



Nat'l Brain Injury Rescue & Rehabilitation Project (N-BIRR)

Why Hyperbaric Oxygen Therapy Works for Chronic Brain Injury Support for the N-BIRR HBOT 1.5 at Observational Study

INTRODUCTION:

This memorandum outlines the scientific basis for why 100% of the casualties of the current war who have been treated with HBOT 1.5 have all made significant recovery. These casualties have suffered from Persistent Post-Concussion Syndrome (PPCS) caused by Traumatic Brain Injury (TBI) with or without PTSD. HBOT uses oxygen as a drug to cause biological repair and regeneration of damaged tissue, a fundamentally different healing process from the symptom relief usually prescribed for these patients. HBOT's mechanisms of action are well understood and HBOT is already FDA-cleared, is safe, and available throughout the nation. This memorandum justifies an observational study to track pre and post testing of patients to provide evidence to policy makers rapidly. This will shorten the time for scientific proof from 2 ½ years for an RCT to six months with FDA-approved scientific validity at a fraction of the cost. The lack of such a Level I study has inhibited the wide-spread adoption and use of HBOT 1.5 for TBI & PTSD. All patients in the observational study receive real treatment, permitting 3rd party payer reimbursement. Thus HBOT 1.5, a legal and ethical treatment already available, will be able to meet the national emergency presented by these war casualties.



HBOT is the use of oxygen in an FDA-cleared medical device, a pressure chamber that uses oxygen at greater than atmospheric pressure as a medication to treat injury and disease processes. There are currently thirteen "indications" or standards of care for which the FDA and Medicare has approved the use of hyperbaric therapy, including three for neurological injuries (decompression illness, carbon monoxide poisoning, and brain abscess). Most of these treatments are done at 2.0 – 2.8 ata (a measurement of oxygen dose). The brain is more sensitive to oxygen¹ and has responded better to

HBOT 1.5, in cumulative repeated treatments.

The HBOT 1.5 National Brain Injury Rescue & Rehabilitation (N-BIRR) project has already saved the government \$6.3 million in retraining costs by restoring five military personnel to duty.² The N-BIRR team, led by Dr. Paul Harch at LSU in New Orleans, has treated 27 combat veterans. Twenty-five were treated with HBOT 1.5 for neurological injuries and two veterans treated for broken vertebrae, off-label, with the wound care protocol HBOT 2.0 for 90 minutes. For those provided with the full battery of neuropsych tests, the results are: Rivermeade Post Concussion Symptom Questionnaire. (Average -37 %Δ. -10% is clinically significant.) PTSD symptoms (Average %Δ = -28, more than clinically significant); Average IQ increase has been 17 IQ points (Most exceeded 20 points in 35 days with ½ the protocol.) A total of 35 will have been treated when the LSU IRB-approved HBOT 1.5 pilot study is completed. They will have clinical evaluation; imaging and most will have an extensive battery of pre and post neuropsychological testing. Each of

¹ The brain is 2% of the body's weight by mass, but uses 20% of its oxygen and 25% of its glucose supply. Therefore it makes sense that a lower dose of oxygen would be needed to heal a hypoxic wound in the brain compared to a hypoxic wound in the foot. Presentation by CAPT Brett Hart, M.D., Dec 2008 DoD HBOT in TBI Consensus Conference.

² Military Replacement Training Costs: Per the "HBOT 1.5 Score Card," costs for recruiting a new service member, \$20,000. Basic Training, \$35,000; Infantry Training: \$150,000 Navy SEAL: \$700,000 Aircraft Pilot: \$5 million

these combat veterans has had significant improvement. Most have had significant improvement or complete remission of their PTSD symptoms and have been able to return to work or other rewarding pursuits.

For those on active duty, their treatment costs were \$62,500. For each dollar spent on HBOT 1.5 treatment, the government saved \$100. This does not include a savings calculation for unneeded disability payments. It does not include the fact that current, less effective treatments cost as much or more than HBOT 1.5. Many more millions of dollars can be saved, and as can hundreds of thousands of shattered lives.

Nature of the Crisis: A new report issued by DoD on March 4, 2009, indicates that 20% of the 1.8 million who have served, or 360,000 service members have suffered wartime brain injuries. Of those retention is a major concern of both the military command and policy makers. In addition, the suicide rate was reported at 17 per day in this population, in 2005, and reports have indicated that rate may have increased. We have seen a surge of county jail inmates from this war, reported at 10% in one rural county, and one of our small cities saw a surge from 35 in November 2008 to nearly 200 just a few months after 3,000 Iraqi war veterans returned to the state. The divorce rate for this population is reported at 80-90%, and the rate of disability, substance abuse and homelessness is alarming. This is with the current “standard of care” medical practices. This argues for compassionate use of the most promising therapy to date, HBOT 1.5.

