

Testimony

“Hyperbaric Medicine and Brain Injured Children”

The International Hyperbaric Medical Association Foundation

Kenneth Stoller, M.D., F.A.A.P.
Chairman of the Pediatrics Committee, IHMA Foundation



Before the

Government Reform & Oversight Hearing --Subcommittee on Wellness & Human Rights

Entitled

**“Autism Spectrum Disorders: An Update of Federal Government Initiatives
and Revolutionary New Treatments of Neurodevelopmental Diseases ”**

United States House of Representatives

May 6, 2004, 2:00PM

International Hyperbaric Medical Association Foundation
46 Draper Circle, Suite B Stafford, Virginia 22554-4754
Office: 540-720-3844 Fax: 540-720-4837

Hyperbaric Medicine and Brain Injured Children

Prepared for the Committee on Government Reform for the May 6th, 2004 Hearing
(Autism Spectrum Disorders: An Update of Federal Government Initiatives and
Revolutionary New Treatment of Neurodevelopmental Diseases)

By: **Kenneth Stoller, M.D., F.A.A.P.**
Chairman of the Pediatrics Committee, IHMA Foundation
Clinical Assistant Professor, University of NM, School of Medicine, Dept of Pediatrics
Diplomat, American Board of Hyperbaric Medicine
Diplomat, American Board of Pediatrics

Hyperbaric Medicine has been repairing brain injuries for 30 years, but neither academia nor the governmental insurance complex took a look at it because everyone “knew” that it was not possible.

Hyperbaric oxygen therapy (HBOT) involves the delivery of oxygen in a pressurized environment created by a chamber. The pressure serves to saturate the tissues of the body, not only the hemoglobin in the blood, but the plasma, lymph and cerebral spinal fluid, all of which go many places that hemoglobin cannot reach, especially in cases of traumatic injury.

Vol. 44 / No. 37 MMWR 697

Birth Defects and Cerebral Palsy — Continued

TABLE 2. Incidence rate and estimated economic costs* of cerebral palsy and 17 of the most clinically important birth defects, by condition and type of cost — United States, 1992

Condition	Incidence rate [†]	Direct costs		Indirect costs** (millions)	Total costs ^{††} (millions)	Cost per new case (thousands)
		Medical [‡] (millions)	Nonmedical [§] (millions)			
Nervous system						
Cerebral palsy [¶]	12.3	\$ 852	\$445	\$1,129	\$2,426	\$503
Spina bifida	4.2	\$ 205	\$ 43	\$ 241	\$ 489	\$294
Cardiovascular						
Truncus arteriosus	1.1	\$ 108	\$ <1	\$ 101	\$ 210	\$505
Single ventricle	1.3	\$ 62	\$ <1	\$ 110	\$ 173	\$344
Transposition						
Double outlet right ventricle	4.9	\$ 166	\$ 4	\$ 344	\$ 515	\$267
Tetralogy of fallot	3.5	\$ 185	\$ 4	\$ 171	\$ 360	\$262
Alimentary tract						
Tracheo-oesophageal fistula ^{¶¶}	2.9	\$ 62	—	\$ 103	\$ 165	\$145

Figure (1) was taken from a 1995 CDC report showing the yearly cost of a child with Cerebral Palsy is \$503K

Children with neurological injuries cost, on average, 2.1 times as much to educate as a non-injured child. There are 6.548 million Individuals with Disabilities Education Act (IDEA) children in the nation, who are costing the state's educational system \$47 billion, for a total of \$55.7 billion. On average, nationally, they cost \$8,510 more per year to educate than a “normal” child. Many cannot learn due to their injuries. Hyperbaric oxygen therapy (HBOT) would cost an average, one time expenditure of between \$7,000 and \$14,000 for most children treated long after the injury, the cost of educating them for a year or two. The effects would be permanent and last throughout their lifetime. For many of these children, if they had been treated immediately upon injury, the costs drop to often less than \$1,000.

Many of these children have neurological injuries that affect their motor skills, learning, speech, etc. They are children injured in birth trauma, accidents, child abuse, fetal alcohol syndrome, maternal drug use, or other such events. HBOT has effectively recovered and rebuilt brain tissue through reactivation of stunned tissue, revascularization and, possibly, stimulation of stems cells in the brain to repair existing neural pathways and grow new ones. In 1992, Rockswold(GL) reported the most exhaustive, rigorous, and important study in acute Traumatic Brain Injury (TBI). Conducted from 1983 to 1989 the study enrolled 168 patients with Glasgow Coma Scale (GCS) of 9 or less in a randomized prospective controlled trial (RPCT). Overall mortality was significantly reduced 50% in the HBOT group (60% in the group with increased ICP).

In 2001, Rockswold(SB), on a group of severe TBI patients similar to those in the 1992 study found that HBOT improved the cerebral metabolic rate for oxygen and decreased CSF lactate (a marker of damaged brain cells), and reduced ICP. These author's showed HBOT's ability to recouple blood flow with metabolism.

