organisms lack antioxidant enzymes such as superoxide dismutase and hydrogen peroxide catalase.[53] Hyperbaric oxygen appears to be bacteriostatic and stops spore germination.[54] In animal studies, HBO was shown to decrease alpha-toxin production although preexisting toxin was still stable.[55] Hyperbaric oxygen also results in vasoconstriction, which reduces tissue edema.

Mortality from gas gangrene is still elevated overall.[56,57] Adjuvant HBO therapy results in a reduced amputation rate (approximately 24% compared to 50%), as when surgery is used alone. Hyperbaric oxygen also appears to improve overall survival when used with surgery and antibiotics. In one study the survival rate was 78.2% with HBO as compared to 55% in the control group.[58] Early aggressive therapy appears to be the most beneficial. Current recommendations are 3 atm absolute for 90 minutes repeated three times within the first twenty-four hours after the diagnosis is initially suspected. Further therapy, twice daily, should continue for four to five days.

Crepitant anaerobic cellutitis is a similar gas producing infection although it tends to spare the muscles and involves only the soft tissues. Organisms responsible include: Bacteroides, Petostreptococcus, Enterbacteriaceae, and Clostridium species. When compared to gas gangrene, systemic involvement and mortality are lower.[58]

Fournier's disease, a similar acute life-threatening infection, is characterized by extensive necrosis of the superficial and deep fascia of the perineum or scrotum. It spreads throughout the tissue planes but does not involve muscle. Both anaerobic and aerobic organisms

have been isolated from these infections. Overall mortality is approximately 30%.

Hyperbaric oxygen appears to be effective because of direct lethal effects of O_2 on anaerobic and microphilic aerobic organisms. HBO may also be useful in combination with antibiotics in reducing necrosis.[59] Current therapeutic recommendations are twice daily treatments at 2.0 to 2.5 atm absolute for 90 to 120 minutes until the patient is stable. Treatment may then be once daily.

Chronic Infections And Osteomyelitis

Osteomyelitis is usually a mixed infection of Staphlococcus aureus, Escherichia coli, Enterobacteria, Klebsiella, Pseudomonas or Proteus species. Factors leading to osteomyletitis include presence of a foreign body, diabetes mellitus, vascular insufficiency, or defects in immune function. Chronic osteomyelitis is defined as continued infection for six months despite antibiotic and surgical therapy. Treatment is difficult because oxygen transport is compromised in avascular bone. Furthermore, oxygen penetration is also complicated by the presence of necrotic and fibrous tissue. Without adequate oxygen, the function of white blood cells, antibiotics, and antibodies are diminished. In animal studies, HBO raised bone oxygen tension.[60] In addition to making previously hypoxic tissue normoxic, hyperbaric oxygen appears to facilitate the transport of aminoglycoside antibiotics across cell membranes.[61,62,63]

In one study 40 patients were treated with surgical debridement, antibiotics, and HBO for an average of 40 treatments. After 23 months, 85% of the patients were clinically free of disease.[64] Similarly, another study using adjuvant HBO therapy, showed 89.5% of patients disease free after 34 months.[65]

Initially, HBO is recommended at 2.0 to 2.5 atm absolute for 90 to 120 mintues twice daily. For chronic management of osteomyelitis, this can be reduced to a once-daily regimen. At least 30 treatments are necessary in addition to surgical wound care.

Acute Ischemic Processes

Both crush injury and compartment syndrome lead to tissue ischemia by a similar mechanism. Edema and swelling tend to reduce perfusion resulting in hypoxic tissue. Concomitant vasodilation will exacerbate this situation. Hyperbaric oxygenation results in vasoconstriction that reduces edema while maintaining adequate tissue oxygenation. HBO therapy is done at twice daily intervals at 2.0 to 2.5 atm absolute for five to seven days. Fasciotomy, surgical debridement, and aggressive wound care are recommended.

Chronic Ischemic Processes

Many chronic conditions exist which predispose to non-healing wounds. The most frequently encountered diseases are: diabetes mellitus, peripheral vascular disease, irradiation, infection, anemia, and malnutrition. Hyperbaric oxygenation intermediately restores hypoxic tissue conditions to normoxic thus promoting healing and growth.