Confusion in Diagnosis: There appears to be confusion within DoD Medicine between blast-induced mild TBI and PTSD in our veteran population. This difficulty is found within the PTSD definition. Careful questioning of over 30 veterans and in-depth interviews with detailed physical examinations of 19 of these veterans exposed to concussive blasts has revealed significant abnormalities in those patients with loss of consciousness from their blast exposure. These abnormalities have been supported by psychological and cognitive testing abnormalities that are consistent with the diagnoses of “TBI” and “PTSD” bestowed by military evaluators. Our experience is reaffirming the findings of the Hoge article of 2008 where servicemen and women with LOC had a much higher rate of TBI and PTSD symptom expression as those without loss of consciousness. Our experience further suggests that the confusion in distinguishing between the residual effects of mild TBI and PTSD may lie in the definition of PTSD which includes symptoms of TBI (sleep cycle disruption, irritability, and difficulty concentrating). Considering the PTSD definition was created before we understood mild TBI and Post Concussion Syndrome as we do today, this mix-up is understandable. This definition of PTSD obscures the diagnosis of mild TBI.

Real Results Now: No other research of the nearly \$1 billion spent by DoD medical for TBI/PTSD research, has yet to deliver return on investment. Announcements have said not to expect anything from that effort for 18 months to five years. Twenty years of clinical experience with TBI patients has shown this lower dose of oxygen (1.5 ata) has caused clinical improvement in TBI patients. It is being used for neurological treatment by scores of physicians throughout the nation. The pilot studies conducted by the N-BIRR team have demonstrated the same expected improvements in these war casualties. The \$62,500 in treatment costs were donated by the physicians or charities serving veterans. Medical professionals cannot donate a sufficient amount of free medical treatment (using a treatment modality already reimbursed by Tricare) to meet the needs of these war veterans and stay in business. Therefore a pathway needs to be found so that services can be delivered so that the states’

National Guard and the military command that are faced with the retention/replacement/ recruitment crisis can have relief. Note that this therapy, HBOT, is already paid for by Tricare and VA and Medicare/Medicaid for 13 other indications, and until recently, was being reimbursed for every HBOT 1.5 case where a war casualty demonstrated significant improvement. If a war veteran is on

the path to being medically discharged and is able to return to duty, it is in the government's interest to have that replicated for at least the admitted 90,000 current symptomatic casualties.

For each casualty, clinical recovery happened over a period of 35 to 150 days, after six months or more of no progress under the care of the current military medical system. It is known that six months after injury, no further significant neurological recovery is expected. Current medical treatment for this population has involved a cocktail of drugs; many of them used off-label (i.e. never FDA-approved for use with traumatic brain injury or PTSD patients). Some of these drugs carry FDA warnings because they increase the risk for suicide.³ Further, active duty personnel lose their security clearances if they take most of these drugs chronically. Further the cost of the current treatments is higher in one or two years for the treatments listed, treatments that treat symptoms, not the cause of the than that of the permanent repair provided by HBOT 1.5.⁴

HBOT has no such FDA warnings, has no impact on a Security Clearance, and has been determined to be safe by the DoD. The official DoD White Paper states, "Side effects from HBOT are uncommon, and severe or permanent complications are rare, especially at the doses of HBOT used "off-label" for TBI patients (approximately 1.5 atm abs for 60 minutes.), compared to HBOT for HHS covered indications (2 to 2.4 atm abs for 120 to 90 minutes.)"⁵

N-BIRR: Real Level I Evidence: We are not advocating an uncoordinated effort of "treat them all and take our word for it." Instead we have developed the National Brain Research and Rehabilitation Project (N-BIRR) that provides an Institutional Review Board-approved protocol and permits data collection through software designed for that purpose. **This will enable results to be gathered and published in peer review journals AND is data that the FDA will accept as being as valid as a randomized-controlled trial.** The data will be FDA/Evidence-based Medicine quality.

HBOT is the only non-hormonal FDA-approved treatment known to repair and regenerate human tissue. HBOT repairs and regenerates tissue by two oxygen-dependent processes, the activation of growth factors at a DNA level and the improvement of blood supply to wounds. These salutary effects of hyperbaric oxygen apply in a variety of FDA-approved indications such as the acute wounds of traumatic loss of blood supply, traumatic hemorrhage, crush injury, and a number of neurological injuries. These effects also apply in FDA-approved conditions with chronic wounds such as diabetic foot wounds, radiation wounds, and chronic bone infections. The salutary effects of HBOT apply regardless of the location of the wounds in the body. As a result, HBOT can be considered a generic drug for repair of acute and chronic wounds in the body. The application of HBOT to chronic traumatic brain wounds is merely

³ The actual FDA warning reads, "Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of (insert name of antidepressant) or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24..." The age group described by this warning would seem to include a significant number of our brain-injured veterans.