The neurosurgeon authors of the Rockswold study conclude that "HBOT should be initiated as soon as possible after acute severe traumatic brain injury." (*Results of a prospective randomized trial for treatment of severely brain injured patients with hyperbaric oxygen. Authors: Rockswold GL, et al Division of Neurosurgery, Hennepin County Medical Center, Minneapolis, Minnesota. J Neurosurg 1992 Jun;76(6):929-34. Effects of hyperbaric oxygenation therapy on cerebral metabolism and intracranial pressure in severely brain injured patients. Authors: Rockswold SB, Rockswold GL et al J Neurosurg March 2001; 94:403-411.*)

Follow children with brain injuries into adulthood and you may discover that many wind up in prison, on welfare, Social Security Disability, in long-term care facilities at state or insurance company expense or become a drain on the system in some other fashion. I served as the pediatrician of the Santa Fe County Youth Development Program for several years and I know first hand that many of these children suffer from a neurological injury incurred prior to incarceration. Many of these children are suffering Mental Retardation or Developmental Disabilities, when they grow to adulthood, cost, on average, \$43,000 per year in group home or institutional settings. HBOT has demonstrated that nearly all of these children can be helped, including many with genetic disorders, and many, many, can lead full, normal and productive lives. This is something current medical practices cannot provide for most of them.

The old concept of cerebral palsy being a "static insult" is no longer tenable. It is now recognized in neurology that deterioration due to brain damage at birth may take place over 28 years. (*St Hilaire MHS, Burke RE, Bressman SB, Brin MF, Fahn S. Delayed-onset dystonia due to perinatal or early childhood asphyxia. Neurology 1991;41:216-222.*) This mirrors the adult situation (*Burke RE, Fahn S, Gold AP. Delayed-onset dystonia in patients with "static" encephalopathy. J Neurol Neurosurg Psychiatry 1980;43:789-797.*) Further over the last decade stem or progenitor cells have been found in the adult brain and they can result in neural regeneration. (*Steindler DA, Pincus DW. Stem cells and neurogenesis in the adult human brain. Lancet 2002;359:1047-54.*) This recovery process is oxygen dependent and on first principles much more likely to take place in a growing child than an adult. There is now conclusive evidence from altitude studies that the capillary density even in the adult mammalian brain can be increased. (*Harik SI, Behmand RA, LaManna JC. Hypoxia increases glucose transport at the blood-brain barrier. J Appl Physiol 1994;77:896-901.*)

Every published research study that has looked at the efficacy of using HBOT to treat children with cerebral palsy has found significant levels of improvement; the most recent study was published in the US Army Medical Journal in 2002, "Adjunctive HBO Treatment of Children with Cerebral Anoxic Injury" by Waalkes et al.⁴

Neurologists have promoted the concept of the ischemic penumbra¹ for many years and both magnetic resonance imaging of children with brain injuries and pathological studies² have shown that the changes are essentially the same as adults. They range from edema, which is treatable, to cystic degeneration, which is not. Stem cells have been demonstrated in the adult brain³ and so must obviously be present during childhood.

Parents have been in the vanguard of the efforts to provide oxygen treatment for children with cerebral palsy in the UK and North America and they actually prompted the funding by the Canadian government of the infamous Quebec/McGill University study. Parents also prompted the study by the US Army⁴ which has confirmed the benefit found in the McGill study. The study conducted at McGill University⁵ published in the Lancet became infamous because the authors used compressed-air at 1.3 atmospheres absolute (ata) for one arm of the study mistakenly believing that such an air pressure could be regarded as a placebo. This was corrected in the Lancet review process and the terms placebo and controlled were not allowed to be

used in the paper. Compressed air at 1.3 ata raises the plasma oxygen tension by almost 50% and that alone was enough for the children with cerebral palsy in that group as well as the treatment arm to show significant gains. Everyone agreed that both groups improved significantly. As a matter of fact none of these children had ever had this type of rapid improvement before. Keep in mind they only received a total of 40 HBOT treatments.

The bottom line is that at an age where one did not expect any dramatic changes, the children in studies conducted by Dr. Marois showed “many tremendous functional improvements.”⁶ “Some children started to walk, to speak, or to sit for the first time in their lives. The motor changes that were seen and measured with GMFM,⁷ were greater, more generalized, and were obtained in a shorter period of time than most of the improvements found in any other studies of recognized conventional therapies in the treatment of children with CP.”

The protocol of treating a minimum of 40 times at 1.5 ATA for non-acute brain injury, is a direct outgrowth of 20 years clinical experience with brain injury of Dr. RA Neubauer in Florida (1970-1990), the published reports of Drs. RA Neubauer and SF Gottlieb, the initial experience of Van Meter and Gottlieb with boxers in New Orleans 1989, and the clinical experience of Harch from 1990-present that was refined to its present state in the prospective trial of chronic brain injury, SPECT, and HBOT by Harch and Gottlieb 1993-9 that tested blocks of 40 HBOT's. At the start of the investigation in 1992 and 1993 Harch and Gottlieb applied HBOT to the first cerebral palsy child in North America (ref #13) The experience in New Orleans was stimulated by the observation that patients with neurological conditions treated with standard HBOT for chronic wound problems experienced concomitant improvement in their neurological problems.

In 1989, Drs. RA Neubauer and SF Gottlieb used a variation of normal SPECT imaging on a 60 year old woman who had experienced a stroke 14 years previously. They performed two consecutive SPECT brain scans with a single exposure to low pressure HBO immediately before the scan. When they compared the after-oxygen scan with the before-oxygen scan they noticed that the after-oxygen scan had a greater uptake of the radioactive tracer, i.e. improved blood flow, and thereby, a decrease in the brain injury. After 60 HBO treatments they were able to recover a fair amount of neurological function in this patient even though the therapy was started 14 years after her stroke. Drs. Neubauer and Gottlieb published this report and two additional cases of near drowning and natural gas poisoning.^{8,9,10}

Subsequently, Drs. Harch and Van Meter performed the same sequence of SPECT scan/HBO therapy/SPECT scan on commercial divers with brain DCS and obtained results similar to those of Neubauer and Gottlieb.^{11,12,13}

This growing body of prospective experience provided the explanation for the phenomena described earlier where patients with neurological problems who were being treated for non-neurological reasons experienced gratuitous neurological improvement as their hyperbaric treatment progressed.

