Low-Pressure Hyperbaric Oxygen Therapy (HBOT) as an Investigational Treatment for Developmental Disabilities including Rett Syndrome and Cerebral Palsy: Theoretical Rationale, Early Results, Protocol, and Risk/Benefit Analysis

by

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This literature review paper should be used for informational purposes only. It does not constitute a medical recommendation either of HBOT or of a particular HBOT protocol for any individual. The author of this paper is the father of a young girl with Rett Syndrome, and is currently completing his Ph.D. dissertation in cognitive developmental psychology. He is not a medical doctor or HBOT practitioner. This paper is unrelated to the author's Ph.D. research, and the UCLA Department of Psychology bears no responsibility for its contents. The author's daughter is scheduled to begin HBOT treatments in August 1999.

Internet links in footnotes are correct as of 5/21/99. This paper can be downloaded from the web site below.

Abstract

Hyperbaric oxygen therapy (HBOT) involves the inhalation of 100% oxygen inside a chamber pressurized above sea-level atmospheric pressure (see Appendix A). HBOT substantially increases the amount of oxygen dissolved in all bodily fluids, including blood plasma, cerebrospinal fluid, and lymph. Increased oxygen in these fluids provides oxygen directly to underoxygenated (**hypoxic**) tissues, supplementing the usual transport system by hemoglobin molecules in the blood.

As a result of extensive civilian and military medical research, HBOT has become a standard, Medicare-reimbursable treatment in the United States for fourteen medical conditions and classes of injury. HBOT is the primary treatment for acute conditions including carbon monoxide poisoning, air/gas embolism, and decompression sickness. HBOT is an accepted adjunctive treatment for both acute and chronic conditions, including crush injuries, radiation osteonecrosis, and poor graft healing after severe burns.

Numerous medical studies show low-pressure HBOT to be an effective treatment for many additional indications in which local or global **tissue hypoxia** is present. Nevertheless, for non-medical reasons, current standard medical practice in the United States does not include the use of HBOT for these indications.

Among the most significant additional indications for which low-pressure HBOT is beneficial is **brain injury** caused by respiratory hypoxia or other brain insult, such as head trauma or stroke. These brain injuries produce regions of chronically reduced blood flow (**hypoperfusion**) in the brain, with consequent tissue hypoxia in these regions. **SPECT** scans (see Appendix B) have conclusively demonstrated that some neurons in these regions remain alive but are "idling" in a low metabolic state which prevents normal function. SPECT scans taken before and after a series of HBOT treatments have shown that HBOT can revive these idling neurons in many cases, producing long term improvement in both brain perfusion and clinical function.

SPECT scans have also shown regions of brain hypoperfusion in several developmental disorders including **Rett Syndrome** (**RS**) (see Appendix C) and **cerebral palsy** (**CP**). These disorders also share many symptomatic parallels with hypoxic brain injuries. The primary regions of brain hypoperfusion seen in RS are the frontal lobes and midbrain, regions which control functions that are typically abnormal in RS. Given the improvements in brain perfusion produced by HBOT in both hypoxic and non-hypoxic brain injuries, HBOT may also be beneficial in treating the brain hypoperfusion seen in RS, CP, and other developmental disorders. Early trials of HBOT for CP have produced promising results, and formal clinical trials are underway.

There is no evidence that **low-pressure HBOT** has any of the side effects associated with high-pressure HBOT (see Appendix D). Therefore, when an appropriate low-pressure protocol is used, the risks of HBOT are minor compared to the potential benefits.

For all these reasons, trials should be conducted to determine whether low-pressure HBOT can improve the brain hypoperfusion and functional abnormalities seen in RS.

1. Rationale for HBOT as an investigational treatment for Rett Syndrome

1.1 Brain injuries produce brain tissue hypoxia, as do neurodevelopmental disorders

Hypoxic brain injuries (those caused by oxygen deprivation) produce **tissue hypoxia** (poor oxygen delivery and uptake) in the brain. Astrup et al. (1981) coined the term "**ischemic penumbra**" to describe a region of neurons that surrounds a hypoxic/ischemic brain lesion (a lesion caused by insufficient oxygen). They referred to the neurons in this surrounding region as "**idling**," because these neurons are electrically non-functional but remain alive. Olsen et al. (1983) verified the existence of idling neurons in a study of rCBF in stroke patients.

With the development of **single photon emission computed tomography (SPECT)** in the late 1980's (see Appendix B), the existence of idling neurons following brain injury has been conclusively demonstrated. These neurons are marked by poor regional cerebral blood flow **(rCBF)**, which leads to **hypoperfusion** and tissue hypoxia. Idling neurons have been observed in patients whose brain injury was caused by stroke (Neubauer et al. 1990), head trauma (Neubauer et al. 1994), and near-drowning (Neubauer et al. 1992). Neubauer & James (1998) report an additional three cases of hypoperfusion documented by SPECT scan (stroke, hypoglycemic encephalopathy, and near-drowning). Hypoperfusion in some cases was diffuse, rather than being located in a penumbra surrounding a focal lesion.

An important distinction must be highlighted between tissue hypoxia (underoxygenated tissues) and what can be called "respiratory hypoxia" (underoxygenated blood due to oxygen deprivation or poor breathing). Respiratory hypoxia leads to a reduced oxygen saturation of the hemoglobin molecules in the blood, and is commonly measured by a fingertip instrument called a pulse oximeter. Normal oxygen saturation is about 98%, but this level can fall sharply as a result of oxygen deprivation or respiratory abnormalities (as seen in Rett Syndrome; see Appendix C).

