Technology Assessment

Technology Assessment Program

A Horizon Scan: Uses of Hyperbaric Oxygen Therapy

Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, Maryland 20850

October 5, 2006

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This report is based on research conducted by the Tufts-New England Medical Center Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-02-0022). The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decision-makers; patients and clinicians, health system leaders, and policymakers, make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Introduction

The Centers for Medicare & Medicaid Services (CMS) has requested the Tufts-New England Medical Center Evidence-based Practice Center (Tufts-NEMC EPC) to conduct a "horizon scan" on the uses of hyperbaric oxygen therapy (HBOT). There are several technology assessments (TA) available for HBOT in wound care and other well-established therapeutic indications. This review is intended to inform CMS of existing and emerging applications of HBOT. As such, this report is a limited systematic review of the literature. It does not synthesize the results or critically appraise individual clinical studies.

Patients undergoing HBOT typically breathe 100% oxygen at a pressure of about 2 to 2.5 atmospheric absolute (ATA). An ATA is defined as the atmospheric pressure at sea level that is equivalent to 101.3 kilo Pascals per square inch. There are two types of chambers – a monoplace chamber or a multiplace chamber – for administering HBOT. In a monoplace chamber only one patient undergoes HBOT, while a multiplace chamber can hold multiple patients and/or medical personnel. HBOT is typically used for treatment of wounds, carbon monoxide (CO) poisoning, and clostridial gas gangrene. The HBOT technique uses systemic blood flow to deliver high concentrations of oxygen to tissues. The treatment duration can vary from 45 to 300 minutes, although a typical HBOT session ranges from 90 to 120 minutes.(1)

Key Questions

This report summarizes the published uses of HBOT in the adult population identified through a systematic literature search. Key questions addressed in this report are:

1. What are the uses of HBOT in the adult population?

2. What kind of evidence (the type and quantity) is available for each use (e.g., systematic reviews with or without meta-analyses, randomized controlled trials (RCT), prospective studies and other)? Case reports of novel uses (i.e., not covered by RCTs or cohort studies) should also be included.
3. What are the overall conclusions reported in systematic reviews? (Include meta-analysis estimate of effect when available).

Methods

We conducted a comprehensive search of the scientific literature to identify relevant studies addressing the key questions. The intent of this review was not to assess the quality of individual studies or to analyze their results. We identified the uses of HBOT in the adult population using the following algorithm (Figure 1):

1. We first searched the websites of CMS, Undersea and Hyperbaric Medical Society (UHMS), and healthcare insurers such as Aetna, Blue Cross and Blue Shield, and CIGNA to come up with an initial list of the covered and non-covered uses of HBOT.
2. We supplemented this list by searching published TAs, systematic reviews and clinical trials that assessed the uses of HBOT.
3. Finally we searched case reports and textbooks for any new uses that were not addressed in RCTs and observational studies

The result of the above search is shown in Table 1. For Question 2, we tallied the number and type of studies for each of the HBOT uses we identified in Question 1, also shown in Table 1. In addition to the summary table, we provided a brief narrative text describing the evidence as reported in these studies for each of the outcomes. For Question 3, we searched for the overall conclusions and estimate of effect, if available, as reported in the systematic reviews and/or RCTs. Because HBOT for CO poisoning and wounds are already covered by CMS, in discussions with CMS and AHRQ, it was decided to include a brief narrative review of the literature on these topics.

Literature Search Strategy

We searched MEDLINE (1966 to December, 2005) for studies of adults in English language to identify articles relevant to each key question. We conducted a supplemental search of the Cochrane Database of Systematic Reviews, National Guidelines Clearinghouse, other appropriate databases for any evidence-based guidelines, and AHRQ databases of technology assessments. We also searched reference lists of selected review articles and textbook chapters on HBOT. In searches of electronic databases, we combined terms for hyperbaric oxygen and relevant research designs (see Appendix A for complete search strategy).

Selection criteria

We included studies of any size and study designs including systematic reviews with or without meta-analysis, RCT, non-randomized comparative studies, cohort studies, case-control studies, and retrospective case series. We included studies reporting any clinical endpoint and intermediate outcomes. Case reports for novel uses of HBOT i.e., not covered by RCTs or cohort studies were also included. For the section on the wounds, we updated studies published after August 2001, the date of the last literature search of the previous Tufts-NEMC EPC TA on HBOT in treatment of hypoxic wounds. We excluded studies that evaluated HBOT in healthy human volunteers and protocols of systematic reviews, and RCTs that evaluated no human subjects. We excluded from analysis studies of well-established indications of HBOT, these included decompression illnesses and air and gas embolism. The adverse events of HBOT were beyond the scope of this report. Studies exclusively of topical HBOT were also excluded. We did not include foreign language publications whose abstracts were indexed in English language. Also excluded were narrative reviews, published commentaries, and letters.

Data abstraction and synthesis

Results from previously conducted TAs and systematic reviews on these topics were sought and used where appropriate. In addition, qualitative reviews on the specific topics from individual studies were conducted. Evidence tables of study characteristics and relevant results were compiled to summarize the uses of HBOT. Because the aim of this report was to identify reported uses of HBOT, individual studies were not critically appraised to determine the validity of their results or conclusions. Items extracted included first author, publication year, country where the study was conducted, study design, number of patients enrolled in the study, topic of the study, and application of the HBOT. For systematic reviews we recorded the overall conclusions and estimate of effect when available. The estimate of effect from any new studies of RCTs identified in our search was also described. Results of data extraction were presented in structured evidence tables (Appendix D) and also as a narrative description.