Commercial divers with decompression sickness of the brain or spinal cord were flown in comatose and/or paralyzed from the oil and gas fields of the Gulf of Mexico. The recoveries of these injured divers showed improvement in neurological levels far exceeded published reports and current expectations. The notable improvement was due to a protocol that treated beyond the medical standard of a few hyperbaric oxygen therapy treatments. Some patients required as many as 100 treatments before reaching a clinical plateau.

Standard diving medicine principles suggest that decompression sickness (DCS) involves bubble formation in the circulatory system thereby interfering with the necessary continuous supply of oxygen and nutrients to the nerve cells in one or more areas of the brain or spinal cord. Minutes to hours after the onset of decompression illness, tissue damage continues to develop because of persistent occlusion of blood vessels by bubbles or secondary damage to the blood vessel caused by passage of the bubbles. This secondary damage is virtually identical to the pathological processes occurring during acute stroke after the blood clot has been dissolved and circulation restored. Even after the initial trauma to the brain and the initial course

of therapy, there may be residual damage to the nerve cells. The initial hyperbaric oxygenation (HBO) treatments are thought to help remove bubbles from the circulatory system of the brain or spinal cord if the patient is being treated in the acute phase of DCS. In 1996 Harch argued that early HBO was also treating the acute aforementioned secondary damage called reperfusion injury, and the downstream tissue damage resulting from interrupted blood flow and oxygen delivery (Harch PG. Late treatment of decompression illness and use of SPECT brain imaging. 45th Undersea and Hyperbaric Medical Society Workshop, Treatment of Decompression Illness, eds. RE Moon, PJ Sheffield. June 18-19, 1995, Palm Beach, Florida. Undersea and Hyperbaric Medical Society, Kensington, MD. 1996) Repetitive hyperbaric oxygen treatments tend to result in improving the function of tissues and nerves that show residual damage resulting from the trauma. The progressive improvement in nerve function seen by Harch and Van Meter in DCS cases is due to the HBO treatment protocols they have used over the last couple of decades (Harch PG. Vide supra. Van Meter KW, article in 45th UHMS Workshop).

In a paper titled “Analysis of the results of a randomized study of hyperbaric oxygen therapy in a treatment of children with cerebral palsy: Placebo or physiological effect?” by Dr. Pierre Marois and Dr. Michel Vanasse (both who were part of the research team to conduct the McGill study), state, “we can therefore establish that the hyperbaric therapy resulted in functional improvements more rapidly and more generalized than conventional treatment. If we accept that the improvement observed in the children having received HBO therapy is due to a placebo, must we then conclude the improvements resulting from the 6-8 months of intensive physical therapy were also due to placebo because the results were identical?” In the same article they write, “another interesting and, in our opinion, very important element that was highlighted by our research was that the improvements persisted at least three months post treatment. The children were systematically re-evaluated three months later and we were able to document beyond doubt the persistence of the gains observed after 40 hyperbaric treatments. To our knowledge, no scientific proof exists confirming the persistence of a placebo for that period of time.”

On May 2, 2002 Dr. Paul G. Harch was invited and presented evidence for a restorative effect of low pressure HBOT on chronic brain injury before the Subcommittee on Labor, Health, Human Services, and Education of the House of Representatives Appropriations Committee. The testimony consisted of functional brain imaging (SPECT) documentation of improvements in brain blood flow in 15 patients with a variety of chronic brain injuries. The diversity of cases in the testimony and the uniform results using a low pressure protocol of HBOT strongly suggest a generic effect of HBOT on the chronically injured brain. The impressive brain scans demonstrate the power of this treatment modality.

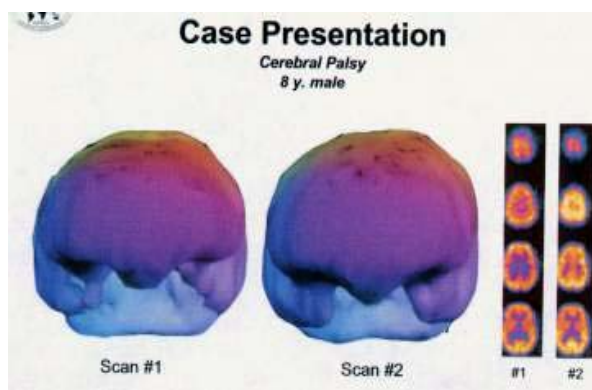


Figure (2) SPECT scan of an eight year old boy with cerebral palsy before and after HBOT as presented by Paul Harch, M.D at a 2002 House of Representatives Appropriations Committee.

It is clear from authoritative medical literature that that SPECT brain blood flow imaging is a respected and scientifically valid measurement of the changes taking place when HBOT is administered to a brain injured child. It is a picture of the biological changes that take place under hyperbaric conditions.

The Case of Augusta

I have brought with me one of my patients – ten year old Augusta Skoog. Augusta was born 11 weeks premature –the product of a precipitous delivery and had an intraventricular hemorrhage at birth from the trauma on her head due to the pressures exerted in the birth canal. She was officially diagnosed with right spastic hemiplegia, hearing impairment, and developmental delay at one year and seven months of age. Augusta was nine years old when we were introduced. Her neurocognitive functions were determined by a computerized neurocognitive test battery (*IMPACT*) developed originally to evaluate sports concussions at the University of Pittsburgh.^{14,15} This is the first time this test has been used to evaluate changes in neurocognitive function from HBOT in a child with cerebral palsy.

