Hyperbaric oxygen therapy (HBOT) involves breathing 100% oxygen at a pressure of more than 1.5 and 3.0 atmospheres (atm). Hyperbaric oxygen therapy is generally applied systemically with the patient inside a hyperbaric chamber. It can also be applied topically; that is, the body part to be treated is isolated e.g., in an inflatable bag and exposed to pure oxygen. HBOT has been investigated for various conditions that have potential to respond to increased oxygen delivery to the tissues.

**Background**

Hyperbaric oxygen therapy (HBOT) is a technique of delivering higher pressures of oxygen to the tissues. Two methods of administration are available. In systemic or large chamber hyperbaric oxygen, the patient is entirely enclosed in a pressure chamber and breathes oxygen at a pressure greater than 1 atmosphere (atm, the pressure of oxygen at sea level). Thus, this technique relies on systemic circulation to deliver highly oxygenated blood to the target site, typically a wound. In addition, systemic hyperbaric oxygen therapy can be used to treat systemic illness, such as air or gas embolism, carbon monoxide poisoning, clostridial gas gangrene, etc. Treatment may be carried out either in a monoplace chamber pressurized with pure oxygen or in a larger, multiplace chamber pressurized with compressed air, in which case the patient receives pure oxygen by mask, head tent or endotracheal tube.

Note that this evidence review does not address topical oxygen therapy in the absence of pressurization.

**Regulatory Status**

In May 2005, the ATA Monoplace Hyperbaric System (ATA Hyperbaric Chamber Manufacturing, Inc.) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing hyperbaric devices.

In 2013, FDA published a statement warning that non-FDA approved uses of HBOT may endanger the health of patients.(1) If patients mistakenly believe that HBOT devices have been proven safe for uses not cleared by FDA, they may delay or forgo other proven medical therapies.

**Related Policies**

None
Systemic hyperbaric oxygen pressurization may be considered medically necessary in the treatment of the following conditions:

- non-healing diabetic wounds of the lower extremities in patients who meet the following 3 criteria:
  1. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes; and
  2. Patient has a wound classified as Wagner grade 3 or higher (see Policy Guidelines); and
  3. Patient has no measurable signs of healing after 30 days of an adequate course of standard wound therapy;
- acute traumatic ischemia e.g. crush injuries, reperfusion injury, compartment syndrome;
- decompression sickness;
- gas embolism, acute;
- cyanide poisoning, acute;
- acute carbon monoxide poisoning;
- soft-tissue radiation necrosis (e.g., radiation enteritis, cystitis, proctitis) and osteoradionecrosis;
- pre- and post-treatment for patients undergoing dental surgery (non-implant-related) of an irradiated jaw;
- gas gangrene (i.e., clostridial myonecrosis);
- profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed; and
- chronic refractory osteomyelitis

Hyperbaric oxygen pressurization is considered not medically necessary in the treatment of the following conditions:

- compromised skin grafts or flaps;
- acute osteomyelitis
- bisphosphonate-related osteonecrosis of the jaw
- necrotizing soft-tissue infections;
- acute thermal burns;
- acute surgical and traumatic wounds;
- chronic wounds, other than those in patients with diabetes who meet the criteria specified in the medically necessary statement;
spinal cord injury;
traumatic brain injury;
inflammatory bowel disease (Crohn disease or ulcerative colitis);
brown recluse spider bites;
bone grafts;
carbon tetrachloride poisoning, acute;
cerebrovascular disease, acute (thrombotic or embolic) or chronic;
fracture healing;
hydrogen sulfide poisoning;
intra-abdominal and intracranial abscesses;
lepromatous leprosy;
meningitis;
Pseudomembranous colitis (antimicrobial agent-induced colitis);
radiation myelitis;
sickle cell crisis and/or hematuria;
demyelinating diseases, e.g., multiple sclerosis, amyotrophic lateral sclerosis;
retinal artery insufficiency, acute;
retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment;
pyoderma gangrenosum;
acute arterial peripheral insufficiency;
acute coronary syndromes and as an adjunct to coronary interventions, including but not limited to, percutaneous coronary interventions and cardiopulmonary bypass;
idioptatic sudden sensorineural hearing loss (ISSNHL);
refractory mycoses: mucormycosis, actinomycosis, canidiobolus coronato;
cerebral edema, acute;
migraine;
in vitro fertilization;
cerebral palsy;
tumor sensitization for cancer treatments, including but not limited to, radiotherapy or chemotherapy;
• delayed onset muscle soreness;
• idiopathic femoral neck necrosis;
• chronic arm lymphedema following radiotherapy for cancer;
• radiation-induced injury in the head and neck; except as noted above in the medically necessary statement;
• early treatment (beginning at completion of radiation therapy) to reduce adverse effects of radiation therapy;
• autism spectrum disorders.
• Bell’s palsy
• acute ischemic stroke;
• motor dysfunction associated with stroke;
• herpes zoster; and
• vascular dementia
• fibromyalgia; and
• mental illness (ie, posttraumatic stress disorder, generalized anxiety disorder or depression).

Policy Guidelines

Systemic Hyperbaric Oxygen
The Wagner classification system of wounds is defined as follows:
• grade 0, no open lesion;
• grade 1, superficial ulcer without penetration to deeper layers;
• grade 2, ulcer penetrates to tendon, bone, or joint;
• grade 3, lesion has penetrated deeper than grade 2 and there is abscess, osteomyelitis, pyarthrosis, plantar space abscess, or infection of the tendon and tendon sheaths;
• grade 4, wet or dry gangrene in the toes or forefoot;
• grade 5, gangrene involves the whole foot or such a percentage that no local procedures are possible and amputation (at least at or below the knee level) is indicated.

Below are suggestions from the Undersea and Hyperbaric Medical Society’s (UHMS) 2008 Hyperbaric Oxygen Therapy Committee report on utilization of hyperbaric oxygen therapy (HBOT) (2):
• Enhancement of healing in problem wounds: Treatments are performed for 90 to 120 minutes. The initial treatment schedule depends on the severity of disease. More serious conditions may require twice daily treatments; when stabilized, this can decrease to once daily. Utilization review is required after the initial 30 days of treatment and at least once every additional 30 days.
• Crush injury, compartment syndrome and other acute traumatic ischemias:
Crush injury: 8 treatments (three times per day for 2 days, then twice a day for 2 days and daily for 2 days)

Compartment syndrome: 3 treatments (twice a day for 1 day and one treatment on day 2)

- Decompression sickness: The majority of cases respond to a single treatment. Patients with residual defects after the initial session should receive additional treatments until they achieve clinical stability (generally no more than 5-10 treatments). Utilization review is recommended after 10 treatments.

- Gas embolism, acute: It is recommended that treatments continue until there is no additional improvement; this typically occurs after 1-2 treatments but occasionally up to 5-10. Utilization review is recommended after 10 treatments.

- Acute carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning: Some patients improve after a single treatment. Patients who fail to demonstrate a full recovery should receive additional treatments. In patients with persistent neurologic dysfunction after the initial treatment, further treatment can occur within 6-8 hours and can be continued once or twice daily until there is no additional improvement in cognitive function. Utilization review is mandatory after the fifth treatment.

- Soft-tissue radiation necrosis (e.g., radiation enteritis, cystitis, proctitis) and osteoradionecrosis: Most treatment courses for radiation injury will be 30-60 treatments (once daily for 90 to 120 minutes). Utilization review is recommended after 60 treatments.

- Mandibular osteoradionecrosis: The initial course of treatment for patients with stage 1 osteoradionecrosis is 30 sessions, followed by only minor bony debridement. If response is adequate, an additional 10 treatments are given. If patients are not responding they are considered stage II and they receive more extensive surgical debridement, followed by 10 additional treatments. Patients who present as stage III patients receive 30 treatments followed by mandibular segmental resection and then an additional 10 treatments.

