Hyperbaric Oxygen Therapy in the Pediatric Patient: The Experience of the Israel Naval Medical Institute

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ABSTRACT. The pediatric patient is to be found in hyperbaric facilities throughout the world, receiving hyperbaric oxygen (HBO) therapy for both life-threatening and chronic diseases.

Objective. To review the experience accumulated at the Israel Naval Medical Institute in the treatment of pediatric patients.

Design. A retrospective analysis and review of all records of patients younger than age 18 years.

Results. Between 1980 and 1997, 139 pediatric patients age 2 months to 18 years (mean, 7.7 years) received HBO treatment at the Israel Naval Medical Institute. Of the children, 111 (79%) suffered from acute carbon monoxide (CO) poisoning; 13 (9.2%) were treated after crush injury, traumatic ischemia, or compartment syndrome; 4 (2.8%) had clostridial myonecrosis; 1 (0.7%) had necrotizing fasciitis; 5 (3.6%) had refractory osteomyelitis; 2 (1.4%) had suffered massive air embolism; 2 (1.4%) had purpura fulminans; and 1 (0.7%) suffered from decompression sickness. Outcome, judged by neurologic sequelae, mortality, and extent of soft tissue loss and limb amputation, was favorable in 129 patients (93%). Two patients (1.4%) died, 1 as a result of CO poisoning and the other, gas gangrene; 2 of the patients in the CO group (1.4%) remained with neurologic sequelae, and 6 patients in the acute traumatic ischemia group (4.3%) underwent limb amputation.

Conclusions. We had a favorable experience with 129 of a total 139 pediatric patients treated at our facility for the indications listed. A basic knowledge of HBO therapy is needed to refer the pediatric patient for treatment when indicated. The needs of the pediatric patient, especially the critically ill, require specific skills and equipment inside the hyperbaric chamber. Close collaboration between the pediatrician and the hyperbaric medicine physician is essential to ensure adequate care for infants and children. *Pediatrics* 1998;102(5). URL: http://www.pediatrics.org/cgi/content/full/102/5/e53; *hyperbaric oxygenation, pediatrics, carbon monoxide poisoning, crush injury, gas gangrene, necrotizing fasciitis, refractory osteomyelitis, purpura fulminans, decompression sickness, arterial gas embolism.*

ABBREVIATIONS. HBO, hyperbaric oxygen; ICU intensive care unit; INMI, Israel Naval Medical Institute; ATA, atmospheres absolute; AGE, arterial gas embolism; DCS, decompression sickness; CNS, central nervous system; CO, carbon monoxide; GG, gas gangrene.

There are numerous reports in the pediatric, hyperbaric, and general medical literature of children treated with hyperbaric oxygen (HBO) therapy. However, there are very few reports that include a broader review of specific approaches to the pediatric patient in the hyperbaric chamber.[1–4]

All branches of pediatric medicine—the general pediatrician, the pediatric intensive care unit (ICU), the neonatal ICU, and the pediatric surgeon and orthopedic surgeon—may be involved in treating a child with one of the conditions that can benefit from HBO therapy.

In the present article, we emphasize the importance of consultation and collaboration between the pediatrician and the staff at the hyperbaric chamber. This starts in the emergency room, pediatric ICU, or neonatal ICU, where the pediatrician should be capable of recognizing those indications for which HBO may be of benefit. It continues during the HBO sessions, with proper management of the pediatric patient, especially critically ill children, to meet their particular requirements.

The results of our experience at the Israel Naval Medical Institute (INMI) will be presented for each of the major clinical indications for hyperbaric treatment. Indications relevant to pediatric patients, based on current clinical practice and reviews, are listed in Table 1.[2–6]

HBO—PRINCIPLES AND MECHANISMS OF ACTION

HBO therapy uses intermittent breathing of 100% oxygen at pressures >1 atmosphere absolute (ATA). Animal studies, clinical trials, and a growing body of clinical experience have shown HBO to be effective in a number of indications.[5,6]

The therapeutic effect of HBO is attributable to the mechanical effect of increased environmental pressure on gas-containing spaces in the body and the physiologic changes induced by hyperoxia. The inspiration of high levels of oxygen has a negligible impact on the total hemoglobin oxygen content. However, HBO increases the amount of oxygen dissolved in plasma, from 0.32 to 6 mL O_2/100 mL of blood when breathing 100% O_2 at 3 ATA. This considerable increase in the amount of oxygen made available to the tissues is of great importance when tissue oxygenation is impaired.

According to Boyle's law, which states that the product of pressure and volume is constant, any increase in environmental pressure will affect gas bubble size. Thus, elevation of the ambient pressure

TABLE 1. Accepted Indications for HBO Therapy for Infants and Children[2–6]

Smoke inhalation, CO intoxication
AGE
Compartment syndrome; acute traumatic peripheral ischemia
GG; complex anaerobic infections
Compromised skin flaps and grafts
Chronic or refractory osteomyelitis
Osteoradionecrosis; radiation-induced soft tissue injury
Purpura fulminans
Chronic, nonhealing wounds
DCS

by a factor of 6 (6 ATA = a depth of 50 m = 165 feet) will reduce bubble volume by the same magnitude. Henry's law states that the amount of gas that will dissolve in a liquid at a constant temperature is directly proportional to the partial pressure of that gas. These physical effects are of great importance in the treatment of arterial gas embolism (AGE) and decompression sickness (DCS), in which inert gas (nitrogen) bubbles are present in tissues and blood vessels. During compression and oxygen breathing, bubble size is reduced, oxygen replaces the inert gas, and surrounding tissues are able to metabolize the oxygen.[7]

Oxygen has a direct antimicrobial effect, particularly on anaerobes. A tissue Po_2 of at least 30 mm Hg of oxygen is considered necessary for normal phagocytosis and oxidative burst to occur. In damaged tissues, the oxygen partial pressure is often lower than this. Increasing the partial pressure of oxygen in hypoxic tissue can lead to the restoration of white blood cell function and the return of adequate antimicrobial action.[8,9]