Not all tissue hypoxia is caused by respiratory hypoxia. In particular, not all brain injuries are caused by respiratory hypoxia (not all brain injuries are hypoxic brain injuries). Many neurodevelopmental disorders should be conceptualized as brain injuries, with the term "brain injury" defined to include developmental brain abnormalities arising from internal causes (such as infections, genetic abnormalities, metabolic abnormalities, or endocrine abnormalities). The brain is injured gradually, as one or more factors prevent normal development and set off a cascade of reactions which can lead to secondary brain injuries. A well-understood example with a metabolic cause is the genetic disorder phenylketonuria (PKU). Children born with PKU are unable to metabolize phenylalanine, leading to a buildup of this substance in the brain followed by irreversible brain damage. This brain damage can be entirely avoided if the child's diet is immediately and permanently restricted to avoid sources of phenylalanine.

Based on their research (reviewed in section 1.2), Neubauer and Gottlieb (1992) have proposed that brain injuries of different etiologies lead to a common pathophysiology involving hypoperfusion, tissue hypoxia, and hypometabolism. Ongoing SPECT research has supported this insight, which should be extended to include a variety of developmental disorders not usually thought of as brain injuries. Brain hypoperfusion has been found in

SPECT studies of children with Rett Syndrome (see section 1.4), cerebral palsy (Lee et al. 1998; Yamada et al. 1995), autism (Chiron et al. 1995; Mountz et al. 1995; Zilbovicius et al. 1995), Angelman Syndrome (Gücüyener et al. 1993), Asperger Syndrome (McKelvey et al. 1995), Landau-Kleffner Syndrome (Guerreiro et al. 1996; Mouridsen et al. 1993), West Syndrome (Sztriha et al. 1997), frontal lobe epilepsy (Harvey et al. 1993), and partial epilepsy (Kuzniecky 1996; Mitsuyoshi et al. 1993; O'Brien et al. 1998). Furthermore, in Rett Syndrome the location of the hypoperfusion correlates well with the particular functional deficits characteristic of that disorder (see section 1.4).

1.2 HBOT produces long-term improvements in brain perfusion and function in brain-injured patients

When a brain injury results in a focal brain lesion with a surrounding ischemic penumbra of idling neurons (see section 1.1), these neurons can potentially recover their function. In stroke patients, this functional recovery sometimes occurs spontaneously. However, such recovery can also be encouraged by medical intervention. Most current interventions after stroke are focused toward this goal (including the prevention of further injury to the region). According to Astrup et al. (1981), "Measures that maintain or raise the residual perfusion in the area of acute focal ischemia are probably all-important determinants of the final outcome in stroke."

HBOT delivers oxygen directly to areas of hypoperfusion and tissue hypoxia, whether in the brain or elsewhere in the body (see Appendix A). Neubauer and colleagues have demonstrated a significant improvement in brain perfusion following a course of HBOT, as seen by a comparison of SPECT scans before and after treatment (Neubauer et al. 1990; Neubauer et al. 1992; Neubauer et al. 1994; Neubauer and James 1998).[1] Corresponding clinical improvements in cognitive and motor functioning were also observed. Improvements appear to be permanent, based on clinical report and long-term follow-up SPECT scans. In some cases, SPECT scans are fully normalized.

HBOT treatments need not be given immediately after a brain injury in order to be effective. Neubauer's published case studies include a successful application of HBOT as much as 12 years after the original brain injury, in the case of a 15-year-old girl who had a near-drowning accident at age 3 (Neubauer et al. 1992). In addition, HBOT is now being used successfully with cerebral palsy patients (see section 1.3) whose brain injuries occurred years prior to treatment.

In addition to documenting long-term improvements by comparing SPECT scans before and after a course of HBOT treatments, Neubauer and colleagues have used SPECT scans before and after a single HBOT treatment as a prospective diagnostic tool (Neubauer and Gottlieb 1993). This technique can identify regions of temporarily improved brain perfusion that could be helped by a course of HBOT treatments. A significant improvement in brain perfusion between SPECT scans taken immediately before and after a single treatment can indicate recoverable areas of hypoperfused, idling neurons. However, this

[1] Sample SPECT images taken before and after a course of HBOT can be viewed on Dr. Neubauer's web site at http://hyperbaric-oxygen.com/spect.htm.

technique may be an over-conservative predictor. According to Neubauer (personal communication), some patients have still shown improvements in perfusion and function after a series of HBOT treatments, even though no improvement was seen in SPECT scans taken before and after a single treatment.

Only Neubauer and colleagues have recently published research in mainstream Western medical journals describing the use of HBOT to treat brain injury (for a review of earlier research, see the recently published third edition of K.K. Jain's Textbook of Hyperbaric Medicine[2]). However, over the past few years, additional research teams have joined the field from the United States, Canada, and around the world. Unpublished studies by these teams have been presented at scholarly conferences (see below and section 1.3), with publication soon to follow.[3]

Undersea and Hyperbaric Medical Society (May 1998). Dr. Paul Harch reported positive HBOT results in a study with Dr. Kevin Barrett of 11 brain-injured patients.[4] Five patients with traumatic brain injury received 80 sessions of HBOT at 1.5 ATA (see Appendix A), followed five months later by another 40 sessions. Six control patients did not receive HBOT treatments. Pre- and post-HBOT SPECT scans of the 5 treated subjects showed a significant increase in rCBF in the damaged areas of their brains (see section 1.1). Significant clinical improvements were also noted. It is likely that these improvements were caused by the HBOT and did not reflect spontaneous recovery, since in all patients at least two years had passed since their brain injury. Further details (including control patient results) should become available when the study is published.