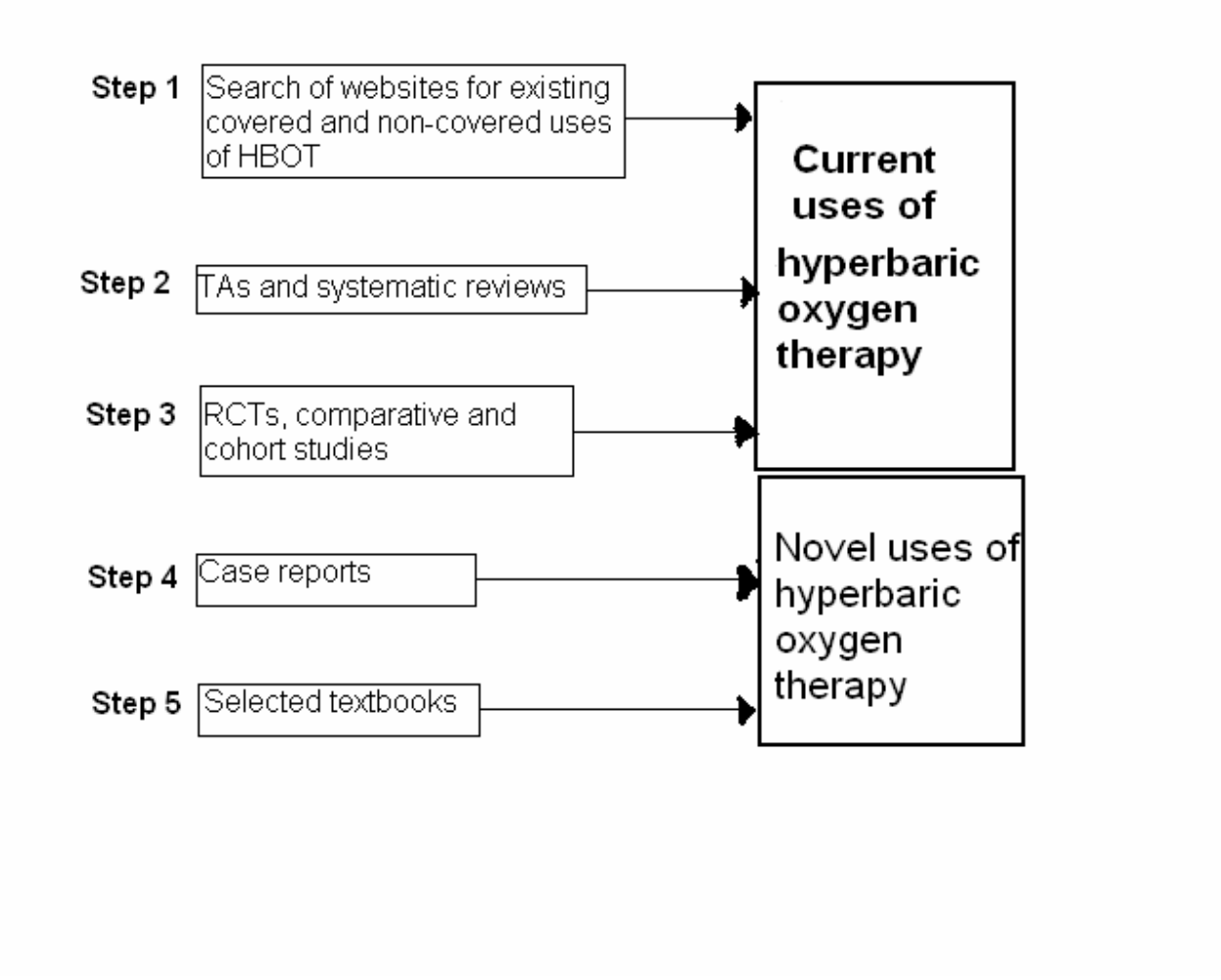

Figure 1. Horizon Scan of hyperbaric oxygen therapy (HBOT). Steps to identify uses of HBOT. Arrows depict studies sought to address key questions.

Results

Fifteen applications of HBOT in the adult population are listed by CMS as usual care and adjunctive therapy for the approval status of reimbursement of applications (Table 1); in addition, 59 non-covered uses of HBOT that were either listed by one or more healthcare organizations and/or identified in the literature (Table 2). Additional uses were identified by a systematic literature search. We identified a total of 10 TAs, 24 systematic reviews (32 publications), 88 RCTs, 95 comparative and cohort studies and 69 case reports that assessed the uses of HBOT.

Table 1. CMS covered uses of hyperbaric oxygen therapy. The number and type of studies found through systematic literature search are shown.

Uses of HBOT [1]	Use status as indicated by one or more healthcare provider	Number of studies found			
		Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies
Actinomycosis[3]	Adjunct care				
Acute air or gas embolism	Standard care				
Carbon Monoxide poisoning	Standard care	4	3	6	13
Cyanide poisoning	Standard care				
Decompression illness	Standard care				
Wounds (total number of studies after yr 2001)	Standard/adjunct	4	8	6	25
Acute traumatic peripheral ischemia	Adjunct care				
Crush injuries and suturing of severed limbs	Adjunct care				
Acute peripheral arterial insufficiency	Standard care				
Compromised skin grafts	Standard care				
Gas gangrene	Standard care				
Progressive necrotizing infections	Standard care				
Chronic refractory osteomyelitis	Standard care				
Osteoradionecrosis	Adjunct care				
Soft tissue radionecrosis	Adjunct care				
Non healing diabetic ulcers	Adjunct care				
Lower wound extremities	Adjunct care				

CMS, The Center for Medicare and Medicaid Services; HBOT, hyperbaric oxygen therapy; RCT, randomized controlled trial
HBOT is widely accepted as standard clinical care in the management of life threatening conditions such as decompression illness and air or gas embolism for which there are limited alternative treatment options.

[1] Identified by one or more healthcare providers
[2] Inclusive of studies found in systematic review and identified by systematic literature search
[3] Refractory to antibiotics and surgical treatment

Table 2. The non-covered uses of hyperbaric oxygen therapy listed by one or more healthcare organizations and identified in the literature. The number and type of studies found through systematic literature search are shown.

Uses of HBOT [1]	Use status as indicated by one or more healthcare provider	Number of studies found			
		Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies
Acute coronary syndrome	Experimental	2	1	5	0
Acute or chronic cerebrovascular insufficiency	Experimental	3	3	4	6
Acute cerebral edema (traumatic brain injury)	Medically necessary[3]	1	3	3	8
Acute renal artery insufficiency	Experimental	0	0	0	0
Acute thermal and chemical pulmonary damage	Experimental	0	0	0	0
Actinic skin damage	Experimental	0	0	0	0
Aerobic septicemia	Experimental	0	0	0	0
Anerobic septicemia - infection other than clostridial	Experimental	0	0	0	0
Arthritic diseases	Experimental	0	0	0	0
Avascular necrosis of the femoral head	Experimental	1	0	0	1
Blood loss (exceptional) or anemia[4]	Recognized[5]	1	0	0	1
Bone grafts or fracture healing	Experimental	0	0	1	0
Cancer	Experimental	1	1	19	1
Cardiogenic shock	Experimental	0	0	0	0
Closed head and/or spinal cord injury	Experimental	0	0	1	3
Chemical poisoning	Experimental	0	0	0	0
Crohn's disease	Experimental	1	0	0	0
Cystic acne	Experimental	0	0	0	0
Dental implants after irradiation	Not stated	1	0	0	8
Facial palsy	Experimental	1	0	1	0
Fibromyalgia	Not stated	0	0	1	0
Fungal infection	Not stated	0	0	0	4
Headaches including migraine or cluster	Experimental	1	0	4	3
Hearing disorders[6]:	Medically necessary[7]	2	1	7	10
Hepatic necrosis	Experimental	0	0	0	0
HIV infection	Experimental	0	0	0	0
Interstitial cystitis	Experimental	0	0	1	0
Intracranial abscess	Recognized[8]	0	0	0	0
Intra-abdominal abscess	Experimental	0	0	0	0
Lepromatous leprosy	Experimental	0	0	0	0
Liver post-operative	Not stated	0	0	1	0
Lyme disease	Experimental	0	0	0	0
Melasma	Experimental	0	0	0	0
Meningitis	Experimental	0	0	0	0
Multiple sclerosis	Experimental	1	2	11	3
Necrotizing arachnidism	Experimental	0	0	0	0
Non diabetic ulcers[9],	Recognized[10]	3	1	1	0

