Regence

Medical Policy Manual Medicine, Policy No. 14

Hyperbaric Oxygen Therapy

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Hyperbaric oxygen therapy (HBOT) is a technique of delivering higher pressures of oxygen to the tissues. Two methods of administration are available, systemic and topical.

MEDICAL POLICY CRITERIA

I. Systemic hyperbaric oxygen therapy may be considered **medically necessary** when both of the following criteria (A. and B.) are met:

   A. Systemic hyperbaric oxygen therapy services must comply with all of the following guidelines which are consistent with the Undersea and Hyperbaric Medical Society criteria:

      1. The individual must breathe 100% oxygen intermittently or continuously while the pressure of the treatment chamber is increased above one atmosphere absolute; and

      2. Systemic hyperbaric oxygen pressurization should be at least 1.4 atmospheres absolute (atm abs) (20.5 psi); and

      3. Treatment is provided in a hospital or clinic setting; and

   B. Treatment meets one or more of the following conditions:

1. Acute carbon monoxide poisoning *(Recommended treatment review threshold*: 5 treatments); or
2. Acute traumatic ischemia (*Recommended treatment review threshold:* Reperfusion injury: one - two treatments; Crush injury: 12 treatments (three times per day for one day, then twice a day for two days, then daily for two days); Compartment syndrome, no fasciotomy: three treatments a day for 36 - 48 hours; Compartment syndrome, after fasciotomy: twice a day up to 14 days.
3. Chronic refractory osteomyelitis (*Recommended treatment review threshold*: 40 treatments; continuation based on clinical response); or
4. Cyanide poisoning, acute (*Recommended treatment review threshold*: five treatments); or
5. Decompression sickness (*Recommended treatment review threshold*: 10 treatments); or
6. Gas or air embolism, acute (*Recommended treatment review threshold*: 10 treatments); or
7. Gas gangrene (i.e., clostridial myositis and myonecrosis; *Recommended treatment review threshold*: 10 treatments); or
8. Non-healing diabetic wounds of the lower extremities as an adjunct to ongoing conventional wound care in individuals who meet **all** of the following Criteria (a. – c.) (*Recommended treatment review threshold*: 30 treatments one or two treatments daily):
    a. Individual has type I or type II diabetes and has a lower extremity wound that is due to diabetes; and
    b. Individual has a wound classified as Wagner grade 3 or higher (see Policy Guidelines); and
    c. Individual has no measurable signs of healing after 30 days of an adequate course of standard wound therapy including **all** of the following:
        i. Assessment of vascular status and correction of any vascular problems in the affected limb if possible; and
        ii. Optimal glycemic control; and
        iii. Optimal nutritional status; and
        iv. Topical wound treatment (e.g., saline, hydrogels, hydrocolloids, alginates) with maintenance of a clean, moist bed of granulation tissue; and
        v. Debridement to remove devitalized tissue, any technique; and
        vi. Pressure reduction or offloading; and
        vii. Treatment to resolve infection (e.g., antibiotics); or
9. Pre- and post-treatment for individuals undergoing dental surgery (non-implant-related) of an irradiated jaw (*Recommended treatment review threshold*: 40 sessions; 10 - 20 before surgery); or

10. Profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed (*Recommended treatment review threshold*: HBOT should be continued with taper of both time and frequency until red blood cells have been satisfactorily replaced by individual regeneration or the individual can undergo transfusion.); or
11. Soft-tissue radiation necrosis (e.g., radiation enteritis, cystitis, proctitis) and osteoradionecrosis *(Recommended treatment review threshold*: 60 treatments); or
12. Idiopathic Sudden Sensorineural Hearing Loss of greater than or equal to 41 decibels and an onset of treatment within 14 days (*Recommended treatment review threshold:* 20 treatments.); or
13. Necrotizing soft tissue infections (*Recommended treatment review threshold*: 30 sessions: twice daily sessions during the acute phase with continuation until extension of necrosis has been halted, typically 10 treatments: followed by once daily sessions; continuation based on clinical response); or
14. Actinomycosis (Recommended treatment review threshold: 20 treatments); or
15. Central retinal artery occlusion (Recommended treatment review threshold: 10 treatments with one to two treatments per day as soon as possible after symptom onset); or
16. Compromised skin grafts and flaps where hypoxia or decreased perfusion has compromised viability acutely (*Recommended treatment review threshold: 40 treatments;* 20 treatments when preparing recipient site and 20 treatments following flap or graft placement with evaluation for continuation based on initial response to hyperbaric oxygen therapy).

II. Systemic hyperbaric oxygen for non-healing diabetic wounds of the lower extremities as an adjunct to conventional wound care is considered **not medically necessary** when Criterion I.B.8 is not met.

III. Continuation of hyperbaric oxygen therapy beyond initial *recommended treatment review thresholds* may be **medically necessary** to reach treatment stabilization, a clinical plateau or continued wound healing. Documentation of initial HBOT treatment response is required for continuation. Note: HBOT treatment continuation will be approved for up to the initial recommended number of sessions at each subsequent review.

IV. Initial or continuing systemic hyperbaric oxygen therapy is considered **investigational** for all other indications including but not limited to other ophthalmologic conditions, non-diabetic wounds, and acute thermal burns.

V. Topical hyperbaric and topical normobaric oxygen therapies are considered **investigational**.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

WAGNER CLASSIFICATION

- 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 the below the knee level) is indicated

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Indication for the requested service including type of HBOT planned
- Treatment plan including the following:
  - Percent of oxygen that the patient will breathe while receiving therapy
  - Pressurization (atm abs, psi)
  - Treatment setting (clinic or hospital)
- Condition being treated including how many treatments being requested
  - If a diabetic wound is being treated, then the request must include the following:
    - Type of diabetes
    - Location of wound
    - Wagner Classification
    - Measurable signs of healing following standard wound therapy including therapy length of time with documentation of the following:
      - Vascular assessment and correction, if possible, of vascular problems to affected area
      - Glycemic data for patient (e.g., A1C)
      - Nutritional status
      - Topical wound treatments utilized including wound bed description
      - Debridement
      - Pressure reduction or offloading
      - Any infection treatment utilized
  - If dental surgery, include description and diagnosis
  - If anemia, include blood loss and ability to transfuse patient
  - If necrosis, include type
  - If idiopathic sudden sensorineural hearing loss, include decibels of loss and onset of treatment
  - For continuation, include documentation of initial treatment response and number of requested treatments

CROSS REFERENCES

None

BACKGROUND

SYSTEMIC HYPERBARIC OXYGEN THERAPY (HBOT)

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 (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 HBOT 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 (class B) chamber pressurized with pure oxygen or in a larger, multiplace (class A) chamber pressurized with compressed air, in which case the patient receives pure oxygen by mask, head tent, or endotracheal tube.

Mild hyperbaric oxygen therapy

Oxygen therapy delivered via soft-sided chambers is referred to as mild hyperbaric oxygen therapy. While this implies that these chambers provide HBOT, the therapy is not considered hyperbaric as they provide pressurization of only about 4.5 psi, compared with true HBOT which is defined as pressurization of 20.5 psi or higher.

TOPICAL OXYGEN THERAPY

Topical hyperbaric oxygen therapy

Topical hyperbaric oxygen therapy is a technique of delivering 100% oxygen directly to an open, moist wound at a pressure slightly higher than atmospheric pressure. It is hypothesized that the high concentrations of oxygen diffuse directly into the wound to increase the local cellular oxygen tension, which in turn promotes wound healing. This therapy has been investigated as a treatment of skin ulcerations resulting from diabetes, venous stasis, postsurgical infection, gangrenous lesion, decubitus ulcers, amputations, skin graft, burns, or frostbite.

Topical hyperbaric oxygen devices consist of an appliance to enclose the wound area (frequently an extremity) and a source of oxygen; conventional oxygen tanks may be used. Topical hyperbaric oxygen therapy may be performed in the office, clinic, or may be self-administered by well-trained patients in the home. Typically, the therapy is offered for 90 minutes per day for 4 consecutive days. After a 3-day break, the cycle may be repeated. The regimen may last for 8 to 10 weeks.

Topical normobaric oxygen therapy

Devices that deliver topical oxygen to a wound at normal atmospheric pressure (normobaric) are not considered hyperbaric oxygen therapy. These devices may also be called low dose tissue oxygenation systems. An example of a normobaric oxygen delivery system is the TransCu O2™, a small handheld device with an attached cannula. According to the manufacturer, the TransCu O2 is “intended for use with wound dressings to treat the following: skin ulcerations due to diabetes, venous stasis, post-surgical infections and gangrenous lesions; pressure ulcers; infected residual limbs; skin grafts; burns; and frostbite.” The device concentrates room air to 99.9% oxygen which is delivered via the cannula which is placed under the wound dressing.

REGULATORY STATUS

In 2013, U.S. Food and Drug Administration (FDA) published a statement warning that non-FDA approved uses of HBOT may endanger the health of patients.[1] "Patients may incorrectly believe that these devices have been proven safe and effective for uses not cleared by FDA, which may cause them to delay or forgo proven medical therapies. In doing so, they may experience a lack of improvement and/or worsening of their existing condition(s)."

The following are examples of oxygen therapy devices:

In February 1999, the Numobag™ Kit (Numotech, Inc) for application of topical hyperbaric therapy was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing devices. Another example is the AOTI Hyper-Box™ (AOTI Ltd., Galway, Ireland) which was cleared by FDA in 2008.

In August 2009, the TransCu O2 (Electrochemical Oxygen Concepts, Inc.) was cleared for marketing by the FDA through the 510(k) process as substantially equivalent to existing devices.

There are numerous FDA-approved hyperbaric oxygen chambers. 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.

EVIDENCE SUMMARY

Current evidence is sufficient to determine the effectiveness of hyperbaric oxygen therapy (HBOT) for the indications that meet the above medical necessity criteria. Assessing the effectiveness and safety of HBOT for the investigational indications requires randomized controlled trials comparing HBOT with the conventional treatments for each indication. Therefore, the following literature review on HBOT focuses on randomized controlled trials (RCTs) and systematic reviews of RCTs for the investigational indications.

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 also be adequate if there is an established link between the intermediate outcome and true health outcomes. When the primary outcomes are subjective (e.g., pain, depression), sham-controlled RCTs are needed to assess the effect of the intervention beyond that of a placebo effect.

Due to the expansive conditions included in this policy, the evidence included below support only the investigational and not medically necessary conditions.

TOPICAL HYPERBARIC OXYGEN

Systematic Reviews

A 2015 Cochrane review of interventions for treating gas gangrene evaluated the safety and efficacy topical HBOT and Chinese herbs as treatments options.[2] Re-analysis if cure rate did not show beneficial effects from either treatment. In 1984, Heng published a controlled study of

topical hyperbaric oxygen therapy in 6 patients with 27 ulcers compared to no treatment in 5 patients with 10 ulcers.[3] Although a greater improvement was noted in the treated group, the results were calculated according to the number of ulcers rather than based on individual patients. Leslie reported on a trial that randomly assigned 18 patients with diabetic foot ulcers to receive either topical hyperbaric oxygen therapy plus standard wound care or standard wound care alone.[4] Changes in ulcer size and depth did not differ between the 2 groups. Other studies consist of anecdotal reports or uncontrolled case series.[5]

Randomized Controlled Trials

Pasek (2023) published a pilot randomized controlled study evaluating the application of topical hyperbaric oxygen therapy (THOT) and Atrauman Ag medical dressings (MD).[6] Patients (n = 30) with chronic arterial ulcers were randomly assigned to MD and THOT (n = 16) or MD alone (n = 14).The treatment was carried out for 4 weeks. The progress of healing ulcers was assessed by using the planimetric method, while the intensity of pain ailments was assessed by the visual analog scale (VAS). In both study groups, a statistically significant reduction in the mean surface area of the treated ulcers from 8.53 ± 1.71 cm2 to 5.55 ± 1.11 cm2 in the THOT group ($p < 0.001$) and 8.43 ± 1.51 cm2 to 6.28 ± 1.13 cm2 in the MD ($p < 0.001$). Intensity of pain reduced from 7.93 ± 0.68 points to 5.00 ± 0.63 points in the THOT group ($p < 0.001$) and 8.00 ± 0.67 points to 5.64 ± 0.49 points in the MD group ($p < 0.001$). The percentage change in ulcer area from baseline in the THOT group (34.6 ± 8.47%) was greater than in the MD group (25.23 ± 6.01%) ($p = 0.003$). The authors conclude that the addition of local hyperbaric oxygen therapy treatments as a supplement to the therapy with the use of specialized medical dressings improves the effectiveness the arterial ulcers treatment of the lower limbs in terms of reducing the ulceration area and pain.

Section Summary

Due to their different methods of delivery, topical and systemic hyperbaric oxygen are distinct technologies such that they must be examined separately.[7] There is minimal published literature regarding topical hyperbaric oxygen therapy.

SYSTEMIC HYPERBARIC OXYGEN THERAPY (HBOT)

In-home hyperbaric oxygen

A position statement from the National Board of Diving & Hyperbaric Medical Technology on in-home HBOT has been published on the Web site for The Undersea and Hyperbaric Medicine Society (UHMS).[8] The statement indicates that in-home HBOT “is inherently unsafe and cannot be condoned.” This position is based on concern for the safety and well-being of patients as well as those people in proximity to the HBOT delivery system because in-home provision of HBOT is likely to:

- Bypass otherwise mandatory federal, state, and local codes related to design, construction, installation, and operation of these devices; and
- Occur without adequate physician oversight and the operational support of appropriately qualified HBOT providers.

Acute Coronary Syndromes

Systematic Reviews

A 2012 Cochrane review by Bennett identified 6 trials with a total of 665 patients evaluating HBO for acute coronary syndrome.[9] All of the studies included patients with acute myocardial infarction (MI); one study also included individuals presenting 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 to a control intervention (RR: 0.58: 0.36 to 0.92). Due to variability of outcome reporting in the 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). The authors noted that, although there is some evidence from small trials that HBOT is associated with a lower risk of death, larger trials with high methodologic quality are needed in order to determine which patients, if any, can be expected to derive benefit from HBOT. Therefore, HBOT is considered investigational in the treatment of acute coronary syndromes.

Autism Spectrum Disorders (ASD)

Systematic Reviews

A 2016 systematic review on hyperbaric oxygen therapy for treatment of children with autism identified one RCT[10] with a total of 60 children. The study quality was rated as low using GRADE criteria with small sample size and wide confidence intervals. The results indicated no improvement in social interaction and communication, behavioral problems, communication and linguistic abilities, or cognitive function. The authors reported minor-grade ear barotrauma as adverse events.

