GROWING IMPATIENCE MARKS THIRD SYMPOSIUM

By David Freels

The Most Passionate Symposium Yet on the use of Hyperbaric Oxygen Therapy for the Brain-Injured Child was held July 16-19, 2003 in Fort Lauderdale, FL. It was sponsored by The Ocean Hyperbaric Neurologic Center and the Research Committee for Space and Underwater Neurology of the World Federation of Neurology. This 3rd Symposium presented pediatric neurologists, hyperbaric physicians, scientists, and researchers from five continents and ten different countries including Australia, Bulgaria, Canada, India, Italy, Mexico, South America, the United Kingdom, and the United States. Once again, there was a common denominator. The off-label use of extra oxygen delivered under increased atmospheric pressure brings healing to the brain-injured child. This overwhelming fact magnified a growing frustration for symposium-attending (and non-attending) caregivers who can't understand the prepetual reimbursement denials by health insurers and other 3rd-party payors for the one treatment that most helps nearly 100% of all brain-injured children.

The First Symposium was held in 1999, and it's believed most of those 1999 attendees had never seen the effects of Hyperbaric Oxygen Therapy on their children. That wasn't true for the attendees at 2001's Second Symposium, where many parents had seen for themselves what HBOT could do. At the Third Symposium, nearly all the parents had seen firsthand the effect of hyperbaric oxygen on their children. That's why most of the hallway chatter and conversations between presentations centered around the frustration of perpetual reimbursement denial from insurance and Medicaid.

UCP: "Where the hell has everybody been for five years?"

Another major contributor to this frustration has been United Cerebral Palsy (UCP). To the general public, UCP holds the 'brand name of expertise' on anything related to CP, thus UCP's opinions are given automatic credibility.

Despite the dozens and dozens of favorable reports presented and published by physicians from around the world at the First and Second symposiums, plus the hundreds (or thousands) of individual reports of improvements in CP children from HBOT, UCP continues to publish disparaging, misleading, and contradictory statements about HBOT on its website.

Repeated requests to UCP to amend and edit its web content on HBOT have not resulted in any changes. At least one caregiver, Julie Gordon, director of MUMS (19,000 members), is openly reviewing the purpose, goals, and accomplishments of UCP by publicly reviewing UCP finances, specifically monies spent toward research. UCP's most recent annual report (2001) reports "research expenses" of $528,203 ($229,242 for salaries), but zero dollars went to "grants or awards." Frustration with UCP and a public request for UCP accountability led to an impromptu presentation by UCP's Dr. Murray Goldstein:

Murray Goldstein: First of all, uh, I think you have to get something straight. There are two cerebral palsy organizations. There's an organization known as United Cerebral Palsy Association which has over 150 chapters--uh, excuse me, over 100 chapters around the country. Bound together. It's a family-oriented organization whose primary service and objectives are service and advocacy. It does no research. It does none. There is a separate corporation, a separate organization, with its own board of directors, its own charter, closely linked to UCPA but not quite called the United Cerebral Palsy Research and Educational Foundation. It has no, no responsibility for patient services or for advocacy. All we are interested in is research, professional education, and public information.

Now, the research foundation does support the investigator initiated research. For five years I have been begging you to submit a scientifically meritorious application to the foundation for research support. I'm delighted to say after five hard years, we finally have two applications presently in a scientific merit review process to study the impact of hyperbaric delivered oxygen. It will be several weeks before we know what the results will be. But in fact, where the hell has everybody been for five years? We've been begging you to submit research proposals. It's not that we turned it down, WE NEVER GOT IT! We now have two. I hope I've answered your question.

Dr. Paul Harch: Wait, wait, wait, wait, wait. Excuse me one second. Hold on. Someone just told me (I've just walked in) that you've been begging for applications, and no one has applied from this group? Murray?

Murray Goldstein: You have never sent us an application.

Dr. Paul Harch: I've asked you how many times about this? You said you only have 50 thousand dollars. You can't do a study with 50 grand. I have a randomized, prospective, controlled, cross-over trial with SPECT brain imaging been approved by IRB for four years with a pediatric neurologist participating, and I have been discouraged from even sending it to you, although you've told me that the corporate board members have money, you don't ever been able to put in touch with the corporate board members. So recently, last month, I sent you another email after you told Julie Gordon you had, what, millions of dollars in research? I asked, has something changed? Under the impression that there's only 50 grand? And you said in the email that you sent, 'Yeah, you're right. We only have 50 grand'. I don't get it.