- Gas gangrene (i.e., clostridial myonecrosis): Recommended are three 90-minute treatments during the first 24 hours and then two treatments per day for the next 2-5 days, depending on the patient’s initial response. Utilization review is indicated after 10 treatments.

- Severe anemia: HBOT can be considered for severe anemia when patients cannot receive blood products due to medical, religious, or strong personal preference reasons. Treatment can occur for periods of up to 3 or 4 hours three to four times a day if patients receive intra-treatment air breaks. HBOT treatment should be continued with taper of both time and frequency until red blood cells have been satisfactorily replaced by patient regeneration or the patient can undergo transfusion.

- Chronic refractory osteomyelitis: No recommendations were made for the total number of treatments required. For patients who respond to initial treatment with antibiotics, surgical debridement and HBOT, therapy should be continued for approximately 4-6 weeks. Utilization review is indicated after 30-40 sessions.
Benefit Applications

The BCBS FEP contract stipulates that FDA-approved biologics, drugs and certain devices may not be considered investigational when used for their intended purpose and thus these products may only be assessed based on medical necessity.

The BCBS FEP contract affects coverage for hyperbaric oxygen therapy. Refer to the current FEP Service Benefit Plan brochure for additional information and guidance.

Rationale

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for a therapeutic intervention is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may be adequate if there is an established link between the intermediate outcome and true health outcomes. When the primary outcomes are subjective (eg, pain, depression), sham-controlled RCTs are needed to assess the effect of the intervention beyond that of a placebo effect.

Systemic Hyperbaric Oxygen

The original policy on systemic HBOT was based on the 1996 guidelines published by the Undersea and Hyperbaric Medical Society (UHMS) and was subsequently revised in 1999 with 3 TEC Assessments. (3-5) The TEC Assessments had conclusions similar to UHMS, except, in contrast to the UHMS guidelines, they concluded that there was insufficient evidence to conclude that HBOT treatment improved the net health outcome for the following indications:

- compromised skin grafts
- acute thermal burns
- chronic refractory osteomyelitis
- necrotizing soft tissue infections
- brown recluse spider bites

The TEC Assessments also concluded that there was insufficient evidence to permit conclusions on the use of HBOT for treatment of brain injury; spinal cord injury; and Crohn’s disease, indications not addressed by the 1996 UHMS Guidelines. Literature updates have focused on identifying new RCTs and meta-analyses of RCTs, particularly on indications considered not medically necessary at the time of the update.

Chronic Diabetic Ulcers

A Cochrane review of RCTs on HBOT for chronic wounds was published by Kranke et al in 2015.(6) Reviewers identified 12 RCTs (total N=577 participants) that compared the effect of HBOT on chronic wound healing with an alternative treatment approach that did not use HBOT. Ten of the 12 trials included in the review evaluated HBOT in patients with diabetes. In a pooled analysis of data from 5 trials, a significantly higher proportion of ulcers had healed at the end of treatment (ie, 6 weeks) in the
group receiving HBOT than in the group not receiving HBOT (relative risk [RR], 2.35; 95% confidence interval [CI], 1.19 to 4.62). However, in a pooled analysis of 5 trials, there was no statistically significant difference in the risk of major amputations in patients assigned to HBOT compared to a control condition (RR=0.36; 95% CI, 0.11 to 2.23). There were insufficient data to conduct pooled analyses of studies evaluating HBOT for treating patients with chronic wounds without diabetes.

A 2016 systematic review by Elraiyah et al evaluated adjunctive therapies used to treat diabetic foot ulcers.(7) A pooled analysis of 6 RCTs found a significantly higher healing rate with HBOT than with control conditions (odds ratio [OR], 0.30; 95% CI, 7.08 to 28.68). Another pooled analysis of the 6 trials found that HBOT was associated with a significantly lower major amputation rate (OR=0.30; 95% CI, 0.10 to 0.89). The studies were rated as low-to-moderate quality.

**Section Summary: Chronic Diabetic Ulcers**

Multiple RCTs and systematic reviews have been published. Pooled analyses of RCTs found significantly higher wound healing rates with HBOT than with control conditions. One meta-analysis, but not the other, found that HBOT was associated with a significantly lower rate of major amputation.

**Carbon Monoxide Poisoning**

A 2011 Cochrane review by Buckley et al included 6 RCTs evaluating HBOT for carbon monoxide poisoning.(8) Two of the 6 RCTs found that HBOT reduced the likelihood of neurologic sequelae at 1 month and 4 others did not find a significant effect. A pooled analysis of RCTs did not find a significant effect of HBOT on risk of neurologic deficits (OR=0.78; 95% CI, 0.54 to 1.12). The trials had substantial methodologic and statistical heterogeneity. Reviewers concluded that there is insufficient evidence to determine whether HBOT reduces the risk of adverse neurologic outcomes after carbon monoxide poisoning.

**Section Summary: Carbon Monoxide Poisoning**

A Cochrane review identified 6 RCTs, the majority of which did not find a significant effect of HBOT on health outcomes. In addition, a pooled analysis of RCT data did not find a significant effect of HBOT on neurologic deficits.

**Radionecrosis, Osteoradionecrosis, and Treatment of Irradiated Jaw**

In 2016, Bennett et al published a Cochrane review on HBOT for late radiation tissue injury.(9) Reviewers identified 14 RCTs. In a pooled analysis of 3 studies, a significantly higher proportion of patients with osteoradionecrosis achieved complete mucosal cover after HBOT than with control treatments (RR=1.30; 95% CI, 1.09 to 1.55). In addition, a pooled analysis of 2 trials found a significantly lower risk of wound dehiscence after surgery to repair mandibular osteoradionecrosis with HBOT than with control treatments (RR=4.23; 95% CI, 1.06 to 16.83). A single trial found a significantly higher likelihood of successful healing with HBOT than with antibiotics for tooth extraction in irradiated jaws (absolute risk reduction, 25%; p=0.02). There were insufficient data to conduct meta-analyses on other outcomes.

**Section Summary: Radionecrosis, Osteoradionecrosis, and Treatment of Irradiated Jaw**

A Cochrane review of RCTs found that HBOT improved some radionecrosis and osteoradionecrosis outcomes and resulted in better outcomes prior to tooth extraction in an irradiated jaw. The number of RCTs evaluating HBOT for these indications, especially in irradiated jaws, is limited.
Chronic Refractory Osteomyelitis

No prospective clinical trials on chronic or acute refractory osteomyelitis were identified in literature searches. The justification for the use of HBOT in chronic osteomyelitis has been primarily based on case series. Among the larger case series, Maynor et al (1998) reviewed the records of all patients with chronic osteomyelitis of the tibia seen at 1 institution. (10) Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBOT sessions (range, 6-99 sessions). Of the 26 patients with at least 2 years of follow-up after treatment, 21 (81%) remained drainage-free. Twelve (80%) of 15 with follow-up data at 60 months had remained drainage-free. A study by Davis et al (1986) reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution. (11) Patients received HBOT until the bone was fully recovered with healthy vascular tissue; this resulted in a mean of 48 daily treatments (range, 8-103 treatments). After a mean posttreatment follow-up of 34 months, 34 (89%) of 38 patients remained clinically free of infection (ie, drainage-free and no tenderness, pain, or cellulitis). Success rates from several smaller case series (N range, 13-15 patients), all conducted in Taiwan (1998-2000), ranged from 79% to 92%. (12-15) A high percentage of refractory patients in these series had successful outcomes.

Section Summary: Chronic Refractory Osteomyelitis

Only case series data are available; no RCTs or comparative nonrandomized trials were identified. Case series tended to find high rates of successful outcomes in patients with chronic refractory osteomyelitis treated with HBOT. However, controlled studies are needed to determine conclusively that HBOT improves health outcomes in patients with chronic refractory osteomyelitis compared to other interventions.

