

HBOT RESEARCH AND SCIENCE

MOST RECENT RESEARCH SHOWING THE SAFETY AND EFFICACY OF HBOT FOR TBI/PTSD

- [0] Doeniyas-Barak K, Catalogna M, Kutz I, Levi G, Hadanny A, Tal S, et al. (2022) ***Hyperbaric oxygen therapy improves symptoms, brain's microstructure and functionality in veterans with treatment resistant post-traumatic stress disorder***: A prospective, randomized, controlled trial. PLoS ONE 17(2): e0264161. <https://doi.org/10.1371/journal.pone.0264161>
- [1] Hadanny A, Daniel-Kotovsky M, Suzin G, Boussi-Gross R, Catalogna M, Dagan K, Hachmo Y, Abu Hamed R, Sasson E, Fishlev G, Lang E, Polak N, Doeniyas K, et al. **Cognitive enhancement of healthy older adults using hyperbaric oxygen: a randomized controlled trial**. Aging (Albany NY). 2020; 12:13740-13761. <https://doi.org/10.18632/aging.103571>
- [2] Harch PG, Andrews SR, Rowe CJ, Lischka JR, Townsend MH, Yu Q, Mercante DE. **Hyperbaric oxygen therapy for mild traumatic brain injury persistent postconcussion syndrome: a randomized controlled trial**. Med Gas Res. 2020;10(1):8-20.
- [3] Douglas Shytle R, Eve DJ, Kim SH, Spiegel A, Sanberg PR, Borlongan CV. **Retrospective Case Series of Traumatic Brain Injury and Post-Traumatic Stress Disorder Treated with Hyperbaric Oxygen Therapy**. Cell Transplant. 2019 May 28:963689719853232. [Epub ahead of print].
- [4] Mozayeni BR, Duncan W, Zant E, Love TL, Beckman RL, Stoller KP. **The National Brain Injury, Rescue and Rehabilitation Study – a multicenter observational study of hyperbaric oxygen for mild traumatic brain injury with post-concussive symptoms**. Med Gas Res. 2019;9(1):1-12. <https://bit.ly/2YGMvJ6>
- [5] Harch PG, Fogarty EF. **Hyperbaric oxygen therapy for Alzheimer's dementia with positron emission tomography imaging: a case report**. Med Gas Res. 2018;8(4):181-184.
- [6] Emily R. Rosario, Stephanie E. Kaplan, Sepehr Khonsari, et al., **"The Effect of Hyperbaric Oxygen Therapy on Functional Impairments Caused by Ischemic Stroke,"** Neurology Research International, vol. 2018, Article ID 3172679, 12 pages, 2018. <https://doi.org/10.1155/2018/3172679>.
- [7] Hadanny A, Abbott S, Suzin G, et al. **Effect of hyperbaric oxygen therapy on chronic neurocognitive deficits of post-traumatic brain injury patients: retrospective analysis**. BMJ Open 2018;8:e023387. <https://bit.ly/2RBOQsd>
- [8] Deng Z, Chen W, Jin J, Zhao J, Xu H. **The neuroprotection effect of oxygen therapy: A systematic review and meta-analysis**. Niger J Clin Pract. 2018 Apr;21(4):401-416.
- [9] Peterson, et. Al. Department of Veteran Affairs. Evidence-based Synthesis Program (ESP). Quality Enhancement Research Institute/QUERI. **Evidence Brief: Hyperbaric Oxygen Therapy (HBOT) for Traumatic Brain Injury and/or Post-traumatic Stress Disorder**, Supplemental Materials, February 2018.

[10] 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;7(3):156-174. <http://bit.ly/2zyFrAr>

[10] Tal S, Hadanny A, Sasson E, Suzin G and Efrati S (2017) **Hyperbaric Oxygen Therapy Can Induce Angiogenesis and Regeneration of Nerve Fibers in Traumatic Brain Injury Patients.** *Front. Hum. Neurosci.* 11:508. doi: 10.3389/fnhum.2017.00508 <http://bit.ly/2l834LT>

[11] HBOT2017, 11th International Symposium. **TBI: No Need to Die! A review of HBOT in Acute Severe Traumatic Brain Injury with an Extension to Acute Concussion, and an Update on Chronic Mild TBI.** Paul G. Harch, M.D. <http://bit.ly/2x4tWUf>

[12] HBOT2017, 11th International Symposium. **Acute Concussion Diagnostics and Treatment: HBOT for Subacute Traumatic Encephalitis Untied with Transcranial Doppler Vascular Lab of the Brain.** Daphne W Denham, M.D. <https://tinyurl.com/ybldktqn>

[13] **A randomized trial of hyperbaric oxygen in U.S. Service Members with post-concussive symptoms** [BIMA]. Weaver et al. 2017. <http://bit.ly/2x6d2EN>