The computer administered test battery consists of seven individual test modules that measure aspects of cognitive functioning including attention, memory, reaction time, and processing speed.

Table 1. Neuropsychological Test Modules of the *IMPACT* test.

Test Module	Ability Area
Word Discrimination	Attentional processes, verbal recognition
Symbol Memory	Visual working memory, visual processing speed
Sequential Digit Tracking	Sustained attention, reaction time
Visual Span	Visual attention, immediate memory
Symbol-Matching	Visual processing speed, learning and memory
Colour Click	Focused attention, response inhibition, reaction time
Three Letters	Working memory, visual-motor response speed

Results from above tests are computed into overall Memory, Reaction Time, and Processing Speed composite scores.

On October 9th of 2003, Augusta completed 40 hyperbaric oxygen treatments and before and after results on her testing are compared. Her Verbal Memory composite score went from 62% (7/24/03) to 82% - (a 46% improvement). Half way through this first set of treatments (8/25/03), her OT (occupational therapist) evaluation noted that “use of both sides of the body together and separately in a smooth coordinated fashion improving by over 40% on a consistent basis.” “Trunk rotation is evidenced at 50% improvement compared to one year ago.”

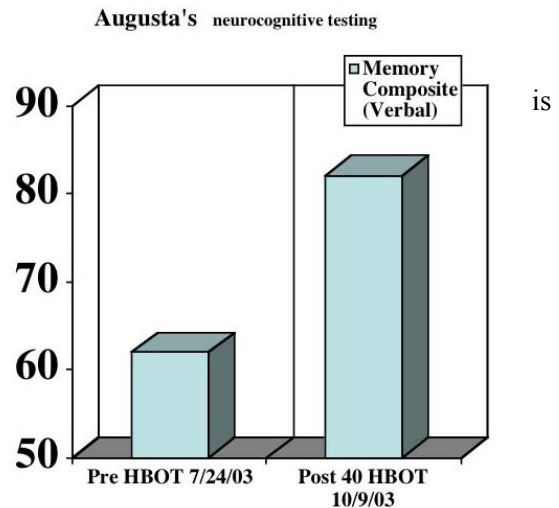


Figure (3) Improvement in Verbal Memory after 40 HBO treatments. (y axis score developed from the clinical research of Drs. Lovell and Collins at the University of Pittsburgh Center for Sports Medicine)

On October 13, 2003, her PT (physical therapist) wrote, “Augusta’s ability to perform activities in a symmetrical way has improved from 50 to 70% (from 7/25/03). Her bilateral skills have improved 25% (from 7/25/03). Endurance improved by 100%.”

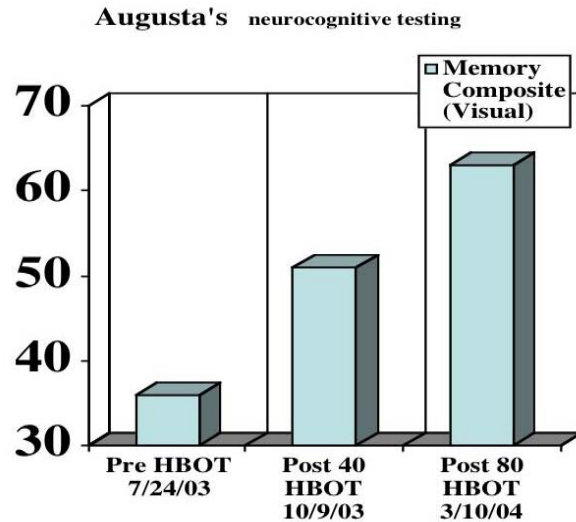


Figure (4) Improvement in Visual Memory after 40 HBO treatments, and 80 HBOT

In March of 2004, Augusta completed her second set of 40 treatments with hyperbaric oxygen and Figure (4) shows the improvement in Augusta’s Visual Memory over the course of two blocks of 40 HBO treatments – a 75% improvement from her pre-HBOT score on 7/24/03.

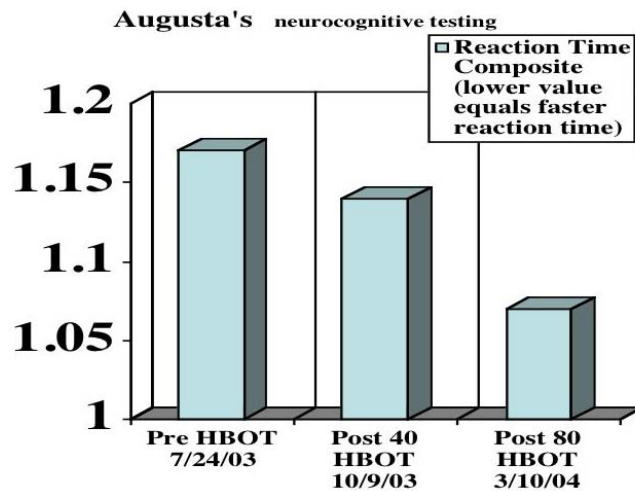


Figure (5) Improvement in Reaction Time after 40 HBO treatments, and 80 HBOT

While still impaired, Figure (5) shows consistent improvement in Reaction Time over the course of Augusta’s HBOT sets. These stellar results are representative of what hyperbaric oxygenation can do for a brain injured child. Now, every brain injury is unique unto itself, and results of HBOT vary from patient to patient influenced by a myriad of factors such as age therapy is initiated the extent of the injury, nutritional status, etc. In Augusta’s case, damage resulted from a single traumatic event, but many neonates and infants can have multiple and prolonged bouts of oxygen deprivation due to prematurity and/or infection. Although each case is different in the extent and type of damage, using hyperbaric oxygenation to preserve

or restore function after brain injury should be considered as fundamental as establishing an airway. Least we forget, the object of intervention in head injury is to maintain an adequate level of oxygen to the brain; although, for some reason this is apparently not obvious.