Acute Thermal Burns

In 2004, a Cochrane review assessed HBOT for thermal burns. (15) Two RCTs were identified. Sample sizes were 16 and 125. Both of these were judged by reviewers to have poor methodologic quality. Reviewers concluded that the evidence was insufficient to permit conclusions on whether HBOT improves health outcomes in patients with acute thermal burns. No additional trials were identified when the Cochrane reviewers conducted an updated literature search in 2009 (the 2004 publication date continues to be used).

Section Summary: Acute Thermal Burns

A Cochrane review identified 2 RCTs on HBOT for thermal burns. Both were judged to have poor methodologic quality. There is insufficient evidence from well-conducted controlled studies to permit conclusions on the impact of HBOT on health outcomes in patients with acute thermal burns.

Acute Surgical and Traumatic Wounds

In 2013, a Cochrane review of RCTs on HBOT for acute surgical and traumatic wounds was published by Eskes et al. (16) HBOT was administered at pressures above 1 atmosphere (atm). To be included, studies had to compare HBOT with a different intervention or compare 2 HBOT regimens; in addition, studies had to objectively measure wound healing. Four RCTs met reviewers’ inclusion criteria. Trials ranged in size from 10 to 135 participants. Due to differences among trials in terms of patient population, comparison intervention, and outcome measurement, results could not be pooled. The primary outcome examined by Cochrane reviewers (wound healing) was not reported in either of the 2 trials comparing HBOT with usual care and was not reported in the 1 trial comparing HBOT with
dexamethasone or heparin. Complete wound healing was reported in the RCT comparing active HBOT with sham HBOT. In this study (N=36), there was a statistically higher rate of wound healing in the group, though the time point for outcome measurement in this trial was unclear. In addition, there was no statistically significant difference between groups in the mean time to wound healing.

A 2014 systematic review of studies on HBOT for acute wounds, published by Dauwe et al, included RCTs and controlled nonrandomized studies.(17) Reviewers included 8 studies, with sample sizes ranging from 5 to 125 patients. Four studies were randomized, 3 were prospective observational studies, and 1 was a retrospective observational study. As in the Eskes systematic review, data were not pooled. Reviewers noted that 7 of the 8 studies reported statistically significant findings for their primary end points, but the end points differed among studies (eg, graft survival, length of hospital stay, wound size). Moreover, the studies were heterogeneous in terms of treatment regimens, patient indications (eg, burns, face lifts), and study designs, making it difficult to draw conclusions about the effect of HBOT on acute wound treatment.

Section Summary: Acute Surgical and Traumatic Wounds

Two systematic reviews identified 4 RCTs; one of the reviews also included nonrandomized studies. Heterogeneity among studies (eg, in patient population, comparison group, outcomes) prevented pooling of study findings and limits the ability to draw conclusions about the impact of HBOT on health outcomes in patients with acute and traumatic wounds. Additional evidence from high-quality RCTs is needed.

Bisphosphonate-Related Osteonecrosis of the Jaw

An unblinded RCT by Freiberger et al (2012) evaluated use of HBOT as an adjunct therapy for patients with bisphosphonate-related osteonecrosis of the jaw.(18) Forty-nine patients were randomized to HBOT plus standard care (n=22) or to standard care alone (n=27). Five patients in the standard care group received HBOT and 1 patient assigned to the HBOT group declined HBOT. The investigators did a per-protocol analysis (actual treatment received) because of the relatively large degree of crossover. Participants were evaluated at 3, 6, 12, and 18 months. Data were available on 46 patients; 25 received HBOT in addition to standard care and 21 received standard care alone. The primary outcome measure was change in oral lesion size or number. When change from baseline to last available follow-up was examined, 17 (68%) of 25 of HBOT-treated patients had improvement in oral lesion size or number compared with 8 (38%) of 21 in the standard care group (p=0.043). When change from baseline to 6, 12, or 18 months was examined, there were no statistically significant differences between groups in the proportion of patients with improvement or in the proportion of those who healed completely at any time point. This trial had a number of methodologic limitations (eg, unblinded, crossover, per-protocol analysis rather than intention-to-treat). A disadvantage of the per-protocol analysis is that randomization is not preserved, and the 2 groups may differ on characteristics that affect outcomes.

Section Summary: Bisphosphonate-Related Osteonecrosis of the Jaw

One RCT has evaluated HBOT for patients with bisphosphonate-related osteonecrosis of the jaw. This unblinded study did not find a significant benefit of HBOT for most health outcomes compared with standard care. Additional evidence from RCTs is needed to permit conclusions on the impact of HBOT on health outcomes in patients with bisphosphonate-related osteonecrosis of the jaw.
Necrotizing Soft Tissue Infections

A 2015 Cochrane review by Levett et al evaluated the literature on HBOT as adjunctive therapy for necrotizing fasciitis. (19) No RCTs were identified. Previously, in 2005, a systematic review by Jallali et al identified only a few retrospective studies with small sample sizes. (20) Findings from these studies were inconsistent. A 2009 retrospective cohort study compared outcomes in 48 patients at 1 center who received adjunctive HBOT for necrotizing soft tissue infections to those in 30 patients at a different center who did not receive HBOT. (21) There was no significant difference in the mortality rate between the 2 groups (8% [4/48]) in the HBOT group vs 13% [4/30] in the non-HBOT group; p=0.48. The median number of days in the intensive care unit and the median number of days in the hospital also did not differ significantly between groups. There was a higher median number of débridement procedures per person in the HBOT group (3.0) than in the non-HBOT group (2.0; p=0.03).

Section Summary: Necrotizing Soft Tissue Infections

No RCTs have evaluated HBOT for necrotizing soft tissue infection. A retrospective cohort study did not find a difference in outcomes after HBOT or standard care.

Acute Coronary Syndrome

A 2015 Cochrane review by Bennett et al identified 6 trials (total N=665 patients) evaluating HBOT for acute coronary syndrome. (22) All studies included patients with acute myocardial infarction (MI); 1 study also included individuals with unstable angina. Additionally, all trials used HBOT as an adjunct to standard care. Control interventions varied; only 1 trial described using a sham therapy to blind participants to treatment group allocation. In a pooled analysis of data from 5 trials, there was a significantly lower rate of death in patients who received HBOT compared with a control intervention (RR=0.58; 95% CI, 0.36 to 0.92). Due to variability of outcome reporting across studies, few other pooled analyses could be conducted. A pooled analysis of data from 3 trials on improvements in left ventricular function did not find a statistically significant benefit of HBOT (RR=0.09; 95% CI, 0.01 to 1.4). Reviewers noted that, although some evidence from small trials correlated HBOT with a lower risk of death, larger trials with high-quality methods are needed to determine which patients, if any, can be expected to derive benefit from HBOT.

Section Summary: Acute Coronary Syndrome

A Cochrane review of 6 RCTs found insufficient evidence that HBOT is safe and effective for acute coronary syndrome. One pooled analysis of data from 5 RCTs found a significantly lower rate of death with HBOT than with a comparison intervention; however, larger, higher quality trials are needed. The other pooled analysis did not find significantly greater improvement in left ventricular function with HBOT versus comparison interventions.

Acute Ischemic Stroke

In a 2014 Cochrane systematic review of RCTs, Bennett et al evaluated HBOT for acute ischemic stroke. (23) Reviewers identified 11 RCTs (total N=705 participants) that compared HBOT with sham HBOT or no treatment. Reviewers could only pool study findings for 1 outcome (mortality at 3-6 months). That pooled analysis of data from 4 trials (n=106 participants) did not find a significant benefit of HBOT compared with a control condition (RR=0.97; 95% CI, 0.34 to 2.75).
Section Summary: Acute Ischemic Stroke

A Cochrane review of RCTs conducted 1 pooled analysis (4 RCTs), which found no significant difference in mortality at 3 to 6 months when patients with acute ischemic stroke were treated with HBOT or a sham intervention. Additional RCT data is needed to permit conclusions on the impact of HBOT on the health outcome in patients with acute ischemic stroke.