⁴ RAND Report: "Invisible Wounds of War: Psychological and Cognitive Injuries, Consequences, and Services to Assist Recovery." Tanielian, Terri; Jaycox, Lisa, April 2008, page xxii-xxiii: Two year costs within the first two years the service member returns home; PTSD \$5,904 to \$10,298 depending on whether we count the lives lost to suicide; Two year costs for major depression, \$15,461 - \$25,757; co-morbid PTSD and major depression; \$12,427 to \$16,884; One year costs for traumatic brain injury diagnosis: \$25,572 to \$30,730 in 2005 for mild cases (\$27,259 to \$32,759 in 2007 dollars), and \$252,251 to \$383,221 for moderate or severe cases (\$268,902 to \$408,519 in 2007 dollars.) These costs, largely treating symptoms, continue to have outyear costs and outyear consequences in terms of disability payments, inability to work, etc. Given that the HBOT ONE TIME cost for service members who need all 80 treatments averages \$16,000 at Medicare Reimbursement rates for a 1 hour treatment. (The cost is lower in some states and higher in urban areas, with known rates set by CMS.) Hyperbaric medicine alone, and hyperbaric medicine in conjunction with other treatments, is very cost effective. If provided acutely within hours of injury, the treatment is even more effective and massively more cost effective.

⁵ DoD "HBOT for TBI" Consensus Conference White Paper, 28 October 2008

the extension of these principles and the science of HBOT to chronic wounds in the brain. When this extension is also underpinned by clinical precedent it meets the criteria for FDA-approval as an off-label application of an FDA-approved drug. For nearly 2000 years prior to the advent of the FDA, “off-label” prescribing was informally known as the practice of medicine according to the Hippocratic Oath. Hyperbaric oxygen therapy for chronic TBI is, therefore, the application of HBOT to chronic TBI according to the Hippocratic Oath.

When devices like hyperbaric chambers are already on the market, and when mechanisms of action are as well known as HBOT's, randomized-controlled trials for new indications are unnecessary. Placebo effect has been long ago ruled out because the non-healing wound in the brain is simply another non-healing wound in the body and has consistently responded to treatment on the same basis as other problem wounds like diabetic foot wound. The demand for an RCT, then, creates an artificial barrier because of the expense of this kind of research. This in turn causes a Type II error⁶, rejecting effective treatment that should be reimbursed, among third party payers.

In addition, with adaptive clinical study design, an entire rehabilitative program, not just a treatment protocol, can be evaluated to determine best practices.⁷ This allows treatment of active duty combat veterans, with their unique set of problems, as well as those who have been returned to the civilian sector with no effective treatment and are homeless, incarcerated, substance-abusers, unable to return to their regular employment, etc. We have strived to structure a complete package that will allow a real time solution to the problem of untreated brain injury among the hundreds of thousands of injured veterans who are still on active duty (treated at DoD facilities and even in theater), have been returned to the care of the VA (as the hundreds of thousands of National Guard personnel have been), have been dishonorably discharged because of their aberrant behavior AFTER having served valiantly in combat, injured, and discharged with no benefits and NO HOPE for the future. The Federal government wishes to abandon these veterans, but the states and local communities must find some way to deal effectively with them other than incarceration. The contemplated N-BIRR research structure will permit determination of best practices and combine effective treatment with all of the adjunct services already available for veterans to deliver real recovery from injuries. It is anticipated this program will be highly compatible with the numerous public and charitable partner's individualized programs to enhance them all.

The crisis is upon our entire nation. Human tragedies in these injured and untreated veterans who served the country when called, faithfully, is playing out across America. Instead of 2 ½ years for a randomized-controlled trial, the anticipated statistical pathway permits ruling out placebo while permitting Level I evidence, plus the roll out of the treatment to the thousands who need it. For those concerned about the 17 suicides per day in this population (2005 data)⁸, these suicides are expected to drop dramatically once it is known that there is a treatment that will restore them to much of their former capability and restore their lives.

HBOT Physiology is Understood & Scientifically Valid: The physiological processes enhanced by hyperbaric oxygen treatments are well understood and characterized in the literature.⁹ Oxygen is

⁶ A type II error is a rejection a use for a device that should be approved.

⁷ Robert Mozayani, M.D. was a Howard Hughes Fellow and NIH Intramural researcher for many years. He is the Administrative Primary Co-Investigator with Paul Harch, M.D. on the national IRB-approved HBOT 1.5 protocol and is skilled at both FDA-Devices Division studies and adaptive trial design.

⁸ http://www.cbsnews.com/stories/2007/11/13/cbsnews_investigates/main3496471.shtml

⁹ For an extensive summary of this literature from the U.S. Air Force, see:

Wright, James K. Wright, Col, USAF, MC, SFS, USAF School of Aerospace Medicine/FEH, “The Relevance of Hyperbaric Oxygen to Combat Medicine,” Paper presented at the RTO HFM Symposium on “Operational Medical Issues in Hypo- and Hyperbaric Conditions”, held in Toronto, Canada, 16-19 October 2000, and published in RTO MP-062.

used in over 200 cellular processes, many of which are damaged after hypoxia. With the well-known clinical and physiological effects of hyperbaric medicine to heal chronic wounds that lack oxygen, the likelihood of the clinical effects being experienced by these combat veterans being attributable to placebo is highly unlikely.

