UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
READINESS

MAY 2 2011

The Honorable Carl Levin
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The enclosed report responds to the Explanatory Statement, page 370, accompanying H.R. 3326, the Department of Defense Appropriations Act, 2010, that requests the Secretary of Defense provide a report to the congressional defense committees on the use of hyperbaric oxygen therapy (HBO_2). The report includes the number of Service members, veterans, and civilians being treated with HBO_2; the types of conditions being treated; the current inventory, location, and rate of use for hyperbaric oxygen chambers; and plans for future use of hyperbaric oxygen for treatment.

This report was due February 17, 2010. We apologize for the late submission. It was delayed due to complex coordination and data collection requirements documented by our previous interim responses of May 12, 2010, and February 1, 2011.

Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,

Clifford L. Stanley

Enclosure:
As stated

cc:
The Honorable John McCain
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

The Honorable Howard P. "Buck" McKeon
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

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The Honorable Adam Smith
Ranking Member

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PERSONNEL AND
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MAY 2 20..

The Honorable Jim Webb
Chairman, Subcommittee on Personnel
Committee on Armed Services
United States Senate
Washington, DC 20510

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The Honorable Lindsey Graham
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
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The Honorable Joe Wilson
Chairman, Subcommittee on Military Personnel
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

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cc:
The Honorable Susan A. Davis
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
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MAY 2 2011

The Honorable Daniel K. Inouye
Chairman
Committee on Appropriations
United States Senate
Washington, DC 20510

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The Honorable Thad Cochran
Vice Chairman

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PERSONNEL AND
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1, 2 2011

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United States Senate
Washington, DC 20510

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PERSONNEL AND
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The Honorable Harold Rogers
Chairman
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

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cc:
The Honorable Norman D. Dicks
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
READINESS

The Honorable C. W. Bill Young
Chairman, Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

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The Honorable Norman D. Dicks
Ranking Member

Report to Congress on the Use of Hyperbaric Oxygen for Medical Care and Research in Response to H.R. 3326, the Department of Defense Appropriations Act for Fiscal Year 2010

Preparation of this study/report cost the Department of Defense a total of approximately $5,511 in Fiscal Years 2010 - 2011.
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March 2011

TABLE OF CONTENTS

LIST OF TABLES

Executive Summary

Hyperbaric oxygen is an approved medical therapy for decompression sickness, gas embolism, carbon monoxide or cyanide poisoning, and rare cases of profound blood loss when blood transfusion cannot be accomplished. The use of hyperbaric oxygen is also approved as adjunctive therapy to support other treatments for approximately ten additional medical conditions, as determined by the Undersea and Hyperbaric Medical Society (UHMS) and the Centers for Medicare and Medicaid Services. The Military Health System of the Department of Defense (DoD) recognizes the medical indications as outlined by these organizations. Like those organizations, the DoD does not recognize traumatic brain injury as an approved medical indication due to lack of medical evidence. With the exception of single person hyperbaric chambers with operational units, DoD has few hyperbaric chambers at its military hospitals. To support its hyperbaric research program for post-concussion syndrome (symptoms resulting from mild traumatic brain injury lasting more than three months), DoD has leased four hyperbaric chambers in addition to the existing DoD chambers, and research is ongoing. Plans for expanding the use of hyperbaric oxygen for treatment will depend on the outcome of these studies.

I. Introduction to Hyperbaric Oxygen (HBO_2)

Hyperbaric oxygen (HBO_2) therapy is a medical procedure in which a patient breathes 100% oxygen while inside a sealed chamber pressurized to a level of at least 1.4 atmospheres absolute (ATA), which is equivalent to a depth of 13 feet of sea water. This delivery of oxygen under pressure results in levels of oxygen in blood and tissue that are generally much higher than normal conditions in the body, and hence HBO_2 is considered a drug by the U.S. Food and Drug Administration (FDA). Hyperbaric oxygen therapy is also known by the acronym, HBOT, but this term should only be used for FDA-approved indications for hyperbaric oxygen.

