Effectiveness of Hyperbaric Oxygen Therapy for Traumatic Brain Injury

Based on an interview of Paul G. Harch, MD by Nancy Faass, MSW, MPH

In the treatment of traumatic brain injury, the research suggests that hyperbaric oxygen is the most effective therapy currently available at all levels of severity and all time points in the disease process. Mortality from acute, severe traumatic brain injury (TBI) can be reduced with just a few treatments, early on, documented in randomized clinical trials. One to three sessions of hyperbaric oxygen therapy (HBOT) in the acute phase can decrease mortality by 50% to 60%, the greatest reduction in mortality of any known therapy. There is also evidence that HBOT is therapeutic for acute concussion, as well as post-concussion symptoms. HBOT is the only therapy that directly treats the underlying disease processes in TBI wounds: decreased oxygen, decreased blood flow, swelling, constriction of blood vessels, acidosis, and anaerobic metabolism.

Significance. In the U.S., accidents are now the leading cause of death among every age cohort from childhood through age 44. Among the survivors, the official number of brain injuries is approximately two million annually in the U.S. and ten million worldwide. This means that more than two million brain-injured individuals are added to our population every year. Over 75% of these brain injuries are concussions. Approximately half of all mild TBI patients develop persistent post-concussion syndrome. characterized by cognitive symptoms such as memory loss, headaches, mood swings (irritability, anxiety, depression, apathy), sleep disruption, fatigue, dizziness, and changes in personality. In terms of potential therapeutics, two randomized trials have been conducted showing significant improvement in moderate to severe TBI in the subacute phase utilizing HBOT. There are multiple randomized trials on mild TBI in the chronic phase, showing the therapeutic benefit of HBOT.

History. Hyperbaric oxygen therapy has been described as a treatment for wounds in any location in the body and of any duration. Initially discovered in England in 1662, hyperbaric therapy was developed in its present form by the U.S. Navy to treat the bends. In the 1950s, surgeons in the Netherlands innovated the use of high-pressure oxygen in the treatment of infections, cases of carbon monoxide poisoning, and during surgery. Today, we are in a new era. In terms of concussion, for example, persistent post-concussion syndrome is no longer considered a psychiatric disease. We now know that it is an organic injury, essentially a wound to the brain. Scientifically, TBI treatment is a logical application of hyperbaric therapy, which is widely acknowledged as an effective intervention for difficult-to-heal wounds. With emerging clinical trials, we have the evidence to confirm the specific effectiveness of HBOT for traumatic brain injury.

Mechanisms of action. Scientific studies over the last 10 years have shown that one of the primary targets of hyperbaric therapy is the DNA. Based on molecular biochemical techniques which became available in 2008, researchers were able to perform mass gene array analysis to determine which genes were upregulated or downregulated by changes in pressure and oxygen. Research has found that a single hyperbaric treatment affects more than 40% of the protein-coding genes in our DNA—8,101 of the 19,000 protein coding genes. Different pressures and different oxygen levels have independent, overlapping, and interactive effects on different clusters of genes. Those effects occur through oxygen and pressure signaling. Understanding these effects, the applications of this therapy can be extended to a wide array of health issues, including genetic syndromes that are not considered wound conditions.

Treatment

Hyperbaric oxygen therapy involves the use of increased atmospheric pressure and elevated levels of oxygen as medications to treat pathophysiology. Therapeutic effects occur through genetic expression and suppression of growth and repair hormone and anti-inflammatory genes, and by improving blood flow and metabolism. These effects are a function of dose and timing of the intervention in the disease process. HBOT doses of 203-304 kPa (kilopascals, equivalent to 29-44 pounds per square inch) are utilized for wound healing and to treat infection. Lesser doses have been used primarily for chronic neurological conditions.