[1] Identified by one or more healthcare providers and in our literature search
[2] Inclusive of studies found in systematic review and identified by systematic literature search
[3] Listed by Aetna
[4] Transfusion impossible
[5] Listed by Aetna, the Undersea and Hyperbaric Medical Society (UHMS)
[6] Includes Idiopathic sudden deafness, acoustic trauma, or noise induced hearing loss
[7] Listed by Aetna
[8] Listed by UHMS
[9] Includes cutaneous, decubitus, and stasis ulcers, chronic peripheral vascular insufficiency
[10] Listed by UHMS

Table 2. The non-covered uses of hyperbaric oxygen therapy listed by one or more healthcare organizations and identified in the literature. (continued)

Uses of HBOT [1]	Use status as indicated by one or more healthcare provider	Number of studies found			
		Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies
Non vascular causes of chronic brain syndrome [3]	Experimental	0	0	0	0
Ophthalmologic diseases	Experimental	0	0	3	2
Opium poisoning	Not stated	0	0	1	0
Organ transplantation	Experimental	0	0	0	0
Osteoporosis	Experimental	0	0	0	0
Periodonitis	Not stated	0	0	1	0
Pneumatosis cystoides intestinalis	Medically necessary[4]	0	0	0	1
Post traumatic complex regional pain syndrome	Not stated	0	0	1	0
Pulmonary emphysema	Experimental	0	0	0	1
Pyoderma gangrenosum	Experimental	0	0	0	0
Reconstructive surgery	Experimental	0	0	0	1
Reflex sympathetic dystrophy	Experimental	0	0	0	0
Senility (cognitive impairment)	Experimental	0	0	1	0
Sickle cell anemia	Experimental	0	0	0	0
Skin burns (thermal)	Recognized[5]	3	2	3	2
Sports injuries	Not stated	0	1	4	1
Systemic aerobic infection	Experimental	0	0	0	0
Sickle cell crisis or hematuria	Experimental	0	0	0	0
Tetanus	Experimental	0	0	0	0
Tinnitus	Experimental	0	0	0	1
Trauma acoustic	Not stated	0	0	1	0
Viral hepatitis	Not stated	0	0	1	0

[1] Identified by one or more healthcare providers and in our literature search
[2] Inclusive of studies found in systematic review and identified by systematic literature search
[3] Pick's, Alzheimer's disease
[4] Listed by Aetna
[5] Listed by UHMS

CMS Covered uses of HBOT

In this section, we describe the literature that evaluated uses of HBOT currently covered by CMS. Information presented here are as reported by the studies' authors.

Carbon monoxide (CO) poisoning

Technology assessment reports

Four TA reports that summarized evidence for the use of HBOT in the treatment of carbon monoxide poisoning included (2-5): 1) Succinct and Timely Evaluated Evidence Review (STEER) 2002 (UK) by Dent; 2) Quẻbec AẺTMIS Canada 2001 report; 3) The Australian Medical Services Advisory Committee (MSAC) 2000 report; and 4) Alberta Heritage Foundation for Medical Research (AHFMR) 1998 (Canada) report.

The STEER and the MSAC TA reports evaluated the uses and efficacy of HBOT for CO poisoning;(2;4) both assessed results of one systematic review.(6) Juurlink assessed six RCTs involving adults acutely poisoned with CO, regardless of severity. The pooled data from the three eligible trials found that non-specific neurological symptoms (e.g., headache, confusion, difficulty concentrating, and sleep disturbances) were present in 34% of the patients in the HBOT group compared to 37% in the non-HBOT group.(7-9) The reports conclude that HBOT use in CO poisoning had insufficient and conflicting evidence. The Steer TA report by Dent also included an update of the systematic review with one additional RCT that found beneficial short and long-term effect of HBOT in reducing the cognitive sequelae in CO poisoning. The result remained non-significant after adding the fourth RCT (odds ratio [OR] 0.68, 95% CI 0.40 to 1.16).(10)

The AĖTMIS TA report assessed two RCTs and three non-randomized comparative trials. The report concluded that level of quantity and quality of scientific evidence was low, but it concluded that the use of HBOT in the treatment of CO poisoning was supported by the clinical results and experimental data.(3)

The fourth TA report (Alberta) examined the effectiveness of HBOT for CO poisoning from one RCT and four non-randomized comparative trials.(5) The report concluded that the literature provided disparate views on the effectiveness of treating CO poisoning with HBOT, and the one best-quality study did not indicate that the majority of CO poisoned patients should be treated with HBOT.

Systematic reviews

Three systematic reviews assessed evidence for the use of HBOT in the treatment of CO poisoning.

Juurlink updated their systematic review, previously published in 2000.(11) No new RCTs were added to or analyzed for this 2005 and 2006 update. Meta-analysis of seven RCTs did not suggest any benefit from HBOT (Odds ratio (OR) for neurological benefits 0.78, 95% CI 0.54 to 1.12). The authors concluded that additional research is necessary to define the role of HBOT in the treatment of patients with CO poisoning.

Saunders assessed the results of four RCTs and the published interim results of two other RCTs.(12) The review concluded that there was no compelling evidence for the beneficial effect of HBOT in the management of either moderately or severely CO poisoned patients.

Tibbles analyzed six comparative studies of HBOT versus non-HBOT in “a critical review of human outcome studies” that favored some support for HBOT.(13)

Individual studies

We did not identify any new RCTs other than the six reviewed in the systematic review. Four of the six RCTs found that HBOT delayed or reduced the risk of neurological or cognitive sequelae, and one RCT found an increased risk of minor neurological symptoms. This latter study also reported that 91% of HBOT subjects with isolated headaches recovered compared to 50% of the controls. The sixth stated that HBOT could be used for acute CO intoxication in pregnant women.

Wounds

This section is an update of the literature on ten diagnostic specific wounds (acute and non-acute) previously addressed in the Tufts-NEMC TA report and includes TAs, systematic reviews and individual studies published after August 2001.(14)

Technology assessment reports

Four TA reports that were published after 2001 summarized evidence for the use of HBOT in the treatment of wounds.(3;15-17) These included: 1) Ontario Health Technology Advisory Committee 2005 (Canada), 2) The 2003 Australian MSAC report, 3) STEER 2003 (UK) by Lawson, and 4) Quebec AĖTMIS 2001.

The Ontario TA report assessed the uses and efficacy of HBOT for ulcers due to diabetes, compared to other therapies. The authors summarized the results from four recent TA reports and one systematic review. The report concluded that the quality of evidence assessing the

effectiveness of HBOT as an adjunct to standard therapy for people with non-healing diabetic ulcers is low with inconsistent results.

The MSAC 2003 TA report assessed the uses and efficacy of HBOT for refractory soft tissue radiation injuries from the results of one systematic review, four RCTs, and two nonrandomized comparative trials. The systematic review by Feldmeier in 2002 found the clinical evidence "likely to be beneficial." One of the four RCTs that examined HBOT for cognitive impairment following brain irradiation showed no significant improvement in neuropsychological function. A second RCT assessed HBOT for radiation-induced brachial plexopathy and showed no significant differences in sensory thresholds or quality of life between those receiving HBOT and controls. A third RCT showed that HBOT improved wound healing in patients at high risk of osteoradionecrosis. The fourth RCT showed that HBOT reduced the likelihood of major wound infection, major wound dehiscence, and delayed wound healing in myocutaneous grafts in patients who had previously undergone radiation therapy. The report concluded that the clinical evidence was inadequate and of insufficient quality to substantiate claims that HBOT was cost effective in the treatment of refractory soft tissue radiation injuries.

