## Evidence Table 1. Brain injury controlled trial data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Control | Randomized? |
|---|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | | |
| Artru 1976[88] France (Fair) | Patients with head injuries and in a coma. | 2.5 atm x 60 minutes x 10 days of treatment alternating with 4 days off until patient regained consciousness or died. Control group received standard therapeutic measures. (Type of chamber not specified) | Standard therapeutic measures were the same in both groups. | Yes |



HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 1. Brain injury controlled trial data (continued)

| Author, year, location (Quality) | Baseline differences between groups | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | | |
| Artru 1976[88] France (Fair) | No information on factors other than those on which they matched participants. Severity of coma (based on Jouvet scale) was 9.39 for HBOT and 9.59 for control group (NS). Types of brain lesions similar except acute subdural hematoma (7 in HBOT and 3 in control group). Age similar (29.9 HBOT, 29.7 control). | 31 HBOT<br>29 control | Mortality rate, coma/conscious. | Mortality assessed at 1 month and 1 year, coma/conscious assessed at 1 month. |



HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 1. Brain injury controlled trial data (continued)

| Author, Year, Location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | |
| Artru 1976[88] France (Fair) | *Persistent coma at 1 month:*<br>32% (HBOT); 38% (control)<br>*Consciousness recovery rate at 1 month:*<br>42% (HBOT); 28% (control)<br>*Death rate at 1 month:*<br>26% (HBOT); 34% (control)<br>*Death rate at 1 year:*<br>48% (HBOT); 55% (control)<br>*Mean duration of coma:*<br>28.2 days (HBOT); 32.7 days (control)<br>Independent in daily activities at 1 year among survivors:<br>45% (HBOT); 41% (control)<br>*p* = NS for all comparisons<br><br>*Subgroup 5 (* n = 9 HBOT, 9 control; patients less than age 30, not reacting in an adapted manner to painful stimuli, and not operated on):<br>*Persistent coma at 1 month:*<br>22% (HBOT); 78% (control); p < 0.03<br>*Consciousness recovery rate at 1 month:*<br>67% (HBOT); 11% (control); p < 0.03<br>*Death rate at 1 month:*<br>11% (HBOT); 11% (control)<br>*Death rate at 1 year:*<br>11% (HBOT);44% (control); p = 0.15 | Major medical reason for interruption was development of pulmonary symptoms indicating an intolerance to HBOT: polypnea with expiratory dyspnea, cyanosis at exit of chamber, and reduced oxygen saturation value. Treatment interrupted in 5 cases where the intolerance was severe enough to suggest impending hyperoxic pneumonia. Treatment interrupted in 6 others with severe pulmonary infections for fear of aggravating the lesions. | Severe chest injury or open brain wounds were excluded. Inclusion in this study depended on availability of the HBOT chamber. All assessed by same examiner at entry. |

HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 1. Brain injury controlled trial data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Control | Randomized? |
|---|---|---|---|---|
| Rockswold 1985,[89] 1992,[90] 1994[91] Minnesota (Fair) | Patients with severe head injury at one institution, admitted 1983-1989.Total GCS score of 9 or less for at least 6 hours. | 1.5 atm x 60 minutes every 8 hours x 2 weeks or until the patient was brain dead or could consistently follow simple commands. Average 21 treatments per patient. (Monoplace) | All patients received intensive neurosurgical care, according to standard medical practice covering stabilization in the emergency department, surgical management, medical treatment and the management of intracranial pressure. However, HBOT patients received closer ICP monitoring. All study patients received phenytoin. | Yes |
| ***Studies of other brain injury*** | | | | |
| Jianhua 1995[106] China (Poor) | Children (age 1-11 years) with viral cerebritis, stable illness but with disturbance of consciousness, aphasia, spasm and dyskinesia, etc. inpatients with confirmed cerebritis. | 1.8-2.0 atm x 90 minutes once daily x 10 days. | Control group received supportive therapy, including drugs naofukang, naofuxin. | Yes |

HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 1. Brain injury controlled trial data (continued)

| Author, year, location (Quality) | Baseline differences between groups | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Rockswold 1985,[89] 1992,[90] 1994[91] Minnesota (Fair) | Small differences in proportion with operable mass lesions, multiple trauma, elevated ICPs and "poor outcome BAEPs (Brainstem Auditory Evoked Potentials) and SSEPs (Somatosensory Evoked Potentials ) | 84 HBOT, 84 control | ICP, mortality, GCS, favorable outcome (GCS score 1-2). | Assessed at baseline and comparisons were done at 12-month exam. Other followup assessments at 6 and 18 months. |
| ***Studies of other brain injury*** | | | | |
| Jianhua 1995[106] China (Poor) | No statistical test performed, but baseline characteristics reported, appear similar. | 47 HBOT 45 control | Curative: disappearance of clinical symptoms, signs, normal EEG and CT; effective: disappearance of some clinical signs and symptoms, better in EEG and CT; ineffective: no change in clinical symptoms through examination of EEG and CT. | Not reported. |

HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 1. Brain injury controlled trial data (continued)

| Author, Year, Location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Rockswold 1985,[89] 1992,[90] 1994[91] Minnesota (Fair) | Mortality at 12 months:<br>14/84 (17%) (HBOT)<br>26/82 (32%) (control)<br>*p* = 0.04<br><br>Favorable outcome at 12 months (independent with or without disability, as assessed by masked neurologist)<br>44/84 (52%) (HBOT)<br>44/82 (54%) (control)<br>*p* = 0.99<br>Results at 6 and 18 months not reported, but stated NS.<br><br>Mean peak ICP<br>No significant difference in peak ICP values between HBOT (all) and control (t = 0.92).<br>HBOT (no myringotomy) subset (37 patients): 33.0 +/ 20.6 (p<0.05 compared to HBOT + myringotomy group)<br>HBOT + myringotomy subset (42 patients): 22.1 +/- 11.7<br>Control: (77 patients): 30.3 +/ 24.3 (*p* <0.05 compared to HBOT + myringotomy group) | Most frequent complication was pulmonary, increasing FiO2 requirement and chest x-ray infiltrates. In 10 patients, HBOT had to be permanently stopped. 2 patients had isolated generalized seizure. 2 had hemotympanum. One patient's family requested HBOT be discontinued. | Assessors at 6, 12 and 18 months were unaware of patient's treatment group. Bilateral myringotomies performed in the last 46 of the 84 patients in the HBOT group. All patients received prophylactic phenytoin. |
| ***Studies of other brain injury*** | | | |
| Jianhua 1995[106] China (Poor) | HBOT group: 18/47 (38%) curative, 25/47 (53%) effective, 3/47 (6%) ineffective (1 missing?).<br>Control group: 8/45 (18%) curative, 20/45 (44%) effective, 17/45 (38%) ineffective.<br>HBOT vs control: % curative *p* < 0.05, % effective p > 0.05, % ineffective *p* < 0.001. | Not reported. | |

HBOT=hyperbaric oxygen therapy; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; atm= atmospheres; NS= non-significant; ICP=intracranial pressure; CT=computerized tomography; EEG=electroencephalogram

## Evidence Table 2. Brain injury observational study data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | |
| Artru 1976[94] France (Fair) | Patients in coma from head injuries with brain stem contusions. 4 of 6 in "deep coma," mean coma duration 2.3 months. | 2.5 atm x 60 minutes (10-minute compression & 20-minute decompression phase before & after), duration, number of treatments not reported. One patient compressed at 2.2 atm due to a bad pulmonary condition. One used respirator, others breathed spontaneously in chamber. (Type of chamber not specified) | None. |
| Hayakawa 1971[95] Japan (Fair) | Patients with acute cerebral damage; 9 with closed head injury in acute post-traumatic period, 4 had craniotomy for brain tumor and were in the immediate postoperative state. All had severe neurological disorders and were comatose. Six were breathing spontaneously, 7 had intermittent positive pressure ventilation. | 2.0 atm x 60 minutes. (Multiplace chamber; oxygen administered with non-rebreathing face mask or endotracheal tube) | None reported. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | | |
| Artru 1976[94] France (Poor) | Before-after | 6 | Cerebral blood flow, other lab tests, change in clinical status. | Tests given immediately following treatment (within hours). |
| Hayakawa 1971[95] Japan (Fair) | Time-series | 13 | Cerebrospinal fluid pressure measured continuously during HBOT with a water manometer connected to a catheter inserted into the lateral ventricle of the cerebrum via a burr hole in the frontal lobe. | Measured before, during and after (up to 100 minutes). |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | |
| Artru 1976[94] France (Poor) | 2 patients (33%) found neurologically improved at exit from the chamber; the first recovered sufficient consciousness to answer simple questions, the second was able to keep his eyes open and showed an improved motor reactivity on one side. However, both patients sunk to pre HBOT status by second cerebral blood flow test (mean time to test = 2hr 20min). No other patients recovered consciousness. 3 of 6 (50%) dead at conclusion of study. | One patient developed a status epilepticus on one side that took 12 hours to control. | |
| Hayakawa 1971[95] Japan (Fair) | 3 patterns of responses noted: Response 1 (69%): ICP fell with HBOT after initial fluctuation eased by the beginning of compression, reverted rapidly with decompression at end of HBOT. After cessation of HBOT, ICP commonly showed temporary rebound & considerably exceeded pretreatment level. Even during HBOT, ICP which had initially fallen by HBOT was liable to increase gradually with passage of time, & upward tendency during HBOT more striking when HBOT continued beyond about 30 minutes. Response 2 (15% pts): ICP showed little rebound & the ICP after HBOT significantly lower than the pretreatment level. Response 3 (15%): ICP showed little response to HBOT, & maintained a consistently low or high level during and after HBOT. | | |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| Mogami 1969[96] Japan (Poor) | Patients with acute cerebral damage (evidence of severe brain damage from any cause). | 2.0 atm x 60 minutes once or twice daily, total number of treatments not stated. 6 treatments given at 3.0 atm x 30 minutes.<br>(Multiplace with non-rebreathing face mask or tracheal tube) | None. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Mogami 1969[96] Japan (Poor) | Before-after | 66<br>51 with TBI | Not clearly stated in methods. Neurologic signs and symptoms, EEG, cerebrospinal fluid pressure, and cerebrospinal fluid lactate and pyruvate levels reported for some patients. | Not clear when or if baseline measurements taken, followup appears to be during and immediately after treatments. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Mogami 1969[96] Japan (Poor) | Of 51 patients with TBI:<br>Clinical improvement (categories not defined) during HBOT treatment:<br>33% "great" improvement, 16% "some," 51% "none."<br>Most of the favorable responses were temporary and regression to pretreatment level occurred immediately after decompression. Authors note that effects more prominent in milder injury.<br>3 patients became convalescent with the definite help of HBOT (diagnosis not reported), especially one (TBI patient) who was discharged with only mild residual neurological deficit.<br>4 (diagnosis not reported) showed clinical improvement during HBOT but became much worse afterward, 1 died. One TBI patient's seizures became worse during HBOT.<br>ICP: Reported that ICP generally fell with HBOT, reverting rapidly with decompression. A rebound phenomenon was noted, with pressures exceeding pretreatment levels. Two cases showed no response, and two showed no rebound. No further details given. | In one patient, seizures caused by head injury slightly increased during HBOT. | |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| Ren 2001[99] China (Poor) | Patients with severe (GCS score < 8) closed head injury. Admitted within 24 hours of injury. Patients with organ injuries or open head injury excluded, patients who died excluded from analysis. | 2.5 atm x 40-60 minutes once daily with 10 minute break x 10 treatments per course x 3-4 courses. After each course a 4-day intermission followed. Begun on third day after stabilization. | Both groups received routine treatment (dehydration, steroid and antibiotics). |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Ren 2001[99] China (Poor) | Cohort | 35 HBOT<br>20 control | GCS and GOS | Baseline measure (GCS) on third day after injury (before HBOT), second week (after 1 course of HBOT), and second month (after 3 courses of HBOT). Prognosis (GOS) at 6 months. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Ren 2001[99] China (Poor) | Mean GCS score,<br>HBOT group: before treatment 5.1, after 1 course 10.1 ($p < 0.01$); after 3 courses 14.6 ($p < 0.01$ compared to initial injury)<br>Control: before treatment 5.3, after 1 course 8.1, after 3 courses 9.5. (NS)<br>After 3 courses of treatment, GCS score vs control group score higher ($p < 0.01$)<br>Good recovery or mild disability at 6 months: 29/35 (HBOT) 6/20 (control), $p < 0.001$<br>GOS: good recovery or mild disability: 29/35 (83.7%) HBOT, 6/20 (30%) control ($p < 0.01$) | Not reported. | Some differences. More women in HBOT group than control (29 vs 15%), CT findings (more subdural hematoma in HBOT group); small difference in baseline GCS (5.3 vs 5.1). |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| Rockswald 2001[97] Minnesota (Fair) | Patients treated for traumatic, severe closed-head injuries at one Level I Trauma Center; mean age 36 +/- 3 years (range 8-84). 27 male, 10 female. Severe brain injury defined as GCS score 8 or less. Mean GCS score at study entry was 5.8 +/- 0.3.<br>Inclusion criteria CT scan score greater than II according to Traumatic Coma Data Bank.<br>Exclusion criteria were condition not compatible with HBOT, such as unstable pulmonary status or pregnant, unstable fracture that prevented placement in chamber, under age 4 years, and patients placed in a barbiturate-induced coma during initial case management. | Compression at a rate of 1 psi per minute x 15 minutes, 1.5 atm x 60 minutes, then decompressed at the same rate. First HBOT treatment performed as soon as entry criteria were met and the patient was deemed clinically stable; mean time from injury to initial treatment was 23 (+/- 2) hours (range 9-49 hours). Second treatment was given the next morning, with a minimum of 8 hours separating the 2 sessions. Subsequent treatments were given 24 hours apart for up to 5 more days (maximum of 7 treatments per patient) or until the patient could consistently obey simple commands or was deemed brain dead. Treatments were stopped if the patient became medically unstable due to sepsis or uncontrolled blood pressure, or if the addition of a pentobarbital-induced coma to the treatment strategy was necessary for control of ICP. A total of 167 HBOT treatments were administered, for an average of 5 treatments per patient. (32 patients used monoplace chamber, 5 multiplace) | Intensive neurosurgical care paralleled Guidelines of the Brain Trauma Foundation, including stabilization with early intubation while patient in ED, surgical evacuation of significant hematomas, continuous monitoring of ICP, treatment of ICPs greater than 15 mm Hg. All received prophylactic phenytoin sodium. All received ventilation therapy throughout entire study period. Bilateral myringotomies performed on all. An ICP over 15 mm Hg was treated, sequentially including hyperventilation, CSF drainage, administration of mannitol, and finally barbiturate therapy. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Rockswald 2001[97] Minnesota (Fair) | Time-series | 37 | ICP monitored using tunneled ventriculostomy. | ICP values recorded hourly in the neurological ICU and every 15 minutes during HBOT treatments. One hour before treatment, during treatment, 1 hour after depressurization to 1 atm, and 6 hours after the session in the chamber. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Rockswald 2001[97] Minnesota (Fair) | Low pretreatment ICP values (<15 mm Hg) were increased 1 hour and 6 hours after the session ($p < 0.001$). High pretreatment ICP values (> 15 mm Hg) were decreased 1 hour and 6 hours after HBOT sessions ($p = 0.006$). ICP values in both categories rose throughout the session ( $p < 0.001$), the only difference being a trend for high pretreatment ICP values to drop during the first 15 minutes of the treatment session. ICP rose linearly during the treatment session in all patients. | Not reported. | |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| Sukoff 1982[98] California (Poor) | Patients with traumatic encephalopathy (cerebral contusion). Sustained depressed level of consciousness, unable to obey commands, decerebrate or decorticate, brain stem dysfunction, and pupillary abnormalities. | 2.0 atm x 45 minutes every 8 hours x 48 hours if ICP was under 15 mm Hg. If over 15 mm Hg after mannitol, every 4 hours for 2-4 days depending on response. (Monoplace chamber.) | Standard therapeutic measures were the same in both groups, except that no barbiturates given to elevated ICP patients under HBOT protocol. |
| ***Studies of other brain injury*** | | | |
| Chuba 1997[107] Michigan (Poor) | Patients with radiation-induced necrosis of the central nervous system. New or increasing neurologic deficits after radiotherapy. Ages 4-23 years. | 2.0-2.4 atm x 90 minutes-2 hours x minimum of 20 treatments. (Multiplace chamber) | None. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Sukoff 1982[98] California (Poor) | Before-after | 50 (10 with ICP data reported) | ICP, neurologic symptoms. | Pre- and post-treatment. |
| ***Studies of other brain injury*** | | | | |
| Chuba 1997[107] Michigan (Poor) | Before-after | 10 | Symptoms and imaging findings attributed to radiation-induced necrosis were scored as improved, worsened or stabilized after HBOT. | Timing of baseline and followup evaluation not stated. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Sukoff 1982[98] California (Poor) | In elevated ICP group (10 patients), all but one patient demonstrated some degree of improvement during initial treatment session, mostly minor. Improvement in chamber was manifested by increased awareness and motor activity. The ability to obey commands was enhanced, and verbalization was more prompt and more appropriate in those patients whose pretreatment status had included some verbal abilities.<br>In the other 40 patients, 22/40 (55%) improved during HBOT treatment. Patients less severely compromised neurologically showed better and more sustained improvement. Details not given, only EEG and CT scan results.<br><br>10 patients had ICP monitoring continuously. ICP decreased during HBOT in all cases. Reduction was 4-21 mm Hg below the pretreatment level. Difference between ICP before and during HBOT $p < 0.001$. Lower pressures were sustained for 2 to 4 hours after HBOT in "most" cases (number not specified). In some instances in 2 patients, at 1 or 2 hours after treatment, ICP was near or slightly higher than pre-HBOT exposure. | In elevated ICP group, one patient died of systemic problems 6 days after the last HBOT exposure. Two patients had seizures. No pulmonary complications attributed to HBOT.<br>In non-elevated ICP group four myringotomies were required for barotrauma, increased restlessness in some patients. Five patients died of systemic problems or progressive cerebral insufficiency. No pulmonary or central nervous system complications attributed to HBOT. | Patients requiring continuous vasopressors for hypotension due to systemic trauma and those with dilated and fixed pupils were excluded. No steroids were given. |
| ***Studies of other brain injury*** | | | |
| Chuba 1997[107] Michigan (Poor) | Following treatment, of 10 patients, symptoms of 40% improved, 20% improved initially, 10% stabilized, 20% stabilized initially, 10% resolved. At followup ranging from 3 to 36 months, 40% died, 10% alive with tumor, 20% alive (not specified if still with disease), 30% alive with no evidence of disease. | One patient developed ear pain and required myringotomy tubes. Treatments discontinued in one patient due to sinusitis. | All patients had failed steroid therapy prior to HBOT. In two of the patients the diagnosis was made on radiological basis, all others by biopsy. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions |
|---|---|---|---|
| Imai 1974[108] Japan (Poor) | Patients with CO intoxication with residual symptoms (N=2). Report also includes patients with chronic alcoholism, presenile dementia, chronic atherosclerosis (results not reported here), and cerebral thrombosis (results reported in stroke table) | 1.3 atm x 60 minutes daily x 5 sessions. (Monoplace chamber) | None. |
| Mathieu 1987[109] France (Poor) | Patients admitted to one emergency unit after unsuccessful hanging from 1971-1981. Age range 10-83. 19 were conscious or slightly "obnubilated," 151 had altered consciousness level. On GCS, 54 grade 1, 26 grade 2, 30 grade 3, 31 grade 4. Brain death was pronounced in 10. Patients admitted to department for unsuccessful hanging, only patients with impaired consciousness levels were selected for HBOT. | 2.5 atm x 90 minutes repeated until the conscious level returned to normal. When several courses were needed, they were separated by 6-hour intervals. 278 courses provided to 136 pts. (Monoplace chamber; pure oxygen chamber used until 1978, then chamber in which oxygen administered by facial mask or assisted ventilation) | Steroids or beta-1-24-tetracosactide was used in every comatose patient until recovery of consciousness or the 3rd day. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|
| Imai 1974[108] Japan (Poor) | Before-after | 32 (report states 30, but numbers total 32); 2 with sequelae from CO poisoning. | Memory testing, that included Bender-Gestalt test as one item of 9, tests given after 1 or 2 courses of treatment | Unclear if and when baseline conducted. Followup conducted after one or two sessions. |
| Mathieu 1987[109] France (Poor) | Before-after | 136 | Recovery, with or without neurological sequelae, mortality. | Not clear. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon monoxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 2. Brain injury observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Imai 1974[108] Japan (Poor) | 5% to 10% improvement in overall score (individual scores not given), with 10% to 15% improvement on visual reproduction (based on Bender-Gestalt test) and story recall (not described) elements. | Not reported. | Results reported only ranges of percentage improvement. Unclear how subjects chosen. |
| Mathieu 1987[109] France (Poor) | 108/136 (79%) recovered without residual effects, 8/136 (6%) recovered with neurological sequelae (chronic coma 3 cases, locked-in syndrome 2 cases, extrapyramidal rigidity 1 case, hemiplegia 1 case, hemiasomatognosia 1 case), 20/136 (15%) treatment failure. | After admission, complications occurred in 10 patients and were cause of death even when neurologic state improved: pulmonary edema 5 cases, pulmonary infection 4 cases, cardiac arrest 1 case. Relationship with HBOT in only 3 of these cases: 2 pulmonary edema occurred during the course of HBOT, and the cardiac arrest patient could not be resuscitated in time because of the monoplace chamber. | |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; GCS=Glasgow Coma Scale; CO=carbon dioxide; GOS= Glasgow Outcomes Scale; ED=emergency department; CSF= cerebrospinal fluid; EEG= electroencephalogram; TBI=traumatic brain injury; psi=pounds per square inch

