Cigna Medical Coverage Policy

Subject **Hyperbaric Oxygen Therapy, Systemic & Topical**

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Coverage Policy

Cigna covers systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) in single or multiple chambers as medically necessary first-line treatment for ALL of the following conditions:

- acute carbon monoxide poisoning
- air or gas embolism
- decompression sickness
- exceptional blood loss when transfusion is not an option

Cigna covers systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) in single or multiple chambers as medically necessary adjunctive treatment for ALL of the following conditions:

- acute cyanide poisoning, after administration of antidote

- acute traumatic peripheral ischemia/insufficiency (e.g., crush injuries, compartment syndrome, suturing of severed limbs)
- central retinal artery occlusion
- clostridial myositis and myonecrosis (i.e., gas gangrene)
- compromised skin grafts and flaps (i.e., preexisting grafts or flaps that are showing signs of failure or necrosis)
- intracranial abscess
- necrotizing soft tissue infections (e.g., necrotizing fasciitis, Meleney's ulcer)
- osteomyelitis unresponsive to conventional medical and surgical interventions
- delayed osteoradionecrosis, including pre- and post-dental extraction(s) from an irradiated mandible
- radiation-induced cystitis or hemorrhagic cystitis (i.e., resulting from chemolytic response, graft-versus-host disease [GVHD])
- soft tissue radionecrosis, delayed (e.g., radiation-induced enterocolitis, proctitis, brain necrosis)
- thermal burns, acute, requiring inpatient hospitalization
- Wagner grade III or higher diabetic wounds/ulcers of the lower extremities that have failed standard wound therapy

Cigna does not cover systemic hyperbaric oxygen therapy in single or multiple chambers for any other indication including the treatment of ANY of the following conditions, because it is considered experimental, investigational or unproven (this list may not be all-inclusive):

- Actinomycosis
- acute cerebral edema
- acute coronary syndrome (ACS)/myocardial ischemia/infarction (MI), cardiogenic shock/preconditioning for coronary artery bypass graft surgery
- acute or chronic cerebral vascular insufficiency
- acute thermal and chemical pulmonary damage (i.e., smoke inhalation with pulmonary insufficiency)
- acute wound, flap, and/or graft
- anorectal disorders (e.g., chronic anal fissure [CAF], internal hemorrhoids, infectious proctitis)
- autism spectrum disorders
- avascular necrosis
- brain injury, closed head injury, traumatic brain injury (TBI), anoxic encephalopathy
- brown recluse spider bites
- cancer
- carbon tetrachloride poisoning
- cerebral palsy
- cerebral radionecrosis
- chronic fatigue syndrome
- chronic peripheral vascular insufficiency
- Crohn's disease
- cutaneous decubitus/pressure ulcers
- dementia
- epilepsy
- fractures, acute, delayed union or nonunion
- headaches (e.g., cluster, migraine)
- hepatic necrosis
- human immunodeficiency virus (HIV)–fatigue
- idiopathic sudden sensorineural hearing loss (ISSHL)
- in vitro fertilization
- Lyme disease
- lymphedema
- malignant otitis externa (e.g., necrotizing external otitis)
- multiple sclerosis
- mycoses

- nonvascular causes of chronic brain syndrome (e.g., Pick's disease, Alzheimer's disease, Korsakoff's disease)
- ophthalmologic conditions other than central retinal artery occlusion (e.g., optic neuropathy, glaucoma)
- organ storage
- organ transplantation
- pulmonary emphysema
- reflex sympathetic dystrophy/complex regional pain syndrome
- rheumatoid arthritis
- sepsis
- sickle cell disease
- soft tissue injury (e.g., delayed onset muscle soreness, sprains, strains)
- spinal cord injury
- stroke
- tetanus
- tinnitus
- venous stasis ulcers

Cigna does not cover topical hyperbaric oxygen (THBO) for any indication because it is considered experimental, investigational or unproven.

General Background

Systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) involves the inhalation of 100% oxygen under increased atmospheric pressure (e.g., 1.4 to 2.8 atmospheres absolutes [ATA]). A hyperbaric oxygen chamber (whether single or multiple chamber [i.e., created to hold several people]) is a device intended to promote the movement of oxygen from the environment to the patient's tissues by means of pressurization. Forcing oxygen into the tissues, organs, brain, and fluids of the body is proposed to stimulate cell growth and regeneration, displace toxins and impurities, and stimulate the immune system. Treatment sessions may last for 30–120 minutes and may be given for up to five times per week. Some conditions may only require one or two treatments (e.g., cyanide poisoning) while others may require 10–40 treatments (e.g., osteonecrosis) depending on the severity of the illness and the clinical response of the patient (i.e., complete response occurs or no improvement is being seen).

Applying these same principles of increased oxygenation, topical hyperbaric oxygen (THBO) has been proposed as an adjunctive therapy for the treatment of open acute and chronic wounds (e.g., on the sacrum or an extremity). With THBO, an airtight chamber or polyethylene bag (e.g., sleeve, boot, pouch) is sealed around a limb by a constriction/tourniquet device or on a part of the body with tape. High flow oxygen (usually 10 liters per minute) is introduced into the bag over the wound. These portable units can be used in a physician's office, clinic, or be self-administered in the home setting. Therapy is typically administered 90 minutes per day on four consecutive days, with a three-day break. In total, therapy may last for up to 10 weeks. The evidence in the published peer-reviewed scientific literature does not support the safety and efficacy of THBO.

U.S. Food and Drug Administration (FDA): Mono- and multiplace hyperbaric chambers are approved by the FDA as a Class II, 510(k) device. Examples of these chambers include the OxyHeal 1000 Monoplace Hyperbaric Chambers (OxyHeal Health Group, LaJolla, CA) and the Multiplace Hyperbaric Chambers (Makai Marine Industries, Inc., Boca Raton, Fl). The devices were approved for the treatment of the conditions recommended by the Undersea Hyperbaric Medicine Society at that time (FDA, 2005; FDA, 2004).

Topical hyperbaric oxygen systems are a Class III device approved by the FDA 510(k) process. An example of a topical system is the Hyper-Box Topical Wound Oxygen System (Qualtech House, Gateway, Ireland). The Hyper-Box is approved for the treatment of open acute or chronic wounds such as decubitus ulcers, infected stumps, skin grafts, gangrenous lesions, burns, frostbite, and skin ulcerations due to diabetes, venous stasis, and/or post-surgical infections (FDA, 2008).

Systemic Hyperbaric Oxygen

Literature Review - HBO as Primary Therapy: Evidence in the published peer-reviewed literature and professional society guidelines support the safety and effectiveness of HBO as a primary treatment option for acute carbon monoxide poisoning, air or gas embolism, decompression sickness, and exceptional blood loss when transfusion is not an option (Agence d'évaluation des technologies et des modes d'intervention en santé [AETMIS], 2008; Bennett, et al., 2012; Undersea & Hyperbaric Medical Society [UHMS], 2011).