Murray Goldstein: Alright, uh. Listen.
Following this exchange there was a burst of thunderous applause from the Audience Despite the obvious discrepancies expressed, Dr. Goldstein did not clarify himself to symposium attendees. It was later learned that Dr. Goldstein has offered to fund a study led by Dr. William Oppenheim of UCLA. Dr. Oppenheim is an orthopedic surgeon who specializes in CP. His study protocol is to do a PET-scan (not SPECT) followed by 20 treatments of HBOT, then followed-up with a 2nd PET-scan six months after the last HBOT treatment. Dr. Oppenheim has no known experience in Hyperbaric Medicine. In 1992, Dr. Paul Harch treated the first CP child in North America with Hyperbaric Oxygen Therapy after discussing the mechanisms of action with Sheldon Gottlieb, Ph.D.

50 Presenters From Five Continents
Despite the institutional denial of HBOT efficacy, 50 presenters from five continents spoke. The evidence mounted one by one. One speaker after another testified to their experience. Nobody said "it doesn't work."
There was Dr. Zerbini of Brazil, who was part of the groundbreaking study led by Dr. Machado in the 1980's. Israel's Dr. Gall has seen improvements in infants with just 1.1 ATA. Dr. Arun Mukherjee of India has seen unprecedented gains in children when HBOT is an adjunctive treatment with Speech, OT, and PT.
The Indian government is now funding a SPECT-based study. Dr. Diaz-Barboza of Mexico is treating with stem cell therapy and HBOT. Dr. Morales also of Mexico is seeing good results when combining chelation therapy with HBOT.
Dr. Jeff Weiss, Ft. Lauderdale resident and Father of Justin, a near-drowning victim, gave a very moving, emotional presentation on his struggle with fellow physicians and his legal fight with the hospital to get HBOT treatments for Justin.
The child who neurologists wanted to take off life support now precociously interacts with his family.
In addition to presentations for neurological conditions, there were presentations on the use of HBOT for cancer. Dr. William Maxfield has extensive experience utilizing HBOT as supportive therapy in pediatric oncology. Dr. Shantha, originally from India and now in Atlanta, has used HBOT to treat children with malignant tumors. Dr. Feingold uses HBOT to treat Lyme disease. Following are just some of the 50 presentations:

Dr. Dan Lacey - USA:
Advances In Diagnosis and Management of Children with Cerebral Palsy
Pediatric neurologist Dr. Dan Lacey was the first speaker. Dr. Lacey has injected off-label Botox into 180 children, with peak effect occurring 2 weeks post injection. He's performed baclofen trials on 70 children, with 43 children getting baclofen pump implants. One child died of medical complications unrelated to the baclofen pump.

Dr. Philip James- United Kingdom:
Pressure and Oxygen Dosage in the Treatment of Brain Injury Hypoxia: Blood Vessel Growth and the Cause of Retinopathy
Canada's Dr. Jean Paul Collet claims his infamous 1.3 ATA ambient air group was placebo even though *The Lancet* refused to publish Collet's paper unless he first removed all references to placebo. Dr. Philip James presented evidence that even a pressure increase of just 0.1 ATA of ambient air can have therapeutic, clinically indisputable, and even lifesaving effects.
Dr. James also gave further proof that hypoxia causes retinopathy of the premature (ROP), as evidenced by Hypoxia Inducible Factor 1 alpha (HIF-1 alpha). Oxygen concentration controls the HIF protein system, and HIF modulates the permeability of small blood vessels. Since low oxygen levels are typical in reperfusion after ischemia, reperfusion injury occurs when blood flow arrests for a time (as in hypoxia from vasodialation in neonates) and is then re-established. An abrupt increase in oxygen levels, possible by using hyperbaric conditions to deliver a high plasma concentration of oxygen, can avoid reperfusion injury after circulatory arrest.

Richard A. Neubauer, M.D. – USA:
"What is Hyperbaric Oxygen Therapy?"
Dr. Neubauer's overview included a reminder that oxygen follows all the gas laws of physics, including Henry's law, which states that as the pressure of a gas increases, there will be a proportional increase in the volume of gas dissolved in a fluid. Since the human body is mostly water, every body fluid becomes hyperoxygenated, delivering free molecular oxygen directly to every cell for immediate metabolic use.
Dr. Neubauer said the USA is behind the rest of the world in taking advantage of the benefits of HBOT. In Mexico City hypoxic, birth-injured infants are taken from the delivery room to a hyperbaric chamber. In Israel, there are portable chambers for diving accidents and near-drownings. The Japanese have hyperbaric chambers on their ambulances. Hopefully the US will catch up when people figure out how cost-effective HBOT is.