HBO_2 administration can be carried out in either a monoplace or multiplace hyperbaric chamber. A monoplace chamber can accommodate just a single patient, and the entire chamber is filled with 100% oxygen that the patient breathes directly. A multiplace chamber holds two or more people (patients, attendants, or treatment personnel). The chamber is pressurized with air from the room, and the patient breathes 100% oxygen delivered through a mask, hood, or endotracheal tube.

HBO_2 treatment was developed during the 1930s as a method to decompress divers in a controlled fashion and to treat decompression sickness (Caisson's Disease) or arterial gas embolism. In the following decades, the U.S. Navy determined the effects of HBO_2 and established the overall safety and treatment levels. Over time, HBO_2 therapy was also evaluated for treating other medical problems and has gained more wide-spread recognition.

In 1976, the Hyperbaric Oxygen Therapy Committee of the Undersea and Hyperbaric Medical Society began reviewing research and clinical data and making evidence-based recommendations

concerning use of HBO_2 therapy. [1] Perhaps even more influential for healthcare providers has been the indications accepted by the Centers for Medicare and Medicaid Services (CMS), as described in the Clinical Indications Manual (CIM section 35-10) and other third party insurance carriers in determination of reimbursement for HBOT.

The FDA considers hyperbaric oxygen a combination product: oxygen, the drug, delivered by a hyperbaric chamber device. Medical grade oxygen is not regulated by the FDA, rather it is regulated through the United States Pharmacopeia (USP), a non-governmental, official public standards setting authority for medicines sold within the United States. Hyperbaric chambers are regulated by the FDA Center for Devices and Radiological Health (CDRH) through the control of intrastate commerce of the chambers and device labeling. Currently, the FDA recognizes 13 medical conditions based on older guidance from the Undersea and Hyperbaric Medical Society that may be advertised in the marketing of hyperbaric chambers:

- Decompression sickness (Caisson's Disease)
- Air or gas embolism
- Carbon monoxide poisoning or cyanide poisoning
- Crush injury, compartment syndrome and other traumatic ischemias
- Acute arterial insufficiency (and central retinal artery occlusion)
- Enhancement of healing for selected wounds, including diabetic ulcers
- Delayed radiation injury (soft tissue and bony necrosis)
- Compromised grafts and skin flaps
- Acute thermal burn injury
- Gas gangrene (clostridial myositis and myonecrosis)
- Necrotizing soft tissue infections (such as flesh-eating bacteria)
- Refractory osteomyelitis (inflammation of bone marrow and adjacent bone)
- Intracranial abscess

The differences in the various organizations' approved indications are a common source of confusion. Differences in the guidelines are summarized in Table 1. Traumatic brain injury (TBI), post concussion syndrome (PCS), and post traumatic stress disorder (PTSD) are not recognized by any of these U.S. organizations.

Table 1: Approved Medical Indications for Hyperbaric Oxygen in the U.S.

Medical Condition	U.S. Food and Drug Administration[a]	Undersea and Hyperbaric Medical Society[b]	Centers for Medicare and Medicaid Services[c]	TRICARE[d]
Decompression sickness	X	X	X	X
Air or gas embolism	X	X	X	X

[1] Undersea and Hyperbaric Medical Society, Hyperbaric Oxygen Therapy Indications, 12th ed., December 2008

Carbon monoxide poisoning or cyanide poisoning	X	X	X	X
Crush injury, compartment syndrome and other traumatic peripheral ischemias	X	X	X	X
Compromised tissues and flaps	X	X	X	X
Delayed Radiation Injury (soft tissue and bone)	X	X	X	X
Acute thermal burns	X	X		
Gas gangrene (clostridial myositis and myonecrosis)	X	X	X	X
Necrotizing soft tissue infections	X	X	X	X
Enhanced healing of select problem wounds, including diabetic ulcers	X	X	X	X
Refractory Osteomyelitis	X	X	X	X
Intracranial Abscess	X	X		
Exceptional Blood Loss Anemia	X	X		X
Central Retinal Artery Occlusion		X		
Acute Peripheral Arterial Ischemia			X	
Refractory Actinomycosis			X	

a Based on CDRH Approval of Hyperbaric Chamber Label, K100268, 28 April 2010.

b UHMS, Hyperbaric Oxygen Therapy Indications, 12th ed., December 2008

c CMS, Medicare Coverage Issues Manual Section 35-10, 2002.

d TRICARE Policy Manual 6010.57-M, Chapter 7, section 20.1, February 1, 2008.