Hyperbaric treatment of diabetic foot wounds has proven to be particularly effective as well as cost effective. It prevents 75% of all amputations.¹⁰ The British military has published a 50% improvement in combat casualty care healing rates using hyperbaric oxygen.¹¹ Treatment for these indications provides the basis for legal and ethical off-label prescription and ongoing treatment of TBI/PTSD cases with HBOT 1.5. There are nearly 1,000 facilities offering hyperbaric treatment across the U. S. delivering an estimated 10,000 treatments per day for these 13 indications. If these facilities were used at emergency capacity, it would be possible to return 10,000 men and women to duty or to functional lives every 150 days to meet this national emergency.

OVERVIEW OF THE SCIENCE :

Oxygen is essential to human life. Appropriate oxygen availability is necessary to optimize bodily functions, sustain life, and repair damaged tissues¹². Oxygen normally is dissolved in the blood through the lungs and distributed throughout the body in the circulatory system. Exposing blood to higher than usual levels of oxygen through breathing oxygen under pressure increases the amount of oxygen available in the body to as much as 7 times normal. When HBOT 1.5 is delivered intermittently, saturating tissues at these higher concentrations, oxygen becomes like a “pill,” stimulating healing processes like a medicinal drug.¹³

HBOT’s healing characteristics include the ability to reduce hypoxia (low oxygen levels in damaged tissue), energize cells damaged by low blood flow, and, in acute injuries, inhibit reperfusion injury (the immune response to injury). Additionally, high levels of oxygen can stimulate release of stem cells from a patient’s bone marrow into their circulatory system where the stem cells can then home to wounded areas in the body.¹⁴ These stem cells address the tasks of repairing or replacing damaged or destroyed cells and tissue, and repairing or replacing the damaged vascular system to restore blood flow.¹⁵

HBOT is now viewed as one of the only growth and repair drugs by virtue of its stimulation of DNA genes that code for growth and repair hormones and their receptors.¹⁶ The net result of this stimulation is growth of new tissue, bone, skin, and blood vessels.¹⁷ All with no adverse side effects when known protocols are followed.

Wright, James K. Wright, Col, USAF, MC, SFS, “Case report: Treatment of Mild Traumatic Brain Injury with Hyperbaric Oxygen,” Manuscript submitted to “Military Medicine,” 2009.

¹⁰ CMS approved diabetic foot wound treatment in 2003. See www.HyperbaricMedicalAssociation.org/Science for the diabetic foot wound argument. In addition, it costs about \$16,000 to rebuild a Wagner Grade III foot wound. By the time the series of surgeries are completed, it costs \$30,000 to treat this conventionally, with a cost of \$150,000 for multiple surgeries, prosthetics, etc., with the patient dead 18 months after the 2nd amputation from cardiovascular complications. It is far less expensive to treat with HBOT and prevents the cascade of events.

¹¹ Schramek A, Hashmonai M. Vascular injuries in the extremities in battle casualties. *Brit J Surg*, 1977;64:644-648.

Radonic V, Baric D, Petricevic A, et al. Military injuries to the popliteal vessels in Croatia. *J Cardiovasc Surg*, 1994;35:27-32.

¹² Sheffield, P.J., *Physiological and Pharmacological Basis of Hyperbaric Oxygen Therapy, Hyperbaric Surgery*, Baker, Dirk, pp 63-109

¹³ Boerema I, Meyne NG, Brummelkamp WK, et al. Life without blood: a study of the influence of high atmospheric pressure and hypothermia on dilution of blood. *J Cardiovasc Surg*, 1960;1:133-146.

¹⁴ Thom et al., 2006, *Am J Physiol Heart Circ Physiol* 290:1378-86.

¹⁵ Zhang, JH et al. *Neuroscience and Critical Care*

¹⁶ Wu, L. *Surgery*, 1995; 117: 570, Sheikh, AY. *Arch Surg*, 2000; 135: 1293-7

¹⁷ Hehenberger, K. *Wound Rep Regen*, 1997; 5: 147-50, Marx, RE. *Am J Surg*, 11/90; 160: 519-24, Manson, PN. *Surg Forum*, 1980; 31: 564-66, Uhl, E. *Plast Reconstr Surg*, 1994; 93: 835-41, Ueng, SWN. *J of Trauma; Injury , Infection & Critical Care*, 1998; 44(4): 676-81