Because of the vasoconstrictive effect of oxygen, HBO is believed to reduce tissue edema.[10] HBO is in wide use for the treatment of problem wounds. When a hypoxic environment is created, wound-healing is compromised by local infection and a decrease in fibroblast proliferation, collagen synthesis, and capillary angiogenesis. The adjunctive use of HBO has been shown to restore a favorable cellular milieu, in which the wound-healing process and host antibacterial mechanism are enhanced.[11]

SIDE EFFECTS OF HBO

The side effects of HBO are related to pressure/volume changes and to oxygen toxicity. The most common side effects seen during hyperbaric treatment are those related to the elevation of chamber pressure and the resultant volume changes in closed, gas-filled spaces (Boyle's law). The middle ear, sinuses, and lung may be commonly affected by pressure changes. Middle ear and sinus barotrauma are the injuries encountered most frequently, especially when congestion is present. They can be prevented most commonly by coaching the patient in ways of equilibrating middle ear pressure and enhancing eustachian tube function (swallowing, yawning, chewing, Frenzel or Valsalva maneuvers). Local or systemic decongestants also can be used. When indicated in the uncooperative patient, tympanocentesis may be performed before starting HBO therapy.

Pulmonary barotrauma is uncommon, but to prevent its occurrence during decompression, it is essential that pulmonary cysts, emphysema, and asthma be ruled out. These are not absolute contraindications to HBO treatment, but special care must be taken when treating a patient in whom any of these diseases are present, especially during decompression. To prevent middle ear and pulmonary barotrauma, the patient must undergo otoscopic examination and chest radiography before treatment is initiated.

The toxic effects of oxygen that may appear during HBO therapy are central nervous system (CNS) and pulmonary oxygen toxicity. CNS oxygen toxicity will develop within a short time on exposure to high oxygen partial pressures. However, in the hyperbaric chamber, CNS toxicity usually will not develop at oxygen partial pressures <2.8 ATA. Factors favoring toxicity are prolonged exposure in the hyperbaric chamber to partial pressures of oxygen >2.0 ATA, exercise, cold, immersion, an increase in end tidal CO_2,[12] fever, steroid treatment, and carbon monoxide (CO) intoxication.[13,14] CNS toxicity is characterized by irritability, decreased visual fields (tunnel vision), nausea, tinnitus, dizziness, muscle twitching, and generalized convulsions. The sequence of symptoms is highly variable, and the appearance of generalized convulsions may not necessarily be preceded by any of the other signs. CNS oxygen toxicity is completely reversible once the oxygen supply is disconnected. The reported incidence of CNS toxicity during HBO exposure is 1:10 000 for therapeutic sessions conducted at oxygen partial pressures between 2 and 3 ATA.[14]

Pulmonary oxygen toxicity may appear during prolonged exposure to a partial pressure as low as 0.5 ATA (50% Fio_2). The higher the partial pressure of oxygen, the shorter will be the time to the appearance of toxicity. The signs of pulmonary toxicity are coughing and irritation of the upper airways and a progressive decrease in vital capacity. Continued exposure eventually will result in the adult respiratory distress syndrome. Whereas susceptibility to CNS oxygen toxicity is highly variable and unexpected, pulmonary oxygen toxicity is related directly to the dose of oxygen delivered, and thus mostly can be avoided.[12] Pulmonary oxygen toxicity is completely reversible, unless permanent structural damage to the alveolo-capillary unit has already developed as a result of adult respiratory distress syndrome.

To minimize the risk of toxicity, HBO therapy is given at oxygen pressures <3 ATA, and oxygen breathing is interrupted by air breaks.

Reversible myopic changes have been reported after >15 to 20 consecutive daily HBO treatments. Reversal of this effect usually occurs within 3 to 6 weeks after the termination of therapy. The development of cataracts after >100 HBO sessions has been reported in patients with previous ocular lens pathology.[15,16]

Because of their susceptibility to retinopathy of prematurity, preterm infants of <35 weeks' postconceptual age should be considered with caution as candidates for HBO treatment at present, until more data are available on the effects of HBO on the de-

veloping retina. Thermoregulation and thermoprotection, which are of critical importance for these patients, are also difficult to achieve and maintain in the hyperbaric environment.

HBO FACILITIES AT THE INMI

Between 1980 and 1997, the period covered by the present review, the INMI was the only hyperbaric center in the northern and central areas of the country, serving a population of 4.5 million. An additional chamber, used primarily for treating victims of diving accidents, was located in Eilat on the Red Sea, with a referral population of 50 000 people. A total of 1634 adult patients were treated at the INMI during the period under study.

The hyperbaric facilities at the INMI comprise a multiplace chamber (Drager, Germany), in which the patient can be accompanied by two attendants if required. The chamber is equipped with all the medical instrumentation required for the treatment of the critically ill patient. Monitoring devices are connected via penetrations in the chamber wall. These include a cardiac monitor, invasive and noninvasive blood pressure monitoring, transcutaneous Po_2 and Pco_2 monitoring, pulse oximetry, and $ETCO_2$. There are battery-operated fluid/drug infusion pumps.

The oxygen delivery system is adapted to patient capacity and cooperation. Built in Breathing System demand masks, free-flow masks, and an oxyhood are available for the nonassisted patient, whereas for the respirator-assisted, we use a Penlon–Oxford pneumatically driven ventilator (Penlon Ltd, Abingdon, Oxfordshire, UK) that is designed for adults but can be adapted to pediatric patients. Changes in ventilator settings are made as required during HBO treatment according to oxygen saturation and blood gas monitoring.

Visual contact during treatment is maintained via the chamber windows and closed-circuit television; verbal communication is by telephone or intercom. The chamber has a small medical or service lock through which medication, food, drink, and other small items may be passed to the attendants inside. If necessary, medical staff can enter or leave the main chamber via a larger airlock or transfer compartment that also may be used to pass larger items of equipment into the main treatment chamber. Temperature inside the chamber is controlled by a specially designed air conditioning system. Items of clothing liable to produce static electricity as well as any electrical devices are prohibited in the chamber as fire hazards. The chamber is fitted with an automatic sprinkler system and manual fire extinguishers, and levels of ambient oxygen are strictly controlled during treatment.

