Hyperbaric Oxygen Pressurization (HBO)

Policy Number: MM.02.012
Line(s) of Business: HMO; PPO; QUEST
Section: Medicine
Place(s) of Service: Outpatient; Inpatient

I. Description

Systemic (large chamber) hyperbaric oxygen therapy (HBO) is a means of delivering higher pressures of oxygen to the tissues of the body. In systemic or large chamber hyperbaric oxygen therapy, the patient is entirely enclosed in a pressure chamber and breathes oxygen at a pressure greater than 1 atmosphere (pressure at sea level). This technique relies on systemic circulation to deliver highly oxygenated blood to the target site, typically a wound. Systemic hyperbaric oxygen therapy can be used to treat a systemic illness such as air or gas embolism. Treatment may be carried out either in a monoplace chamber pressurized with pure oxygen or in a larger, multiplace chamber pressurized with compressed air, delivered to the patient through oxygen mask, head tent, or endotracheal tube.

II. Criteria/Guidelines

A. Systemic hyperbaric oxygen pressurization is covered (subject to Limitations/Exclusions and Administrative Guidelines) for treatment of the following conditions:
   1. Non-healing wounds of the lower extremities in patients with type 1 or type 2 diabetes and who meet all of the following criteria:
      a. Patient has a wound classified as Wagner grade 3 or higher as defined in the table below:

<table>
<thead>
<tr>
<th>Grade Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>No open lesion</td>
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<tr>
<td>1</td>
<td>Superficial ulcer without penetration to deeper layers</td>
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<tr>
<td>2</td>
<td>Ulcer penetrates to tendon, bone, or joint</td>
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<tr>
<td>3</td>
<td>Lesion has penetrated deeper than grade 2 and there is</td>
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abscess, osteomyelitis, pyarthrosis, plantar space abscess, or infection of the tendon and tendon sheaths

| 4 | Wet or dry gangrene in the toes or forefoot |

| 5 | Gangrene involves the whole foot or such a percentage that no local procedures are possible and amputation (at least at below the knee level) is indicated |

b. Patient has no measurable signs of healing after a 30-day course of standard wound therapy which includes the following:

i. The following standard wound treatment measures have been accomplished for all chronic ulcers and complex wounds:
   a. Evaluation of wound with documentation of measurements (length, width and depth) at baseline and at least weekly by a licensed medical professional.
   b. Debridement of necrotic tissue, if present
   c. Treatment of infection, if present
   d. Management of diabetes mellitus, if applicable
   e. Evaluation and management of peripheral artery disease, if applicable

ii. The following standard wound treatment measures have been accomplished for chronic neuropathic ulcers:
   a. Patient’s diabetes is managed by a physician who is responsible for diagnosing and treating the diabetes through a comprehensive plan of care.
   b. Reduction in pressure on a foot ulcer has been accomplished with appropriate modalities.

(Criteria/Guidelines, continued – II.A.1.)

2. Acute traumatic ischemia e.g. crush injuries, reperfusion injury, compartment syndrome
3. Decompression sickness
4. Gas embolism, acute
5. Cyanide poisoning, acute
6. Acute carbon monoxide poisoning
7. Gas gangrene (i.e., clostridial myonecrosis)
8. Profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed
9. Soft-tissue radiation necrosis (e.g., radiation enteritis, cystitis, proctitis) and osteoradionecrosis
10. Pre- and post-treatment for patients undergoing non-implant related dental surgery (including tooth extraction) of an irradiated jaw
   a. The patient has had prior radiation to the head or neck and has received greater than or equal to a cumulative dose of 60 gray of radiation.
11. Chronic osteomyelitis refractory to conventional medical and surgical management
B. A treatment plan must be submitted for wounds, osteoradionecrosis, and soft tissue radiation necrosis.
C. Wounds, osteoradionecrosis, and soft tissue radiation necrosis must be evaluated and documented by the treating physician for signs of healing after every 15 treatments or every 14 days of treatment (whichever comes first).
D. Continued treatment with HBO therapy is covered if signs of healing have been demonstrated and documented in the medical record.