Buckley et al. (2011) conducted a systematic review of randomized controlled trials (n=1361) that compared normobaric oxygen therapy (NBO) to HBO for the treatment of CO poisoning. Six randomized controlled trials involving non-pregnant adults with acute CO poisoning regardless of severity met inclusion criteria. The primary outcome measure was the presence of signs or symptoms possibly indicative of neurologic injury at follow-up (approximately 4 to 6 weeks) after randomization. Two trials reported a reduction in neurologic sequelae at one month, one of which was an abstract of an interim analysis. Of these two trials, the "conclusions of one positive trial may have been influenced by failure to adjust for multiple hypothesis testing" and the other trial may have been influenced by a "high risk bias". The three negative trials had "low power" to detect a benefit of HBO and "very poor follow-up" in the other. One trial had never reported final analysis. Although meta-analysis did not suggest a significant improvement from the administration of HBO (odds ratio [OR] for neurological deficits 0.78, 95%CI 0.54 to 1.12), the authors stated that the results should be interpreted cautiously due to the "significant methodologic and statistical heterogeneity" of the trials. These trials did not establish whether the administration of HBO reduced the incidence of adverse neurological outcomes in patients with CO poisoning.

Annane et al. (2011) conducted two prospective randomized controlled trials (n=385) to assess the efficacy of HBO for the treatment of carbon monoxide (CO) poisoning. Patients were age 15 years or older and had experienced domestic CO poisoning within 12 hours of the initiation of treatment. In trial A, patients with a transient loss of consciousness (i.e., malaise or syncope) (n=179) were randomized to six hours of normobaric oxygen therapy (NBO) (n=86) or to four hours of NBO plus one HBO session (n=93). In trial B, patients with initial coma (n=206) were randomized to four hours of NBO plus one HBO session (n=101) or four hours of NBO plus two HBO sessions (n=105). The primary outcome measure was the number of patients with complete recovery one month following initiation of therapy. In trial A, 26 patients were lost to follow-up and there was no significant difference in recovery between the two groups. In trial B, recovery was significantly lower in patients who received two HBO sessions compared to one session (p=0.007). In trial A, NBO was stopped prematurely in one patient because of a panic attack. In trial B, HBO was stopped prematurely in seven patient because of claustrophobia (n=4), ear pain (n=2), and seizures (n=1). Barotrauma was confirmed for six patients in trial B. Both studies were terminated at the end of one month.

Literature Review - HBO as Adjunctive Therapy: HBO has been shown to be effective and is an established adjunctive therapy used in combination with other established therapies for the treatment of acute cyanide poisoning; acute traumatic peripheral ischemia/insufficiency (e.g., crush injuries, compartment syndrome, suturing of severed limbs); central artery occlusion, clostridial myositis and myonecrosis (i.e., gas gangrene); compromised skin grafts and flaps (i.e., preexisting grafts or flaps that are showing signs of failure or necrosis); intracranial abscess; necrotizing soft tissue infections such as necrotizing fasciitis or Meleney's ulcer; osteomyelitis that is unresponsive to conventional medical and surgical interventions; delayed radiation damage of non-neurologic tissue (i.e., osteoradionecrosis, including pre- and post dental extraction in an irradiated mandible, and mandibular radionecrosis), soft tissue radionecrosis (e.g., radiation-induced enterocolitis, cystitis, proctitis; laryngeal and brain necrosis) and acute thermal burns requiring hospitalization (Bennett, et al., 2012; Eskes, et al., 2011; Fritz, et al., 2011; Nabil and Samman, 2011; UHMS, 2011; Latham, et al., 2013; American Cancer Society [ACS], 2011; AETMIS, 2008; Bennett , et al., 2008; Goldman, 2009).

HBO is also a recognized adjunctive therapy for the treatment of radiation-induced cystitis or hemorrhagic cystitis resulting from chemolytic response or graft-versus-host disease, and radiation-induced enterocolitis (Fink, 2006; Bennett, 2005; Chong, 2005; Fine, 2005; El-Zimaity, 2004; Lazzarini, 2004; Hailey, 2003; Wang, 2003; Kalayoglu-Besisik, 2003; Cesaro, 2003).

Randomized controlled trials and prospective case series support the safety and efficacy of HBO as an effective adjunctive therapy for the treatment of Wagner grades III–V diabetic wounds/ulcers of the lower extremity that are refractory to aggressive medical management including wound care, glucose control and surgical debridement or surgical revascularization. A Wagner grade III wound involves a deep ulcer that contains an abscess, osteomyelitis, or both; grade IV is an ulcer that has led to gangrene of the toes and/or forefoot; and a

grade V ulcer has caused gangrene of the entire foot or enough of the foot that it cannot be salvaged (Kranke, et al., 2012; Goldman, 2009; Roeckl-Wiedmann, et al., 2005).

Professional Societies: In the Infectious Diseases Society of America (IDSA) 2012 guidelines on the treatment of diabetic foot infections, IDSA stated that it did not recommend HBO as an adjunctive treatment for a patient with osteomyelitis of the foot. However in selected diabetic wounds that are slow to heal, HBO may be considered as an adjunctive therapy (strong/moderate recommendation).

The American College of Foot and Ankle Surgeons (ACFAS) (2006) reported that systemic HBO therapy has shown promise in the treatment of diabetic foot wounds with hypoxia severe enough to interfere with healing. However, most of the HBO studies had been hampered by methodological errors that prevented defining a role for this modality in the routine treatment of diabetic foot ulcers. The benefit of HBO therapy for this indication has not been proven conclusively in large multicenter randomized clinical trials.

The Undersea and Hyperbaric Medical Society (UHMS) (2011) approved the following indications for systemic HBO:

- air or gas embolism
- carbon monoxide poisoning
- carbon monoxide poisoning complicated by cyanide poisoning
- central retinal artery occlusion
- clostridial myositis and myonecrosis (gas gangrene)
- crush injury, compartment syndrome, and other acute traumatic ischemias
- decompression sickness
- enhancement of healing in select problem wounds
- exceptional blood loss (severe anemia)
- intracranial abscess
- necrotizing soft tissue infections
- osteomyelitis (refractory)
- delayed radiation injury (soft tissue and bony necrosis)
- skin grafts and flaps (compromised)
- thermal burns (acute)
- idiopathic sudden sensorineural hearing loss

Literature Review - Other Proposed Indications for Systemic HBO: There is insufficient evidence in the published peer-reviewed scientific literature to support HBO as a primary or adjunctive treatment of the conditions discussed below (this list may not be all inclusive). HBO is not FDA approved for these other indications.

Actinomycosis: Actinomycosis is a rare chronic, indolent, suppurative, tissue-destructive infection presenting with lumps and sinus formation, usually involving the head and neck, although it can affect other parts of the body, such as the abdomen and thorax. Adjunctive HBO has been proposed as a treatment option for patients who are unresponsive to medical and surgical intervention; however, studies are primarily in the form of case reports.

Acute Cerebral Edema: Cerebral edema accompanies a wide variety of pathologic processes and may be present in head/brain injury, stroke, brain tumor, cerebral infections (e.g., brain abscess, encephalitis and meningitis), lead encephalopathy, hypoxia, disequilibrium syndrome associated with dialysis and diabetic ketoacidosis, Reye's syndrome, fulminant hepatic encephalopathy, and hydrocephalus (Rowland, 2005). HBO has not been established as a treatment option for cerebral edema.

Acute Coronary Syndrome (ACS)/Myocardial Ischemia/Infarction (MI), Cardiogenic Shock/Preconditioning for Coronary Artery Bypass Graft Surgery): ACS includes acute MI and unstable angina. HBO therapy has been proposed as an adjunct to standard therapy to improve oxygen supply to the heart and possibly decrease the amount of myocardial ischemic death that could occur and/or to prevent cardiogenic shock. HBO has also been investigated for preconditioning coronary artery disease (CAD) patients

prior to elective surgery to improve left ventricular stroke work postoperatively. However, there is insufficient evidence to support the effectiveness of HBO for these conditions.