The STEER TA report analyzed two systematic reviews, neither of which contained any relevant RCTs evaluating HBOT for the treatment of osteomyelitis.

The Quebec TA report assessed two RCTs and two nonrandomized comparative trials, and concluded that HBOT was an accelerating factor in cases of complete healing of radiation therapy-induced tissue and bony necrosis with promising results for soft-tissue necrosis.

Systematic reviews

Eight systematic reviews published after 2001 assessed the evidence for the use of HBOT in the treatment of wounds.(12;18-24)

Bennett assessed six RCTs.(18) There was a significantly improved chance of healing following HBOT for radiation proctitis (Risk ratio [RR] 2.7, 95% CI 1.2 to 6.0) and following both surgical flaps (RR 8.7, 95% CI 2.7 to 27.5) and hemimandibulectomy (RR 1.4, 95% CI 1.1 to 1.8). There was also a significantly improved probability of healing irradiated tooth sockets following dental extraction (RR 1.4, 95% CI 1.1 to 1.7). There was no evidence of benefit in clinical outcomes with established radiation injury to neural tissue, and no data reported on the use of HBOT to treat other manifestations of late radiation injury affecting tissues of the head, neck, anus and rectum.

Denton assessed four retrospective case series and one prospective observational study in the use of HBOT for perineal and vaginal radiation injuries.(19) In one study, eight of the 12 patients with vaginal vault or perineal necrosis showed marked or complete healing. In a second study of 12 patients, there was no response or even partial healing. There was treatment failure in the third study of 14 patients. The response rate in the fourth study showed a positive response rate of eight of 12 patients with HBOT as an adjunct treatment for delayed radiation injuries of the abdomen and pelvis. The review concluded that the evidence was weak and the studies were not recent, and the treatment response was variable.

Roeckl-Wiedmann included six RCTs evaluating HBOT for chronic wounds and found no appropriate trials were identified for arterial or pressure ulcers.(23) Pooled data from five trials on diabetic ulcers (118 patients) suggested a significant reduction in the risk of major amputation with HBOT (RR=0.31, 95% CI 0.13 to 0.71). The authors concluded that there was no evidence of the effectiveness of HBOT for wound healing in general (except for diabetic ulcers), or for the prevention of minor amputation.

Pasquier assessed approximately 30 studies of mixed and unclear design.(22) The authors concluded there was sufficient evidence from a large number of positive retrospective studies to support the use of HBOT combined with surgery in the treatment of mandibular osteonecrosis. A majority of studies including a few retrospective studies favored the use of HBOT in osteonecrosis of the head and neck; case reports of benefit for osteonecrosis of the skull, extremities, and pelvis have been reported. The review also concluded that HBOT has a beneficial effect in the management of laryngeal necrosis. Despite the lack of RCTs, the results of one prospective and nine retrospective studies suggest that HBOT is effective in patients with radiation cystitis. The authors concluded that the evidence to support the use of HBOT for patients using curative doses for cervical, prostate, and rectal cancers is weak. In myelitis, HBOT has shown to be effective only in one case report. Likewise, only retrospective studies are available for optic neuropathy and brain necrosis. The data from the literature concerning the efficacy of HBOT in the treatment of neurological side effects in radiotherapy is scarce (case reports and one small RCT). The authors concluded that the evidence of efficacy in the treatment of complications of the central nervous system is very weak and the negative results of the RCT do not therefore justify its use in the treatment of plexopathy.

The 2000 HBOT TA by Wang (Tufts-NEMC EPC) assessed seven TAs or systematic reviews, seven RCTs, 16 nonrandomized comparative trials, and 34 case series involving more than 2000 patients and recommended that more research needed to be done to assess the effectiveness of HBOT in diabetic patients.(24) The authors concluded that HBOT is beneficial as an adjunct therapy for patients with chronic refractory wounds. The TA found there was also sufficient objective evidence that HBOT aids in wound healing for compromised skin grafts,

osteoradionecrosis, gas gangrene, progressive necrotizing infections, and chronic non-healing wounds.

Saunders assessed the results of six RCTs and concluded that there was some evidence of benefit in the treatment of leg ulcers and gas gangrene but no convincing evidence of benefit for osteoradionecrosis, skin grafts, or crush injury.(12)

Johnston cited five small nonrandomized comparative trials but provided no analysis. (21) The authors stated without elaboration that there was some improvement in up to 65 % of patients with severe proctitis.

Feldmeier reviewed three RCTs, two nonrandomized comparative trials, and 69 case series to evaluate the efficacy of HBOT in treating delayed radiation injuries.(20) All but seven publications reported beneficial results for the use of HBOT in the treatment or prevention of radiation injuries. Specifically, the authors recommend HBOT for delayed radiation injuries for soft tissue or bony injuries of most sites: necrosis of the mandible, head and neck, chest wall and breast, abdominal wall and pelvic injuries, the nervous system, the extremities, radiation cystitis, proctitis and enteritis. The review concluded that an increasing body of evidence supports HBOT for radiation-induced necrosis of the brain.

Individual studies

We identified three new RCTs other than those cited in the most recent systematic review.(25-27) One RCT showed enhanced healing of ischemic diabetic leg ulcers, one other study showed a doubling of the mean healing rate of nonischemic diabetic foot ulcers, and the third study showed no benefit in patient with overt mandibular osteonecrosis. In addition we identified two nonrandomized comparative trials, eight prospective cohorts, and 15 retrospective studies.

Non-covered uses of HBOT

Acute coronary syndrome (ACS)

Technology assessment reports

Two TA reports (2;3) assessed the evidence for the use of HBOT in ACS including acute myocardial infarction (AMI) and angina: 1) Quebec AĖTMIS 2001, and 2) The 2000 Australian MSAC report.

The Quebec TA report assessed one RCT for MI and concluded there was insufficient evidence for the use of HBOT. The 2000 MSAC TA identified two RCTs, published 25 years apart with variations in patient criteria and outcomes. It concluded that there was no firm evidence to support the use of HBOT in AMI.

Systematic reviews

One systematic review assessed the evidence for the use of HBOT in ACS.(28) Bennett included four RCTs involving 462 patients with ACS. There was a non-significant trend of decreases in the risk of death with HBOT (RR=0.64, 95% CI 0.38 to 1.06) There was evidence from individual trials of reductions in the risk of major adverse coronary events (RR=0.12, 95% CI 0.02 to 0.85) and some dysrythmias following HBOT (RR=0.59, 95% CI 0.39 to 0.89), particularly complete heart block (RR=0.32, 95% CI 0.12 to 0.84). Time to relief from pain was reduced with HBOT (weighted mean difference 353 minutes shorter, 95% CI 219 to 488). The authors concluded against the routine application of HBOT in ACS.