Harch is the Director of Hyperbaric Medicine at the Jo Ellen Smith Memorial Baromedical Center, and is now coordinating a formal trial of HBOT entitled "Low Pressure Hyperbaric Oxygen Therapy in the Diagnosis and Treatment of Perfusion/ Metabolism Encephalopathies" (personal communication). This study is being conducted in New Orleans under the auspices of the Baromedical Research Institute.[5] Participants in the study include children with cerebral palsy. Harch is also the co-author with Neubauer of a chapter on brain trauma and HBOT in the new Jain textbook (see above).

World Federation of Neurology (May 1998). Several papers on HBOT and hypoxic brain injury were presented to the Space and Underwater Research Group. Dr. Philip James reported on the successful use of HBOT in the treatment of spinal cord injuries in which the spinal cord is bruised (but not severed).[6] Neubauer and others reported on early trials of HBOT in the treatment of stroke, and a study of HBOT and stroke was planned.[7]

"Hyper-acute Hyperbaric Oxygen Therapy for Cerebral Ischemia" (Bowman Gray School of Medicine, Winston-Salem, North Carolina, 1997). This conference focused on the

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[2] See publisher information at http://www.hhpub.com/catalogue/Jain2.html.
[3] Some of this research is summarized at http://mondenet.com/~chrisck/HBOTresrch.htm.
[4] An informal description of this study can be found at http://www.neosoft.com/~tlc/pressrel.htm, and a news article about the study can be found at http://hyperbaric-therapy.com/news/reuters/index.html.
[5] A list of BRI researchers can be found at http://www.baromedicine.com/sites/bri.html.
[6] See news article at http://www.erols.com/nscia/newsroom/archive/disability/HighPressure.html.
[7] See news articles at http://www2.nando.net/newsroom/ntn/health/051498/health14_13240_noframes.html and http://www.techmall.com/techdocs/TS980508-7.html.

possibility of using HBOT with stroke patients (see previous paragraph) to extend the window of opportunity for the use of tissue plasminogen activator. Dutka (1998) briefly reviews the conference, and the conference proceedings are now in press.

1.3 Early results indicate that HBOT also produces improvements in function in children with cerebral palsy

SPECT studies have shown that the brain injuries that produce CP result in regions of tissue hypoxia in the brain, particularly in the midbrain region. In an unpublished manuscript, Dr. Philip James describes the location and cause of this tissue hypoxia:

> "The areas affected in CP are in the middle of the hemispheres of the brain and one side or both sides may involved. These critical areas, called the internal capsules, are where the fibres from the controlling nerve cells in the grey matter of the brain pass down on their way to the spinal cord. In the spinal cord they interconnect with the nerve cells whose fibers activate the muscles of the legs and arms…. Unfortunately, the internal capsules have a poor blood supply, shown by the frequent occurrence of damage to these areas in younger patients with multiple sclerosis and in strokes in the elderly by Magnetic Resonance Imaging (MRI). When any event causes lack of oxygen the blood vessels leak, the tissues become swollen and there may even be leakage of blood. The increased water content, termed oedema, reduces the transport of oxygen."

Several private hyperbaric clinics in the United States[8] as well as groups of parents in the United Kingdom[9] and United States[10] have begun to use HBOT for children with cerebral palsy. While preliminary results of these treatments remain anecdotal, formal research on HBOT and CP is now underway at several sites in the United States, Canada, the United Kingdom, and Brazil. This research will be presented at the 1st International Conference for Hyperbaric Oxygenation in Cerebral Palsy and the Brain Injured Child, to be held in Boca Raton, Florida (July 23-25,1999).[11] Speakers will include Drs. Neubauer, Harch, and James. Also speaking will be Dr. Michael Uszler, Medical Director of Nuclear Medicine at the UCLA Medical Center - Santa Monica Hospital, who has considerable experience with evaluating SPECT scans before and after HBOT treatment.

One presentation at this conference will be given by Dr. Pierre Marois, who leads a Canadian research team from McGill University. In their pilot study, 25 children with CP between the ages of 3 and 8 received 20 one-hour HBO treatments at 1.75 ATA (see

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[8] For example, http://hyperbaric-oxygen.com, http://www.hbot.com, http://www.hyperbaric-clinics.com, and http://www.abilitycamp.com. For a list of clinics, see http://mondenet.com/~chrisck/HBOTlist.htm.
[9] Hyperbaric Oxygen Trust, http://www.fseng.demon.co.uk/hot4cp/index.html.
[10] See Hyperbaric Oxygen Therapy 4 Cerebral Palsy at http://www.jumpoint.iperweb.com/hot4cp/, and Mothers United for Moral Support (MUMS) at http://www.waisman.wisc.edu/~rowley/mums/index.htmlx, which offers an HBOT information packet (portions of this packet are at http://mondenet.com/~chrisck/).
[11] The schedule and speakers list for this conference is available at several HBOT web sites including http://members.home.net/anothercapitalidea/hot/conference.html.