Harch Protocols. Over the last 34 years I have developed algorithmic approaches and flexible protocols to assess and treat different medical conditions with HBOT. One methodology for brain-based neurological conditions involves the following protocol:

- Pretreatment screening by phone
- Day 1. History, physical exam, and SPECT brain imaging to establish baseline
- Day 2. First HBOT session at a specific dose, followed in 3-4 hours by a second SPECT imaging
- Days 3 on: 39 additional daily HBOT sessions at that specific dose, five days per week, for eight weeks
- Periodic evaluation to check progress, response, and dosage

SPECT scans. We began doing SPECT scans in 1989. The protocol for SPECT scanning described above evolved from Dr. Richard A. Neubauer's use of SPECT imaging before and after a first HBOT in a stroke patient in the late 1980s. We adapted this to the first-ever use in divers with residual brain injury from decompression illness and in boxers, and over time, treated patients with more than 80 different neurological conditions. What we typically would see on the second scan after the very first HBOT was an improvement in overall brain circulation, and an improvement in the pattern of blood flow, which becomes more normalized. (Note that the SPECT scan provides images of circulation or lack thereof that is a snapshot of brain blood flow at the time the SPECT dye is injected. In contrast, a PET scan documents activity involving glucose metabolism.)

Oxygen toxicity. The most extreme form of oxygen toxicity is a grand mal seizure. Although this is generally rare, I strongly recommend that HBOT is delivered by and under the supervision of a physician knowledgeable regarding HBOT. Lin, Tsai, & Lee (2008), treating moderate to severe TBI at 203 kPa, reported a 9% incidence of grand mal seizures. However, accumulating data and experience have demonstrated that toxicity can occur at lower pressures of oxygen. In 2018 four patients were reported to the FDA as part of a traumatic brain injury study who developed signs of oxygen sensitivity or overdosing with less than 40 treatments at 150 kPa. Children with seizure disorders can exhibit oxygen toxicity at far lower levels and with lesser numbers of treatments. In my own practice, when treating patients with a history of seizure disorder, I start at lower pressures and observe the patient carefully, adjusting the dose based on their response.

It is possible that hyperbaric oxygen therapy can worsen existing conditions. Having documented these cases over the course of 30 years in practice, my observation is that too much oxygen can result in deterioration. In the majority of these cases (both in the U.S. and overseas), the treating facilities had no physicians involved and the technicians were operating under the precept that hyperbaric oxygen therapy could only improve patients, so negative effects were puzzling, often ignored, or commonly blamed on the patient. (I reported these results at the 2001 Symposium on Hyperbaric Oxygenation and the Brain Injured Child. The Proceedings are available from Best Publishing Company.)

Mild adverse effects. In our study of mild TBI and PTSD (2017), six of thirty participants experienced mild, reversible middle-ear barotrauma (five of these patients had mild upper respiratory infections at the beginning of the study). Other patients, seven of the total 30 in the study, had a transient deterioration or re-expression of pre-existing symptoms approximately halfway through the 40-treatment course. These resolved over the next four to six HBOT treatments. In general practice, mild symptoms most likely to occur involve clearing pressure in the ears, or sometimes the sinuses.

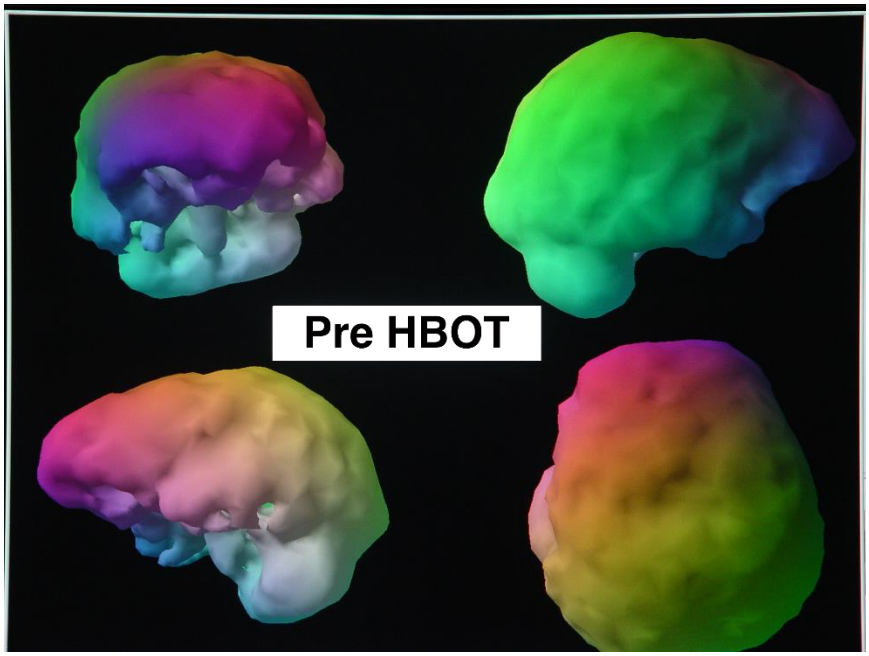
Therapeutic Effects Achieved with Delayed Treatment for TBI