While these are all approved indications in the U.S., some are rarely used. In a survey of hyperbaric oxygen use billed to Medicare between 1995-1998, the Department of Health and Human Services (DHHS) Office of Inspector General determined that nearly a third of billed cases did not fall under an approved indication for hyperbaric oxygen use as shown in Table 2. [2] Since its addition to the list of approved indications in 2002, treatment of non-healing diabetic ulcers became a primary use of hyperbaric oxygen in civilian practice, which has led to a proliferation of multi-place chamber to treat this common condition.

[2] Department of Health and Human Services, Office of Inspector General. Hyperbaric Oxygen Therapy: Its Use and Appropriateness (OEI 06-99-00090). October 2000.

The effectiveness of the hyperbaric treatment for many of these medical conditions is difficult to establish. Hyperbaric oxygen is first-line therapy for the medical emergencies of decompression sickness, air/gas embolism, and carbon monoxide poisoning. For the remaining indications, hyperbaric oxygen is an adjunctive therapy and is not to be used as sole therapy. As part of a combination of therapies, it is difficult to determine the contribution of each component individually. Moreover, hyperbaric oxygen is often ordered as an adjunctive therapy after all else has been tried and has failed.

It is important to note that outside of United States, medical uses for HBO_2 are viewed with much less conservatism. Some international hyperbaric groups cite 20 types of treatment covering 66 medical conditions, including several classes of brain injury, even traumatic brain injury. It is from this perspective that the International Hyperbaric Medical Association (IHMA) and its lobbyists are advocating for immediate access to and reimbursement for HBO_2 therapy for soldiers or veterans within the United States with traumatic brain injury.

Table 2: Indications for Hyperbaric Oxygen based on Billing to Medicare 1995-1998[2]

CIM 35-10 Indication for Treatment	% of Beneficiaries
Acute Peripheral Arterial Insufficiency	20.9
Effects of Radiation (Osteoradionecrosis and Soft Tissue Radionecrosis)	15.1
Preparation and Preservation of Skin Grafts	15.0
Chronic Refractory Osteomyelitis	8.6
Progressive Necrotizing Infections	4.0
Gas Gangrene	1.3
Decompression Sickness	0.8
Carbon Monoxide Poisoning	0.6
Acute Traumatic Peripheral Ischemia	0.2
Non-covered Primary Indications	33.5

II. Hyperbaric Chambers and their Use in the Military

Hyperbaric chambers in DoD fall into four groups:

- Hyperbaric/hypobaric chambers used for military training at depth or altitude, respectively. These are not used for medical care.
- Portable chambers used for evacuating casualties to an emergency room or larger hospital hyperbaric chambers. DoD has a limited number of these chambers, and

they are used in support of United States Central Command (CENTCOM) combat operations.

- Monoplace chambers used in the operational units to treat occupational health emergencies such as decompression sickness, air/gas embolism, or carbon monoxide poisoning.
- Fixed monoplace or multiplace chambers in medical treatment facilities used primarily to treat the 13-15 approved medical conditions listed in the previous section. These multiplace chambers are best suited to use for medical research when not in use for patient care.

The portable hyperbaric chamber or Gamow bag was developed and cleared by FDA for the treatment of acute mountain sickness. Pressurized by a foot pump, it can decrease the effective altitude by nearly 5000 feet, which can relieve symptoms of high altitude pulmonary or cerebral edema. They can also be used in medical transport. These bags are limited to low pressure (4.1 PSI or 1.3 ATA) and cannot truly administer hyperbaric oxygen (<1.4 ATA). Many brands are now being marketed as "mild hyperbaric oxygen", and are available for use at home, in athletic training facilities, and at spas for non-medical consumers. There is no medical evidence that "mild hyperbaric oxygen" can treat any medical condition outside of acute mountain sickness.