Dr. Sheldon Gottlieb – USA:
Hyperbaric Oxygen Delivery Systems
Hyperbaric oxygen can be administered in either monoplace or multiplace chambers. Monoplace chambers are single occupancy and have a maximum pressure of 3 ATA and need to be flushed with a fixed flow rate of oxygen to remove (1) exhaled carbon dioxide and (2) prevent increases in intra-chamber temperature due to heat production by the patient. Multiplace chambers can hold two or more people for simultaneous treatment. They usually have a maximum working pressure of 6 ATA. During operation they are continuously flushed with air to prevent heat build-up and expel leaked oxygen from patient hoods or masks. Hyperbaric Oxygen Therapy is equally effective in either type chamber.

Virginia Neubauer – USA:
History of Hyperbaric Oxygenation In Cerebral Palsy and the Brain Injured Child
After World War II, oxygen supplementation at levels of 60-80% increased survival of premature neonates, with development of cerebral palsy from hypoxic-ischemic encephalopathy occurring less than 7% of the time; however, the ROP rate was 25%. Fearing oxygen toxicity as the ROP cause, oxygen levels were reduced to 40%, eliminating ROP, but cerebral palsy increased over 600%.
The UK, 1964. Hutchison treated asphyxiated newborns with 100% oxygen for just 20 minutes at 4 ATA. 54% resuscitated and survived.
Italy, 1988. When a small or deformed fetus is found in utero, pregnant mothers are treated with HBOT. Normal birth weights and reduction in cerebral damage is demonstrated.
Brazil, 1989. Machado and Zerbini report 230 cp children treated with HBOT. 218 experience at least a 50% reduction of spasticity. Parents report improvements in balance, intelligence, and reduced frequency of seizure activity.
The UK, 1995. A small pilot study of HBOT for cp children leads to the formation of the Hyperbaric Oxygen Trust, a charity to treat brain-injured children.
USA, 1995. Dr. Richard Neubauer and Dr. Paul Harch begin treating CP and brain-injured children with HBOT. The evidence of efficacy continues to accumulate.

USA, 1999. Upon the insistence of the MUMS group, Dr. Maurine Packard of Cornell University undertakes a study of HBOT for CP children. The results are positive; even cognitive skills improved.
USA, 1999. United States Army undertakes a pilot study of eight brain injured children, volunteered by parents who are serving in the Army. More positive results.
Canada, 1999. The first McGill study demonstrates significant improvements in fine motor, gross motor, and spasticity from Hyperbaric Oxygen Therapy in 23 brain-injured children.
Canada, 2000. The second McGill study. This time it's double-blind. 111 children. One group receives 1.3 ATA of ambient air; the second 1.5 ATA of 100% oxygen. Both groups improved.
Mexico, 2002. Dr. E. C. Sanchez takes severely hypoxic neonates straight from the delivery room to the hyperbaric chamber, giving a single 45-minute dose of 100% oxygen at 2 ATA, which dramatically reduces the rate of morbidity and also results in typical neurological development.

Kevan Corson (presented by Mike Milligan) – USA:
Pediatric Cerebral Palsy treated by 1.5 ATA Hyperbaric Oxygen - A Pilot Study
To achieve maximum metabolism, 14 cp children (average age 38 months) received 60 one-hour treatments of HBOT at 1.5 ATA. Measureable improvements in gross motor and fine motor skills were observed in modified GMFM scores for all patients completing the study (13). Decreased spasticity, as measured by a modified Ashworth spasticity score, also occurred. One patient with cortical blindness was assessed with visual evoked potentials; they were absent before HBOT and measureable after HBOT. Functional reorganization in the visual cortex is suggested by the reappearance of visual-evoked potentials.