## Evidence Table 3. Cerebral palsy controlled trial data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Control | Randomized? | Baseline differences between groups? |
|---|---|---|---|---|---|
| Collet 2001[119] Hardy 2002[120] Canada (Fair) | Children with CP with history of hypoxia in perinatal period, age 3-12 years, motor development age of 6 months to 4 years, and psychological development age 24 months or more. | 100% oxygen at 1.75 atm x 60 minutes x 40 sessions. Sessions 5 days/week x 8 weeks.<br><br>(Monoplace or multiplace chamber, depending on facility used) | Room air at 1.3 atm x 60 minutes x 40 sessions. Sessions 5 days/week x 8 weeks. | Yes | Some differences in presumed cause and type of CP. |
| Packard 2000[118] New York (Poor) | Children age 15 months to 5 years, with CP secondary to prenatal insults, premature birth, birth asphyxia, and post-natal hemorrhage. Criteria for enrollment were age between 1 and 5 years, moderate to severe CP, no evidence of brain malformation, developmental delay of at least 33% in one area, and no active seizures for the previous 6 months. | 1.5 atm x 60 minutes twice daily x 40. Five days per week for 4 weeks.<br>(Chamber type not given) | Delayed HBOT treatment. | Yes | Not reported beyond subjects "matched roughly to age and severity." |

HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; NS=non-significant; PEDI= Pediatric Evaluation of Disabilities Inventory; GMFM=Gross Motor Function Measure

## Evidence Table 3. Cerebral palsy controlled trial data (continued)

| Author, year, location (Quality) | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|
| Collet 2001[119] Hardy 2002[120] Canada (Fair) | 111 (57 HBOT, 54 control) for motor function based tests, 75 for neuropsychiatric tests | Primary outcome measure: Gross motor function as assessed by the GMFM. Other outcomes measured using a variety of tests/protocols, including neuropsychological testing based on 5 measures. | Assessed at baseline, after 20 and 40 treatments, and 3 months later. |
| Packard 2000[118] New York (Poor) | 26 (12 immediate treatment group, 14 delayed treatment group) | Weekly parent diaries, neuro-developmental assessment, Bayley II (cognitive assessment) Preschool Language Scale (language assessment), Peabody Motor Scales (assessment of gross and fine motor skills), PEDI (Parental report of specific skill in mobility, self-care, and social interactions). | Assessments at T1 (at enrollment), T2 (after the immediate group received treatment), T3 (prior to the delayed group's HBOT, 5 months after enrollment), and T4 (after the delayed group's treatments). |

HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; NS=non-significant; PEDI= Pediatric Evaluation of Disabilities Inventory; GMFM=Gross Motor Function Measure

## Evidence Table 3. Cerebral palsy controlled trial data (continued)

| Author, year, location (Quality) | Results |
|---|---|
| Collet 2001[119] Hardy 2002[120] Canada (Fair) | Change in Global GMFM<br>Post-intervention (after 40 treatments):<br>HBOT: 2.9 (95% CI, 1.9, 3.9)<br>Control: 3.0 (95% CI, 2.1, 3.9)<br>$p$ = 0.54<br>At 3 months:<br>HBOT: 3.4 (95% CI, 2.2, 4.5)<br>Control: 3.1 (95% CI, 2.2, 4.1)<br>$p$ = 0.97<br>Secondary outcome measures:<br>NS for between group comparisons for all tests, including neuropsychological tests. |
| Packard 2000[118] New York (Poor) | Parental diaries:<br>83% of parents noted a marked improvement in mobility, 43% saw a marked increase in attention, and 39% reported a marked increase in language skills. There was some improvement in mobility in 21 of 23 children (91%), attention in 18/23 (78%), language in 20/23 (87%), and play in 12/23 (52%). One family saw no improvement and 6 saw minimal improvement (30%). Five families (22%) reported major gains in skills and 11 (48%) reported modest gains.<br>Improvement in vision:<br>4/9 (44%) children with cortical visual impairment had improvement in vision noted by families, vision therapists, and ophthalmologists.<br>PEDI Results:<br>Improved scores on mobility sub-domains of PEDI for time period T2 minus T1 in favor of immediately treated group (p<0.05), trend favoring recently treated delayed group for time period T4 minus T3 ($p$ <0.058).<br>For social function sub-domain, trend favoring more recent treated group (p not given).<br>Blinded Assessments:<br>No statistical difference in the change scores on any of the blinded assessments (change in Peabody scores for T2 minus T1 and T4 minus T3; change in Bayley II and PLS scores for T3 minus T1),<br>($p$ values not given).<br><br>In followup interviews with parents after 6 months, it was found that changes in spasticity were most likely to diminish over time, but the improvement in attention, language, and play remained. |

HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; NS=non-significant; PEDI= Pediatric Evaluation of Disabilities Inventory; GMFM=Gross Motor Function Measure

## Evidence Table 3. Cerebral palsy controlled trial data (continued)

| Author, Year, Location (Quality) | Adverse effects | Comments |
|---|---|---|
| Collet 2001[115] Hardy 2002[116] Canada (Fair) | One withdrawal for side effects, not stated which group. 27 patients in HBOT group and 12 in control group had ear problems (p = 0.004) | Masking of parents and assessors, statistical analysis described, loss to followup reported. Patients with physical disability preventing them from using a computer with at least one hand were excluded from neuropsychologic testing. |
| Packard 2000[114] New York (Poor) | 3/26 (12%) patients developed seizures and could not complete treatment. Nine children and 7 parents required ventilation tube placement or myringotomies for barotrauma to the middle ear. | 11/12 (92%) in immediate group and 12/14 (86%)in delayed group completed 40 sessions. |

HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; NS=non-significant; PEDI= Pediatric Evaluation of Disabilities Inventory; GMFM=Gross Motor Function Measure