III. Limitations/Exclusions
A. The use of HBO is not covered for other indications as payment determination criteria are not met. This includes, but is not limited to:
   1. Compromised skin grafts or flaps
   2. Acute osteomyelitis, refractory to standard medical management
   3. Necrotizing soft-tissue infections
   4. Acute thermal burns
   5. Acute surgical and traumatic wounds
   6. Spinal cord injury
   7. Traumatic brain injury
   8. Severe or refractory Crohn’s disease
   9. Brown recluse spider bites
   10. Bone grafts
   11. Carbon tetrachloride poisoning, acute
   12. Cerebrovascular disease, acute (thrombotic or embolic) or chronic
   13. Fracture healing
   14. Hydrogen sulfide poisoning
   15. Intra-abdominal and intracranial abscesses
   16. Lepromatous leprosy
   17. Meningitis
   18. Pseudomembranous colitis (antimicrobial agent-induced colitis)
   19. Radiation myelitis,
   20. Sickle cell crisis and/or hematuria
   21. Demyelinating diseases, (e.g., multiple sclerosis, amyotrophic lateral sclerosis)
   22. Retinal artery insufficiency, acute
   23. Retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment
   24. Pyoderma gangrenosum
   25. Acute arterial peripheral insufficiency
   26. Acute coronary syndromes and as an adjunct to coronary interventions, including but not limited to percutaneous coronary interventions and cardiopulmonary bypass
   27. Idiopathic sudden sensorineural hearing loss
   28. Refractory mycoses: mucormycosis, actinomycosis, canidiobolus coronato
   29. Cerebral edema, acute
   30. Migraine
31. In vitro fertilization
32. Cerebral palsy
33. Tumor sensitization for cancer treatments, including but not limited to, radiotherapy or chemotherapy
34. Delayed onset muscle soreness
35. Idiopathic femoral neck necrosis
36. Chronic arm lymphedema following radiotherapy for cancer
37. Radiation-induced injury in the head and neck
38. Early treatment (beginning at completion of radiation therapy) to reduce adverse effects of radiation therapy; and
39. Autism Spectrum Disorders
40. Acute ischemic stroke
41. Bell’s palsy

B. Topical hyperbaric oxygen therapy is not a covered benefit.

IV. Administrative Guidelines
A. Precertification is required for wounds, osteoradionecrosis, soft tissue radiation necrosis and chronic refractory osteomyelitis. To precertify, please complete HMSA’s Precertification Request and mail or fax the form as indicated.
B. A treatment plan must be submitted for wounds, osteoradionecrosis, soft tissue radiation necrosis and chronic refractory osteomyelitis.
C. Documentation of previous medical and surgical interventions including outcomes must be submitted.
D. For continuation of therapy, documentation from the medical record showing objective signs of wound healing from wounds, osteoradionecrosis, soft tissue radiation necrosis and chronic refractory osteomyelitis must be submitted.

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ICD-10 codes are provided for your information. These will not become effective until 10/1/2014:

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<td>S45.101A to S45.199S</td>
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### Scientific Background

#### Chronic Wounds

A Cochrane review of RCTs on HBO treatment for chronic wounds was published by Kranke and colleagues in 2004. (8) The authors reported finding insufficient evidence to demonstrate benefits with use of HBO for arterial, venous, or pressure ulcers or wounds or other pathologies due to limited trial data. However, they found that, in diabetic patients with foot ulcers, HBO significantly reduced the risk of major amputations based on an analysis of 5 trials and concluded that HBO therapy may be justified in this group of patients when appropriate facilities are available. A 2011 double-blind RCT from Sweden evaluated HBO therapy in 75 diabetic patients with chronic wounds who had failed at least 2 months of treatment at a diabetic foot clinic. (9) After 12 months, the healing rate was 61% in the hyperbaric oxygen group and 27% in the sham hyperbaric group; this difference was statistically significant, p=0.009. This new study supports the findings of the 2004 Cochrane review, which has not been updated. Thus, HBO therapy for chronic severe diabetic ulcers may be considered medically necessary, and HBO treatment for other types of chronic wounds is considered investigational.
Acute surgical and traumatic wounds

In 2011, a Cochrane review of RCTs on HBO therapy for acute wounds (e.g., surgical wounds, lacerations, traumatic wounds, and animal bites) was published by Eskes and colleagues. (10) To be included, studies needed to compare HBO with a different intervention or compare 2 HBO regimens; in addition, studies needed to objectively measure wound healing. A total of 7 potentially relevant studies were identified; 3 of these met the review’s inclusion criteria. The 3 studies ranged in size from 36 to 135 participants. Due to differences among studies in terms of patient population, comparison intervention, outcome measurement, etc., study results could not be pooled. In addition, investigators identified biases in the studies such as insufficient reporting of randomization procedures and selective reporting of outcome data. Findings of individual studies were mixed. For example, one study found a significantly higher rate of complete wound healing with HBO compared to sham HBO treatment, and another study did not find a significant difference in complete healing rates between HBO therapy and dexamethasone or heparin treatment. The authors concluded that there is insufficient high-quality data on the effect of HBO therapy on treatment of acute wounds.