Figure (6) Ten year old Augusta with fellow patients inside the hyperbaric chamber in Santa Fe.

The Case of Slava

Slava was found abandoned and wandering a Rustov, Russia train station as a toddler. When brought to the USA by his adoptive mother he was diagnosed with Fetal Alcohol Syndrome (FAS). Slava, now in his mid teens, has just begun his HBOT but already has shown significant neurocognitive gains as documented by the IMPACT test.

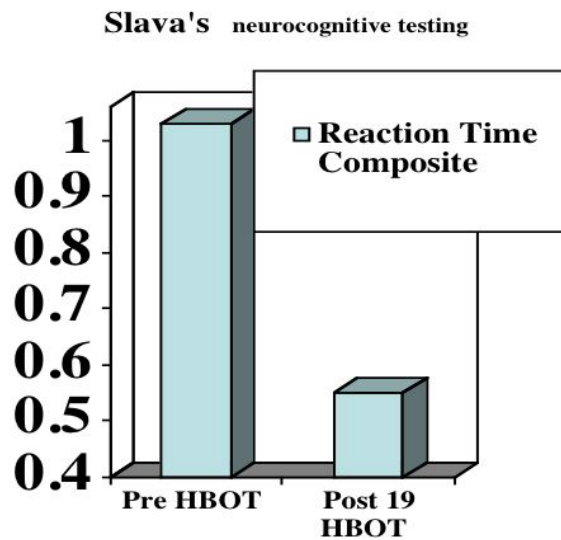


Figure (7) Improvement in Reaction Time after 19 HBO treatments (4/23/04), an improvement of 53%.

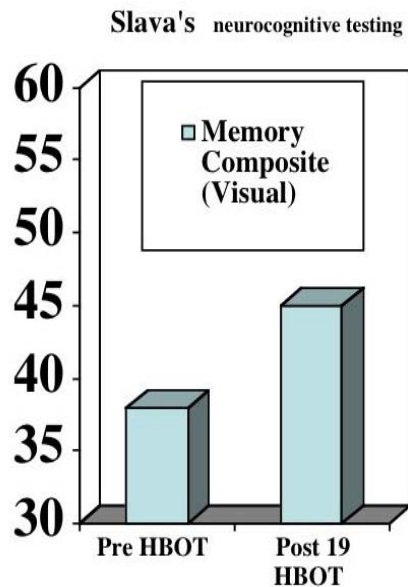


Figure (8) improvement in Visual Memory after 19 HBO treatments (4/23/04), an 18% increase in performance.

The data/documentation that can be generated using a tool, such as the IMPACT neurocognitive evaluation system, demonstrates not only the remarkable improvement children such as Slava and Augusta can make with HBOT, but shows that these children can act as their own controls for the purpose of evaluating the efficacy and effectiveness of HBOT for brain injured children.

Fetal Alcohol Syndrome is one of the leading causes of mental retardation and birth defects in this country. This syndrome is considered irreversible and there is no treatment for it. Slava is the first child with FAS to be getting a therapy that is drastically improving his neurocognitive abilities and he is having these dramatic changes documented as Figure 7 & 8 attest.

Oxygen: An Orphan Drug

Why is there such resistance to giving more oxygen under hyperbaric conditions, not only in the new or “controversial” areas such as neuro-rehabilitation, but also in a wide variety of diseases where it could save lives and improve the outcome of treatment? The principle reason is the current “culture” of medicine will not embrace a therapy that is neither taught in medical school nor promoted by a big pharmaceutical house. There are also those that have a vested interest in protecting an agenda who have had great influence on suppressing HBOT to the point of misrepresentation and prevarication. The bottom line is that the current generation of teachers at our medical schools do not themselves understand the importance of barometric pressure in oxygen delivery. If such fundamental concepts as pressure and tissue oxygenation are not grasped properly before a doctor qualifies or matriculates, then it is almost impossible for them to be taught later.

HBOT was first defined as a drug in 1977 by Gottlieb. Unfortunately, this critical definition has been long forgotten and substitute definitions have mischaracterized HBOT as a therapy for “certain recalcitrant, expensive, or otherwise hopeless medical problems.” In 1999, the drug definition of HBOT was refined and restated as the use of greater than atmospheric pressure oxygen as a drug to treat basic pathophysiologic

processes and their diseases. For the first time, this definition permitted an understanding of how all the conditions, which HBOT can help treat, can be connected as cohesive sets where a common pathophysiology is shared. Yet, medical students are taught little about oxygen except that it can be toxic in excess. Oxygen is toxic when given in excessive amounts for too long, but this is only relevant to divers. We know more about the actions of oxygen and the safe limits of its delivery than we do about any drug.