## Evidence Table 4. Cerebral palsy observational study data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Chavdarov 2002[121] Bulgaria (Fair) | Children with CP selected from a population of children treated and followed at one residential treatment center. 15 females and 35 males, mean age 5 years 9 months (range 1 year 7 months to 19 years); No history of seizures, age over 1 year 6 months, not having complaints about lungs, heart, ears, or naso-pharynx; parental consent. | 1.5 to 1.7 atm x 40 to 50 minutes (including 10 minutes compression, 20 to 30 minutes iso-compression, and 10 minutes decompression) once daily x 20 consecutive days. (Multiplace, oxygen administered through a hood) | Vitamin C | Time-series | 50 |
| Machado 1989[122] Brazil (Poor) | Children with CP age under 1 year to 15 years. | 1.5 atm x 1 or 2 maximum hours per day x 20 sessions. (Monoplace) | Not reported | Time-series | 230 |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 4. Cerebral palsy observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Chavdarov 2002[121] Bulgaria (Fair) | Motor developmental level classified by Gross Motor Function Classification System at baseline, motor abilities measured by Holt's Assessment of Motor Abilities, mental abilities by Munich's Functional Developmental Diagnostic, Wechsler's test for children, Raven's test for children, Frostig's test, Goppinger's test; speech abilities assessed by Munich's Functional Developmental Diagnostic, Nancie Finnie's Questionnaire, Wechsler's test for children. Assessments by physiotherapists, psychologists, speech therapists. | All measurements repeated on two consecutive days before and after the period of HBOT by the same specialist. |
| Machado 1989[122] Brazil (Poor) | Neurological exam, including a spasticity rating of 0 to 100. Some patients also had EEG and/or CT scans. | Baseline, immediately after, and "6 or more months after" HBOT |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 4. Cerebral palsy observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Chavdarov 2002[121] Bulgaria (Fair) | Change after HBOT:<br>Motor abilities: moderate improvement 6/46 (13%), mild improvement 13/46 (28%), no improvement 27/46 (59%).<br>Mental abilities: 2/34 (6%) moderate improvement, 10/34 (29%) mild improvement, 22/34 (65%) no improvement.<br>Speech abilities: moderate improvement 3/41 (7%), mild improvement 15/41 (37%), no improvement 23/41 (56%). | 4/50 (8%) stopped treatments because of unwanted effects, including seizures, oral automatic movements, hyperesthesia of the face, extreme increasing pulse rate. | |
| Machado 1989[122] Brazil (Poor) | Immediately after HBOT: 218/230 (95%) patients had clear reduction of spasticity (nearly 50% less). Frequently, clonus or Babinski sign would disappear, with better plantar support and abolition of leg "scissoring."<br>12/230 (5%) remained unchanged.<br>In 82 patients followed for 6 or more months: 76% had persisting reduction of spasticity & better motor control. Parents reported other types of improvement, such as better balance, more attentive, more "intelligent" with reduced frequency of convulsions & episodes of bronchitis.<br>24% were apparently unchanged. | One parent found daughter to be worse, with convulsions some time after the course of HBOT. | This is acknowledged to be only a reporting of this facility's experiences, is not intended as a scientific study. |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 4. Cerebral palsy observational study data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Montgomery 1999[123] Canada (Fair) | Children with CP and a functional diagnosis of spastic diplegia. Age 3 to 8 years (mean 5.6 years). | 95% oxygen at 1.75 atm x 60 minutes x 20 sessions. 10 of the patients received 1 treatment daily x 5 days per week x 4 weeks in a monoplace chamber. The other 15 received 2 treatments daily x 5 days per week x 2 weeks in a multiplace chamber. (Either monoplace or multiplace) | None | Before-after | 25 |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 4. Cerebral palsy observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Montgomery 1999[123] Canada (Fair) | GMFM; fine motor function by Jebsen's test, and spasticity level by the modified Ashworth scale. Videotapes of motor function also assessed by physical therapists. Oral questionnaires on physical functioning administered by physical therapists. | Pre- and post-treatment evaluations separated by a mean of 37.2 (+/- 8) days. |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 4. Cerebral palsy observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Montgomery 1999[123] Canada (Fair) | On GMFM, significant improvements ($p < 0.05$) observed for 3 of 5 dimensions: sitting, standing, walking/running/jumping. Not on lying/rolling or crawling/kneeling. Average improvement in total GMFM score was 5.3%.<br>Functional evaluation of hand: Significant improvement on 3 of 6 tests: turning cards, moving large cans, and moving weighted cans. Not on picking up small objects & placing in a container, stacking checkers, or simulated eating.<br>Spasticity: Physician determined significant reduction in spasticity in hip abductors, hamstrings, ankle plantar flexors. Physical therapist noted improvement only in left quadriceps femoris.<br>Video analysis of gross motor function: better movement post-test in 16/24 (67%) children, better pre-test in 7/24 (29%), and equal for 1/24 (4%).<br>On parent questionnaire, significant improvement occurred for 4 of 9 activities: walking, high kneeling, sitting on the floor, and sitting on a bench. The proportion of patients whose scores improved for each of these items were 38%, 33%, 50%, and 42%, respectively. Scores were not improved for crawling, undressing ($p = 0.07$), eating, personal hygiene, or communication. | Pressure equalization tubes inserted in 13 children, all using multiplace chamber, none using monoplace chamber. | Pressure equalization tubes were given to 13 children in the multiplace unit to aid in compression discomfort. Subjects selected randomly from a total pool of 60 potential then randomly assigned to the HBOT protocol administered. |



HBOT=hyperbaric oxygen therapy; CP=cerebral palsy; atm=atmospheres; GMFM=Gross Motor Function Measure; EEG=electroencephologram; CT=computerized tomography

## Evidence Table 5. Stroke controlled trial data

| Author, year, location (Quality) | Population | HBOT Protocol (Type of chamber) | Control |
|---|---|---|---|
| Anderson 1991[127] Minnesota (Fair) | Patients with ischemic cerebral infarction. | 100% oxygen at 1.5 atm x 60 minutes every 8 hours x 15 treatments. Standard ICU plus physical and occupational therapy. Vitamin E 400 units given with each HBOT session. (Monoplace) | Room air at 1.5 atm x 60 minutes every 8 hours x 15 treatments. Standard ICU plus physical and occupational therapy. |
| Marroni 1987[129] Italy (Poor) | Stabilized stroke patients no longer undergoing any form of therapy or rehabilitation, 69% male, mean age 59.7 (range 24-78), who had a stroke from 2 to 172 months earlier (average 29.2 months). | Group C1: HBOT at 2.0 atm x 60 minutes x 30 sessions<br>Group C2: Same as C1 at 1.5 ata<br>Group D1: HBOT + Rehab: 30 in-water, 40-minute morning rehab sessions (water temperature 30 degrees celsius) and HBOT 2.0 atm x 60minutes x 30 afternoon sessions.<br>Group D2: Same as D1 at 1.5 ata<br>Group E1: HBOT Rehab: 30 simultaneous, 60-minute HBOT and 40-minute in-water rehab sessions (water temp 30 degrees celsius) in specially-built hyperbaric pool at 2.0 ata.<br>Group E2: Same as E1 at 1.5 ata.<br>(BIBS mask overboard dump system)? | Group A: No treatment,<br>Group B: 30 in-water physical therapy sessions x 40 minutes in 30 degree celsius water. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Randomized? | Baseline differences between groups | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Anderson 1991[127] Minnesota (Fair) | Yes | Small difference in age, other factors similar, including baseline neurologic scores. | 20 HBOT<br>19 control | Graded neurological exam (0 to 100), volume of hypodensity on CT scan. | Neurological exam administered at entry, 5 days, 6 weeks, 4 months, and 1 year. Hypodensity measured at 4 months. |
| Marroni 1987[129] Italy (Poor) | No | Not reported. | 80 total:<br>11 A<br>7 B<br>15 C1<br>10 C2<br>9 D1<br>7 D2<br>12 E1<br>9 E2 | All patients evaluated using Kurtzke scale before entering protocol, then at days 10, 20, and 30 of treatment and 1 and 3 months after treatment . At the same time, all pts scored according to an original neuromotor disability evaluation scale (given in paper). | Patients evaluated before entering protocol, then at days 10, 20, and 30 of treatment and 1 and 3 months after treatment. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Anderson 1991[127] Minnesota (Fair) | Average graded neurological exam scores<br>Baseline: 44.6 (control), 45.5 (HBOT):<br>Day 5: 38.5 (control), 43.8 (HBOT) $p = 0.54$<br>Week 6: 28.3 (control), 38.5 (HBOT) $p = 0.25$<br>Month 4: 25.6 (control), 34.5 (HBOT) $p = 0.33$<br>Year 1: 25.8 (control), 31.4 (HBOT) $p = 0.53$ | 2 complications (group not clear): 1 patient with a history of psychiatric illness became acutely psychotic in the chamber, 1 developed atelectasis the authors believe was exacerbated by sedation and suspension of pulmonary toilet during treatment. No seizures. 8/39 (21%) patients refused to continue treatments (not specified from which groups). | Study suspended after enrollment of 39 patients when a safety monitoring committee detected an outcome trend favoring sham treatment. |
| Marroni 1987[129] Italy (Poor) | Evaluation of general disability according to the Kurtzke functional scale showed improvement between 1 and 1.8 degrees in HBOT groups; non-HBOT groups did not show notable changes. Using an unvalidated scale developed by the authors, all dry HBOT groups showed greater improvement in their motor ability, but no clear-cut difference could be observed among the 4 groups that scored improvements of from 3.1 to 3.8 degrees. HBOT 1.5 atm rehab group reached 8.1 degrees 1 month after treatment, leveling off to 7.7 at 3 months, and the 2.0 atm HBOT rehab group showed an 11.6 degree improvement still present 3 months after treatment. The scale ranged from 17 (best) to 111 (worst) points. No statistical analysis, data presented graphically as means only. | Not reported. | |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Population | HBOT Protocol (Type of chamber) | Control |
|---|---|---|---|
| Nighoghossian 1995[126] France (Poor) | Patients with ischemic stroke in middle cerebral artery confirmed by CT and seen within 24 hours of onset. | 100% oxygen at 1.5 atm x 40 minutes daily x 10 treatments. (Monoplace) | Room air at 1.5 atm x 40 minutes daily x 10 treatments. |
| Rusyniak 2003[131] Indiana (Fair) | Patients presenting to Emergency Department within 24 hours of onset of symptoms and measurable deficit by NIHSS and without evidence of hemorrhage by CT scan. | 100% oxygen at 2.5 atm x 1 hour x 1 session (Monoplace) | Control: 100% oxygen at 1.14 atm x 1 hour x 1 session |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Randomized? | Baseline differences between groups | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Nighoghossian 1995[126] France (Poor) | Yes | Not clear, Orgogozo scale lower in control group at baseline (not statistically significant). | 17 HBOT<br>17 control | Three scales: Orgogozo scale, Rankin disability scale, and Trouilla scale. | Only Orgogozo scale administered at baseline, all three administered at 6 months and 1 year. |
| Rusyniak 2003[131] Indiana (Fair) | Yes | Some differences in age gender and race (HBOT group older, fewer women, more Black patients) | 17 HBOT<br>16 control | Primary outcome = Proportion with "good" outcome on NIHSS at 24 hours and 90 days (score of 0 or improvement of >4 points) and on Barthel Index (score 95 or 100), Modified Rankin score (score </= 1), and GOS (score = 5) at 90 days<br>Secondary outcomes = mortality and adverse events | Only NIHSS at baseline. Follow up at 24 hours and 90 days |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Nighoghossian 1995[126] France (Poor) | Difference in mean score (HBOT-Control) on Orgogozo scale:<br>6 months: 18.2 (-3.4, 39.9) (NS)<br>1 year: 27.9 (6.0, 50.0) ($p$ = 0.02)<br>*On Trouillas scale:*<br>6 months: -1.5 (-3.3, 0.3) (NS)<br>1 year: -2.2 (-4.2, -0.2) ($p$ = 0.13)<br>*On Rankin scale:*<br>6 months: -0.6 (-1.5, 0.2) (NS)<br>1 year: -0.6 (1.5, 0.2) (NS)<br><br>Pretherapeutic and posttherapeutic differences (HBOT-Control)<br>*On Orgogozo scale:*<br>Difference (6 months -baseline): 7.1 (-14.6, 28) $p$ = 0.51<br>Difference (1 year - baseline): 16.8 (-6.9, 40.4) $p$ = 0.16<br>*On Trouillas scale:*<br>Difference (1 year - 6 months): -0.6 (-1.6, 0.4) $p$ = 0.50<br>*On Rankin scale:*<br>Difference (1 year - 6 months): 0.1 (-0.3, 0.5) $p$ = 0.78 | Treatment discontinued in 7 patients (21%): 4 due to worsening of neurological status in first week (3 died), 3 patients had myocardial infarction, worsening of neurological condition related to ischemic injury, and claustrophobia. | |
| Rusyniak 2003[131] Indiana (Fair) | Proportion with good outcome on NIHSS at<br>24 hours: HBOT 18%, control 31%, p=0.44<br>90 days: HBOT 29%, control 50% p=0.30 (ITT)<br>90 days: HBOT 31%, control 80% p=0.04 (PP)<br><br>Proportion with good outcome at 90 days on:<br>Barthel Index: HBOT 47%, control 56%, p=0.73 (ITT)<br>HBOT 50%, control 82%, p=0.12 (PP)<br>Modified Rankin score: HBOT 29%, control 56%, p=0.17 (ITT)<br>HBOT 31%, control 82% p=0.02 (PP)<br>GOS: HBOT 35%, control 63% p = 0.17 (ITT)<br>HBOT 38%, control 91% p = 0.01 (PP) | HBOT: 2 patients (ear pain, claustrophobia)<br>Control: 3 patients (claustrophobia) (p=0.44)<br>Deaths: HBOT: 1, Control 2 (p=0.6) | Planned as a pilot study, no power calculations. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Population | HBOT Protocol (Type of chamber) | Control |
|---|---|---|---|
| Sarno, JE 1972[128]<br>Sarno, MT 1972[130]<br>New York<br>(Fair) | Patients with vascular stroke at least 3 months post-stroke. Mean age 60.5 years, range 42-82. In MT Sarno, subset of 16 patients with left-brain damage, right hemiplegic patients. Mean age 62, range 44-82. | 100% oxygen at 2.0 atm x 1.5 hours x 1 session. (Multiplace. In early phase of the study, plastic hood sealed with tape was used, but patients complained of confinement and claustrophobia. Changed to mask) | 10.5% oxygen at 2.0 atm x 1.5 hours x 1 session. |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Randomized? | Baseline differences between groups | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Sarno, JE 1972[128] Sarno, MT 1972[130] New York (Fair) | Yes (randomized crossover) | Not reported. | 32 (all received both HBOT and control) (subset of 16 reported in MT Sarno) | Cognitive-perceptual testing (Token Test and Functional Communication Profile) and communication testing (those with right brain damage were only given the cognitive-perceptual tests). | Communication baseline done 24 hours prior to exposure, immediately after HBOT treatment. Baseline cognitive test given in the chamber with mask in place. The followup done in chamber after exposed to 2.0 atm for 30 minutes. |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 5. Stroke controlled trial data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Sarno, JE 1972[128] Sarno, MT 1972[130] New York (Fair) | No significant effect on any measure. | Not reported. | |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; CT=computerized tomography; ICU=intensive care unit; NS=non-significant; NIHSS=National Institutes of Health Stroke Scale; GOS=Glascow Outcomes Scale; ITT=intention-to-treat-analysis; PP=per-protocol analysis