Monoplace chambers are less mobile, but are widely used in the military to treat occupational emergencies (decompression sickness, air/gas embolism, or carbon monoxide poisoning). The Navy operates 81 of these chambers around the globe. In FY10, the Navy treated 135 individuals (mostly active duty) for decompression sickness. The Air Force and the Army Special Operations and Engineer Diving Units also maintain a number of operational monoplace chambers to treat service members with emergency conditions. Individuals in the local beneficiary population with non-emergency approved medical conditions are occasionally treated in these chambers on a space available basis. These chambers are not readily available for research.

Within the Military Health System, fixed hyperbaric chambers are available at limited facilities for treatment of emergency and non-emergency medical conditions. Multiplace or monoplace chambers are installed at:

- San Antonio Military Medical Center/Wilford Hall, Lackland Air Force Base, San Antonio, TX
- David Grant USAF Medical Center, Travis Air Force Base, CA
- Kettering Medical Center, Wright-Patterson Air Force Base, OH
- Dwight David Eisenhower Army Medical Center, Ft. Gordon, GA
- Walter Reed National Military Medical Center (planned: monoplace chamber to be installed in FY11 for traumatic wound/flap care)

These facilities treat the spectrum of approved medical conditions, and some have sharing arrangements to provide care to Veterans Affairs (VA) beneficiaries. The use of these DoD chambers in FY10 is summarized in Table 3.

Table 3: Hyperbaric Oxygen Treatments in Military Health System Facilities in FY10

Site	Total HBO_2 Sessions	Total Beneficiaries Treated	% Active Duty (AD)	% Non-AD DoD Beneficiaries	% VA Beneficiaries
Lackland AFB	2913	151	95%	-	5%
Travis AFB	23,147	890	3%	54%	43%
Wright Patterson AFB	2012	106	-	-	106
Ft. Gordon	454	25	36%	57%	7%
TOTAL	28,526	1172	-	-	-

Information provided by the Service medical departments.

DoD health practitioners follow the approved uses of hyperbaric oxygen as outlined in the guidelines of the Hyperbaric Oxygen Therapy Committee of the Undersea and Hyperbaric Medical Society. TRICARE guidelines allow coverage for HBO_2 when provided by an approved institutional provider and only when provided as treatment for an approved indication from the same guidelines. [3]

A summary of TRICARE referrals for hyperbaric oxygen (CPT procedure code 99183) from 2008-2010 is provided in Table 4. In this time frame, there were 815 referrals for hyperbaric oxygen, and 25% were for active duty members. It is important to note that this table summarizes referrals based on medical diagnosis coding. Some referrals, especially for non-approved indications such as traumatic brain injury, may have been denied. The duration of hyperbaric therapy and outcomes are not provided.

[3] TRICARE Policy Manual 6010.57-M, February 1, 2008. Chapter 7, section 20.1.

Table 4: Medical Conditions for Referred for HBO_2 Therapy (CPT 99183) from the TRICARE Database from 2008 to 2010

Medical Condition	No. of TRICARE Beneficiaries Referred [a]	% of Total
Decompression sickness	35	4.3%
Air or gas embolism	1	0.1%
Carbon monoxide poisoning or cyanide poisoning	7	0.5%
Crush injury, compartment syndrome and other traumatic peripheral ischemias	36	4.4%
Compromised tissues and flaps	118	14.5%
Delayed Radiation Injury (soft tissue and radioosteonecrosis)	227	27.9%
Gas gangrene (clostridial myositis and myonecrosis)	0	0%
Necrotizing soft tissue infections	19	2.3%
Enhanced healing of select problem wounds, including diabetic ulcers	141	17.3%
Refractory Osteomyelitis	53	6.5%
Exceptional Blood Loss Anemia	1	0.1%
Central Retinal Artery Occlusion or Acute Nontraumatic Peripheral Ischemia	13	1.6%
Referral for Non-Approved Indications (all)	94	11.5%
Referral for Traumatic Brain Injury	21	2.6%
Code Incomplete	49	6.0%
TOTAL	**815**	-

[a] Research participants, such as those in the brain injury research trials, are not included.