Motor Dysfunction Associated With Stroke

In 2013, Efrati et al published an RCT evaluating HBOT for treatment of neurologic deficiencies associated with a history of stroke.(24) The trial included 74 patients with at least 1 motor dysfunction who had an ischemic or hemorrhagic stroke 6 to 36 months prior to study participation. Participants were randomized to 2 months of HBOT (40 daily sessions, 5 d/wk, n=30) or to delayed treatment (n=32). Patients were evaluated at baseline and 2 months. For patients in the delayed treatment control group, outcomes were evaluated at 4 months after crossing over and receiving HBOT. Twenty-nine (91%) of 32 patients in the delayed treatment group crossed over to the active intervention. Outcome measures included the National Institutes of Health Stroke Scale (NIHSS), which was measured by physicians blinded to treatment group, and several patient-reported (QOL) and functional status measures.

At the 2-month follow-up, there was statistically significantly greater improvement in function in the HBOT group than in the control group, as measured by the NIHSS, QOL scales, and the ability to perform activities of daily living (ADLs). These differences in outcome measures were accompanied by improvements in single-photon emission computed tomography imaging in the regions affected by stroke. For the delayed treatment control group, there was a statistically significant improvement in function after HBOT than before HBOT. This RCT raises the possibility that HBOT may induce improvements in function and QOL for poststroke patients with motor deficits. However, the results are not definitive for a number of reasons. This RCT was small and enrolled a heterogeneous group of poststroke patients. It was not double-blind and most outcome measures, except for NIHSS, were patient-reported and thus prone to the placebo effect. Also, there was a high total dropout rate (20%) at the 2-month follow-up. Therefore, larger, double-blind studies with longer follow-up are needed to corroborate these results.

Section Summary: Motor Dysfunction Associated With Stroke

One crossover RCT identified evaluated HBOT in patients with a recent history of stroke. The RCT found better outcomes at 2 months with HBOT versus delayed treatment. However, the trial had a number of methodologic limitations, which make it difficult to draw conclusions about the efficacy of HBOT for this indication. Double-blind RCTs that address potential bias in subjective outcomes and studies with adequate follow-up are needed.

Bell Palsy

In 2012, Holland et al published a Cochrane review evaluating HBOT in adults with Bell palsy.(25) Reviewers identified 1 RCT with 79 participants, but this trial did not meet reviewers’ selection standards because the outcome assessor was not blinded to treatment allocation.
Section Summary: Bell Palsy

There is a lack of evidence on HBOT for Bell palsy. A Cochrane review did not identify any eligible RCTs; the single RCT identified lacked blinded outcome assessment. Well-conducted RCTs are needed.

Traumatic Brain Injury

A 2016 meta-analysis by Wang et al addressed HBOT for treatment of traumatic brain injury (TBI). (26) The review included RCTs or nonrandomized 2-arm trials comparing HBOT and normobaric oxygen therapy in patients with mild or severe TBI. Eight studies (total N=519 participants) met the eligibility criteria. HBOT protocols varied across studies in the levels of oxygen and the length and frequency of treatments. The primary outcome was change in the Glasgow Coma Scale (GCS) score. Only 2 of the 8 included trials had data on GCS scores suitable for pooling. A pooled analysis of 2 studies found a significantly greater improvement in the mean GCS score in the HBOT than with control groups (mean difference, 3.13; 95% CI, 2.34 to 3.92; p<0.001). Mortality (a secondary outcome) was reported in 3 of the 8 studies. Pooled analysis of these 3 studies found a significantly lower overall mortality rate in the HBOT group than in the control group (OR=0.32; 95% CI, 0.18 to 0.57; p<0.001).

Another 2016 systematic review, by Crawford et al, did not conduct pooled analyses. (27) Reviewers identified 12 RCTs evaluating HBOT for patients with TBI. Four trials, all rated as having acceptable quality, addressed patients with mild TBI and compared HBOT with sham. None found statistically significant differences between groups on outcomes (ie, postconcussive symptom severity, psychological outcomes). Seven trials evaluated HBOT for acute treatment of patients with moderate-to-severe TBI. Four were rated as acceptable quality and 3 as low quality. Study protocols and outcomes varied and none used a sham control. Three acceptable quality studies with standard care controls reported the Glasgow Outcome Scale (GOS) score and mortality rate. In 2 of these, outcomes were better with HBOT than standard care; in the third study, outcomes did not differ significantly.

Previously, in 2012, a Cochrane review on HBOT as adjunctive therapy for TBI was published. (28) Reviewers identified 7 RCTs (total N=571 participants) comparing a standard intensive treatment regimen with the same treatment regimen plus HBOT. Reviewers did not include studies with interventions in specialized acute care settings. The HBOT regimens varied among studies; eg, the total number of individual sessions varied from 3 to 40. None of the trials used sham treatment or blinded staff treating patients, and only 1 had blinding of outcome assessment. Allocation concealment was inadequate in all studies. The primary outcomes of the review were mortality and functional outcomes. A pooled analysis of data from 4 trials reporting this outcome found a statistically significantly greater reduction in mortality when HBOT was added to a standard treatment regimen (RR=0.69; 95% CI, 0.54 to 0.88). However, in additional pooled analysis with the same data from these 4 trials, the difference in the proportion of patients with an unfavorable functional outcome at final follow-up was not statistically significant (RR=0.71; 95% CI, 0.50 to 1.01). Unfavorable outcome was commonly defined as a GOS score of 1, 2, or 3, which are described as “dead,” “vegetative state,” or “severely disabled,” respectively. Studies were generally small and judged to have substantial risk of bias.

In addition, several trials on mild TBI in military populations have been published; they did not find significant benefits of HBOT compared with sham treatment. (29-31) For example, in 2015, Miller et al evaluated HBOT in 72 military service members with continuing symptoms at least 4 months after mild TBI. (31) Patients were randomized to 40 daily HBOT sessions at 1.5 atm, 40 sham sessions consisting
of room air at 1.2 atm, or standard care with no hyperbaric chamber sessions. The primary outcome was change in Rivermead Post-Concussion Symptoms Questionnaire (RPQ) score. A cutoff of 15% improvement was deemed clinically important, which translates to a change score of at least 2 points on the RPQ-3 subscale. The proportion of patients who met this prespecified change on the RPQ-3 was 52% in the HBOT group, 33% in the sham group, and 25% in the standard care-only group. The difference between rates in the HBOT and sham groups was not statistically significant (p=0.24). None of the secondary outcomes significantly favored the HBOT group. A criticism of this study, as well as the other military population studies, was that patient response in the sham group was not due to a placebo effect but to an intervention effect of slightly increased atmospheric pressure (1.2 atm).(32) Other researchers have noted that room air delivered at 1.2 atm would not be considered an acceptable therapeutic dose for any indication, and especially for a condition with persistent symptoms like postconcussive syndrome.

Section Summary: Traumatic Brain Injury

A number of RCTs and systematic reviews have been published. RCTs were heterogenous in terms of intervention protocols, patient populations, and outcomes reported. Pooled analyses were only conducted on a minority of the published RCTs, and these analyses had mixed findings. There is a lack of consistent evidence from well-conducted trials that HBOT improves the health outcome for patients with TBI.