## Evidence Table 6. Stroke observational study data

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Hart 1973[149] California (Poor) | Patients referred with middle cerebral artery ischemia. Neurologic state unchanging for at least 3 weeks and at least 4 weeks from onset of ischemic attack. Excluded if untreated malignancy, severe emphysema, or uncontrollable claustrophobia. Had to refrain from nicotine use. | 2.5 atm x 90 minutes daily x 15 days. Allowed to rest for 30 days and if measurable improvement had occurred, a second series of 15 treatments administered. (Monoplace) | Methyldopa, 250 mg tid, acetazolamide 500 mg 1 hour prior to treatment, or cyclandelate 200 mg bid, alpha-tocopheroll 25 mg qid, anticoagulation (coumadin preferred). Idiazepam 10 mg im tid if apprehensive; physical therapy, gait training, and speech therapy. | Before-after | 40 |
| Heyman 1966[133] North Carolina (Poor) | Patients with neurologic deficits caused by various forms of cerebral vascular disease. Clinical manifestations of cerebral ischemia were sudden in onset, clearly defined, and usually consisted of hemiplegia, hemisensory loss, aphasia, and coma. One hour to 30 days since onset of symptoms. | 2.0 to 3.0 ata. Duration and extent of compression selected in each patient to minimize the risk of oxygen toxicity. In initial studies patients had 3.04 atm for less than 1 hour. In later treatments, used 2.5 atm to allow prolonged exposure (duration not specified). (Chamber type not reported, used mask or head tent) | Myringotomies performed prior to compression. | Time-series | 22 |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Hart 1973[149] California (Poor) | Improved neurological exam (tests not specified), death. | Complete neurological exam and EEG prior to onset of therapy, not clear when followup exams done. |
| Heyman 1966[133] North Carolina (Poor) | Clinical and neurologic changes (observations). | Not clear how long followup was, clinical and neurologic changes monitored throughout HBOT procedure and at frequent intervals thereafter. |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Hart 1973[149] California (Poor) | 7/40 (17.5%) died, 33 (82.5%) improved; 11/15 (73%) aphasic improved. | One patient became worse during therapy (found at autopsy to have a cerebral metastasis). | |
| Heyman 1966[133] North Carolina (Poor) | Of 15 patients whose symptoms began within the preceding several hours, 4 (27%) improved dramatically during HBOT, with complete or almost complete restoration of neurologic and mental function, immediate reversal of paralysis with return of strength and ability to perform fine controlled movements, striking improvement in consciousness, increased awareness and responsiveness, aphasic patients regained speech and comprehension. Only 2 of these maintained recovery. In 6 other patients, favorable responses were less dramatic, moderate but significant improvement in mentation immediately following HBOT, but definite neurologic dysfunction persisted, and immediately after decompression clinical picture reverted to pretreatment level. None of the remaining 12 patients improved during HBOT. | One patient developed hemolysis similar to that observed in tocopherol-deficient mice exposed to toxic levels of oxygen pressure. Jaundice and anemia occurred shortly after treatment, and blood pressure rose strikingly during procedure. Patient ultimately recovered from the anemia, but died 3 months later from complications of his cerebrovascular disease. | |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Holbach 1977[141] Germany (Poor) | Patients with cerebral infarction, including occlusive lesion of internal carotid or middle cerebral artery, TIA or completed stroke. | 1.5 atm x 40 minutes. TIA patients received one session. Stroke patients received 15 daily sessions. (Chamber type not reported) | None reported. | Time-series | 101: 27 TIA 38 complete stroke 36 chronic stroke |
| Holbach 1977[142] Germany (Poor) | Patients with internal carotid artery occlusion in chronic post-stroke state, with distinct neurologic deficits persisting beyond the 4th week following stroke. Internal carotid artery occlusion and the availability of a superficial temporal artery of sufficient caliber were determined by angiography. | 1.5 atm x about 40 minutes daily x 10-15. (Chamber type not reported) | Patients with superficial temporal artery of sufficient caliber were considered suitable to undergo EIAB if necessary. | Before-after | 20 |
| Imai 1974[105] Japan (Poor) | Patients with cerebral thrombosis. | 1.3 atm x 60 minutes daily x 5 sessions. (Monoplace chamber) | None. | Before-after | 18 |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Holbach 1977[141] Germany (Poor) | Neurologic exam and EEG. | Neurologic and EEG exams at beginning, middle, and conclusion of series of sessions. EEGs also during HBOT. |
| Holbach 1977[142] Germany (Poor) | Neurological exam. | Neurological exam given before and after each HBOT session. Patients assessed by an independent neurologist prior to HBOT treatment, during the course of treatment, at conclusion of treatment, and 6 weeks after conclusion of treatment or after EIAB. |
| Imai 1974[105] Japan (Poor) | Psychological and physical tests, Bender-Gestalt, memory scale. | Unclear if and when baseline conducted. Followup conducted after one or two sessions. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Holbach 1977[141] Germany (Poor) | Complete stroke due to occlusion of the internal carotid artery (23 patients): 72% had marked improvement of neurological deficit at conclusion of HBOT treatment.<br>Complete stroke due to middle cerebral artery occlusion (15 patients): 66% had a marked improvement of neurological deficit at conclusion of HBOT treatment.<br>Chronic stroke (36 patients): 45% had a marked improvement of neurological deficit at conclusion of HBOT treatment.<br>No neurological outcome data reported on patients with TIAs. | Not reported. | Neurologic exams not described, results of these reported in very general way. |
| Holbach 1977[142] Germany (Poor) | 11 patients (55%) favorably affected by HBOT all received EIAB after HBOT therapy complete; 9 patients (45%) affected little by HBOT (little or no improvement immediately after HBOT and 6 to 12 months later). | Not reported. | |
| Imai 1974[105] Japan (Poor) | Bender-Gestalt test and memory scale after 1 or 2 courses of treatment:<br>In 18 cases of cerebral thrombosis, orientation improved 20% or more, mental control and associate learning improved 10%-15%, visual reproduction, color recognition, body image improved 15%-20%, and logical memory, digit span, and story recall improved 1%-4%. Total score improved 15%-20%.<br>Aphasia, old memory, neurological signs improved, disturbance of recent memory not improved. | Not reported. | Results reported only ranges of percentage improvement. Unclear how subjects chosen. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Jain 1989[134] Germany (Poor) | Patients with cerebrovascular occlusive disease, age 44-64 years, with clinically assessible spasticity and radiographically documented diagnosis. | 1.5 atm x 45 minutes daily x 5 weeks. The first HBOT session was given without physical therapy, subsequent sessions conducted simultaneously with physical therapy. (Chamber type not reported, but HBOT occurred simultaneously with physical therapy, so assume multiplace) | Stroke rehabilitation, including physical therapy. Outpatient physical therapy continued after HBOT treatments completed. | Time-series | 21 |
| Jain 1990[143] Germany (Poor) | Patients with occlusive cerebrovascular disease and residual hemiparesis or hemiplegia, referred from acute-care stroke facilities. Stable chronic post-stroke state (3 weeks to 5 years) and no day-to-day neurological changes during the first week of admission to the clinic. Only patients who were available to senior author for clinical examination before, during, and after HBOT therapy are included in the paper. | 1.5 atm x 30 minutes daily x up to 5 weeks. (Chamber type not reported, but grip strength measured in the chamber, so assume multiplace) | Physical therapy simultaneously with HBOT. | Before-after | 25 |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Jain 1989[134] Germany (Poor) | Motor power of the hand using a hand-held dynamometer and measured in the paralyzed hand only (graded as 0-5). Spasticity assessed on a scale of 0-5. | Followup measurements of spasticity at 24 hours after each HBOT session. Timing of motor power tests not stated. Followup continued every 3 months. |
| Jain 1990[143] Germany (Poor) | Spasticity (graded 0 - 5), handgrip by dynamometer, neurological and functional assessment. | Assessments at admission and discharge, handgrip measured during first week of stay. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Jain 1989[134] Germany (Poor) | Of 21 patients: A rapid improvement of spasticity was noted in all the patients during the first HBOT session. This was significantly more than that observed with physical therapy, normobaric oxygen, or hyperbaric air. Improvement was transitory and receded during first 24 hours, but effects were more durable when physical therapy was carried out with HBOT and repeated daily for 5 weeks. Improvement maintained at 6 months to 1 year followup. Recovery of motor function was sometimes not detectable until after a few HBOT sessions. Recovery of motor function was slower but more durable. In patients with marked spasticity of lower extremities, improved gait resulted after "retraining" to walk. No change in tendon reflexes, clonus diminished.<br>(Grade changes are given for during HBOT, after 6 weeks of HBOT, and at 6 months to 1 year followup) | No complications. Two patients showed a transient tremor of the hand at the end of the session but this did not recur. | Results include only hand spasticity grades during, 6 weeks post, and 6-12 months post HBOT - no baselines and no motor power results. |
| Jain 1990[143] Germany (Poor) | All patients with spasticity grade 2-5 had spasticity reduced by 1 or 2 grades during HBOT. Improvement initially transient, regressed 1-8 hours after treatment, prolonged up to 12 hours by conducting physical therapy in chamber. Many patients kept their improvement at 3 months followup without additional HBOT treatments. | Not reported. | |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Kapp 1981[144] Florida (Poor) | Patients with angiographic evidence of carotid or middle cerebral artery occlusion, weakness on opposite side or speech impairment, and less than age 80. | 1.5 atm x 40 minutes daily x 14 days. (Chamber type not reported, used mask) | None reported. | Time-series | 22 |
| Li, 1998[135] China (Poor) | Patients with cerebral thrombosis at one hospital (390 male, 100 female, age 28-79), with disturbance of consciousness and cognition, aphasia, etc., confirmed by neurologist. | 2.5 atm x 90 minutes with a 15-minute break, daily. One course = 15 treatments. Patients usually had 3 to 4 courses, rarely more. (Chamber type not reported) | None reported. | Before-after | 490 |
| Neubauer 1980[139] Florida (Poor) | Consecutive patients with acute or chronic completed cerebrovascular accident: 34 acute, 88 chronic; mean age 66 (range 44-88). | For patients with onset of symptoms 4 hours or less: Pressure not specified. 60 minutes every 12 hours (some increased to every 2-6 hours). After 10 treatments, reduced to weekly, then monthly. Mean total treatments = 16 (range 12-20). For > 4 hours since onset of symptoms: 2.0 atm x 60 minutes daily x 10, then weekly x 4, then monthly thereafter. Average total treatments = 10 (range 10-90). (Monoplace used in all but 6 patients) | None reported. | Before-after | 122 |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Kapp 1981[144] Florida (Poor) | Neurological function, specifically grip strength, mental status, speech, 2-point discrimination, and repetitive thumb/finger movements. | Evaluation before, twice during, and after every HBOT treatment. |
| Li, 1998[135] China (Poor) | Evaluation: completely cured (signs & symptoms disappeared completely, patients lead normal, active lives without difficulty); markedly improved (most signs & symptoms disappeared, "myodynamia" improved more than 2 degrees); improved (symptoms & signs disappeared partially, some difficulty in walking, cannot care for self entirely, "myodynamia" improved less than 2 degrees); no effect (no improvement in signs & symptoms); not reported how these were measured or when, or by whom. | Not reported. |
| Neubauer 1980[139] Florida (Poor) | No standard tests; changes in ambulation reported for some patients based on assessments from neurologists, physical therapists, nurses, MDs, and family. Reported increased quality of life for some patients - measure not given. | Not reported. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Kapp 1981[144] Florida (Poor) | 10/22 (45%) had improved motor function during HBOT.<br>6/14 (43%) with infarction of left hemisphere with dysplasia had improvement in speech.<br>7/10 (70%) responders to HBOT subsequently had successful revascularization with no further cerebral infarcts from 4-20 months following surgery (3 had no or unsuccessful revascularization). | No complications definitely related to HBOT. One patient developed pulmonary infiltrate after 5 days, 1 had a pulmonary embolus after 10 days. | Study intended to identify candidates for cerebral revascularization procedure. |
| Li, 1998[135] China (Poor) | 108/409 (26%) completely cured, 157/409 (38%) markedly improved, 166/409 (41%) improved, 59/409 (14%) no effect.<br>Also report: In a group receiving HBOT and conventional treatment 10/25 (40%) markedly improved, 15/25 (60%) improved. In a group receiving conventional treatment alone, 4/25 (16%) markedly improved, 19/25 (76%) improved, 2/25 no effect (8%). | Not reported. | |
| Neubauer 1980[139] Florida (Poor) | Treatment begun when patient bedridden (11 patients):<br>9% improved enough to use a wheelchair, 18% to walk with aids, 27% to walk independently, 45% no improvement.<br>Treatment begun when patient wheelchair bound (31 patients):<br>26% improved enough to walk with aids, 45% to walk independently, 29% no improvement.<br>Treatment begun when patient walking with aids (48 patients):<br>56% improved enough to walk independently, 44% no improvement.<br>49/79 (62%) who received HBOT 5 months-10 years after onset of stroke reported improvement in quality of life (increased ability to communicate with family members, willingness to participate in social activities, interest in constructive self-regulatory behavior).<br>Compared to patients with stroke at another hospital without HBOT, HBOT patients had fewer days in the hospital (HBOT 177 days vs standard treatment 287 days) | 5%-6% of patients developed barotrauma which was usually minor and easily controlled with medication (type not stated).<br>Myringotomies were required in 1% of patients. | Selection of comparison sample not defined. Very little discussion of differences for acute/chronic. Results presented for only 90 patients. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Noguchi 1983[136] Japan (Poor) | Patients treated with HBOT from April 1980 to March 1983 at one emergency medical center, 42.2% with central nervous system diseases which were probably due to systemic or local circulatory disturbances or hypoxia (cerebrovascular spasm, brain infarction, brain hypoxia, carbon monoxide intoxication, and spinal cord disease). | 2.0 to 3.0 atm x 45-60 minute (compressed within 20-25 minutes, decompressed over 5-30 minutes). Standard procedure was once daily, but twice daily was done at "critical stages, or in cases in which rapid improvement was expected." When symptoms became more stable, one treatment per day was done. Course was 3 weeks. (Multiplace) | None reported. | Before-after | 316 overall, 46 with cerebral infarction |
| Pilotti 1991[147] Italy (Poor) | Patients with clearly demonstrable completed stroke in the chronic phase, all had a stroke between 1977 and 1985 and received HBOT in 1985 at one research center. Control group recruited from neurology department at another hospital, matched for age at time of stroke, did not receive HBOT. | 1.5 - 2.0 atm x 90 minutes once daily x 30. (Chamber not reported, but reports patients are those reported in Marroni 1986, 1987) | No HBOT. | Retrospective comparison of cohorts | 65 HBOT 65 control |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Noguchi 1983[136] Japan (Poor) | Patients' response in the HBOT chamber, clinical signs and symptoms, clinical course, physical examination, and CT findings. Divided into marked improvement, improvement, and no improvement (not defined). When treatment was stopped too early to notice its effects, classified as "no improvement." GCS also used in cases of disturbance of consciousness. Cases recovered to 6-7 in GCS score were classified as "marked improvement," to 4-5 as "improvement," and to 3 "no improvement." | Not clear. |
| Pilotti 1991[147] Italy (Poor) | Patients in control and treatment groups were treated at 2 different institutions. Small differences with respect to age, sex, clinical history. Respiratory insufficiency, vascular insufficiency of inferior limbs, and arterial hypertension were higher in HBOT-treated group ($p < 0.05$) | Mortality 5 years post-stroke. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Noguchi 1983[136] Japan (Poor) | Of 46 cases of cerebral infarction: 21 (45.7%) marked improvement, 14 (30.4%) improvement, and 11 (23.9%) no improvement. | Not reported. | |
| Pilotti 1991[147] Italy (Poor) | Retrospectively examined mortality incidence in 5-year period after HBOT was received. | 21/65 deaths in HBOT group (32%), 31/65 in control group (48%) ($p$ = 0.048) | Not reported. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Saltzman 1965[145] North Carolina (Poor) | Patients with cerebral ischemia with neurologic deficits (hemiplegia, hemisensory loss, aphasia, and loss of consciousness). | 2.0 - 2.04 atm x less than 1 hour to 5 hours. Number of treatments not reported. (Chamber type not reported, used mask or head tent) | Myringotomies performed on most patients prophylactically. | Before-after | 25 |
| Steenblock 1998[137] California (Poor) | Patients with stroke (49) and brain injury (1). Mean age 61.8 (range 31-89). | 1.5 to 2.0 atm x 90 minutes daily 6 days a week. "Some" patients received treatment twice a day. Average total number of treatments = 55. (Monoplace) | Physical therapy 5 times per week and biofeedback therapy 5 times per week. | Before-after | 50 |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Saltzman 1965[145] North Carolina (Poor) | No standard test; changes in neurologic deficits described for each patient who improved either permanently or temporarily. | No baseline reported. Followup varies from patient to patient. |
| Steenblock 1998[137] California (Poor) | Patient self-evaluation of 16 functions graded ranging from "negative change" to "back to normal." Physical therapist evaluation of 33 functions (including range of movement, extremity strength, bed mobility, transfer, and balance) divided into "improvement," "no improvement," or NA if function was normal at baseline. | Patient evaluations prior to and after the series of HBOT, physical therapist evaluations prior to and at the "end of the program." |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Saltzman 1965[145] North Carolina (Poor) | Of 25 patients:<br>48% no improvement<br>32%: favorable responses during treatment, including cleared mentation & partial restoration of motor activity. However, definite neurologic dysfunction persisted, in most instances clinical picture reverted to pretreatment level immediately after decompression.<br>20% improved dramatically during treatment, with complete or almost complete restoration of neurologic & mental function, including immediate reversal of paralysis, within 5 to 10 minutes of beginning HBOT. In 2 of these, improvement was permanent. In 3, improvement dramatic but temporary, with return of symptoms 2 hours after HBOT. | One patient developed hemolysis. Jaundice and anemia occurred shortly after HBOT treatment, and blood pressure rose strikingly during procedure. | Difficult to know if TIA vs. stroke. 18 patients had onset of neurologic symptoms within 7 hours of starting HBOT. |
| Steenblock 1998[137] California (Poor) | At end of program, 96.7% of patients reported total improvement in at least one of the 16 functions. 3.3% reported no improvement, 30% considered the program "good," 46.7% considered program "excellent," 20% considered program "stupendous." Physical therapist evaluations found all patients showed one or more improvements among the 33 functions: 10% minimal gains, 7% mild gains, 48% good gains, 34% excellent gains.<br>Patients reported chronically cold arm or leg changed to warm during therapy. Fingernails and hair began to grow normally again, chronic fatigue generally relieved by the program. | "Only insignificant problems were encountered." Three of over 500 patients overall required tympanostomy tubes placed. | Exact timing of followup assessments not clear. One subject included had a diagnosis of "car accident". |



HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Population | HBOT protocol (Type of chamber) | Other interventions | Study design | Number of patients |
|---|---|---|---|---|---|
| Tsuro[138] 1983 Japan (Poor) | Part 1: patients with ischemic cerebrovascular disease, average age 50, neurological signs marked in 15, moderate in 9, and slight in 6.<br><br>Part 2: patients who developed mental signs lasting more than 2 weeks following surgery for cerebral aneurysm; 53% operated on within 2 weeks of subarachnoid hemorrhage, 47% later than 2 weeks after attack. | Part 1: 2.0 atm x 60 minutes daily x 6 to 30 times (average 13).<br><br>Part 2: 2.0 atm x 60 minutes daily, number of treatments not specified.<br><br>(Monoplace) | None reported. | Before-after | part 1: 30; part 2: 49 |
| Wassman 1986[146] Germany (Poor) | Completed stroke patients (74% male) who showed definite increase of EPE (electrical power equivalent) values after an HBOT series. All had persisting neurological deficits about 3 months after stroke as a result of occlusion of an internal carotid artery. | 1.5 atm x about 40 minutes, once daily x 10 to 15 treatments. (Chamber type not reported, states "specially constructed") | None reported. | Time-series | 73: 38 had EIAB surgery following HBOT series 35 did not |
| Zhou Shn-rong 1995[110] China (Poor) | Men & women age 1 month - 73 years, in coma due to acute cerebral ischemia & hypoxia in 95 cases: drowning (23), hanging (44), electric shock (2), narco-operation accident (14), Adam-Stoke's Syndrome (1), barbital poisoning (4), asphyxia (2), and cover-bedding syndrome (11). 3 cases head trauma, 226 carbon monoxide poisoning, 12 acute hydrogen sulfide poisoning. | 2.0-2.5 atm x 2 hours twice daily in the first 2 to 3 days, and then 2.0 atm once daily. Timing of treatment depends on change in patient's condition. Course of treatment may reach 40-60 treatments.<br>(Chamber type not reported) | Not reported. | Before-after | 336 |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Outcomes measured | Baseline and followup |
|---|---|---|
| Tsuro[138] 1983 Japan (Poor) | *Part 1:* Neurological signs (motor, sensory, amnestic aphasia, hemiparesis) *Part 2:* Severity of mental signs classified into 4 grades: absent (no mental signs), slight (slight disturbance of mental signs, for example slight disturbance in recent memory), moderate (moderate disturbance of mental signs, presumed to have trouble in social life), and marked (marked disturbance of mental signs, not able to return to previous social life). Efficacy of HBOT ranked into 4 groups: excellent (improvement by 2 grades), moderately improved (improvement by 1 grade), slightly improved (improvement without promotion to higher grade), and unchanged (no change). Method of determining grades not specified. | Not reported. |
| Wassman 1986[146] Germany (Poor) | EEG, changes in motor function. | Neurological examinations carried out before, during, and after HBOT therapy. Patients followed for 4.5 years after HBOT or after EIAB surgery. |
| Zhou Shn-rong 1995[110] China (Poor) | Criteria for treatment effect: cure (consciousness and labor ability recovered with no sequelae, curative effect is stable during followup); notable effect (consciousness and labor ability recovered, with low-grade sequelae); improvement (consciousness recovered, patient can take care of self partly and has sequelae); no effect (patient's condition has no improvement or deterioration). Not reported how or when assessed. | Not reported. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 6. Stroke observational study data (continued)