Oxygen has been extensively used in military and commercial diving for over sixty years and millions of hours of oxygen breathing have been completed underwater since the midget submarine charioteers bravely attacked ships in the Second World War. Similarly, pure oxygen breathing is necessary in military aircraft and for extra vehicular activity (EVA) in the space program. Although these activities have involved thousands of scientists and engineers, very few doctors have been involved, and so it should be no surprise that most physicians know very little about hyperbaric conditions and the need for the higher dosages of oxygen made possible at increased atmospheric pressure. But aren't physicians monitoring oxygen levels routinely in clinical practice? No, they measure the oxygenation of hemoglobin (the molecule that carries oxygen within the red blood cells). This value gives no direct indication of the amount of oxygen reaching the body's tissues. So, in major conditions, such as with heart attacks or strokes, the amount of oxygen being carried by the blood may be normal but the tissues of the heart or brain are dying of hypoxia – lack of oxygen, yet third party payers and their physician advisors often do not see HBOT as a medical necessity.

How does a therapy become a Medical Necessity?

How do Medicaid, Medicare and other third party payers decide what diagnoses are considered covered expenses and what diagnoses are considered investigational and does that determine whether a therapy is or isn't a medical necessity? What specific standard is applied to all diagnoses?

Both the 1999 Tec Assessment from BlueCross/BlueShield (BCBS) and the Undersea Hyperbaric Medical Society (UHMS) make it quite clear that HBOT is approved and reimbursed for conditions that lack any blinded, randomized controlled clinical trials. The UHMS also admitted that there exist no definitive criteria to determine what is approved and what is unapproved. It is Blue Cross Blue Shield's position that HBOT continues to be used and reimbursed for specific diagnoses despite the lack of controlled studies. Medicare, Medicaid and all other third party payers readily reimburse for those "experimental" and "investigational" applications of HBOT such as decompression sickness and air embolism.

Most of the medical therapies we offer children with neurological injuries do not meet the criteria of peer-reviewed double blind controlled studies published in authoritative journals to support their use with certainty for a particular diagnosis. For example, a recent article in the New England Journal of Medicine (NEJM) titled "Phenobarbital Compared with Phenytoin for the Treatment of Neonatal Seizures" states that both of the above mentioned drugs are ineffective in treating seizures in neonates and that phenobarbital may have negative effects on the developing brain and phenytoin can be toxic to heart tissue. Yet both these drugs are a covered "benefit" across the United States by all insurance carriers for neonates having seizures. Most seizure medications for the pediatric population lack any studies to support their use.

As a matter of fact there are few peer-reviewed double blind controlled studies published in authoritative journals for any drug given to the pediatric population.

Almost every drug given to a child is an off-label use of a drug that has Federal Drug Administration (FDA) approval for adults. According to the American Academy of Pediatrics only a small fraction of all drugs marketed in the United States has been studied in pediatric patients, and a majority of marketed drugs are not labeled, or are insufficiently labeled, for use in pediatric patients (Committee on Drugs, American Academy of Pediatrics, Guidelines for Ethical Conduct of Studies to Evaluate Drugs in Pediatric Populations, Pediatrics, 95(2);286-294, 1995.)

Hyperbaric chambers are a FDA approved and regulated medical device, and medical grade oxygen is a FDA approved and regulated drug. It is also a well established fact that both Medicare and Medicaid

reimburse for both medical grade oxygen and for HBOT. Furthermore, all insurance plans including Medicaid will reimburse for drugs or therapies given to children even though those drugs or therapies are “off-label.” What does it mean that a drug or device is used “off-label”?

When a drug or device is approved for marketing by the FDA it has to state a list of indications of use. The list would include what diagnoses this drug or device would be used to treat. When the drug or device is used for a particular diagnosis that does not appear on the original list then for that indication it is considered “off-label”. (Device Labeling Guidance, FDA Guidance Doc. No. G-91, pt. III May 8, 1991) Off-label uses are neither risky nor investigational. The off-label designation by the FDA is simply a term they use to mean they are silent on the indicated use. The off-label use of a drug or medical device may be less risky than the approved indications. All drugs and devices contain inherent risks. Off-label simply means it is being used for an indication that was not originally thought of when the drug or device was presented for approval. In their article “FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions” Beck and Azari state the following: The notion that off-label use is itself a “risk” is one of two common misperceptions addressed in this article. The second is that all off-label treatment is *ipso facto* “investigational” or “experimental.” It is an accepted principle that once FDA determines that a drug or device can be marketed, a physician’s discretionary use of that product (the practice of medicine) is not restricted to the uses indicated on FDA-regulated labels. Off-label use is widespread in the medical community and often is essential to giving patients optimal medical care, both of which medical ethics, FDA, and most courts recognize. Even so, the public (and an occasional court) mistakenly presumes that all off-label treatment is investigational or experimental.” (Beck, James and Elizabeth Azari. “FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions.” *Food and Drug Law Journal*, 53 (1998): 71 – 104.)

The term investigational only applies when a new drug or device has been submitted for approval or when a manufacturer wants to market an approved drug or device for an off-label use. The FDA regulates the marketing of approved drugs and devices but not the prescribing of those drugs or devices. Furthermore the Food and Drug law Journal states the following:

“Off-label uses of medical devices and drugs perform an important therapeutic role in many, if not most, areas of medical practice. Prescriptions for off-label uses of drug products “may account for more than 25% of the approximately 1.6 billion prescriptions written each year, with some recent estimates running as high as 60%.” Pediatric uses also are mostly off-label. Thus, “in some cases, if you didn’t use the drug in the off-label way, you’d be guilty of malpractice.”(Beck, p. 80)

HBOT for brain injuries is simply the off-label use of a FDA approved drug and device. HBOT for brain injuries is clearly an acceptable off-label use. Not only is it an acceptable off-label use but HBOT for brain injuries is a reimbursable diagnosis covered by many state Medicaid plans and Medical Insurance plans. Clearly there is no policy that forbids HBOT for brain-injuries to be a reimbursable diagnosis.