Individual studies

We identified one new RCT (two articles) published by the Hyperbaric Oxygen and Thrombolysis (HOT) in AMI group that concluded no adjuvant benefit of HBOT on left ventricular diastolic filling in patients with AMI.(29;30)

Cerebrovascular disease

Technology assessment reports

Three TA reports (2;3;31) assessed evidence for the use of HBOT in acute ischemic stroke: 1) AHRQ Evidence report/TA by Oregon EPC (Publication No. 85, 2003), 2) Quebec AĖTMIS 2001, and 3) 2000 MSAC TA.

The Oregon EPC TA concluded that the evidence was insufficient to address mortality in any subgroup of stroke patients – there were no controlled trials available to assess this outcome. Three RCTs found no difference in neurological measures, but the fourth RCT and the nonrandomized comparative trial found that HBOT improved neurological outcomes. Most observational studies reported favorable results but failed to prove that these results could be attributed to HBOT; the authors concluded that the observational studies provided insufficient evidence to establish a clear relationship between physiological changes after sessions with HBOT and measures of clinical improvement.

The Quebec TA report assessed two RCTs and two case series, and concluded there was insufficient evidence to support the use of HBOT in cerebral ischemia.

The 2000 MSAC TA assessed the uses and efficacy of HBOT therapy for middle cerebral artery occlusion and ischemic cerebral infarction. For this indication, there were two RCTs that provided evidence. One study reported statistically significant differences at 1 year based on the

Orgogozo and Trouillas scores. The second trial reported significant improvements by the non HBOT group in a graded neurological scale sensitive to deficits referable to the region of the brain perfused by branches of the internal carotid artery. The authors concluded, on the basis of conflicting results, that there was "no firm and generalizable" evidence available to support the use of HBOT in cerebrovascular disease**.**

Systematic reviews

One systematic review assessed the evidence for the use of HBOT in acute ischemic stroke.(32) Bennett included three RCTs involving 106 patients who had acute ischemic stroke. There were no important differences in mortality rate at 6 months (RR=0.61, 95% CI 0.17 to 2.2). Only two of 15 scale measures of disability and functional scores indicated an improvement following HBOT, both at 1 year follow up: the mean Trouillas Disability Scale was lower (mean difference 2.2 points reduction, 95% CI 0.15 to 4.3) and the mean Orgogozo Scale was higher (mean difference 27.9, 95% CI 4.0 to 51.8). The authors concluded there was no evidence that HBOT improved clinical outcomes.

Individual studies

We identified no new studies.

Traumatic brain injury (TBI)

Technology assessment reports

One TA report – AHRQ Evidence/TA report by Oregon EPC in 2003 that assessed two RCTs and six observational studies for the use of HBOT in TBI.(31) One RCT provided fair evidence that HBOT might reduce mortality or the duration of coma in severely injured TBI

patients; however, HBOT also increased the chance of poor functional outcomes. A second fair-quality RCT found no differences in mortality or morbidity overall, but a significant reduction in one subgroup. The authors concluded that the evidence was conflicting and inconclusive.

Systematic reviews

Three systematic reviews assessed the evidence for the use of HBOT in TBI.(33-35)

Bennett included four RCTs to evaluate the use of HBOT: pooled data from three trials with 327 patients reported a significant reduction in mortality with HBOT (RR 0.69, 95% CI 0.54 to 0.88) and the numbers needed to analysis derived that seven patients would have to be treated to avoid one extra death. The authors concluded against the routine application of HBOT to patients with TBI.

McDonagh (who was also the principal investigator of the Oregon EPC technology assessment report) reviewed two fair-quality RCTs that reported conflicting morbidity and mortality results and five observational studies examining the short-term effect of HBOT on brain physiologic parameters such as intracranial pressure. The authors concluded that the evidence for use of HBOT for TBI was insufficient even though there is a small chance of a mortality benefit among selected subgroup of patients with TBI.

The third systematic review found no benefit for HBOT use in TBI from six RCTs and two case reports.(33)

Individual studies

We identified no new studies other than those reported in TAs and systematic reviews.

Cancers and tumor sensitization to radiotherapy

Technology assessment reports

One TA report that assessed the evidence for the use of HBOT in the treatment of cancers – Quebec AĖTMIS 2001. (3)

The Council on the Evaluation of Health Technologies assessed two RCTs for adjuvant use of HBOT in the cancer of the uterine cervix. The results of one trial showed no benefit while the other showed significant improvement of locally advanced tumors in patients less than 55 years of age. The authors found one RCT for adjuvant use of HBOT in the treatment of bladder cancer and the results showed no benefit. The authors found two RCTs for adjuvant use of HBOT in the treatment of head and neck cancer and concluded the following: the role of HBOT in head and neck cancer therapy is in the experimental stage.

Systematic reviews

Two systematic reviews assessed the evidence for the use of HBOT to improve the ability of radiotherapy to kill hypoxic cancer cells.(36;37)

Bennett included 19 trials involving 2286 patients of whom 785 had head and neck tumors, 1089 carcinoma of the cervix, and 343 carcinoma of the bladder. The others were dispersed over bronchus, glioblastoma, rectum, and esophagus. With HBOT, there was a reduction in mortality for head and neck tumors at both 1 (RR 0.83, 95% CI 0.70 to 0.98) and 5 years follow-up (RR .82, 95% CI 0.69 to 0.98) as well as improved local tumor control at the same periods. The local tumor recurrence was lower with HBOT in uterine cancer cervix at 2 years (RR 0.60, p=0.04, NNT=5). The effect of HBOT varied with different fractionation schemes. The authors

concluded there was some evidence that HBOT demonstrated benefit as an adjuvant for the treatment of certain cancers.

Widmark analyzed three RCTs in assessing the effectiveness of HBOT in combination with radiation therapy in urinary bladder cancer. The author concluded that HBOT did not improve the efficacy of radiotherapy in muscle invasive cancer compared to radiation in normal atmosphere.

Individual studies

We identified no new studies published after 1999 for the adjuvant treatment of HBOT in bladder, brain, breast, bronchus, cervical, GI, head and neck, or multiple sites cancers.

Headache

Technology assessment reports

Two TA reports (2;3;37) provided evidence for the use of HBOT in the treatment of headache: 1)Quebec AĖTMIS 2001 ; and 2) The Australian MSAC report 2000.

The Quebec TA and MSAC 2000 TA assessed the uses and efficacy of HBOT therapy for cluster headaches from two nonrandomized comparative trials that showed evidence of a beneficial effect on pain relief. Only one study, however, measured clear, clinically relevant outcome such as mean number of attacks. The authors concluded that the evidence was insufficient to support the use of HBOT. For the use of HBOT in migraine, there were two RCTs one of which found statistical significance for overall severity and the other statistical significance for pain using a visual analogue scale. The Quebec TA concluded that the evidence was insufficient to support the use of HBOT for this indication. The authors of MSAC 2000 TA

concluded that exposure to HBOT seems to provide pain relief, but more evidence was necessary.

Systematic reviews

We identified no systematic reviews.

Individual studies

We identified two new RCTs other than those included in the TAs.(38;39) Each RCT assessed a different outcome: one assessed the use of HBOT in migraine headache and found no significant reduction in hours of headache. The other RCT assessed cluster headache patients and found no difference between HBOT and sham in reducing the Headache Index and interrupting headache period.