In our previously mentioned study involving 30 military personnel with mild TBI, 90% reported improvement in cognitive symptoms after 40 HBOTs, and that improvement increased at the 6-month follow-up. The veterans' post-concussion symptom scores (headaches, neurological, cognitive, vestibular, and emotional symptoms) decreased by 36%. Wechsler IQ testing was administered, and showed on average a gain in IQ points of 14.2 points, which is exceptional. Evaluation of anxiety using the GAD-7 showed an average decrease of 5.4 points on a scale of 21. Similar improvements were documented in depression with an average 7.9-point decrease on a scale of 27 using the PHQ-9. Reductions in PTSD symptoms averaged 16.6 points on the 80-point Military PTSD Checklist. This represents the greatest improvement in PTSD symptoms in the shortest period of time for any clinical study on PTSD. Overall, there was a self-reported 95% improvement in emotional control. All findings had a *P*-value of 0.001 or better.

Symptoms in Order of Prevalence	Percentage of Subjects' Symptoms better after 40 HBOT Treatments	Percentage of Subjects' Symptoms better at 6-Month Follow-up
Headaches	**93%**	**86%**
Depression	**92**	**87**
Cognition (100% of participants reported cognitive symptoms)	**90**	**96**
Short temper	**90**	**95**
Low energy	**86**	**93**
Mood swings	**84**	**96**
Short-term memory loss	**83**	**91**
Speech problems	**78**	**87**
Sleep disruption	**73**	**80**
Poor balance	**65**	**88**
Tinnitus	**47**	**56**
Hearing loss	**10**	**22**

Figure 1. Symptoms reported for 30 military personnel in study (Harch *et a*l., 2017) and improvement after received HBOT for mild TBI.

Case study: Delayed treatment of traumatic brain injury. Rusty had been in the military and was back in civilian life, a family man, serving as a law enforcement officer, and running a small business in the Midwest, when 9/11 occurred. He was so outraged that he reenlisted, and found himself in Iraq, age 45, escorting translators around the Green Zone. When his area was hit with more than 300 rounds of enemy mortar, he was knocked unconscious. He started having headaches and went to the sick bay, but no one there realized that he had been in an explosion. He continued to suffer from debilitating headaches, vertigo, short-term memory loss, and constant fatigue, was medically boarded out of the military, and diagnosed with a psychiatric disorder. One year later, a military caseworker happened to note his symptoms and called me. When I screened him over the phone and took a detailed history, I realized that he had a brain injury, so I entered him in our study, and he came to Louisiana. One aspect of the study was brain imaging and the resulting images were dramatic, in fact, the most exceptional of any of the 30 participants in the study. The entire left side of his brain showed a reduction in brain-blood flow (the side on which the blast had occurred). He also complained about intense itching and periodic blistering on his left arm. We subsequently X-rayed his arm, which showed 16 pieces of embedded shrapnel. Here was the evidence that he had experienced a concussive blast injury. Over the course of treatment, his symptoms and imaging improved. He was eventually awarded a Purple Heart and now serves as liaison to the North Dakota State Legislature on matters related to veterans.



Figures 2-4: Four-view three-dimensional surface reconstructions of SPECT brain imaging of 45-year-old veteran with blast-induced persistent post-concussion syndrome. Figure 2. Imaging pre-HBOT shows deficits in brain blood flow that are registered as scalloped indentations on the surface of the brain. Note the asymmetric injury to the left side of the brain (in the left upper quadrant scan, the area of the brain on the right side of the image), the side from which the mortar blast occurred. The left frontal, temporal, and cerebellar lobes are severely affected.