INDICATIONS FOR HBO THERAPY

Acute CO Poisoning

CO is produced by the incomplete combustion of carbon-containing materials. CO poisoning is not uncommon among children.[17–20] The many sources of CO poisoning include coal heaters left to burn in closed or unventilated spaces, gas heater malfunc-tion, fires in which the victims suffer from concomitant smoke inhalation,[21] and accidental or intentional poisoning (homicide, suicide) from motor vehicles.

CO has a high affinity for hemoglobin, 200 times that of oxygen.[22] It binds competitively with hemoglobin to form carboxyhemoglobin, shifting the oxygen dissociation curve to the left. Thus, less than the normal amount of oxygen is carried and delivered to the tissues.[23] At the cellular level, CO binds with cytochrome oxidase A3 in the mitochondria, establishing a hypoxic milieu.[24] In animal experiments of CO-mediated brain injury, neutrophils seem to participate in an enzymatic process, leading to the formation of free oxygen radicals and cellular damage from lipid peroxidation. This is consistent with the view that CO-mediated brain injury is a type of postischemic reperfusion phenomenon.[25,26]

Clinical signs and symptoms of CO intoxication include headache, nausea and vomiting, dyspnea, vision abnormalities, muscular weakness, syncope, convulsions, coma, and death. Children may present with nausea, vomiting, and diarrhea, and be mistakenly diagnosed as suffering from gastrointestinal disease.[19] History of exposure and the measurement of carboxyhemoglobin levels can help confirm the diagnosis. The syndrome of delayed neuropsychiatric sequelae, which can appear from 3 days to 3 weeks after recovery, is well known in children.[20,27]

HBO is the treatment of choice for acute CO poisoning.[28] High concentrations of oxygen are immediately made available to the hypoxic tissues and are capable of supplying all of their metabolic needs at rest. Breathing 100% oxygen at 3 ATA shortens the half-time for the elimination of carboxyhemoglobin from 5 hours (breathing room air) to 23 minutes.[29] There is evidence from animal experiments that HBO accelerates the elimination of CO bound to cytochrome oxidase and has a protective effect on the brain. However, the mechanism by which this is accomplished is not yet understood completely.[30] Data exist suggesting that HBO may reduce the incidence of the late neuropsychiatric manifestations related to acute CO intoxication.[28]

The indications we have adopted for treating victims of CO intoxication are any neurologic symptom or sign (including transient loss of consciousness), metabolic acidosis, angina or ischemic changes in the ECG, and a carboxyhemoglobin level >25%. It must be noted that even brief loss of consciousness without other major complaints is an indication for HBO treatment.

The treatment protocol consists of breathing 100% oxygen for 90 minutes at an ambient pressure of 2.5 to 3 ATA. Most children recover in the course of this treatment. If residual signs remain, the same protocol is repeated every 8 to 12 hours until recovery is achieved.

A total of 111 pediatric patients suffering from CO intoxication were treated at our facility between January 1980 and August 1997. There were 50 boys and 61 girls, with a median age of 8 years (range, 2 months to 18 years). Most (75%) were referred from

the Jerusalem area, a mountainous region with a particularly cold climate in winter.

The sources of CO for our patients were gas heaters in 69 (62%), coal and kerosene heaters in 28 (25%), and fire with smoke inhalation in 9 (8%). In 5 cases (4.5%), the source was noted as unclear in the patients' charts. The trend over the years is toward a reduction in the number of accidents related to the use of coal heating devices, whereas the number of victims related to the use of gas heaters has remained almost unchanged. This is despite the involvement of the health authorities and public information services.

The most prevalent of the presenting symptoms and signs in our patients were transient loss of consciousness (54%), headaches (23%), vomiting (12%), and drowsiness (11%). Five of the 6 patients who arrived in coma were fire victims suffering from smoke inhalation, and 1 had become intoxicated as a result of a gas heater malfunction. Three of the 6 made a complete recovery, 2 remained with severe sequelae, and 1 died. Carboxyhemoglobin levels as first measured in the emergency department were available for 90 of the 111 patients. In 39, COHb levels were >20% (in 1 case as high as 51%), but there was no correlation with the severity of the presenting symptoms. These measurements are influenced greatly by the time that had elapsed between exposure to CO and patients' arrival at the referral center, breathing of oxygen, and ventilation. Unfortunately, these important data were not detailed in most of the charts reviewed, thus, it was impossible to estimate the level of carboxyhemoglobin immediately after exposure by retrograde extrapolation. Nineteen percent of the patients reached our facility >10 hours after the incident, either because of delay in seeking medical advice or severe complications (in fire victims).

Seventy-eight percent of the children underwent treatment together with family members inside the chamber. In 92% of these cases, this was because more than one member of the family had been affected by CO intoxication. In the remaining 8%, it was for the purpose of parental support inside the chamber.

Tympanic membrane paracentesis was performed electively in 22 of the patients before HBO treatment to prevent middle ear barotrauma during pressurization. It was indicated in children younger than 3 years old, in older children with active otitis media, and in those unable to perform middle ear clearing or pressure equalization during the otoscopic examination before treatment. It also was performed in all patients who were comatose or stuporous, and thus unable to equalize middle ear pressure.

One of the 2 children who remained with neurologic sequelae was an 8-year-old boy who had residual visual impairment attributable to cerebral infarction. The second was a 3-year-old boy who had severe brain edema and remained with severe neurologic deficits, subsequently developing hydrocephalus. The patient who died was a 2-year-old girl, the victim of a gas heater malfunction. She underwent full resuscitation at the scene, including chest compressions, which resulted in a right pneumothorax. Her condition was complicated further by severe hypothermia, and she died despite intensive care support and HBO therapy.

No cases of CNS oxygen toxicity (convulsions) or other complications related to HBO therapy were registered in this group of patients.

CO Intoxication in Pregnancy

Treatment is indicated in the case of the pregnant patient to prevent neurologic damage or death in both the mother and the fetus. Current recommendations are that HBO therapy should be administered if the mother has neurologic signs, if her carboxyhemoglobin level is >20%, or if there are signs of fetal distress on the monitor.[31,32] Three women (18 to 36 years of age) who suffered acute CO intoxication during pregnancy received HBO treatment. All three were at the end of the first trimester of pregnancy. Follow-up during and after HBO treatment was uneventful. All three delivered healthy term babies. On long-term follow-up, only one of the three children was reported at age 8 years to have minor developmental disabilities (cognitive and motor). This may not necessarily be related to the CO intoxication.