In the over-40-year science of treating divers for decompression sickness, from which the science of HBOT 1.5 has been evolved,¹⁸ the purpose of the pressurized delivery of oxygen through HBOT was initially thought necessary to eliminate bubbles occurring in the blood due to sudden decompression. By 1989, however, Navy research had revealed that the bubbles disappeared quickly, even without treatment.¹⁹ It was found that the effect of the HBOT treatment was to provide healing oxygen to the reperfusion damage caused by the bubbles as they passed through the brain.¹⁹ By adapting the acute treatment protocol to a lower dose of HBOT, Dr. Harch found in the early 1990s that divers with more chronic injuries from decompression sickness could be rehabilitated with HBOT similar to divers with acute injuries.¹⁹

With the advent of advanced brain-scanning technologies, the similarity of the divers' brain damage could be compared to brain damage from other causes (such as TBI, stroke and cerebral palsy). The potential of HBOT for treatment of other brain injuries began to be realized from the research and clinical experience of Dr. Harch and others.¹⁹ HBOT 1.5 was determined to be the optimum pressure for the treatment of brain injury, combining rapid recovery times with low – virtually no – downside risks. As the Attachments show, the related, preceding and underlying science is relevant to the accumulated scientific knowledge on which proposed Trial is based and justified.

The HBOT 1.5 protocol is extremely safe²⁰ and effective, and is a direct extension of the U.S. Navy Diving Tables. In the United States Navy as well as the world navies injured divers are treated for decompression sickness shortly after emerging from the water and experience a 90% cure rate on the first treatment. Those who do not have complete remission are treated repetitively with a tapered dose of HBOT until they reach a treatment plateau. Unfortunately injured commercial divers and recreational scuba divers have hours to days delay to treatment and are often left with significant neurological residual damage. In the late 1980s Dr. Harch used the Navy concept of tapered dose to extend the Navy dive tables and found that commercial and SCUBA divers neurologically improved far after plateau on the U.S. Navy protocol. Divers with residual neurological injury months to years after typical U.S. Navy treatment also improved. These findings were then successfully applied to over 60 other chronic neurological conditions, including TBI and PTSD. Essentially, this protocol was derived by simply reducing the oxygen pressure from 2.4 ATA [Atmosphere Absolute or 20.6 pounds per square inch-gauge (psig)], commonly used in wound care, to 1.5 ATA (7.35 psig). This 38% reduction in dose of HBOT was found to be not only safe (could repair seizures instead of causing them), but also effective on both subacute and chronic neurological wounds.

Gaylan Rockswold, M.D., the neurosurgeon who reduced death by 59% in the most fragile of acutely brain injured patients wrote, “Based on our own past and continuing investigations ... placing severe

¹⁸ Harch PG. Late treatment of decompression illness and use of SPECT brain imaging. In Treatment of Decompression Illness, 45th Workshop of the Undersea and Hyperbaric Medical Society (eds RE Moon, PJ Sheffield). UHMS, Kensington, 1996, 203-242.; Harch PG, Van Meter KW, Gottlieb SF, Staab P. HMPAO spect brain imaging of acute CO poisoning and delayed neuropsychological sequelae (DNSS). Undersea & Hyperbaric Medicine, 1994;21(Suppl):15.; Harch PG, Van Meter KW, Gottlieb SF, Staab P. The effect of HBOT tailing treatment on neurological residual and SPECT brain images in type II (cerebral) DCI/CAGE. Undersea & Hyperbaric Medicine, 1994;21(Suppl):22-23.; Harch PG, Gottlieb SF, Van Meter KW, Staab P. HMPAO SPECT brain imaging and low pressure HBOT in the diagnosis and treatment of chronic traumatic, ischemic, hypoxic and anoxic encephalopathies. Undersea & Hyperbaric Medicine, 1994; 21(Suppl):30.; Paul G. Harch, Keith W. Van Meter, Sheldon F. Gottlieb, Paul Staab. Delayed treatment of type II DCS: the importance of low pressure HBOT and HMPAO SPECT brain imaging in its diagnosis and treatment. Undersea & Hyperbaric Medicine, 20(Suppl):51, 1993.; Paul G. Harch, Sheldon F. Gottlieb, Keith Van Meter, Paul K. Staab. SPECT brain imaging in the diagnosis and treatment of type II decompression sickness. Undersea Hyper Med, 1992;19(Suppl):42.

¹⁹ Cockett ATK, Zehl DN, Hanley J, Adey WR, Roberts AP. Effects of emboli on the neurocirculatory system in decompression sickness. In: Trapp WG, Banister EW, Davison AJ, Trapp PA, editors. Proceedings of the 5th International Hyperbaric Congress, Vol. II, 1973. Simon Fraser University, Burnaby 2, B.C., Canada, 1974. Gorman DF, Browning DM. Cerebral vasoreactivity and arterial gas embolism. Undersea Biomed Res, 1986 Sept;13(3):317-35. Moon RE, Gorman DF. Treatment of the Decompression Disorders, Chapter 18. In: The Physiology and Medicine of Diving, 4th Edition, eds. Bennett P, Elliott D. W. B. Saunders Company, Ltd. London, 1993.