Bennett et al. (2011) conducted a systematic review of randomized controlled trials comparing the treatment of ACS with HBO and without HBO. Six trials (n=665) met inclusion criteria. Overall, HBO resulted in a significant decrease in the risk of death (p=0.02), a significantly lower extent of heart muscle damage measured by lesser rise in muscle enzymes (p=0.005) and a significantly better left ventricular ejection fraction (p=0.001). Evidence from individual trials reported a reduction in the risk of major adverse coronary events (MACE) (p=0.003), re-infarction (p=0.04), dysrhythmias (p=0.01) and less time to relief of pain (P<0.00001). However, the authors warned that because of the "modest number of patients, methodological shortcomings and poor reporting, these results should be interpreted cautiously, and an appropriately powered trial of high methodological rigor is justified to define those patients (if any) who can be expected to derive the most benefit from HBOT. The routine application of HBOT to these patients cannot be justified from this review."

Yogaratnam et al. (2010) conducted a randomized controlled trial (n=81) to determine if preconditioning coronary artery disease (CAD) patients with HBO prior to first-time, elective coronary artery bypass graft surgery (CABG) with on-pump cardiopulmonary bypass (CPB), would improve postoperative myocardial left ventricular stroke work (LVSW). Preoperatively, the study group (n=41) received HBO for two 30-minute intervals, five minutes apart. The control group (n=40) was not treated with HBO. Hemodynamic monitoring was performed on 22 HBO patients and 25 control group patients. Immediately following HBO, the study group had a significant reduction in pulmonary vascular resistance (PVD) (p=0.03), but the significant difference was not maintained. Intraoperatively, the HBO group had a significant reduction in blood loss (p=0.05). There was no significant difference in the rise in the serum troponin T level, but the rise was greater in the control group. This indicated that HBO-treated patients had less postoperative myocardial injury than the control group. Postoperatively, the HBO group had a significantly improved stroke volume (p=0.01) and LVSW (p=0.05), spent 24 minutes longer on mechanical ventilation and was intubated 36 minutes longer than the control group. The HBO group had a significantly shorter length of stay in the intensive care unit (p=0.05). The study group also had a reduction in blood loss (11.6%), blood transfusion (34%), low cardiac output syndrome (10.4%), inotrope use (8%), atrial fibrillation (11%), pulmonary complications (12.7%), and wound infections (7.6%), but the differences were not statistically significant. No renal or neurological complications were reported in the HBO group compared to 5% and 2.5%, respectively in the control group. Author-noted limitations of the study included the small patient population, recruitment of low-risk patients, and lack of comparison to patients who underwent CAPG without the use of CPB and to patients with controlled ischemia. Another limitation of the study is that all patients were not hemodynamically monitored during the postoperative period.

In a randomized controlled trial by Dekleva et al. (2004), 74 patients were assigned to HBO and streptokinase treatment versus streptokinase treatment alone within the first 24 hours after diagnosis. This study was small in sample size, showed treatment effectiveness limited to the first three days following HBO, and excluded patients with significant electrical complications. Due to these limitations, the effectiveness of HBO for the treatment of acute MI cannot be determined.

Acute or Chronic Cerebral Vascular Insufficiency: Cerebral vascular insufficiency is defined as insufficient blood flow to the brain that can lead to a stroke or transient ischemic attack (TIA). Although HBO has been proposed as a treatment option for cerebral vascular insufficiency, there is insufficient evidence in the peer-reviewed scientific literature to support its use for this indication.

Acute Thermal and Chemical Pulmonary Damage: HBO for the treatment of acute thermal and chemical pulmonary damage including smoke inhalation and pulmonary insufficiency in the absence of acute carbon monoxide poisoning is not supported by the evidence in the peer-reviewed literature.

Acute Wound, Flap and/or Graft: HBO has been proposed for the treatment of acute wounds, flaps and grafts. Published studies have included randomized controlled trials, case series and retrospective reviews. Dauwe et al. (2014) conducted a systematic review of the literature to evaluate the role of HBO in the treatment of acute wounds, flaps and grafts. Four randomized controlled trials, three prospective studies and one retrospective review met inclusion criteria. The studies included treatment of burn patients, crush injuries, postoperative ecchymosis following face lift surgery, post mastectomy and free parascapular flaps for lower extremity reconstruction. Due to the heterogeneity of the small patient populations (n=5–125), the poor methodology of

the studies and conflicting outcomes, the authors concluded that the data did not support HBO for these indications.

Anorectal Disorders: HBO has been proposed as a treatment option for anorectal disorders (e.g., chronic anal fissure, internal hemorrhoids, infectious proctitis). The efficacy of HBO as primary or adjunctive treatment for anorectal disorders has not been established. Randomized controlled trials comparing HBO to standard care (e.g., non-steroidal anti-inflammatory medications, steroid enemas, cauterization or surgical excision) are lacking (Rao, 2004; Schwartz, 2004).

Autism: Autism is the most common condition in the group of developmental disorders known as autism spectrum disorders (ASD). HBO has been proposed as a potential treatment modality for improving cognitive function by increasing tissue oxygenation and improving cerebral blood flow. There are a limited number of randomized controlled trials evaluating HBO for the treatment of autism. Published studies have been primarily in the form of case series with small, heterogeneous patient populations (n=6-18) and involved various HBO treatment regimens (Rossignol, et al, 2007; Rossignol and Rossignol, 2006).

Ghanizadeh (2012) conducted a systematic review of randomized controlled trials to evaluate the efficacy of HBO for the treatment of autism in children. Two randomized controlled trials met inclusion criteria. One study was the Rossignol et al. study discussed below. The second study (n=42) reported that HBO was not more effective than placebo.

Rossignol et al. (2009) conducted a multicenter, randomized, double-blind, controlled trial to evaluate the efficacy of HBO in the treatment of children (n=62), ages 2–7 years, diagnosed with autistic disorder. The children were randomly assigned to the study group (n=33) treated with HBO at 1.3 atmosphere and 24% oxygen or to the control group (n=29) treated with slightly pressurized room air and 21% oxygen. Forty, one-hour sessions (two sessions per day for five days) were administered over four consecutive weeks. Compared to the control group, the treatment group had significantly improved outcomes in the mean physician Clinical Global Impression (CGI) scale in overall functioning ($p=0.0008$), receptive language ($p<0.0001$), social interaction ($p=0.0473$), and eye contact ($p=0.0102$). Significantly more children in the treatment group were rated as “very much improved” ($p=0.0471$) or “much improved” ($p=0.0024$). Significant improvements were also reported by the treatment group in the parental CGI scores in overall functioning ($p=0.0336$), receptive language ($p=0.0168$), and eye contact ($p=0.0322$). Significant improvements were noted in total score, irritability, stereotypy, hyperactivity and speech ($p<0.03$ for each) on the Aberrant Behavior Checklist in the treatment group. The treatment group also showed significant improvement in the Autism Treatment Evaluation Checklist sensory/cognitive awareness score ($p=0.0367$) compared to the control group. Children over age five years with lower initial autism severity showed the most significant improvements. Due to the short-term duration of this study, the authors stated that studies with long-term outcomes were needed to formally validate the results. It is also unknown what the ideal HBO treatment regimen is for this patient population.

A systematic review of the literature produced no studies that met inclusion criteria investigating HBO for the treatment of autism in adults (age ≥ 18 years). Therefore, the 2012 National Institute for Health and Clinical Excellence (NICE) (United Kingdom) guideline on the diagnosis and management of adults with autism recommendation stated: “Do not use hyperbaric oxygen therapy for the management of core symptoms of autism in adults”.