Out of 18 patients with diabetic foot wounds who were treated with HBO, 16 had complete healing as opposed to 1 patient in 10 in a control group.[66] Strict glucose control, surgical therapy, and debridement are also required.

Radiation Necrosis

Radiation therapy leads to microvascular injury and eventually tissue necrosis. Specifically, osteoradionecrosis seems to respond favorably to hyperbaric oxygen. HBO increases angiogenesis,[67] collagen formation,[68] and osteoneogenesis.[69] For facial reconstruction of irradiated tissues, use of HBO prior to surgery resulted in a success rate of 92% with a complication rate of only 9%.[70]

In a prospective trial of HBO versus penicillin, for patients with prior irradiation of the mandible, osteoradionecrosis after tooth extraction was reduced from 29% to 5.4%.[71]

The current recommendation for treatment is HBO at 2.0 to 2.4 atm absolute for 60 to 120 minutes daily for 40 days.

Exceptional Blood Loss-Anemia

At 3 atm absolute enough oxygen can be dissolved in plasma to maintain tissue oxygen demands without hemoglobin being present.[72] This might be used transitorily in situations where a patient's blood may be difficult to crossmatch or if a patient refuses transfusion.[73]

Contraindications To Hyperbaric Oxygen Therapy

The most common situation which may be a contraindication to HBO is chronic obstructive pulmonary disease (COPD). With this condition, the risk of pulmonary barotrauma and toxicity from HBO may outweigh its benefits. This conflict may arise in the elderly and debilitated in whom chronic obstructive pulmonary disease is prevalent. Those patients with a history of seizure disorder should receive anticonvulsant medication without interruption during hyperbaric therapy. If a history of seizure disorder is suspected, prophylaxis may be warranted.

Myringotomy tubes may be necessary if evidence exists that there may be blockage of the eustachian tubes or if the patient is unconscious and thus cannot swallow. Decongestants may be helpful for those patients with symptomatic sinus obstruction.

Claustrophobic patients need reassurance when enclosed in multiplace chambers and especially in

monoplace chambers. Sedation, when necessary, can be achieved with benzodiazepines.

Bleomycin, a cancer chemotherapeutic agent, is associated with pulmonary fibrosis. Patients who have been exposed to this drug may be particularly prone to pulmonary manifestations of oxygen toxicity.[74] Use of hyperbaric oxygen in these patients could possibly result in severe pulmonary complications.

Conclusion

Hyperbaric oxygen therapy is based upon rational scientific principles and is useful in a variety of diseases. It is the treatment of choice for bubble mediated disease as well as air and gas emboli. It is also ideal for carbon monoxide poisoning and may be useful in other conditions of toxicosis. Additionally, current clinical research has shown HBO to be beneficial adjuvant therapy in ischemic and infectious conditions. Future research must further elucidate its multiple mechanisms of action and may lead to more narrowly defined applications.

REFERENCES

1. Moon RE, Camporesi EM, Shelton DI: Prediction of arterial PO_2 during hyperbaric Physiology IX: Proceedings of the Ninth International Symposium on Underwater and Hyperbaric Physiology. Bethesda: Undersea and Hyperbaric Medical Society, 1987; pp 1127-1131.

2. Kitamura H, Sawa T, Ikezono E: Postoperative hypoxemia: The contribution of age to the maldistribution of ventilation. *Anesthesiology* 36:244-252, 1972.

3. Kilmartin JV, Rossi-Bernardi L: Interaction of hemoglobin with hydrogen ions, carbon dioxide, and organic phosphates. *Physiol Rev* 53:836-890, 1973.

4. Benesch R, Benesch RE: Intracellular organic phosphates as regulators of oxygen release by haemoglobin. *Nature* 221:618-622, 1969.

5. Jain KK: Textbook of Hyperbaric Medicine, Physical, Physiological and Biochemical Aspects of Hyperbaric Oxygenation. Toronto and Lewiston, NY: Hogrete and Huber 1990; pp 11-25.