Appendix A). Comparison of formal evaluations before and two weeks after treatment revealed statistically significant improvements in aspects of gross-motor and fine-motor functioning, as well as reductions in spasticity in hip adductors, hamstrings, and ankle plantar flexors. Significant improvements in walking and sitting were also reported on post-treatment parent questionnaires. Based on this pilot study, Marois and colleagues have now obtained a $1.2 million grant for a full double-blind trial.

Cerebral palsy (CP) was once thought to be predominantly caused by oxygen deprivation during birth and delivery ("birth hypoxia" or "fetal distress"). However, several large-scale studies have failed to find a strong correlation between birth hypoxia and the subsequent onset of CP (Naeye et al. 1989; Naulty et al. 1994; Nelson et al. 1998; Nelson and Ellenberg 1985; Nelson and Ellenberg 1986; Nelson and Grether 1998; O'Shea et al. 1998; Spinillo et al. 1997; Torfs et al. 1990).[12] Birth asphyxia does occur in some cases of CP, but many more cases are associated with risk factors such as prematurity and infection. However, this debate is irrelevant to the question HBOT's usefulness for CP: what matters is the presence of brain tissue hypoxia in children with CP (see section 1.1), and not whether the brain injuries in CP result from birth hypoxia. Brain hypoperfusion in CP has been demonstrated by two SPECT studies (Lee et al. 1998; Yamada et al. 1995).

1.4 SPECT studies show brain tissue hypoxia in Rett Syndrome patients

Rett Syndrome (RS) is a severe neurodevelopmental disorder that almost exclusively affects females (see Appendix C).[13] To date, five independent SPECT studies of RS patients have been published. Each of these studies found hypoperfusion and reduced blood flow (see section 1.1) in the frontal lobes and midbrain:

- Bjure et al. (1997) compared 16 RS girls and 1 RS woman with 16 normal children, and found hypoperfusion in the frontal lobes and parts of the midbrain (appearing no later than age 3 or 4) compared to the controls.
- Burroni et al. (1997) compared 12 RS girls with 12 normal children, and found global cerebral hypoperfusion in the RS girls compared to the controls.
- Lappalainen et al. (1997) found hypoperfusion in 11 of 13 RS patients, in all brain structures except the occipital lobes, and most strongly in the frontal lobes.
- Uvebrant et al. (1993) compared 9 RS girls and 1 RS woman (all but three under age 5) with 10 age-matched controls, and found hypoperfusion in the frontal lobes, midbrain, and upper brainstem.
- Nielsen et al. (1990) compared 7 RS girls with 9 normal children, and described the distribution of cerebral blood flow in the RS group as "very similar to the distribution of brain metabolic activity in infants of a few months of age." RS patients showed a 30% lower antero-posterior flow ratio than the control group.

[12] See news article at http://www.mylifepath.com/article/iac/100052184.
[13] See the International Rett Syndrome Association web site at http://www.rettsyndrome.org.

The locations of the observed hypoperfusion (frontal lobes and midbrain) are consistent with the locations of the brain regions normally responsible for functions that are abnormal in RS, particularly motor planning and autonomic nervous system control.

1.5 HBOT may produce long-term improvements in brain perfusion and function in girls with Rett Syndrome

As with most cases of cerebral palsy (see section 1.3), the brain tissue hypoxia observed in RS (see section 1.4) is probably not caused by respiratory hypoxia (see discussion of this distinction in section 1.1). RS is a disorder of early brain maturation, rather than an injury to developed brain structures as seen in cases of stroke or head trauma. Neurological and neuroanatomical abnormalities have been identified in RS (see Appendix C), but it is not known which of these abnormalities are primary causal factors in the disorder. Some of these abnormalities may be secondary consequences, as the brain attempts to adapt to the primary abnormalities.

The outcome of abnormal brain maturation in RS is similar in many ways to the outcome seen in both traumatic brain injury and cerebral palsy. In particular, SPECT scans show hypoperfusion in one or more brain structures. Accordingly, there is reason to believe that HBOT may improve brain perfusion in RS patients by the same mechanisms that it improves brain perfusion in other brain-injured patients (see section 1.2) and cerebral palsy patients (see section 1.3). The clinical profile of RS overlaps substantially with the profile of disabilities seen in patients with CP and hypoxic brain injuries. Given this overlap, it should be useful to look to therapies for brain injuries as a source of potential help for girls with RS.

It is noteworthy that in children with cerebral palsy who benefited from HBOT, treatments were given years after the events which led to their brain injuries. These children missed many milestones of development and brain maturation, and yet HBOT was able to help their brains re-establish functions that normally develop at a much earlier age. Children with Rett Syndrome are in a similar position to children with CP, in that HBOT treatments are usually possible only after years of milestones have been missed. Since HBOT is helpful to CP children in early or middle childhood, years after the age at which they should have achieved certain developmental milestones, it could similarly be helpful to girls with RS.