Dr. George Mychaskiw – USA:
Hyperbaric Oxygenation Prevented Brain Injury Induced By Hypoxia Ischemia in a Neonatal Rat Model.
Hypoxia–ischemia (HI) was induced in seven-day-old rat pups by unilateral carotid artery ligation followed by 2.5 hours of hypoxia via 8% O2 at 37° C. No effective treatment is currently available for HI and this study is the first to use hyperbaric oxygen as treatment for neonatal HI.
HBO treatment was administered by subjecting pups to 3 ATA for 1 hour, 1 hour after hypoxia exposure. Sensorimotor functional tests were given 5 weeks later. After HI, the ipsilateral hemisphere was 52.65 and 57.64% ($P<0.001$) of the contralateral hemisphere at 2 and 6 weeks, respectively. In HBO treated pups, the ipsilateral hemisphere was 77.77 and 84.19% ($P<0.001$) at 2 and 6 weeks. HBO pup brains were nearly 50% larger, with much less atrophy and apoptosis (cell death).
Sensorimotor function also improved by HBO at 5 weeks after hypoxia exposure (Chi-square, $P<0.050$). The results suggest that HBO is able to attenuate the effects of HI on the neonatal brain by reducing the progression of neuronal injury and increasing sensorimotor function.

Dr. Michael Uszler – USA:
SPECT Imaging of Brain "Injury" and its "Healing"
While many believe brain injury is always permanent, SPECT imaging can demonstrate improvements made from Hyperbaric Oxygen Therapy, even years after occurrence of the injury. Brain SPECT imaging is recognized as a scientifically valid, physiologic, objective, and evaluative test of brain perfusion (blood flow) and related regional brain function. When compared with reference databases, objective regional function analysis can be made on individual before and after scans.

Dr. Paul Harch – USA:
Low Pressure Hyperbaric Oxygen Therapy In Chronic Brain Injury: Proof of Efficacy In Humans With An Animal Model
After successfully treating divers after weeks, months, and even years post-injury with Low Pressure Hyperbaric Oxygen Therapy (LPHBOT), it was determined the underlying pathology in acute and subacute brain decompression sickness is subacute ischemic brain injury. The diver success resulted in an IRB approved protocol and eventual treatment of nearly 500 patients and over 50 different neurological conditions, including the first cerebral palsy child treated in North America.
Controversy followed, as did demand for proof of HBOT efficacy with animal models. A small 1995 trial provided statistically significant improvements in cognition and brain vascularity in HBOT rat groups. A co-investigator remained unbelieving and a 2001 study replicated the 1995 results with five times the number of rats. LPHBOT was found to significantly improve spatial memory and induced cerebrovascular changes in a rat model of chronic TBI. This is the only demonstration of improvement in chronic brain injury in an animal model and underpins the human experience, suggesting the possibility of a common underlying mechanism triggered by LPHBOT in numerous human neurological conditions, including cerebral palsy.

Dr. Andrew Campbell – USA:
Neurophysiological and Immunological Abnormalties in Children with Exposure to Molds and Mycotoxins
A statistically significant number of children (52) with documented chronic exposure to toxigenic molds developed immunologic and neurophysiologic abnormalities. Environmental studies on the homes of these children were positive for specific levels of exposure to toxigenic molds including Penicillium, Aspergillus, Cladosporium, Chaetomium, and Stachybotrys. A Test of Variables of Attention (TOVA) was performed and 78% of the children showed symptoms of ADHD and 11% showed symptoms of ADD. These findings demonstrate the effect toxigenic molds can have on the neurological and immunological systems of environmentally-exposed children.

Ivan Chavdarov - Bulgaria
Developmental Outcome After Early Hyperbaric Oxygenation For "CP-Risk" Infants
Just like in the US Army Study, children receiving HBOT in combination with Speech Therapy, Occupational Therapy, and Physical Therapy did much better than just receiving therapies alone. Dr. Chavdarov found developmental outcome of central motor disturbances (CMD) in "CP-risk infants" were significantly better when they received a combination of neuro-developmental physiotherapy (NDP) and HBOT instead of just receiving NDP alone.

Dr. E.C. Sanchez - Mexico:
Emergency Life Saving Uses of Oxygen In High Doses For Neonates.
Dr. Sanchez has taken hypoxic newborns from the delivery room to the hyperbaric chamber for just one session (sometimes two) of 100% oxygen delivered at 2 ATA for just 45 minutes (20 min oxygen, 5 min air brake, 20 min oxygen).
Lab exams, transfontanelar ultrasound, EEG, x-rays, and funduscopic studies were performed before and after treatment(s). The result? Significant modifications to hemoglobin, hematocrit, proteins, serum sodium, triglicerides, direct bilirubin and PH. Dramatic improvement was observed in EEG, transfontanelar ultrasound, and x-rays. All the funduscopic studies were

negative, i.e., no retinopathy--even from *high dosages* of oxygen. Best of all, a two year follow-up found adequate neurological development. Worst of all, naysayers still insist on controlled trials.