6. Nunn JF: Applied Respiratory Physiology 3rd Edition Chapter 29. Hyperoxia and oxygen toxicity. London: Butterworths 1987; pp 478-482.

7. Davis JC: Enhancement of Healing. In: Camporesi EM, Barker AC (eds): Hyperbaric Oxygen Therapy a Critical Review. Bethesda: Undersea and Hyperbaric Medical Society, 1991; pp 127-140.

8. Saltzman HA, Smith WW, Fuson RL, et al.: Hyperbaric Oxygenation. *Monogr Surg Sci* 2:1-68, 1965.

9. Krogh A: The anatomy and physiology of capillaries. New Haven: Yale University Press 1922; pp 266-292.

10. Gonzalez-Fernandez JM, Atta SE: Transport and Consumption of Oxygen in Capillary-Tissue Structures. *Math Biosci* 2:225-262, 1968.

11. Blum JJ: Concentration profiles in and around capillaries. *Am J Physiol* 198:991-998, 1960.

12. Middleman S: Transport Phenomena in the Cardiovascular System. Chapter 3: Transcapillary Exchange. New York: Wiley-Interscience 1972; pp 116-177.

13. Salzano JV, Camporesi EM, Stolp BW et al.: Physiological Response to Exercise at 47 and 66 ATA. *J Appl Physiol* 57:1055-1068, 1984.

14. Whalen RE, Saltzman HA, Holloway DH: Cardiovascular and Blood Gas Responses to Hyperbaric Oxygenation. *Am J Cardiol* 15:638-646, 1965.

15. Savitt MA, Elbeery JR, Owen CH, Rankin JS, Camporesi EM: Mechanism of decreased coronary and systemic blood flow during hyperbaric oxygenation. *Undersea Biomed Res* 16(Suppl) #25, 1989.

16. Klein J: Normobaric Pulmonary Oxygen Toxicity. *Anesth Analg* 70:195-207, 1990.

17. Phelps DL: Retinopathy of Prematurity. *Pediatr Clin North Am* 40:705-714, 1993.

18. Hyperbaric Oxygen Therapy: A Committee Report. Myers RAM, Chairman. Bethesda: Undersea and Hyperbaric Medical Society, 1986.

19. Davis JC, Elliott DH: Treatment of Decompression disorders. In: Bennett PB, Elliott DH (eds): The Physiology and Medicine of Diving, 3rd ed. Bailliere, London: Tindall, 1982, pp 473-486.

20. Stoney WS, Alford WC Jr., Burrus GR, Glassford DM Jr., Thomas CS Jr.: Air embolism and other accidents using pump oxygenators. *Ann Thorac Surg* 29:336-340, 1980.

21. Halpern P, Greenstein A, Melamed Y et al.: Arterial air embolism after penetrating chest injury. *Crit Care Med* 11:392-393, 1983.

22. Vourc'h G, Berreti E, Trichet B, Moncorge C, Camey M: Two unusual cases of gas embolism following urethral surgery under laser. *Int Care Med* 8:239-240, 1982.

23. Hallenbeck JM, Bove AA, Moquin RB, Elliott DH: Accelerated coagulation of whole blood and cell-free plasma by bubbling in vitro. *Aerospace Med* 44:712-714, 1973.

24. Peirce EC: Cerebral gas embolism (arterial) with special reference to iatrogenic accidents. *Hyperbaric Oxygen Rev* 1:161-184, 1980.

25. Gillen HW: Symptomatology of cerebral gas embolism. *Neurology* 18:507-512, 1968.

26. Warren LP, Djang WT, Moon RE et al.: Neuroimaging of scuba diving injuries to the CNS. *J Neuroradiol* 9:933-938, 1988.

27. Sukoff MH, Ragatz RE: Hyperbaric oxygenation for the treatment of acute cerebral edema. *Neurosurg* 10:29-38, 1982.

28. Sukoff MH, Hollin SA, Espinosa OE, Jacobson JH: The protective effect of hyperbaric oxygena-

tion in experimental cerebral edema. *J Neurosurg* 29:236-241, 1968.