A 2012 systematic review[11] of RCTs on hyperbaric oxygen therapy for treatment of children with autism identified two RCTs[12, 13]with a total of 89 participants. In both RCTs the active hyperbaric treatment was 24% oxygen delivered at an atmospheric pressure of 1.3 atmospheres (atm). Although this regimen was referred to as HBOT in the article, it differed from standard HBOT which uses 100% oxygen and a pressure of at least 1.4 atm. A detailed analysis of these RCTs is provided below. Briefly, one of the two RCTs found better outcomes after hyperbaric oxygen compared with placebo treatment, and the other did not find significant differences in outcomes. The author concluded that additional sham-controlled trials with rigorous methodology are needed in order to draw conclusions about the efficacy of HBOT for treating autism.

Randomized Controlled Trials (RCTs)

The following is a summary of the 2 RCTs reported in the above systematic review:

One of the above two RCTs was by Rossignol.[12] This study was a double-blind RCT that included 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 HBOT 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 two 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 included 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 HBOT.[14]

The other RCT included in the systematic review was a double-blind RCT that began with 46 children with autism, ages 2-14 years, who were matched in pairs according to age and the number of hours of Applied Behavior Analysis (ABA) treatment they were receiving at the start of the study. Randomized[13] treatment allocation of the matched pairs was by coin toss. Both groups received 80 1-hour sessions of active treatment (24% oxygen at 1.3 atm) or sham treatment (room air at ambient pressure) for up to 15 weeks. Participants were allowed to undergo ABA, take any supplements, pharmacological interventions, and dietary modifications. Twelve patients withdrew from the trial, leaving 18 patients in the treatment group and 16 in the control group.

The primary outcome of change in symptoms was based on direct observation and the scales

noted in the Rossignol et al. study above in addition to the Behavior Rating Inventory of Executive Functioning (BRIEF), Parent Stress Index (PSI), Peabody Picture Vocabulary Test (PPVT-III), Repetitive Behavior Scale (RBS), and the Vineland Adaptive Behavior Scales (VABS-II). Direct observation and intention to treat analysis of test scores found no significant difference on any outcome measures between the treatment and sham groups. No participants experienced adverse effects attributable to barotrauma (e.g., pressure injury to tympanic membranes or sinuses).

A limitation of this study was the small sample size which was determined to be adequate to detect only large effects, which were not present in this study. In addition, since some patients in both groups received intensive ABA interventions during the study period, any potential effects of HBOT could not be isolated. The authors concluded that the active treatment had no significant beneficial effect on ASD and was not recommended for the treatment of ASD symptoms.

One additional RCT not included in the systematic review above was identified:

A 2012 RCT published after the systematic review randomly assigned 60 children with autism to receive 20 one-hour sessions with HBOT or sham air treatment (n=30 per group).[15] The primary outcome measures were change in the ATEC and CGI, evaluated separately by clinicians and parents. There were no statistically significant differences between groups on any of the primary outcomes. For example, post-treatment clinician-assessed mean scores on the ATEC were 52.4 in the HBOT group and 52.9 in the sham air group.

Section Summary

There is insufficient evidence from well-designed RCTs that HBOT improves health outcomes for patients with autism spectrum disorder; therefore, HBOT therapy for this indication is considered investigational.

Bell's Palsy

Systematic Review

In 2012, Holland published a Cochrane review evaluating HBOT in adults with Bell's palsy.[16] The authors identified one RCT with 79 participants, and this study did not meet the Cochrane review methodologic standards because the outcome assessor was not blinded to treatment allocation. Therefore, the evidence is insufficient to permit conclusions and HBOT is considered investigational for the treatment of Bell's palsy.

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2012 Cochrane review.

Bisphosphonate-related Osteonecrosis of the Jaw (BRONJ)

Randomized Controlled Trials (RCTs)

An unblinded RCT was published by Freiberger in 2012 on use of HBOT as an adjunct therapy for patients with bisphosphonate-related osteonecrosis of the jaw.[17] Forty-nine patients were randomly assigned to HBOT in addition to standard care (n=22) or 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 decided to do a *per* protocol

(PP) 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 of 25 (68%) of HBO-treated patients had improvement in oral lesion size or number compared to 8 of 21 (38%) in the standard care group, p=0.043. When change from baseline to 6, 12 or 18 months was examined, there was not a statistically significant difference between groups in the proportion of patients with improvement. In addition, the proportion of patients who healed completely did not differ significantly between groups at any time point. This single trial does not report consistent findings of benefit across outcome measures. It also has a number of methodologic limitations, e.g., unblinded, cross-over, and analysis performed on a *per-protocol* basis rather than intention to treat. A disadvantage of the *per-protocol* analysis is that randomization is not preserved, and the two groups may differ on characteristics that affect outcomes. As a result, this trial is insufficient to conclude that HBOT improves health outcomes for patients with bisphosphonate-related osteonecrosis of the jaw.

Section Summary

Current evidence is insufficient to determine the safety and efficacy of HBOT in the treatment of bisphosphonate-related osteonecrosis of the jaw. Therefore, HBOT is considered investigational for this indication.

Cancer Treatment

Randomized Controlled Trials (RCTs)

In an RCT of 32 patients, Heys found no increase in 5-year survival in patients treated with HBOT prior to chemotherapy for locally advanced breast carcinoma to increase tumor vascularity.[18] This approach is being studied since studies in animal models have suggested that HBOT increases tumor vascularity and thus may make chemotherapy more effective. In a Cochrane review, Bennett concluded that HBOT given with radiotherapy may be useful in tumor control; however, the authors expressed caution since significant adverse effects were common with HBOT and indicated further study would be useful.[19]

Section Summary

Current evidence is insufficient to determine the safety and efficacy of HBOT in the treatment of cancer of any type and location. Therefore, HBOT is considered investigational for this indication.

Cerebral Palsy

Randomized Controlled Trials (RCTs)

In 2012, Lacey published a double-blind RCT that included 49 children age 3-8 years with spastic cerebral palsy.[20] Participants were randomized to receive 40 treatments with either 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 study 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 time of the interim analysis, there was no significant between-group difference in the post-treatment GMFM-88 global score (p=0.54).

In the largest RCT to date, Collet et al. randomly assigned 111 children with cerebral palsy to 40 treatments over a 2-month period of either HBOT (n=57) or slightly pressurized room air (n=54).[21] The authors found HBOT and slightly pressurized air produced similar improvements in both groups for outcomes such as gross motor function and activities of daily living.

Section Summary

Current evidence is insufficient to determine the safety and efficacy of HBOT in the treatment of cerebral palsy. Therefore, Therefore, HBOT is considered investigational for this indication.

Compromised Skin Grafts and Flaps

Systematic Reviews

Gao (2025) published a systematic review examining flap necrosis reduction after autologous breast reconstruction. Sixty-eight studies were selected identifying risk factors and treatment strategies including local wound care, hyperbaric oxygen therapy, and pharmacological treatments for improving flap survival. HBOT was examined in 12 studies with sample sizes ranging from 15 to 89 patients showing reduced partial flap necrosis rates from 15-25% to 5-12% and complete flap loss from 8-15% to 2-6% when used prophylactically or therapeutically. HBOT protocols typically involved 2.0 to 2.5 ATA for 90 to 120 minutes over 10 to 30 sessions. Other interventions included nitroglycerin patches, pentoxifylline, and various wound care protocols.

In a 2010 Cochrane review, Estes found a lack of high quality evidence regarding HBOT in the treatment of skin grafts and flaps.[22, 23] The authors found one randomized controlled trial (RCT) on skin grafts for burn wounds (n=48) which reported significantly higher graft survival with HBOT, and one RCT on flap grafting (n=135) which reported no significant differences in graft survival with HBOT compared with dexamethasone or heparin. However, these data are unreliable due to various methodologic limitations such as biased analysis, omitted data, and small size.

In 2006, Friedman published a systematic review of literature on use of HBOT for treating skin flaps and grafts.[24] No RCTs were found. The authors identified 2 retrospective case series on use of HBOT 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.

Randomized Controlled Trials (RCTs)

Uniyal (2025) published a randomized controlled trial examining HBOT effects on split-thickness skin graft uptake in posttraumatic wounds. Sixty-four patients were randomized to HBOT (n=32) or control groups (n=32) with mean graft uptake of 92.44% ± 4.87% in HBOT group versus 88.12% ± 6.23% in control group on postoperative day four (p=0.002). Donor site recovery was significantly faster in HBOT group (15.16 ± 2.18 days versus 17.97 ± 2.84 days, p<0.001). Complete graft take (>95%) was achieved in 78.1% of HBOT patients versus 53.1% of controls (p=0.034). HBOT protocol involved 2.0 ATA for 90 minutes daily for 10 sessions starting 24 hours post-surgery. Wound infection rates were lower in HBOT group (6.25%

versus 18.75%, p=0.127). Limitations included single-center design, relatively small sample size, short follow-up period of 30 days, exclusion of patients with significant comorbidities, and potential observer bias in graft assessment despite standardized photography protocols.

Carbon Monoxide Poisoning

A 2011 Cochrane review of seven RCTs concluded that the available evidence is insufficient to determine whether adverse neurologic outcomes in patients with carbon monoxide poisoning are reduced with HBOT.[25] In 2008, the American College of Emergency Physicians (ACEP) published a clinical policy on critical issues in carbon monoxide poisoning.[26] Their literature review indicated there was only level C evidence (preliminary, inconclusive, or conflicting evidence) for treatment of acute carbon monoxide poisoning. The 2008 UHMS guidelines, however, list carbon monoxide poisoning as an indication for HBOT.

Two blinded randomized trials were discussed in both the Cochrane and ACEP reviews. One is a study by Scheinkestel, a double-blind, RCT comparing HBOT with normobaric oxygen in patients with carbon monoxide poisoning.[27] The authors reported that HBOT did not benefit patient outcomes of neuropsychologic performance when HBOT 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 administrating 100% normobaric oxygen for at least 72 hours between treatments, which has been called a toxic dose of oxygen.[28] 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, also compared hyperbaric and normobaric oxygen.[29] Patients received either 3 sessions of HBOT 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 using 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 HBOT 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 HBOT to be effective. A follow-up study, which included 147 patients from the randomized trial and 75 who had been eligible for the trial but had not enrolled, was published in 2007.[30] Of the group treated with HBOT (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 HBOT (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.)

Delayed-Onset Muscle Soreness

Systematic Review

In a 2005 Cochrane review, Bennett concluded that available evidence is insufficient to demonstrate beneficial outcomes with HBOT for delayed-onset muscle soreness and closed soft-tissue injury.[31] It was noted that HBOT possibly even increases pain initially and further studies are needed. Therefore, use of HBOT for this indication is considered investigational.

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2005 Cochrane review.

Dementia

Systematic Review

A 2012 Cochrane review identified 1 RCT evaluating HBOT for the treatment of vascular dementia.[32] The 2009 study compared HBOT plus donepezil to donepezil-only in 64 patients. The HBOT and donepezil group had significantly better cognitive function after 12 weeks of treatment, as assessed by the Mini-Mental State Examination. However, the Cochrane investigators judged the trial to be of poor methodologic quality because it was not blinded and the methods of randomization and allocation concealment were not discussed.

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2012 Cochrane review.

Section Summary

The current evidence for HBOT as a treatment of dementias of any cause is limited to a single short-term clinical trial on vascular dementia. This evidence is insufficient to permit conclusions about the safety and efficacy of HBOT on vascular dementia. No other randomized controlled trials were found for HBOT as a treatment of dementia from any cause. Due to the lack of sufficient evidence, HBOT is considered investigational for treatment of dementias.

Femoral Neck Necrosis, Idiopathic

Cao (2025) published a systematic review and meta-analysis evaluating HBOT effectiveness for osteonecrosis of femoral head. Ten studies involving 568 participants were included comprising six randomized controlled trials and four cohort studies. Pre-post analyses showed significant improvements in visual analog scale pain scores (MD=-2.94, 95% CI: -3.87 to -2.01, p<0.001), SF-12 Physical Component Summary (MD=17.28, 95% CI: 12.45-22.11, p<0.001), SF-12 Mental Component Summary (MD=4.26, 95% CI: 1.83-6.69, p<0.001), and modified Harris Hip Score (MD=44.31, 95% CI: 35.67-52.95, p<0.001). However, controlled studies showed no significant differences between HBOT and control groups for pain relief (MD=-0.45, 95% CI: -1.23 to 0.33, p=0.26) or functional improvement. HBOT protocols typically involved 2.0 to 2.5 ATA for 90 to 120 minutes over 20 to 40 sessions. Limitations included significant heterogeneity between studies (I^2>75% for most outcomes), varying stages of osteonecrosis, different HBOT protocols, inconsistent outcome measures, and potential placebo effects in unblinded studies.

Randomized Controlled Trials (RCTs)

In 2010, Camporesi published the results of a double-blind RCT that evaluated HBOT in 20 adult patients with idiopathic unilateral femoral head necrosis.[33] Patients received 30 treatments over 6 weeks with either HBOT 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 HBOT 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. At the end of the initial treatment period, extension, abduction and adduction, but not flexion, were significantly greater in the HBOT group compared to the

control group. Longer-term comparative data were not available because the control group was offered HBOT at the end of the initial 6-week treatment period.

Current evidence is insufficient to determine the safety and efficacy of HBOT in the treatment of idiopathic femoral head necrosis. Therefore, HBOT is considered investigational for this indication.

Fibromyalgia

Randomized Controlled Trials

Ablin (2023) published a RCT investigating the utility of HBOT in patients (n = 58) with fibromyalgia who had a history of traumatic brain injury (TBI).[34] They compared HBOT (n =29) to pharmacological intervention (n = 29). The HBOT protocol comprised 60 daily sessions, breathing 100% oxygen by mask at two absolute atmospheres (ATA) for 90 minutes. Pharmacological treatment included Pregabalin or Duloxetine. Results demonstrated a significant group-by-time interaction in pain intensity post-HBOT compared to the medication group ($p = 0.001$), with a large net effect size ($d = -0.95$) in pain intensity reduction following HBOT compared to medications. Fibromyalgia related symptoms and pain questionnaires demonstrated significant improvements induced by HBOT as well as improvements in quality of life and increase in pain thresholds and conditioned pain modulation. This study is limited by the small sample size, high dropout rate, no long-term follow-up, and lack of sham control.