Dr. Philip James- United Kingdom:
Brain-injury in Neonates is Birth Related: The MRI and Pathological Evidence
In 1999 the International Cerebral Palsy Taskforce claimed, "new insights have recently transformed the old concept that most cases of cerebral palsy begin in labour" and that birth injuries are responsible for cp less than 10% of the time. Absent from this statement was confirming data from neuroimaging. MRI neuroimaging has now been published in The Lancet, whose authors state that events in the immediate perinatal period are the most important in neonatal brain injury, a finding diametrically opposed to the concensus statement of the International Cerebral Palsy Taskforce.
In addition, Magnetic Resonance Spectroscopy (MRS) has uncovered clear markers for hypoxia and energy failure, dictating the necessity for higher levels of oxygen for the mother during delivery and for newborns during the postnatal period. In some cases this will require the use of hyperbaric conditions.

Dr. Pierre Marois – Canada:
HBOT in Neurological Conditions in Children
Despite overwhelmingly favorable results in the first double-blind study (two groups: 1.3 ATA 21% O2 and 1.75 ATA 100% O2) of HBOT for cp, the causes of these changes remain controversial. The Lancet agreed to publish only if all references to an HBOT "placebo" were removed; however, the lead author, Jean-Paul Collet has consistently and publicly declared the 1.3 group to be placebo, creating great confusion. Collet contradicts all other HBOT studies for CP, which have clearly demonstrated some improvements: the first McGill, Galveston, Cornell, US Army, and Machado studies. In addition, thousands of anecdotal changes have been described worldwide.
Historically there has never been any placebo improvements in any double-blind controlled study for cerebral palsy, nor have there been improvements from any "participation effect."
More research on HBOT for CP is mandatory, not to prove efficacy but to refine dosages and better understand the underlying mechanisms.
[NOTE: In a private meeting, Dr. Marois disclosed that a class-action lawsuit against the Quebec government by parents of brain-injured children is in progress. This suit is supported in large part by a substantial paper trail that documents a deliberate effort to withhold HBOT from cp children. Over 250 pages plus video have been compiled into a CD that will be used in the case.

Dr. Daniel Fitzpatrick - Eisenhower Army Medical Center – USA:
The Effect of Adjunctive Hyperbaric Oxygen Treatment on Functional Outcome in Children with Cerebral Anoxic Injury
Do improvements from HBOT ever reach a plateau? Eight children with cp and one near-drowning victim received 80 HBOT treatments at 1.7 ATA for 60 minutes. Baseline and serial evaluations after every 20 treatments included WeeFIM, GMFM, MAS, video recording, and 24-hour time of care analysis. Parent questionnaires were completed at baseline, 40, and 80 treatments. Using pretreatment scores as baseline, each child served as his/her own control. For the cp group, GMFM testing showed significant ($p<0.05$) improvements in four of the five functional areas. Improvements continued to the end of the study. The younger children demonstrated a 58.6% improvement in total score on the WeeFIM. Video evaluation recorded improved range of motion in four children and improved gross motor function in three children. Total time parents spent providing care for their child decreased significantly ($p=0.03$).
These findings suggest adjunctive HBOT significantly improves functional capacity in children with cp, but not near drowning when treatment is delayed.
An optimum number of treatments remains undetermined since improvements were noted at the end of the study.

Making HBOT Mainstream Medicine
Historically, numerous roadblocks have prevented HBOT from becoming mainstream medicine. In the US, Hyperbaric Oxygen Therapy is simply not taught as standard curriculum in any American medical school so most physicians have never even heard of it. The Undersea and Hyperbaric Medical Society (UHMS) has refused to add brain-injury to their list of recommended uses. UHMS recommendations directly influence what 3rd-party payors will reimburse, particularly Medicare. However, with the creation of the International Hyperbaric Medical Association (IHMA), policy makers have found another source for expert opinions. Recent court decisions fought by parents seeking Medicaid reimbursement are helping to facilitate a change as well. Hearings before the US Congress on these issues are planned for Spring, 2004 (see back cover, this issue). The Fourth Symposium is scheduled for July 2004 and we hope to see you there.