29. Bove AA, Clark JM, Simon AJ, Lambertsen CJ: Successful therapy of cerebral air embolism with hyperbaric oxygen at 2.8 atm absolute. *Undersea Biomed Res* 9:75-80, 1982.

30. Takahashi H, Kobayashi S, Hayase H, Sakakibara K: Iatrogenic air embolism: A review of 34 cases. 9th International Symposium on Underwater and Hyperbaric Physiology. Bethesda: Undersea and Hyperbaric Medical Society, 1987, pp 931-948.

31. Massey EW, Shelton DL, Moon RE, Camporesi EM: Hyperbaric treatment of iatrogenic air embolism. *Undersea Biomed Res* 16 (Suppl) #159, 1989.

32. U.S. Navy Department. U.S. Navy Diving Manual Vol 1: Air Diving. NAVSEA 0994-LP-001-9010. San Pedro, CA: Best Publishing Company, 1993.

33. Rivera JC: Decompression sickness among divers: an analysis of 935 cases. *Military Med* 129:314-334, 1964.

34. Moon RE, Camporesi EM, Kisslo JA: Patent foramen ovale as a risk factor for decompression sickness in compressed air divers. *Lancet* 1:513-515, 1989.

35. Myers RAM, Bray P: Delayed treatment of serious decompression sickness. *Annals Emerg Med* 14:254-257, 1985.

36. Davis JC, Sheffield PJ, Schuknecht L et al.: Altitude Decompression Sickness: Hyperbaric therapy results in 145 cases. *Aviat Space Env Med* 48:722-730, 1977.

37. Norkool DM, Kirkpatrick JN: Treatment of acute carbon monoxide poisoning with hyperbaric oxygen: A review of 115 cases. *Ann Emerg Med* 14:1168-1171, 1985.

38. Myers RAM, Snyder SK, Emhoff TA: Subacute sequelae of carbon monoxide poisoning. *Ann Emerg Med* 14:1163-1167, 1985.

39. Sokal JA: Lack of the correlation between biochemical effects on rats and blood carboxyhemoglobin concentrations in various conditions of single acute exposure to carbon monoxide. *Arch Toxicol* 34:331-336, 1975.

40. Haldane J: The relation of the action of carbonic oxide to oxygen tension. *J Physiol* 18:201-217, 1895.

41. Sendroy J Jr., Liu SH, Van Slyke DD. The gasometric estimation of the relative affinity constant for carbon monoxide and oxygen in whole blood at 38° C. *Am J Physiol* 90:511, 1929.

42. Piantadosi CA: Carbon monoxide, oxygen transport, and oxygen metabolism. *J Hyperbaric Med* 2:27-44, 1987.

43. Pace N, Strajman E, Walker EL: Acceleration of carbon monoxide elimination in many by high pressure oxygen. *Science* 111:652-654, 1950.

44. Goulon M, Barois A, Rapin M et al.: Carbon monoxide poisoning and acute anoxia due to breathing coal gas and hydrocarbons. (Republished in 1986) *J Hyperbaric Med* 1:23-41, 1969.

45. Van Hoesen KB, Camporesi EM, Moon RE, Hage ML, Piantadosi CA: Should hyperbaric oxygen be used to treat the pregnant patient for acute carbon monoxide poisoning?: A case report and literature review. *JAMA* 261:1039-1043, 1989.

46. Baund F, Barriot P, Véronique T: Elevated Blood Cyanide Concentrations In Victims of Smoke Inhalation. *New Engl J Med* 325:1761-1766, 1991.

47. Litovitz TL, Larkin RF, Myers RAM: Cyanide poisoning treated with hyperbaric oxygen. *Am J Emerg Med* 1:94-101, 1983.

48. Trapp WG: Massive cyanide poisoning with recovery: A Boxing Day story. *Can Med Assoc J* 102:517, 1970.

49. Davis FM, Ewer T: Acute cyanide poisoning: Case report of the use of hyperbaric oxygen. *J Hyperbaric Med* 3:103-106, 1988.