[14] E.G. Wolf, **Traumatic Brain Injury and Hyperbaric Oxygen Therapy: Dawn of a New Day.** Presented at APWCA 16th Annual National Clinical Conference, 7-9 Sep 17. <http://bit.ly/2x8WDiT>

[15] Harch PG, Fogarty EF. **Subacute normobaric oxygen and hyperbaric oxygen therapy in drowning, reversal of brain volume loss: a case report.** *Med Gas Res* 2017;7:144-9 <http://bit.ly/2yCfZdq>

[16] Xavier A. Figueroa, PhD and James K. Wright, MD (Col Ret), **USAF Hyperbaric Oxygen: B-Level Evidence in Mild Traumatic Brain Injury Clinical Trials.** *Neurology*® 2016;87:1–7 "There is sufficient evidence for the safety and preliminary efficacy data from clinical studies to support the use of HBOT in mild traumatic brain injury/ persistent post concussive syndrome (mTBI/PPCS). The reported positive outcomes and the durability of those outcomes has been demonstrated at 6 months post HBOT treatment. Given the current policy by Tricare and the VA to allow physicians to prescribe drugs or therapies in an off-label manner for mTBI/PPCS management and reimburse for the treatment, it is past time that HBOT be given the same opportunity. This is now an issue of policy modification and reimbursement, not an issue of scientific proof or preliminary clinical efficacy." <http://bit.ly/2xEZS9>

[17] DJ Eve, MR Steele, PR Sanberg, Cesar V Borlongan. **Hyperbaric oxygen therapy as a potential treatment for post-traumatic stress disorder associated with traumatic brain injury.** *Neuropsychiatric Disease and Treatment* 2016;12 2689–2705. "A proportion of the returning soldiers also suffer from post-traumatic stress disorder (PTSD), and in some cases, this may be a consequence of TBI. . . . a possible therapeutic candidate is hyperbaric oxygen therapy (HBOT). Some clinical trials have been performed which suggest benefits with regard to survival and disease severity of TBI and/or PTSD. . . . HBOT has been shown to reduce apoptosis, upregulate growth factors, promote antioxidant levels, and inhibit inflammatory cytokines in animal models, and hence, it is likely that HBOT could be advantageous in treating at least the secondary phase of TBI and PTSD."

[18] Amir Hadanny & Shai Efrati (2016): **Treatment of persistent post-concussion syndrome due to mild traumatic brain injury: current status and future directions,** *Expert Review of Neurotherapeutics*, DOI: 10.1080/14737175.2016.1205487. Persistent post-concussion syndrome caused by mild traumatic brain injury has become a major cause of morbidity and poor quality of life. Unlike the acute care of

concussion, there is no consensus for treatment of chronic symptoms. Moreover, most of the pharmacologic and non-pharmacologic treatments have failed to demonstrate significant efficacy on both the clinical symptoms as well as the pathophysiologic cascade responsible for the permanent brain injury. This article reviews the pathophysiology of PCS, the diagnostic tools and criteria, the current available treatments including pharmacotherapy and different cognitive rehabilitation programs, and promising new treatment directions. ***A most promising new direction is the use of hyperbaric oxygen therapy, which targets the basic pathological processes responsible for post-concussion symptoms; it is discussed here in depth.***

[19] Wang F, et al. *Hyperbaric oxygen therapy for the treatment of traumatic brain injury: a meta-analysis*. *Neurol Sci*. 2016 Jan 8. PubMed PMID: 26746238. **"Compelling evidence suggests the advantage of hyperbaric oxygen therapy (HBOT) in traumatic brain injury. ...Patients undergoing hyperbaric therapy achieved significant improvement....with a lower overall mortality, suggesting its utility as a standard intensive care regimen in traumatic brain injury."**

[20] E.G. Wolf, L.M. Baugh, C.M.S. Kabban, et al. ***Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial***. *UHM* 2015, Vol. 42, No. 4, 2015. Dr. Wolf is a principle co-author of the first Army study. This recent USAF paper reanalyzing the data in the cornerstone DOD/VA/Army study concludes: "This pilot study demonstrated no obvious harm [and] both groups showed improvement in scores and thus a benefit. Subgroup analysis of cognitive changes and PCL-M results regarding PTSD demonstrated a relative risk of improvement There is a potential gain and no potential loss. The VA/Clinical Practice Guidelines define a "B evidence rating" as "a recommendation that clinicians provide (the service) to eligible patients. ***At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.*** . . . [emphasis added] Hyperbaric oxygen therapy for mild traumatic brain injury and PTSD should be considered a legitimate adjunct therapy if future studies demonstrate similar findings or show comparable improvement to standard-of-care or research-related treatment modalities." [NOTE: subsequent worldwide studies already published and those underway show comparable improvements.] <http://bit.ly/2faBldN>

[21] Leila H Eadie (editorial). ***New technology and potential for telemedicine in battlefield brain injury diagnostics***. *Concussion* (2016) 1(4), CNC22. "In severe cases, [TBI] injury occurs due to bleeding and inflammation, having several different effects: contact with blood causes brain tissue to swell (cerebral edema), and pooled blood within the confines of the skull also puts pressure on nearby tissue, constricting blood flow and depriving the brain of oxygen, killing neurons and leading to a chemical cascade that reinforces the injury. . . . People suffering from TBI can deteriorate suddenly and die, and in some cases swift treatment can help reduce mortality. Others will have minor initial symptoms, yet untreated brain hemorrhage can have insidious long-term effects. The etiology of postconcussive syndrome is debated, but may be caused by diffuse axonal injury or persistent metabolic alterations resulting in neuronal dysfunction and develops in 38–80% of patients with TBI...."