2. An appropriate pediatric protocol reduces HBOT risks to minimal levels

Like many substances, oxygen can be either therapeutic or toxic depending on dosage. Not all applications of hyperbaric oxygen are therapeutic, and therefore not all HBO should be referred to as HBOT. In particular, **"low-pressure" HBOT** at 1.5 or 1.75 ATA is very different from **"high-pressure" HBO** at 2.0 ATA or higher (see Appendix A). The safety and intensity of HBO are determined by the following factors:

- preparatory measures (assessment for contraindications)
- session protocol (pressure, duration, and rate of compression/decompression)
- safety measures and patient monitoring during treatment
- chamber certification and operator training
- session frequency and overall treatment duration

When properly developed based on research and clinical experience, a pediatric HBOT treatment plan and session protocol can address the following concerns (Kindwall 1995c; Santamaria et al. 1995; Thombs and Martorano 1995; Waisman et al. 1998):[14]

- General contraindications
- Physical safety and comfort
- Oxygen toxicity to the central nervous system
- Oxygen toxicity to the pulmonary system
- Free radical production
- Visual side effects
- Auditory side effects
- SPECT scan risks

Appendix D addresses each of these concerns in detail, and includes a detailed review of the literature on each side effect. To summarize that Appendix, there is no evidence that any side effects are associated with low-pressure HBOT (1.5 or 1.75 ATA).

3. Pediatric protocol summary

(Please read the Disclaimer on page 1)

The following protocol is currently used by most private clinics and research teams using HBOT to treat children with cerebral palsy.

Preparatory Measures. Pneumothorax should be ruled out by a chest examination or chest x-ray (see Appendix D1). Bilateral myringotomies may be performed to prevent ear barotrauma, but in most cases this procedure is unnecessary (see Appendix D7).

Chamber and Safety. The construction and maintenance of the hyperbaric chamber must be properly certified (as by the American Society of Mechanical Engineers, ASME), and the operator properly trained. Items or materials which could cause sparks or static

[14] The full text of the Waisman et al. article is at http://www.pediatrics.org/cgi/content/full/102/5/e53.

electricity must not be taken into the hyperbaric chamber. All clothes must be 100% cotton. In general, HBOT is extremely safe when administered by a trained operator in a certified chamber. According to Dr. Philip James, individuals in the United Kingdom (outside of formal hospital settings) have administered over 1.3 million hours of HBOT treatment over the past 17 years without a single safety incident.

Session and Treatment Protocol. HBOT should be administered in daily or twice daily sessions of 60 minutes at 1.5 or 1.75 ATA (see Appendix A). The chamber should be compressed and decompressed slowly, over the course of 15 minutes. The patient must be continuously monitored for symptoms of oxygen toxicity (see Appendices D3 and D4) and barotrauma (see Appendix D7).

Evaluation and Treatment Duration. The patient should be assessed for clinical improvement after an initial program of 40 HBOT treatments, although in some cases improvement may begin up to a month after treatment. If possible, this clinical assessment should be supplemented with a comparison of SPECT scans taken before and after the treatments. This comparison should be made by an experienced medical doctor who specializes in nuclear medicine, ideally one with direct experience in comparing pre- and post-HBOT SPECT scans. One such doctor is Dr. Michael Uszler, the Medical Director of Nuclear Medicine at the UCLA Medical Center-Santa Monica Hospital in Santa Monica, California.

4. Conclusion

In all likelihood, formal clinical trials of HBOT as an investigational treatment for Rett Syndrome will be conducted only if several case studies “go first” and demonstrate significant improvements in brain perfusion and clinical function. Some medical doctors might object to this course of action, considering untested therapies for developmental disability to be unethical because of cost or the risk of creating “false hope” in parents. However, in the case of HBOT, there is a solid theoretical and empirical basis for real hope. Informed parents (not their doctors) should be the ones to make decisions for their children that balance risk, cost, and a reasonable expectation for clinical improvement.

The administration of HBOT should pose minimal risks to RS patients when a highly safety-conscious and low-pressure protocol is used (see sections 2 and 3). The potential benefits to RS patients, their families, and society are enormous. HBOT has been shown to improve brain perfusion in patients with brain injuries and cerebral palsy, and girls with RS have neurological and clinical abnormalities which overlap substantially with the abnormalities of these patients. Therefore, the hypothesis that HBOT will improve brain perfusion and clinical function in Rett Syndrome patients deserves investigation.

Appendices

Appendix A. Hyperbaric Oxygen Therapy (HBOT)

Hyperbaric oxygen therapy (HBOT) involves the inhalation of 100% oxygen inside a chamber pressurized above sea-level atmospheric pressure. Hyperbaric chambers are classified as monoplace or multiplace, according to their capacity. Most monoplace chambers are pressurized with 100% oxygen, while multiplace chambers are pressurized with air and patients wear a hood supplied with 100% oxygen.

Following the basic gas laws of chemistry, HBOT substantially increases the amount of oxygen dissolved in all bodily fluids including blood plasma, cerebrospinal fluid, and lymph. This hyper-oxygenation greatly outweighs the minor reduction in oxygen delivery via hemoglobin that results from blood vessel constriction. The effects of the resulting hyper-oxygenation include the short-term delivery of additional oxygen to otherwise under-oxygenated tissues, improved long-term blood flow to these tissues via the growth of new blood vessels (angiogenesis), and possibly a direct stimulation of metabolic processes in idling neurons (see section 1.1).

The pressure and duration of a HBOT session are the major determinants of its efficacy and safety (see section 2). Normal atmospheric pressure at sea level is referred to as 1.0 **atmospheres absolute** (**ATA**), and HBOT therefore involves pressures greater than 1.0 ATA. HBOT sessions are sometimes informally referred to as "dives," because diving underwater similarly subjects the body to pressures greater than 1.0 ATA. HBOT at 1.5 ATA is equivalent in pressure to diving to a depth of 16.5 feet of seawater (fsw). Most studies showing adverse effects from HBOT have involved pressures substantially higher than 2.0 ATA (equivalent to 33 fsw), and many animal studies have used pressures of 5.0 ATA (equivalent to 132 fsw) or higher.