50. Smilkstein MJ, Bronstein AC, Pickett HM, Rumack BH. Hyperbaric oxygen therapy for severe poisoning. *J Emerg Med* 3:27-30, 1985.

51. Hsu P, Li H-W, Lin Y-T: Acute poisoning treated with hyperbaric oxygen. *J Hyperbaric Med* 2:215-221, 1987.

52. Bakker DJ. Clostridial myonecrosis. In: Davis JC and Hunt TK (eds) Problem Wounds. New York: Elsevier, 1988, pp 153-172.

53. McCord JM, Keele BB Jr., Fridovich I: An enzyme-based theory of obligate anaerobiosis: The physiologic function of superoxide dismutase. *Proc Natl Acad Sci USA* 68:1024-1027, 1971.

54. Demello FJ, Hashimoto T, Hitchcock CR, Haglin JJ: The effect of hyperbaric oxygen on the

germination and toxin production of Clostridium perfringens spores. In: Wada J, Iwa T (eds): Proceedings of the Fourth International Congress on Hyperbaric Medicine, Baltimore: Williams & Wilkins, 1970, pp 276-281.

55. Van Unnik AJM: Inhibition of toxin production in Clostridium perfringens in vitro by hyperbaric oxygen. *Antonie Van Leeuwenhoek* 31:181-186, 1965.

56. Hart GB, Lamb RC, Strauss MB: Gas gangrene. *J Trauma* 23:991-1000, 1983.

57. Hitchcock CR, Demello FJ, Haglin JJ: Gangrene infection: New approaches to an old disease. *Surg Clin North Am* 55:1403-1410, 1975.

58. Mader JT: Mixed anaerobic and aerobic soft tissue infections. In: Davis JC and Hunt TK (eds) Problem Wounds. New York: Elsevier, 1988, pp 173-186.

59. Knighton DR, Halliday B, Hunt TK: Oxygen as an antibiotic: A comparison of the effects of inspired oxygen concentration and antibiotic administration on in vivo bacterial clearance. *Arch Surg* 121:191-195, 1986.

60. Strauss MB: Refractory osteomyelitis. *J Hyperbaric Med* 2:147-159, 1987.

61. Adams KR, Sutton TE, Mader JT: *In Vitro* Potentiation of Tobramycin Under Hyperoxic Conditions. *Undersea Biomed Res* (Suppl) #69, 1987.

62. Adams KR, Mader JT: Aminoglycoside potentiation with adjuntive hyperbaric oxygen therapy in experimental *Ps. aeruginosa* osteomyelitis. *Undersea Biomed Res* (Suppl) #70, 1987.

63. Raval G, Park MK, Myers RAM, Marzella L: Hyperoxia Modulates Aminoglycoside Activity in Gram-Negative Bacteria. *Undersea Biomed Res* (Suppl) #21, 1992.

64. Morrey BF, Dunn JM, Heimbach RD, Davis JC: Hyperbaric oxygen and chronic osteomyelitis. *Clin Orthop* 144:121-127, 1979.

65. Davis JC: Adjunctive hyperbaric oxygen in chronic refractory osteomyelitis: Long-term follow-up results (letter). *Clin Orthop* 205:310, 1986.

66. Baroni G, Porro T, Faglia E et al.: Hyperbaric oxygen in diabetic gangrene treatment. *Diabetes Care* 10:81-86, 1987.

67. Marx RE, Ehlere WJ, Tayapongsak P, Pierce LW: Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg* 160:519-524, 1990.

68. Hunt TK, Pai MP: The effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. *Surg Gynecol Obstet* 135:561-567, 1972.

69. Marx RE, Kline SN: Principles and methods of osseous reconstruction. In: Murphy AP, ed. International advances in surgical oncology. New York: Alan R. Liss, Inc., 1983, pp 176-228.