Inflammatory Bowel Disease

A 2014 systematic review by Dulai et al examined the evidence on HBOT for inflammatory bowel disease (Crohn disease, ulcerative colitis).(33) The review was not limited by study design. Reviewers included 17 studies: 1 RCT, 2 case-control studies, 3 case series, and 11 case reports. The studies reported on a total of 613 patients, 286 with Crohn disease and 327 with ulcerative colitis. The only RCT identified was published in 2013; it was open-label and included 18 patients with ulcerative colitis.(34) Patients were randomized to standard medical therapy only (n=8) or medical therapy plus HBOT (n=10). The hyperbaric oxygen intervention consisted of 90 minutes of treatment at 2.4 atm, 5 days a week for 6 weeks (total of 30 sessions). The primary outcome was the Mayo score, which has a potential range of 0 to 12.(35) Patients with a score of 6 or more are considered to have moderate-to-severe active disease. At follow-up, there was no significant difference between groups in the Mayo score; the median score at 6 months was 0.5 in the HBOT group and 3 in the control group (p value not reported). In addition, there were no significant differences in any secondary outcomes, including laboratory tests and fecal weight. This small study may have been underpowered. Overall, reviewers found that the selected studies had a high risk of bias, particularly in the areas of attrition and reporting bias.

Section Summary: Inflammatory Bowel Disease

Only 1 small RCT has been published, and it did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy. A systematic review of RCTs and observational studies found high rates of bias in the literature (eg, attrition, reporting bias).

Idiopathic Sudden Sensorineural Hearing Loss

A 2012 Cochrane review on HBOT for idiopathic sudden sensorineural hearing loss (ISSNHL) and tinnitus identified 7 RCTs (total N=392 participants).(36) All trials included patients with ISSNHL with and/or without tinnitus; 2 trials also included patients with tinnitus in the absence of ISSNHL.
Randomization procedures were only described in 1 study, and only 1 study stated they blinded participants to treatment group assignment using sham therapy. Six studies included time-based entry criteria for hearing loss and/or tinnitus (48 hours in 3 studies, 2 weeks in 2 studies, 6 months in 1 study). The dose of oxygen per treatment session and the treatment protocols varied across studies (eg, the total number of treatment sessions ranged from 10-25).

All trials reported on change in hearing following treatment; but specific outcomes varied. Two trials reported the proportion of participants with greater than 50% return of hearing at the end of therapy. A pooled analysis of these studies did not find a statistically significant difference in outcomes between the HBOT and the control groups (RR=1.53; 95% CI, 0.86 to 2.78). In contrast, a pooled analysis of 2 trials reporting the proportion of participants with greater than 25% return of hearing at the end of therapy found a significantly higher rate of improvement after HBOT than after a control intervention (RR=1.39; 95% CI, 1.05 to 1.84). Moreover, a pooled analysis of 4 trials found a significantly greater mean improvement in hearing over all frequencies with HBOT compared with control (mean difference, 15.6 dB; 95% CI, 1.5 to 29.8 dB). Reviewers stated that, due to methodologic shortcomings of the trials and the modest number of patients, results of the meta-analysis should be interpreted cautiously; they did not recommend use of HBOT for treating ISSNHL.

In 2013, Cvorovic et al published an RCT that included 50 patients with ISSNHL who had failed primary therapy with intravenous steroids.(37) Patients were randomized to HBOT (20 sessions, 5 daily sessions per week) or to intratympanic steroid injection (4 injections in 13 days). The HBOT sessions consisted of 10 minutes of compression on air, 60 minutes of 100% oxygen at 2 atm, and 10 minutes of decompression on air. Outcomes were change in the mean hearing thresholds at each of 5 frequencies (0.25, 0.5, 1, 2, and 4 kHz). After treatment, there were no statistically significant differences in mean hearing thresholds at 4 of the 5 frequencies. The exception was 2 kHz, and at that frequency, the improvement was significantly greater in the HBOT group.

**Section Summary: Idiopathic Sudden Sensorineural Hearing Loss**

A Cochrane review of RCTs had mixed findings. Some outcomes (ie, improvement in hearing of all frequencies, >25% return of hearing) were better with HBOT than with a control intervention, but more than 50% return of hearing did not differ significantly between groups. The Cochrane reviewers noted methodologic imitations and variability across published studies.

**Delayed-Onset Muscle Soreness**

In a 2005 Cochrane review, Bennett et al identified 7 small RCTs on HBOT for delayed-onset muscle soreness.(38) Pooled analysis showed significantly higher pain at 48 and 72 hours in the group receiving HBOT compared with a control condition. There were no between-group differences in long-term pain outcomes or other measures (eg, swelling, muscle strength).

**Section Summary: Delayed-Onset Muscle Soreness**

A Cochrane review of RCTs found worse short-term pain outcomes with HBOT than with a control condition and no difference in longer term pain or other outcomes (eg, swelling).

**Autism Spectrum Disorder**

A 2016 Cochrane review by Xiong et al identified 1 RCT evaluating systemic HBOT for people with autism spectrum disorder who met reviewers’ eligibility criteria.(39) Criteria included a hyperbaric oxygen intervention using 100% oxygen at more than 1 atm. The trial, published by Sampanthaviat
(2012), randomized 60 children with autism to receive 20 one-hour sessions with HBOT or sham air (n=30 per group).(40) The primary outcome measures were change in Autism Treatment Evaluation Checklist (ATEC) and Clinical Global Impression scores, evaluated separately by clinicians and parents. There were no statistically significant differences between groups for any primary outcomes. For example, posttreatment clinician-assessed mean scores on ATEC were 52.4 in the HBOT group and 52.9 in the sham air group. Other studies identified in the search were excluded from the Cochrane review, including Rossignol et al (2009), which used 24% oxygen, not 100% oxygen.(41)

Section Summary: Autism Spectrum Disorder

A Cochrane review identified 1 RCT on HBOT for autism spectrum disorder and that trial did not find significantly improved outcomes with HBOT versus sham.

Cerebral Palsy

Two published RCTs were identified on HBOT for cerebral palsy. In 2012, Lacey et al published a double-blind RCT that included 49 children ages 3 to 8 years with spastic cerebral palsy.(42) Participants were randomized to 40 treatments with HBOT (n=25) or hyperbaric air to simulate 21% oxygen at room air (n=24). The primary efficacy outcome was change in the Gross Motor Function Measure (GMFM-88) global score after the 8-week treatment period. The trial was stopped early due to futility, when an interim analysis indicated that there was less than a 2% likelihood that a statistically significant difference between groups would be found. At the interim analysis, the posttreatment GMFM-88 global score was a mean of 40.8 in the HBOT group and 41.2 in the hyperbaric air group (p=0.54).

Previously, Collet et al (2001) randomized 111 children with cerebral palsy to 40 treatments over a 2-month period of HBOT (n=57) or slightly pressurized room air (n=54).(43) Reviewers found HBOT produced similar improvements in outcomes such as gross motor function and ADLs in both groups as slightly pressurized air.

Section Summary: Cerebral Palsy

Two RCTs were identified. One was stopped early due to futility and the other did not find significantly better outcomes with HBOT than with a sham intervention.

Vascular Dementia

A 2012 Cochrane review identified 1 RCT evaluating HBOT for vascular dementia.(44) This 2009 RCT study, conducted in China, compared HBOT plus donepezil to donepezil-only in 64 patients. The HBOT plus donepezil group had significantly improved cognitive function after 12 weeks of treatment, as assessed by the Mini-Mental State Examination. Reviewers judged the trial to be of poor quality because it was not blinded and the methods of randomization and allocation concealment were not discussed.

Section Summary: Vascular Dementia

A Cochrane review identified 1 RCT judged to be of poor quality. This trial provides insufficient evidence to permit conclusions on the impact of HBOT on health outcomes in patients with vascular dementia.
Radiotherapy Adverse Effects

In 2010, Spiegelberg et al conducted a systematic review of studies on HBOT to prevent or treat radiotherapy-induced head and neck injuries associated with treatment of malignant tumors. (45) Reviewers identified 20 studies. Eight studies included control groups; their sample sizes ranged from 19 to 78 subjects. Four studies with a control group concluded that HBOT was effective; the other 4 did not. Reviewers noted a paucity of RCTs; they did not state how many RCTs they identified in their literature search.