In 2015, Efrati published an RCT that included 60 female patients who had fibromyalgia for at least two years and were symptomatic.[35] Patients were randomized to an immediate two month course of HBOT or delayed HBOT after two months. The HBOT protocol was forty 90-minute sessions of 100% oxygen at two ATA (one session per day, five d/wk). Forty-eight of 60 patients (80%) completed the study and were included in the analysis. After the initial two months, outcomes including number of tender points, pain threshold, and quality of life (SF-36) were significantly better in the immediate treatment group compared with the delayed treatment group (which received no specific intervention during this time). After the delayed treatment group had undergone HBOT, outcomes were significantly improved compared with scores prior to HBOT treatment. These findings are consistent with a clinical benefit of HBOT, but also with a placebo effect. A sham-control 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.

One quasi-randomized trial and 1 delayed-treatment RCT on HBOT for fibromyalgia were identified. In 2004, a study by Yildiz included 50 patients with fibromyalgia who had ongoing symptoms despite medical and physical therapy.[36] On an alternating basis, patients were assigned to HBOT or a control group. The HBOT consisted of fifteen 90-minute sessions at 2.4 ata (1 session per day, 5 d/wk). The control group breathed room air at 1 ata on the same schedule. Baseline values on the 3 outcomes were similar in the 2 groups. After the course of HBOT treatment, the mean (SD) number of tender points were 6.04 (1.18) in the HBO group and 12.54 (1.10) in the control group. The mean (SD) pain threshold was 1.33 kg (0.12) and 0.84 kg (0.12), respectively, and the mean VAS was 31.54 (8.34) and 55.42 (6.58), respectively. In the study abstract, the authors stated that there were statistically significant differences between the HBO and control groups after 15 therapy sessions, but the table presenting outcomes lacked the notation used to indicate between-group statistical significance. It is not clear whether the control group actually received a sham intervention that would minimize any placebo effect (i.e., whether or not the control intervention was delivered in

a hyperbaric chamber). The authors stated that the study was double-blind but did not specify any details of patient blinding.

Section Summary

The above studies are few with relatively small sample sizes and have methodological limitations, e.g., quasi-randomization and no or uncertain sham control for a condition with subjective outcomes susceptible to a placebo effect. Moreover, the HBO protocol varied (e.g., 15 vs 40 HBOT sessions). Thus, the evidence is insufficient to draw conclusions about the impact of HBOT on health outcomes for patients with fibromyalgia.

Fracture Healing

Systematic Review

In 2012, Bennett published a Cochrane review on HBOT to promote fracture healing and treat non-union fractures.[37] The investigators did not identify any published RCTs on this topic that compared HBOT to no treatment, sham treatment, or another intervention and reported bony union as an outcome.

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2012 Cochrane review.

Section Summary

Due to the lack of RCTs, it is not possible to conclude whether the use HBOT to promote fracture healing improves outcomes; therefore, the use of HBOT for this indication is considered investigational.

Headaches

When assessing any treatment focused on pain relief, randomized, placebo-controlled trials are necessary to investigate the extent of any placebo effect and to determine whether any improvement with the treatment exceeds that associated with a placebo.

The following is a summary of the available evidence:

Migraine headaches

Systematic Review

A 2008 Cochrane review by Bennett identified RCTs that evaluated the effectiveness of systemic hyperbaric oxygen therapy for preventing or treating migraine headache compared to another treatment or a sham control.[38] Five trials with a total of 103 patients were identified that addressed treatment of acute migraine with HBOT. 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 HBOT (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 did 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. There was no evidence that HBOT could prevent episodes of migraine headache.

Randomized Controlled Trials (RCTs)

In 2004 Eftedal reported the results of a randomized, double-blind, placebo-controlled trial to assess whether HBOT had a prophylactic effect on migraine headache.[39] Forty patients were randomly assigned to either a treatment group receiving 3 sessions of HBOT or a control group receiving 3 hyperbaric treatments with room air. Thirty-four patients completed the study. Efficacy was measured as the difference between pre- and post-treatment hours of headache per week. There was no significant reduction in hours of headache with HBOT compared with hyperbaric air treatments. Nor was there a significant difference in either group in pre- and post-treatment levels of endothelin-1 in venous blood. The authors concluded that that HBOT had no significant prophylactic effect on migraine headache or on the endothelin-1 level in venous blood.

Cluster headaches

Systematic Reviews

Two 2008 systematic reviews, including the Cochrane review noted above, reported few studies comparing HBOT with sham treatment for cluster headaches.[38, 40] Available randomized, placebo-controlled trials measuring effect on symptoms are unreliable due to very small size.[41, 42]

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2008 systematic reviews.

Section Summary

Due to the lack of sufficient evidence from well-designed clinical trial, HBOT for the treatment of headaches from any cause is considered investigational.

Herpes Zoster

Randomized Controlled Trial (RCT)

In 2012, Peng published an RCT evaluating HBOT as a treatment of herpes zoster.[43] 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 of patients who were healed (i.e., complete subsidence of pain and rash) or improved (i.e., significant pain relief and rash subsistence). Rates of therapeutic efficacy were 97.2% in the HBOT group and 81.3% in the medication group ($p<0.05$). Limitations of the study included a lack of blinding and lack of long-term follow-up.

Section Summary

The evidence from the single randomized controlled trial is insufficient to permit conclusions about the effect of HBOT on health outcomes for patients with herpes zoster; therefore, HBOT is considered investigational for this indication.

Idiopathic Sudden Sensorineural Hearing Loss (ISSHL)

Systematic Reviews

Alter (2025) published a systematic review and meta-analysis examining the efficacy of hyperbaric oxygen therapy in treating sudden sensorineural hearing loss. [44] The review included 20 studies (16 randomized controlled trials and four non-randomized prospective studies) with 1087 patients receiving hyperbaric oxygen therapy and 600 receiving medical therapy alone, and found that patients receiving hyperbaric oxygen therapy in combination with medical therapy had 2.61 higher odds of experiencing hearing recovery than those treated with medical therapy alone (95% CI 1.86-3.68, $p < 0.001$). Subgroup analyses showed higher odds of hearing recovery with hyperbaric oxygen therapy plus systemic steroids versus systemic steroids alone (OR 2.54, 95% CI 1.63-3.97, $p < 0.001$) and hyperbaric oxygen therapy plus systemic steroids plus intratympanic steroids versus systemic steroids plus intratympanic steroids alone (OR 2.64, 95% CI 1.39-5.02, $p < 0.001$). The authors noted limitations including the need for standardized treatment protocols and data reporting to allow for more definitive conclusions.

Moghib (2025) published a systematic review and meta-analysis evaluating HBOT as adjunct to corticosteroids for sudden sensorineural hearing loss. Fourteen studies with 794 participants were included comprising 11 randomized controlled trials and three cohort studies. Combined therapy significantly improved low-frequency hearing thresholds (SMD: 0.83, 95% CI: 0.34-1.32, p=0.001) and increased odds of complete recovery (OR: 2.05, 95% CI: 1.42-2.96, p<0.001) compared to corticosteroids alone. High-frequency thresholds also improved (SMD: 0.45, 95% CI: 0.09-0.81, p=0.01). However, significant heterogeneity was observed (I^2=78% for complete recovery). HBOT protocols ranged from 2.0 to 2.5 ATA for 60 to 120 minutes over 10 to 30 sessions. Limitations included substantial heterogeneity between studies, varying corticosteroid regimens, different HBOT protocols, inconsistent timing of treatment initiation, and potential language bias as most studies were from non-English speaking countries.

Lin (2025) published a systematic review and network meta-analysis examining salvage therapy for refractory sudden sensorineural hearing loss. The study included 34 articles with 1,456 patients comparing intratympanic steroids, hyperbaric oxygen therapy, prostaglandin E1 injection, combined ITS and HBO therapy, and continued systemic steroids. Prostaglandin E1 injection showed greater mean hearing gain (11.1 dB, 95% CI: 6.2-16.0) than intratympanic steroids (7.7 dB, 95% CI: 4.8-10.6), while ITS combined with HBO therapy showed largest improvement (14.5 dB, 95% CI: 8.1-20.9) when restricted definition was used. Network meta-analysis ranked treatments by SUCRA values with ITS+HBO (89.2%), PSI (71.8%), and ITS alone (45.6%) showing highest probabilities of being most effective. Limitations included heterogeneity in treatment protocols, varying definitions of treatment response, potential publication bias, and limited direct comparisons between some treatment modalities.

Meliante (2025) published a comprehensive review and meta-analysis of salvage treatment strategies for refractory sudden sensorineural hearing loss. Forty-one articles were included examining intratympanic steroids, hyperbaric oxygen therapy, and combined treatments with a total of 2,847 patients. Intratympanic steroids and hyperbaric oxygen therapy, especially when combined, were most effective salvage therapies with response rates of 65.2% for ITS alone, 58.7% for HBO alone, and 78.9% for combined therapy. Methylprednisolone offered better outcomes than dexamethasone (OR=1.84, 95% CI: 1.12-3.02, p=0.016). The studies included 28 retrospective studies, eight prospective studies, and five randomized controlled trials. Limitations included predominance of retrospective studies, heterogeneity in treatment protocols, varying definitions of treatment response, and potential selection bias in treatment allocation.

Joshua (2021) published a SR which included 3 RCTs comparing HBOT with medical treatment, all published in 2018 and none of which were included in either the Bennett or Rhee systematic reviews below.[45] Inclusion criteria for studies in the Joshua review differed from the previous reviews in that: 1) only randomized studies were included and 2) diagnosis of ISSNHL was based on American Academy of Otolaryngology Head and Neck Surgery criteria. In addition, the literature search was limited to studies published beginning in January 2020. HBOT interventions were 60 or 90 minutes in duration, for time periods ranging from 10 to 20 days and medical treatment included a use of steroids (oral and/or intravenous) alone or in combination with antiviral medications and/or hemorheologic therapy. The patients included in the studies were clinically heterogenous, with baseline hearing loss ranging from moderate to profound in 2 studies and was unreported in the third study. The proportion of patients with hearing recovery, based on a ≥10 point audometric gain, was significantly higher with HBOT compared with control based on pooled analysis of 2 studies (OR, 4.32; 95% CI, 1.60 to 11.68; I2=0%). Limitations of these results include the fact that the included studies were judged to have moderate (2 studies) and high (1 study) risk of bias and the small number of participants in both HBOT (n=88) and medical treatment (n=62) groups.

Eryigit (2018) published a qualitative SR assessing the effectiveness of HBOT to treat patients with ISSNHL.[46] Sixteen clinical trials were included, with a total of 1759 operative ears, 580 of which received HBOT. All patients also received steroid treatment, (systemic, intravenous, or intratympanic injection). Most studies found that patients with severe or profound hearing loss who received steroids (any route of administration) plus HBOT saw statistically significant improvements (specified p-value range across studies:0.0014 to 0.012), whereas those with a lower level of hearing loss did not see these improvements. Several studies reported no significant difference between case and control groups, but the studies that broke down the results by levels of hearing loss all showed that profound (or severe and profound) loss benefited from the addition of HBOT to steroid treatment.

Rhee (2018) published a systematic review and meta-analysis comparing HBOT plus medical therapy (HBOT + MT) with MT alone for ISSNHL treatment.[47] Randomized clinical trials and nonrandomized studies were included. The main outcomes considered were complete hearing recovery, any hearing recovery, and absolute hearing gain. Nineteen studies (3 randomized and 16 nonrandomized) with a total of 2401 patients (mean age, 45.4 years; 55.3% female) were included. In the HBOT+ MT group, rates of complete hearing recovery and any hearing recovery were 264/897 (29.4%) and 621/919 (67.6%), respectively, and in the MT alone group were 241/1167 (20.7%) and 585/1194 (49.0%), respectively. Pooled HBOT+MT also showed favorable pooled results from random-effects models for both complete hearing recovery (OR, 1.61; 95% CI, 1.05 to 2.44) and any hearing recovery (OR, 1.43; 95% CI, 1.20 to 1.67). Limitations include differences in clinical and methodological characteristics of selected studies heterogeneity, possible measurement confounder effects, and difficulty in evaluating the benefit of treatment due to a substantial proportion of patients experiencing spontaneous recovery.

A Cochrane review by Bennett (2012) on HBOT for ISSNHL and/or tinnitus identified seven RCTs (n = 392).[48] 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 to 25). All trials reported on the change in hearing following treatment, but specific outcomes varied. Two trials reported the proportion of participants with more than 50% and more than 25% 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 at the level of 50% or higher but did find a significantly higher rate of improvement at the level of 25% or higher. A pooled analysis of 4 trials found a significantly greater mean improvement in hearing over all frequencies with HBOT compared with control. Studies were small and generally of poor quality. Randomization procedures were only described in 1 study, and only 1 study stated they blinded participants to treatment group assignment using sham therapy.

Randomized Controlled Trial (RCT)

Cavaliere (2022) published a RCT comparing HBOT and oral steroids, alone and in combination, in adults (n = 171) with ISSNHL.[49] Pure tone audiometry (PTA) testing was conducted at baseline and 20 days after treatment. ISSNHL was characterized at baseline as upsloping (hearing loss affecting 250 to 500 herz [Hz] more), flat (<20 decibel [dB] difference between the highest and lowest pure tone average threshold), downsloping (hearing loss affecting 4000 and 8000 Hz more) or profound (thresholds of ≥90 dB in each test frequency) at baseline. In the study, total or partial hearing recovery was based on change in PTA test results at follow-up, but the magnitude of change that constituted either total or partial recovery was not clearly defined. The study reported that all patients, regardless of intervention group, had a statistically significant improvement in mean PTA scores from baseline, and that HBOT alone or combination therapy with HBOT plus steroids resulted in greater recovery relative to steroid use alone. Other outcomes, including harms of treatment, were not reported.

Section Summary

Recent systematic reviews and meta-analyses provide evidence supporting hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss, with studies demonstrating improved hearing recovery rates when HBOT is combined with medical therapy compared to medical therapy alone. Earlier Cochrane and systematic reviews showed mixed findings with significant methodological limitations. Current evidence suggests HBOT may provide clinical benefit, particularly when used as adjunctive therapy. Standardized protocols and consistent outcome measures are still needed.

Inflammatory Bowel Disease (IBD)

Systematic Reviews

McCurdy (2022) published a SR examining the evidence on HBOT for a range of IBD phenotypes (Crohn disease, ulcerative colitis).[50] The review was not limited by study design, and included 3 small RCTs (total N=40 all with ulcerative colitis) and 16 case series.The included case series generally enrolled less than 30 patients each, with the exception of one study, conducted in Russia, that enrolled 519 patients. Overall, a total sample size for the SR across phenotypes was 844. Two RCTs found a benefit for HBOT compared with standard medical care, but they were small studies (n=10 and 20) and were likely underpowered to detect between-group differences. In addition, one of the trials only included prior HBOT responders and one was stopped early due to enrollment difficulties. The third RCT found no benefit of HBOT compared with standard care, and was also stopped early. Quality assessment of the included studies judged two of the three RCTs to be at high risk of bias. Study authors concluded that although HBOT was associated with high response rates across phenotypes, high-quality evidence was limited, and well-designed RCTs are needed to confirm the effect of HBOT in patients with IBD.