70. Marx RE, Johnson RP: Problem wounds in oral and maxillofacial surgery: The role of hyperbaric oxygen. In: Davis JC and Hunt TK (eds) Problem Wounds. New York: Elsevier, 1988, pp 65-124.

71. Marx RE, Johnson RP, Kline SN: Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen versus penicillin. *J Am Dent Assoc* 111:49-54, 1985.

72. Boerema I, Meijne NG, Brummelkamp WK et al.: Life without blood: A study of the influence of high atmospheric pressure and hypothermia on dilution of the blood. *J Cardiovasc Surg* 13:133-146, 1960.

73. Hart GB, Lennon PA, Strauss MB: Hyperbaric oxygen in exceptional acute blood-loss anemia. *J Hyperbaric Med* 2:205-210, 1987.

74. Goldiner P, Carlon GC, Cvitkovic E et al.: Factors influencing postoperative morbidity and mortality in patients treated with bleomycin. *Br Med J* 1:1664-1667, 1978.

THESE QUESTIONS ARE TO BE ANSWERED ON A DATA CARD

IMPORTANT! USE NUMBER 2 PENCIL ONLY: MARK ONLY THE ONE BEST ANSWER

SELF-ASSESSMENT QUESTIONS: THEORY AND APPLICATION OF HYPERBARIC OXYGEN THERAPY

Choose the one correct response to each question.

1. The partial pressure of oxygen within the alveoli is calculated using all of the following EXCEPT:
   A. Barometric pressure
   B. F_IO_2
   C. Respiratory quotient
   D. End-tidal CO_2
   E. Water vapor pressure

2. From the blood to the tissues, oxygen delivery is facilitated by all the following EXCEPT:
   A. Increased pH
   B. Increased partial pressure of oxygen
   C. Increased 2,3 DPG
   D. Increased temperature
   E. Increased P_{50}

3. Factors NOT taken into account with the Krogh model of oxygen diffusion include:
   A. The solubility of oxygen in tissue
   B. The diffusion of oxygen in tissue
   C. Approximate capillary radius
   D. Approximate capillary length
   E. Partial pressure of oxygen

4. Cardiovascular effects of HBO therapy include:
   A. Increased vascular resistance
   B. Decreased cardiac output
   C. Increased blood pressure
   D. Decreased heart rate
   E. All of the above

5. The first step in the initial treatment of a seizure during HBO therapy would be:
   A. Switching from oxygen to air
   B. Immediate decompression to atmospheric pressure
   C. Partial reduction in chamber pressure
   D. Administration of an intravenous anticonvulsant
   E. Switching from oxygen to a combination of 50% oxygen and 50% nitrogen

6. Which clinical condition is LEAST likely to benefit from HBO?
   A. A pregnant patient with carbon monoxide poisoning
   B. Gas gangrene
   C. Compartment syndrome
   D. Diabetic foot ulcer
   E. Sickle cell anemia

7. The advantages of monoplace over multiplace chambers include all EXCEPT:
   A. Decreased cost
   B. Decreased size
   C. Ability to work directly with the patient
   D. Patients can be monitored (ECG, BP, arterial line, pulmonary artery catheter)
   E. Patients can receive mechanical ventilation if necessary

8. Which clinical condition is LEAST likely to benefit from HBO?
   A. Clostridial myonecrosis
   B. Carbon monoxide poisoning
   C. Adult respiratory distress syndrome (ARDS)
   D. Air embolism
   E. Compartment syndrome

9. Oxygen toxicity is reduced by:
   A. Using the lowest possible chamber pressure
   B. Frequent "air breaks"
   C. Antioxidants
   D. Limiting chamber time
   E. All of the above

10. Which of the following is NOT TRUE concerning carbon monoxide poisoning:
    A. Clinical status correlates with HbCO levels
    B. Hyperbaric oxygen hastens recovery despite delayed treatment
    C. A pregnant patient with CO poisoning should receive HBO if necessary
    D. A patient complaining of chest pain and having ST segment depression, following CO exposure, should receive IV nitroglycerin and hyperbaric oxygen.
    E. Psychometric testing can assess neurological sequela of carbon monoxide poisoning.