[22] Christine L. Mac Donald, Jason Barber, Mary Jordan, Ann M. Johnson, Sureyya Dikmen, Jesse R. Fann, Nancy Temkin. ***Early Clinical Predictors of 5-Year Outcome After Concussive Blast Traumatic Brain Injury***. *JAMA Neurology*, 2017; DOI: 10.1001/jamaneurol.2017.0143 "Together these findings indicate progression of symptom severity beyond one year after injury We believe that by being informed from longitudinal studies such as this one, the medical community can be proactive in combating the potentially negative and extremely costly effect of these wartime injuries."

[23] Daniel Nicoara, Raymond M. Quock et al. **Hyperbaric oxygen treatment suppresses withdrawal signs in morphine-dependent mice.** *Brain Research*, 2016; 1648:434
DOI:10.1016/j.brainres.2016.08.017 Groundbreaking research from Washington State University found that hyperbaric oxygen treatment (HBOT) can halve the pain and symptoms of opiate withdrawal/detox.

1. Other Peer-reviewed published articles

[a] Hu Q, Manaenko A, Xu T, Guo Z, Tang J, Zhang JH. **Hyperbaric oxygen therapy for traumatic brain injury: bench-to-bedside.** *Med Gas Res* 2016;6:102-10 <http://bit.ly/2aasAxb>

[b] Malek M, et al. **Hyperbaric oxygen and hyperbaric air treatment result in comparable neuronal death reduction and improved behavioral outcome after transient forebrain ischemia in the gerbil.** *Experimental Brain Research Experimentelle Hirnforschung Experimentation Cerebrale*. 2013;224(1):1-14. doi:10.1007/s00221-012-3283-5.

[c] Fife CE, Eckert KA, Carter MJ. **An Update on the Appropriate Role for Hyperbaric Oxygen: Indications and Evidence.** *Plast Reconstr Surg*. 2016;138(3 Suppl):107S-16S.

[d] Shi XY, Tang ZQ, Sun D, He XJ. Evaluation of hyperbaric oxygen treatment of neuropsychiatric disorders following traumatic brain injury. *Chin Med J (Engl)*. 2006;119(23):1978-82.
<http://www.ncbi.nlm.nih.gov/pubmed/17199942>

[e] Hardy P, Johnston KM, De Beaumont L, Montgomery DL, Lecomte JM, Soucy JP, et al. Pilot case study of the therapeutic potential of hyperbaric oxygen therapy on chronic brain injury. *J Neurol Sci*. 2007;253(1-2):94-105. <http://www.ncbi.nlm.nih.gov/pubmed/17234213>

[f] Lin JW, Tsai JT, Lee LM, Lin CM, Hung CC, Hung KS, et al. Effect of hyperbaric oxygen on patients with traumatic brain injury. *Acta Neurochir Suppl*. 2008;101:145-9.
http://www.researchgate.net/publication/51416688_Effect_of_hyperbaric_oxygen_on_patients_with_traumatic_brain_injury_injury

[g] Wright JK, Zant E, Groom K, Schlegel RE, Gilliland K. Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen. *Undersea Hyperb Med*. 2009; 36(6):391-9.
<http://www.echa.net/36-6%20UHM-P391-399.pdf>

[h] Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report. *Cases J*. 2009;2:6538.
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2740054/>

[i] Rockswold, Rockswold, Zaun and Liu. A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury. *Journal of Neurosurgery*, Jun 2013 / Vol. 118 / No. 6 / Pages 1317-1328
<http://www.ncbi.nlm.nih.gov/pubmed/23510092>

[j] Sahni T, Jain M, Prasad R, Sogani SK, Singh VP. Use of hyperbaric oxygen in traumatic brain injury: Retrospective analysis of data of 20 patients treated at a tertiary care centre. Br J Neurosurg. 2011. <http://www.ncbi.nlm.nih.gov/pubmed/22085249>

[k] Paul G. Harch, Susan R. Andrews, Edward F. Fogarty, Daniel Amen, John C. Pezzullo, Juliette Lucarini, Claire Aubrey, Derek V. Taylor, Paul K. Staab, and Keith W. Van Meter. A phase I study of low-pressure hyperbaric oxygen therapy for blast-induced post-concussion syndrome and post-traumatic stress disorder. J Neurotrauma. 2012 Jan 1;29(1):168-85. <http://online.liebertpub.com/doi/pdf/10.1089/neu.2011.1895>

[l] Stoller KP. All the right moves: the need for the timely use of hyperbaric oxygen therapy for treating TBI/CTE/PTSD. Medical Gas Research. 2015;5:7. doi:10.1186/s13618-015-0028-0.