The therapeutic effect of HBOT in the treatment of many acute conditions is quite rapid. By contrast, the therapeutic effect of HBOT on chronic conditions such as brain injury is rarely immediate. In the studies reviewed in this paper (see sections 1.2 and 1.3), a series of 40 or more treatments was typically required, with some subjects receiving as many as 130 treatments. For chronic conditions, therefore, HBOT is truly a therapy whose speed and outcome cannot be precisely predicted. This situation is shared with most other standard therapies for brain injury, such as physical therapy, occupational therapy, and speech therapy. HBOT is not a cure, and should supplement existing therapies rather than replacing them.

Recent reviews of HBOT and its generally accepted medical indications have appeared in mainstream Western medical journals including the British Medical Journal (Leach et al. 1998),[15] the New England Journal of Medicine (Tibbles and Edelsberg 1996), Advances in Pediatrics (Santamaria et al. 1995), and the Journal of the American Medical Association (Grim et al. 1990).[16] The primary textbooks of the field are the Textbook of Hyperbaric Medicine (Jain 1990) and Hyperbaric Medicine Practice (Kindwall 1995b). The

[15] The full text of this article can be found at http://www.bmj.com/cgi/content/full/317/7166/1140.
[16] The full text of this article can be found at http://www.livelinks.com/sumeria/oxy/hot.html.

third edition of the Jain textbook has just been published, and includes chapters on HBOT, brain injury, and SPECT scanning.[17]

As a result of extensive civilian and military research, HBOT has become a standard, Medicare-reimbursable treatment in the United States for fourteen medical conditions and classes of injury (Jain 1990, Ch. 8). The Undersea and Hyperbaric Medicine Society[18] (UHMS) produced this list of HBOT indications, and in the opinion of some HBOT researchers, their management of the list has been both over-conservative and idiosyncratic. Some indications have been added with minimal research support, while other indications (such as brain injury) have been omitted despite significant research support. The American College of Hyperbaric Medicine[19] (ACHM) is another organization that oversees hyperbaric medicine in the United States and advocates for issues including Medicare reimbursement.

For economic and other reasons, formal research on new applications for HBOT has progressed slowly in the USA. By contrast, HBOT is used widely in many other countries. In England, HBOT is used to treat children with cerebral palsy and adults with multiple sclerosis (over 1.3 million treatment hours during the past 17 years, according to Dr. Philip James). According to Dr. Neubauer, stroke patients in West Germany are routinely given a three-week course of intensive HBOT to supplement their physical rehabilitation. In some areas of Italy, a physician can have his or her license revoked for failing to use HBOT when indicated. Over 1000 HBOT chambers are in use in Russia and China. Many positive HBOT studies have been published in Russian and Chinese medical journals, and also at the Eleventh International Congress on Hyperbaric Medicine held in China in 1993 (Li and Cramer 1995).

Ongoing research in the United States is now extending the indications for HBOT, particularly to conditions that involve poor oxygenation, hypoperfusion, and tissue hypoxia in the brain (Bakker 1992; James 1997; Kindwall 1993; Neubauer and Walker 1998).[20] The field of hyperbaric medicine appears to be poised on the brink of a new expansion, based on valid research rather than the anecdotal reports and claims of the past.

Appendix B. Single-Photon Computed Emission Tomography (SPECT)

Single-photon computed emission tomography (SPECT) was developed in the late 1980's as an outgrowth of positron emission tomography (PET)[21]. Unlike computed axial tomography (CAT) and magnetic resonance imaging (MRI), which image anatomical structures in the brain, the SPECT scan reveals the functional structure of the brain as it metabolizes a radioactive tracer that has been injected into the bloodstream. Variations in regional cerebral blood flow (rCBF) reflect regional differences in metabolic activity in the brain, making the SPECT scan an ideal tool for identifying areas of brain hypoperfusion (Neubauer et al. 1992).

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[17] See publisher information at http://www.hhpub.com/catalogue/Jain2.html.
[18] http://www.uhms.org
[19] http://www.hyperbaricmedicine.org
[20] The full text of the Kindwall article can be found at http://www.livelinks.com/sumeria/oxy/kindwall.html.
[21] An online medical course about SPECT is at http://www.bae.ncsu.edu/bae/courses/bae590f/1995/scarfone/.

SPECT studies of brain perfusion in normally developing children have revealed significant maturational changes during childhood (Chiron et al. 1992). According to Chiron et al., "Cognitive development of the child seems to be related to changes in blood flow of the corresponding brain regions." Similar maturational changes have been observed in PET studies of glucose consumption in the brain. Kuzniecky (1996) summarizes these maturational changes as follows:

> "At birth, metabolic function is high in the thalamus, central region, and cerebellar vermis. At 3 months, activity increases in the striatum, occipitoparietal regions, and cerebellar cortex, with the frontal lobes remaining relatively hypometabolic. At 12 months of age, metabolic activity reaches adult values. From ages 2 years to age 6 to 7, values are double those seen in adults. Thereafter, glucose consumption decreases progressively to adult values, which are reached by age 15 years. These changes should be considered when studies at different ages are interpreted." (p. S15)

The technology and interpretation of SPECT scans remain an active area of research. For recent reviews of the application of SPECT to pediatrics, abnormal brain development, and epilepsy, see Kuzniecky (1996), Barkovich and Kuzniecky (1996), Gordon (1996), and Treves and Connolly (1995).