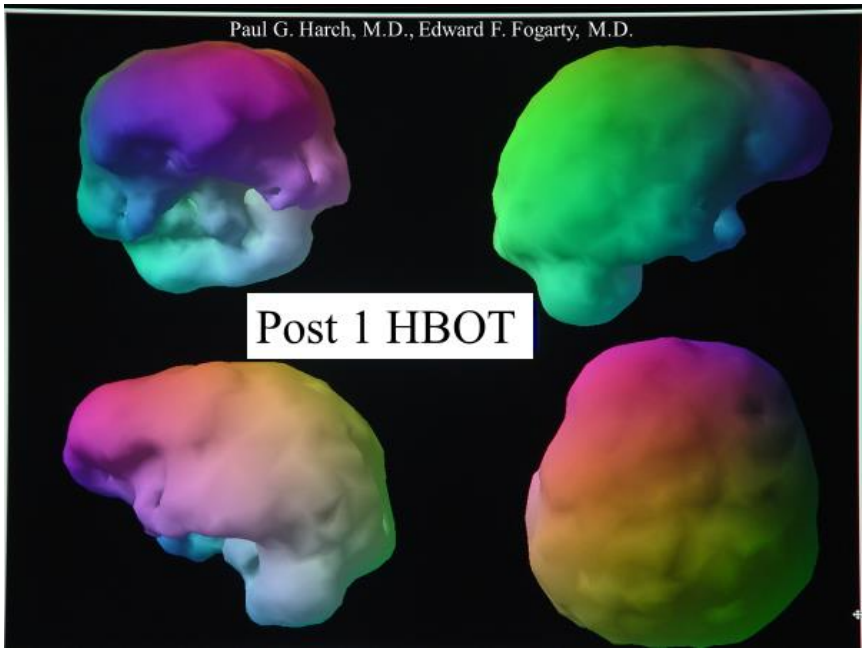


Figure 3. After the first HBOT intervention there is diffuse improvement in the brain blood flow, especially the most damaged left temporal, frontal, and cerebellar lobes.

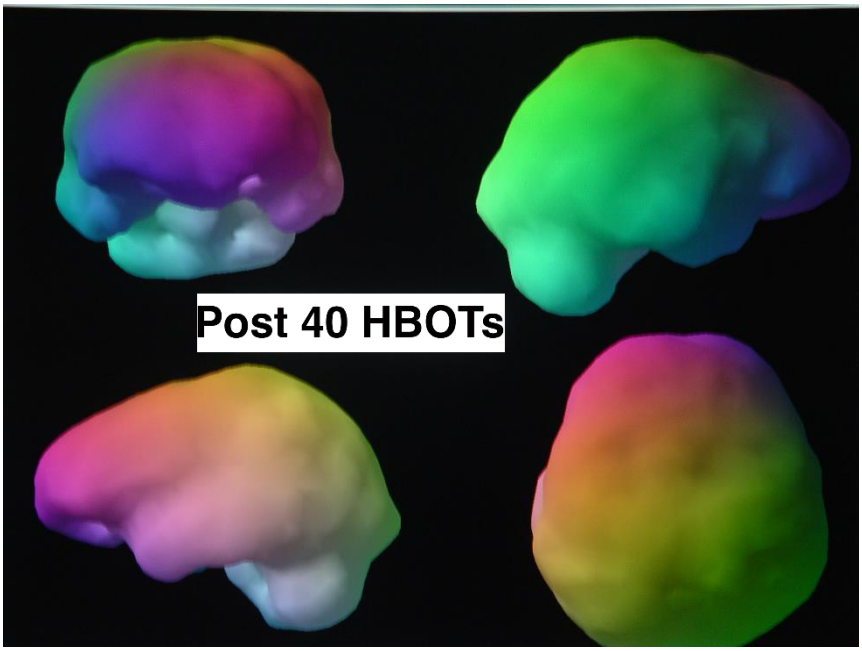


Figure 4. After 40 HBOTs, there is a near normalization of brain blood flow compared to the pre-HBOT study. Simultaneously, the veteran experienced improvement in his symptoms and cognition.

Achieving More Precise Diagnosis and Treatment with EEG

For much of my career, I have been searching for an effective means of pinpointing dose-response for the individual patient and for their specific disease process. Dosage was guided by cumulative case experience, my research, the research of others, and the use of pre- and post-treatment SPECT scans. However, we were unable to see what was occurring in the brain during actual treatment, until now. In the past 4 years I have adapted our hyperbaric chambers to perform real-time qEEG in the chamber to monitor a patient's response to hyperbaric therapy. This process is patent pending.