[m] Stoller KP. Hyperbaric oxygen therapy (1.5 ATA) in treating sports related TBI/CTE: two case reports. Med Gas Res. 2011;1(1):17. PMID: 3231948. <http://www.medicalgasresearch.com/content/pdf/2045-9912-1-17.pdf>

[n] Lei Huang and Andre Obenaus. Hyperbaric oxygen therapy for traumatic brain injury Medical Gas Research, September 6, 2011.

2. Peer-reviewed Israeli research on stroke and TBI, neurogenesis and angiogenesis

[1] Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0079995>

[2] Hyperbaric Oxygen Induces Late Neuroplasticity in Post Stroke Patients - Randomized, Prospective Trial <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0053716>

[3] Hyperbaric oxygen may induce angiogenesis in patients suffering from prolonged post-concussion syndrome due to traumatic brain injury. Restor Neurol Neurosci. 2015 Oct 7. <http://www.ncbi.nlm.nih.gov/pubmed/26484702>

[4] Hyperbaric oxygen can induce neuroplasticity and improve cognitive functions of patients suffering from anoxic brain damage. Restorative Neurology and Neuroscience 33 (2015) 471–486 <http://www.ncbi.nlm.nih.gov/pubmed/26409406>

[5] Reflections on the neurotherapeutic effects of hyperbaric oxygen <http://informahealthcare.com/doi/pdf/10.1586/14737175.2014.884928>

3. Animal studies showing positive effects of HBOT on brain injury

[a] Kent MacLaughlin, et al. **The Effect of Intermittent Normobaric Hyperoxia on Stem Cell Mobilization and Cytokine Expression.** Report of research conducted at University of Wisconsin and reported at HBOT2018, Denver, CO, August 2018. Together these findings support the likelihood of biologic activity, consubstantial with HBOT, being activated at much lower dose of hyperoxia than previously postulated. The results demonstrate that the Army's and UHMS's claims

that hyperbaric medicine only occurs at pressures higher than 1.4ata are fallacious. Any increase in oxygen concentration and/or pressure is a medical intervention.

[b] Blast Exposure Induces Post Traumatic Stress Disorder-Related Traits in a Rat Model of Mild Traumatic Brain Injury. Gregory A. Elder, Nathan P. Dorr, Rita De Gasperi, Miguel A. Gama Sosa, Michael C. Shaughness, Eric Maudlin-Jeronimo, Aaron A. Hall, Richard M. McCarron, and Stephen T. Ahlers. Journal of Neurotrauma. <http://online.liebertpub.com/doi/abs/10.1089/neu.2012.2510>

[c] Research Report: Hyperbaric oxygen therapy improves spatial learning and memory in a rat model of chronic traumatic brain injury. Paul G. Harch, Christopher Kriedt, Keith W. Van Meter, Robert James Sutherland, BRAIN RESEARCH 1174 (2007) 120-129. http://www.researchgate.net/publication/5971941_Hyperbaric_oxygen_therapy_improves_spatial_learning_and_memory_in_a_rat_model_of_chronic_traumatic_brain_injury

[d] The effect of hyperbaric oxygen on intracephalic angiogenesis in rats with intracerebral hemorrhage. Peng ZR, Yang AL, Yang QD. J Neurol Sci. 2014 May2. <http://www.ncbi.nlm.nih.gov/pubmed/24836574>

[e] Kraitsy K, Uecal M, Grossauer S, Bruckmann L, Pflieger F, et al. (2014) Repetitive Long-Term Hyperbaric Oxygen Treatment (HBOT) Administered after Experimental Traumatic Brain Injury in Rats Induces Significant Remyelination and a Recovery of Sensorimotor Function. PLoS ONE 9(5): e97750. <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0097750>

[f] Calvert, Zhou, Nanda, and Zhang. Effect of hyperbaric oxygen on apoptosis in neonatal hypoxia-ischemia rat model. J Appl Physiol 95: 2072–2080, July 21, 2003.