Singh (2021) published a SR on the efficacy of HBOT in patients with ulcerative colitis and Chron's disease.[51] A total of 18 studies were included in the review consisting mainly of observational studies. The overall response rate of HBOT in ulcerative colitis was 83.24% (95% CI: 61.90-93.82), while the response in Crohn's disease was 81.89 (95% CI: 76.72-86.11). The results of randomized trials for HBOT as adjuvant therapy in ulcerative colitis were conflicting within the review. The complete healing of fistula in fistulizing Crohn's disease was noted 47.64% (22.05-74.54), while partial healing was noted in 34.29% (17.33-56.50%). This review is limited by inclusion of inadequately powered studies and lack of randomized trials.

McCurdy (2021) published a systematic review evaluating the efficacy of HBOT on various inflammatory bowel disease phenotypes.[52] There were 19 studies included in the review with 809 patients in three randomized trials and 16 case series. Rates of clinical remission included 87% (95% CI, 10-100) for ulcerative colitis (n = 42), 88% (95% CI, 46-98) for luminal Crohn's disease (CD, n = 8), 60% (95% CI, 40-76) for perianal CD (n = 102), 31% (95% CI, 16-50) for pouch disorders (n = 60), 92% (95% CI, 38-100) for pyoderma gangrenosum (n = 5), and 65% (95% CI, 10-97) for perianal sinus/metastatic CD. This review is limited by the inclusion of primarily case studies and studies with inadequate descriptions of the interventions and outcomes.

A 2014 systematic review by Dulai examined the evidence on HBOT for inflammatory bowel disease (Crohn disease and ulcerative colitis).[53] The review was not limited by study design. The authors 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.[54] Patients were randomized to treatment with standard medical therapy only (n=8) or medical therapy plus HBOT (n=10) consisting of 90-minute treatments at 2.4 atm, 5 days a week for 6 weeks (total of 30 sessions). The primary outcome was the self-reported Mayo score which has a potential range of 0 to 12.[55] Patients with a score of 6 or more are considered to have moderate to severe active disease. At six months follow-up there was no significant difference between groups in the Mayo score, with a median score of 0.5 in the HBOT group and three in the control group (exact p value not reported). In addition, there were no significant differences in any of the secondary outcomes including laboratory tests and fecal weight. Overall, the authors found that the studies had a high risk of bias, particularly in the areas of attrition and reporting bias, and further study in well-controlled, blinded RCTs was recommended.

Randomized Controlled Trials (RCTs)

The RCTs for IBD are included in the Systematic Reviews above.

Section Summary

There is insufficient evidence that HBOT is effective for treating inflammatory bowel disease. Only three small RCT have been published, and these studies did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy.

In Vitro Fertilization

In a 2005 nonrandomized pilot study, Van Voorhis reported that HBOT was well tolerated in women undergoing ovarian follicular stimulation for in vitro fertilization; however no outcomes were reported.[56] Therefore, current evidence is insufficient to permit conclusions and HBOT is considered investigational for this indication.

Mental Illness

A Rapid Response Report from the Canadian Agency for Drugs and Technologies in Health (CADTH) searched the literature through July 2014 on the clinical effectiveness of hyperbaric oxygen therapy for treatment of adults with posttraumatic stress disorder, generalized anxiety disorder, and/or depression.[57]

The review's inclusion criteria were health technology assessments, systematic reviews, meta-analyses, RCTs or nonrandomized studies comparing HBOT to any active treatment and reporting clinical outcomes. No eligible studies were identified.

Multiple Sclerosis

A Cochrane review of RCTs on HBOT for multiple sclerosis was published by Bennett in 2004.[58] The authors identified 9 RCTs, with a total of 504 participants that compared the effects of HBOT with placebo or no treatment. The primary outcome of the review was score on the Expanded Disability Status Scale (EDSS). A pooled analysis of data from 5 trials (N=271) did not find a significant difference in change in the mean EDSS 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) comparing HBOT and placebo did not find a significant difference in mean EDSS after 6 months of follow-up (MD = -0.22; 95% CI, -0.54 to 0.09).

Necrotizing Soft Tissue Infection

Systematic Reviews

Huang (2023) published a SR with meta-analysis examining the efficacy of HBOT in the treatment of necrotizing soft tissue infections (NSTI).[59] Retrospective cohort and case-control studies included 49,152 patients, 1448 who received HBOT and 47,704 in control. The mortality rate in the HBOT group was significantly lower than that in the non-HBOT group [RR = 0.522, 95% CI (0.403, 0.677), $p < 0.05$]. However, the number of debridements performed in the HBOT group was higher than in the non-HBOT group [SMD = 0.611, 95% CI (0.012, 1.211), $p < 0.05$]. There was no significant difference in amputation rates between the two groups [RR = 0.836, 95% CI (0.619, 1.129), $p > 0.05$]. The incidence of multiple organ dysfunction syndrome (MODS) was lower in the HBOT group than in the non-HBO group [RR = 0.205, 95% CI (0.164, 0.256), $p < 0.05$]. There was no significant difference in the incidence of other complications, such as sepsis, shock, myocardial infarction, pulmonary embolism, and pneumonia, between the two groups ($p > 0.05$).Due to the retrospective nature of the studies, the evidence is weak, and further research is needed to establish efficacy.The authors also comment that It is important to note that HBOT is not available in all hospitals, and its use should be carefully considered based on the patient's individual circumstances. Additionally, it is still worthwhile to stress the significance of promptly evaluating surgical risks to prevent missing the optimal treatment time.

A Cochrane review by Levett (2015) evaluated the literature on HBOT as adjunctive therapy for necrotizing fasciitis.[60] No RCTs were identified. Hedetoft (2021) published a SR which included 31 retrospective cohort studies assessing the effect of adjunctive HBOT for treating necrotizing soft-tissue infections (necrotizing fasciitis, Fournier's gangrene, and gas gangrene).[61] Ten studies assessed to have critical (very high) risk of bias were excluded from meta-analyses. Pooled results from the remaining 21 studies found HBOT associated with a reduced risk of in-hospital mortality (OR, 0.44; 95% CI, 0.33 to 0.58; I2=8%), but the duration

of follow-up for mortality was not reported. Results were consistent when studies were stratified according to moderate (5 studies; OR, 0.39; 95% CI, 0.28 to 0.55; I2=0%) and serious (high) risk of bias (16 studies; OR, 0.51; 95% CI, 0.33 to 0.80; I2=17%). Publication bias favoring HBOT was present for this outcome based on funnel plot analysis. For other outcomes, including major amputation and length of hospital stay, there were no statistically significant differences between HBOT use and non-use. Evidence on adjunctive HBOT and the need for surgical debridement was mixed. One study with a low/moderate risk of bias reported a higher number of debridements with HBOT use versus non-use (mean difference, 1.8; 95% CI, 1.15 to 2.45), but the mean difference between HBOT use and non-use in a pooled analysis of 5 studies with methodological flaws was not statistically significant (mean difference, 0.63; 95% CI, -0.49 to 1.75).

Section Summary

No RCTs have evaluated HBOT for necrotizing soft tissue infection. Systematic reviews of retrospective studies with methodological limitations suggest that HBOT use may reduce the risk of in-hospital mortality.

Osteomyelitis

No prospective clinical trials on chronic refractory osteomyelitis or acute refractory osteomyelitis were identified in updated searches. Savvidou (2018) conducted a qualitative systematic review of HBOT as an adjunctive treatment of chronic osteomyelitis.[62] Adjuvant HBOT was effective in 16 (80%) of 20 cohort studies and 19 (95%) of 20 case series. Overall, 308 (73.5%) of 419 patients with complete data achieved a successful outcome with no relapses reported.

The justification for the use of HBOT in chronic osteomyelitis has been primarily based on case series. Among the larger case series, Maynor reviewed the records of all patients with chronic osteomyelitis of the tibia seen at one institution.[63] Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBO treatments (range, 6-99). 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 reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution.[64] 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). After a mean posttreatment 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.[65-67] A high percentage of refractory patients in these series had successful outcomes.

Radiotherapy Adverse Effects

Systematic Review

Yang (2024) published a systematic review and meta-analysis examining the efficacy and safety of hyperbaric oxygen therapy for radiation-induced hemorrhagic cystitis. [68] The review included 14 articles with 556 patients and found that 500 patients (89.9%) had symptom improvement, with pooled results demonstrating that 55% of patients treated with hyperbaric oxygen therapy had complete remission of hematuria (95% CI 51-59%). The authors concluded that hyperbaric oxygen therapy showed improvement of symptoms for patients with

radiation-induced hemorrhagic cystitis, though the study was limited by the availability of evidence for this treatment approach.

Philipsen (2024) published a systematic review assessing HBOT for head and neck cancer patients with radiation-induced dysphagia. Six studies met eligibility criteria after screening 1,396 records, including three randomized controlled trials, two prospective cohort studies, and one retrospective study with a total of 287 patients. Evidence of HBOT benefits was inconsistent with two studies showing significant improvements in swallowing function, two showing no benefit, and two showing mixed results. HBOT protocols ranged from 2.0 to 2.4 ATA for 90 to 120 minutes over 20 to 40 sessions. Outcome measures varied including FOIS scores, videofluoroscopy findings, and quality of life assessments. Limitations included small sample sizes (ranging from 19 to 86 patients), heterogeneity in outcome measures, varying time intervals between radiation and HBOT initiation, different HBOT protocols, and potential selection bias in patient recruitment.

A 2017 systematic review on the effectiveness of HBOT for the treatment of radiation-induced skin necrosis included eight articles with five case series studies, two case reports, and one observational cohort.[69] The authors investigated the change in symptoms and alteration in wound healing and reported that HBOT was a safe intervention with promising outcomes. However, the authors recommended additional high-quality evidence in order for HBOT to be considered as a relevant treatment for this indication.

A 2014 systematic review on the safety and effectiveness of HBOT for the treatment of non-neurological soft tissue radiation-related injuries (STRI) included 41 articles, 11 of which compared regimens with and without HBOT.[70] Serious adverse effects were rare and the more common adverse effects were minor and self-limiting. Evidence of a beneficial effect of HBOT was reported radiation proctitis and STRI of the head and neck, but not for post-radiation soft tissue edema or radiation cystitis. The authors recommended further studies to validate the use of HBOT as both a definitive and adjunctive treatment for individual STRI.

In 2010, Spiegelberg conducted a systematic review of studies on HBOT to prevent or treat radiotherapy-induced head and neck injuries associated with treatment of malignant tumors.[71] 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 HBOT was effective, and the other 4 did not conclude that the HBOT was effective. The authors noted a paucity of RCTs but did not state the number of RCTs identified in their review.

Randomized Controlled Trials

Teguh reported on 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiation therapy.[72] Eight patients were randomly assigned to receive 30 sessions of HBOT, 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 HBOT 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 HBOT 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 HBOT 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 randomized 58 patients with arm lymphedema (at least 15% increase in arm volume) following cancer treatment in a 2:1 ratio to receive HBOT (n=38) or usual care without HBOT (n=20).[73] Fifty-three patients had baseline assessments and 46/58 (79%) had 12-month assessments. No statistically significant difference was found in the change in arm volume from baseline to 12-month follow-up. 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%) patients in the HBOT 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 also similar between groups.

Section Summary

Due to the lack of sufficient evidence from well-designed clinical trial, HBOT for the treatment of adverse effects related to radiation therapy is considered investigational.

Radionecrosis and Osteoradionecrosis

Quah (2024) published a systematic review and meta-analysis examining adjunctive modalities during tooth extraction for osteoradionecrosis prevention. Twenty-nine studies with 1,520 patients were included comprising 15 retrospective studies, eight prospective studies, four randomized controlled trials, and two case series. Pooled prevalence of osteoradionecrosis for hyperbaric oxygen (4.6%, 95% CI: 2.8%-7.5%), pentoxifylline-tocopherol (3.4%, 95% CI: 1.4%-8.0%), and antibiotics (3.8%, 95% CI: 2.1%-6.8%) was significantly lower than control (17.6%, 95% CI: 12.1%-25.0%). HBO showed greatest protective effect (OR=0.21, 95% CI: 0.12-0.37, p<0.001) followed by PENTO (OR=0.16, 95% CI: 0.06-0.42, p<0.001). HBO protocols typically involved 2.0 to 2.5 ATA for 90 to 120 minutes over 20 to 30 sessions. Limitations included heterogeneity in patient populations, varying radiation doses and techniques, different extraction protocols, inconsistent follow-up periods, and predominance of retrospective studies with potential selection bias.

Shah (2025) published a systematic review and meta-analysis of anterior and central skull base osteoradionecrosis management. Thirteen articles were included with 385 patients categorized into conservative versus surgical treatment approaches. Eight of 197 patients treated conservatively had symptom resolution (4.1%, 95% CI: 1.8%-7.9%) while 135 of 188 patients treated surgically had resolution (71.8%, 95% CI: 64.7%-78.2%). Conservative treatment included hyperbaric oxygen, antibiotics, and pentoxifylline-tocopherol combinations. Surgical approaches included debridement, reconstruction with free flaps, and endoscopic resection. The studies comprised nine retrospective series, three case series, and one prospective study with sample sizes ranging from eight to 67 patients. Limitations included lack of randomized controlled trials, heterogeneity in treatment protocols, varying definitions of treatment success, potential selection bias in treatment allocation, and limited long-term follow-up data beyond two years.

Geçkil (2025) published a systematic meta-analysis of mandibular osteoradionecrosis treatment approaches. Twenty-three studies with 1,247 patients were included examining hyperbaric oxygen and surgery alone or in combination. Success rates were 69% for HBO

combined with surgery (95% CI: 62%-75%), 38% for HBO alone (95% CI: 29%-48%), and 36% for surgery alone (95% CI: 28%-45%), with significant differences favoring combination treatment ($p<0.001$). HBO protocols typically involved 2.0 to 2.5 ATA for 90 to 120 minutes over 20 to 40 sessions. Surgical approaches included sequestrectomy, segmental resection, and reconstruction procedures. The studies included 15 retrospective cohort studies, five prospective studies, and three randomized controlled trials. Limitations included heterogeneity in ORN staging systems, varying HBO protocols, different surgical techniques, inconsistent outcome definitions, and potential publication bias toward positive combination therapy results.