Indications for Treatment

I have two practices: one is an academic medical practice in which we treat reimbursable conditions, both outpatient and inpatient. At the present time, 13 indications are approved for the marketing of hyperbaric chambers by the FDA, and 15 are typically reimbursed. (The typically reimbursed indications appear in the table below identified by an asterisk.) The second practice is a private practice where I treat off-label indications, which for the most part are not reimbursable. It becomes a matter of discretionary income in order for patients to obtain this type of therapy. The additional problem is that the number of people who understand this therapy is relatively limited. Hospital facilities that have a chamber and have trained staff will not treat off-label indications such as neurological disorders, because these conditions are not reimbursed at this high level. In addition, there have been threats in the past of disciplinary action by one of the medical societies against their members should they treat off-label conditions "for profit." This has inhibited many hyperbaric physicians from offering HBOT for off-label conditions in the hospital setting.

Indications for Hyperbaric Oxygen Therapy

Neurological Conditions	**Injuries and Wound Healing**
*Air or Gas Embolism	*Compartment Syndrome/Crush Injury/Other
Anoxic Brain injury	*Delayed Radiation Injury (soft tissue and bony necrosis)
Autism	*Diabetic and Selected Problem Wounds
Birth Injury	*Exceptional Blood Loss Anemia
Brain Aneurysm, Post-Rupture	*Skin Grafts and Flaps, Compromised
Brain Injury, Acquired (ABI) (lack of oxygen, exposure to toxins, pressure of a tumor)	Spinal Cord Compression Injury
Brain Injury caused by Substance Abuse	*Thermal Burns
Brain Injury, Chronic Traumatic Encephalopathy	*Traumatic Ischemias
Brain Injury from Chemotherapy ("Chemo Brain")	
Brain Injury from Radiation	**Pain Conditions**
Brain Injury, Traumatic	Pain Syndrome, Complex Regional
Brain Injury, Traumatic with Post-Traumatic Stress Disorder	Pain Syndrome, Fibromyalgia
	Peripheral Neuropathy
Brain Injury-Related Depression	
Brain Insult, Concussion	**Rehabilitation**
Brain Insult, Post-Concussion Syndrome	Arthritis
*Central Retinal Artery Occlusion	*Decompression Sickness, Acute (The Bends)
Cerebral Palsy	Decompression Sickness, Chronic
Dementia	Multiple Sclerosis
Dementia, Early (Mild Cognitive Impairment)	Recovery from Surgery
Drowning	Sports Injuries and Sports Performance Recovery
Encephalopathy, Hypoxic Ischemic	
Fetal Alcohol Syndrome	**Infectious Processes**
Hypoxia (Near-hanging)	*Actinomycosis
*Intracranial Abscess	Chronic Infection
Migraine Headache	*Gas Gangrene
Post-Anesthesia Brain Injury	Lyme Disease
Shaken Baby Syndrome	*Necrotizing Soft Tissue Infection
Stroke	*Osteomyelitis (refractory
Toxic Exposure	
*Carbon Monoxide Poisoning, Acute and Acute Carbon Monoxide Poisoning complicated by Cyanide Poisoning	Autoimmune Disorders
Carbon Monoxide Poisoning, Chronic	Chronic Fatigue Syndrome
	Inflammatory Conditions

* FDA-approved indications for treatment.

Resources

Training Resources

One-year fellowship. These fellowships are currently offered at eight institutions across the U.S., which teach the treatment of 13-15 indications that have FDA-approval for marketing and 3rd party reimbursement. Louisiana State University has the largest fellowship program in the country. Fellowship programs are also offered at Duke, State University in New York (SUNY), U.C. San Diego, and other universities. The problem is that no training is provided for off-label indications, which means that there is no training for the vast majority of neurological conditions that can be ameliorated with hyperbaric treatment. Additional information is available at: acgme.org, using the search term "hyperbaric medicine fellowship".

Forty-hour CME training. There is a forty-hour continuing medical education introductory course provided nationwide, available online and in other cases, by physical attendance. The forty-hour course enables providers to bill Medicare, Medicaid, and insurance companies for hyperbaric therapy for reimbursable indications. This is essentially an entry point to the field. For an example of these CME offerings, see: uhms.org/education/courses-meeting/introductory-courses.html

Upcoming trainings. In the next year, we anticipate offering additional training in hyperbaric therapy via an educational platform. For updates on this training, please check HBOT.com periodically.