Carbon Monoxide Poisoning

A 2005 Cochrane review of 7 RCTs concluded that the available evidence is insufficient to determine whether adverse neurologic outcomes in patients with carbon monoxide poisoning are reduced with HBO therapy. (11) In 2008, the American College of Emergency Physicians published a clinical policy on critical issues in carbon monoxide poisoning. (12) Their literature review indicated there was only Level C evidence (preliminary, inconclusive, or conflicting evidence) for treatment of acute carbon monoxide poisoning. The 2008 Undersea and Hyperbaric Medical Society (UHMS), however, lists carbon monoxide poisoning as an indication for HBO therapy.

Two blinded randomized trials were discussed in both the Cochrane and American College of Emergency Physicians reviews. One is a study by Scheinkestel and colleagues, a double-blind, RCT comparing HBO to normobaric oxygen in patients with carbon monoxide poisoning. (13) The authors reported that HBO therapy did not benefit patient outcomes of neuropsychological performance when HBO therapy was completed and at 1-month follow-up. This study was limited, however, by a high rate (46%) of patients who were lost to follow-up. Moreover, the trial has been criticized for administering 100% normobaric oxygen for at least 72 hours between treatments, which has been called a toxic dose of oxygen. (14) The critiques also mention that there was an unusually high rate of neurologic sequelae after the treatment period, which could be due in part to the high dose of oxygen and/or the high rate of cognitive dysfunction in the study population (69% were poisoned by carbon monoxide through suicide attempts).

The other blinded trial by Weaver and colleagues also compared HBO and normobaric oxygen. (15) Patients received either 3 sessions of HBO or 1 session of normobaric oxygen plus 2 sessions of exposure to normobaric room air. The primary outcome was the rate of cognitive sequelae at 6 weeks. Cognitive function was assessed by a battery of neuropsychological tests. At the 6-week follow-up, the intention to treat analysis found that 19 of 76 (25.0%) in the HBO group and 35 of 76 (46.1%) in the control group had cognitive sequelae; the difference was statistically significant, p=0.007. There was a high rate of follow-up at 6 weeks, 147 of 152 (97%) of randomized patients. Enrollment in the study was stopped early because an interim analysis found HBO to be effective.
A follow-up study, that included 147 patients from the randomized trial and 75 who had been eligible for the trial but had not enrolled, was published in 2007. (16) Of the group treated with HBO (n=75), cognitive sequelae were identified in 10 of 58 (17%) at 6 months and 9 of 62 (14%) at 12 months. Of the group not treated with HBO (n=163), 44 of 146 (30%) at 6 months and 27 of 149 (18%) at 12 months had cognitive sequelae. (The follow-up rate was higher at 12 months because the investigators received additional funding for data collection.) Thus, in light of the clinical studies, including the limitations of trials noted above, and given the strong clinical support for this treatment (see Clinical Input section below), the use of hyperbaric oxygen therapy for acute carbon monoxide poisoning was changed to medically necessary.

Radionecrosis and Osteoradionecrosis

In a 2005 Cochrane review, Bennett and colleagues concluded that there was “some evidence that HBO improves the probability of healing in radiation proctitis and following hemimandibulectomy and reconstruction of the mandible; improves the probability of achieving mucosal coverage and the restoration of bony continuity with ORN (osteoradionecrosis); prevents the development of ORN following tooth extraction from a radiation field; and reduces the risk of wound dehiscence following grafts and flaps in the head and neck.” (17) They also concluded that there was no benefit using HBO in important clinical outcomes with radiation brachial plexus lesions or cerebral tissue injury. No data were reported from randomized trials for other manifestations of late radiation tissue injury.