III. DoD Plans for Expansion of Treatment with HBO_2

As outlined in the previous section, the Military Health System's use of hyperbaric oxygen as treatment is consistent with the Undersea and Hyperbaric Medical Society-endorsed and DHHS Centers for Medicare and Medicaid Services approved uses. DoD continues to use an evidence-based approach to developing policy on hyperbaric oxygen use to ensure that any new indication is documented by reliable evidence as safe, effective, and comparable or superior to standard care. At this time there are no plans to expand the use of HBO_2 for treatment beyond any of these approved medical conditions; however, research on hyperbaric oxygen for war injuries is being strongly encouraged. DoD approved uses for HBO_2 will be frequently re-assessed by the Senior Military Medical Advisory Council and the Traumatic Brain Injury Subcommittee of the Defense Health Board.

IV. HBO_2 is Not a Proven Therapy for Traumatic Brain Injury

A. Reviews of Use of HBO_2 for Brain Injury

HBO_2 has been used by many foreign and limited U.S. health practitioners for treatment of various brain injuries, including stroke, cerebral palsy, autism, severe traumatic brain injury within 72 hours of injury, and more recently the persistent symptoms of mild traumatic brain injury (post concussion syndrome). Publications in the medical literature documenting the use of HBO_2 for treating traumatic brain injury within 72 hours of injury, cerebral palsy, and stroke date back to the 1970s.

Despite many anecdotal publications and a small number of more conclusive trials, several independent reviews of the data in the past decade have concluded that there is still insufficient evidence to warrant an endorsement of HBO_2 for the acute treatment of traumatic brain injury typically within 72 hours or for the rehabilitation of traumatic brain injury:

- The Undersea and Hyperbaric Medical Society, in a 2003 position statement, reported that there was insufficient evidence to support an endorsement for HBO_2 in treating chronic brain injury and called for prospective randomized controlled clinical trials. [4]
- The DHHS Agency for Healthcare Research and Quality reviewed the literature involving the use of HBO_2 in treating acute brain injury, cerebral palsy, and stroke in 2003, and concluded "Evidence from well-conducted clinical studies is limited. The balance of benefits and harms of HBOT for brain injury, cerebral palsy, or stroke has not been adequately studied. Future research of HBOT should include dose-ranging (multiple dose) and safety studies to establish the optimum course of HBOT to evaluate in outcome studies." [5]

[4] Hyperbaric Oxygen for Chronic Brain Injury. Undersea and Hyperbaric Medical Society Position Statement, November 2003

[5] McDonagh M, Carson S, Ash J, et al. Hyperbaric Oxygen Therapy for Brain Injury, Cerebral Palsy, and Stroke. Evidence Report/Technology Assessment No. 85 (Prepared by the OregonHealth & Science University Evidence-based Practice Center under Contract No 290-97-0018). AHRQ Publication No. 03-E050. Rockville, MD: Agency

- The Cochrane Collaboration, a non-profit organization dedicated to reviewing medical literature for evidence-based decision making, conducted an academic review of the available data in 2008 and concluded that routine application of HBO_2 for the treatment of acute traumatic brain injury cannot be justified based on the existing scientific evidence, and stated "an appropriately powered trial of high methodological rigor is required to define those patients (if any) who can be expected to derive the most benefit from HBOT." This report did not assess the role of HBO_2 for rehabilitation after brain injury. [6]
- A report prepared for the Department of Veterans Affairs by the Technology Assessment Advisory Group exploring potential clinical uses of HBO_2 for the symptoms of traumatic brain injury in the veteran population stated, "the clinical value of HBO_2 in treating [traumatic brain injury] is unknown due to insufficient evidence proving the effectiveness or ineffectiveness." [7]

There have been no reviews solely focused on the use of HBO_2 for the experimental treatment of chronic symptoms of mild traumatic brain injury (post concussion syndrome) due to the lack of published data. Current published literature is limited to 2 case reports in 3 individuals.