4. Expert Opinion

[a] Richard A. Neubauer, M.D. and William S. Maxfield, M.D. **The Polemics of Hyperbaric Medicine.** Journal of American Physicians and Surgeons, Vol. 10 Number 1 Spring 2005, 15-17 www.jpands.org

[b] **Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment.** The National Academies. The Institute of Medicine. Washington DC: The National Academies Press, 2014. <https://bit.ly/2oYJ17I> Significant finding: “DoD and VA are spending substantial time, money, and effort on the management of PTSD in service members and veterans [\$9.3Billion+ through 2014]. Those efforts have resulted in a variety of programs and services for the prevention and diagnosis of, treatment for, rehabilitation of, and research on PTSD and its comorbidities. **Nevertheless, neither department knows with certainty whether those many programs and services are actually successful in reducing the prevalence of PTSD in service members or veterans and in improving their lives.**”

[c] **"What the *Bleep* is going on with Hyperbaric Oxygen Therapy?** Brain Health and Healing Foundation. Xavier Figueroa. PhD has been performing neurological clinical research since 1995 in the field of Alzheimer’s research, as well as basic research in neuron biology, cancer research, bioengineering and the biophysics of water in cells. He has a long history of involvement with research using hyperbaric oxygen therapy for brain injury.

**<http://braininjury.org/blog/2014/05/01/what-the-bleep-is-going-on-with-hyperbaric-oxygen-therapy/>

**<http://braininjury.org/blog/2014/07/03/what-the-bleep-is-wrong-with-the-dodva-hbot-studies/>

**<http://braininjury.org/blog/2014/11/23/what-the-is-going-on-with-hyperbaric-oxygen-therapy-part-3/>

[d] UHM 2012, Vol. 39, No. 4 – How many deaths will it take? AN EDITORIAL PERSPECTIVE. Undersea & Hyperbaric Medical Society, Inc. **How many deaths will it take till they know?** Monkeys, madmen and the standard of evidence. George Mychaskiw II, DO, FAAP, FACOP, Editor-in-Chief Chair, Department of Anesthesiology, Nemours Children's Hospital, Orlando, Florida USA. The Journal of Hyperbaric Medicine is the most prestigious journal on Hyperbaric Medicine in the world. "Hyperbaric oxygen is a safe, easily used treatment that, in many cases, has resulted in a dramatic improvement in the symptoms of patients with [TBI]. Every day we are.... gathering more data validating its efficacy.... I feel, as do many of my colleagues, that there is sufficient clinical and research evidence to justify the use of [HBOT] as a standard-of-care treatment for [TBI] that should be reimbursed by CMS and Tricare.... I have no doubt that, over the next several years, [HBOT] will be proven beyond a reasonable doubt to be one of the most effective treatments for [TBI].... There is a preponderance of evidence now to justify the use and funding for the treatment...." http://www.therapiehyperbare.com/images/hyperbare/2012-06_uhms_editorial.pdf

[e] **Chamber of Hopes for Brain Repair.** Eshel Ben-Jacob , PhD. January, 27, 2013. <http://www.assafh.org/sites/en/Documents/Chamber%20of%20Hopes%20for%20Brain%20Repair.pdf>

[f] **Hyperbaric oxygen in chronic traumatic brain injury: oxygen, pressure, and gene therapy.** Paul G. Harch. Medical Gas Research (2015) 5:9 DOI 10.1186/s13618-015-0030-6

[g] **Hyperbaric Oxygen Therapy for Brain Injury, Cerebral Palsy, and Stroke.** Summary, Evidence Report/Technology Assessment: Number 85. AHRQ Publication Number 03-E049, September 2003. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/clinic/epcsums/hypoxsum.htm>

5. Data from DoD/Army studies, with responses

Summary of positive findings in Army Studies: Army medicine has run trials investigating the use of Hyperbaric Oxygen to treat and help heal Traumatic Brain Injury. They have shown that HBOT is both safe and effective: "**Randomization to the chamber . . . offered statistical and in some measures clinically significant improvement over local routine TBI care.**" Also: "**.... total scores for [both] groups revealed significant improvement over the course of the study for both the sham-control group and the HBO2 group.....**" Expert outside consultants to DOD declared that "**[HBOT] is a healing environment.**" The Army's premier researcher, Dr. Scott Miller, says on the Veterans Affairs web site: "**People did get better and we can't ignore those results.**"

[1] **A randomized trial of hyperbaric oxygen in U.S. Service Members with post-concussive symptoms** [BIMA]. Weaver et al. 2017. <http://bit.ly/2x6d2EN>

[2] E.G. Wolf, **Traumatic Brain Injury and Hyperbaric Oxygen Therapy: Dawn of a New Day.** Presented at APWCA 16th Annual National Clinical Conference, 7-9 Sep 17. <http://bit.ly/2x8WDiT>

[3] E.G. Wolf, L.M. Baugh, C.M.S. Kabban, et al. **Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial.** UHM 2015, Vol. 42, No. 4, 2015.