In 2007, Hampson and colleagues reported results on a series of 65 patients with radiation enteritis/proctitis and 94 patients with cystitis at one institution. (18) In this series, response was better in patients receiving 30 or more total treatments as compared with fewer treatments. In a review of management of radiation-induced necrosis, Delanian and Lefaix comment on the role of HBO as part of the “vascular” treatment of this condition. (19) In the earlier Cochrane review, Bennett and colleagues had concluded that “these small trials suggest that for people with LRTI (Late Radiation Tissue Injury) affecting the head, neck, anus, and rectum, [HBO] is associated with improved outcome. HBO also appears to reduce the chance of osteoradionecrosis following tooth extraction in an irradiated field. There was no such evidence of any important clinical effect on neurological tissues. The application of [HBO] to selected patients and tissues may be justified.” (17) The authors of this review also note that intermittent application of HBO is the only intervention that has been shown to increase the number of blood vessels in irradiated tissue; as noted, this work was first reported in the late 1980s by Marx.

A 2008 Cochrane review by Esposito et al. reviewed the use of HBO therapy in patients requiring dental implants. (20) The authors identified 1 randomized trial involving 26 patients. The authors concluded that despite the limited amount of clinical research available, it appears that HBO therapy in irradiated patients requiring dental implants may not offer any appreciable clinical benefits. They indicate that there is a definite need for more RCTs to ascertain the effectiveness of HBO in irradiated patients requiring dental implants. In summary, given the longstanding use of this technology, the existing literature base and the Cochrane review noted above, the policy statement was changed to indicate that use of HBO therapy for treatment of soft tissue and bone radiation necrosis and for pre- and post-treatment of dental surgery (non-implant-related) in an irradiated jaw may be considered medically necessary.
Osteomyelitis

No prospective clinical trials on chronic refractory osteomyelitis or acute refractory osteomyelitis were identified in updated searches. The justification for the use of HBO in chronic osteomyelitis has been primarily based on case series. Among the larger case series, Maynor and colleagues reviewed the records of all patients with chronic osteomyelitis of the tibia seen at one institution. (21) Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBO treatments (range, 6 to 99). Of the 26 patients with at least 2 years of follow-up after treatment, 21 (81%) remained drainage free. Twelve of 15 (80%) with follow-up data at 60 months had remained drainage free. A study by Davis and colleagues reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution. (22) Patients received HBO treatment until the bone was fully recovered with healthy vascular tissue; this resulted in a mean of 48 daily HBO treatments (range, 8 to 103). After a mean post-treatment follow-up of 34 months, 34 of 38 (89%) patients remained clinically free of infection (i.e., drainage free and no tenderness, pain, or cellulitis). Success rates from several smaller case series, all conducted in Taiwan, are 12 of 13 (92%) patients, 11 of 14 (79%) patients, and 13 of 15 (86%) patients. (23–25) Given the high percentage of refractory patients in these series who had successful outcomes and the clinical support for HBO as a treatment option for chronic refractory osteomyelitis (see Clinical Input section below), the use of HBO therapy for chronic refractory osteomyelitis was changed to medically necessary. HBO treatment for acute osteomyelitis refractory to medical treatment remains investigational.

Compromised Skin Grafts and Flaps

In 2006, Friedman and colleagues published a systematic review of literature on use of HBO for treating skin flaps and grafts. (26) No RCTs were found. The authors identified 2 retrospective case series on use of HBO for clinically compromised skin grafts and flaps. The series had sample sizes of 65 and 26, respectively; both were published in the 1980s based on treatment provided in the 1970s and 1980s. Given the limited published data and lack of recent data, this indication remains investigational.

Necrotizing Soft Tissue Infections

A 2005 systematic review by Jallali and colleagues evaluated the literature on HBO as adjunctive therapy for necrotizing fasciitis. (27) They did not identify any RCTs. There were only a few retrospective studies with small sample sizes and findings were inconsistent. The authors concluded that more robust evidence is needed before widespread use of HBO is recommended. A 2009 retrospective cohort study compared outcomes in 48 patients at 1 center who received adjunctive HBO for necrotizing soft issue infections to those in 30 patients at a different center who did not receive HBO. (28) There was not a significant difference in the mortality rate between the 2 groups; this was 4 of 48 (8%) in the HBO group and 4 of 30 (13%) in the non-HBO 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. There was a higher median number of debridement procedures per person in the HBO group, 3.0 compared to 2.0 in the non-HBO group (p=0.03). Thus, based on the available evidence, HBO for necrotizing soft tissue infections remains investigational.
**Refractory Mycoses**

No clinical trials on refractory mycoses (mucormycosis, actinomycosis, canidiobolus coronato) and cerebral edema were found. Therefore, these indications were changed to investigational.