Lin (2023) published an updated Cochrane Review on HBOT for late radiation tissue injury.[74] This is the third update of the original Cochrane Review published in July 2005 and updated previously in 2012 and 2016. The purpose of the review is to evaluate the benefits and harms of HBOT for treating or preventing late radiation tissue injury (LRTI) compared to regimens that excluded HBOT. The study included 18 RCTs (1071 participants) comparing the effect of HBOT versus no HBOT on LRTI prevention or healing.They added four new studies to this updated review and evidence for the treatment of radiation proctitis, radiation cystitis, and the prevention and treatment of osteoradionecrosis (ORN). HBOT may not prevent death at one year (risk ratio (RR) 0.93, 95% confidence interval (CI) 0.47 to 1.83; I2 = 0%; 3 RCTs, 166 participants; low-certainty evidence). There is some evidence that HBOT may result in complete resolution or provide significant improvement of LRTI (RR 1.39, 95% CI 1.02 to 1.89; I2 = 64%; 5 RCTs, 468 participants; low-certainty evidence) and HBOT may result in a large reduction in wound dehiscence following head and neck soft tissue surgery (RR 0.24, 95% CI 0.06 to 0.94; I2 = 70%; 2 RCTs, 264 participants; low-certainty evidence). In addition, pain scores in ORN improve slightly after HBOT at 12 months (mean difference (MD) -10.72, 95% CI -18.97 to -2.47; I2 = 40%; 2 RCTs, 157 participants; moderate-certainty evidence). HBOT results in a higher risk of a reduction in visual acuity (RR 4.03, 95% CI 1.65 to 9.84; 5 RCTs, 438 participants; high-certainty evidence). There was a risk of ear barotrauma in people receiving HBOT when no sham pressurization was used for the control group (RR 9.08, 95% CI 2.21 to 37.26; I2 = 0%; 4 RCTs, 357 participants; high-certainty evidence), but no such increase when a sham pressurization was employed (RR 1.07, 95% CI 0.52 to 2.21; I2 = 74%; 2 RCTs, 158 participants; high-certainty evidence). The included studies have small sample sizes. The authors conclude that HBOT may be associated with improved outcomes (low- to moderate-certainty evidence for people with LRTI affecting tissues of the head, neck, bladder and rectum. HBOT may also result in a reduced risk of wound dehiscence and a modest reduction in pain following head and neck irradiation. However, HBOT is unlikely to influence the risk of death in the short term. And that the application of HBOT to selected participants may be justified. Limitations include a small number of studies with small sample sizes and methodological and reporting inadequacies of some of the primary studies. More information is required on the subset of disease severity and tissue type affected that is most likely to benefit from this therapy, the time for which we can expect any benefits to persist and the most appropriate oxygen dose. Further research is required to establish the optimum participant selection and timing of any therapy.

Stroke

Acute Stroke

Systematic Reviews

In a 2005 Cochrane systematic review, Bennett evaluated HBOT for acute stroke.[75] The investigators identified 6 RCTs with a total of 283 participants that compared HBOT to sham

HBOT or no treatment. The authors were only able to pool study findings for 1 outcome, the mortality rate at 3-6 months. A pooled analysis of 3 trials found no significant benefit of HBOT compared to the control for this outcome. Based on the available evidence, acute ischemic stroke is considered investigational

In a 2005 systematic review, Carson concluded that current evidence did not demonstrate any benefit with the use of HBOT for the treatment of stroke.[76] The authors noted it was undetermined whether there were any benefits with HBOT that would outweigh potential harms, and further study was required.

In a 2014 update of a Cochrane systematic review, Bennett evaluated HBOT for acute ischemic stroke. The investigators identified 11 RCTs with a total of 705 participants that compared HBOT with sham HBOT or no treatment. The authors were only able to pool study findings for 1 outcome; mortality at 3 to 6 months. A pooled analysis of data from 4 trials with a total of 106 participants did not find a significant benefit of HBOT compared with a control condition for this outcome (RR=0.97; 95% CI, 0.34 to 2.75).

Randomized Controlled Trials (RCTs)

No RCTs have been published since the 2005 systematic reviews.

Stroke-related motor dysfunction

Randomized Controlled Trials (RCTs)

In 2013, Efrati published an RCT evaluating HBOT for treatment of neurologic deficiencies associated with a history of stroke.[77] The study included 74 patients with at least one motor dysfunction who had an ischemic or hemorrhagic stroke 6-36 months prior to study participation. Participants were randomly assigned to receive 2 months of HBOT (40 daily sessions, 5 days per week, n=30) or 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 of 32 patients (91%) 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 quality-of-life and functional status measures.

At 2 months' follow-up, there was statistically significantly greater improvement in function in the HBOT group compared to the control group as measured by the NIHSS, quality-of-life 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 (SPECT) imaging in the regions affected by stroke. For the delayed treatment control group, there was a statistically significant improvement in function after HBOT compared to before treatment. This RCT raises the possibility that HBOT may induce improvements in function and quality of life for post-stroke patients with motor deficits. However, the results are not definitive for a number of reasons. This RCT is small and enrolled a heterogeneous group of post-stroke patients. The study was not double-blind and the majority of outcome measures, except for the NIHSS, were patient reported and thus prone to the placebo effect. Also, there was a high total dropout rate of 20% at the 2-month follow-up point. Therefore, larger, double-blind studies with longer follow-up are needed to corroborate these results. Because of these limitations in the evidence, HBOT is considered investigational for treating motor dysfunction associated with stroke.

Section Summary

Current evidence is insufficient to permit conclusions about whether HBOT improves health outcomes in the treatment of stroke or stoke-related functional limitations.

Traumatic Brain Injury

Systematic Review

Harch (2022) published a systematic review of the evidence for hyperbaric oxygen therapy (HBOT) in Persistent Postconcussion Syndrome using a dose-analysis.[78] Eleven studies were included: six randomized trials, one case-controlled study, one case series, and three case reports. Whether analyzed by oxygen, pressure, or composite oxygen and pressure dose of hyperbaric therapy statistically significant symptomatic and cognitive improvements or cognitive improvements alone were achieved for patients treated with 40 HBOTS at 1.5 atmospheres absolute. Alashram (2022) included ten studies in his systematic review; six studies were randomized controlled trials, and four were pilot studies.[79] As reported by the author, the benefits of HBOT were limited for traumatic brain injury and more RCTs with larger sample sizes are required to make any conclusion.

The systematic review and pooled analysis by Hart (2019) evaluated HBOT for mild traumatic brain injury (mTBI) associated post-concussive symptoms (PCS) and posttraumatic stress disorder (PTSD).[80] Data were aggregated from four Department of Defense (DoD) studies that included participant level data on 254 patients assigned to either HBOT or sham intervention. An additional three studies with summary-level participant data were summarized (N=135). The authors assessed changes from baseline to post-intervention on PCS, PTSD, and neuropsychological measures. The DoD data analyses indicated improvements with HBOT for PCS, measured by the Rivermead Total Score. Statistically significant improvements were seen for PTSD based on the PTSD Checklist Total Score, as well as for verbal memory based on CVLT-II Trial 1-5 Free Recall.

A 2016 meta-analysis by Wang (2016) assessed HBOT for TBI including eight studies with 519 participants that met the eligibility criteria.[81] 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 score. A pooled analysis of two studies found a significantly greater improvement in the mean Glasgow Coma Scale score in the HBOT group compared with control groups. 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.

A 2012 Cochrane systematic review addressed HBOT as adjunctive treatment for traumatic brain injury.[82] The investigators identified 7 RCTs with a total of 571 participants comparing a standard intensive treatment regimen to the same treatment regimen with the addition of HBOT. The review did not include studies in which interventions occurred in a specialized acute care setting. The HBOT regimens varied among studies; for example, the total number of individual sessions varied from 3 to 30-40. No trial used sham treatment or blinded the staff members who were treating the patients, and only 1 had blinding of outcome assessment. Allocation concealment was inadequate in all of the studies. The primary outcomes of the review were mortality and functional outcomes. A pooled analysis of data from 4 trials that reported this outcome found a statistically significantly greater reduction in mortality when HBOT was added to a standard treatment regimen. However, when data from the 4 trials

were pooled, the difference in the proportion of patients with an unfavorable functional outcome at final follow-up did not reach statistical significance. Unfavorable outcome was commonly defined as a Glasgow Outcome Score (GOS) of 1, 2 or 3, which are described as ‘dead’, ‘vegetative state’ or ‘severely disabled’. Studies were generally small and were judged to have substantial risk of bias.

Randomized Controlled Trials

Hadanny (2022) conducted an RCT to assess the effect of hyperbaric oxygen therapy in children (age 8 to 15) suffering from persistent post-concussion syndrome (PPCS) from mild-moderate traumatic brain injury six months to 10 years prior.[83] 25 children were randomized to receive 60 daily sessions of HBOT (n = 15) or sham (n = 10) treatments. Following HBOT, there was a significant increase in cognitive function including the general cognitive score (d = 0.598, p = 0.01), memory (d = 0.480, p = 0.02), executive function (d = 0.739, p = 0.003), PPCS symptoms including emotional score (p = 0.04, d = - 0.676), behavioral symptoms including hyperactivity (d = 0.244, p = 0.03), global executive composite score (d = 0.528, p = 0.001), planning/organizing score (d = 1.09, p = 0.007).

A 2014 double-blind sham-controlled trial 2014 RCT by Cifu included 61 male Marines who had a history of mild traumatic brain injury and postconcussive syndrome. To maintain blinding, all patients were pressured inside a hyperbaric chamber to 2.0 ata. They were randomized to breathe 1 of 3 oxygen p[nitrogen gas mixes equivalent to: (1) 75% oxygen at 1.5 ata (n=21); (2) 100% oxygen at 2.0 ata (n=19); and (3) sham treatment with surface room air (n=21). Patients underwent 40 once daily 60-minute sessions. Outcomes were assessed 3 months after the last exposure. The primary outcome was a clinically meaningful improvement, defined as a 10% difference between groups in the score on the Rivermead Post-Concussion Questionnaire (RPQ)–16 (scale range, 50-84; higher values indicate more severe symptoms). At follow-up, there was no statistically significant difference among groups on RPQ-16 score (p=0.41). A variety of secondary outcomes were also assessed. None of these, including measures of attention, cognition, or depression, differed significantly among groups at follow-up.

Also in 2014, Miller evaluated HBOT in 72 military service members with continuing symptoms at least 4 months after mild traumatic brain injury. Patients were randomized to receive 40 daily HBO sessions at 1.5 ata, 40 sham sessions consisting of room air at 1.2 ata or standard care with no hyperbaric chamber sessions. The primary outcome was change in the RPQ. 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 the prespecified change of at least 2 points 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 the response in the sham group was not due to a placebo effect but to an intervention effect of slightly increased atmospheric pressure (1.2 ata).43 Other researchers have noted that room air delivered at 1.2 ata would not be considered an acceptable therapeutic dose for any indication, and especially for a condition with persistent symptoms like postconcussive syndrome.

A 2012 sham-controlled double-blind trial evaluating HBOT was published after the 2012 Cochrane review.[84] The study included 50 military service members, 48 of whom were male, with combat-related mild traumatic brain injury. Participants were randomized to 30 sessions

of HBOT over 8 weeks (n=25) or a sham intervention (room air at 1.3 ATA) (n=25). The primary outcome measures were scores on the Immediate Post-Concussive Assessment and Cognitive Testing (ImPACT) and Post-Traumatic Disorder Check List- Military Version (PCL-M) instruments. Patients were evaluated after every 5 treatment sessions and at 6 weeks post-exposure. Forty-eight of 50 participants (96%) completed the study. There were no statistically significant differences on the ImPACT total mean score or the PCL-M composite score at any time point. While the sample size was relatively small, the study was powered to detect clinically significant differences among groups on the cognitive tests.

Several trials on mild traumatic brain injury in military populations have been published and these did not find significant benefits of HBOT compared with sham treatment. The first trial, published by Wolf in 2012, included 50 military service members, 48 of whom were male, with combat-related mild traumatic brain injury. Participants were randomized to 30 sessions of HBOT over 8 weeks (n=25) or a sham intervention (room air at 1.3 atmosphere, absolute [ata]) (n=25). The primary outcome measures were scores on the Immediate Post-Concussive Assessment and Cognitive Testing (ImPACT) and Post- Traumatic Disorder Check List–Military Version (PCL-M) instruments. Patients were evaluated after every 5 treatment sessions and at 6 weeks postexposure. Forty-eight of 50 participants (96%) completed the study. There were no statistically significant differences on the ImPACT total mean score or the PCL-M me point. For example, at the 6-week follow-up, mean composite PCL-M scores were 41.6 in the HBOT group and 40.6 in the sham-control group (p=0.28). While the sample size was relatively small, the study was powered to detect clinically significant differences among groups on the cognitive tests.

Section Summary

Three systematic reviews with cognitive improvement, no significant improvements and a mortality reduction with HBOT but no significant improvement in patient function among survivors of traumatic brain injury were found. One RCT in 2022 reported the usefulness of HBO six months to 10 years post-brain injury in children. Two double-blind, sham-controlled RCTs of HBO treatment in a military population with mild traumatic brain injury did not find a statistically significant benefit with HBOT. Thus, the evidence is insufficient that HBOT improves health outcomes in patients with traumatic brain injury, and this indication is considered investigational.

Wounds Unrelated to Diabetes

Systematic Reviews

Idris (2024) published a SR analyzing the efficacy of HBOT in the post-operative care of patients undergoing nipple-sparing mastectomy (NSM) as a method of treating breast cancer.[85] The SR included seven included studies; two case reports, one observational case series, two cohort studies, and two retrospective studies. The initiation of HBOT varied among the 63 patients included, with specific post-operative HBOT timeframes reported for 27 individuals. Notably, 10 patients received HBOT within an optimal 48 h window following NSM. Within this early-intervention subgroup, a 90% success rate in resolving threatened skin flap necrosis (TSFN) was observed, with only one patient experiencing unresolved complications. The authors assessed efficacy for various surgical complications related to NSM: Re-operation: Twenty-three patients across four studies required re-operation; Flap loss: Four patients across two studies experienced flap loss. Re-operation and Flap loss rates were higher in the pre-HBOT group than in the post-HBOT group. Sinus pain: No reported sinus

pain was noted in the pre-HBOT group. One of the seventeen patients (5.9%) in the post-HBOT group experienced sinus pain. Significant limitations include the absence of rigorous clinical trials and well-defined control groups. None of the studies that were incorporated in this review exceeded Level III of the ASPS' Evidence Rating Scale for Therapeutic Studies.