Several RCTs were identified in literature searches. A 2009 trial by Teguh et al included 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiotherapy; the trial was conducted in The Netherlands. (46) HBOT was used to prevent adverse events following radiotherapy. Eight patients were randomized to 30 sessions of HBOT, beginning within 2 days of completing radiotherapy, and 9 patients to no additional treatment. QOL outcomes were assessed, and the primary outcome was xerostomia at 1 year. QOL measures did not differ significantly between groups in the acute phase (first 3 months). For example, 1 month after treatment, the mean visual analog scale (VAS) score for xerostomia (0-to-10 scale) was 5 in the HBOT group and 6 in the control group. However, at 1 year, there was a statistically significant difference between groups in several outcomes. For example, the mean QOL score for swallowing (0-to-100 scale) was 7 in the HBOT group and 40 in the control group (p<0.001). The trial is limited by its small sample size and wide fluctuations over the follow-up period in QOL ratings.

In 2010, Gothard et al in the U.K. published findings of an RCT using HBOT for arm lymphedema occurring after radiotherapy for cancer. (47) Fifty-eight patients with arm lymphedema (at least 15% increase in arm volume) following cancer treatment were randomized in a 2:1 ratio to HBOT (n=38) or to usual care without HBOT (n=20). Fifty-three patients had baseline assessments and 46 (79%) of 58 had 12-month assessments. At the 12-month follow-up, there was no statistically significant difference in the change from baseline in arm volume. Median change from baseline was -2.9% in the treatment group and -0.3% in the control group. The study protocol defined response as at least an 8% reduction in arm volume relative to the contralateral arm. By this definition, 9 (30%) of 30 of patients in the HBOT group were considered responders compared with 3 (19%) of 16 in the control group (p=NS). Other outcomes (eg, QOL scores on the 36-Item Short-Form Health Survey [SF-36]) also did not differ significantly between groups.

Section Summary: Radiotherapy Adverse Effects

A systematic review noted a lack of RCTs evaluating HBOT for radiotherapy adverse effects. The available RCTs had mixed findings. One found no short-term benefit and some benefits of HBOT 12 months after radiotherapy, while the other did not find a significant benefit of HBOT 12 months after radiotherapy.

Idiopathic Femoral Neck Necrosis

A double-blind RCT evaluating HBOT for treatment of femoral head necrosis was published in 2010 by Camporesi et al. (48) The trial included 20 adults with idiopathic unilateral femoral head necrosis. Patients received 30 treatments over 6 weeks with HBOT at 2.5 atm (n=10) or to a sham treatment of hyperbaric air (n=10). Mean severity of pain on a 0-to-10 scale was significantly lower in the HBOT group than in the control group after 30 sessions (p<0.001) but not after 10 or 20 sessions. (The article did not report exact pain scores.) Several range-of-motion outcomes were reported. At the end of the
initial treatment period, extension, abduction, and adduction, but not flexion, were significantly greater in the HBOT group than in the control group. Longer term comparative data were not available because the control group was offered HBOT after the initial 6-week treatment period.

Section Summary: Idiopathic Femoral Neck Necrosis

One small RCT (N=20) was identified. It only reported 6-week outcomes and results were mixed. This RCT does not provide sufficient data to permit conclusions about the efficacy of HBOT for femoral head necrosis.

Migraine

A 2015 Cochrane review by Bennett et al identified RCTs comparing the effectiveness of systemic HBOT for preventing or treating migraine headache to another treatment or a sham control.(49) Eleven trials (total N=209 patients) were identified that addressed treatment of acute migraine with HBOT. A pooled analysis of 3 trials (n=58 patients) found a statistically significant increase in the proportion of patients with substantial relief of migraine within 45 minutes of HBOT (RR=6.21; 95% CI, 2.41 to 16.00; p=0.001). No other pooled analyses were conducted due to variability in outcomes reported across trials. The meta-analysis did not report data on treatment effectiveness beyond the immediate posttreatment period, and the methodologic quality of selected trials was moderate to low (eg, randomization was not well-described in any trial).

Section Summary: Migraine

A Cochrane review identified 11 RCTs on HBOT for migraine headache. However, only 1 pooled analysis was conducted and it included only 3 of the 11 trials selected. Pooled analysis found significantly greater relief of migraine symptoms with HBOT than a comparator intervention within 45 minutes of treatment. Limitations included availability of outcomes specific to the immediate posttreatment period, variability of outcomes across trials, and generally low methodologic quality of trials.

Herpes Zoster

In 2012, Peng et al in China published an RCT evaluating HBOT for herpes zoster.(50) Sixty-eight patients with herpes zoster diagnosed within the previous 2 weeks were randomized to 30 sessions of HBOT (n=36) or medication treatment (n=32). Pharmacotherapy included antiviral, pain, nerve nutritive, and antidepressive medication. Therapeutic efficacy was calculated at the end of the 3-week treatment period and included the proportion who were healed (ie, complete subsidence of pain and rash) or improved (ie, significant pain relief and rash subsistence). Rates of therapeutic efficacy were 97.2% in the HBOT group and 81.3% in the medication group. The difference between groups was statistically significant (p<0.05). In the HBOT group, 22 (61%) of 36 patients were considered to be healed and 13 (36%) were improved. In the medication group, 17 (53%) of 32 patients were healed and 9 (28%) were improved. Limitations of the study included a lack of blinding and long-term follow-up.

Section Summary: Herpes Zoster

One RCT was identified. Only short-term outcomes were reported. Outcomes at the end of the treatment period were significantly better in the HBOT group compared with the medication group. Limitations include lack of blinding and long-term outcomes.
Fibromyalgia

One quasi-randomized trial and 1 delayed-treatment RCT on HBOT for fibromyalgia were identified. In 2004, Yildiz et al assessed 50 patients with fibromyalgia who had ongoing symptoms despite medical and physical therapy.(51) On an alternating basis, patients were assigned to HBOT or to a control group. HBOT consisted of fifteen 90-minute sessions at 2.4 atm (1 session per day, 5 d/wk). The control group breathed room air at 1 atm on the same schedule. Baseline values on the 3 outcomes were similar. After HBOT treatment, the mean (SD) number of tender points were 6.04 in the HBOT group and 12.54 in the control group. Mean pain thresholds were 1.33 kg and 0.84 kg, respectively, and mean VAS scores were 31.54 and 55.42, respectively. Inconsistent reporting by the authors between the abstract and outcomes table make it difficult to determine whether results between the HBOT and the control groups after 15 therapy sessions were statistically significant. It is also unclear whether the control group received a sham intervention that would minimize any placebo effect (ie, whether the control intervention was delivered in a hyperbaric chamber). The authors stated that the study was double-blind but did not provide details of patient blinding.

In 2015, Efrati et al published an RCT that included 60 symptomatic female patients who had fibromyalgia for at least 2 years.(52) Patients were randomized to an immediate 2-month course of HBOT or to delayed HBOT after 2 months. The HBOT protocol was forty 90-minute sessions of 100% oxygen at 2 atm (1 session per day, 5 d/wk). Forty-eight (80%) of 60 patients completed the study and were included in the analysis. After the initial 2 months, outcomes including number of tender points, pain threshold, and QOL (SF-36) were significantly improved in the immediate treatment group than in the delayed treatment group. After the delayed treatment group had undergone HBOT, outcomes were significantly improved compared with scores in the 2 months prior to HBOT treatment. These findings are not only consistent with a clinical benefit of HBOT, but also with a placebo effect. A sham-control trial is needed to confirm the efficacy of HBOT in the treatment of fibromyalgia and other conditions where primary end points are pain and other subjective outcomes.