**Acute Peripheral Arterial Insufficiency**

While Medicare has long listed acute peripheral arterial insufficiency as a medically necessary indication, this application was not addressed by previous versions of this policy. No clinical trial publications were identified that demonstrated benefit in HBO therapy for acute peripheral arterial insufficiency, and thus the evidence basis of the Medicare policy is unclear. (29) Due to the lack of published literature, acute peripheral arterial insufficiency was added as an investigational indication in this policy.

**Acute Coronary Syndromes**

A 2005 Cochrane review by Bennett and colleagues of 4 trials with a total of 462 patients concluded there were no significant benefits for patients with acute coronary syndromes receiving HBO therapy. (30) One trial was by Sharifi and colleagues and randomly assigned 69 patients with unstable angina or acute myocardial infarction (MI) to receive or not receive HBO after a percutaneous coronary intervention (PCI). (31) The 24 patients randomly assigned to the HBO group reported only 1 adverse event (death, MI, coronary artery bypass, or revascularization of target lesion), compared to 13 in the 37 control patients. However, this study lacked adequate detail, e.g., on the type of PCI performed, to permit scientific conclusions. In another RCT of 64 patients, Alex and colleagues concluded both neuropsychometric dysfunction and inflammatory response can be reduced post cardiopulmonary bypass when HBO pretreatment is given. (32) Based on the above evidence, acute coronary syndromes was added to the investigational statement in 2005, and in 2006, the statement was modified to specify “as an adjunct to coronary interventions, including but not limited to percutaneous coronary interventions and cardiopulmonary bypass.”

**Stroke**

In 2003, Rusyniak and colleagues reported on the results of a randomized, double-blind sham controlled study of 33 patients presenting with acute ischemic stroke who were randomly assigned to active or sham HBO. (33) No beneficial effect was reported for HBO therapy. In a 2005 systematic review, Carson and colleagues concluded that current available evidence does not demonstrate any benefit with the use of HBO therapy for the treatment of stroke. (34) The authors noted it is undetermined whether there are any benefits with HBO therapy that would outweigh potential harms and further study is required. Based on the available evidence, acute ischemic stroke was added to the list of investigational indications.

**Hearing Loss**

Topuz and colleagues reported on a trial that randomly assigned 51 patients with sudden idiopathic sensorineural hearing loss to receive conventional therapy (i.e., steroids, plasma expanders) with or without HBO. (35) Audiologic assessment was performed immediately after treatment. While the HBO group reported gains in hearing at some frequencies, this small trial with short follow-up is inadequate to permit scientific conclusions. A Cochrane review of 5 trials
Hyperbaric Oxygen Pressurization (HBO)

with a total of 254 patients also concluded that the data are insufficient to determine the clinical significance of hearing improvement with the use of HBO in patients with idiopathic sudden sensorineural hearing loss, and thus this was added to the list of investigational indications. (36)

**Migraine**

In a randomized, double-blind, placebo-controlled study of 40 patients, Eftedal and colleagues reported no significant reductions in migraine occurrence with HBO compared to hyperbaric air treatments. (37) Thus, migraine was added to the list of investigational indications.

**Amyotrophic Lateral Sclerosis**

In the updated searches, no randomized trials were found evaluating HBO for treatment of amyotrophic lateral sclerosis. In a small case series, Steele et al. treated 5 patients with HBO and reported some improvements in fatigue but noted that further study is needed, and attention to placebo effects must be given. (38) Thus, amyotrophic lateral sclerosis was added to the policy as an investigational indication.

**In Vitro Fertilization**

Van Voorhis and colleagues reported that HBO was well-tolerated in women undergoing ovarian follicular stimulation for in vitro fertilization; however, no outcomes were reported, and further study is needed. (39) In vitro fertilization was added to the list of investigational indications for HBO.

**Cerebral Palsy**

Collet et al. randomly assigned 111 children with cerebral palsy to 40 treatments over a 2-month period of either HBO (n=57) or slightly pressurized room air (n=54). (40) The authors found HBO produced similar improvements in outcomes such as gross motor function and activities of daily living in both groups as slightly pressurized air. Thus, cerebral palsy was added as an investigational indication of HBO therapy.