Following a review of the evidence, which included one randomized controlled trial and three case series, Undersea and Hyperbaric Medical Society (UHMS) (2009) concluded that although there is a strong case for further studies on the role of HBO in the treatment of autism, HBO cannot be recommended as a routine treatment option.

Avascular Necrosis: Avascular necrosis (AVN), also called osteonecrosis or aseptic necrosis, is a disease in which there is a lack of blood supply to the bone causing death of bone tissue. Ultimately, AVN may lead to collapse of the bone and joint surface. AVN most often occurs in the hip joint in the femoral head and usually leads to osteoarthritis. Risk factors include hip injury, alcohol abuse and/or excessive corticosteroid use. AVN may be associated with other disease entities (e.g., Gaucher disease, sickle cell disease) and in some cases there may be no underlying disease (idiopathic AVN). Treatment depends on the severity of symptoms and may include limited weight bearing, physical therapy, cessation of alcohol usage, and/or surgical intervention. HBO has been proposed for the treatment of AVN. However, there is insufficient evidence in the published peer-

reviewed literature to support HBO for the treatment of AVN. Studies are primarily in the form of case series and retrospective reviews with small patient populations (n=12-109) (Comporesi et al., 2010; Reis, et al., 2003).

Comporesi et al. (2010) conducted a randomized controlled trial (n=20) using HBO to treat Ficat stage II patients with unilateral femoral head necrosis (FHN). Patients were treated with either 30 treatments of HBO or compressed air (HBA) for six weeks. After 20 treatments, significant pain improvement (p=0.002) and improvement in extension, adduction and abduction (p<0.001) were reported for HBO-treated patients. At the end of six weeks all HBA patients were offered HBO. At the seven-year follow-up (n=17), patients were substantially pain-free and none required surgical intervention. Substantial radiographic healing of osteonecrosis was observed in seven of nine hips. Limitations of the study include the small patient population and following cross-over the study became observational.

The Institute for Quality and Efficiency in Health Care in Germany (IQWiG) (2007) conducted a systematic review of randomized and non-randomized controlled trials to evaluate HBO for the treatment of adult, idiopathic osteonecrosis of the femoral head. One non-randomized study (n=44) was found. The study was excluded due to "major deficiencies in its methods and content". Therefore, there were no data available and no evidence to support HBO for this indication.

Brain Injury, Closed Head Injury, Traumatic Brain Injury (TBI), Anoxic Encephalopathy: In patients with moderate or severe TBI, the goal is to resuscitate the patient adequately to prevent further brain injury. The available evidence on adjunctive HBO treatment for severe traumatic brain injury is limited, and patient outcomes following HBO therapy are uncertain (Rowland, 2005).

In a Cochrane review of randomized controlled trials, Bennett et al. (2012) evaluated the benefits and harms of adjunctive HBO for the treatment of patients with TBI. The authors concluded that the combined results of the studies, involving 571 patients, suggested that HBO may reduce the risk of death and improve the final Glasgow Coma Scale. However, there was "little evidence that survivors had a good outcome". Based on this review, "the routine application of HBOT to these patients cannot be justified".

Brown Recluse Spider Bites: Brown recluse spider (i.e., loxosceles reclusa) venom contains enzymes that cause local (e.g., dermonecrosis) and systemic toxicity. There are a limited number of case studies that administered HBO as a treatment option. The studies did not show that HBO therapy produced better patient outcomes than standard aggressive wound care and antibiotic administration (Arnold, 2013; Norris, 2006; Wasserman, 2005).

Cancer: HBO therapy has been proposed for use as a cure for cancer and as a means of enhancing tumor response to chemotherapeutic treatment. According to AETMIS (2008), the efficacy evidence for HBO is still insufficient and additional studies are needed. The ACS (2011) stated available scientific evidence does not support claims that HBO "destroys disease-causing microorganisms, cures cancer, relieves chronic fatigue syndrome, and decreases allergy symptoms".

Carbon Tetrachloride Poisoning: Poisoning from carbon tetrachloride, which is used in industrial solvents, grain fumigants, insecticides, and the production of fluorocarbons, may cause nausea, vomiting, abdominal pain, diarrhea, confusion, coma, respiratory depression, hypotension, convulsions and even death (Harwood-Nuss, 2001). Although HBO has been proposed as a treatment option for carbon tetrachloride poisoning, there is insufficient evidence to support its effectiveness.

Cerebral Palsy: Cerebral palsy (CP) is an umbrella term covering a group of nonprogressive, but often changing, motor-impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development. The evidence in the peer-reviewed literature does not support HBO for the treatment of CP.

Lacey, et al. (2012) conducted a randomized controlled trial (n=46) to determine if HBO would improve functional abilities in children (ages 3–8 years) with spastic CP. One group received HBO (n=24), 100% oxygen at a pressure (or depth) of 1.5atm; and the second group received hyperbaric air (HBA) (n=22), a mixture of gases (14% oxygen) at 1.5atm to simulate 21% oxygen at room air. Eighty-minute sessions took place once a day for eight weeks for a total of 40 treatments. At the six month follow-up there were no changes from baseline in the Gross Motor Function Measure (GMFM)-88 and GMFM-66 or dimension A-D scores (i.e., lying and rolling,

sitting, crawling and kneeling, standing) in either group. There were no significant differences between groups. The HBA group showed a significant increase in dimension E score (walking, running and jumping). Although both groups showed improvement, there was also no significant difference between the groups in the Pediatric Evaluation of Disability Inventory (PEDI) scores. The study was stopped because "the calculated conditional probability of obtaining a difference between groups if the study continued to the end was only between 0.5% and 1.6%". The results of the study do not support HBO in the treatment of this patient population.

In a 2007 systematic review including two randomized controlled trials and four observational studies evaluating the benefits and adverse effects of HBO for the treatment of CP, McDonagh et al., reported that the improvements in motor function when compared to baseline for both HBO and room air were not significantly different. The evidence to support HBO therapy for CP is insufficient at this time.

In a clinical report for the American Academy of Pediatrics (AAP) regarding the treatment of children and youth with CP, Liptak et al. (2011) listed HBO as a therapy for which some evidence exists to refute its effectiveness. "Because CP is so heterogeneous, it is unlikely that all children would improve with a single therapy; benefits have not been proven".

Cerebral Radionecrosis: Cerebral radionecrosis is a complication of radiation therapy of intracranial and extracranial tumors. Delayed radionecrosis may appear as an intracranial mass and is typically surgically removed. Although HBO has been suggested as a treatment option when surgery is not feasible, clinical trials demonstrating the efficacy of HBO for this indication are lacking.

Chronic Fatigue Syndrome: Chronic fatigue syndrome (CFS) is a disorder of unknown etiology, which may have an infectious basis. It involves a state of chronic fatigue that can be accompanied by cognitive difficulties and typically, exists for a year or more. Because most cases of CFS may be based on a viral infection, no effective therapy exists (Cunha, 2012). Evidence supporting HBO for the treatment CFS is lacking.

Chronic Peripheral Vascular Insufficiency: Peripheral vascular insufficiency is most commonly a disease of the arteries and is caused by atherosclerosis which results in insufficient tissue perfusion. Although HBO has been proposed as a treatment option for peripheral vascular insufficiency, there is insufficient evidence in the peer-reviewed literature to support HBO for this indication.

Crohn's Disease: Crohn's disease is a chronic inflammatory disease of the gastrointestinal tract, the cause of which remains unknown. The available evidence is limited and is considered insufficient to determine the effect of HBO treatment on the health outcomes of patients with Crohn's disease.