Section Summary: Fibromyalgia

There are few RCTs assessing HBOT for fibromyalgia, and those available have relatively small sample sizes and methodologic limitations (eg, quasi-randomization, no or uncertain sham control for a condition with subjective outcomes susceptible to a placebo effect). Moreover, the HBOT protocol varied. Thus, across studies the evidence is insufficient to permit conclusions on the impact of HBOT on health outcomes for patients with fibromyalgia.

Multiple Sclerosis

A 2004 Cochrane review of RCTs on HBOT for multiple sclerosis was published by Bennett et al.(53) Reviewers identified 9 RCTs (total N=504 participants) that compared the effects of HBOT with placebo or no treatment. The primary outcome of the review was Expanded Disability Status Scale (EDSS) score. A pooled analysis of data from 5 trials (n=271 patients) did not find a significant difference in mean EDSS score change after 20 HBOT treatments versus control (mean difference [MD], -0.07; 95% CI, -0.23 to 0.09). Moreover, a pooled analysis of data from 3 trials (n=163 patients) comparing HBOT and placebo did not find a significant difference in mean EDSS score after 6 months of follow-up (MD = -0.22; 95% CI, -0.54 to 0.09).
Section Summary: Multiple Sclerosis

A Cochrane review of RCTs did not find a significant difference in outcomes when patients with multiple sclerosis were treated with HBOT versus a comparison intervention.

Cancer and Chemotherapy

In an RCT of 32 patients, Heys et al (2006) found no increase in 5-year survival for patients treated with HBOT prior to chemotherapy for locally advanced breast carcinoma to increase tumor vascularity.(54) In a 2005 Cochrane review, Bennett et al concluded that HBOT given with radiotherapy may be useful in tumor control; however, reviewers expressed caution because significant adverse effects were common with HBOT.(55)

Section Summary: Cancer and Chemotherapy

A Cochrane review and 1 RCT were identified. The RCT did not find a significant difference in survival in cancer patients who received HBOT prior to chemotherapy.

Other Indications

For the indications listed below, insufficient evidence to support the use of HBOT was identified. Since 2000, there have been no published controlled trials or large case series (ie, ≥25 patients):

- bone grafts;
- carbon tetrachloride poisoning, acute;
- cerebrovascular disease, acute (thrombotic or embolic) or chronic;
- fracture healing;
- hydrogen sulfide poisoning;
- intra-abdominal and intracranial abscesses;
- lepromatous leprosy;
- meningitis;
- pseudomembranous colitis (antimicrobial agent-induced colitis);
- radiation myelitis;
- sickle cell crisis and/or hematuria;
- amyotrophic lateral sclerosis;
- retinal artery insufficiency, acute;
- retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment;
- pyoderma gangrenosum;
- tumor sensitization for cancer treatments, including but not limited to, radiotherapy or chemotherapy;
• compromised skin grafts and flaps;
• brown recluse spider bites;
• spinal cord injury;
• fracture healing;
• refractory mycoses;
• acute peripheral arterial insufficiency;
• in vitro fertilization;
• amyotrophic lateral sclerosis;
• mental illness.

Practice Guidelines and Position Statements

Undersea and Hyperbaric Medical Society

In 2015, the Undersea and Hyperbaric Medical Society (UHMS) published a guideline on use of HBOT for treating diabetic foot ulcers. (56) Recommendations are:

- Suggest against using HBOT in patients with “Wagner Grade 2 or lower diabetic foot ulcers….”
- Suggest adding HBOT in patients with “Wagner Grade 3 or higher diabetic foot ulcers that have now shown significant improvement after 30 days of [standard of care] therapy….”
- Suggest “adding acute post-operative hyperbaric oxygen therapy to the standard of care” in patients with “Wagner Grade 3 or higher diabetic foot ulcers” who have just had foot surgery related to their diabetic ulcers.

In 2011, the Undersea and Hyperbaric Medical Society (UHMS) updated their list of indications considered appropriate for hyperbaric oxygen therapy. (70) These indications are as follows:

- Air or gas embolism
- Carbon monoxide poisoning and carbon monoxide complicated by cyanide poisoning
- Clostridial myositis and myonecrosis (gas gangrene)
- Crush injury, compartment syndrome and other acute traumatic ischamias
- Decompression sickness
- Arterial insufficiencies:
  - Central retinal artery occlusion;
  - Enhancement of healing in selected problem wounds
- Severe anemia
- Intracranial abscess
- Necrotizing soft tissue infections
• Osteomyelitis (refractory)
• Delayed radiation injury (soft tissue and bony necrosis)
• Skin grafts and flaps (compromised)
• Acute thermal burn injury
• Idiopathic sudden sensorineural hearing loss (ISSNHL) (patients with moderate to profound ISSNHL who present within 14 days of symptom onset)

American Academy of Otolaryngology-Head and Neck Surgery

In 2012, the American Academy of Otolaryngology-Head and Neck Surgery published a clinical guideline on treatment of sudden hearing loss. (58) The guideline includes a statement that HBOT may be considered a treatment option for patients who present within 3 months of a diagnosis of idiopathic sudden sensorineural hearing loss. The document states, “Although HBOT is not widely available in the United States and is not recognized by many U.S. clinicians as an intervention for ISSNHL, the panel felt that the level of evidence for hearing improvement, albeit modest and imprecise, was sufficient to promote greater awareness of HBOT as an intervention for [this condition].”