**Cancer Treatment**

In an RCT of 32 patients, Heys and colleagues found no increase in 5-year survival in patients treated with HBO prior to chemotherapy for locally advanced breast carcinoma to increase tumor vascularity. (41) This approach is being studied since studies in animal models have suggested that HBO increases tumor vascularity and thus may make chemotherapy more effective. In a Cochrane review, Bennett and colleagues concluded that HBO given with radiotherapy may be useful in tumor control; however, the authors expressed caution since significant adverse effects were common with HBO and indicated further study would be useful. (42) Therefore, a policy statement was added to indicate HBO for tumor sensitization for cancer treatments, including but not limited to radiotherapy or chemotherapy, is considered investigational.

**Delayed-onset Muscle Soreness**

In a Cochrane review, Bennett and colleagues concluded that available evidence is insufficient to demonstrate beneficial outcomes with HBO for delayed-onset muscle soreness and closed soft tissue injury. (43) It was noted that HBO possibly even increases pain initially and further studies...
Hyperbaric Oxygen Pressurization (HBO)

are needed. Therefore, a policy statement was added to indicate HBO for delayed-onset muscle soreness is considered investigational.

**Autism Spectrum Disorders**

Rossignol and colleagues published the first controlled study on use of HBO therapy to treat children with autism. (44) The new study was a double-blind RCT including 62 children, ages 2-7, meeting DSM-IV criteria for autistic disorder. The active treatment was hyperbaric treatment at 1.3 atmospheres (atm) and 24% oxygen in a hyperbaric chamber. (This regimen differs from standard HBO treatment which uses 100% oxygen and a pressure of at least 1.4 atm.) The other group received a sham treatment consisting of 1.03 atm and ambient air (21% oxygen). Both groups received 40 sessions of active or sham treatment lasting 60 minutes each over a period of 4 weeks. The equipment, procedures, etc. in the 2 groups were as similar as possible to maintain blinding. The investigators, participants, parents, and clinic staff were blinded to treatment group. Only the hyperbaric technician, who had no role in outcome assessment, was aware of group assignment. After completion of the 4-week study, families with children in the control group were offered the active intervention. When asked at the end of the study, there was no significant difference in the ability of parents to correctly guess the group assignment of their child.

The outcomes were change compared to baseline after 4 weeks on the following scales: Aberrant Behavior Checklist (ABC) total score and 5 subscales; Autism Treatment Evaluation Checklist (ATEC) total score and 4 subscales; and Clinical Global Impression-Improvement (CGI) overall functioning score and 18 subscales. P values of <0.05 were considered statistically significant; there was no adjustment for multiple comparisons. The analysis included all children who completed at least one complete session. Of the 33 children assigned to active treatment, 30 were included in the analysis, and 29 completed all 40 treatments. Of the 29 children assigned to the control treatment, 26 completed all 40 sessions and were included in the analysis.

There was no significant between-group improvement on the ABC total score, any of the ABC subscales, or on the ATEC total score. Compared to the control group, the treatment group had a significant improvement in 1 of 4 subscales of the ATEC, the sensory/cognitive awareness subscale. The change from baseline on this subscale was a mean of 16.5 in the treatment group and a mean of 5.4 in the control group, a difference of 11.1 (p=0.037). (Note: due to an administrative error, baseline ATEC was not collected at one site, and thus data were not available for 23 children in the treatment group and 21 children in the control group). On the physician-rated CGI total score, 9/30 (30%) children in the treatment group had a score of 1 (very much improved) or 2 (much improved) compared to 2/26 (8%) in the control group (p=0.047). On the parental-rated CGI total score, 9/30 (30%) children in the treatment group had a score of 1 or 2 compared to 4/26 (15%) in the control group (p=0.22, not statistically significant). (The exact numbers receiving scores of 1 vs. 2 were not reported). Change in mean CGI scores were also reported, but this may be a less appropriate way to analyze these data. Among the parental-rated CGI subscales, significantly more children were rated as improved in the treatment group compared to control on 2 out of 18 subscales, receptive language (p=0.017) and eye contact (p=0.032).
A key limitation of this study was that the authors reported only outcomes at 4 weeks, directly after completion of the intervention. It is not known whether there are any long-term effects. Additional follow-up data cannot be obtained because members of the control group crossed over to the intervention after 4 weeks. Other limitations include lack of adjustment for multiple comparisons and unclear clinical significance of the statistically significant outcomes. The Undersea and Hyperbaric Medical Society (UHMS) issued a position paper after publication of the Rossignol et al. study stating that they still did not recommend routine treatment of autism with HBO. (45) Based on limitations of the Rossignol and colleagues RCT and the lack of other controlled studies, autism was added to the policy as an investigational indication for HBO.