[4] 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(17):2606-12. (DoD) (USA)

<http://biawa.org/docs/pdf/MTBI%20PCS%20J%20Neurotrauma%202012.pdf>

[5] Paul G. Harch, MD. Letters to the Editor. Journal of Neurotrauma. **Hyperbaric Oxygen Therapy for Post-Concussion Syndrome: Contradictory Conclusions From a Study Mischaracterized as Sham-Controlled.** 2014 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3837504/>

[6] Cifu DX, Hart BB, West SL, Walker W, Carne W. The Effect of Hyperbaric Oxygen on Persistent Postconcussion Symptoms. J Head Trauma Rehabil. 2013. (DoD) (USA)
http://journals.lww.com/headtraumarehab/Fulltext/2014/01000/The_Effect_of_Hyperbaric_Oxygen_on_Persistent.2.aspx

[7] Weaver LK, Cifu D, Hart B, Wolf G, Miller RS. Hyperbaric oxygen for post-concussion syndrome: Design of Department of defense clinical trials. Undersea Hyperb Med 2012; 39(4); 807-814.

[8] Paul G. Harch, MD. Letters to the editors, UHM 2013, Vol. 40, No. 5 – LETTERS. Department of Defense trials for hyperbaric oxygen and TBI: Issues of study design and questionable conclusions. <http://www.ncbi.nlm.nih.gov/pubmed/24224289>

[9] Walker WC, Franke LM, Cifu DX, Hart BB. Randomized, Sham-Controlled, Feasibility Trial of Hyperbaric Oxygen for Service Members With Postconcussion Syndrome: Cognitive and Psychomotor Outcomes 1 Week Postintervention. Neurorehabil Neural Repair. 2013. DoD/USA
<http://nnr.sagepub.com/content/28/5/420>

[10] Cifu DX, Walker WC, West SL, Hart BB, Franke LM, Sima A, et al. Hyperbaric oxygen for blast-related postconcussion syndrome: Three-month outcomes. Ann Neurol. 2014;75(2):277-86. (DoD) (USA). Available upon request.

[11] Army Trials Report from UHMS Conference, June 2013. Press Release: " DoD announces results of first three DoD-Sponsored trials using hyperbaric oxygen for mild traumatic brain injury." Available upon request.

[12] R. Scott Miller, M.D., COL, US Army, Director, Hyperbaric Oxygen Research Program, US Army Medical Materiel Development Activity, Ft. Detrick, MD. **Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms.** JAMA Intern Med. doi:10.1001/jamainternmed.2014.5479. Published online November 17, 2014.

6. Additional Relevant Science and Brain Wound Research.

1. Burns PB, Rohrich RJ, Chung KC. The Levels of Evidence and their role in EvidenceBased Medicine. Plast Reconstr Surg . 2011 July ; 128(1): 305–310. doi:10.1097/PRS.0b013e318219c171.

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4. <https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Traumatic-Brain-Injury>. Sourced 11/7/2020.
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12. Schoettle RJ, Kochanek PM, et al: Early polymorphonuclear leukocyte accumulation correlates with the development of posttraumatic cerebral edema in rats. *J Neurotrauma* 1990; 7(4):207-217.
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16. McIntosh TK, Smith DH, Garde E (1996): Therapeutic approaches for the prevention of secondary brain injury. *European Journal of Anaesthesiology* 1996; 13:291-309.
- 17.a Hovda DA, Lee SM, et al: The neurochemical and metabolic cascade following brain injury: moving from animal models to man. *J Neurotrauma* 1995; 12(5): 903-906.
- 17.b Giza, C.C., M.D. and Hovda, D.A., Ph.D., "The New Neurometabolic Cascade of Concussion," *Neurosurgery*. 2014 October; 75(0 4): S24–S33. doi:10.1227/NEU.0000000000000505.
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J Trauma September 1993; 35(3):415-422.

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Johns Hopkins reports that the brains of Iraq and Afghanistan combat veterans who survived blasts from improvised explosive devices and died later of other causes show a honeycomb of broken and swollen nerve fibers in critical brain regions, including those that control executive function. The pattern is different from brain damage caused by car crashes, drug overdoses or collision sports, and may be the never-before-reported signature of 'shell shock' suffered by World War I soldiers.

<http://www.sciencedaily.com/releases/2015/01/150114140600.htm>

Blast injury, and the accompanying role of air embolism in invisible wounds to the brain, is still not widely studied and thus seldom treated. Hyperbaric Oxygen Therapy is recognized worldwide as the definitive treatment for air embolism. Air/gas embolism is already an on-label, approved indication for HBOT.

This is a page out of the Textbook of Military Medicine, updated in 2006; this same algorithm is in the textbook in the 1980s. The "definitive therapy" then and is HBOT treatment for TBI.