Cutaneous, Decubitus/Pressure Ulcers: Cutaneous, decubitus (pressure) ulcers are typically localized to an area of tissue necrosis that develops when soft tissue is compressed between a bony prominence and an external surface. HBO for the treatment of decubitus or pressure ulcers has generally been considered ineffective or not extensively evaluated (Gifford, 2007).

Dementia: Dementia is characterized by progressive deterioration that interferes with social or occupational functions, such as: memory, orientation, abstraction, ability to learn, visuospatial perception, language function, and constructional praxis. Alzheimer's disease accounts for more than 50% of cases of dementia (Rowland, 2005). There is insufficient evidence in the peer-reviewed literature to support the treatment of dementia with HBO.

Xiao et al. (2012) conducted a Cochrane systematic review to assess HBO for the treatment of vascular dementia. One randomized controlled trial (n=64), "of poor methodological quality" met inclusion criteria. There is insufficient evidence to support HBO for the treatment of this condition.

Epilepsy: Epilepsy, or seizure disorder, is characterized by the tendency to have recurring seizures. HBO is proposed for the treatment of this condition as a means to improve cerebral circulation to the brain and decrease cerebral edema. HBO for the treatment of epilepsy has not been established.

Fractures (e.g., Acute, Delayed Union and/or Nonunion): The primary goal in the treatment of fractures is the realignment and stabilization of the fractured bone and restoration of function. HBO has been proposed to assist

in improving the healing outcomes in delayed or nonunion fractures, but improvement in clinical outcomes has not been established.

In a Cochrane systematic review, Bennett et al. (2012) concluded that, although HBO has been proposed for many years for the treatment of fractures, there is insufficient evidence within the literature to support or refute that it aids in the healing of acute injuries and fractures, and/or assists in the healing process of a nonunion fracture. No studies met inclusion criteria.

Headaches (Cluster and Migraine): Cluster headaches are an extremely painful but uncommon type of migraine headache. According to the International Headache Society, a migraine headache is a chronic condition with recurrent, episodic attacks. Although HBO has been proposed as a treatment option for headaches, there is insufficient evidence in the peer-reviewed literature supporting the efficacy of HBO for the treatment of this condition.

Bennett et al. (2008) conducted a systematic review and meta-analysis to evaluate the safety and efficacy of HBO compared to normal pressure oxygen therapy (NPOT) used for the prevention and treatment of migraine and cluster headaches. The review included nine randomized controlled trials (n=201) including five trials that compared HBO to sham for acute migraines, two that compared HBO to sham therapy for cluster headaches and two that evaluated HBO only for cluster headaches. Pooled data suggested that HBO was effective in relieving migraines compared to sham therapy (p=0.01), but provided no evidence that HBO could prevent migraines or reduce nausea, vomiting or medication requirements. One trial reported better outcomes using HBO in the treatment of cluster headaches (p=0.08). The authors concluded that additional research was necessary to support HBO over NPOT.

In an evidence-based guideline on the treatment and prevention of migraines, the American Academy of Neurology (AAN) (2012) concluded that the evidence was inadequate to either support or refute HBO for the treatment of migraines. Only one study was included and no differences were found in patients treated with HBO.

Hepatic Necrosis: Hepatic necrosis is a severe and progressive form of hepatitis associated with hepatocellular death and hepatic failure. Although HBO has been proposed as a treatment option for hepatic necrosis, there is insufficient evidence in the peer-reviewed literature to support its use for this condition.

Human Immunodeficiency Virus (HIV)–Fatigue: Fatigue is often a chronic, debilitating symptom of individuals infected with HIV. It has been hypothesized that increased oxygenation by HBO may help to relieve the fatigue. However, evidence in the peer-reviewed literature supporting this hypothesis is lacking.

Idiopathic Sudden Sensorineural hearing loss (ISSHL): Sudden sensorineural hearing loss (SSHL) is an acute hearing impairment defined as a 30 decibel (dB) or greater hearing loss occurring in at least three contiguous audiometric frequencies over 72 hours or less. Sensorineural hearing loss indicates an abnormality of the cochlea, auditory nerve, or higher aspects of central auditory perception or processing. With sudden hearing loss (SHL), the loss is typically defined in relation to hearing in the opposite ear because pre-event audiometry is generally not available. Idiopathic means that there is no identifiable cause of the sudden hearing loss and 85%–90% of SHL is idiopathic. SHL is considered an emergency situation that requires immediate medical intervention. There is a lack of consensus on the accepted treatment options for ISSHL. The standard treatment is systemic and/or intratympanic corticosteroids. Other treatments that have been proposed include: antivirals, antibiotics, diuretics, vasodilators, osmotic agents, plasma expanders, anticoagulants, mineral supplements, and hyperbaric oxygen or carbon dioxide–rich gases (American Academy of Otolaryngology – Head and Neck Surgery [AAO-HNS], 2012; National Institute on Deafness and Other Communication Disorders [NICDC], 2010). The efficacy of HBO, patient selection criteria and treatment regimens for ISSHL have not been established. Studies are primary in the form of retrospective reviews and case series. The few available randomized controlled trials include small patient populations and short-term follow-ups.

Cvoric et al. (2013) conducted a randomized controlled trial (n=50) to compare HBO to intratympanic (IT) steroid injection in patients with ISSHL Patients who had less than a 10-dB hearing gain following systemic steroid therapy were randomized to either HBO or IT steroids. Treatment began after unsuccessful primary treatment but no later than four weeks of the onset of ISSHL. HBO was given in 20 treatments, one per day, Monday-Friday, 2ATA at 100% O2 (10 minutes of compression on air, 60 minutes of oxygen breathing, and 10 minutes

of decompression on air). The IT steroid group received four intratympanic injections in 13 days. The primary outcome measure was hearing gain at 0.25, 0.5, 1, 2, and 4 kHz following treatment. Patients were classified into three subgroups: pure tone average (PTA) less than 60, PTA 61 to 81, and PTA greater than 80 dB. There were significant differences between hearing thresholds at all frequencies before and after the HBO treatment as well as, after IT steroid injections with the exception of the 2 kHz. Patients with a PTA less than 81dB and age less than 60 years had a better response to HBO. There were no significant differences between the two groups at any of the five frequencies tested except at 2 kHz, at which HBO treatment resulted in better outcomes than IT steroids. Patients with a PTA of more than 81 dB had significantly higher hearing gain on IT steroid than on HBO treatment. Hearing recovery was significantly worse in the HBO group in patients with PTA greater than 80 dB. The majority of patients failed to improve completely. Final hearing levels were reached at one month in 78% of patients and by three months in 97% of patients. As noted by the authors a “major” limitation of the study was that the patients in the two groups were not matched and not similar. Another limitation was the small patient population and the short-term follow-up. Large randomized controlled trials are needed to identify the subgroup of patients with ISSHL who might benefit from HBO therapy.