²⁰ Ibid, DoD Consensus Conference White Paper, October 2008.

TBI patients in either a monoplace or multiplace HBO chamber at 1.5 ATA for 60 minutes is a very low risk procedure.”²¹ The official DoD White Paper states, “Side effects from HBOT are uncommon, and severe or permanent complications are rare, especially at the doses of HBOT used “off-label” for TBI patients (approximately 1.5 atm abs for 60 minutes.), compared to HBOT for HHS covered indications (2 to 2.4 atm abs for 120 to 90 minutes.)”²² **For the mild traumatic brain injury patient, clinical experience demonstrates this treatment is far less risky to patients than leaving them untreated. It is also less risky than being in Iraq or Afghanistan.**

Preliminary results from the pilot study protocol approved by Louisiana State University’s IRB to treat 30 veterans of the war, 15 with TBI and 15 with TBI/PTSD, have demonstrated that blast-injured war veterans respond very positively to HBOT 1.5. **There have been NO adverse events or side-effects in blast injury patients.** Clinical symptoms on the Rivermeade Post-concussion Symptoms Questionnaire²³ have shown a 40% reduction in symptoms on a majority of patients. Further, a majority of casualties treated have recorded a 20+ point IQ jump, and most have experienced a 40% decrease in PTSD symptoms, just with the first ½ of the protocol. This study is underway and still recruiting patients. Everyone receives treatment and recruiting and treatment are being completed as quickly as possible so that data can be utilized by policy makers striving to solve the national crisis these untreated casualties are adding to the other challenges the nation is facing.

It is well to note that animal studies utilizing the HBOT 1.5 protocol have now replicated the experience with HBOT 1.5 in humans. This is the first improvement of chronic brain injury in animals in the history of science. A copy of this research report, “Hyperbaric Oxygen Therapy Improves Spatial Learning and Memory in a Rat Model of Chronic Traumatic Brain Injury” is at www.HyperbaricMedicalAssociation.org/Science .

Placebo Effect: A major argument lodged against starting treatment right now is that HBOT 1.5 might be a placebo effect. “The **Placebo effect** is the medical phenomena in which a person’s beliefs about an inert substance or a sham therapy results in that treatment having the expected consequences of those beliefs upon health.”²⁴ Thirty Five percent of patients are expected to get some improvement because of placebo effect. HBOT 1.5 has significantly improved 100% of the treated patients.

There are several reasons it is highly unlikely that improvement in war casualties treated with HBOT 1.5 is the result of a placebo effect.

- 1) **Oxygen can never be a placebo because it violates one component of the placebo definition, that the substance has the potential to be inert. Oxygen is a biologically active element and hence is not inert.**
- 2) Placebo effects are not expected to show improvement in 100% of the subjects treated.
- 3) Placebos do not show independently verifiable clinical effect. DoD’s own invited expert, Dr. Orrison, stated clearly that neuroimaging demonstrates a rebuilding of neural issue within as little as 30 days. A placebo does not do that. It is a clear clinical effect that rules out placebo. As John Eisenberg, MD, Ph.D., founder and director of AHRQ stated, “This is an N of 1 study where each patient serves as their own control. When there is 30 days between one image and other, and the only intervention was HBOT 1.5, the cause of the repair can only logically have been HBOT.”²⁵
- 4) The laws of physics and the gas laws show that HBOT 1.5 delivers 7 times as much oxygen to plasma as normally breathed. The known science of how oxygen works and how the body uses oxygen to heal indicates that this oxygen delivery begins healing at the DNA level, activates stem cells, and increases blood vessel

²¹ Rockswold, Sarah B; Rockswold, Gaylan L.; *Neurological Research*, Vol. 29, March 2007, pp. 162 – 172.

²² DoD “HBOT for TBI” Consensus Conference White Paper, 28 October 2008

²³ This Questionnaire is the standard measure of post concussion injury and was selected by the DoD HBOT Consensus Conference as the measure they were going to use to determine clinical effectiveness. A 10% reduction is considered significant. All HBOT 1.5 treated veterans have had between 13% and nearly 43% improvement on this scale.

²⁴ Wikipedia, “Placebo Effect”

²⁵ Meeting with Drs. Duncan, Harch and Neubauer in 2002. This is when Dr. Eisenberg ordered the HBOT 1.5 literature review on HBOT in TBI and stroke. Unfortunately it was completed after his death and did not actually examine the evidence for HBOT.