The Management of Primary Blast Injury

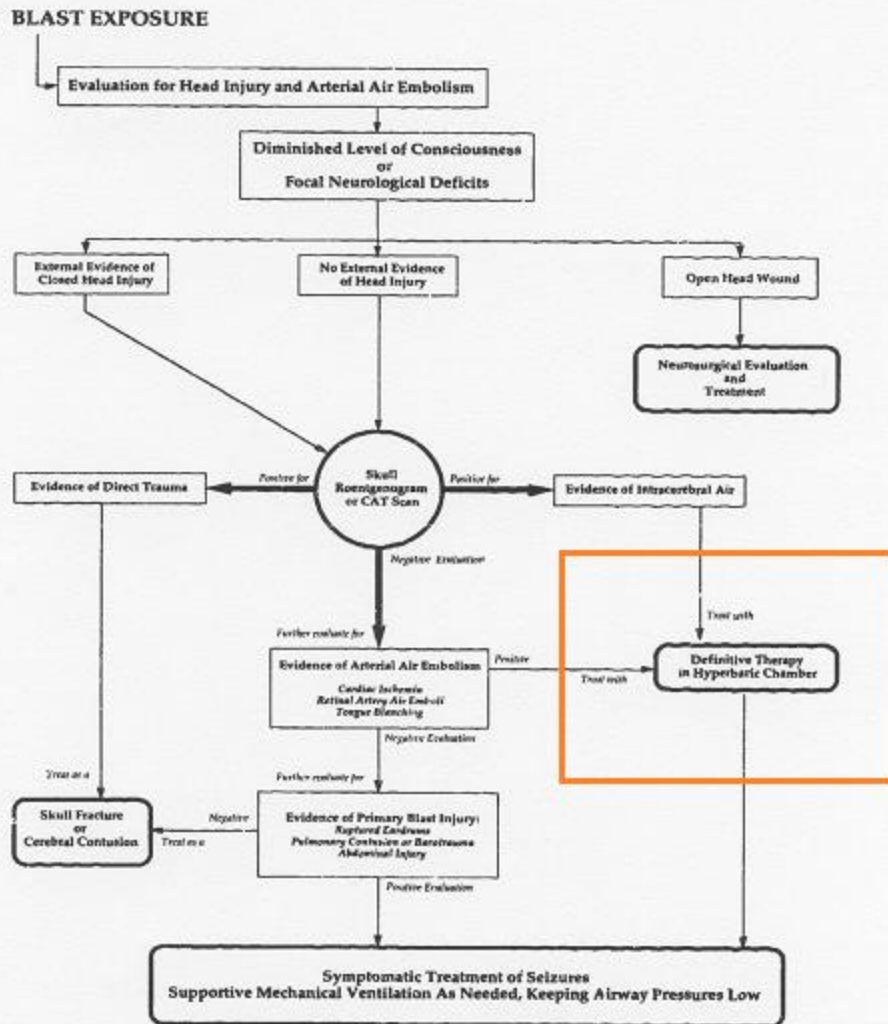


Fig. 9-10 Algorithm for the evaluation of neurological abnormalities in a blast casualty

Textbook of Military Medicine - Series on Combat Casualty Care Part 1 Volume 5 pg 313 Conventional Warfare - Ballistic Blast and Burn Injuries Published by the Office of the Surgeon General Department of the Army, United States of America. Editor in Chief Colonel Russ Zajchuk, MC US Army, Deputy Commander, Walter Reed Army Medical Center. Managing Editor Donald P Jenkins PhD Uniformed Services University of the Health Sciences. 313
 Walter Reed Army Medical Center, Walter Reed Army Institute of Research, Washington DC.
 Uniformed Services University of the Health Sciences, Bethesda Maryland.
 United States Army Institute for Surgical Research, San Antonio Texas.
 Printed in the United States 2006