The possibility of teratogenicity induced by HBO has been suggested by the results of animal experiments involving prolonged exposures, but there was no evidence of this in humans who received HBO therapy.[33]

Gas Gangrene (GG) (Clostridial Myonecrosis) and Necrotizing Fasciitis

GG is a severe, rapidly progressing infection attributable to specific clostridium strains, of which *Clostridium perfringens* is the most common. Their systemic effects are produced by exotoxins, particularly α toxin (a lecithinase), which are able to destroy membranes and alter capillary permeability. GG is most commonly seen in combat injuries,[34] as a result of soil contamination, and entry of foreign bodies.[35] Hypoxic tissue attributable to vascular compromise and vast soft tissue damage provide the anaerobic environment required for the bacteria to proliferate.

A considerable number of cases also can be found in the civilian adult and pediatric population, in whom clostridial myonecrosis may be associated with trauma, surgical procedures, venipunctures, insect bites, diagnostic gynecological and urologic examinations, parenteral drug abuse, or de novo occurrence in the immunocompromised patient.[36–38] Atraumatic infection with *C septicum* has been reported in children suffering from different forms of neutropenia.[39,40]

A diagnosis of GG might be suspected from the history, appearance of the wound, odor, presence of bullae, drainage from the wound, fever, tachycardia, severe pain, stupor or coma, crepitation of tissue, and presence of gas in x-ray. Pain can be out of proportion to the apparent severity of the wound. However, a finding of Gram-positive rods in a Gram stain is required to confirm the diagnosis and indicates the need for urgent intervention.[38,41]

In the attempt to reduce the high mortality rate and the extent of limb amputation, the best results may be obtained from a combination of wide surgical excision, high dose antibiotics (penicillin), and early administration of HBO. The results are improved further if HBO is started within the first 24 hours of diagnosis.[6,37,41,42] Although no prospective human data are available, retrospective data from human subjects and animal experiments indicate that a combination of antibiotics, surgery, and early HBO therapy can reduce mortality significantly.[43] In view of the knowledge and experience accumulated, it is considered unethical by some researchers to conduct a randomized study for this type of patient.[44]

A tissue Po_2 >300 mm Hg arrests clostridial development and the production of toxins and also inhibits their systemic effects, improving cardiovascular status and the patient's general condition. HBO therapy must be administered immediately after surgery. The treatment profile of 90 min at 3 ATA is repeated every 6 to 8 hours until the patient is stable and the wound clean.[4,6,38]

Necrotizing fasciitis, a rapidly progressive infection of the soft tissues, with typical sparing of the underlying muscle, may be produced by a combination of aerobic and anaerobic flora. Mortality is high, and progression of the disease is usually less rapid but may be similar to that of clostridial myonecrosis. This type of infection is more common in immunocompromised adults and diabetics, but it also has been described in neonates in association with omphalitis, necrotizing enterocolitis, varicella, staphylococcal skin infections, and balanitis after circumcision. The use of HBO has been reported for newborn infants who developed necrotizing fasciitis of the abdominal wall.[45] The use of HBO in the treatment of necrotizing fasciitis is still controversial, most reports being retrospective analyses of adult patients.[46,47]

Five pediatric patients were treated at our facility, 4 suffering from GG and 1 from necrotizing fasciitis with a mixed aerobic and anaerobic infection. Mean age was 10.1 ± 4 years (range, 5 to 16 years). There were 4 boys and 1 girl. Two cases were related to traumatic injuries, 1 with a gunshot injury and the other the victim of an explosion. The remaining 3 patients had spontaneous infections related to immunodeficiency secondary to cyclic neutropenia. Clostridium septicum was isolated in these 3 patients, and clostridium septicum in the fourth patient suffering from GG.

All but 1 patient survived after rapid institution of aggressive antibiotic therapy, surgery, and HBO.

AGE

The introduction of air into the arterial system can result in cerebral air embolism, which may lead to severe neurologic damage and death. Air also may enter the coronary arteries and produce myocardial infarction. Signs and symptoms depend on the particular organ for which blood supply is arrested.

Most cases of AGE reported in the literature are iatrogenic, in which embolism is the result of an invasive medical procedure or surgery. These include umbilical catheterization in newborn babies, the introduction of central venous lines, neurosurgical procedures, open heart surgery, and pulmonary barotrauma as a complication of ventilator therapy. AGE also may be seen after diving as a result of pulmonary barotrauma or secondary to acute decompression. Diving-related pulmonary barotrauma often is accompanied by vascular rupture. Air under high pressure thus might enter the systemic arterial vasculature, resulting in AGE. In acute decompression, a large number of venous nitrogen bubbles are introduced into the systemic circulation, either because of a preexisting right to left shunt (such as via a patent foramen ovale) or by overwhelming the pulmonary filtration mechanism.[48–52]

AGE has a complex pathophysiology. The primary mechanism is vessel occlusion, but at the same time, a thromboinflammatory response is initiated causing additional injury to the surrounding tissue.[53]

There is no diagnostic method that makes it possible to reach a definitive diagnosis of AGE unless a massive amount of air has entered the circulation, as can happen during open-heart surgery. Only computed tomography has been investigated formally as a diagnostic tool for cerebral air embolism.[53] Embolic episodes also have been recorded using transcranial cerebral Doppler and end tidal CO_2 capnography. However, sometime only supportive therapy is given when embolism is diagnosed, either because the possible outcome is underestimated or because the prognosis is considered to be so ominous that treatment would be futile.

HBO is the treatment of choice for AGE. Treatment is provided by initial compression to 6 ATA breathing a mixture of 50% oxygen and 50% nitrogen (nitrox).[54–59] Some researchers recommend that treatment should be initiated by compression to 2.8 ATA and increased to 6 ATA according to the clinical response.[60]

Any delay in diagnosis and the institution of HBO therapy can jeopardize the outcome. If a large amount of air is observed entering the circulation, the patient must be transferred promptly to the nearest hyperbaric chamber and receive HBO treatment.