| Author, year, location (Quality) | Results | Adverse effects | Comments |
|---|---|---|---|
| Tsuro[138] 1983 Japan (Poor) | Part 1: 8/30 (27%) excellent recovery; 9/30 (30%) moderate improvement; 8/30 (27%) slight improvement; 3/30 (10%) unchanged neurological signs.<br><br>Part 2: 3/49 (6%) excellent improvement, 23/49 (47%) moderate improvement, 15/49 (31%) slight improvement, 8/49 (16%) unchanged. | Part 1: No patient showed aggravation of neurological signs after HBOT, Part 2 none reported. | |
| Wassman 1986[146] Germany (Poor) | 6 months after HBOT, both groups showed increases of 4 points in recovery from motor deficit. After bypass surgery (3-6 months after HBOT?), patients who had surgery showed an additional improvement of nearly 3 points during the next 8 months. This level of improvement continued in most patients during the remaining 3 years of the followup period. | States in 10,000 HBOT sessions conducted since 1967, no complications worth mentioning occurred. | |
| Zhou Shn-rong 1995[110] China (Poor) | Of 95 cases of cerebral ischemia and hypoxia:<br>68% cured, 2% notable effect, 4% improvement, 24 (25%) no effect.<br>Of 3 traumatic brain injury: 100% regained consciousness after 7 to 20 HBOT treatments. | Not reported. | |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; TIA=transient ischemic attack; EEG=electroencephalogram; EIAB=extra- intracranial arterial bypass; GCS=Glasgow Coma Scale; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| ***Patients with traumatic brain injury*** | | | | |
| Barrett 1998 | Patients with chronic stable TBI, at least 3 years post-injury. Controls = healthy volunteers for CBF measurements after one HBOT session. | Meeting abstract | Not reported. | 1.5 atm x 60 minutes x 120 sessions. 5 month rest between first 80 sessions and final 40 sessions. |
| Gelety 1983 | Patients in chronic coma from closed head injury. In vigil coma for 3 weeks-27 months, age 3-67 years. | Meeting abstract | Not reported. | 1.5 - 2.0 atm x 60 to 90 minutes x 40 to 80 treatments. |
| Guo 1996 | Patients with post-traumatic brain injury (26 male and 5 female). Manifestation of disease was intellectual stimulation and "hypomnesis". | Meeting abstract | Not reported. | Under 2.5 atm x 40 minutes twice with a break of 10 to 20 minutes in between, daily x 20 days. |
| Jianhui 2000 | Patients with brain stem damage without cerebral hernia, unconscious. GCS grade 4 to 7. | Conference proceedings | Not reported. | 2.0 atm x 80-90 minutes once daily x 10 per course x 1 to 6 courses, varying according to patient's condition. |
| Kondratenko 1981 | Patients with severe craniocerebral injury. | Meeting abstract | Not reported. | 1.90-1.45 atm x 30-60 minutes. Number of sessions depended on patient's condition. |
| Neubauer 2001 | Patients with varying degrees of TBI, age 3 to 80. Onset since injury: 6 months to 16 years. GCS 3-12. | Conference proceedings | Not reported. | Most received 1.5 atm x 60minutes, but those with seizure disorder received 1.1 to 1.25 ata. From 80 to 500 consecutive treatments. (monoplace chamber) |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| ***Patients with traumatic brain injury*** | | | | | |
| Barrett 1998 | None reported. | Controlled trial | 5 HBOT 6 control (no TBI) | Cerebral blood flow, speech fluency, neurologic, cognitive, and progressive exercise testing. | Not reported. |
| Gelety 1983 | None reported. | Before-after | 16 | Glasgow Coma Scale. | Not reported. |
| Guo 1996 | None reported. | Before-after | 31 post-traumatic brain injury. | Digital symbol test (from Wechsler adult intelligence scale). | Outcome measured pre- and post- therapy, but timing not specified. |
| Jianhui 2000 | Control group received routine therapy, including dehydration, antibiotics, cortex hormone, etc. | Controlled trial | 32 HBOT 25 control | GCS grade; cure (consciousness, symptoms disappear, can care for self), marked effect (consciousness, main symptoms disappear, can care for self on the whole, accompanying sequelae), positive effect (consciousness, on the mend, cannot care for self), no effect (still not conscious), death. | Not reported. |
| Kondratenko 1981 | None reported. | Before-after | 101 | Mortality. | Not reported. |
| Neubauer 2001 | All modalities of PT, OT, speech therapy, biofeedback, nutritional counseling, accupunture, herbal medications when indicated. | Before-after | 60 | Removal of G-tube, closing of tracheostomy, and communication ability. | Not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| ***Patients with traumatic brain injury*** | | |
| Barrett 1998 | In the HBOT group, no changes were seen in progressive exercise and neurologic testing. Speech fluency universally improved, as did group mean scores of memory, attention, and executive function. Improvement peaked at 80 treatments. (no scores given, scales used not given, p values not given) | |
| Gelety 1983 | 10/16 cases responded (63%); 6 were successfully rehabilitated and 4 had a lightening of the coma and became semi-responsive; 6 showed no change, there was no worsening in any patient. | |
| Guo 1996 | Change in digital symbol test (post test mean-pre test mean):<br>cerebral thrombosis: 6.1 (+/- 5.5) (14.7-8.6)<br>p < 0.0001 | See stroke section for stroke results |
| Jianhui 2000 | HBOT group: 22/32 (69%) cure, 4/32 (13%) marked effect, 0/32 (0%) positive effect, 1/32 (3%) no effect, 5/32 (16%) death.<br>Control group: 9/25 (36%) cure, 3/25 (12%) marked effect, 1/25 (4%) positive effect, 2/25 (8%) no effect, 10/25 (40%) death.<br>*p* < 0.05 (for all comparisons? Not clear)<br>Return to consciousness by 2 weeks: 18/32 (56%) HBOT, 4/25 (16%) control. (*p* not given) | |
| Kondratenko 1981 | For patients with craniocerebral injury in the acute period, favorable effect observed in 69% of cases, mortality decreased by 38.1% as compared to the control group. No uniform effect of HBOT was obtained in both groups in the rehabilitation period. | |
| Neubauer 2001 | In nearly all cases the G-tube was removed, in 80% the tracheostomy was closed. Few with GCS at lower level returned fully to society. 70% some degree of improvement to point of being able to communicate verbally, with word-board, computer or sign language. No patient regressed. | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Rockswold 1985 | Patients with head trauma at one medical center. | Meeting abstract | Unable to obey commands or pronounce recognizable words. | Not reported. |
| ***Patients with other brain injury*** | | | | |
| Harch 1994 | Patients with chronic traumatic, ischemic, hypoxic, and anoxic brain injuries. | Meeting abstract | All referrals with chronic stable encephalopathies manifested by perfusion/ metabolism deficits on HMPAO SPECT scans that improved on repeat scan immediately after a 1.5 or 1.75 ata/90 min HBOT treatment. | Primarily 1.5 atm x 90 minutes once or twice daily x 40 (1 patient), 60 (1 patient), or 80 (16 patients) treatments. |
| Juan 1992 | Patients with congenital heart diseases who had anoxic encephalopathy after open heart surgery done under extracorporeal circulation. Age 3 to 16 years; time in coma was 30, 35, 9, and 12 days. | Meeting abstract | Not reported. | Dose, total number of treatments not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Rockswold 1985 | All patients receive intensive neurosurgery care, treatment group also receives HBOT. | Randomized controlled trial | 30 (first admitted into the study) | Intracranial pressure, neurological exams, CT scans of the brain, multimodal evoked responses, neuropsychological tests, and neurological followup evaluations. This abstract reports mortality data only on the first 30 patients. | Monitored during hospital and post-hospital course (not specified). |
| ***Patients with other brain injury*** | | | | | |
| March 1994 | Standard rehabilitation when possible. | Before-after | 18 | Neurologic changes were noted by combinations of history, exam, video, occupational and physical therapists, neuropsychologists, referring doctors, and final SPECT scans. | Not clear. |
| Juan 1992 | None reported. | Time-series | 4 | Regained consciousness, intelligence, and limb function (not specified how measured). | Not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Rockswold 1985 | Mortality rate of those with GCS score of 7-9 show no significantl difference between groups; patients with GCS of 3 had 100% mortality rate. Patients with GCS of 4-6 results suggest increased survival among HBOT-treated group (p = 0.100). | Numbers of patients in each group are not given, states that number with GCS 4-6 is "small". |
| ***Patients with other brain injury*** | | |
| March 1994 | 18/18 patients (100%) showed motor, behavioral, personality, or cognitive gains. 6/18 patients (33%) noted neurological changes on the intervention either in chamber or later that day, 16/18 (89%) noted neurological changes by 18 treatments (range 7-33) including emotional lability and personality changes. All noted changes by 40 treatments, many had further gains at 60-70, and all were improved at 80 treatments. 16/18 patients (89%) or their parents requested continuous treatment beyond the study endpoint of 80 treatments, 2 patients (11%) (40 and 60 treatments) stopped for personal reasons and sinusitis. | |
| Juan 1992 | 4 patients (100%) regained consciousness on 6th, 2nd, 10th, and 4th HBOT treatment, respectively. They walked without help on the 50th, 10th, 20th, and 20th treatment. 3 (75%) had perfect intelligence restored on the 30th, 25th, and 20th treatment, 1 (25%) had partial intelligence restored after 10 treatments and then stopped treatment for some reason. | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Keim 1997 | Patients age 4-72 with brain injury from carbon monoxide (4 patients), closed head trauma (4 patients), and ischemia/asphyxia (2 patients). | Meeting abstract | Not reported. | 2.0 atm x 90 minutes or 1.5 atm x 90 minutes (not specified which patients had which treatment) for time intervals determined by clinical course or IRB protocol (maximum 120 treatments over 390 days). Time interval from injury to treatment ranged from 6 hours to 11 years. |
| Lantsev 1981 | Newborn infants with asphyxia delivered by Caesarian section. | Meeting abstract | Not reported. | 3.0 atm x first 15 minutes, then 1.5-1.3 atm x 1.5-2 hours. Started within 5 minutes after birth. |
| Lianbi 2002 | Children with brain injury (23 post-operation for cerebral tumor, 39 with cerebral trauma), average age 6.5 years (5.4), all with severe or moderate cerebral edema, in coma 3-12 days. | Conference proceedings | Not reported. | 0.2 Mpa once daily, average number of treatments was 30. |
| Mathieu 1982 | Patients admitted to one emergency unit for unsuccessful hanging between 1970 and 1981. | Meeting abstract | Not reported. | 136 patients had 278 HBOT courses at 2.0 atm x 90 minutes. 34 patients with only minor neurological troubles received normobaric oxygen. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Keim 1997 | None reported. | Before-after | 10 | Clinical improvement, SPECT imaging. | Not reported. |
| Lantsev 1981 | Artificial pulmonary ventilation. | Before-after | 56 | | 3-10 year followup. |
| Lianbi 2002 | None reported. | Time-series | 62 | Neuropediatric and neurophysiologic evaluation, change in functional outcomes. | Before treatment and at 1, 2, and 3 months after HBOT. |
| Mathieu 1982 | All had supportive and anticerebral edema measures. | Before-after | 170 (136 received HBOT, but results are reported for entire group) | Mortality, survival without sequelae, survival with neurologic sequelae. | Not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Keim 1997 | Clinical improvement was seen in all 10 patients (100%). | |
| Lantsev 1981 | 33 infants delivered by caesarian section followed for 3-10 years. Only in one child (3%), at age 3 1/2, epilepsy and deaf-mutism were revealed. The other children (97%) developed normally. | |
| Lianbi 2002 | Satisfactory curative effect was observed in all patients (100%), especially within the early time of lesion (sooner after injury?), results are invariable and permanent, no evidence that HBOT promoted growth or metastasis of tumor. | |
| Mathieu 1982 | 132/170 (78%) recovered completely without any sequelae, 8/170 (5%) recovered with neurological sequelae, and 30/170 (17%) died. Neurological recovery was obtained after 0.8 HBOT course in patients in grade I coma, 1.5 courses in patients in grade II, 2.5 courses in grade III, and 3.9 courses in grade IV. In any case, recovery was obtained after the fifth course. Results were significantly better when HBOT treatment began before the third hour after the unsuccessful hanging. | Same study as Wattel 1981 with one more years' data, more patients |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Pilinoga 1981 | Neonates with intracranial birth injuries. | Meeting abstract | Not reported. | 1.2-1.5 atm x 20-30 minutes; number of sessions depended on severity of neonate's state, range 5-12 sessions. Started 3-9 days after delivery. |
| Yi Zhi 1996 | Patients with persistent vegetative state from head injury, cerebral hemmorhage, cerebral infarction, surgery for meningioma. Longest coma lasted 281 days prior to HBOT. | Meeting abstract | Not reported. | 0.2 Mpa x 80 minutes per session, with a break of 10 minutes, one session per day. One treatment course was 10 sessions. Minimum sessions 20 and maximum 86. |
| ***Patients with cerebral palsy*** | | | | |
| Barrett 2001 | Children with cerebral palsy, average age 41.8 months. | Meeting abstract | Not reported. | 1.5 atm x one hour daily x five days per week x 60 treatments. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Pilinoga 1981 | None reported. | Time-series | 80 infants with intracranial birth injuries received HBOT (48 severe, 21 moderate, 11 mild). 52 followed up 6 months to 6 years. | Elimination of pathological disorders in respiration, cardiovascular, thermal regulation, and regression of neurological impairments, observation by pediatrician and neuropathologist after discharge from hospital. | 6 months to 6 years followup. |
| Yi Zhi 1996 | Conventional therapy. | Before-after | 8 | Resumed consciousness. | Not reported. |
| ***Patients with cerebral palsy*** | | | | | |
| Barrett 2001 | None reported. | Before-after | 5 (results on 4 only, one patient dropped before completion) | Modified test of gross motor and fine motor function (GMFM-m) and modified Ashworth Spasticity Scale. | Outcomes measured before and after HBOT therapy. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; CBF=cerebral blood flow; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ= memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Pilinoga 1981 | Functions of cardiovascular system and thermal regulation reached usual age norms following 2-3 HBOT sessions. Neurological symptoms regressed at a slower rate depending on severity of intracranial birth injuries. Of 52 children under observation from 6 months to 6 years found no deviations from the age norm. | |
| Yi Zhi 1996 | All 8 patients (100%) resumed consciousness upon completion of the HBOT courses. | |
| ***Patients with cerebral palsy*** | | |
| Barrett 2001 | Modest decreases in spasticity and improvements in the modified GMFM scores for all patients completing the study. | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Kazantseva 2002 | Children under age 14 with brain injury (47 hypertensive headache, 25 epilepsy, 8 cerebral palsy). | Conference proceedings | Not reported. | HBOT: 1.2 atm x 20 minutes x 1-4 sessions (47 children); MHT (minimized hyperbaric treatment): 1.05-1.1 atm with 30% oxygen x 20 minutes x 5-10 sessions (54 children, 40 of them received Q10 10-30 mg and picnogenol 15-30 mg). 21 children received HBOT and later were administered MHT. |
| Lobov 2002 | Children age 6 months to 15 years with various forms of clinical cerebral palsy. | Conference proceedings | Not reported. | "The whole spectra of mild standard isopressure regimens" up to 2.0 atm with 40-60 minute exposures, the whole course lasting 1-10 exposures. |
| Marois 1998 | Children with cerebral palsy, with a functional diagnosis of spastic diplegia, 10 girls and 15 boys, mean age 5.6 years, range 3.1-8.2 years. | Abstract (there is reference to a website that may contain full results, but is no longer available). | Not reported. | 1.75 atm x 60 minutes x 20. |
| Zerbini, 2002 | Children with chronic encephalopathy. | Conference proceedings | Not reported. | Not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Kazantseva 2002 | 40/54 MHT children received Q10 10-30 mg and picnogenol 15-30 mg. | Retrospective cohort | 80 | Neurological exam. | Not reported. |
| Lobov 2002 | None reported. | Before-after | 60 | Clinical improvement. | Not reported. |
| Marois 1998 | None reported. | Time-series | 25 | The same evaluators (physician, physical and occupational therapist) conducted pre and post evaluations. Gross Motor Function Measure, Jebsen Test for hand function, modified Ashworth Scale (evaluation by both physical therapist and physician), evaluation of reflexes. | Evaluations before treatment and at 2 weeks post-treatment and 3 months post-treatment. |
| Zerbini, 2002 | None reported. | Before-after | 232 | Spasticity, global motor coordination, attention, memory, comprehension, reasoning, interest, visual perception, control of the sphincter, control of the sialorrhea (?), increasing sociability. | Evaluated 1-6 months after HBOT. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Kazantseva 2002 | Minimized hyperbaric treatment accompanied by a more pronounced therapeutic effect than HBOT. Use of antioxidants noticeably increased the efficacy of HBOT and duration of the after effect period. | Results of neurological exam not reported, only intermediate outcomes. |
| Lobov 2002 | Good or satisfactory outcome up to clinical convalescence was obtained in 20 patients with hypoxic-and-dyscirculatory cerebral lesions. Results insignificant or doubtful in 30 patients (50%). Efficacy of HBOT depended on disease severity and patient's age. Better results in children under 1 year, at risk of cerebral palsy development, and in those with spastic hemiplegia and diplegia. | |
| Marois 1998 | Results of 3-month follow up evaluation not available at time of publication.<br>Pre and post-treatment (2 weeks):<br>GMFM significantly improved for items B,D, and E ($p$ <0.001); Jebsen Test significant for card turning, lifting objects, and stacking checkers ($p$ < 0.05); spasticity decreased in the hip abductors, hamstrings, and ankle plantarflexors for the evaluation by physician (p < 0.01); spasticity decreased in quadriceps as measured by the physical therapist ($p$ < 0.05); patellar tendon and Achilles tendon reflexes significantly reduced ($p$ < 0.05); questionnaire revealed significant improvement for walking and sitting ($p$ < 0.01) and knee walking ($p$ < 0.05). | |
| Zerbini, 2002 | 41.8% had decrease in spasticity, 33.2% improved global motor coordination, improvement in attention 40.1%, memory 10.8%, comprehension 13.3%, reasoning 5.6%, interest 6.9%, visual perception 12.9%, control of the sphincter 6.5%, control of the sialorrhea 4.3%, which made it possible to improve daily activities, increasing sociability in 13.8% of cases. | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| ***Patients with stroke*** | | | | |
| Guo 1996 | Patients with cerebral thrombosis (24 male 16 female). Manifestation of disease was intellectual stimulation and "hypomnesis". | Meeting abstract | Not reported. | Under 2.5 atm x 40 minutes, twice with a break of 10 to 20 minutes in between. Every day x 20 days. |
| Holbach 1979 | Stroke patients with persisting neurological deficits due to occlusive lesions in the internal carotid or middle cerebral artery. | Meeting abstract | Not reported. | All patients received 15 single HBOT sessions given daily (dose/duration not reported) before either surgical treatment (extra-intracranial arterial bypass) or medical treatment. |
| Jain 1988 | Post-stroke with no day-to-day changes in neurological status despite physical therapy. | Meeting abstract | Not reported. | 1.5 atm x 60 minutes x 1 |
| Jain 1989 | Patients in chronic post-stroke stage with severe spasticity of the hemiplegic side. | Meeting abstract | Not reported. | Normobaric 100% oxygen, hyperbaric air, and HBOT at 1.5 atm, duration not clear (40 minutes daily for 5 weeks?). |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| ***Patients with stroke*** | | | | | |
| Guo 1996 | None reported. | Before-after | 40 | Digital symbol test (from Wechsler adult intelligence scale). | Outcome measured pre- and post- therapy, but timing not specified. |
| Holbach 1979 | Surgery or medical treatment. | Randomized controlled trial (randomized to either surgery or medical treatment, after all received HBOT) | 112 | Improvement, favorable EEG or neurological response (not described). | Long-term neurological and EEG analytical exams regularly carried out (not specified when). |
| Jain 1988 | None reported. | Before-after | 4 | The patients were accompanied into the HBOT chamber and had motor power (hand grip) and spasticity measured manually by the author. | Baseline not reported, followup varied, up to two weeks post-treatment |
| Jain 1989 | Physical therapy. | Before-after | 18 | Clinical and video-recording of the gait, dynamography, and photography of the spastic hand. | Spasticity measured during HBOT treatment, effect of physical therapy was observed both prior to and during HBOT. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| ***Patients with stroke*** | | |
| Guo 1996 | Change in digital symbol test (post test mean-pre test mean): cerebral thrombosis: 12.2 (+/- 5.5) (28.6-16.4) $p < 0.0001$ | See brain injury section for traumatic brain injury results. |
| Holbach 1979 | Nearly all patients with a favorable EEG or neurological response, or both, to HBOT showed a positive response to extra-intracranial arterial bypass surgery, while in patients where HBOT was considered to be ineffective there was little or no change in impaired neuronal functions following surgery. | Both groups received HBOT, study designed to assess HBOT as predictor of surgical success |
| Jain 1988 | 3 patients with spasticity: relief of spasticity which was maximal 15 minutes after start of HBOT and the effect persisted on average 1 hour following the session. During this period motor function improved. Range of motion of the limbs and finger movements on the paralyzed side improved, and posture of the hand improved. In one patient in which handgrip was measured, it increased from 2 to 4 kg during the first session, and 2 weeks later handgrip was 12 kg. In one patient with no spasticity, grip increased from less than 1 kg to 4 kg during the first session and dropped to 2 kg one hour later. No change in tendon reflexes. Improvement in motor power was observed again in the following HBOT session and improvement to 4 kg maintained for the rest of the day. | Results reported on a per-patient basis. |
| Jain 1989 | Maximum relief was seen under HBOT in all patients. Improvement was transient initially but combined HBOT and physical therapy for 40 minutes daily for 5 weeks led to persisting improvement of spasticity and contributed to improvement of motor function. | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Nagayoshi 1991 | Patients with cerebral embolism treated with HBOT from 1981 to 1989. | Meeting abstract | Not reported. | Dose, duration not reported, patients analyzed according to period when HBOT was started from onset of disease (0-24 hours, 24-48 hours, 48-72 hours, 3 days-1 week, 1-2 weeks, 2-3 weeks, and 3-4 weeks). |
| Oshima 1990 | Patients with acute cerebral infarction, admitted to one hospital within 2 weeks of onset. | Meeting abstract | Not reported. | 2.0 atm x 90 minutes once daily, and in severe cases, twice daily. 20-30 sessions. |
| Sansone 1997 | Patients with focal cerebral ischemia due to occlusion of middle or anterior cerebral arteries. Mean age 61 (range 43 - 76). | Meeting abstract | Not reported. | HBOT=100% oxygen at 1.5-1.8 atm x 60 minutes daily (3x20 minutes separated by 3 minutes of breathing air) daily x 8-10 treatments. Control =room air x 60 minutes daily (3x20 minutes separated by 3 minutes of breathing air) daily x 8-10 treatments. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Nagayoshi 1991 | None reported. | Before-after | 158 | Consciousness, motor, sensory, speech, and other "subjective symptoms." Each item evaluated on 4-point scale, improvement rate classified as excellent, good, fair, or poor. | Before treatment and after 20 treatments |
| Oshima 1990 | None reported. | Controlled trial? | 67 (26 mild, 21 moderate, 20 severe). Patients in each severity group divided into 2 groups with or without HBOT, but numbers in each group not given. | Lactic acid of cerebrospinal fluid, CT of the brain, infarction index (size of maximum forcus/hemicerebral space X 100), clinical symptoms. | Outcomes measured before, during, and after therapy (not specified). |
| Sansone 1997 | None reported. | Randomized controlled trial | 17 (9 intervention, 8 control) | Neurologic Recovery Score (assume 10 = no disability, 0 = dead, but unclear due to typographical error in report). | Baseline, 6 and 12 months |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Nagayoshi 1991 | In groups that started within 48 hours, rates of excellent and good cases were higher than any other group ($p$ <0.05). | |
| Oshima 1990 | Effects of HBOT were remarkable in the moderate group, effects were not significant in mild or severe group. Improvement of clinical symptoms correlated with decrease in lactic acid of cerebrospinal fluid and infarction index. | |
| Sansone 1997 | Difference in neurological recovery score<br>(10= no disability, 0 = dead),<br>(HBOT-Control)<br>6 months: -0.8 (sd 0.9), $p$ = 0.21<br>12 months: -2.2 (sd 1.0), $p$ = 0.031 | Does not give baseline data, only reports change in score within group, not compared to change in control group. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Population | Type of publication | Inclusion criteria | HBOT protocol |
|---|---|---|---|---|
| Shalkevich 2000 | Patients with ischemic stroke. | Meeting abstract | Not reported. | HBOT: 1.5 atm x 40-60 minutes x 4-6 procedures. HBOT applied once every 6 months. Control no HBOT. |
| Vysotsky 1981 | Patients with air embolism of the cerebral vessels developing mainly during open heart surgery, and patients with thrombosis and thromboembolic complications. | Meeting abstract | Not reported. | Patients with air embolism (17): 6-8 atm for 40-35 minutes. "On subsequent stepwise regression beginning at 3-2.8 atm artificial ventilation of the lungs with 100% oxygen while under pressure" Patients with thrombosis (7): intermittent HBOT of 6 sessions at 3 atm for 60 minutes. |
| Ystrokeu 1981 | Patients with ischemic stroke and cerebral injuries and intracranial hematomas. Most were in grave condition in coma and stupor and severe focal symptoms. | Meeting abstract | Not reported. | 1.6-2.0 atm x 40-60 minutes x 6-15 sessions. Treatment started in 80% of cases on day 2-7 after onset, in 20% on day 7-20. |
| Yu 1981 | Patients with ischemic stroke and cerebral injuries and intracranial hematomas. Most in critical condition with coma and stupor with severe focal symptoms. | Meeting abstract | Not reported. | Course: 4 sessions at 1.6-2.0 atm x 40-60 minutes x 6-15 treatments. Started on 2nd-7th day after insult in 80%, 7th-20th day in 20%. |
| Zhem 1986 | Patients age 40-70 with cerebral thrombosis. | Meeting abstract | Not reported. | Not reported. |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Other interventions | Study design | Number of patients | Outcomes measured | Baseline and followup |
|---|---|---|---|---|---|
| Shalkevich 2000 | Both groups received low-dose aspirin, antihypertensive and antisclerotic agents. | Controlled trial | 48 treatment, 49 control | Recurrent stroke/TIA. | 5 years of followup. |
| Vysotsky 1981 | None reported. | Before-after | Says 32 patients studied, but report on only 24. | Recovery of consciousness, focal neurological symptomatology. | Not reported. |
| Ystrokeu 1981 | None reported. | Before-after | 264 (140 ischemic stroke;124 cerebral injuries and intracranial hematomas) | Neurological symptoms, specifics or how measured not reported (also reports other clinical data, such as cerebral blood flow). | Not reported. |
| Yu 1981 | None reported. | Before-after | 140 stroke, 124 cerebral injuries and intracranial hematomas. | Neurological symptoms. | Not reported. |
| Zhem 1986 | None reported. | Before-after | 36 | Short-term memory (MQ of individual event scale, observation of the character of memory function in different hemispheres). | Not reported- results "after treatment by HBOT." |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 7. Conference proceedings and abstract-only study data (continued)