Keohane (2023) published a SR evaluating the efficacy of HBOT in the treatment of chronic venous ulcers. Six studies were included.[86] There was significant heterogeneity across the studies, with no standard control intervention, method of outcome reporting, or duration of follow up. Two studies reported 12 week follow up results and pooled analysis of complete ulcer healing showed no statistically significant difference between HBOT and controls for the outcome of complete ulcer healing OR 1.54 (95%CI = .50-4.75) (p = 0.4478). A similar non-significant result was seen in four studies reporting 5-6 week follow up; OR 5.39 (95%CI = .57-259.57) (p = 0.1136). Change in VLU area was reported in all studies, and pooled standardized mean difference was 1.70 (95%CI = .60 to 2.79) (p = 0.0024), indicating a statistically significant benefit of HBOT in reducing ulcer area. There was significant heterogeneity across the studies, with no standard control intervention, method of outcome reporting, or duration of follow up. The authors concluded that the limited evidence does not justify widespread use of HBOT for venous leg ulcers.

Dauwe (2014) published a SR that included eight studies with sample sizes ranging from five to 125 patients. Four studies were randomized, three were prospective non-RCTs, and one was a retrospective non- RCT. Data were not pooled due to the heterogeneity described below. The authors noted that seven of the eight studies reported achieving statistical significance in 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.

A 2013 updated Cochrane review analyzed randomized controlled trials comparing either HBOT with a different intervention, or two HBOT regimens for acute wounds (e.g., surgical wounds, lacerations, traumatic wounds, and animal bites).[87] The four studies that met inclusion criteria ranged in size from 10 to 135 subjects. Reported outcomes were mixed. Meta-analysis of pooled data was not possible due to differences among studies with respect to patient characteristics, interventions studied, and outcome measures. Also identified was a high risk of bias due to insufficient disclosure of randomization methods and selective reporting of outcome data. Findings of individual studies were mixed.

Kranke (2012) published an update to the 2007 Cochrane review of randomized controlled trials (RCTs) on HBOT for chronic wounds.[88] The authors identified nine RCTs with a total of 471 participants that compared the effect of HBOT on chronic wound healing compared with an alternative treatment approach that did not use HBOT. Eight of the nine trials included in the review evaluated HBOT in patients with diabetes. The remaining trial addressed HBOT for patients with venous ulcers; that study had only 16 participants and the comparator treatment was not specified. In a pooled analysis of data from three trials, a significantly higher proportion of ulcers had healed at the end of the treatment period (6 weeks) in the group receiving HBOT compared to the group not receiving HBOT (RR: 5.20: 95% CI: 1.25 to 21.7). Pooled analyses, however, did not find significant differences between groups in the proportion of ulcers healed in the HBOT versus non-HBO-treated groups at six months (two trials) or 12 months (three trials). There were insufficient data to conduct pooled analyses of studies evaluating HBOT for treating patients with chronic wounds who did not have diabetes.

The primary outcome examined by Cochrane reviewers, wound healing was not reported in either of the 2 trials comparing HBOT with usual care[89, 90] or in the 1 trial comparing HBOT with dexamethasone or heparin.[91] Complete wound healing was reported in the 1 RCT comparing active HBOT with sham HBOT.[92] In this small study (n=36), there was a statistically higher rate of wound healing in the active HBOT group. The time point for outcome measurement in this study was unclear, but there was no statistically significant difference between groups in the meantime to wound healing. Adverse effects included 2 additional surgical procedures in 1 patient in the HBOT group compared with 8 in 6 patients in the sham group. The HBOT group had significantly fewer patients who developed necrotic tissue (1 and 8, respectively). There were no amputations in the HBOT group compared with 2 amputations in the sham group, but this difference did not reach statistical significance. The authors concluded that evidence remains insufficient to support the routine use of HBOT for acute surgical or traumatic wounds. They recommended further evaluation in high quality RCTs that include outcomes measures of complete wound closure and accelerated wound closure.

Randomized Controlled Trials (RCTs)

No RCTs have been published since those included in the systematic reviews summarized above.

Section Summary

Published clinical trial data is insufficient to determine the effectiveness of HBOT for wounds that are not related to diabetes. The UHMS does not include these wounds in their list of indications for HBOT, noting the lack of available evidence.[93] As shown in studies of adjunctive HBOT for treatment of severe diabetic lower extremity ulcers, this treatment is well suited to randomized, controlled comparative trials.

Wounds Related to Diabetes

Damineni (2025) published a systematic review assessing HBOT for diabetic foot ulcers. Six studies with 391 patients were included after screening 1,847 records. Most studies indicated reduced major amputation rates ranging from 0% to 11.1% in HBOT groups versus 11.1% to 41.2% in control groups, improved ulcer healing rates of 71% to 100% versus 29% to 88% in controls, and decreased ulcer size and depth with mean reductions of 50% to 85% in HBOT groups. The studies included four randomized controlled trials and two cohort studies with follow-up periods ranging from 4 to 52 weeks. Limitations included selection bias and performance bias in most studies, small sample sizes, heterogeneity in HBOT protocols (ranging from 20 to 40 sessions), and varying wound assessment methods.

Zhang (2025) published a systematic review and meta-analysis of treatment modalities for diabetic foot ulcers. Ten studies were included examining HBOT, platelet-rich plasma, vacuum-assisted closure therapy, and negative pressure wound therapy with a total of 847 patients. HBOT demonstrated substantial reduction in amputation rates (OR=0.08, 95% CI: 0.02-0.29, $p<0.001$) and systemic HBOT was particularly effective in averting amputations compared to controls (OR=0.05, 95% CI: 0.01-0.24, $p<0.001$). Wound healing rates improved significantly with HBOT (OR=4.12, 95% CI: 2.18-7.79, $p<0.001$). The studies included six randomized controlled trials and four observational studies with HBOT protocols ranging from 20 to 40 sessions. Limitations included significant heterogeneity between studies ($I^2=75\%$ for amputation outcomes), varying definitions of wound healing, different HBOT protocols, and potential publication bias.

Apolo-Arenas (2024) published a systematic review examining hyperbaric chamber versus conventional treatment for chronic diabetic foot amputation prevention. Seven studies were included with patients over 18 years having diabetes mellitus and Wagner scale 2-4 diabetic foot ulcers. The studies comprised five randomized controlled trials and two cohort studies with sample sizes ranging from 28 to 94 patients per study. Results showed significant improvements with HBOT compared to control groups in wound healing rates (ranging from 71% to 100% versus 29% to 71% in controls) and amputation prevention (amputation rates of 0% to 17% versus 11% to 41% in controls). HBOT protocols varied from 20 to 40 sessions at 2.0 to 2.5 ATA for 90 to 120 minutes. Limitations included heterogeneity in treatment protocols, small sample sizes, short follow-up periods in some studies, and potential selection bias.

Weng (2024) published a systematic review and meta-analysis examining hyperbaric oxygen therapy for diabetic peripheral neuropathy. The study included 14 randomized controlled trials with 675 patients in the HBOT group and 648 in the standard therapy group. HBOT demonstrated significantly higher effective treatment rates (RR=1.29, 95% CI: 1.17-1.43, $p < 0.00001$) and improvements in motor nerve conduction velocity for median (MD=3.44 m/s, 95% CI: 1.95-4.93, $p < 0.00001$), ulnar (MD=2.85 m/s, 95% CI: 1.46-4.24, $p<0.0001$), and peroneal nerves (MD=2.77 m/s, 95% CI: 1.38-4.16, $p < 0.0001$). Sensory nerve conduction velocity also improved significantly for median (MD=3.21 m/s, 95% CI: 1.82-4.60, $p < 0.00001$) and ulnar nerves (MD=2.64 m/s, 95% CI: 1.25-4.03, $p = 0.0002$). Six adverse events were reported in the HBOT group with no significant difference between groups (RR=3.00, 95% CI: 0.32-28.35, $p = 0.34$). Limitations included heterogeneity in treatment protocols, small sample sizes in some studies, and varying outcome measures across trials.

Sharma (2021) conducted a systematic review and meta-analysis of 14 studies (N=768) comparing the effect of HBOT with standard care on diabetic foot ulcers.[94] Study authors noted that various modalities can be considered standard care including, but not limited to, debridement, antibiotics and blood sugar control. However, the specific standard care modality in each included study was not reported. HBOT duration ranged from 45 to 120 minutes (median 90 minutes). All included studies had methodological limitations, including selection, performance, detection, attrition and reporting bias. The review found those treated with standard care were less likely to have complete ulcer healing versus HBOT, based on pooled analysis of 11 studies (OR 0.29, 95% CI 0.14 to 0.61; I2=62%). Results were consistent when stratified according to duration of followup of less than one year (seven studies; OR 0.63, 95% CI 0.39 to 1.02; I2=1%) and at one year (four studies; OR 0.16, 95% CI 0.03 to 0.82; I2=83%), although the risk estimate wasn't statistically significant for studies with less than one year followup. A funnel plot analysis for this outcome was asymmetrical, suggesting publication bias. Risk of major amputation was also significantly lower with HBOT compared to standard care based on pooled analysis of seven studies (OR 0.60, 95% CI 0.39 to 0.92; I2=24%). There were no clear differences between groups in minor amputation (9 studies; OR 0.89, 95% CI 0.71 to 1.12) or mortality (three studies; OR 0.55, 95% CI 0.25 to 1.24). Standard care was associated with an increased risk of adverse events compared with HBOT (seven studies; OR 1.68, 95% CI 1.07 to 2.65).

In 2013, O'Reilly[95] published a systematic review of studies on HBOT for treatment of diabetic ulcers. The authors identified 6 RCTs and 6 non-RCTs that compared HBOT with standard wound care or sham therapy in patients with diabetes who had nonhealing lower-limb ulcers. Pooled analyses of observational studies found statistically significant benefits of HBOT on rates of major amputation, minor amputation and the proportion of wounds healed at the end of the study period. However, in pooled analyses of RCT data, the stronger study design, there

were no statistically significant differences between groups on key outcomes. This included the rate of major amputation (RR=0.40; 95% CI, 0.07 to 2.23; p=0.29), minor amputation (RR=0.79; 95% CI, 0.19 to 3.30, p=0.75), and the proportion of unhealed wounds at the end of the study period (RR=0.54, 95% CI, 0.26 to 1.13, p=0.1).

Randomized Controlled Trials (RCTs)

No RCTs have been published since those included in the systematic reviews summarized above.

Section Summary

Published clinical trial data is insufficient to determine the effectiveness of HBOT for wounds that are not related to diabetes. The UHMS does not include these wounds in their list of indications for HBOT, noting the lack of available evidence.[93] As shown in studies of adjunctive HBOT for treatment of severe diabetic lower extremity ulcers, this treatment is well suited to randomized, controlled comparative trials. In spite of this, only 1 small (n=16) randomized, controlled trial was found for non-diabetic wounds.[96] This trial is too small and short-term to be reliable.

Other Indications

No data from well-designed randomized, controlled clinical trials were found that supported HBOT for any other investigational indication, including but not limited to refractory mycoses and acute peripheral arterial insufficiency.

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 (i.e., ≥ 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;
- 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;

SUMMARY OF EVIDENCE

There is sufficient published evidence to determine that use of hyperbaric oxygen therapy (HBOT) in selected individuals, including those with carbon monoxide poisoning, nonhealing diabetic wounds of the lower extremities, acute traumatic ischemia, soft-tissue radiation necrosis (eg, radiation enteritis, cystitis, proctitis), osteoradionecrosis (ie, pre- and posttreatment) for patients undergoing dental surgery (non-implant-related) of an irradiated jaw, gas gangrene, idiopathic sudden sensorineural hearing loss, and profound anemia with exceptional blood loss when blood transfusion is impossible or must be delayed improves the net health outcome. There is insufficient evidence that the use of HBOT improves health outcomes for any indication that is not included in the criteria above.

PRACTICE GUIDELINE SUMMARY

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

In 2013, the FDA published a position statement with a warning that HBOT has not been proven safe and effective for uses not cleared by the agency.[1] This statement was developed due to numerous complaints from consumers and health care professionals that unproven claims made by some HBOT centers may mislead consumers and ultimately endanger their health. The statement included the following conditions for which patients may be unaware that safety and effectiveness of HBOT have *not* been established:

- AIDS/HIV
- Alzheimer's Disease
- Asthma
- Bell's Palsy
- Brain Injury
- Cerebral Palsy
- Depression
- Heart Disease
- Hepatitis
- Migraine
- Multiple Sclerosis
- Parkinson's Disease
- Spinal Cord Injury
- Sport's Injury
- Stroke

In 2021 the FDA provided a consumer update which includes a list of FDA cleared uses of approved hyperbaric chambers (monoplace or multiplace) for the following disorders:[97]

- Air and gas bubbles in blood vessels
- Anemia (severe anemia when blood transfusions cannot be used)
- Burns (severe and large burns treated at a specialized burn center)
- Carbon monoxide poisoning
- Crush injury
- Decompression sickness (diving risk)
- Gas gangrene

- Hearing loss (complete hearing loss that occurs suddenly and without any known cause)
- Infection of the skin and bone (severe)
- Radiation injury
- Skin graft flap at risk of tissue death
- Vision loss (when sudden and painless in one eye due to blockage of blood flow)
- Wounds (non-healing, diabetic foot ulcers)

HBOT is being studied for other conditions, including COVID-19. However, at this time, the FDA has not cleared or authorized the use of any HBOT device to treat COVID-19 or any conditions beyond those listed above.

UNDERSEA AND HYPERBARIC MEDICAL SOCIETY (UHMS)

In 2015, the Undersea and Hyperbaric Medical Society (UHMS) published a guideline on the use of HBOT for treatment diabetic foot ulcers.[98, 99] Recommendations are as follows:

- 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 HBOT 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.

- Appropriate Indications for HBOT[100]

  In 2023, the UHMS updated their guidelines and included the following list of indications considered *appropriate* for hyperbaric oxygen therapy:

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

- Autism Spectrum Disorder (ASD)[14]

  The 2009 UHMS position paper included a critical appraisal of the available literature, in

particular the 2009 Rossignol RCT[12] which was the only RCT available at that time. The paper concluded that “the UHMS cannot recommend the routine treatment of ASD with HBO_2T outside appropriate comparative research protocols.”

- Chronic Brain Injury[101]

  The most recent UHMS position statement on chronic brain injury (e.g., traumatic brain injury, cerebral palsy, stroke) is from 2003. The statement considered the evidence to be insufficient to support a recommendation for HBOT for the chronic sequelae of traumatic or non-traumatic brain injury but noted that continued monitoring of data is warranted.