Two children with massive air embolism have been treated at our facility, a 4-year-old girl and a 2-year-old boy. Both events were associated with cardiopulmonary bypass for correction of tetralogy of Fallot. Both patients began to improve during the initial compression to 6 ATA, according to US Department of the Navy treatment Table 6A,[60] and subsequently made a complete recovery.

Crush Injury, Acute Traumatic Ischemia, Compartment Syndrome

HBO therapy is indicated for acute posttraumatic ischemia resulting from crush injury or tissue hypoxia persisting after the successful repair of an injured main arterial axis.

Microcirculatory and perfusion disturbances secondary to the increased interstitial pressure leading to compartment syndrome often are observed after crush injury. Reperfusion injury, with a paradoxical

increase in soft tissue and neurologic damage, might be the consequence of delayed repair of traumatic rupture of a main limb vascular axis.

The purpose of HBO therapy is to save partially damaged hypoxic tissue and to reduce the extent of necrosis. The vasoconstrictive effect of HBO reduces edema while still increasing tissue oxygenation. This breaks the vicious circle of ischemia–edema–ischemia, improves tissue and cellular oxygenation, and enhances phagocytosis and bacterial killing by the leucocytes.[8,61–64]

We treated 13 patients (mean age, 9.7 ± 5.1 years; range, 4 months to 17 years). They received an average of four treatments (range, one to nine). Two patients made a full recovery. Five made a partial recovery, with a marked reduction in the extent of amputation required according to the surgeon's estimation before and after the administration of HBO. Six patients did not benefit from treatment. The best results were obtained when the main vascular axis was not damaged completely and treatment was instituted promptly.

Purpura Fulminans

This life-threatening, mutilating entity was first described by Hjort.[65] It appears in the form of progressive purpuric lesions of the skin, primarily on the lower limbs, that eventually become necrotic. Purpura fulminans has been described in association with previous infection by varicella or streptococcus; sepsis or septic shock associated with *Escherichia coli*, *Haemophilus* or *Meningococcus*; and protein C or protein S deficiency. The development of disseminated intravascular coagulation with small vessel thrombosis, and endothelial damage with massive capillary leak and bleeding into tissues and skin, may precede the patient's death or lead to peripheral ischemia and limb loss if the patient survives. There have been reports of a mortality rate as high as 90%.[66–70]

Several researchers have reported success in reducing mortality and the amount of amputated limb tissue by HBO adjunctive to the intensive care treatment.[71–73] HBO therapy should be instituted as soon as possible to reduce the extent of necrosis. The rationale for HBO is similar to that described for the treatment of acute peripheral ischemia.

Two patients suffering from purpura fulminans have been treated at our facility, a 17-month-old girl suffering from severe pneumococcal sepsis and a 4-month-old girl with sepsis and meningitis attributable to *H influenza* B. In both cases, hemodynamic status and limb perfusion deteriorated, with progressive ischemic compromise. Slow progressive improvement was achieved after adjunctive HBO therapy was started, and only minor amputations were required. Follow-up after 1 year was uneventful in both children.

Refractory Osteomyelitis

Chronic osteomyelitis that has persisted or recurred after appropriate interventions or acute osteomyelitis that fails to respond to intensive medical and surgical treatment within a reasonable time may benefit from adjunctive HBO treatment. The thera-

peutic action of HBO is associated with the improvement of oxygenation in infected ischemic and hypoxic tissue, thereby enhancing the white blood cell killing index and osteoclast activity and potentiating the antibiotic action of the aminoglycosides. Reviews in the literature report good results achieved with HBO in the treatment of chronic refractory osteomyelitis, in combination with appropriate surgical procedures and antibiotics.[6,74,75]

Five pediatric patients have been treated for refractory osteomyelitis at our hyperbaric facility. The median age was 9 years (range, 5 to 13); there were 4 boys and 1 girl. Patients had been treated with a combination of antibiotics and surgical interventions for an average of 4 months before referral. This group included 2 boys suffering from familial dysautonomia, 1 of whom developed chronic osteomyelitis of the left femur and toe after septic arthritis of the hip, whereas the other had chronic osteomyelitis of the toe. Other etiologies included shrapnel wound infection and hematogenous spreading after infection of pressure sores in a boy with paraplegia. All patients recovered without the need for ablative surgery. Some received up to 45 HBO sessions (average, 32) at 2.5 ATA, in most cases twice a day. Treatments were continued until the wound was clean, and in some cases until the tissue was ready for skin transplant.

DCS

DCS is caused by the release of inert gas (eg, nitrogen) from body tissues, where it was dissolved after prolonged exposure to high environmental pressures, into the vascular system in the form of bubbles after transition to lower environmental pressures. The disease was originally described in mine and tunnel workers exposed to high pressures of compressed air (caisson disease) and is a relatively common problem in commercial and sport diving, as well as in aviation and space medicine.

Depending on the organs affected, the disease may be classified as type I (affecting skin or joints) or type II (affecting the CNS or lungs). The two types have a different presentation and prognosis, but the treatment of both, in most cases, is based on recompression in a hyperbaric chamber.[3,7,76]

We have treated 1 case of suspected DCS type I in a pediatric patient. A 10-year-old boy dove with an instructor to a depth of 10 m for 30 minutes twice on the same day. Three hours after the second dive, the patient made an hour-long flight in an aircraft. He developed subsequent acute pain in the knees, hip joints, and abdomen. The patient was transferred to the hyperbaric chamber with suspected DCS type I and received treatment according to US Navy Table 5,[60] during which his symptoms resolved.

Although the patient had made two dives to a relatively shallow depth without violating the decompression tables, the child then flew in an aircraft, during which he was subjected to an additional reduction in atmospheric pressure. The clinical symptomatology was highly suggestive of DCS type I. It should be kept in mind that in cases of type II DCS,

treatment is given according to US Navy Table 6 or oxy-helium therapeutic tables.

There are no data in the medical literature concerning the susceptibility of children to decompression and bubble formation. Most decompression tables are based on empiric data from animal research or adult divers, but none relates to children. We know also that bubble formation can occur in shallow water dives, primarily during exercise. With the increasing accessibility of sport diving and future developments in aviation and space flight, there is a distinct possibility that pediatricians will be faced with these problems.