Hearing disorders

Technology assessment reports

Two TA reports (2;3) assessed the evidence for the use of HBOT in sudden deafness, acoustic trauma, and tinnitus: 1) Quebec AĖTMIS 2001and 2) The Australian MSAC report 2000,.

The Quebec TA found a literature survey that analyzed 50 studies – the authors of the survey concluded that HBOT may have a beneficial effect in patients with the condition lasting less than 3 months' duration. Other case series advocated the use of HBOT in other chronic ear conditions. However, the TA concluded that in the absence of rigorous studies, they could draw no conclusion as to the efficacy of HBOT in these disorders.

The MSAC 2000 TA assessed the uses and efficacy of HBOT therapy for sudden deafness, acoustic trauma, and tinnitus. For these indications, there were two RCTs and two nonrandomized comparative trials that provided evidence. Only one study reported statistically significant improvements in average absolute gain in hearing but it was the only one that used a retrospective observational design. One study found that the HBOT intervention promoted recovery if therapy began within 72 hours. The other two studies found no differences. The authors concluded that the conflicting studies required more rigorous evidence, and thus could not support the use of HBOT in these conditions.

Systematic reviews

One systematic review assessed the evidence for the use of HBOT in sudden deafness, acoustic trauma, and tinnitus.(40)

Bennett included five RCTs involving 254 patients who had idiopathic sudden hearing loss. Pooled data from two trials suggested a trend towards, but no significant increase in, the chance of a 50% increase in hearing threshold on Pure Tone Average over 4 frequencies with HBOT. The chance of achieving a 25% increase was statistically significant (RR=1.39, 95% CI 1.05 to 1.84). Compared to 56% of control subjects, 78% of HBOT subjects achieved this outcome. Only one trial involving 50 patients also suggested a significant improvement in the mean PTA threshold expressed as percentage of baseline (62% improvement with HBOT versus 24% with control.) The effect in tinnitus could not be assessed due to poor reporting. In one study there was no significant improvement in hearing or tinnitus to examine the effect of HBOT on a chronic presentation (6 months). The authors concluded there was no evidence of a beneficial effect: routine application of HBOT cannot be justified.

Individual studies

We identified two new RCTs other than those included in the systematic review.(41;42) In addition, there were four nonrandomized comparative trials, one prospective cohort, and five retrospective studies. In the case of acute acoustic trauma, HBOT significantly improved hearing recovery. For hearing loss, two RCTs found significant improvement in hearing gains, and one study found no differences in recovery from cochlear vestibular symptoms.

Multiple sclerosis

Technology assessment reports

One TA report – Quebec AĖTMIS 2001 assessed the evidence for the use of HBOT in the treatment of multiple sclerosis(3) from three RCTs, all of which proved negative, and concluded that HBOT is ineffective in the treatment of multiple sclerosis.

Systematic reviews

Two systematic reviews assessed the evidence for the use of HBOT in the treatment of multiple sclerosis.(43;44)

Bennett updated the systematic review previously published in 2001. The authors identified ten reports of nine RCTs: two RCTs had generally positive results, while the remaining seven reported generally no evidence of a treatment effect. Three of 21 analyses indicated some benefit: for example, the mean Expanded Disability Status Scale (EDSS) at 12 months was improved with HBOT (group mean reduction compared to sham -0.85 of a point, 95% CI -1.28 to - 0.42). The authors concluded that there was no consistent evidence to confirm the beneficial effect of HBOT.

Kleijnen reviewed the evidence from thirteen RCTs and one nonrandomized comparative trial and concluded there was no justification for the use of HBOT in the treatment of multiple sclerosis.

Individual studies

We identified two more RCTs other than those included in the systematic reviews.(45;46) One trial showed symptomatic improvement in a majority of subjects, and one showed no difference between groups. In the third study there was no difference in the Functional System Scale but a slight trend for visual evoked potentials.

Non diabetic ulcers

Technology assessment reports

Three TA reports that provided evidence for the use of HBOT in the treatment of non-diabetic ulcers included:(2;3;15) 1) The Australian MSAC report 2003; 2) Quebec AĖTMIS 2001; 3) The Australian MSAC report 2000

These three TAs assessed the results from one small RCT. Exposure to HBOT was associated with a statistically significant decrease in the wound area at 4 and 6 weeks.
The Australian authors concluded that more studies were needed to provide more generalizable evidence; the Quebecois authors concluded that since the only rigorous study showed HBOT effective as an adjunct to conventional treatments, this proof constituted a sufficient level of evidence for justifying the use of HBOT in this condition.

Systematic reviews

Two systematic reviews assessed the evidence for the use of HBOT in the treatment of venous wounds.(47;48)

Kranke reviewed the evidence from the same RCT as analyzed by the previous three TA reports (wound area reduction WMD 33%, $p<0.00001$) and concluded there were no data available for evaluating the efficacy of HBOT.

Roeckl-Wiedmann assessed data from one trial on venous ulcers and suggested significant wound size reduction at the end of treatment, but not at follow-up.

Sports injuries

Technology assessment reports

We identified no TA reports.

Systematic reviews

One systematic review assessed the evidence for the use of HBOT for the treatment of sport injuries.(49) Bennett reviewed nine randomized, or quasi-randomized trials evaluating the efficacy of HBOT for soft tissue injuries in 219 patients. Two trials compared HBOT to sham therapy on acute injuries: ankle sprain injury and injury to the medial collateral ligament of the knee. Seven studies assessed delayed onset muscle soreness following eccentric exercise in unconditioned volunteers. Pooling of data from the seven trials showed significantly and consistently higher pain at 48 and 72 hours in the HBOT group (mean difference in pain score 0.88, 95% CI 0.09 to 1.67) in trials where HBOT started immediately. The studies reported no difference between groups for various outcomes including functional outcomes, long-term pain,

swelling, muscle strength. The authors concluded there was insufficient evidence to establish the effectiveness of HBOT on acute injuries or delayed onset muscle soreness.

Individual studies

We identified no new RCTs for the treatment of acute soft tissue injury.

Thermal burns

Technology assessment reports

Three technology assessments that assessed the evidence for the use of HBOT for the treatment of thermal burns included:(2;3;5;49) 1)Quebec AĔTMIS 2001; 2) The Australian MSAC report 2000; 3) Alberta TA report 1998

The Quebec TA assessed two RCTs and concluded that the use of HBOT was still in the experimental stage as its efficacy was inconclusive.

The MSAC 2000 TA assessed the safety and effectiveness of HBOT in three RCTs and five nonrandomized comparative trials. The disparities of the reporting of the studies were outlined as well as the differences in the protocol design. The report concluded that there was lack of good evidence as well as lack of well-conducted studies to recommend the use of HBOT for thermal burns.

The Alberta TA examined the effectiveness of HBOT for acute burns. Four RCTs and one review were assessed. The report concluded that the available evidence supporting the use HBOT to reduce morbidity, surgical procedures in acute burn patients were contradictory.

Systematic reviews

Two systematic reviews assessed the evidence for the use of HBOT for the treatment of thermal burns.(12;50)

Villanueva described two RCTs, one study reporting no differences between treatment and control arms, and a small study of 16 patients showing shorter healing times with HBOT treatment. The authors concluded that there was insufficient evidence to support the use of HBOT for the management of thermal burns.