U.S. Preventive Services Task Force Recommendations

Not applicable

Summary of Evidence

For individuals who have chronic diabetic ulcers who receive systemic HBOT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms and change in disease status. Meta-analyses of RCTs found significantly higher diabetic ulcer healing rates with HBOT than with control conditions. One meta-analysis, but not the other, found that HBOT was associated with a significantly lower rate of major amputation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have carbon monoxide poisoning who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival and symptoms. A meta-analysis of available RCT data in a Cochrane review did not find that HBOT is associated with a significantly lower risk of neurologic deficits after carbon monoxide poisoning. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have radionecrosis, osteoradionecrosis, or treatment of irradiated jaw who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and change in disease status. A Cochrane review of RCTs found evidence that HBOT improved radionecrosis and osteoradionecrosis outcomes and resulted in better outcomes prior to tooth extraction in an irradiated jaw. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have chronic refractory osteomyelitis who receive systemic HBOT, the evidence includes case series. Relevant outcomes are symptoms and change in disease status. The case series tended to find high rates of successful outcomes in patients with chronic refractory osteomyelitis treated with HBOT. However, controlled studies are needed to determine conclusively the impact of HBOT on
health outcomes compared with other interventions. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute thermal burns who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, and change in disease status. Only 2 RCTs were identified and both were judged to have poor methodologic quality. Evidence from well-conducted controlled trials is needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute surgical and traumatic wounds who receive systemic HBOT, the evidence includes RCTs, controlled nonrandomized studies, and systematic reviews. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. Four RCTs were identified. There was considerable heterogeneity across trials (eg, patient population, comparison group, outcomes). This heterogeneity prevented pooling of study findings and limits the ability to draw conclusions about the impact of HBOT on health outcomes for patients with acute surgical and traumatic wounds. Additional evidence from high-quality RCTs is needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have bisphosphonate-related osteonecrosis of the jaw who receive systemic HBOT, the evidence includes 1 RCT. Relevant outcomes are symptoms and change in disease status. The RCT was unblinded and did not find a significant benefit of HBOT for most health outcomes compared with standard care. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have necrotizing soft tissue infections who receive systemic HBOT, the evidence includes systematic reviews and a retrospective cohort study. Relevant outcomes are overall survival, symptoms, and change in disease status. A Cochrane review did not identify any RCTs. Another systematic review identified a retrospective cohort study, which did not find better outcomes after HBOT than after standard care without HBOT in patients with necrotizing soft tissue infections. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute coronary syndrome who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. A Cochrane review identified 6 RCTs. There were 2 pooled analyses, with mixed findings. The analyses found significantly lower rates of death with HBOT but not a significant improvement in left ventricular function. Additional RCT data are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have acute ischemic stroke who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. Cochrane reviewers could only pool data for 1 outcome (mortality at 3-6 months) and for that outcome there was no significant difference between active and sham HBOT treatments. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have motor dysfunction associated with stroke who receive systemic HBOT, the evidence includes 1 RCT. Relevant outcomes are symptoms and functional outcomes. The RCT, which used a crossover design, found better outcomes with HBOT at 2 months than with delayed treatment. However, the trial had a number of methodologic limitations (eg, lack of patient blinding, heterogeneous
population, high dropout rate) that make it difficult to draw conclusions about the efficacy of HBOT. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Bell palsy who receive systemic HBOT, the evidence includes a systematic review. Relevant outcomes are symptoms, change in disease status, and functional outcomes. A Cochrane review did not identify any RCTs meeting selection criteria; the single RCT found did not have a blinded outcome assessment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have traumatic brain injury who receive systemic HBOT, the evidence includes RCTs and systematic reviews. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. RCTs were heterogenous in terms of intervention protocols, patient populations, and outcomes reported. Systematic reviews conducted pooled analyses only on a minority of the published RCTs and these findings were mixed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have inflammatory bowel disease who receive systemic HBOT, the evidence includes RCTs, observational studies and a systematic review. Relevant outcomes are symptoms, change in disease status and functional outcomes. Only 1 small RCT has been published, and this study did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy. A systematic review of RCTs and observational studies found a high rate of bias in the literature eg attrition and reporting bias. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have idiopathic sudden sensorineural hearing loss (ISSHL) who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. A Cochrane review of RCTs had mixed findings. Some outcomes (ie, improvement in hearing of all frequencies, >25% return of hearing) were better with HBOT than with a control intervention, but more than 50% return of hearing did not differ significantly between groups. The RCTs had methodologic limitations. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have delayed-onset muscle soreness who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and functional outcomes. A Cochrane review of RCTs found worse short-term pain outcomes with HBOT than with a control condition and no difference in longer term pain or other outcomes (eg, swelling). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have autism spectrum disorder who receive systemic HBOT, the evidence includes 1 RCT and a systematic review. Relevant outcomes are symptoms and functional outcomes. A Cochrane review identified 1 RCT on HBOT for autism spectrum disorder and this trial did not find did not find significantly better outcomes with HBOT than with sham. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cerebral palsy who receive systemic HBOT, the evidence includes 2 RCTs. Relevant outcomes are symptoms and functional outcomes. One RCT was stopped early due to futility and the other did not find significantly better outcomes with HBOT than with a sham intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.
For individuals who have vascular dementia who receive systemic HBOT, the evidence includes 1 RCT and a systematic review. Relevant outcomes are symptoms and functional outcomes. The Cochrane review identified only 1 RCT with methodologic limitations. Well-conducted controlled trials are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have radiotherapy adverse effects who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and functional outcomes. A systematic review concluded that more RCTs are needed. The 2 RCTs identified had mixed findings. One found no short-term benefit with HBOT, but some benefits 12 months after radiotherapy; the other RCT did not find a significant benefit of HBOT 12 months after radiotherapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have idiopathic femoral neck necrosis who receive systemic HBOT, the evidence includes 1 RCT. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCT had a small sample and only reported short-term (ie, 6-week) outcomes. Larger well-conducted RCTs reporting longer term outcomes are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have migraine who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The Cochrane review conducted only 1 pooled analysis, and that outcome was reported in the immediate posttreatment period. Meta-analysis of 3 RCTs found significantly greater relief of migraine symptoms with HBOT than a comparator intervention within 45 minutes of treatment. Longer term data are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have herpes zoster who receive systemic HBOT, the evidence includes 1 RCT. Relevant outcomes are symptoms and change in disease status. The RCT was unblinded and only reported short-term (ie, 6-week) outcomes. Additional well-conducted RCTs with longer follow-up are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have fibromyalgia who receive systemic HBOT, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status and functional outcomes. There were only 2 RCTs and they had relatively small samples and methodologic limitations (eg, quasi-randomization, no or uncertain sham control for a condition with subjective outcomes susceptible to a placebo effect). Moreover, the HBOT protocols varied. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have multiple sclerosis who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and functional outcomes. A Cochrane review of RCTs did not find a significant difference in outcomes when patients with multiple sclerosis were treated with HBOT versus a comparator intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cancer and are undergoing chemotherapy who receive systemic HBOT, the evidence includes 1 RCT and a systematic review. Relevant outcomes are overall survival and change in disease status. The single RCT did not find a significant difference in survival for cancer patients who received HBOT prior to chemotherapy compared with usual care. The evidence is insufficient to determine the effects of the technology on health outcomes.
Medicare National Coverage

As of April 1, 2003, the Centers for Medicare and Medicaid (CMS) added Medicare coverage of hyperbaric oxygen therapy for diabetic wounds of the lower extremities meeting certain criteria. Medicare coverage is provided for HBOT administered in a chamber for the following conditions:

1. Acute carbon monoxide intoxication,
2. Decompression illness,
3. Gas embolism,
4. Gas gangrene,
5. Acute traumatic peripheral ischemia. HBOT therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
6. Crush injuries and suturing of severed limbs. As in the previous conditions, HBOT therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
7. Progressive necrotizing infections (necrotizing fasciitis),
8. Acute peripheral arterial insufficiency,
9. Preparation and preservation of compromised skin grafts (not for primary management of wounds),
10. Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management,
11. Osteoradionecrosis as an adjunct to conventional treatment,
12. Soft tissue radionecrosis as an adjunct to conventional treatment,
13. Cyanide poisoning,
14. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment,
15. Diabetic wounds of the lower extremities in patients who meet the following three criteria:
   a. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
   b. Patient has a wound classified as Wagner grade III or higher; and
   c. Patient has failed an adequate course of standard wound therapy.

The use of HBOT therapy is covered as adjunctive therapy only after there are no measurable signs of healing for at least 30 days of treatment with standard wound therapy and must be used in addition to standard wound care. Standard wound care in patients with diabetic wounds includes: assessment of a patient’s vascular status and correction of any vascular problems in the affected limb if possible, optimization of nutritional status, optimization of glucose control, debridement by any means to remove devitalized tissue, maintenance of a clean, moist bed of granulation tissue with appropriate moist dressings, appropriate off-loading, and necessary treatment to resolve any infection that might be present. Failure to respond to standard wound care occurs when there are no measurable signs of
healing for at least 30 consecutive days. Wounds must be evaluated at least every 30 days during administration of HBOT therapy. Continued treatment with HBOT therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.

Note: Medicare differs from BCBS policy in that it provides coverage for systemic HBOT therapy for acute carbon monoxide intoxication, actinomycosis, acute peripheral arterial insufficiency, compromised skin grafts or flaps, chronic refractory osteomyelitis, and necrotizing soft tissue infections. However, as noted here, literature searches did not reveal sufficient evidence to consider these appropriate indications for HBOT therapy.

References

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<td>Subsection: Medicine</td>
<td>Original Policy Date: September 13, 2012</td>
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<tr>
<td>Subject: Hyperbaric Oxygen Therapy</td>
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</tbody>
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fibromyalgia and (2) mental illness (ie, posttraumatic stress disorder, generalized anxiety disorder or depression) added to the not medically necessary statement.

March 2017 Update Policy Policy updated with literature review through November 8, 2016; references 6-7, 15, 22, 26-27, 39, 48, and 56 added. Policy statements unchanged.

Keywords

Hyperbaric Oxygen Therapy (HBOT)
Oxygen, Hyperbaric Pressurization
Topical Hyperbaric Oxygenation

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 17, 2017 and is effective April 15, 2017.

Signature on File
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