Radiotherapy Adverse Effects

In 2010, Spiegelberg and colleagues conducted a systematic review of studies on HBO therapy to prevent or treat radiotherapy-induced head and neck injuries associated with treatment of malignant tumors. (46) The authors identified 20 studies. Eight of the studies included control groups, their sample sizes ranged from 19 to 78 individuals. Four (50%) of the studies with a control group concluded that HBO was effective, and the other 4 did not conclude that the HBO was effective. The authors noted a paucity of RCTs but did not state the number of RCTs that they identified in their review.

A study by Teguh and colleagues published in 2009 included 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiation therapy; the study was conducted in The Netherlands. (47) HBO therapy was used to prevent adverse events following radiotherapy. Eight patients were randomly assigned to receive 30 sessions of HBO, beginning within 2 days of completing radiation therapy, and 9 patients received no additional treatment. All patients were included in the analysis. Quality-of-life outcomes were assessed, and the primary outcome was specified as xerostomia at 1 year. Quality-of-life 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 HBO group and 6 in the control group. However, at 1 year, there was a statistically significant difference between groups; the mean VAS score for xerostomia was 4 in the HBO group and 7 in the control group (p=0.002). Also at 1 year, the mean quality-of-life score for swallowing (0-to-100 scale) was 7 in the HBO group and 40 in the control group (p=0.0001). The study is limited by the small sample size and the wide fluctuation over the follow-up period in quality of life ratings.

In 2010, Gothard and colleagues in the U.K. published findings of a RCT using HBO therapy to treat arm lymphedema occurring after radiotherapy for cancer. (48) Fifty-eight patients with arm lymphedema (at least 15% increase in arm volume) following cancer treatment were randomized in a 2:1 ratio to receive HBO (n=38) or usual care without HBO (n=20). Fifty-three patients had baseline assessments and 46/58 (79%) had 12-month assessments. At the 12-month follow-up, there was not a statistically significant difference in the change from baseline in arm volume. The 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. According to this definition, 9 of 30 (30%) of patients in the HBO group were considered responders compared with 3 of 16 (19%) in the control group; the difference between
groups was not statistically significant. Other outcomes, e.g., quality-of-life scores on the Short-Form (SF)-36, were similar between groups.

Due to the limited data, use of HBO to treat arm lymphedema or radiation-induced injury in the head and neck after radiotherapy, as well as early use of HBO after radiation therapy to reduce side effects are considered investigational.

**Idiopathic femoral neck necrosis**

A double-blind RCT that evaluated HBO therapy to treat femoral head necrosis was published in 2010 by Camporesi and colleagues. (49) The study included 20 adult patients with idiopathic unilateral femoral head necrosis. Patients received 30 treatments over 6 weeks with either HBO at 2.5 ATA (n=10) or a sham treatment consisting of hyperbaric air (n=10). The mean severity of pain on a 0-to-10 scale was significantly lower in the HBO group than 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 also reported; degrees were the unit of measurement. At the end of the initial treatment period, extension, abduction and adduction, but not flexion, were significantly greater in the HBO group compared to the control group. Longer-term comparative data were not available because the control group was offered HBO at the end of the initial 6-week treatment period. This single, small short-term RCT represents insufficient data on which to draw conclusions about the efficacy of HBO for treating femoral head necrosis.

**Migraine**

A Cochrane review by Bennett and colleagues identified RCTs that evaluated the effectiveness of systemic HBO therapy for preventing or treating migraine headache compared to another treatment or a sham control. (50) In a search of the literature through May 2008, 5 trials with a total of 103 patients were identified that addressed treatment of acute migraine with HBO. A pooled analysis of 3 trials (total of 43 patients) found a statistically significant increase in the proportion of patients with substantial relief of migraine within 45 minutes of HBO treatment (relative risk [RR]: 5.97, 95% confidence interval [CI]: 1.46-24.38, p=0.001). No other pooled analyses were conducted due to variability in the outcomes reported in the trials. The meta-analysis does not report data on treatment effectiveness beyond the immediate post-treatment period, and the methodologic quality of trials was moderate to low, e.g., randomization was not well-described in any trial. Based on the above limitations of the meta-analysis, use of HBO to treat migraine remains investigational.