- density. It does this in bone, skin and other hypoxic tissues throughout the body. Why would the brain be different?
- 5) HBOT 2.0-2.4 clearly heals diabetic foot wounds. These are hypoxic wounds that we can see, and HBOT has a clinical effect. HBOT has been proven in RCTs and placebo effect was eliminated as a reason for healing. Wounds in the brain are also hypoxic wounds. It is logical that HBOT heals the hypoxic wounds in the brain and in the foot. Thus the HBOT clinical experience is consistent with the scientific validity of the rest of the HBOT treatment indications.
 - 6) After 6 months, no further natural healing is expected in brain injured patients. Therefore, even 45 years after injury, to have these injuries heal, permanently, within a 30 day period, can only be attributed to a clinical effect.
 - 7) The improvement in the above cases that allowed return to duty occurred in cases that were facing being medically boarded out of the military. None of these service members wanted this. This desire to avoid medical boarding generated a placebo effect for every therapy prior to HBOT that was offered to these men to improve their condition. However, only HBOT 1.5 provided the objective improvement that allowed them to return to duty. The decision to return to duty was made by independent physicians who did not deliver the HBOT. These were the same physicians who were initially recommending them for a medical board. If HBOT is in fact a placebo every service member who is facing medical boarding should be offered the placebo effect of HBOT 1.5 to avoid medical boarding when all other therapies have failed. This is nonsense.

Blast-Induced TBI/PTSD is NOT a Concussive Sport Injury

The belief that, “90% of these concussed war veterans get better in six months with no treatment” is simply untrue and not based in sound science. It reflects the “belief” or “paradigm” that there is no treatment for brain injury.

John T. Povlishok, M.D., editor of the journal, *Neurotrauma*, presented to the DoD HBOT Consensus Conference. He showed this injury is from multiple causes. It is stretching of neurons by the blast wave, sheer and twisting injury, concussive injury from striking solid objects or being struck by objects. The standard sports concussion model did not apply.²⁶ Further, he showed the extensive deterioration in neural pathways without intervention that takes place over just weeks following an injury. This explains why a few HBOT treatments shortly after injury provide effective treatment to heal these tissues. These few treatments will prevent deterioration. HBOT works just like this for decompression sickness (DCS). This deterioration also explains why many more treatments are necessary to repair pathways months to years after an injury.

Since the DoD HBOT in TBI Consensus Conference, a paper on blast injury has been produced showing that blast waves cause lungs to rupture which can lead to bubbles in circulation like we see with DCS.²⁷ So, if the correct acute and chronic treatment for bubbles in the brain from DCS sickness is hyperbaric oxygen, then it stands to reason that the correct acute and chronic treatment for bubbles caused by a concussive blast wave from lungs rupturing is also hyperbaric oxygen.

The doctrine that the brain adjusts to a concussion in 90% of concussive sports injuries and neuropsych test scores return to near normal, assumes there are no further injuries to these athletes. A second injury is known to prevent recovery. This is why the “readiness to play” concept has become standard practice. The assumption, that these battle casualties are the same as sports concussions is an incorrect model for this application. These battle casualties have successive concussions within a six month period that prevent recovery. Further, blood brain flow and long term cognitive function does not return to normal in athletes as previously believed. A new article in *Brain: A Journal of Neurology* published by Oxford, now shows that 30 years post injury there is not the recovery that had previously been reported. They state, “There is a growing body of evidence suggesting that there are cumulative effects of concussions that manifest as increased susceptibility to subsequent concussions as well as an increase in their severity. More recent findings suggest that the effects of a concussion far outlast the acute phase.” They further point out that there is an earlier onset of mild cognitive impairment and an earlier onset of Alzheimer’s disease. Thus for military

²⁶ Povlishok, JT., etc.

²⁷ Reimers, et. Al.

medicine and policy makers to assume “90% of concussed veterans get better in six months with no treatment” is simply not true and is preventing effective treatment from being explored.²⁸

Further, brain blood flow is decoupled even in these sports concussions.²⁹ Even though neuropsychological tests show a return to normal cognitive function, brain blood flow in these individuals remains decoupled. The brain is not able to control its blood circulation as it did previously. Drs. Rockswold, Harch, Orrison, and Fogarty have now all demonstrated that HBOT recouples brain-blood flow, with even a single hyperbaric treatment, thus restoring the physiology in the brain that helps start a healing process.³⁰

Any period of unconsciousness is known to cause permanent organic injury. We have many more injured veterans than even the Rand report claims. The N-BIRR team to date has found that almost all of the combat arms war veterans have suffered at least one concussion, and 50% of the combat support and combat service support war veterans have suffered blast related injuries. These injuries are easily diagnosed on the ANAM tests being given now as a standard measure pre and post deployment. Oklahoma’s National Guard command was able to identify 200 45th Infantry veterans who had been concussed in a 3 day period. Those veterans can now be treated and the majority of them returned to deployable status in 150 days.

High Altitude Mortality Reduction (HAMR) Project: Placing HBOT in the Battle Area:

It has been reported that casualty deaths at Afghanistan altitudes is higher than in Iraq. The HBOT literature and experience with HBOT indicate that acute treatment in theater for TBI/PTSD could prove even more effective, requiring only 1-5 rather than 40 - 80 treatments. The result is expected to be reduced casualties (59% for acute TBI in the civilian sector), and improved individual readiness and performance among deployed forces and reduced disability in combat veterans.