SUMMARY AND CONCLUSIONS

Over the past 17 years, we have treated 139 pediatric patients with a median age of 7.7 years (range, 2 months to 18 years). The patients' characteristics are shown in Table 2. Outcome was favorable in 129 (93%) of the 139 patients treated in our facility. Two patients (1.4%) died, 1 after CO poisoning and 1 as a result of GG. Two patients (1.4%) in the CO group remained with neurologic sequelae, and 6 (4.3%) in the acute traumatic ischemia group underwent limb amputation.

Of the patients in the present series, only 2 suffered side effects of HBO. One was a 17-month-old infant with purpura fulminans, who developed a single generalized convulsion that ended when the oxygen supply was interrupted. The child had no neurologic sequelae. The second infant, a 4-month-old girl, developed pulmonary oxygen toxicity during treatment for ischemia of the left arm. Symptoms improved shortly after an interval between treatments.

Pediatricians are not always aware of the potential benefit of HBO in the treatment of the diseases for which it is indicated, whereas the HBO staff are not always familiar with the specific management requirements of the pediatric patient, especially those who are critically ill. The physician inside the chamber caring for a ventilated, critically ill infant or child should be familiar with this type of treatment, ventilator settings, and eventual intubation or reintubation of the patient, as well as with medication management.

A number of issues must be considered before treating a child in the hyperbaric chamber. A chest x-ray is important for two reasons. Even a small pneumothorax can be dangerous during the reduction of pressure at the end of the treatment session, when it may become a tension pneumothorax. Any pneumothorax should be drained before treatment begins, but can be drained inside a multiplace chamber if imperative. In the presence of pneumonia or pulmonary infiltrates, the magnitude of the intrapulmonary shunt should be evaluated. The presence of a large shunt will greatly reduce the efficacy of HBO therapy in achieving tissue oxygenation. One might argue that the same problem will be present in infants with cyanotic heart disease, but successful treatments have been reported in these infants.[77]

Children as young as 5 years of age can perform a pressure compensation maneuver (clearing the ears) by closing both nose and mouth and elevating the pressure against a closed glottis. Younger or disoriented children as well as babies should undergo myringotomy to prevent middle and inner ear barotrauma. Giving the baby a bottle to suck on is an uncertain method of equalizing pressure and can delay or jeopardize treatment.

In the majority of children, endotracheal intubation is performed using an uncuffed endotracheal tube. However, if the child is intubated with a low-pressure balloon, the air inside must be replaced by fluid. The same applies to a urinary bladder catheter.

The child may be frightened and unwilling to enter the chamber. In some cases, it is advisable to allow a family member to enter the chamber with the patient, after otoscopic examination and chest x-ray are performed, exactly as for the patient.

Among the other special requirements of the pediatric patient that must be taken care of in the hyperbaric chamber are the adaptation or preparation in advance of medical instruments suited to the patient's age. Suitable oxygen delivery systems also must be made available, such as an oxyhood or a free flow or demand mask for the more cooperative child. Mechanical ventilators may be adapted or their settings changed when treating infants, to prevent pulmonary barotrauma.

There is a fundamental need for pediatricians and institutions engaged in pediatric health care to be actively involved in the decision-making process for HBO therapy in the pediatric patient. Wise decision-making, based on an understanding of the known benefits of this modality of treatment, may reduce the mortality and severe sequelae of those diseases for which HBO is indicated.

TABLE 2. Total Number of Pediatric Patients Treated at the INMI Between 1980 and 1997

Diagnosis	Number of Patients (% Total)	Age (Median and Range)	Male/Female
CO intoxication	111 (79%)	8 y (2 mo–18 y)	50/61
GG	4 (2.8%)	10 y (5–14)	3/1
Necrotizing fasciitis	1 (0.7%)	16 y	1/0
AGE	2 (1.4%)	3 y (2–4)	1/1
Chronic osteomyelitis	5 (3.6%)	9 y (5–13)	4/1
Acute peripheral ischemia, crush injury	13 (9.2%)	10 y (4 mo–17 y)	10/3
Purpura fulminans	2 (1.4%)	10 mo (4–17 mo)	0/2
DCS	1 (0.7%)	10 y	1/0
Total	139	7.7 y (2 mo–18 y)	70/69