In a Cochrane review, Bennett et al. (2012) evaluated seven randomized controlled trials (n=392) that assessed the effectiveness of HBO for the treatment of ISSHL in adults. “The studies were small and of poor quality” and were published from 1985 to 2004. No trials were found from 2004 to 2012. Treatment regimens, outcome measures and comparators (multimodal pharmacological approach, vasodilator alone) varied between studies. Follow-ups ranged from 10 days to three months. Two studies evaluated HBO for chronic hearing loss. When the data from the two trials were pooled (n=114), no significant improvement in the chance of a 50% increase in hearing threshold on pure-tone average with HBO was seen. The data did show a significantly increased chance of a 25% increase in pure-tone average (p=0.02), a 22% greater chance of improvement with HBO, and the number needed to treat to achieve one extra good outcome was five. There was also an “absolute improvement in average pure-tone audiometric threshold following HBO (mean difference 15.6 dB greater with HBO) (p=0.03) (n=91; two studies). Although HBO improved hearing, “the clinical significance was unclear”. The significance of a percentage improvement in hearing from baseline was not clear and would depend on the starting level of impairment. It was also noted that improved hearing may only be true if HBO is used within two weeks of the onset of problems. The authors noted that because of the “modest number of patients, methodological shortcomings and poor reporting, the results should be interpreted cautiously”. There was “no evidence of a beneficial effect of HBO on chronic ISSHL (six months)”.

Conlin and Parnes (2007) conducted a systematic review of randomized controlled trials to identify, evaluate and review treatments of ISSHL. A total of 21 trials were identified and one study included the use of HBO (n=34) as an adjunctive treatment to pharmacotherapy. A greater rate of improvement was reported with HBO.

In an informational brief (2013), the National Institute for Excellence in Health and Social Services (INESSS), Quebec, concluded that that the efficacy of HBO in the treatment of idiopathic sudden sensorineural hearing loss (ISSHL) remains uncertain. Systematic reviews and other studies stated that the clinical significance of HBO is not clear, results are conflicting, the methodology of the studies was flawed and sample sizes were heterogeneous and small.

The American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) (2012) developed evidence-based clinical practice guidelines for the management of sudden hearing loss with a special emphasis on managing sudden sensorineural hearing loss (SSNHL) in adult patients (aged 18 years and older). Following a systematic review of randomized controlled trials “with methodological limitations”, AAO-HNS stated that HBO may be offered to patients within three months of diagnosis of ISSNHL. The evidence supports possible benefit of HBO as an adjuvant treatment in cases of acute SSNHL when used within 3 months of the onset of the hearing loss, with potentially more benefit noted in cases of severe to profound loss”. AAO-HNS’s “value judgment” stated that although the level of evidence was “modest and imprecise”, it was “sufficient to promote greater awareness of HBO for the treatment of SSNHL”. The report went on to say that “given the small number of patients in the trials reviewed, methodological shortcomings, and poor reporting, the reported findings of benefit should be interpreted cautiously”. “The authors also noted that HBO is “not recognized by many United States clinicians as an intervention for ISSNHL” and is not FDA approved for this condition.

The Undersea and Hyperbaric Medical Society (2011) support HBO for the treatment of ISSHL stating that patients who meet the criteria for ISSHL may benefit from HBO. Candidates for HBO include those patients with “moderate to profound ISSHL (≥ 41 dB) who present within 14 days of symptom onset”. According the UHMS,

patients presenting after this time may experience improvement when treated with HBO, however, the medical literature suggests that early intervention is associated with improved outcomes. “The best evidence supports the use of HBO within two weeks of symptom onset”.

In Vitro Fertilization (IVF): Infertility may be the result of endometriosis, or abnormalities in tubal, uterine, endometrial, cervical, or ovulatory functions. It has been proposed that increasing oxygenation by HBO may aid in egg maturation and alignment of chromosomes during meiosis but there insufficient evidence to report this claim.

Lyme Disease: Lyme disease is a clinical diagnosis, and currently the early use of antibiotics can prevent persistent, recurrent and refractory conditions. The duration of therapy is determined by each individual's clinical response, but the adjuvant use of HBO therapy is not recommended as part of this treatment.

In their 2010 final report on Lyme disease, the Infectious Diseases Society of America (IDSA) lists HBO as a treatment modality that is not recommended for the management of this disease.

Lymphedema: Approximately 10–38% of all women who have breast-conserving surgery (BCS) or modified radical mastectomy have postsurgical irradiation to the lymph nodes, and 10% of those women develop lymphedema. HBO has not been established as an effective adjunctive treatment for the reduction of lymphedema. Studies have primarily been in the form of case series with small patient populations (n=10) and reported that the total limb volume did not change significantly from baseline measurements (Teas, et al., 2004).

Gothard et al. (2010) conducted a randomized controlled trial (n=58) to investigate the effectiveness of HBO in the treatment of patients with ipsilateral arm lymphedema, ≥ 15% increase in arm volume, following treatment for cancer. Diagnosis included breast cancer (n=56) and Hodgkin lymphoma (n=2). All patients had undergone surgery and radiation therapy. The average interval of time from radiation therapy to randomization was 2.1–21.5 years. Patients were randomized to HBO (n=38) or to the control group (n=20). The study group received 30 HBO treatments while the control group continued best standard care for lymphedema according to the 2006 Lymphoedema Framework Best Practice for the Management of Lymphoedema International Consensus. At the 12-month follow-up (n=46), there were no statistically significant differences from baseline to follow-up in the median volume of the ipsilateral limb (expressed as a percentage of contralateral limb volume) and change over time in either group. There was no clear within-patient improvement from baseline to 12 months with either group. Author-noted limitations of the study included the small patient population and the interval of time from radiation therapy to randomization.

Malignant Otitis Externa: Malignant otitis externa (i.e., necrotizing external otitis) is an uncommon, yet potentially fatal infection of the external auditory canal and may involve surrounding tissue and soft bone. HBO therapy has been proposed as an adjunct to traditional therapy (e.g., diabetic control, administration of antibiotics, repeat debridement and surgical resection). However, the efficacy of HBO for this condition has not been established.

Phillips et al. (2013) conducted a Cochrane systematic review to determine the effectiveness of HBO when used as an adjunct to the traditional treatment protocols for malignant otitis externa. The researchers could not locate any randomized controlled trials that had measured the effectiveness of HBO within this population. A small number of case reports and case series were found, but there was no clear evidence that demonstrated the effectiveness HBO therapy for this condition.

Multiple Sclerosis: Multiple sclerosis (MS) is a chronic neurological disease in which there is patchy inflammation, demyelination and gliosis in the central nervous system. HBO has been proposed as a treatment modality for MS based on the demonstrated ability of HBO to produce vasoconstriction with increased oxygen delivery and some anecdotal evidence of efficacy.

In a Cochrane systematic review, Bennett and Heard (2010) investigated the use of HBO for the treatment of MS. Two randomized controlled trials reported generally positive results, but the remaining seven randomized trials reported no evidence of treatment effects. Due to the paucity of evidence to confirm beneficial effects of HBO, the authors did not believe that routine use of HBO was justified.

Mycoses: Mycosis is an infection or a disease caused by a fungus (e.g., candidiasis, aspergillosis, cryptoccocus). Zygomycosis (e.g., mucormycosis, phycomycosis) is an infection caused by "bread mold fungi" and can infect immunosuppresant individuals (e.g., HIV). HBO has been proposed as a treatment option for some forms of invasive mycosis (e.g., zygomycosis), but its efficacy remains unproven (McAdam and Sharpe, 2005).

Nonvascular Causes of Chronic Brain Syndrome (e.g., Pick's Disease, Alzheimer's Disease, Korsakoff's Disease): Chronic Brain Syndrome, also called dementia, is a loss of brain function. Alzheimer's disease and Pick's disease are forms of dementia. Alzheimer's is a primary degenerative dementia that typically involves diffuse atrophy of the brain, while Pick's disease is a classical frontotemporal dementia. Korsakoff's is a psychosis that results from a thiamine deficiency and is primarily a memory disorder. The efficacy of HBO for these conditions has not been established (Smith and Seirafi, 2006).