Annual meetings. Hyperbaric Medicine International (HMI) provides annual meetings focused on the science and applications, with information on dosing. See: hyperbaricmedicineinternational.org

Professional Organizations

Hyperbaric Medicine International (HMI). I am one of the founders of this association, which was originally called the International Hyperbaric Medical Society (IHMA, 2001), a nonprofit that supports research, education, and treatment. The website of HMI provides a wealth of information and resources for both medical professionals and patients. For more information, see: hyperbaricmedicineinternational.org

American College of Hyperbaric Medicine. The hyperbaric society originally founded by Dr. Richard Neubauer and colleagues in 1983 and now re-incorporated by another group, this society focuses primarily on reimbursable applications in wound care, certification, regulatory issues, practice protocols, quality assurance, and Medicare. See: hyperbaricmedicine.org

The Undersea and Hyperbaric Medical Society. The first of the hyperbaric medical societies, UHMS holds national and regional meetings. The society established the majority of the current reimbursable diagnoses and continues to focus on the treatment of those 15 conditions. uhms.org

Referrals

Referring to providers of HBOT. If you have patients with neurological disorders, and you wish to refer them within your metropolitan area for treatment, you must perform due diligence. Search for facilities in your area on the internet and then screen providers by phone and in person, just as you would any provider in an emerging field to whom you want to refer vulnerable patients.

With hyperbaric therapy, the range of training, experience, and quality of care is so broad, this personal research is essential. Currently HBOT is provided by practitioners whose background varies from no training to 40 hours of CME to 20 years or more of training and experience. In other cases, HBOT may simply be provided as a business, by a technician who receives a prescription signed by a physician (the MD may be knowledgeable or not). This range in training and experience within the field explains why the outcomes are so varied.

These varied outcomes also characterize recent studies by the Dept. of Defense using HBOT, which were performed with what were judged to be highly sophisticated study designs. These designs instead revealed a fundamental misunderstanding of hyperbaric oxygen therapy, which is that HBOT is a dual-component drug composed of increased pressure and increased oxygen. Those patients in the control group received low-doses of hyperbaric therapy—low pressures and low doses of oxygen labeled as sham treatment. In fact, they turned out to be effective doses of hyperbaric therapy. Consequently, rather than comparing HBOT with sham therapy, the clinical trial inadvertently compared HBOT at different dosages. Unfortunately, the mixed outcomes from these Federally sponsored studies have tended to prejudice other institutional healthcare providers.

SPECT Scanning. The majority of hospitals in the U.S. have SPECT brain scan capability, but rarely perform this type of brain imaging. My recommendation is that you find a facility that frequently performs SPECT brain scanning, and insist on a dedicated nuclear technologist and radiologist to perform and interpret all of your patients' scans in order to minimize variability in technique and interpretation.

Most radiologists are not familiar with or accustomed to seeing the type of changes evident on SPECT after HBOT. (More detailed suggestions are offered on numerous aspects of HBOT protocol in my book, *The Oxygen Revolution*, 3rd edition.)

Information Resources

Website. The website of Harch Hyperbarics features extensive patient videos, taken at various points in treatment which provide an encouraging and realistic sense of what can be achieved in cases of traumatic brain injury. News articles and informational resources are also available on the site at HBOT.com.

Online. Interviews of a number of Harch Hyperbarics patients are also available on YouTube.com. Additional videos about HBOT on YouTube include Joe Namath speaking on hard-chamber treatment for post-concussion symptoms (years post-injury) and LeBron James describing how he uses soft-chamber HBOT for training and recovery.

Journal articles. My randomized study on use of hyperbaric therapy for the treatment of traumatic brain injury will be published in March/April in a peer-reviewed instant-access online journal. The journal will be announced at that time. The article will be easily accessed through any search engine using "Harch, traumatic brain injury, hyperbaric oxygen therapy." A number of journal articles are available for download in free full-text versions on PubMed, including our study of 30 military personnel with TBI, published in 2017.

Book. Paul Harch, MD, and Virginia McCullough. *The Oxygen Revolution, 3rd edition.* Hobart, NY: Hatherleigh Press, 2016, 310 pp. Written for both providers and patients, the book contains information and resources, with insight into numerous aspects of treatment, reimbursement, and healthcare policy.

More than 100 pages are devoted to the treatment of TBI, birth injuries, strokes, autism, Alzheimer's, and alcohol abuse, as well as diabetes, bone and joint disorders, AIDS, and antiaging therapies.

Textbook. Kewal K. Jain, editor. *Textbook of Hyperbaric Medicine, 6th edition*. New York, NY: Springer; 2016.