Readiness

With the quality of recruits down, with large numbers of TBI/PTSD casualties sitting in barracks on military payroll, with thousands of previously able men and women returned to their states and sitting in their rooms unable to function, and with a need to send fit troops to Afghanistan, the readiness of the U.S. Military forces are in crisis. There is no greater threat to the All-Volunteer Army than hundreds of thousands of casualties in society. Many highly qualified special operations war veterans are injured and are hiding that injury because they wish to continue their careers. HBOT 1.5 and the N-BIRR project make it possible to restore the vast majority of these people to full function and make it possible to prevent creation of future casualties.

Altitude in Afghanistan

There are a considerable number of injured members of the Armed Forces who have been able to cope and hide their brain injury to date (Rand Report of estimated numbers of TBI and PTSD-afflicted service members vs. those diagnosed to date). Now that war is moving back to Afghanistan, living at 7,000 feet and fighting at 10,000 feet, the lack of oxygen at those altitudes will cause previously undiagnosed injuries to become problematic and symptoms can manifest that were not seen at lower altitudes. This is well known from hypoxia studies conducted by the military in altitude chambers. The military command needs to be aware of this and prepare appropriately to treat war veterans in theater with HBOT 1.5. There is going to be a significant degradation of combat readiness in previously concussed individuals at this new altitude unless they are treated.

²⁸ De Beaumont, Louis, et. al., “Brain Function Decline in Healthy Retired Athletes Who Sustained Their Last Sports Concussion in Early Adulthood.” *Brain: A Journal of Neurology, Oxford Journals, November 26, 2008:*

<http://brain.oxfordjournals.org/cgi/reprint/awn347v1>

²⁹ Tegeler CH, et. al, “Dynamic Vascular Assessment of Brain Circulation for Sports-Related Concussion”

³⁰ See HBOT 1.5 Restores brain Blood Flow & Metabolism, N-BIRR Casualty Case Reports.

N-BIRR: Real Treatment in Real Time

There is great logic to insurance companies not paying for treatment in clinical trials. In these trials, some number of patients would receive fake treatment. Further most of the time, the molecules used are of unknown efficacy. With N-BIRR, that is not the case. The National study will involve every veteran treated getting real treatment with a molecule, O2, that has well known effects and that is clearly safe, and certainly safer than leaving these injuries untreated. N-BIRR is an observational study under IRB-supervision. Data can be collected, reported, published, and given to the FDA Devices Division for a 14th approved indication, along with the N-BIRR data.

Military personnel are not supposed to be treated with placebo treatments. Their commanders are reluctant to allow them to be enrolled in “studies” where they could receive no treatment. N-BIRR gets around that completely. By statistically tracking outcomes, the N-BIRR study can be a phase III efficacy study providing Level I evidence acceptable to the FDA. The congress has already funded the DoD-BIRR, being coordinated at Louisiana State University, where subjects will be treated by in a randomized-controlled study, with a placebo arm. That study will rule out placebo and be completed in time for presentation to the FDA.

Therefore N-BIRR can justify having REAL HBOT 1.5 treatments paid for by state Medicaid and even Tri-Care and the VA. To date all subjects (who are enrolled in an IRB-approved protocol) have made significant improvement, after previous standard protocols had failed to improve them. All subjects get real treatment and treatment results are tracked. To make sure that the public purse is protected, both state Medicaid, Tri-Care and the VA could even implement a rule where payments are only made for persons who improve on neuro-psych testing, approved survey instruments, imaging, or clinical symptom assessment. They are certainly not seeing these results and current treatments are more expensive than HBOT.

N-BIRR will help the nation solve the crisis caused throughout our society by the huge numbers of persons with untreated brain injury being returned from the war to our society. It is far more expensive to the federal, state and local governments to leave these war casualties untreated than to treat them with HBOT 1.5. We are already spending billions on these veterans, trying to provide them new job skills, etc. They will be able to learn new jobs if their results are typical of HBOT 1.5 treated patients to date. Lost ability to learn and have executive function is one of the chief reasons “rehabilitation” has not worked, both for disabled veterans and in the prison system. It is simply hard to function as a rational human being without a brain that functions properly.

HBOT 1.5 and N-BIRR offer a path to the future that is likely to restore much of the ability of the current military forces to continue to fight our nation’s battles. It can be expected to greatly reduce VA disability payments by restoring people to greater function. It will likely restore the National Guard’s capacity to provide war veterans for further service, and restore the men and women to higher levels of function who have served our nation. It can be expected to help clear our legal and prison system of this population, and provide the civilian sector with an effective treatment for its thousands of untreated brain injuries from the normal accident rate in the nation.

**The choice belongs to the policy makers.
Are the effects happening combat casualties from “standard of care”
TBI/PTSD treatment working for you?**

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