REFERENCES

1. Jain KK. Hyperbaric oxygenation in obstetrics and neonatology. In: Jain KK. *Textbook of Hyperbaric Medicine*. Toronto, Ontario: Hogrefe & Huber Publishers; 1990:389–393
2. Thombs PA, Martorano FJ. Hyperbaric medicine in pediatric practice. In: Kindwall EP, ed. *Hyperbaric Medicine Practice*. Flagstaff, AZ: Best Publishing Co; 1995:261–275
3. Santamaria JP, Williams ET III, Desautels DA. Hyperbaric oxygen therapy in pediatrics. *Adv Pediatr*. 1995;42:335–366
4. Sukoff MH, Gottlieb SF. Hyperbaric oxygen therapy. In: Nussbaum E, ed. *Pediatric Intensive Care*. 2nd ed. Mount Kisko, NY: Futura Publishing Company, Inc; 1989:483–507
5. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med*. 1996;334:1642–1648
6. Camporesi EM, ed. *Hyperbaric Oxygen Therapy: A Committee Report*. Kensington, MD: Undersea and Hyperbaric Medical Society; 1996
7. Melamed Y, Shupak A, Bitterman H. Medical problems associated with underwater diving. *N Engl J Med*. 1992;326:30–35
8. Forman HJ, Thomas MJ. Oxidant production and bactericidal activity of phagocytes. *Annu Rev Physiol*. 1986;48:669–680
9. Hohn DC, MacKay RD, Halliday B, Hunt TK. Effect of O_2 tension on microbicidal function of leukocytes in wounds and in vitro. *Surg Forum*. 1976;27:18–20
10. Nylander G, Nordstrom H, Lewis D, Larsson J. Metabolic effects of hyperbaric oxygen in postischemic muscle. *Plast Reconstr Surg*. 1987;79:91–97
11. Meltzer T, Myers B. The effect of hyperbaric oxygen on the bursting strength and rate of vascularization of skin wounds in the rat. *Am Surg*. 1986;52:659–662
12. Clark JM. Oxygen toxicity. In: Bennett PB, Elliott DH, eds. *The Physiology and Medicine of Diving*. 4th ed. London, UK: WB Saunders Co; 1993:121–169
13. Sloan EP, Murphy DG, Hart R, et al. Complications and protocol considerations in carbon monoxide-poisoned patients who require hyperbaric oxygen therapy: report from a ten-year experience. *Ann Emerg Med*. 1989;18:629–634
14. Hampson NB, Simonson SG, Kramer CC, Piantadosi CA. Central nervous system oxygen toxicity during hyperbaric treatment of patients with carbon monoxide poisoning. *Undersea Hyperb Med*. 1996;23:215–219
15. Palmquist BM, Philipson B, Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. *Br J Ophthalmol*. 1984;68:113–117
16. Butler FK Jr. Diving and hyperbaric ophthalmology. *Surv Ophthalmol*. 1995;39:347–366
17. Zimmerman SS, Truxal B. Carbon monoxide poisoning. *Pediatrics*. 1981;68:215–224
18. Gozal D, Ziser A, Shupak A, Melamed Y. Accidental carbon monoxide poisoning. Emphasis on hyperbaric oxygen treatment. *Clin Pediatr (Phila)*. 1985;24:132–135
19. Gemelli F, Cattani R. Carbon monoxide poisoning in childhood. *Br Med J*. 1985;291:1197
20. Binder JW, Roberts RJ. Carbon monoxide intoxication in children. *Clin Toxicol*. 1980;16:287–295
21. Parish RA. Smoke inhalation and carbon monoxide poisoning in children. *Pediatr Emerg Care*. 1986;2:36–39
22. Douglas CG, Haldane JS, Haldane JBS. The laws of combination of haemoglobin with carbon monoxide and oxygen. *J Physiol (Lond)*. 1912;44:275–304
23. Benesch RE, Maeda N, Benesch R. 2,3-Diphosphoglycerate and the relative affinity of adult and fetal hemoglobin for oxygen and carbon monoxide. *Biochim Biophys Acta*. 1972;257:178–182
24. Goldbaum LR, Orellano T, Dergal E. Mechanism of the toxic action of carbon monoxide. *Ann Clin Lab Sci*. 1976;6:372–376
25. Thom SR. Dehydrogenase conversion to oxidase and lipid peroxidation in brain after carbon monoxide poisoning. *J Appl Physiol*. 1992;73:1584–1589
26. Thom SR. Leukocytes in carbon monoxide-mediated brain oxidative injury. *Toxicol Appl Pharmacol*. 1993;123:234–247
27. Lacey DJ. Neurologic sequelae of acute carbon monoxide intoxication. *Am J Dis Child*. 1981;135:145–147
28. Myers RAM, Snyder SK, Linberg S, Cowley RA. Value of hyperbaric oxygen in suspected carbon monoxide poisoning. *JAMA*. 1981;246:2478–2480
29. Pace N, Strajman E, Walker EL. Acceleration of carbon monoxide elimination in man by high pressure oxygen. *Science*. 1950;111:652–654
30. Thom SR. Functional inhibition of leukocyte B_2 integrins by hyperbaric oxygen in carbon monoxide-mediated brain injury in rats. *Toxicol Appl Pharmacol*. 1993;123:248–256
31. Ginsberg MD, Myers RE. Fetal brain injury after maternal carbon monoxide intoxication. Clinical and neuropathologic aspects. *Neurology*. 1976;26:15–23
32. 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*. 1989;261:1039–1043
33. Elkharrat D, Raphael JC, Korach JM, et al. Acute carbon monoxide intoxication and hyperbaric oxygen in pregnancy. *Intensive Care Med*. 1991;17:289–292
34. Workman WT, Calcote RD. Hyperbaric oxygen therapy and combat casualty care: a viable potential. *Mil Med*. 1989;154:111–115
35. Melamed Y, Bursztein S. Hyperbaric medicine. In: Reis ND, Dolev E, eds. *Manual of Disaster Medicine. Civilian and Military*. Berlin, Germany: Springer-Verlag; 1989:149–160
36. Feigin RD. Gas gangrene. In: Behrman RE, Vaughan VC III, Nelson WE, eds. *Nelson Textbook of Pediatrics*. 13th ed. Philadelphia, PA: WB Saunders Co; 1987:620–621
37. Brook I. Facial gas gangrene after penetrating injury. *Pediatr Infect Dis J*. 1990;9:222–223
38. Hart GB, Lamb RC, Strauss MB. Gas gangrene. I. A collective review. II. A 15-year experience with hyperbaric oxygen. *J Trauma*. 1983;23:991–1000
39. Seidel M, Weiss M, Nicolai T, Roos R, Grantzow R, Belohradsky BH. Gas gangrene and congenital agranulocytosis. *Pediatr Infect Dis J*. 1990;9:437–440
40. Bar-Joseph G, Halberthal M, Sweed Y, Bialik V, Shoshani O, Etzioni A. *Clostridium septicum* infection in children with cyclic neutropenia. *J Pediatr*. 1997;131:317–319
41. Weinstein L, Barza MA. Gas gangrene. *N Engl J Med*. 1973;289:1129–1131
42. Shupak A, Halpern P, Ziser A, Melamed Y. Hyperbaric oxygen therapy for gas gangrene casualties in the Lebanon War, 1982. *Isr J Med Sci*. 1984;20:323–326
43. Stephens MB. Gas gangrene: potential for hyperbaric oxygen therapy. *Postgrad Med*. 1996;99:217–220
44. Peirce EC II. Gas gangrene: a critique of therapy. *Surg Rounds*. 1984;7:17–25
45. Sawin RS, Schaller RT, Tapper D, Morgan A, Cahill J. Early recognition of neonatal abdominal wall necrotizing fasciitis. *Am J Surg*. 1994;167:481–484
46. Riseman JA, Zamboni WA, Curtis A, Graham DR, Konrad HR, Ross DS. Hyperbaric oxygen therapy for necrotizing fasciitis reduces mortality and the need for debridements. *Surgery*. 1990;108:847–850
47. Shupak A, Shoshani O, Goldenberg I, Barzilai A, Moskuna R, Bursztein S. Necrotizing fasciitis: an indication for hyperbaric oxygenation therapy? *Surgery*. 1995;118:873–878
48. Fok TF, Shing MK, So LY, Leung RKW. Vascular air embolism—possible survival. *Acta Paediatr Scand*. 1990;79:856–859
49. Stoney WS, Alford WC Jr, Burrus GR, Glassford DM Jr, Thomas CS Jr. Air embolism and other accidents using pump oxygenators. *Ann Thorac Surg*. 1980;29:336–340
50. Marini JJ, Culver BH. Systemic gas embolism complicating mechanical ventilation in the adult respiratory distress syndrome. *Ann Intern Med*. 1989;110:699–703
51. Lau KY, Lam PKL. Systemic air embolism: a complication of ventilator therapy in hyaline membrane disease. *Clin Radiol*. 1991;43:16–18
52. Banagale RC. Massive intracranial air embolism: a complication of mechanical ventilation. *Am J Dis Child*. 1980;134:799–800
53. Dexter F, Hindman BJ. Recommendations for hyperbaric oxygen therapy of cerebral air embolism based on a mathematical model of bubble absorption. *Anesth Analg*. 1997;84:1203–1207
54. Toscano M, Chiavarelli R, Ruvolo G, Macchiarelli A, Scibilia G, Marino B. Management of massive air embolism during open-heart surgery with retrograde perfusion of the cerebral vessels and hyperbaric oxygenation. *Thorac Cardiovasc Surg*. 1983;31:183–184
55. VanRynen JL, Taha AM, Ehrlich R, Parlette DM. Treatment of cerebral air embolism in the pediatric patient. *J Hyperbaric Med*. 1987;2:199–204
56. Kol S, Ammar R, Weisz G, Melamed Y. Hyperbaric oxygenation for arterial air embolism during cardiopulmonary bypass. *Ann Thorac Surg*. 1993;55:401–403
57. Dunbar EM, Fox R, Watson B, Akrill P. Successful late treatment of venous air embolism with hyperbaric oxygen. *Postgrad Med J*. 1990;66:469–470