Appendix C. Rett Syndrome (RS)

Rett Syndrome (RS) is a severe neurodevelopmental disorder that almost exclusively affects females (Armstrong 1997; Naidu 1997).[22] Estimates of the prevalence of RS range between 1 in 10,000 to 1 in 22,000 girls. The cause of RS is not yet known, but current research is focusing on a genetic abnormality on the X chromosome, which causes reduced brain size, microcephaly, and abnormalities in neural growth factors, the cholinergic system, and the serotonergic system.

Although RS is not caused by a traumatic or oxygen-related brain injury (see section 1.1), the clinical profile of RS overlaps substantially with the symptoms of children with these brain injuries. Shared symptoms include hypotonia and/or spasticity, seizures, EEG abnormalities, ataxia (poor motor control), and apraxia (poor motor planning). In addition, five separate SPECT studies of RS girls have shown characteristic patterns of brain hypoperfusion (see section 1.4).

Rett Syndrome was once thought to be a degenerative disorder, like Parkinson's Syndrome, but it is now recognized as a neurodevelopmental disorder involving delayed and arrested brain maturation. In terms of behavioral consequences, the primary neuroanatomical abnormality in RS has been described by Niedermeyer (1998) as a "frontal lobe – motor cortex disconnection due to the lack of inhibitory influences" (p.83). According to Niedermeyer, these abnormalities in frontal and motor cortex produce common RS symptoms including a lack of mental drive (apathy), difficulties with perceptual integration, loss of speech, ataxia, apraxia, grasp reflexes, and repetitive hand movements.

[22] See the International Rett Syndrome Association web site at http://www.rettsyndrome.org.

Abnormalities in the midbrain and brainstem may also be responsible for the abnormal autonomic nervous system control commonly seen in RS, in the regulation of functions including breathing (Kerr 1992), sleep, peripheral circulation, and bowel motility. Almost all RS girls have characteristic EEG abnormalities (Niedermeyer et al. 1997; Sheth 1998; Trauner and Haas 1987), although fewer than half have true seizures (Glaze et al. 1998). Additional neurological abnormalities in RS are reviewed in Murakami et al. (1992), Naidu (1992), and Wenk (1997).

Appendix D. Review of HBOT Side Effects (none associated with low-pressure HBOT)

D1. General contraindications

HBOT is absolutely contraindicated in patients who have pneumothorax or are taking certain chemotherapeutic or antibacterial medications (Kindwall 1995b, Chapter 4). Pneumothorax and spontaneous pneumothorax are extremely rare in children, and an external examination can reveal asymmetries in breath sounds that might indicate an undiagnosed pneumothorax.

Caution must be observed when administering HBOT to patients with several types of conditions. Neurological conditions include seizure disorders and high fever, which could increase the risk of oxygen-induced seizures during HBOT (but see Appendix D3). Pulmonary conditions include upper respiratory infections and emphysema, in which trapped gases in the lungs could expand during decompression. Kindwall (1995c) states that these concerns can be addressed by adding or adjusting medication, or by suspending treatment when the problems will resolve in a few days. None of these conditions are contraindications to HBOT when an appropriate protocol is followed.

D2. Physical safety and comfort

A major safety consideration in HBOT is fire prevention. Fire can occur only in the presence of fuel, oxygen, and an ignition source. Oxygen is a powerful fire accelerant, but oxygen itself does not burn except in rare circumstances. FDA-approved HBOT protocols must be followed to eliminate ignition sources and minimize potential fuel. These protocols strictly prohibit items or materials which could cause sparks or static electricity from being taken into the hyperbaric chamber. For example, all clothes must be 100% cotton, and no electronic devices are permitted. Chamber fires are very rare in the history of HBOT, occurring to date only in cases of chambers outside the United States which have not been properly certified (as by the American Society of Mechanical Engineers, ASME).

Psychological issues including claustrophobia and boredom are affected by the type of hyperbaric chamber used, since chambers vary in their spaciousness and the extent to which the patient can see outside. All multiplace chambers and even some monoplace chambers are sufficiently large that an adult can accompany a young pediatric patient. Distractions such as music and television can be helpful, transmitted through the walls or windows of the chamber. Many of the accepted medical indications for HBOT are equally or

more common in children as in adults, and the logistics of pediatric HBOT are therefore well understood (Santamaria et al. 1995; Thombs and Martorano 1995; Waisman et al. 1998).[23]

Physical comfort issues such as increased temperature and humidity can be regulated by the chamber operator during treatment. Temperature increases with pressure according to Charles Law, and water vapor exhaled by the patient can increase humidity. To regulate these levels, the oxygen or air in the chamber is periodically replaced during treatment.

D3. Oxygen toxicity to the central nervous system

When administered in sufficient quantity, oxygen is toxic to the central nervous system **(CNS)** and can provoke seizures. Even if convulsions do occur, HBOT research and clinical experience have shown no residual effects to the patient (even at high pressures), as long as physical trauma is avoided.

The intensity with which HBOT delivers oxygen to the body is determined by the pressure, session duration, session frequency, and overall number of sessions (see section 2). HBOT does not produce CNS oxygen toxicity when levels of these factors are sufficiently low, and this should be true even in a patient at increased risk for seizures (such as in Rett Syndrome). For reviews of oxygen toxicity and HBOT, see Clark (1995) and Jain (1990).