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Paul G. Harch, MD is an emergency medicine and hyperbaric medicine clinician, clinical professor of medicine at Louisiana State University Health Sciences Center, New Orleans, and former director of the Hyperbaric Medicine Department and Hyperbaric Medicine Fellowship at Louisiana State University School of Medicine, New Orleans. He is a graduate of the University of California, Irvine (magna cum laude/Phi Beta Kappa), and Johns Hopkins University School of Medicine. Dr. Harch initiated and maintains both an academic and a private practice that have resulted in the largest case experience in neurological hyperbaric medicine in the world. In his private practice he has adapted the concepts of conventional hyperbaric oxygen therapy to disorders of the central nervous system. Working initially with brain-injured divers and boxers he treated the first case of chronic traumatic encephalopathy (CTE) in 1989 (boxer) and dementia (diver) then adapted this protocol to the treatment of traumatic brain injury in 1991, cerebral palsy in 1992, autism in 1995, and numerous other cerebral disorders. He has also seen the positive effects of HBOT firsthand through the treatment of patients with toxic brain injury, stroke, dementia, and learning disabilities. Dr. Harch has successfully treated U.S. servicemen with TBI and PTSD, and his clinical studies for brain-injured veterans have continued with a recently completed randomized trial funded by a Louisiana-generated congressional appropriation. He has also presented his clinical experience and research four times to the U.S. Congress and has been a semifinalist for the NIH Director's Pioneer Award. A founder and the first president of Hyperbaric Medicine International, Dr. Harch is active in conferences and training. His book, *The Oxygen Revolution, 3rd edition,* (2016) co-authored with Virginia McCullough, explains HBOT as an epigenetic therapy with potentially widespread application in medicine and neurology.

Dr. Harch's work focuses on the development of HBOT treatment protocols for neurological disorders, based on the needs of each specific patient, their disease process, and the patient's response to HBOT. SPECT scans and qEEG-directed dosing facilitate additional precision, but are optional. His patients are from all over the world, and all are treated at his center in New Orleans.

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References

Boussi-Gross R, Golan H, Fishlev G, et al. Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury-randomized prospective trial. *PLOS ONE*. 2013;8:1-18.

Golden ZL, Neubauer R, Golden CJ, et al. Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy. *Int. J. Neurosci*. 2002;112:119-131.

Golden Z, Golden CJ, Neubauer RA. Improving neuropsychological function after chronic brain injury with hyperbaric oxygen. *Disability and Rehabilitation*. 2006;28(22):1379-86.

Harch PG. Hyperbaric oxygen therapy for post-concussion syndrome: contradictory conclusions from a study mischaracterized as sham-controlled. *J Neurotrauma*. 2013;30:1995-1999.

Harch PG. Hyperbaric oxygen in chronic traumatic brain injury: oxygen, pressure, and gene therapy. *Med Gas Res*. 2015:5:9. doi: 10.1186/s13618-015-0030-6.

Harch PG, Andrews SR, Fogarty EF, Lucarini J, Van Meter KW. Case control study: hyperbaric oxygen treatment of mild traumatic brain injury persistent post-concussion syndrome and post-traumatic stress disorder. *Med Gas Res*. 2017 Oct 17;7(3):156-174.

Harch PG, Fogarty EF. Hyperbaric oxygen therapy for Alzheimer's dementia with positron emission tomography imaging: a case report. *Med Gas Res*. 2019 Jan 9;8(4):181-184.

Harch PG. HBO therapy in global cerebral ischemia/anoxia and coma. In KK Jain, ed. *Textbook of Hyperbaric Medicine*, *6th ed*. Cham, Switzerland. Springer; 2017: 269-319.

Harch PG. HBO in the management of cerebral palsy. In KK Jain, ed. *Textbook of Hyperbaric Medicine, 6th ed*. Cham, Switzerland. Springer; 2017: 351-364.

Lin JW, Tsai JT, Lee LM, et al. Effect of hyperbaric oxygen on patients with traumatic brain injury. *Acta Neurochir Suppl*. 2008;101:145-149.

Moon RE (ed). *Hyperbaric Oxygen Therapy Indications, 14th ed*. North Palm Beach, FL. Best Publishing Company; 2019.

Neubauer RA, Gottlieb SF, Kagan RL. Enhancing "idling" neurons. *Lancet*. 1990:335(8688):542

Wolf G, Cifu D, Baugh L, Carne W, Profenna L. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. *J Neurotrauma*. 2012;29:2606-2612.