Ophthalmologic Conditions Other Than Central Retinal Artery Occlusion (e.g., Optic Neuropathy, Glaucoma): HBO has been proposed as an adjunctive treatment option for various ophthalmologic conditions, including, optic neuropathy, and glaucoma. There is insufficient evidence to determine the health outcomes of HBO for the treatment of ophthalmologic conditions other than central retinal artery occlusion.

Organ Transplant/Storage: Researchers have hypothesized that HBO may enhance the performance and growth in pancreatic islet grafts, when they are subjected to high levels of oxygen prior to transplant. HBO has also been proposed for administration following organ transplantation to reduce the risk of organ rejection (e.g., liver) as well as, keeping donated organs viable for a longer period of time. However, additional research is required to establish the efficacy of HBO therapy on organ transplantation and storage (Muralidharan, et al., 2007; Juang, 2002).

Pulmonary Emphysema: Emphysema is defined as an abnormal permanent enlargement of air spaces in the distal bronchioles that is associated with chronic bronchitis. HBO has been proposed as a treatment option for emphysema, however, improvements in health outcomes have not been established in clinical trials.

Reflex Sympathetic Dystrophy (RSD)/Complex Regional Pain Syndrome (CRPS): CRPS, also known as RSD or causalgia, is a neuropathic condition that causes intense pain primarily in the arms, hands, legs or feet. HBO has been proposed as a treatment option for the pain associated with CRPS. Evidence in the peer-reviewed literature does not support the effectiveness of HBO for the treatment of CRPS.

Kiralp et al. (2004) conducted a double-blinded, randomized, placebo-controlled study (n=71) to assess the effectiveness of HBO for treating patients with CRPS. The patients were allocated alternately to receive fifteen, 90-minute therapy sessions of HBO therapy (n=37) or normal air therapy (n=34). The visual analog scale score indicated that pain decreased starting from the first day until day 45 of treatment. An increase in wrist flexion was observed with the HBO group after 15 therapy sessions. A decrease in wrist circumference in the HBO group was also reported. There was a statistically significant difference for all variables except wrist extension. The study is limited by the small patient population and short-term follow-up. Additional studies with larger populations and long-term follow-ups are needed to validate the results of this clinical trial.

Rheumatoid Arthritis: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause that primarily affects the peripheral joints leading to joint destruction and limited mobility. Although HBO has been proposed for the treatment of RA to decrease pain and inflammation, there is insufficient evidence supporting its efficacy.

Sepsis: Sepsis is a group of disorders that result from infection by bacteria, viruses, fungi, or parasites or the toxic products of these microorganisms. Sepsis involves early signs of circulatory compromise to full-blown circulatory collapse with potentially multi-organ system failure and death. The role of HBO as an adjunctive therapy in the treatment of sepsis remains controversial.

Sickle-Cell Disease: Sickle-cell disease is a hereditary disorder of hemoglobin structure and function. The anemia of sickle-cell disease is due to both chronic and acute hemolysis. Several new approaches to treatment of sickle-cell disease are currently under evaluation; however, these approaches do not include HBO (Lodewijk, 2007). Studies supporting HBO for the treatment of sickle-cell anemia are lacking.

Soft Tissue Injury (e.g., Delayed Onset Muscle Soreness, Closed Soft Tissue Injury, Sprains, Strains): Soft tissue injuries can range from abrasions and bruising to disruptions of tendons, ligaments and muscles. Muscle soreness and damage are commonly associated with athletic activity. HBO has been proposed as an adjunct to conventional therapies (e.g., rest, elevation, pharmacotherapy) to expedite the healing process, but its beneficial impact on health outcomes has not been established.

According to Bennett et al. (2010) in a Cochrane systematic review including nine randomized controlled trials (n=219), there was insufficient evidence to conclude that HBO in the treatment of delayed onset of muscle soreness or closed soft tissue injury is efficacious.

Spinal Cord Injuries: Bruising, pressure, cutting or severance of the spinal cord may result in partial or complete loss of sensation and movement below the site of injury. Studies investigating the adjunctive use of HBO for the treatment of spinal cord injuries are primarily in the form of small, uncontrolled case series with a range of spinal cord injuries. Overall, results were not favorable. HBO therapy for the management of spinal cord injury has not been widely accepted (Rowland, 2005).

Stroke: Medical therapies for stroke are designed to minimize or prevent ischemic brain infarction, optimize functional recovery and avert stroke recurrence. Specific therapies depend on the stroke syndrome. In a Cochrane review conducted by Bennett et al. (2008), the authors assessed the safety and effectiveness of adjunctive HBO therapy in the treatment of acute ischemic stroke. Three randomized controlled trials (n=106) met inclusion criteria. The authors determined that there is insufficient evidence to make any determinations regarding the safety and efficacy of HBO therapy for stroke patients.

Tetanus: Tetanus is caused by the bacteria clostridium tetani and is characterized by an acute onset of hypertonia and generalized muscle spasms. Although HBO has been proposed as a treatment option for tetanus, there is insufficient evidence in the peer-reviewed literature to support its efficacy.

Tinnitus: Tinnitus, also commonly referred to as “ringing in the ears” or “head noise,” is defined as the perception of sound in the head when no external sound is present. This symptom can occur in one ear or bilaterally, as well as internal and external to the auricle. HBO has been investigated as a treatment option in order to increase the supply of oxygen to the ear and brain in an attempt to decrease the severity of hearing loss and tinnitus. Overall, improved clinical outcomes have not been reported following HBO.

Bennett, et al. (2012) conducted a systemic review of seven randomized controlled trials (n=392) to assess the benefits and harms of HBO for the treatment of tinnitus and/or sudden sensorineural hearing loss. The significance of any improvement in tinnitus could not be assessed by pooled data and the routine use of HBO for the treatment of tinnitus could not be recommended.

In a study to analyze the effectiveness of HBO treatment on tinnitus, Porubsky et al. (2007) randomized 360 patients into two HBO treatment protocols (2.2 bar vs. 2.5 bar). Twelve patients (3.3%) experienced complete remission of tinnitus, in 122 (33.9) the intensity lessened, and 44 (12.2%) had a subjectively agreeable change of noise characteristics. No change was found in 157 cases (43.6%) and 25 (6.9%) experienced deterioration. There was no statistically significant difference between the two groups ($p>0.05$). Out of 68 patients with a positive expectation of HBO effects, 60.3% stated that the tinnitus had improved compared to 47.2% of patients (n=271) who underwent therapy with an indifferent expectation and 19% (n=21) of patients with a negative expectation. The influence of subjective expectation on the outcome was statistically significant ($p<0.05$).

Venous Stasis Ulcers: Venous stasis ulcers are the result of chronic venous insufficiency and can lead to life-threatening infections of the lower extremities. Although HBO therapy has been proposed for the treatment of this population, its efficacy has not been established by clinical trials. A Cochrane systematic review of randomized controlled trials evaluating HBO for the treatment of chronic wounds (Kranke, et al., 2012) included one trial with 16 patients who had venous ulcers. At six weeks the author reported significant reduction in the ulcer area. Large randomized controlled trials with long-term follow-ups are needed to validate the results of this study.

Other Indications: Studies, primarily in the form of case series (n=5-20), case reports and retrospective reviews have investigated HBO as a primary or adjunctive therapy for various other indications including: altitude sickness, avascular necrosis, Bell’s palsy, comatose patients, cutaneous polyarteritis nodosa lesions,

frostbite, femoral head necrosis, fibromyalgia, Fournier's gangrene, gastrointestinal ulcers, heat stroke, myofascial pain, Parkinson disease, chronic periodontitis, scleroderma, venomous snake bites, and to improve the success of osseointegration following maxillofacial implants. Overall, improved health outcomes following HBO for the treatment of these conditions has not been established (European Association of Urology, 2013; Nogueira-Filho, et al., 2010; ACS, 2008).