58. Murphy BP, Harford FJ, Cramer FS. Cerebral air embolism resulting from invasive medical procedures. Treatment with hyperbaric oxygen. *Ann Surg.* 1985;201:242–245

59. Bitterman H, Melamed Y. Delayed hyperbaric treatment of cerebral air embolism. *Isr J Med Sci.* 1993;29:22–26

60. US Dept of the Navy. *US Navy Diving Manual, Vol 1 (Air Diving).* NAVSEA publication 0994-LP-001-9110. Washington, DC: US Dept of the Navy; 1993;8:53-8-54

61. Zamboni WA, Roth AC, Russell RC, Graham B, Suchy H, Kucan JO. Morphologic analysis of the microcirculation during reperfusion of ischemic skeletal muscle and the effect of hyperbaric oxygen. *Plast Reconstr Surg.* 1993;91:1110–1123

62. Skyhar MJ, Hargens AR, Strauss MB, Gershuni DH, Hart GB, Akeson WH. Hyperbaric oxygen reduces edema and necrosis of skeletal muscle in compartment syndromes associated with hemorrhagic hypotension. *J Bone Joint Surg.* 1986;68:1218–1224

63. Badwey JA, Karnovsky ML. Active oxygen species and the functions of phagocytic leukocytes. *Annu Rev Biochem.* 1980;49:695–726

64. Zamboni WA, Mazolewski PJ, Erdmann D, et al. Evaluation of penicillin and hyperbaric oxygen in the treatment of streptococcal myositis. *Ann Plast Surg.* 1997;39:131–136

65. Hjort PF, Rapaport SI, Jorgensen L. Purpura fulminans. Report of a case successfully treated with heparin and hydrocortisone. Review of 50 cases from the literature. *Scand J Haematol.* 1964;1:169–192

66. Dudgeon DL, Kellogg DR, Gilchrist GS, Woolley MM. Purpura fulminans. *Arch Surg.* 1971;103:351–358

67. Canale ST, Ikard ST. The orthopaedic implications of purpura fulminans. *J Bone Joint Surg.* 1984;66:764–769

68. Watson CHC, Ashworth MA. Growth disturbance and meningococcal septicemia. Report of two cases. *J Bone Joint Surg.* 1983;65:1181–1183

69. Nogi J. Physeal arrest in purpura fulminans. A report of three cases. *J Bone Joint Surg.* 1989;71:929–931

70. Mahasandana C, Suvatte V, Chuansumrit A, et al. Homozygous protein S deficiency in an infant with purpura fulminans. *J Pediatr.* 1990;117:750–753

71. Kuzemko JA, Loder RE. Purpura fulminans treated with hyperbaric oxygen. *Br Med J.* 1970;4:157

72. Rosenthal E, Benderly A, Monies-Chass I, Fishman J, Levy J, Bialik V. Hyperbaric oxygenation in peripheral ischaemic lesions in infants. *Arch Dis Child.* 1985;60:372–374

73. Dollberg S, Nachum Z, Klar A, et al. *Haemophilus influenzae* type b purpura fulminans treated with hyperbaric oxygen. *J Infect.* 1992;25:197–200

74. Strauss MB. Refractory osteomyelitis. *J Hyperbaric Med.* 1987;2:147–159

75. Mader JT, Adams KR, Wallace WR, Calhoun JH. Hyperbaric oxygen as adjunctive therapy for osteomyelitis. *Infect Dis Clin North Am.* 1990;4:433–440

76. Elliott DH, Moon RE. Manifestations of the decompression disorders. In: Bennett PB, Elliott DH, eds. *The Physiology and Medicine of Diving.* 4th ed. London, UK: WB Saunders Co; 1993:481–505

77. Vazquez RL, Spahr RC. Hyperbaric oxygen use in neonates. A report of four patients. *Am J Dis Child.* 1990;144:1022–1024

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