B. Anecdotal Data on Use of HBO_2 to Treat Post Concussion Syndrome

Persistent symptoms lasting more than three months after one or more mild traumatic brain injuries (concussions) are properly called post-concussion syndrome. This condition has been labeled by the general public and DoD as chronic or persistent mild traumatic brain injury, and these terms can be used interchangeably. The standard case definition [8] of post-concussion syndrome is:

A. A history of head trauma that has caused significant cerebral concussion.

B. Evidence from neuropsychological testing or quantified cognitive assessment of difficulty in attention (concentrating, shifting focus of attention, performing simultaneous cognitive tasks), or memory (learning or recalling information).

C. Three (or more) of the following occur shortly after the trauma and last at least three months:

   1. Becoming fatigued easily
   2. Disordered sleep
   3. Headache

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for Healthcare Research and Quality. September 2003.

[6] Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. *Cochrane Database of Systematic Reviews* 2004, Issue 4. Art. No.: CD004609. DOI: 10.1002/14651858.CD004609.pub2.

[7] Flynn K. Bibliography: Hyperbaric Oxygen Therapy for Traumatic Brain Injury. VA Technical Assessment Program. Sept 2009.

[8] American Psychiatric Association. *Diagnosis and Statistical Manual of Mental Disorders (DSM-IV-TR)*. 4th ed. Washington, DC: American Psychiatric Association; 2000.

4. Vertigo or dizziness
5. Irritability or aggression with little or no provocation
6. Anxiety, depression, or affective lability
7. Changes in personality (eg, social or sexual inappropriateness)
8. Apathy or lack of spontaneity

D. The symptoms in criteria B and C have their onset following head trauma or else represent a substantial worsening of preexisting symptoms.

E. The disturbance causes significant impairment in social or occupational functioning and represents a significant decline from a previous level of functioning.

F. The symptoms do not meet criteria for dementia due to head trauma and are not better accounted for by another mental disorder (eg, amnestic disorder due to head trauma, personality change due to head trauma).

Symptoms of post concussion syndrome commonly exist without the formal diagnosis, as the head injury or concussion may not be well documented or attributed as a cause of symptoms. Interest in this diagnosis has substantially increased in recent years, due to the war-related blast traumatic brain injuries and a variety of sports injuries.

Two case reports of three individuals over the past two years have indicated HBO_2 relieved symptoms and improved social or occupational function in persistent mild traumatic brain injury, and no evidence to the contrary has been reported. Other anecdotes have been noted in testimony, but not published. It is important to note, however, that authors tend to publish positive findings more often than those of equivocal or negative findings.

The first case report published in *Undersea and Hyperbaric Medicine* [9] described improvement in sleep, headaches, and thought processes in two airmen who suffered persistent symptoms six months after being injured by an improvised explosive device (IED). A second case report described a 25-year-old Marine veteran who suffered from post concussion syndrome and post traumatic stress disorder three years after an IED blast.[10] After 39 sessions of HBO_2 he no longer had headaches or post traumatic stress disorder symptoms, and his sleep and depression symptoms improved.

C. Unpublished data on HBO_2 for TBI

In March 2010, Dr. Paul Harch and his colleagues at Louisiana State University (LSU) reported preliminary results from an interim analysis of a case series of 15 veterans with post concussion

[9] Wright JK. et al. 2009. Case report: treatment of mild traumatic brain injury with hyperbaric oxygen. UHM, 36 (6): 391-9.

[10] Harch PG et al. 2009. 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 Journal, 2: 6538.

syndrome treated one to four years after war-related mild traumatic brain injury (International Brain Injury Association Meeting, abstract #0653). Volunteers received 60-minute sessions of HBO_2 twice daily for 40 days for a total of 80 HBO_2 sessions, and all volunteers reported improvement. Results immediately post testing revealed:

- Up to 51% improvement in anxiety and depression symptom scores
- Improvement of 10% in memory and thought processes by neuropsychometric tests
- Significant perceptions in improvement in thought processes and overall well being as reported by volunteers
- Improvement in blood flow in the first five volunteers
- No serious safety concerns from the HBO_2, but onset of emotional lability during the treatment was noted in some individuals

This study was completed in the summer of 2010, and unfortunately no further information has become available.