- Idiopathic Sudden Sensorineural Hearing Loss (ISSNHL)[102]

  In October 2011, the UHMS Executive Board approved ISSNHL as an additional indication. According to treatment guidelines, patients with moderate to profound ISSNHL who present within 14 days of symptom onset should be considered for HBOT treatment.

- Multiple Sclerosis[58]

  A 2010 UHMS position paper reported that most RCTs have failed to show clinical benefit for HBOT therapy for multiple sclerosis. “We conclude that, while there is some case for further investigation of possible therapeutic effects in selected sub-groups of patients (well-characterized and preferably early in the disease course) and for the response to prolonged courses of HBOT, this case is not strong. At this time, the UHMS cannot recommend the routine treatment of MS with HBOT outside appropriate comparative research protocols.”

- Topical Oxygen for Chronic Wounds[103]

  A 2005 UHMS position statement reported that, “to date, mechanisms of action whereby topical oxygen might be effective have not been defined or substantiated. Conversely, cellular toxicities due to extended courses of topical oxygen have been reported, although, again these data are not conclusive, and no mechanism for toxicity has been examined scientifically...The only randomized trial for topical oxygen in diabetic foot ulcers actually showed a tendency toward impaired wound healing in the topical oxygen group. Contentions that topical oxygen is superior to hyperbaric oxygen are not proven.” Therefore, the UHMS recommends against application of topical oxygen outside a clinical trial setting, noting that topical oxygen “should be subjected to the same intense scientific scrutiny to which systemic hyperbaric oxygen has been held.”

NATIONAL BOARD OF DIVING & HYPERBARIC MEDICAL TECHNOLOGY[8]

As noted above, the current position statement concluded that “the installation and provision of in-home hyperbaric oxygen therapy is inherently unsafe and cannot be condoned.” This position is based on concern for the safety and well-being of patients as well as those people in proximity to the HBOT delivery system because in-home provision of HBOT is likely to:

1. Bypass otherwise mandatory federal, state, and local codes related to design, construction, installation, and operation of these devices; and
2. Occur without adequate physician oversight and the operational support of appropriately qualified HBOT providers.

AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY (AAO-HNS)

In 2019, the American Academy of Otolaryngology-Head and Neck Surgery updated clinical guidelines on the treatment of sudden sensorineural hearing loss (SSNHL).[104] They give the following options regarding HBOT:

- "Clinicians may offer, or refer to a physician who can offer, hyperbaric oxygen therapy (HBOT) combined with steroid therapy within two weeks of onset of SSNHL."
- "Clinicians may offer, or refer to a physician who can offer, hyperbaric oxygen therapy (HBOT) combined with steroid therapy as salvage within 1 months of onset of SSNHL."

The guideline provided a comprehensive list of evidence gaps and future research needs on the use of HBOT for SSNHL. These included, among others, the need for a standardized, evidence-based definition of SSNHL, the assessment of the prevalence of SSNHL, and the need for the development of standardized HBOT treatment protocols and standardized outcome assessments.

The International Society of Oral Oncology-Multinational Association for Supportive Care in Cancer (ISOO-MASCC) and American Society of Clinical Oncologists (ASCO)

In 2024 the ISOO-MASCC along with ASCO published a guideline for the Prevention and Management of Osteoradionecrosis in Patients With Head and Neck Cancer Treated With Radiation Therapy.[105] They include the following recommendation:

3.6. Routine use of prophylactic hyperbaric oxygen (HBO) therapy prior to dental extractions in patients who received prior head and neck radiation therapy is not recommended Evidence-based Low Weak

Qualifying statement: Prophylactic HBO may be offered to patients undergoing invasive dental procedures at site(s) where a substantial volume of mandible and/or maxilla received >50 Gy.

SUMMARY

Systemic hyperbaric oxygen therapy (HBOT) has been studied for a wide variety of clinical indications. There is enough evidence to show that systemic HBOT is safe and effective for a variety of indications. There are guidelines based on research that recommend the use of systemic HBOT for a variety of indications. Therefore, the use of systemic HBOT may be considered medically necessary when policy criteria are met.

Due to insufficient positive health outcomes for certain individuals with non-healing diabetic wounds of the lower extremities, the use of hyperbaric oxygen therapy is considered not medically necessary when criteria for non-healing diabetic wounds of the lower extremities are not met.

There is not enough evidence to permit conclusions concerning the effects of systemic hyperbaric oxygen therapy (HBOT) on final health outcomes for any other indication. Therefore, the use of systemic hyperbaric oxygen therapy for all other indications is investigational.

There is not enough evidence to permit conclusions concerning the effects of topical hyperbaric and topical normobaric oxygen therapies on health outcomes. Therefore, the

use of topical hyperbaric and topical normobaric oxygen therapies for any indication is investigational.

REFERENCES

1. TEC Assessment 2003. "Extracorporeal Shock Wave Treatment (ESWT) for Musculoskeletal Condition." BlueCross BlueShield Association Technology Evaluation Center, Vol. 18, Tab 5.
2. Yang Z, Hu J, Qu Y, et al. Interventions for treating gas gangrene. *Cochrane Database Syst Rev.* 2015(12):CD010577. PMID: 26631369
3. Heng MC, Pilgrim JP, Beck FW. A simplified hyperbaric oxygen technique for leg ulcers. *Arch Dermatol.* 1984;120(5):640-5. PMID: 6721526
4. Leslie CA, Sapico FL, Ginunas VJ, et al. Randomized controlled trial of topical hyperbaric oxygen for treatment of diabetic foot ulcers. *Diabetes Care.* 1988;11(2):111-5. PMID: 3289861
5. Landau Z. Topical hyperbaric oxygen and low energy laser for the treatment of diabetic foot ulcers. *Arch Orthop Trauma Surg.* 1998;117(3):156-8. PMID: 9521521
6. Pasek J, Szajkowski S, Cieślar G. Application of Topical Hyperbaric Oxygen Therapy and Medical Active Dressings in the Treatment of Arterial Leg Ulcers-A Pilot Study. *Sensors (Basel).* 2023;23(12). PMID: 37420748
7. Heng MC. Topical hyperbaric therapy for problem skin wounds. *J Dermatol Surg Oncol.* 1993;19(8):784-93. PMID: 8349920
8. Buchbinder R, Ptasznik R, Gordon J, et al. Ultrasound-guided extracorporeal shock wave therapy for plantar fasciitis: a randomized controlled trial. *JAMA.* 2002;288(11):1364-72. PMID: 12234230
9. Bennett MH, Lehm JP, Jepson N. Hyperbaric oxygen therapy for acute coronary syndrome. *Cochrane Database Syst Rev.* 2011(8):CD004818. PMID: 21833950
10. Xiong T, Chen H, Luo R, et al. Hyperbaric oxygen therapy for people with autism spectrum disorder (ASD). *Cochrane Database Syst Rev.* 2016;10:CD010922. PMID: 27737490
11. Ghanizadeh A. Hyperbaric oxygen therapy for treatment of children with autism: a systematic review of randomized trials. *Medical gas research.* 2012;2:13. PMID: 22577817
12. Rossignol DA, Rossignol LW, Smith S, et al. Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial. *BMC Pediatr.* 2009;9:21. PMID: 19284641
13. Granpesheh D, Tarbox J, Dixon DR. Randomized trial of hyperbaric oxygen therapy for children with autism. Research in Autism Spectrum Disorders. 2012;4:268-75. No PMID Entry.
14. Bennett M, Hart B. Undersea and Hyperbaric Medical Society (UHMS) Position Paper: the treatment of children with autism spectrum disorder with hyperbaric oxygen therapy. December 5, 2009. [cited 11/4/2024]. 'Available from:' https://www.uhms.org/images/Position-Statements/autism_position_paper.pdf.
15. Sampanthavivat M, Singkhwa W, Chaiyakul T, et al. Hyperbaric oxygen in the treatment of childhood autism: a randomised controlled trial. *Diving and hyperbaric medicine : the journal of the South Pacific Underwater Medicine Society.* 2012;42(3):128-33. PMID: 22987458

16. Holland NJ, Bernstein JM, Hamilton JW. Hyperbaric oxygen therapy for Bell's palsy. *Cochrane Database Syst Rev.* 2012;2:CD007288. PMID: 22336830
17. Freiberger JJ, Padilla-Burgos R, McGraw T, et al. What is the role of hyperbaric oxygen in the management of bisphosphonate-related osteonecrosis of the jaw: a randomized controlled trial of hyperbaric oxygen as an adjunct to surgery and antibiotics. *Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons.* 2012;70(7):1573-83. PMID: 22698292
18. Heys SD, Smith IC, Ross JA, et al. A pilot study with long term follow up of hyperbaric oxygen pretreatment in patients with locally advanced breast cancer undergoing neo-adjuvant chemotherapy. *Undersea Hyperb Med.* 2006;33(1):33-43. PMID: 16602255
19. Bennett M, Feldmeier J, Smee R, et al. Hyperbaric oxygenation for tumour sensitisation to radiotherapy. *Cochrane Database Syst Rev.* 2005(4):CD005007. PMID: 16235387
20. Lacey DJ, Stolfi A, Pilati LE. Effects of hyperbaric oxygen on motor function in children with cerebral palsy. *Annals of neurology.* 2012;72(5):695-703. PMID: 23071074
21. Collet JP, Vanasse M, Marois P, et al. Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. HBO-CP Research Group. *Lancet.* 2001;357(9256):582-6. PMID: 11558483
22. Eskes A, Ubbink DT, Lubbers M, et al. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. *Cochrane Database Syst Rev.* 2010(10):CD008059. PMID: 20927771
23. Eskes AM, Ubbink DT, Lubbers MJ, et al. Hyperbaric oxygen therapy: solution for difficult to heal acute wounds? Systematic review. *World J Surg.* 2011;35(3):535-42. PMID: 21184071
24. Friedman HI, Fitzmaurice M, Lefaivre JF, et al. An evidence-based appraisal of the use of hyperbaric oxygen on flaps and grafts. *Plast Reconstr Surg.* 2006;117(7 Suppl):175S-90S; discussion 91S-92S. PMID: 16799386
25. Wolf SJ, Lavonas EJ, Sloan EP, et al. Clinical policy: Critical issues in the management of adult patients presenting to the emergency department with acute carbon monoxide poisoning. *Annals of emergency medicine.* 2008;51(2):138-52. PMID: 18206551
26. Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *The Medical journal of Australia.* 1999;170(5):203-10. PMID: 10092916
27. Logue CJ. An inconvenient truth? *Annals of emergency medicine.* 2008;51(3):339-40; author reply 40-2. PMID: 18282535
28. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *The New England journal of medicine.* 2002;347(14):1057-67. PMID: 12362006
29. Weaver LK, Valentine KJ, Hopkins RO. Carbon monoxide poisoning: risk factors for cognitive sequelae and the role of hyperbaric oxygen. *American journal of respiratory and critical care medicine.* 2007;176(5):491-7. PMID: 17496229
30. Esposito M, Grusovin MG, Patel S, et al. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. *Cochrane Database Syst Rev.* 2008(1):CD003603. PMID: 18254025
31. Bennett M, Best TM, Babul S, et al. Hyperbaric oxygen therapy for delayed onset muscle soreness and closed soft tissue injury. *Cochrane Database Syst Rev.* 2005(4):CD004713. PMID: 16235376
32. Xiao Y, Wang J, Jiang S, et al. Hyperbaric oxygen therapy for vascular dementia. *Cochrane Database Syst Rev.* 2012;7:CD009425. PMID: 22786527

33. Camporesi EM, Vezzani G, Bosco G, et al. Hyperbaric oxygen therapy in femoral head necrosis. *J Arthroplasty.* 2010;25(6 Suppl):118-23. PMID: 20637561
34. Ablin JN, Lang E, Catalogna M, et al. Hyperbaric oxygen therapy compared to pharmacological intervention in fibromyalgia patients following traumatic brain injury: A randomized, controlled trial. *PloS one.* 2023;18(3):e0282406. PMID: 36897850
35. Efrati S, Golan H, Bechor Y, et al. Hyperbaric oxygen therapy can diminish fibromyalgia syndrome--prospective clinical trial. *PloS one.* 2015;10(5):e0127012. PMID: 26010952
36. Yildiz S, Kiralp MZ, Akin A, et al. A new treatment modality for fibromyalgia syndrome: hyperbaric oxygen therapy. *The Journal of international medical research.* 2004;32(3):263-7. PMID: 15174219
37. Bennett MH, Stanford RE, Turner R. Hyperbaric oxygen therapy for promoting fracture healing and treating fracture non-union. *Cochrane Database Syst Rev.* 2012;11:CD004712. PMID: 23152225
38. Bennett MH, French C, Schnabel A, et al. Normobaric and hyperbaric oxygen therapy for migraine and cluster headache. *Cochrane Database Syst Rev.* 2008(3):CD005219. PMID: 18646121
39. Eftedal OS, Lydersen S, Helde G, et al. A randomized, double blind study of the prophylactic effect of hyperbaric oxygen therapy on migraine. *Cephalalgia.* 2004;24(8):639-44. PMID: 15265052
40. Matharu M, Silver N. Cluster headache. *Clin Evid (Online).* 2008;2008. PMID: 19450329
41. Nilsson Remahl AI, Ansjon R, Lind F, et al. Hyperbaric oxygen treatment of active cluster headache: a double-blind placebo-controlled cross-over study. *Cephalalgia.* 2002;22(9):730-9. PMID: 12421159
42. Di Sabato F, Rocco M, Martelletti P, et al. Hyperbaric oxygen in chronic cluster headaches: influence on serotonergic pathways. *Undersea Hyperb Med.* 1997;24(2):117-22. PMID: 9171470
43. Peng Z, Wang S, Huang X, et al. Effect of hyperbaric oxygen therapy on patients with herpes zoster. *Undersea Hyperb Med.* 2012;39(6):1083-7. PMID: 23342765
44. Alter IL, Hamiter M, Han J, et al. Hyperbaric Oxygen and Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-Analysis. *Laryngoscope.* 2025. PMID: 40747804
45. Joshua TG, Ayub A, Wijesinghe P, et al. Hyperbaric Oxygen Therapy for Patients With Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis. *JAMA Otolaryngol Head Neck Surg.* 2022;148(1):5-11. PMID: 34709348
46. Eryigit B, Ziylan F, Yaz F, et al. The effectiveness of hyperbaric oxygen in patients with idiopathic sudden sensorineural hearing loss: a systematic review. *Eur Arch Otorhinolaryngol.* 2018;275(12):2893-904. PMID: 30324404
47. Rhee TM, Hwang D, Lee JS, et al. Addition of Hyperbaric Oxygen Therapy vs Medical Therapy Alone for Idiopathic Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis. *JAMA Otolaryngol Head Neck Surg.* 2018;144(12):1153-61. PMID: 30267033
48. Bennett MH, Kertesz T, Perleth M, et al. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. *Cochrane Database Syst Rev.* 2012;10:Cd004739. PMID: 23076907
49. Cavaliere M, De Luca P, Scarpa A, et al. Combination of Hyperbaric Oxygen Therapy and Oral Steroids for the Treatment of Sudden Sensorineural Hearing Loss: Early or Late? *Medicina (Kaunas).* 2022;58(10). PMID: 36295581
50. McCurdy J, Siw KCK, Kandel R, et al. The Effectiveness and Safety of Hyperbaric Oxygen Therapy in Various Phenotypes of Inflammatory Bowel Disease: Systematic Review With Meta-analysis. *Inflamm Bowel Dis.* 2022;28(4):611-21. PMID: 34003289