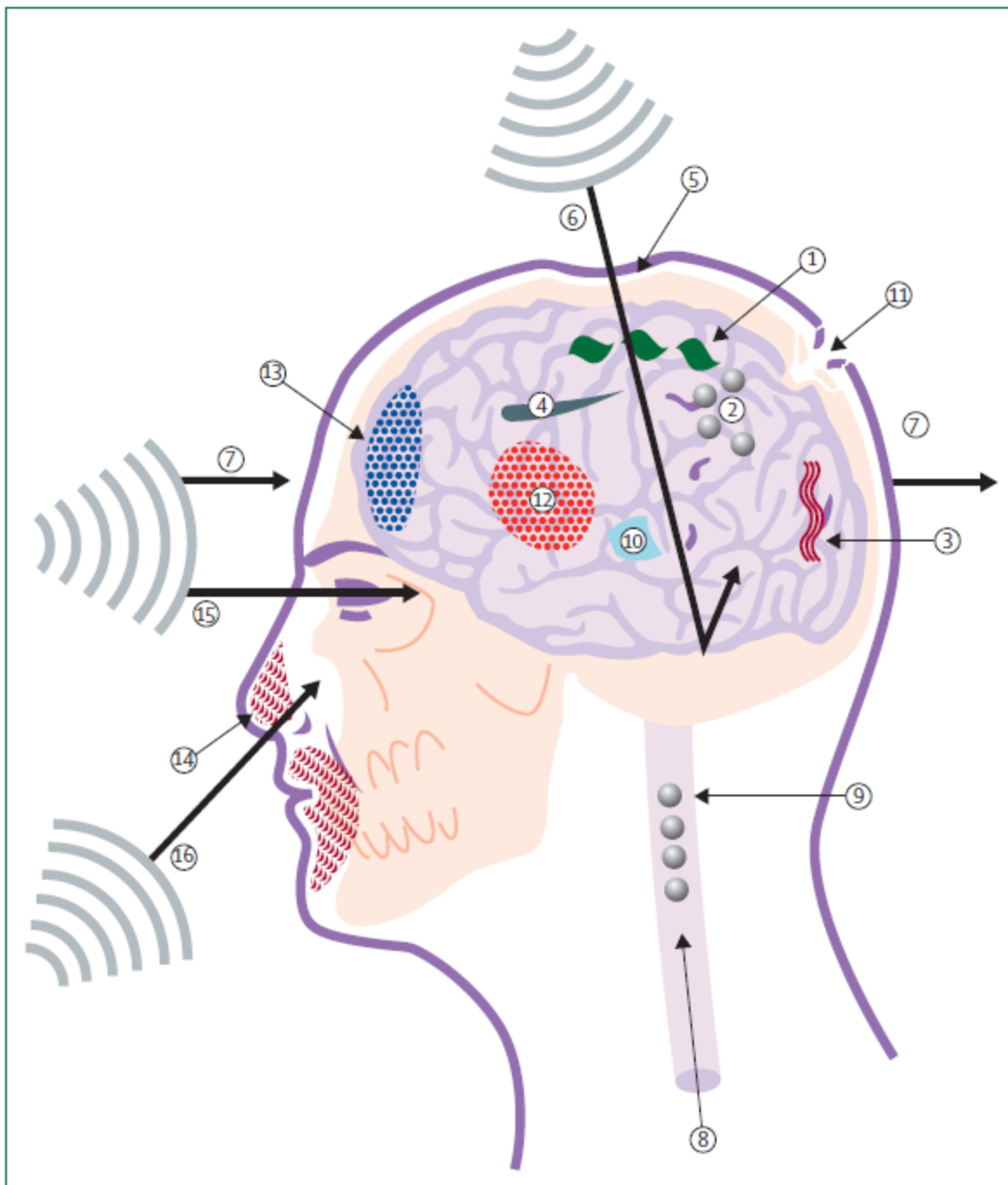


Figure 1: Schematic diagram of the mechanisms of blast-related traumatic brain injury

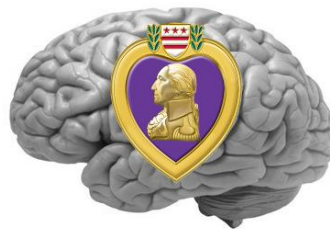
Figure shows local effects (1-7) and systemic effects (8, 9) of primary blast injury, secondary blast injury (10-12), tertiary blast injury (13), quaternary blast injury (14), and portals for blast wave transmission to the brain (15, 16). (1) Acoustic impedance mismatch causes spallation. (2) Shock-bubble interaction. (3) Shear stress causing diffuse axonal injury. (4) Cavitation. (5) Skull deformation with elastic rebound. (6) Reflection of the blast wave within the skull. (7) Bobblehead effect of acceleration-deceleration. (8) Blood surge from the torso damages the microvasculature. (9) Air embolism from blast lung injury. (10) Penetrating fragments. (11) Compound fractured skull. (12) Intracerebral haemorrhage. (13) Contrecoup contusion. (14) Burns. (15) Blast wave transmitted through the orbits. (16) Blast wave transmitted through the nasal sinuses.

Blast-related traumatic brain injury. Jeffrey V Rosenfeld, et al *Lancet Neurol* 2013; 12: 882-93 July 22, 2013 [http://dx.doi.org/10.1016/S1474-4422\(13\)70161-3](http://dx.doi.org/10.1016/S1474-4422(13)70161-3)

15 on-label indications for HBOT are already approved and insured

1. **Air or Gas Embolism****
2. **Carbon Monoxide Poisoning****
Carbon Monoxide Poisoning Complicated By Cyanide Poisoning
3. **Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias****
4. **Decompression Sickness****
5. Arterial Insufficiencies:
Central Retinal Artery Occlusion**
Enhancement of Healing In Selected Problem Wounds
6. Clostridial Myositis and Myonecrosis (Gas Gangrene)
7. Severe Anemia
8. Intracranial Abscess
9. Necrotizing Soft Tissue Infections
10. Osteomyelitis (Refractory)
11. Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
12. Compromised Grafts and Flaps
13. Acute Thermal Burn Injury
14. Idiopathic Sudden Sensorineural Hearing Loss (Approved on October 8, 2011 by the UHMS Board of Directors)
15. CMS Covered Condition: Diabetic wounds of the lower extremities in patients who meet the following three criteria [August 30, 2002]
 - a. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
 - b. Patient has a wound classified as Wagner grade III or higher; and
 - c. Patient has failed an adequate course of standard wound therapy.

**** These indications are similar to conditions found in brain injury**



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