In a 2012 Cochrane systematic review of the literature, Holland et al. reported that one low quality randomized controlled trial (n=79) suggested that HBO may be effective for the treatment of Bell's palsy. Further randomized controlled trials are indicated.

Esposito et al. (2013) conducted a systematic review of randomized controlled trials to investigate the effectiveness of HBO administered with dental implants. Only one randomized controlled trial with 26 patients met inclusion criteria. One year after implantation, four patients died from each group. There were no statistically significant differences for prosthesis and implant failures, postoperative complications and patient satisfaction between the two groups.

Topical Hyperbaric Oxygen (THBO)

Literature Review –There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of THBO for the treatment of acute or chronic wounds. The available studies have been primarily in the form of nonrandomized studies and case series with small patient populations and short-term follow-ups.

Blackman et al. (2010) conducted a prospective controlled study to compare the efficacy of THBO (n=17) to silver-based dressing (control group, n=11) for the treatment of diabetic foot ulcers. Wounds were more severe and ulcer durations were longer in the treatment group compared to the control group. The THBO group received therapy five times per week for 90 days. Wounds were debrided in each group as indicated. The number of ulcers with complete healing in the THBO group compared to the control group was statistically significant (p=0.04). Fourteen of 17 ulcers (82.4%) in the treatment group and five of 11 ulcers (45.5%) in the control group healed after a median of 56 and 93 days, respectively. At the 24-month follow-up no ulcers had reoccurred in either group. The authors noted that there was a possible selection bias with the more serious wound patients being assigned to THBO. Limitations of the study include the small patient population and nonrandomization.

Tawfick and Sultan (2009) conducted a prospective comparative study to evaluate the safety and efficacy of THBO for the treatment of chronic venous ulcers refractory to medical management. A total of 46 ulcers were treated with THBO and debridement, and 37 ulcers were treated with dressings and debridement. Patients selected the treatment option they preferred. Treatment was continued for 12 weeks or until complete healing occurred. Compared to the control group, a significant number of ulcers in the THBO group showed a reduction in surface area by week three and complete healing by week 12 ($p=0.016$ and $p<0.001$, respectively). At 12 weeks, the mean reduction in ulcer surface area was 96% in the THBO group, compared to 61% in the control group. The median time to full healing was 45 days in the THBO group and 182 days in the control group ($p<0.001$). Nine of 19 methicillin resistant staphylococcus aureus (MRSA) positive ulcers in the THBO group were negative after five weeks of therapy compared to none of 17 in the control group ($p=0.007$). During the follow-up period none of the 37 THBO-treated healed ulcers showed signs of recurrence compared to 5 of 13 ulcers in the control group and two control group ulcers begin to deteriorate prior to complete healing. Limitations of the study include the small patient population, selection of treatment option by the patients, and nonrandomization.

Professional Societies/Organizations: Regarding topical oxygen, Undersea and Hyperbaric Medical Society (UHMS) stated (Feldmejer, et al., 2005) "Topical oxygen should not be termed hyperbaric oxygen since doing so intentionally or unintentionally suggests that topical oxygen treatment is equivalent or even identical to hyperbaric oxygen. Mechanisms of action or clinical study results for hyperbaric oxygen cannot and should not be co-opted to support topical oxygen since hyperbaric oxygen therapy and topical oxygen have different routes and probably efficiencies of entry into the wound and their physiology and biochemistry are necessarily different. The application of topical oxygen cannot be recommended outside of a clinical trial at this time based on the volume and quality of scientific supporting evidence available."

Use Outside of the US
Professional societies outside of the US have published guidance documents for the use of HBO for conditions such as autism spectrum disorder, cerebral palsy, diabetic foot ulcers, and radiation-induced GI bleeding.

According to the British Society of Gastroenterology (BSG) (Andreyev, et al., 2012), "the best current evidence for effective treatment of radiation-induced GI bleeding is with sucralfate enemas and hyperbaric oxygen therapy, and HBO is "probably the treatment of choice for radiotherapy-induced bleeding occurring at multiple sites throughout the small and/or large bowel". Regarding rectal bleeding from radiation-induced telangiectasia after pelvic radiotherapy, BSG stated that HBO is one of only four treatments with any evidence (of very variable quality) of benefit from randomized controlled trials and lists HBO as one of three definitive treatments for telangiectasia. BGS noted that the advantages of HBO include that it may reverse progressive changes caused by radiotherapy and improve other symptoms (e.g., urinary problems). Disadvantages of HBO include the fact that it is time-consuming (8 weeks of daily treatment), expensive and patients may need to travel a long distances to the nearest HBO facility.

In a 2011 diabetic inpatient clinical guideline, NICE (United Kingdom) recommended that HBO not be offered as an adjunctive treatment for diabetic foot problems unless part of a clinical trial. The evidence was of "low to moderate quality". However, two of five outcomes demonstrated significant positive effects indicating that additional assessment is needed.

A 2008 update on the indications for HBO by the Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) (Quebec) concluded that the recommendations for the indication for HBO as previously published remain "basically unchanged" and the evidence still does not support the effectiveness of HBO for all other conditions. The role of HBO remains experimental for the treatment of cerebral palsy and autism.

An AETMIS technology assessment (2007) of three case series, one randomized controlled trial and five unpublished studies included small patient populations (n=10–60) and variations in the oxygen and pressure parameters. Although the studies seemed to indicate a reduction in autism symptoms, AETMIS concluded that "there is insufficient evidence to build a strong case for the efficacy of hyperbaric oxygen therapy in the management of autistic disorders."

Summary
Although there is there is a paucity of data in the form of randomized controlled trials and studies are primarily in the form of case series and retrospective reviews, systemic hyperbaric oxygen therapy (HBO) is an established treatment option for a carefully selected subgroup of conditions. Recent published studies have called into question the safety and effectiveness of systemic HBO for some of these conditions and additional, well designed clinical trials are indicated to validate these outcomes.

There is insufficient evidence in the published, peer-reviewed scientific literature to support systemic HBO for all other conditions and to support the effectiveness of topical hyperbaric oxygen for any indication. Overall, studies are primarily in the form of case series and retrospective reviews with small heterogeneous patient populations, short-term follow-ups and have reported conflicting and various outcome data. For some conditions, systematic reviews and randomized controlled trials have shown that systemic HBO and topical HBO were ineffective therapies resulting in no improvements in the clinical status of the patients. Systemic HBO for these other conditions and topical HBO have not been proven to improve net health outcomes.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.
3) ICD-10-CM Diagnosis Codes are for informational purposes only and are not effective until 10/01/2015

Systemic Hyperbaric Oxygen Therapy

Covered when medically necessary:

CPT®* Codes	Description
99183	Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session

HCPCS Codes	Description
C1300	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval

Topical Hyperbaric Oxygen

Experimental/Investigational/Unproven/Not Covered:

HCPCS Codes	Description
A4575	Topical hyperbaric oxygen chamber, disposable

ICD-9-CM Diagnosis Codes	Description
	All codes

ICD-10-CM Diagnosis Codes (Effective 10/01/2015)	Description
	All codes

***Current Procedural Terminology (CPT®) ©2013 American Medical Association: Chicago, IL.**

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