The Medicaid Law for Children and HBOT

Currently, Medicaid reimbursement for hyperbaric oxygen for pediatric brain-injury is "governed" by the 15 indications as "approved" by Centers for Medicare & Medicaid Services (CMS) for the Medicare plan.

Thus, most state Medicaid agencies have decided their reimbursement policies for HBOT should be modeled after Medicare policy, but the Medicare policy on HBOT was devised and created for use by people aged 65 and older as part of their retirement benefits.

How can a Medicaid HBOT policy for children truly provide services for children if its plan is based on a government model that was not designed for children but was designed instead for elderly adults aged 65 and older?

Remember, over 80% of everything prescribed for children are prescribed off-label, and for brain-injured children that number is closer to 100%.

This means the government model for children's healthcare should be that model which will most-include the occurrence of off-label treatments and/or services. This was the exact purpose of the Medicaid Law as discovered by the Georgia father of a cerebral palsy child, Mr. David Freels when he read Paragraph 5 of the EPSDT statute:

so children would not be denied treatments and/or services that are "necessary to correct or ameliorate" their physical or mental illnesses or defects "whether the treatment is covered by the state plan or not."

CMS has two lists on HBOT reimbursement for Medicare recipients: one is termed a "covered" uses list; the second is a "non-covered" uses list.

The "covered" uses list

For purposes of coverage under Medicare, hyperbaric oxygen (HBO) therapy is a modality in which the entire body is exposed to oxygen under increased atmospheric pressure.

A. Covered Conditions.--Program reimbursement for HBO therapy will be limited to that which is administered in a chamber (including the one person unit) and is limited to the following conditions:

1. Acute carbon monoxide intoxication.
2. Decompression illness.
3. Gas embolism.
4. Gas gangrene.
5. Acute traumatic peripheral ischemia. HBO therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
6. Crush injuries and suturing of severed limbs. As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
7. Progressive necrotizing infections (necrotizing fasciitis).
8. Acute peripheral arterial insufficiency.
9. Preparation and preservation of compromised skin grafts.
10. Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management.
11. Osteoradionecrosis as an adjunct to conventional treatment.
12. Soft tissue radionecrosis as an adjunct to conventional treatment.
13. Cyanide poisoning.
14. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment.
15. Diabetic Wounds (Wagner grade 3&4)

No other drug has a "non-covered" list. So, why does HBO have one?

The "non-covered" uses list:

1. Cutaneous, decubitus, and stasis ulcers.
2. Chronic peripheral vascular insufficiency.
3. Anaerobic septicemia and infection other than clostridial.
4. Skin burns (thermal).
5. Senility.
6. Myocardial infarction.
7. Cardiogenic shock.

8. Sickle cell anemia.
9. Acute thermal and chemical pulmonary damage, i.e., smoke inhalation with pulmonary insufficiency.
10. Acute or chronic cerebral vascular insufficiency.
11. Hepatic necrosis.
12. Aerobic septicemia.
13. Nonvascular causes of chronic brain syndrome (Pick's disease, Alzheimer's disease, Korsakoff's disease).
14. Tetanus.
15. Systemic aerobic infection.
16. Organ transplantation.
17. Organ storage.
18. Pulmonary emphysema.
19. Exceptional blood loss anemia.
20. Multiple Sclerosis.
21. Arthritic Diseases.
22. Acute cerebral edema.

Many of these indications are for conditions that afflict many elderly people: bedsores (#1), senility (#5), heart attack/heart condition (#6, #7), stroke--cerebral vascular insufficiency (#10), Alzheimer's (#13), organ transplant (#16, #17), blood loss (#19), arthritis (#21), etc.

It makes no financial sense whatsoever for a Medicaid healthcare plan for children to use a Medicare model on which to base health care decisions for children, particularly brain-injured children.

On November 19, 2002, in the Court of Appeals of Georgia, the Presiding Judge, P.J. Ruffin ruled in favor of a five-year-old child with cerebral palsy by the name of James Freels. Freels' parents had to take Georgia Medicaid to court in order to get reimbursed for HBOT.

The Court said that while state Medicaid programs are "to be given great weight and deference" when it comes to administering this federal program; "nevertheless, the Department must comply with the applicable federal law, and having chosen to participate in the Medicaid program, the State must provide services required under the program."

"Federal law governing the Medicaid program provides that eligible recipients under the age of 21 are entitled to early and periodic screening, diagnostic, and treatment ('EPSDT') services. Specifically, 42 USC 1396d(r)(5) provides that EPSDT services include: 'Such other necessary health care, diagnostic services, treatment, and other measures...to correct or ameliorate defects and physical and mental illnesses and conditions by the screening services, whether or not such services are covered under the State plan.'"

"In its final decision, the Department (Georgia Medicaid) noted that it 'reimburses only for services which are **medically necessary** and within accepted professional standards'." "The Department denied Medicaid coverage to Freels because it found that...Petitioner failed to satisfy the requisite burden of proof that HBOT treatments are an acceptable standard of medical practice and has not proven the HBOT is medically necessary for Petitioner."

But the Court of Appeals said, "the federal (*Medicaid*) statute does not require that a treatment also be 'an acceptable standard of medical practice' to be eligible for reimbursement. As the superior court ruled, 'instead of requiring proof that HBOT is the accepted standard medical practice, or that it meets the definition of medical necessity reserved for adult Medicaid recipients, the [Department] should have focused its inquiry on whether HBOT was necessary to **correct or ameliorate** [Freels'] physical condition.' The Department's findings show that the proper legal standard was not used in making its reimbursement determination, and we affirm the superior court's reversal of the Department's decision on this basis."