| Author year | Results | Comments |
|---|---|---|
| Shalkevich 2000 | Within 5 years, rare TIA in 2 patients (4.8%) in HBOT group, in the arterial system where a stroke previously occurred, in control group, 3 patients (5.9%) had a recurrent stroke, 2 within 2 years and 1 within 4 years. | No data on baseline severity or risk factors, selection of patients into HBOT/no-HBOT not described. |
| Vysotsky 1981 | Consciousness returned in 13/24 (54%) patients in Group 1 (air embolism). In Group 2 (thrombosis), 1/6 patients (17%) regained consciousness. Focal neurological symptomatology regressed much more slowly. | |
| Ystrokeu 1981 | In patients with ischemic strokes, 80% had a regression of neurological symptomatology (i.e., symptoms improved) and in 52% of observations the onset of diminishing neurological deficiency coincided with the beginning of the HBOT course. Data on neurological symptoms in patients with brain injury not reported. | Notes "sporadic convulsive fits." |
| Yu 1981 | Neurological symptoms regressed in 80% of patients with ischemic stroke and in 52% the onset of improvement coincided with the start of HBOT. | |
| Zhem 1986 | After HBOT treatment, memory of patients improved significantly, MQ of individual event scale value, $p < 0.001$ (no details given) | |

HBOT=hyperbaric oxygen therapy; TBI=traumatic brain injury; atm=atmospheres; GCS=Glasgow Coma Scale; GMFM=Gross Motor Function Measure; HMPAO SPECT=99mTc-hexamethyl propylene-amine-oxime single photon emission computed tomography; MPa = miliPascals TIA=transient ischemic attack; MQ=memory quotient; MHT=minimized hyperbaric treatment; PT=physical therapy; OT=occupational therapy; CT=computerized tomography

## Evidence Table 8. Quality assessment of controlled studies

| Author, year (Quality) | Randomization/ allocation concealment | Baseline comparability | Timing of baseline measures sufficiently close to intervention? | Intervention the same for all patients within groups? | Outcome measures stated and objective? |
|---|---|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | | | |
| Artru 1976[88] (Fair) | Randomization, allocation methods not reported. | Similar. | Yes (coma scored at admission to study) | No, other medical factors delayed or disrupted treatments. | Yes (mortality and duration of coma, pulmonary complications) |
| Rockswold 1985,[89] 1992,[90] 1994[91] (Fair) | Randomization, allocation methods not reported. | Small differences in proportion with operable mass lesions, multiple trauma, elevated ICP and "poor outcome BAEPs (Brainstem Auditory Evoked Potentials) and SSEPs (Somatosensory Evoked Potentials )" | Yes | No, number of treatments could vary. | Yes |
| ***Studies of other types of brain injury*** | | | | | |
| Jianhua 1995[106] (Poor) | Randomization, allocation methods not reported. | No statistical test performed, but baseline characteristics reported, appear similar. | Not stated | Similar HBOT treatments (not exactly the same). Control interventions actually used not stated. | Stated, but not objective |
| ***Studies of cerebral palsy*** | | | | | |
| Collet 2001[119] (Fair) | Yes, centralized randomization, concealment by sealed envelopes. | Some differences in presumed cause and type of CP and in baseline GMFM scores. | Yes | Yes | Yes (GMFM) |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Timing of follow-up measurements stated and adequate? | Followup adequacy (loss to followup) | Handling of dropouts or missing data | Masking | Statistical analysis |
|---|---|---|---|---|---|
| ***Studies of traumatic brain injury*** | | | | | |
| Artru 1976[88] (Fair) | Yes (1 month) | All 60 followed for 12 months | No dropouts. | Not reported | Chi-squared test presented for some outcomes. |
| Rockswold 1985,[89] 1992,[90] 1994[91] (Fair) | Yes | Good; 1 lost to follow up | Unclear - 24 protocol violations occurred, including medical condition not compatible with study and/or HBOT, but unclear how these handled. Two missing data in control group, lost to followup and excluded from analysis. | Single masked. Assessments done by masked neurologist | Stratified chi-squared analyses by GCS score and age, comparisons based on 12-month followup exam. Chi-squared test and survival analysis presented for some outcomes. |
| ***Studies of other types of brain injury*** | | | | | |
| Jianhua 1995[106] (Poor) | Not stated | Dropouts not reported | Dropouts not reported. | Not reported | Groups had "obvious differences (p<0.001) through the processing of statistics," no details. |
| ***Studies of cerebral palsy*** | | | | | |
| Collet 2001[119] (Fair) | Yes (3 months) | Good, 96% | Intention-to-treat analysis. | Double-masked | Groups compared by analysis of covariance. Non-parametric tests also used. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Comments | External validity |
|---|---|---|
| ***Studies of*** | | |
| Artru 1976[88] (Fair) | More acute subdural hematomas developed and required surgery in the HBOT group. Because of highly stratified groups, sample sizes very small for some analyses. | 60/185 (32%) screened were enrolled "not particularly selected, inclusion depended on availability of chamber." |
| Rockswold 1985,[89] 1992,[90] 1994[91] (Fair) | Not ITT based on exclusion of two patients lost to followup in control group, but was ITT for HBOT group. HBOT group received closer monitoring of ICPs. | Severity of head injury was moderate, with mean GCS 6.2. Selection of subjects is unclear, 168 of 272 (62%) potential subjects included. |
| ***Studies of other types of brain injury*** | | |
| Jianhua 1995[106] (Poor) | | Poor. Not enough details, difference in terminology. Viral cerebritis, age 1-11. No information on selection of patients. |
| ***Studies of*** | | |
| Collet 2001[119] (Fair) | | Children with asthma, seizures or recent otitis media, surgery, botulinum toxin or rhizotomy excluded. Medications stopped 6 weeks prior to trial. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Randomization/ allocation concealment | Baseline comparability | Timing of baseline measures sufficiently close to intervention | Intervention the same for all patients within groups? | Outcome measures stated and objective? |
|---|---|---|---|---|---|
| Packard 2000[118] (Poor) | Randomization, allocation methods not reported. | Not reported beyond subjects "matched roughly to age and severity." | Yes | Yes | Yes |
| ***Studies of stroke*** | | | | | |
| Anderson 1991[127] (Fair) | Randomization, allocation methods not reported. | Small difference in age, other factors similar, including baseline neurologic scores. | Yes | Yes | Yes (graded neurological exam) |
| Marroni 1987[129] (Poor) | Not randomized (assigned by "first come first to get the free position"). | Not reported. | Not stated | Yes | Yes (Kurtzke scale and author's scale) |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Timing of follow-up measurements stated and adequte? | Followup adequacy (loss to followup) | Handling of dropouts or missing data | Masking | Statistical analysis |
|---|---|---|---|---|---|
| Packard 2000[118] (Poor) | Yes | 3/26 did not complete treatment (12%). Assessment data for both time points available for 20/26 patients (77%). | Results not reported for 3 patients who did not complete treatment. | Physical therapists who completed Peabody Motor Scales, child psychologists who completed Bayley II and Preschool Language Scale tests were masked. Parents were not. | P-values given for mean change scores, analysis not described. |
| ***Studies of stroke*** | | | | | |
| Anderson 1991[127] (Fair) | Yes | Fair- 25/39 (64%) randomized followed for one year, 70% at 4 months. | Not included in analysis, reasons for dropouts reported. | Double-masked | Paired t-tests on difference between exam score at onset and at 4 months. |
| Marroni 1987[129] (Poor) | Yes | Dropouts not reported. | Dropouts not reported. | Single masked (examiner) | Plotted mean improvement in disability index. P-values reported for some measures, no details given. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Comments | External validity |
|---|---|---|
| Packard 2000[118] (Poor) | Enrolled children of different ages and disabilities, excluded patients with seizures in last 6 months. No information on screening process. | Not enough information to assess. |
| ***Studies of stroke*** | | |
| Anderson 1991[127] (Fair) | Subjects in the control group had a mean age of 69.1 years, in HBOT group was 63.7 years. Randomization was stratified by baseline neurological exam. Mean number of treatments completed was 10 in control group, 8.9 in HBOT.<br><br>Data analyzed cross-sectionally, rather than as mean change in score for each group. | 39/92 patients screened were enrolled, reasons for exclusion given; only patients with new, moderate, stable deficits included. |
| Marroni 1987[129] (Poor) | | No information on selection, all were no longer undergoing any form of therapy or rehabilitation. |

HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Randomization/ allocation concealment | Baseline comparability | Timing of baseline measures sufficiently close to intervention | Intervention the same for all patients within groups? | Outcome measures stated and objective? |
|---|---|---|---|---|---|
| Nighoghossian 1995[126] (Poor) | Randomization, allocation methods not reported. | Not clear, Orgogozo scale lower in air group at baseline (not statistically significant). | Not stated | Yes | Yes |
| Sarno JE 1972,[128] Sarno MT 1972[130] (Fair) | Randomization, allocation methods not reported. | Not reported. | No | No | Yes |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Timing of follow-up measurements stated and adequte? | Followup adequacy (loss to followup) | Handling of dropouts or missing data | Masking | Statistical analysis |
|---|---|---|---|---|---|
| Nighoghossian 1995[126] (Poor) | Yes | Poor- 7 of 34 (21%) discontinued (13 control and 14 HBOT completed), 4 because of worsening (3 died), 1 MI, claustrophobia, ischemic damage | Not included in analysis | Patients may have been masked, unclear if assessors masked (says "double-masked" in title, but not described) | T-test of means pre and post therapy and comparison of differences of post scores at 6 months and 1 year. |
| Sarno JE 1972,[128] Sarno MT 1972[130] (Fair) | No, only immediately after HBOT | Dropouts not reported | Dropouts not reported | Double-masked | States data did not warrant a detailed statistical analysis, results of token test and Functional Communication Profile were statistically treated to illustrate and confirm absence of improvement. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 8. Quality assessment of controlled studies (continued)

| Author, year (Quality) | Comments | External validity |
|---|---|---|
| Nighoghossian 1995[126] (Poor) | | Radiologic evidence (CT scan) of recent ischemic stroke, and significant deficit on Orgogozo scale required. Excluded: patients with previous stroke, seizures with stroke, significant improvement within 1 hour of stroke, metabolic encephalopathy, significant pulmonary disease, congestive heart failure or uncontrolled hypertension. |
| Sarno JE 1972,[128] Sarno MT 1972[130] (Fair) | Effects are those during treatment only. Documented stroke, but unclear how/why patients selected for study. | N of 60 was planned, but difficulty due to negative patient attitudes changed it to 32. Some patients refused participation when they learned of the absence of beneficial effects. 14 patients rejected for a variety of contraindications. All were examined for pulmonary tests, eliminated if pulmonary status would interfere with the development of high blood oxygen levels, patients with hearing loss excluded. |



HBOT=hyperbaric oxygen therapy; ICP=intracranial pressure; CP=cerebral palsy; GMFM=Gross Motor Function Measure; ITT=intention-to-treat; GCS=Glasgow Coma Scale; CT=computerized tomography; MI=myocardial infarction

## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| ***Traumatic Brain Injury*** | | | | | |
| Artru 1976[94] (Fair) | Before-after | Yes, except one compressed at 2.2 atm instead of 2.5 because of a bad pulmonary condition. | No | Severity, diagnosis of each patient reported. | Not reported |
| Hayakawa 1971[95] (Fair) | Time-series | Yes for dose, number of treatments varied from 10 to 15 | No | No | No |
| Mogami 1969[96] (Poor) | Before-after | No | No | No | Not reported |
| Ren 2001[99] (Poor) | Retrospective cohort | Similar HBOT treatments (not exactly the same). Control interventions actually used not stated. | No | No | No |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| ***Traumatic Brain Injury*** | | | | | |
| Artru 1976[94] (Fair) | Not reported when or how clinical status measured, other measures taken in close proximity. | CBF, metabolic rates for oxygen, glucose and lactate and CSF parameters measured 2 hours after exit from the chamber, clinical status seemed to be measured immediately after exit. | No for clinical status, yes for other measures. | | Not reported how patients selected, no standard assessment of severity of illness, only 6 patients. |
| Hayakawa 1971[95] (Fair) | Yes | Yes | Yes | | Very small sample from one institution, no info on patient selection. |
| Mogami 1969[96] (Poor) | Not reported, "before treatment". | Yes | Subjective, observation (e.g., increased awareness and responsiveness) | | Not clear, some patients comatose, some requiring ventilation, others with only mild deficits. No information on selection of patients, no description of patients except diagnosis and symptoms. |
| Ren 2001[99] (Poor) | Yes | Yes | Yes | | No information on selection. Uneven numbers in groups, reason not given. Mean GCS = 5.3 a& 5.1, not enough other details to assess. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Rockswold 2001[97] (Fair) | Time-series | Dose and duration the same, number of treatments varied according to response. | No | Yes- time from injury to treatment, type of brain injury and types of multiple trauma. | Yes |
| Sukoff 1982[98] (Poor) | Before-after | No- frequency changed based on ICP and clinical response. | No | No | No |
| ***Other Brain Injury*** | | | | | |
| Chuba 1997[107] (Poor) | Before-after | No | No- all patients presented with new or increasing neurologic deficits. | Some confounding factors listed (e.g., tumor); not controlled for. | Not reported |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Rockswold 2001[97] (Fair) | Yes | Yes | Yes | | Patients were from one Level I trauma center, number screened not given, excluded patients placed in barbiturate-induced coma. |
| Sukoff 1982[98] (Poor) | Not reported | Yes | Subjective | Vague reporting of results, other than ICP measurements. | Only a series of patients in whom HBOT was effective in reducing ICP and showed improved neurological status. No information on how many other patients treated without improvements. Patients requiring vasopressors or with dilated and fixed pupils excluded. |
| ***Other Brain Injury*** | | | | | |
| Chuba 1997[107] (Poor) | Not clear | Yes | No- symptoms, method not described | Very few outcome measures reported. | Children with radiation-induced necrosis of CNS, mostly in supratentorial location. All patients had increasing neurologic deficits and had failed steroids. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Imai 1974[108] (Poor) | Before-after | Yes | No- not reported | No | Not reported |
| Mathieu 1987[109] (Poor) | Before-after | Dose the same, but number of treatments varied according to condition | No | No | No |
| ***Studies of Cerebral Palsy*** | | | | | |
| Chavdarov 2002[121] (Poor) | Before-after | Yes | No | Reports data grouped by level of severity. | No |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Imai 1974[108] (Poor) | Not clear | "After one or two treatments" | Yes | Few details about how subjects selected or if/when baseline tests done. | No information on selection of patients, no description of patients except diagnosis; very mixed group selected: patients with presenile dementia, chronic alcoholism, cerebral vascular disease, and CO intoxication. |
| Mathieu 1987[109] (Poor) | Baseline information not reported except for GCS measure on admission, timing not clear in relation to HBOT | Timing not reported | Death, neurological sequelae described, "recovery without sequelae" not defined, not objective. Method of measuring outcomes not reported. | | All patients at one institution with attempted hanging, 71 (42%) had psychiatric illness. |
| ***Studies of Cerebral Palsy*** | | | | | |
| Chavdarov 2002[121] (Poor) | Yes | Yes | Yes, but measured by the same assessor before and after treatment | | Not clear how patients selected, all were from one hospital in Bulgaria, described inclusion criteria (history of seizures excluded, among other). |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Machado 1989[122] (Poor) | Time-series | No | No | No | No |
| Montgomery 1999[123] (Fair) | Before-after | No, varied by center | Yes. Inclusion criteria stated functional plateau in rehabilitation for 12 months (defined as no measurable functional changes in gross motor performance as documented by their physical therapists. | Potential effect of age is addressed by type of test given. | Not clear: outcome assessors had "no contact" with children during HBOT; but not necessarily masked. |
| ***Studies of Stroke*** | | | | | |
| Hart 1973[149] (Poor) | Time-series | No, same pressure and time, but different drug therapies and a second course given if improvement seen | No- criteria were 3 weeks stable and at least 4 weeks from onset of ischemic attack. | No- all patients received physical therapy, gait training, and speech therapy. Only age and other medications given in different recovery groups were reported, but not controlled for. | No |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Machado 198122 (Poor) | Not clear ("had been reviewed before and after therapy") | Yes | Subjective-observations | Few details about intervention, or outcome measurements | Retrospective review of CP patients treated at one institution, states that report is observations based on clinical findings and without scientific documentation, followed up only 39% (only those that lived in Sao Paolo). Diagnosis not defined. |
| Montgomery 1999[123] (Fair) | Pre and post evaluations separated by 37.2 +/- 8 days | Pre and post evaluations separated by 37.2 +/- 8 days | Stated, some subjective, some objective | This study randomized subjects to two weeks of HBOT or 4 weeks of HBOT, with no control group. | Excluded were those with recent rhizotomy, thoracic surgery, epilepsy, cancer, asthma, VP shunts, previous HBOT, anti-spasticity meds, or behavior problems. |
| ***Studies of Stroke*** | | | | | |
| Hart 1973[149] (Poor) | Not reported | Not clear (period of 7 days reported for improved patients, but duration of follow-up not clear). | Stated, but not clearly objective (neurologic exam, EEG, radioisotope scans) | | Defined as middle cerebral artery ischemia (proven by angiography or radioisotope scan), neurologic state stable for at least 3 weeks, and at least 4 weeks from onset. No information on patient selection. |

HBOT=hyperbaric oxygen therapy; atm=atmospheres; ICP=intracranial pressure; TIA=transient ischemic attack; CBF=cerebral blood flow; CSF=cerebrospinal fluid; GCS=Glasgow Coma Scale; CO=carbon monoxide; CP=cerebral palsy; PT=physical therapy; EEG=electroencephalogram; CNS=central nervous system

## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Holbach 1977a[141] (Poor) | Time-series | Yes, except TIA patients had only 1 treatment ("test treatment"), but results are reported separately. | No States 38 patients had complete stroke, 36 were chronic stroke patients, but timing of HBOT since onset of stroke not reported. | No | Not reported |
| Holbach 1977b[142] (Poor) | Time-series | Yes for dose, number of treatments varied from 10 to 15. | No | Patients selected for surgery based on initial response to HBOT. | Not reported |
| Imai 1974[108] (Poor) | Before-after | Yes | No- not reported. | No | Not reported |
| Jain 1989[134] (Poor) | Before-after | Yes | No- time since onset ranged from 3 months to 5 years, all were undergoing stroke rehabilitation. | No, all patients had simultaneous physical therapy. | No |

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## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Holbach 1977a[141] (Poor) | "Before HBOT treatment" | "During and at conclusion of HBOT" sessions | States neurological exam, but not described | Outcome measurements unclear. | Diagnosis vague, no information on patient selection. |
| Holbach 1977b[142] (Poor) | Yes | Yes | Neurological exam and neurological deficits, not specified | | All patients were judged suitable to undergo surgery if necessary, no other information on patient selection. |
| Imai 1974[108] (Poor) | Not clear | "After one or two treatments" | Yes | Few details about how subjects selected or if/when baseline tests done. | No information on patient selection, no description except diagnosis; mixed group selected: patients with presenile dementia, chronic alcoholism, cerebral vascular disease & CO intoxication. |
| Jain 1989[134] (Poor) | Yes | Yes | Yes | Results on spasticity are very difficult to interpret (stratification of results not explained), also subjects continued to receive PT after HBOT during followup. | 21/50 patients already undergoing rehabilitation with PT in HBOT chamber, only those with clinically assessable spasticity are included. Diagnosis vague. |

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## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Jain 1990[143] (Poor) | Time-series | Yes | No One patient was 5 years post-stroke, all others less than 12 months (range 3 weeks-11 months); no day-to-day neurological changes during first week of admission to clinic. | No, all patients had simultaneous physical therapy. | Not reported |
| Kapp 1981[144] (Poor) | Time-series | Yes. | No- HBOT started on day of diagnosis or after obtaining consent from family. | Yes, stratified results but no attempt to control statistically. | Not reported |

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## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Jain 1990[143] (Poor) | Yes | Yes | Yes | Only patients seen by senior authors included, only 10 of 25 had spasticity measurements recorded. Data for grip strength in table not discernable (e.g. before = 0/32 and after = 8). A footnote refers to stronger/weaker hand strength. First 8 patients recevied PT immediately after HBOT, and noticed that this significantly helped with spasticity, so the rest received PT during HBOT treatments. | Almost no description of patients given, except that they had occlusive cerebrovascular disease, 24 had hemiplegia. Spasticity grade at baseline ranged from 2-5 (scale 0-5), mean 3.4 (only 10 patients with this data). |
| Kapp 1981[144] (Poor) | Yes | Yes | Some measures objective and some subjective | Purpose of study was to use HBOT to identify subjects who are candidates for revascularization | Inclusion criteria described, all patients seen by author in 2-year period who fit criteria enrolled, number screened and eligible not given. |

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## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Li 1998[135] (Poor) | Before-after | Dose and duration the same, but course of 15 treatments varied from 3-4, and "rarely" more. | No- some patients were 3 years post-stroke but results are not reported separately by time since stroke. Range was < 1 month to over 3 years. | No. | Not reported |
| Neubauer 1980[139] (Poor) | Before-after | No. | Yes for some patients (time of HBOT treatment from onset ranged from 4 hours to 10 years). | No- patients received simultaneous physical therapy "when indicated". Severity reported, no statistical tests done. Results reported by timing of treatment from onset of stroke. | No |
| Noguchi 1983[136] (Poor) | Before-after | No. Number of treatments per day and total varied based on condition of patient. Varied from one time to 60 times, average of 17.2 per case. | No. | No. | Not reported |

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## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Li 1998[135] (Poor) | Not reported | Not reported | Stated, not objective (assessment of clinical symptoms by neurologists) | Too few details to assess. A subset was compared to "controls" - no details on how either gorup selected | No information on selection of patients, limited description of patients. |
| Neubauer 1980[139] (Poor) | Not reported | Not reported | Subjective | | Some information on patients given, no info on selection process. Because consecutive patients, may be good but baseline characteristics not reported. |
| Noguchi 1983[136] (Poor) | Not reported | Not reported | No, clinical assessment, signs and symptoms, physical exam, not described. | | No information on patient selection, diagnosis vague |

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## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Pilotti 1991[147] (Poor) | Retrospective comparison of cohorts | Similar HBOT treatments (not exactly the same). Control interventions actually used not stated. | NA | Patients in control and treatment groups were treated at 2 different institutions. Small differences with respect to age, sex, clinical history. Respiratory insufficiency, vascular insufficiency of inferior limbs and arterial hypertension were higher in HBOT-treated group ($p < 0.05$). | Yes |
| Saltzman 1965[145] (Poor) | Time-series | No In 18 patients, HBOT given within 7 hours of onset of symptoms, in 7 patients, given 7-30 days after onset. Myringotomies performed before in "most" patients. Initial studies used 3.04 atm for < 1 hour, in later treatments, pressure below 2.5 ata, permitting "prolonged" exposure. | No- patients had treatment <7 hours to 30 days after onset of stroke. | Describe separately patients who received HBOT soon after onset, but other factors not addressed | No |
| Steenblock 1998[137] (Poor) | Before-after | No. Treatment plans and physical therapy adjusted as the patient's condition warranted. | Yes for some patients (time of HBOT treatment from onset ranged from 1 month to 10 years, average 29 months). | No- all patients received physical therapy, electrical stimulation, hot or cold packs, ultrasound, short wave diathermy, paraffin bath therapy, and biofeedback. | No |

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## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Pilotti 1991[147] (Poor) | Yes | NA (retrospective cohort) | No dropouts or missing data reported | Overall mortality rates at the 2 hospitals are not given for comparison. | No information on patient selection |
| Saltzman 1965[145] (Poor) | Not reported | Unclear. One patient reported out to 10 days, others only immediately after HBOT. | Subjective (observation) | Very vague description of improvements seen during and shortly after HBOT. | No information on selection of patients, no description of patients except diagnosis. Diagnosis vague |
| Steenblock 1998[137] (Poor) | Evaluation at the "beginning of the program and at the end" | "At the end" | Stated, subjective | Results are presented as % improvement or improvement no/yes. | No information on selection of patients, reports that 100% of patients improved on one or more functions, little description of patients. Baseline severity of disability not presented. |

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## Evidence Table 9. Quality assessment of observational studies (continued)

| Author year (Quality) | Study design | Exposure measurement (HBOT therapy same for all participants?) | Stable baseline established? | Confounding factors addressed? (severity of disease, other treatment); control for confounders? | Masking (patients, outcome assessors) |
|---|---|---|---|---|---|
| Tsuro[138] 1983 (Poor) | Before-after | Dose the same, but number of treatments varied. | No. | No. | No |
| Wassman 1986[146] (Poor) | Time-series | Yes for dose, number of treatments varied from 10 to 15. | No- patients were about 3 months post-stroke. | No. | Not reported |
| Zhou Shn-rong 1995[110] (Poor) | Before-after | No, dose the same but number of treatments varied. | No- HBOT given 2-3 days after stroke. | No. | No |

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## Evidence Table 9. Quality assessment of observational studies

| Author year (Quality) | Timing of baseline measures stated and sufficiently close to intervention? | Timing of followup measurements stated and adequte? | Outcome measures stated and objective? | Comments | External validity |
|---|---|---|---|---|---|
| Tsuro[138] 1983 (Poor) | Not reported | Not reported | Observations, not objective, not stated how determined | | Series of cases treated with HBOT at one institution, no information on selection of patients for treatment. Only 79 cases of "over a hundred" treated are presented. |
| Wassman 1986[146] (Poor) | Yes | Yes | "Motor deficit" method of measurement not described. | | Only includes patients who showed a definite increase of electrical power equivalent on EEG after an HBOT series. |
| Zhou Shn-rong 1995[110] (Poor) | Not reported | Not reported | Yes, but not objective | Few details about how subjects selected or if/when baseline tests done. | No info on selection of patients, no way to compare patients, e.g. described as 'deep coma' |

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