Saunders identified three RCTs on HBOT therapy for thermal burns; Villanueva has previously discussed two of these RCTs in their systematic review. A third small study enrolled volunteers and created standardized burn wounds and reported short-term benefits from HBOT. The authors concluded that there was insufficient evidence for the effectiveness of HBOT on thermal burns.

Individual studies

We identified no new studies.

Miscellaneous uses

Avascular necrosis of bone

One technology assessment – Hong Kong 2003 report assessed the use of HBOT in the treatment of avascular necrosis.(51)

The Hong Kong report concluded from their analysis of four systematic reviews, one comparative study and one observational study that there was insufficient evidence to support the clinical efficacy of HBOT in AVN.

Dental implants and tooth extractions in irradiated tissues

One systematic review published by Pasquier assessed this topic.(22) The authors identified no RCTs for dental implants, and they concluded that the use of HBOT to reduce loss in irradiated jaws was not clearly defined. For tooth extractions, the authors identified one RCT, which showed that HBOT before and after tooth removal significantly reduced osteoradionecrosis. They advised that indications should nevertheless be considered by individual case and reserved for patients with the most considerable risk. We identified observational studies that assessed the use of HBOT in this topic (Appendix D)

Eye disorders

No TA reports or systematic reviews assessed the use of HBOT for the totality of eye disorders. However, we identified two RCTs on HBOT therapy in eye disorders. The first RCT that assessed HBOT use in glaucoma found a significant improvement in visual fields but no influence on intraocular pressure.(52) The achieved visual field improvements remained stable for 3 months except for the I3 and I4 isopters of the left. The same RCT studied open angle glaucoma and found no significant differences for visual acuity or intraocular values. The second RCT for retinitis pigmentosa found an increase in electroretinographic mean values.(53) The third RCT found improved visual acuity after HBOT use in keratoendotheliosis.(54)

Facial palsy

One TA report assessed the use of HBOT for facial palsy.(2) A single RCT reported a statistically significant difference in total recovery, average duration in days of symptoms. Nerve excitability was also found to be positive.

Other uses

There was at least one RCT available for the use of HBOT in the following disease conditions: periodonitis, fibromyalgia, tibial shaft fractures, opium poisoning, complex regional pain syndrome, post-operative liver damage, chronic hepatitis B and C, and cognitive impairment that are summarized in Table 3.

Table 3. Randomized controlled trials of HBOT uses in miscellaneous treatments

Author UI	Indications of HBOT	Grouping	Nature of HBOT care	Total number of patients	Country of the study	Preliminary conclusions of the RCTs only
Alex 2005 16308008	Evaluation of neuropsychometric dysfunction among patients undergoing cardiopulmonary bypass	Cardiac surgery	Adjunct	64	United Kingdom	The atmospheric oxygen group (A) had a significant postoperative increase in the inflammatory markers soluble E-selectin, CD18, and heat shock protein 70. This was not observed in the hyperbaric oxygen therapy group (B). Neuropsychometric dysfunction was also significantly higher in group A compared with group B. There was no difference in any other early postoperative clinical outcome.
Kiralp 2004 15174218	Treatment of post traumatic complex regional pain syndrome	Pain	ND	71	Turkey	Significant decrease in pain and edema and a significant increase in the range of motion of the wrist. Comparing the two groups HBOT and control, HBOT group had significantly better results with the exception of wrist extension.
Yildiz 2004 15174219	Effect on fibromyalgia	Fibromyalgia	Primary	50	Turkey	Significant improvement for pain threshold, VAS score, reduction of tender points for HBOT vs control group
Chen T 2002 12670118	Effect of HBOT on severe periodonitis	Dental	Refractory and adjunct	24	China	Statistically greater differences in clinical indices, gingival blood flow, subgingival anerobe number and number of rods, curved rods , fusiforms and spirochetes between HBOT, HBOT+scaling and scaling groups. No significant differences were observed in gingivitis
Liu 2002 12215281	Treatment of chronic hepatitis B and C	Viral hepatitis	Primary	60	China	No reduction in the fibrosis and fat storing cells in the liver in HBOT group (P >0.05) and the expression of HBsAg and HBcAg in the liver was not weakened (P <0.05) in the HBOT group. There was a decrease in the liver enzymes levels in the serum and the degeneration and necrosis of hepatocytes were remarkably decreased (P <0.05)
Epifanova 1999 CN-00320116	Opium poisoning	Opium poisoning	Primary	86	Russia	HBOT normalizes lipid peroxdation/antioxidant system, decreased neuropsychological sequelae
Ueno 1999 10430348	Modification of acute HBOT affects the post-operative sinusoidal endothelial cell damage caused by activated neutrophils	Liver post-operative	Primary	24	Japan	HBOT especially at 3 hours after hepatectomy has favorable effects on the activation of neutrophils decreasing post-operative sinusoidal endothelial cell damage.

Table 3. Randomized controlled trials of HBOT uses in miscellaneous treatments (continued)

Author UI	Indications of HBOT	Grouping	Nature of HBOT care	Total number of patients	Country of the study	Preliminary conclusions of the RCTs only
Lindstrom 1998 9670433	Effects of HBOT on perfusion parameters and transcutaneous oxygen measurements in patients with intramedullary nailed tibial shaft fractures	Fractures	Adjunct	20	Finland	A statistically significant improvement in tibialis posterior arterial values in the nailed legs in the HBOT group compared to controls. Also a statistically significant improvement in transcutaneous oxygen values in the nailed legs of the HBOT group
Racic 1997 9068154	Therapy of Bell's palsy	Facial palsy	Primary	79	Croatia	HBOT is more effective than prednisosne in treatment of Bell's palsy with greater % of those in HBOT group showed recovery. The average time to complete the recovery in HBOT group was shorter than in the control group (P <0.001)
Raskin 1978 619839	Effects on cognitive impairment	Cognitive function	Primary	82 elderly	USA	No difference between normo- or hyperbaric oxygen vs normo- or hyperbaric air for cognitive functioning or symptom reduction

Novel uses of HBOT identified in textbooks

We identified an additional list of uses for which HBOT has been used as an experimental treatment. The following examples have been supplied from three textbooks.(1;55;56) HBOT has been used as an adjunct therapy with proven antibiotics for intracranial abscess. HBOT has been used experimentally in dermatological diseases such as toxic epidermal necrolysis and pemphigus vulgaris, pyoderma gangrenosum, Hansen's disease, Lyell's syndrome, and purpura fulminans. Textbooks cite case reports that have been published describing HBOT in the treatment of adhesive ileus associated with abdominal surgery, and for the use of HBOT in the treatment of neurological disorders such as benign intracranial hypertension, polyradiculoneuritis, and Susac's syndrome.

Case reports identified in MEDLINE search

Table 4 summarizes the novel uses of HBOT and the number of case reports that described their uses.