In other words, the Appeals Court reaffirmed that Paragraph five of the EPSDT circumvents the “medical necessary” barrier applied to adults seeking any given therapy by having its own standard for whether a service is reimbursable, and this standard or requirement is only whether that service is necessary to correct or ameliorate. It is no typographical error that “medically necessary” is not found in Paragraph five. The authors knew it can take decades before a treatment, procedure, drug, or device is finally categorized as “medically necessary,” and it should be clear now that there really is no process for that to happen anyway, in fact, what is or isn’t a medical necessity is often determined by what seem to be arbitrary and capricious machinations that are neither based in science nor economics.

Summary

Today, neonatologists and pediatricians are willing to vigorously resuscitate almost all newborns that are born before 28 weeks gestational age if they appear viable. Of this group we know that about 25% will have an outcome with a major disability. Another 10% are destined for a life of total dependency and an additional 30%-50% will have cognitive, perceptual and behavior problems severe enough to interfere with school performance. According to the Centers for Disease Control (CDC) the average cost of a child with cerebral palsy per year is over half a million dollars with a lifetime cost of \$40 million (CDC: Economic costs of Birth Defects and Cerebral Palsy, United States–1992. MMWR 1995: 44;47,695 [see figure #1]). So, the combined savings to the government and the economy of returning function to a child with cerebral palsy are almost im-measurable, but the improved quality of life cannot always be quantified. After all, what is the price of a CP child being able to feed themselves or walk?

If we are willing to resuscitate these children knowing the odds and knowing the cost then why are we so unwilling to accept a treatment that is safe under the right conditions and which seems to benefit some patients and their families with improvements in function and decreased burden of care? The answer is multifaceted, but oxygen is not a patentable drug; therefore, there is not a well funded pharmaceutical marketing campaign behind it. Add to that fact that the principles of hyperbaric or oxygen saturation medicine are not taught in medical school for similar reasons, and most physicians have no exposure to it at all during their training. Do you know what physicians say when you approach them and tell them all the things HBOT can do and has been doing all these years? They say if this were true they would already know about it or point to (non) evidence based reports/assessments that continue to ignore the truth. Having the perfect Randomized, Double Blinded, Controlled (cross-over designed) trial is sought after by medical technocrats as if it were the Holy Grail. Four decades ago the National Academy of Sciences called for a different benchmark when it came to hyperbaric medicine:

"In some [patients], changes in manifestations or course of disease may be such as to permit each patient to serve as his own control. In any situation where application of appropriate measurements gives concrete evidence of changes induced by treatment, the significance of limited numbers of patients is increased"

--from page 13 of a 1963 white paper issued by the US National Academy of Science-National Research Council entitled: "Hyperbaric Oxygenation: Potentialities and Problems".

Children like Augusta, children who have strong documentation showing how hyperbaric oxygenation has changed the clinical course of their illness are being denied this therapy by third party payers and technocrats. Medicaid law, the science of HBOT, and prudent economics are all present behind this therapy, and it is time for it to be made known and available to all brain injured children as Congress originally intended when Medicaid was first created – even if it takes another act of Congress.

Thank you.

Kenneth P. Stoller, M.D.

1. Astrup J, Siesjo BK, Symon L. Thresholds in cerebral ischemia - the ischemic penumbra. *Stroke* 1981;12:723-25.
2. Rutherford MA. MRI of the neonatal brain. WB Saunders London 2002.
3. Finkel E Stem cells in brain have regenerative potential. *Lancet* 1996;347:751.
4. Waalkes P, Fitzpatrick DT, Stankus S, Topolski R. Adjunctive HBO treatment of children with cerebral anoxic injury. *US Army Med Dept Journal* 2001;April-June:13-21.
5. Collett J-M, Vanasse M, Marois P, Amar M, Goldberg J, Lambert J, Lassonde M, Hardy P, Fortin J, Tremblay SD, Montgomery D, Lacroix J, Robinson A, Majnemar A and the HBO-CP Research Group. Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. *Lancet* 2001;357:582-6.
6. Marois P et al (2003) Hyperbaric oxygen therapy and cerebral palsy. *Dev Med Child Neurol* 45:646+
7. Trahan J et al (1999) Changes in Gross Motor Function Measure in children with different types of cerebral palsy. *Pediatric Physical Therapy* 11:12-17
8. Neubauer RA et al (1990): Enhancing "idling" neurons. *Lancet* 335:542.
9. Neubauer RA et al (1992): Identification of hypometabolic areas in the brain using brain imaging and hyperbaric oxygen. *Clin Nucl Med* 1992;17(6):477-481.
10. Neubauer RA (1990). Severe natural gas poisoning successfully treated with hyperbaric oxygen—2 years later. Presented in Prague, Yugoslavia, Proceedings of the 5th International Congress on Neurotoxicology and Occupational Neurology, Sept 24-7, 1990, page 10.
11. Harch PG et al: HMPAO spect brain imaging of acute CO Poisoning and delayed neuropsychological sequelae (DNSS). *Undersea & Hyperbaric Medicine*, 1994;21(Suppl):15.
12. Harch PG et al: 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):30.
13. Harch PG et al: 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.
14. Collins MW, Lovell MR, Mckeag DB. Current Issues in Managing Sports-Related Concussion. *JAMA*, 1999; 282:2283.
15. Collins MW, Grindel SH, Lovell, MR, et al. Relationship between Concussion and Neuropsychological Performance in College Football Players. *JAMA*, 1999; 282:964.