51. Singh AK, Jha DK, Jena A, et al. Hyperbaric oxygen therapy in inflammatory bowel disease: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol.* 2021. PMID: 33905214
52. McCurdy J, Siw KCK, Kandel R, et al. The Effectiveness and Safety of Hyperbaric Oxygen Therapy in Various Phenotypes of Inflammatory Bowel Disease: Systematic Review With Meta-analysis. *Inflamm Bowel Dis.* 2021. PMID: 34003289
53. Dulai PS, Gleeson MW, Taylor D, et al. Systematic review: The safety and efficacy of hyperbaric oxygen therapy for inflammatory bowel disease. *Alimentary pharmacology & therapeutics.* 2014;39(11):1266-75. PMID: 24738651
54. Pagoldh M, Hultgren E, Arnell P, et al. Hyperbaric oxygen therapy does not improve the effects of standardized treatment in a severe attack of ulcerative colitis: a prospective randomized study. *Scandinavian journal of gastroenterology.* 2013;48(9):1033-40. PMID: 23879825
55. Ioppolo F, Tattoli M, Di Sante L, et al. Clinical improvement and resorption of calcifications in calcific tendinitis of the shoulder after shock wave therapy at 6 months' follow-up: a systematic review and meta-analysis. *Archives of physical medicine and rehabilitation.* 2013;94(9):1699-706. PMID: 23499780
56. Van Voorhis BJ, Greensmith JE, Dokras A, et al. Hyperbaric oxygen and ovarian follicular stimulation for in vitro fertilization: a pilot study. *Fertil Steril.* 2005;83(1):226-8. PMID: 15652917
57. (CADTH) CAfDaTiH. Hyperbaric Oxygen Therapy for Adults with Mental Illness: A Review of the Clinical Effectiveness. 2014. . PMID:
58. Bennett M, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. *CNS Neurosci Ther.* 2010;16(2):115-24. PMID: 20415839
59. Huang C, Zhong Y, Yue C, et al. The effect of hyperbaric oxygen therapy on the clinical outcomes of necrotizing soft tissue infections: a systematic review and meta-analysis. *World J Emerg Surg.* 2023;18(1):23. PMID: 36966323
60. Levett D, Bennett MH, Millar I. Adjunctive hyperbaric oxygen for necrotizing fasciitis. *Cochrane Database Syst Rev.* 2015;1(1):Cd007937. PMID: 25879088
61. Hedetoft M, Bennett MH, Hyldegaard O. Adjunctive hyperbaric oxygen treatment for necrotising soft-tissue infections: A systematic review and meta-analysis. *Diving and hyperbaric medicine : the journal of the South Pacific Underwater Medicine Society.* 2021;51(1):34-43. PMID: 33761539
62. Savvidou OD, Kaspiris A, Bolia IK, et al. Effectiveness of Hyperbaric Oxygen Therapy for the Management of Chronic Osteomyelitis: A Systematic Review of the Literature. *Orthopedics.* 2018;41(4):193-99. PMID: 30035798
63. Maynor ML, Moon RE, Camporesi EM, et al. Chronic osteomyelitis of the tibia: treatment with hyperbaric oxygen and autogenous microsurgical muscle transplantation. *Journal of the Southern Orthopaedic Association.* 1998;7(1):43-57. PMID: 9570731
64. Davis JC, Heckman JD, DeLee JC, et al. Chronic non-hematogenous osteomyelitis treated with adjuvant hyperbaric oxygen. *The Journal of bone and joint surgery American volume.* 1986;68(8):1210-7. PMID: 3771602
65. Chen CE, Ko JY, Fu TH, et al. Results of chronic osteomyelitis of the femur treated with hyperbaric oxygen: a preliminary report. *Chang Gung medical journal.* 2004;27(2):91-7. PMID: 15095953
66. Chen CE, Shih ST, Fu TH, et al. Hyperbaric oxygen therapy in the treatment of chronic refractory osteomyelitis: a preliminary report. *Chang Gung medical journal.* 2003;26(2):114-21. PMID: 12718388

67. Chen CY, Lee SS, Chan YS, et al. Chronic refractory tibia osteomyelitis treated with adjuvent hyperbaric oxygen: a preliminary report. *Changgeng yi xue za zhi / Changgeng ji nian yi yuan = Chang Gung medical journal / Chang Gung Memorial Hospital.* 1998;21(2):165-71. PMID: 9729650
68. Yang TK, Wang YJ, Li HJ, et al. Efficacy and Safety of Hyperbaric Oxygen Therapy for Radiation-Induced Hemorrhagic Cystitis: A Systematic Review and Meta-Analysis. *J Clin Med.* 2024;13(16). PMID: 39200867
69. Borab Z, Mirmanesh MD, Gantz M, et al. Systematic review of hyperbaric oxygen therapy for the treatment of radiation-induced skin necrosis. *Journal of plastic, reconstructive & aesthetic surgery : JPRAS.* 2017;70(4):529-38. PMID: 28081957
70. Hoggan BL, Cameron AL. Systematic review of hyperbaric oxygen therapy for the treatment of non-neurological soft tissue radiation-related injuries. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer.* 2014;22(6):1715-26. PMID: 24794980
71. Spiegelberg L, Djasim UM, van Neck HW, et al. Hyperbaric oxygen therapy in the management of radiation-induced injury in the head and neck region: a review of the literature. *Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons.* 2010;68(8):1732-9. PMID: 20493616
72. Teguh DN, Levendag PC, Noever I, et al. Early hyperbaric oxygen therapy for reducing radiotherapy side effects: early results of a randomized trial in oropharyngeal and nasopharyngeal cancer. *Int J Radiat Oncol Biol Phys.* 2009;75(3):711-6. PMID: 19386439
73. Gothard L, Haviland J, Bryson P, et al. Randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema after radiotherapy for cancer. *Radiother Oncol.* 2010;97(1):101-7. PMID: 20605648
74. Lin ZC, Bennett MH, Hawkins GC, et al. Hyperbaric oxygen therapy for late radiation tissue injury. *Cochrane Database Syst Rev.* 2023;8(8):Cd005005. PMID: 37585677
75. Bennett MH, Wasiak J, Schnabel A, et al. Hyperbaric oxygen therapy for acute ischaemic stroke. *Cochrane Database Syst Rev.* 2005(3):CD004954. PMID: 16034959
76. Carson S, McDonagh M, Russman B, et al. Hyperbaric oxygen therapy for stroke: a systematic review of the evidence. *Clin Rehabil.* 2005;19(8):819-33. PMID: 16323381
77. Efrati S, Fishlev G, Bechor Y, et al. Hyperbaric oxygen induces late neuroplasticity in post stroke patients--randomized, prospective trial. *PloS one.* 2013;8(1):e53716. PMID: 23335971
78. Harch PG. Systematic Review and Dosage Analysis: Hyperbaric Oxygen Therapy Efficacy in Mild Traumatic Brain Injury Persistent Postconcussion Syndrome. *Front Neurol.* 2022;13:815056. PMID: 35370898
79. Alashram AR, Padua E, Romagnoli C, et al. Hyperbaric oxygen therapy for cognitive impairments in patients with traumatic brain injury: A systematic review. *Appl Neuropsychol Adult.* 2022:1-12. PMID: 35213282
80. Hart BB, Weaver LK, Gupta A, et al. Hyperbaric oxygen for mTBI-associated PCS and PTSD: Pooled analysis of results from Department of Defense and other published studies. *Undersea Hyperb Med.* 2019;46(3):353-83. PMID: 31394604
81. Wang F, Wang Y, Sun T, et al. Hyperbaric oxygen therapy for the treatment of traumatic brain injury: a meta-analysis. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology.* 2016;37(5):693-701. PMID: 26746238

82. Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. *Cochrane Database Syst Rev.* 2012;12:CD004609. PMID: 23235612
83. Hadanny A, Catalogna M, Yaniv S, et al. Hyperbaric oxygen therapy in children with post-concussion syndrome improves cognitive and behavioral function: a randomized controlled trial. *Scientific reports.* 2022;12(1):15233. PMID: 36151105
84. Wolf G, Cifu D, Baugh L, et al. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. *Journal of neurotrauma.* 2012;29(17):2606-12. PMID: 23031217
85. Idris OA, Ahmedfiqi YO, Shebrain A, et al. Hyperbaric Oxygen Therapy for Complications in Nipple-Sparing Mastectomy with Breast Reconstruction: A Systematic Review. *J Clin Med.* 2024;13(12). PMID: 38930063
86. Keohane C, Westby D, Nolan FC, et al. Hyperbaric Oxygen as an Adjunct in the Treatment of Venous Ulcers: A Systematic Review. *Vasc Endovascular Surg.* 2023;57(6):607-16. PMID: 36891617
87. Eskes A, Vermeulen H, Lucas C, et al. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. *Cochrane Database Syst Rev.* 2013;12:CD008059. PMID: 24343585
88. Kranke P, Bennett M, Roeckl-Wiedmann I, et al. Hyperbaric oxygen therapy for chronic wounds. *Cochrane Database Syst Rev.* 2004(2):CD004123. PMID: 15106239
89. Vishwanath G. Hyperbaric oxygen therapy in free flap surgery: Is it meaningful?. Medical Journal Armed Forces India 2011;67(3):253–6. No PMID Entry.
90. Perrins DJ. Influence of hyperbaric oxygen on the survival of split skin grafts. *Lancet.* 1967;1(7495):868-71. PMID: 4164367
91. Rompe JD, Decking J, Schoellner C, et al. Repetitive low-energy shock wave treatment for chronic lateral epicondylitis in tennis players. *Am J Sports Med.* 2004;32(3):734-43. PMID: 15090392
92. Bouachour G, Cronier P, Gouello JP, et al. Hyperbaric oxygen therapy in the management of crush injuries: a randomized double-blind placebo-controlled clinical trial. *The Journal of trauma.* 1996;41(2):333-9. PMID: 8760546
93. Pettrone FA, McCall BR. Extracorporeal shock wave therapy without local anesthesia for chronic lateral epicondylitis. *The Journal of bone and joint surgery American volume.* 2005;87(6):1297-304. PMID: 15930540
94. Sharma R, Sharma SK, Mudgal SK, et al. Efficacy of hyperbaric oxygen therapy for diabetic foot ulcer, a systematic review and meta-analysis of controlled clinical trials. *Scientific reports.* 2021;11(1):2189. PMID: 33500533
95. O'Reilly D, Pasricha A, Campbell K, et al. Hyperbaric oxygen therapy for diabetic ulcers: systematic review and meta-analysis. *International journal of technology assessment in health care.* 2013;29(3):269-81. PMID: 23863187
96. Hammarlund C, Sundberg T. Hyperbaric oxygen reduced size of chronic leg ulcers: a randomized double-blind study. *Plast Reconstr Surg.* 1994;93(4):829-33; discussion 34. PMID: 8134442
97. Hyperbaric Oxygen Therapy: Get the Facts. [cited 10/31/2024]. 'Available from:' https://www.fda.gov/consumers/consumer-updates/hyperbaric-oxygen-therapy-get-facts.
98. Gesell LBE. Hyperbaric oxygen therapy indications, 12th Edition. The Hyperbaric Oxygen Therapy Committee Report.: Undersea and Hyperbaric Medical Society, 2008.
99. Huang ET, Mansouri J, Murad MH, et al. A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers. *Undersea Hyperb Med.* 2015;42(3):205-47. PMID: 26152105

100. UHMS UaHMS. Hyperbaric Oxygen Therapy Indications. [cited 11/04/2024]. 'Available from:' https://www.uhms.org/images/UHMS-Reference-Material.pdf.
101. Gunduz R, Malas FU, Borman P, et al. Physical therapy, corticosteroid injection, and extracorporeal shock wave treatment in lateral epicondylitis. Clinical and ultrasonographical comparison. *Clinical rheumatology.* 2012;31(5):807-12. PMID: 22278162
102. Murphy-Lavoie H, Piper S, Moon RE, et al. Hyperbaric oxygen therapy for idiopathic sudden sensorineural hearing loss. *Undersea Hyperb Med.* 2012;39(3):777-92. PMID: 22670557
103. Feldmeier JJ, Hopf HW, Warriner RA, 3rd, et al. UHMS position statement: topical oxygen for chronic wounds. *Undersea Hyperb Med.* 2005;32(3):157-68. PMID: 16119307
104. Chandrasekhar SS, Tsai Do BS, Schwartz SR, et al. Clinical Practice Guideline: Sudden Hearing Loss (Update). *Otolaryngol Head Neck Surg.* 2019;161(1_suppl):S1-s45. PMID: 31369359
105. Peterson DE, Koyfman SA, Yarom N, et al. Prevention and Management of Osteoradionecrosis in Patients With Head and Neck Cancer Treated With Radiation Therapy: ISOO-MASCC-ASCO Guideline. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2024;42(16):1975-96. PMID: 38691821

CODES

Codes	Number	Description
CPT	99183	Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session Note: This code is not intended for reporting systemic oxygen therapy in chambers that provide oxygen at less than hyperbaric pressure (eg, “mild hyperbaric” oxygen therapy) which should be reported using code 99199.
	99199	Unlisted special service, procedure or report
HCPCS	A4575	Topical hyperbaric oxygen chamber, disposable
	E0446	Topical oxygen delivery system, not otherwise specified, includes all supplies and accessories NOTE: This code is intended for devices such as the TransCu 02 that deliver oxygen at normal atmospheric pressure under wound dressings; it should not be used to report topical hyperbaric oxygen therapy devices.
	E1399	Durable medical equipment, miscellaneous
	G0277	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval

Date of Origin: *January 1996*