Table 4. Case reports on the novel uses of HBOT

New Uses of HBOT	Number of case reports
Acne with chronic recurrent multifocal osteomyelitis	1
Acute blood loss anemia (ineligible for transfusion)	1
Alveolar proteinosis	2
Anterior spinal artery ischemia	1
Cannabis arteritis	1
Chronic idiopathic intestinal pseudo-obstruction	1
Claustrophobia	1
Cochlear implant flap necrosis	2
Dupuytren's contracture	1
Enteric Behcet syndrome	1
Ergotism	1
Esophageal perforation	1
Eye Ocular quinine toxicity	1
Eye Transient visual loss after licorice	1
Hepatic artery thrombosis	1

Table 4. Case reports on the novel uses of HBOT (continued)

New Uses of HBOT	Number of case reports
Hypoxic demyelination	1
IBD Crohn's disease or diverticulitis	7
Intractable livedoid vasculopathy	1
Ischemic glans penis after circumcision	1
Life threatening epistaxis	1
Lupus erythemetosus panniculitis	1
Malignant external otitis	2
Mechanical root pain	1
Necrobiosis lipoidica diabeticorum	2
Parkinsonism	1
Pneumocystis Carini Pneumonia	1
Persistent left hemiface hyperalgesia	1
Poisoning hydrogen sulfide	4
Poisoning methylene chloride	1
Poisoning potassium chlorate	1
Poisoning chloroform	1
Postoperative hypoxia	1
Postoperative liver failure	1
Prolonged epidural blockade	1
Pulmonary edema	1
Pulmonary TB	1
Reflex sympathetic dystrophy syndrome	1
Rheumatic diseases	1
Rhizopus infection	1
Sagittal sinus thrombosis	1
Secondary abdominal pregnancy	1
Snake bites	5
Stingray puncture	1
Subdural spinal granuloma resulting from Candida albicans	1
Symptomatic vasospasm	1
Tetanus	1
Toxic megacolon	1
Tracheal tear	1
Transient osteoporosis associated with hyperhomocystinemia	1
Ulcerative colitis	3
Ventricular tachysystole	1
Werner's syndrome	1

Summarized in Table 5 are the uses of HBOT, the number of studies found that reported on the specific use, and the conclusions of authors of those studies.

Table 5. Conclusions from the studies evaluating non-covered uses of hyperbaric oxygen therapy.

Uses of HBOT [1]	Number of studies found				Conclusions from the studies
	Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies	
Acute coronary syndrome	2	1	5	0	The authors concluded no firm evidence to support the use of HBOT in acute myocardial infarction or acute coronary syndrome.
Acute or chronic cerebrovascular insufficiency	3	3	4	6	The authors concluded that there is insufficient evidence to support the use of HBOT in cerebral ischemia to improve clinical outcomes.
Acute cerebral edema (traumatic brain injury)	1	3	3	8	The authors conclude that evidence was conflicting, and inconclusive. The authors concluded against the routine application of HBOT to patients with traumatic brain injury.
Avascular necrosis of the femoral head	1	0	0	1	The authors concluded that there is insufficient evidence to support the clinical efficacy of HBOT in avascular necrosis.
Blood loss (exceptional) or anemia[3]	1	0	0	1	Insufficient data
Bone grafts or fracture healing	0	0	1	0	Insufficient data
Cancer	1	1	19	1	No benefit in the treatment of cancers
Closed head and/or spinal cord injury	0	0	1	3	Insufficient data
Crohn's disease	1	0	0	0	Insufficient data

[1] Identified by one or more healthcare providers and in our literature search
[2] Inclusive of studies found in systematic review and identified by systematic literature search
[3] Transfusion impossible

Table 5. Conclusions from the studies evaluating non-covered uses of hyperbaric oxygen therapy. (continued)

Uses of HBOT [1]	Number of studies found				Conclusions from the studies
	Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies	
Dental implants after irradiation	1	0	0	8	The authors advise that indications should be considered by individual case and reserved for patients with the most considerable risk.
Facial palsy	1	0	1	0	Insufficient data
Fibromyalgia	0	0	1	0	Insufficient data
Fungal infection	0	0	0	4	Insufficient data
Headaches including migraine or cluster	1	0	4	3	The authors concluded that the evidence was insufficient to support the use of HBOT.
Hearing disorders[3]:	2	1	7	10	The authors concluded that the conflicting studies required more rigorous evidence and there was no evidence of a beneficial effect. Routine application of HBOT cannot be justified.
Interstitial cystitis	0	0	1	0	Insufficient data
Liver post-operative	0	0	1	0	Insufficient data
Multiple sclerosis	1	2	11	3	The authors concluded that HBOT is ineffective in the treatment of multiple sclerosis.
Non diabetic ulcers[4],	3	1	1	0	The authors reached mixed conclusions, two of whom favored use of HBOT, while three others did not.
Ophthalmologic diseases	0	0	3	2	The authors found some to no benefit from HBOT in various eye disorders
Opium poisoning	0	0	1	0	Insufficient data
Periodonitis	0	0	1	0	Insufficient data

[1] Identified by one or more healthcare providers and in our literature search
[2] Inclusive of studies found in systematic review and identified by systematic literature search
[3] Includes Idiopathic sudden deafness, acoustic trauma, or noise induced hearing loss
[4] Includes cutaneous, decubitus, and stasis ulcers, chronic peripheral vascular insufficiency

Table 5. Conclusions from the studies evaluating non-covered uses of hyperbaric oxygen therapy. (continued)

Uses of HBOT [1]	Number of studies found				Conclusions from the studies
	Technology Assessment	Systematic review	RCT[2]	Comparative and cohort studies	
Pneumatosis cystoides intestinalis	0	0	0	1	Insufficient data
Post traumatic complex regional pain syndrome	0	0	1	0	Insufficient data
Pulmonary emphysema	0	0	0	1	Insufficient data
Reconstructive surgery	0	0	0	1	Insufficient data
Senility (cognitive impairment)	0	0	1	0	Insufficient data
Skin burns (thermal)	3	2	3	2	The authors conclude that evidence was conflicting, and inconclusive to recommend the use of HBOT for thermal burns.
Sports injuries	0	1	4	1	The authors concluded there was insufficient evidence to establish the effectiveness of HBOT on acute injuries or delayed onset muscle soreness.
Tinnitus	0	0	0	1	Insufficient data
Trauma acoustic	0	0	1	0	Insufficient data
Viral hepatitis	0	0	1	0	Insufficient data

[1] Identified by one or more healthcare providers and in our literature search
[2] Inclusive of studies found in systematic review and identified by systematic literature search

Discussion / Limitations

This report summarizes the published uses of HBOT in the adult population identified through a systematic literature search. The main purpose of this review was to identify studies that reported or assessed the uses of HBOT but not to perform critical evaluations of the studies for each of the uses we identified. Because HBOT for CO poisoning and wounds are already covered by CMS, in discussions with CMS and AHRQ, it was decided to include a brief narrative review of the literature on these topics. Our report relied primarily on the published TAs and systematic reviews but did not evaluate both included and rejected primary studies reviewed by them. We included only those individual studies published subsequent to the most recent TAs and systematic reviews. We did not critically appraise TAs, systematic reviews and individual studies, as the intent of this review was not to assess the quality of studies or analyze their results. We reported authors' conclusions without critical assessment. We also did not include any published commentaries that critically addressed the deficiencies and flaws of the included TAs, systematic reviews, and individual studies on the uses of HBOT.

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