The Hyperbaric Medicine Department at LDS Hospital/Intermountain Healthcare, Salt Lake City, Utah conducted a six year case series assessing HBO_2 in the rehabilitation phase of various brain injuries. Volunteers who experienced symptoms lasting more than one year after various brain injuries, including stroke, anoxia, and traumatic brain injury, were recruited. This trial was designed to answer three questions:

1) Is the HBO_2 regimen safe in this population?
2) Is it feasible to recruit subjects?
3) Will subjects follow-up as directed?

Sixty-four civilian volunteers were enrolled. Twenty-one had suffered moderate or severe traumatic brain injury and were an average of six and a half years post injury. Over 3,400 HBO_2 sessions were conducted. Analysis of the data revealed that the intervention was safe. No deaths or expected serious complications such as seizures, severe ear trauma, or pulmonary or heart complications were reported. Minor complications such as ear and sinus pressure were common, and worsening vision (myopia) was seen in 5% of volunteers. An interim analysis of the traumatic brain injury subset suggests modest improvement in volunteer-reported symptoms, which were out of proportion to the minimal improvement noted by caregiver assessment or objective cognitive testing.

These limited case reports and case series are compelling observations, but it is important to note that they do not meet the scientific rigor requested by Agency for Healthcare Research and Quality or the Undersea and Hyperbaric Medical Society for determination of efficacy of the HBO_2 intervention. None included comparisons to a placebo or sham group. A placebo or sham is a type of treatment where the volunteers believe that they receive a procedure that appears to be but is not the research intervention. This helps distinguish the true effects of treatment from

the psychological and physical effects of being a research participant (also known as the placebo effect). The placebo effect could easily account for the 50% improvement in symptoms observed in the case reports and studies. Given this possibility, the role of the hyperbaric oxygen in the improvements in these cases is unknown. The DoD and VA opinion is that in 2011 there is still insufficient evidence to endorse HBO_2 as treatment of post concussion syndrome.

The International Hyperbaric Medical Foundation and Dr. Paul Harch have embarked on a large new observational trial to evaluate HBO_2 for long-term symptoms of mild-to-moderate traumatic brain injury (NBIRR-1), and have also now opened enrollment to persons with post traumatic stress disorder without brain injury. Unfortunately, this observational design will not be able to assess contribution of HBO_2 to the resolutions of post traumatic stress disorder symptoms because it does not include a sham or comparator drug group. This project is expected to be completed in 2014.

V. DoD/VA Research Program on HBO_2 for Post Concussion Syndrome

In response to the promising anecdotes, DoD has instituted a comprehensive research program to evaluate the safety and effectiveness of HBO_2 for the treatment of post concussion syndrome. Two pilot studies were initiated, and then a formal development program was launched. An investigational new drug application (IND) was filed with the Center for Drug Evaluation and Research, U.S. Food and Drug Administration by the Defense Centers of Excellence for TBI and Psychological Health (DCoE). The program subsequently moved under the supervision of the U.S. Army Medical Research and Materiel Command.

To support the robust DoD HBO_2 research program for war related casualties (such as post concussion syndrome), four new multi-place hyperbaric chambers have been leased by the TRICARE Management Activity to conduct the research without affecting the occupational and medical missions of the current DoD chambers. These chambers are placed at hospitals near the troops to minimize their time away from families to receive experimental therapy. The four leased chambers are located at:

- Naval Hospital Camp Pendleton, Camp Pendleton, CA (12 person chamber)
- Naval Hospital Camp Lejeune, Camp Lejeune, NC (6 person chamber)
- Evans Army Community Hospital , Ft. Carson, CO (18 person chamber)
- Madigan Army Medical Center, Joint Base Lewis McChord, WA (6 person chamber) – to be installed in May 2011.

At maximum capacity and staffing, they are capable of supporting approximately 150 HBO_2 treatments daily and will meet DoD requirements for traumatic brain injury research.