**Clinical Input Received through Physician Medical Societies and Academic Medical Centers**

In response to requests, input was received through 6 Physician Specialty Societies and 5 Academic Medical Centers while this policy was under review in 2010. While the various Physician Specialty Societies and Academic Medical Centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the Physician Specialty Societies or Academic Medical Centers, unless otherwise noted. The clinical input was variable depending on the condition. There was universal agreement that topical hyperbaric therapy and systemic hyperbaric oxygen therapy for autism spectrum disorders and headache/migraine are investigational. There was also wide
support for changing acute carbon monoxide poisoning, compromised skin grafts or flaps, chronic refractory osteomyelitis, and necrotizing soft tissue infections to the list of medically necessary indications for hyperbaric oxygen treatment. Several reviewers acknowledged that there is a paucity of clinical trials on hyperbaric oxygen treatment for compromised skin grafts/flaps, necrotizing soft tissue infections, and chronic refractory osteomyelitis. These reviewers commented on the support from basic science, animal studies, and retrospective case series, as well as lack of effective alternative treatments for these conditions.

Based on the available evidence and clinical input, acute carbon monoxide poisoning and chronic refractory osteomyelitis were changed in 2010 to medically necessary indications for hyperbaric oxygen therapy. However, despite the clinical input and given the limited published evidence, compromised skin grafts and flaps and necrotizing soft tissue infections are still considered investigational.

**Technology Assessments, Guidelines and Position Statements**

In 2008, the Undersea and Hyperbaric Medical Society (UHMS) updated their list of indications considered appropriate for HBO therapy. (1) 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 ischemias
- 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

**Medicare National Coverage**

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

- Acute carbon monoxide intoxication (ICD-9-CM diagnosis 986)
- Decompression illness (ICD-9-CM diagnosis 993.2, 993.3)
- Gas embolism (ICD-9-CM diagnosis 958.0, 999.1)
- Gas gangrene (ICD-9-CM diagnosis 0400)
- Acute traumatic peripheral ischemia. HBO 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 (ICD-9-CM diagnosis 902.53, 903.01, 903.1, 904.0, 904.41).
- Crush injuries and suturing of severed limbs. As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened (ICD-9-CM diagnosis 927.00-927.03, 927.09-927.11, 927.20-927.21, 927.8-927.9, 928.00-928.01, 928.10-928.11, 928.20-928.21, 928.3, 928.8-928.9, 929.0, 929.9, 996.90-996.99).
- Progressive necrotizing infections (necrotizing fasciitis) (ICD-9-CM diagnosis 728.86)
- Acute peripheral arterial insufficiency (ICD-9-CM diagnosis 444.21, 444.22, 81)
- Preparation and preservation of compromised skin grafts (not for primary management of wounds) (ICD-9CM diagnosis 996.52; excludes artificial skin graft)
- Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management (ICD-9-CM diagnosis 730.10-730.19)
- Osteoradionecrosis as an adjunct to conventional treatment (ICD-9-CM diagnosis 526.89)
- Soft tissue radionecrosis as an adjunct to conventional treatment (ICD-9-CM diagnosis 990)
- Cyanide poisoning (ICD-9-CM diagnosis 987.7, 989.0)
- Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment (ICD-9-CM diagnosis 039.0-039.4, 039.8, 039.9)
- Diabetic wounds of the lower extremities in patients who meet the following three criteria:
  - Patient has type 1 or type 2 diabetes and has a lower extremity wound that is due to diabetes;
  - Patient has a wound classified as Wagner grade III or higher; and
  - Patient has failed an adequate course of standard wound therapy.

The use of HBO 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 HBO therapy. Continued treatment with HBO therapy is not covered if measurable signs of healing have not been demonstrated within any 30-day period of treatment.

Medicare continues to consider topical HBO therapy ineligible for coverage.

Note: Medicare differs from BCBS policy in that it provides coverage for systemic HBO 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 HBO therapy.
VI. **Important Reminder**

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. **References**