Three HBO_2 trials are currently underway within the military, and to date, 62 active duty military volunteers have received HBO_2 or sham treatment (normal or room air). In these studies volunteers are put in a chamber and pressured to simulate the dive, then they breathe oxygen (the

treatment) or room air (the sham treatment). These trials are blinded, that is neither the volunteers nor the investigators know which intervention is given to each volunteer until the study is over.

The first of these studies, started in 2009, has completed enrollment and is in data analysis. Results are expected in the spring of 2011. This study, conducted by researchers at the US Air Force School of Aerospace Medicine (USAFSAM) using a research hyperbaric chamber at Brooks City Base, Texas (now closed at part of the Defense Base Closure and Realignment Commission) compared two groups: one receiving 30 sessions of HBO_2 at 2.4 atmospheres absolute (ATA) and the other receiving 30 sham chamber sessions (regular air). Computerized assessments of brain function were performed before the first treatment session, after every five treatments, and six weeks after the last treatment session. Preliminary results have shown HBO_2 to be safe in over 700 sessions.

The second DoD study, sponsored by the Defense Advanced Research Projects Agency (DARPA) in a grant to Virginia Commonwealth University/McGuire VA Medical Center, is enrolling 60 volunteers with persistent symptoms of mild traumatic brain injury. The VA has no hyperbaric chambers, so it is utilizing the research multiplace chamber and the expertise in dive medicine at the Naval Operational Medicine Institute, Pensacola FL. This study compares multiple oxygen dosing regimens (1.5 and 2.0 ATA) to sham treatment. A variety of questionnaires, brain function testing, and functional MRI (fMRI) testing, which assesses blood flow, will be performed before and after the study and at a 6 month follow-up visit.

The third DoD pilot study underway is a multi-site study evaluating various measurements of treatment effects and safety and is being conducted under the Investigational New Drug application with the FDA. This study compares routine medical care alone, routine care plus HBO_2 (at 1.5 ATA), and routine care plus room air (sham treatment) in military volunteers with post concussion syndrome. Symptom questionnaires and cognitive testing will be performed before and after 40 hyperbaric sessions. In addition, a group of volunteers with post traumatic stress disorder (PTSD) will also complete the testing to evaluate the contributions of concomitant PTSD to the outcome measurements. This study will take approximately six months to complete.

Additional scientifically robust trials are planned in DoD. One study will compare symptom improvement to a state-of-the-art radiology, balance, and physiology assessment. The results of all of these studies will provide the information necessary to plan a larger trial designed to conclusively demonstrate if HBO_2 is an effective drug to treat post concussion syndrome or chronic mild traumatic brain injury. This larger trial is planned for FY12. Safety data and interim reports from these studies will be reviewed by an independent data and safety monitoring board set up by DoD, and a five-year follow up study is planned for all DoD service members treated in the HBO_2 trials. This follow-up will be done to assess long-term outcomes and the duration of any improvements seen in the initial studies. Taken in aggregate, these studies will answer many critical questions on safety, dose, effectiveness, and longevity of any improvements attributable to HBO_2.

VI. Conclusions

Since its refinement by the U.S. Navy in the 1940s, hyperbaric oxygen has continued to serve as primary medical treatment of occupational and recreational diving and aerospace injuries (decompression syndrome and gas embolism). The role of hyperbaric oxygen to serve as primary or adjunctive medical treatment for other conditions has expanded in recent years but remains controversial due to lack of quality clinical trials. DoD recognizes the medical indications endorsed by the Undersea and Hyperbaric Medical Society, which are generally also recognized by the Food and Drug Administration and Department of Health and Human Services Centers for Medicare and Medicaid services with minor variations. Traumatic brain injury and post traumatic stress disorder are not approved indications by any organizations due to the lack of evidence supporting its effectiveness.

DoD and their VA partners are the only groups conducting scientifically robust trials of HBO_2 for post concussion syndrome to provide data for the development of treatment guidelines. Several trials are currently underway, and results are expected in the coming months. Plans for expanding the use of hyperbaric oxygen for treatment will depend on the outcome of these studies.