In a study with brain-injured patients, who are at increased risk for seizures, Holbach and colleagues (1977) administered HBOT session protocols at 1.5 and 2.0 ATA (see Appendix A). They found that at 2.0 ATA, AVD (arteriovenous difference) oxygen levels decreased, while at 1.5 ATA they remained constant and the glucose oxidation quotient (GOQ) remained normal. Consistent with Holbach et al.'s study, Clark's (1995) review reports that oxygen toxicity from HBOT can cause grand mal convulsions at pressures of 2.0 ATA or greater. Based on these findings, Neubauer and colleagues use a protocol of either 1.5 or 1.75 ATA for 60 minutes, once or twice daily (see sections 2 and 3).

HBOT protocols include monitoring for the standard symptoms of CNS oxygen toxicity, such as sweating followed by nausea, vomiting, apprehension, shortness of breath, tunnel vision, or muscle twitching (Kindwall 1995c). At the appearance of these symptoms, the oxygen supplied to the chamber or hood can be replaced with normal air, thereby quickly reducing the oxygen level to the patient without the need to quickly decompress the chamber.

D4. Oxygen toxicity to the pulmonary system

Exposure to hyperbaric oxygen can produce respiratory symptoms including intratracheal and bronchial irritation, chest tightness, cough, and a reduction in vital capacity. Again, the degree of oxygen toxicity to the pulmonary system is determined by the pressure, session duration, session frequency, and overall number of sessions (see section 2). The concept of a Unit Pulmonary Toxicity Dose (UPTD) has been developed to quantify the relationship between these HBO factors and pulmonary oxygen toxicity. Tables of depths,

[23] The full text of the Waisman et al. article is at http://www.pediatrics.org/cgi/content/full/102/5/e53.

durations, and UPTD levels have been produced based on extensive experience with diving and HBOT applications (Clark 1995). According to Clark, "doses of 600 UPTD given in two treatment sessions have been administered on a daily basis with no evidence of cumulative toxicity." When HBOT is administered at 1.75 ATA for 60 minutes, the UPTD is only 129. This level is substantially below the daily threshold of 600 UPTD. Pulmonary oxygen toxicity is therefore not a concern when HBOT is given daily or twice daily at 1.75 ATA.

Many girls with Rett Syndrome have respiratory abnormalities while awake, including hyperventilation and/or breathholding (Kerr 1992). For divers, breathholding during rapid ascent can cause a potentially fatal air embolism. However, there is no risk of air embolism during normal decompression from a HBOT session, because the chamber is decompressed gradually over the course of 15 minutes.

D5. Free radical production

The HBO research literature provides substantial evidence that high-pressure HBO (≥2.0 ATA; see Appendix A) can cause the production of harmful free radicals (Jamieson et al. 1986). Narkowicz, Vial et al (1993) exposed human subjects to HBO at 2.7 ATA and found evidence of increased free radical levels in blood samples using electron spin resonance (ESR) spectroscopy. These levels returned to baseline in blood samples taken within 10 minutes of cessation of HBO, indicating the successful action of antioxidant defenses. Yamaguchi, Stewart et al. (1992) exposed rabbits to HBO at 2.5 ATA and found ESR spectra indicating significant free radical production. The same results were found by Torbati, Church et al. (1992), who exposed rats to 5.0 ATA.

At low pressures such as 1.5 or 1.75 ATA (see section 3), there is no evidence that HBOT produces significant levels of harmful free radicals. In a study of free radical formation and lipid peroxidation in rat brain *in vitro*, Dirks and Faiman (1982) found that exposure to HBO as high as 2.5 ATA did not cause any significant increase in free radical formation compared to untreated controls.

Antioxidants may play a role in preventing the damage from free radicals associated with high-pressure HBO. Etlik, Tomur et al. (1997) showed that administration of vitamins E and C significantly reduced oxidative damage to erythrocytes in rats exposed to HBO for 60 minutes daily at 2.8 ATA for 45 days. A deficiency of antioxidants can also lead to certain types of damage from free radicals during high-pressure HBO. Stone, Henderson et al. (1989) found that rats fed a diet deficient in vitamin E and selenium had retinal damage after exposure to HBOT (90 minutes at 3.0 ATA, 5 days/week for 4 or 15 weeks) relative to rats fed the same diet but not exposed to HBO. Finally, Kaelin, Im et al (1990) found that HBO increased the survival rate of skin flaps in rats. They concluded that HBO caused an increase in the activity of superoxide dismutase (SOD), an important antioxidative defense mechanism.

Some girls with Rett Syndrome have abnormalities of oxidative metabolism, including elevated serum levels of lactate and pyruvate (Haas et al. 1995a; Haas et al. 1995b). In the absence of these abnormalities, when the protocol in section 3 is used, the diagnosis of Rett Syndrome should not be a particular contraindication for the use of HBOT.

D6. Visual side effects

HBOT has been used to treat eye diseases including vascular insufficiency and hypoxic disorders of the anterior segment (see Jain 1990, Ch. 28), as well as retinitis pigmentosa.[24] However, with long-term or high-pressure courses of HBOT, adverse side effects on the visual system sometimes occur. These side effects are reviewed by Jain and by Kindwall (1995a).

Myopia (shortsightedness) is a temporary side effect sometimes seen after an extended course of 20 or more high-pressure HBOT treatments (≥2.0 ATA; see Appendix A), typically in older patients (Anderson and Farmer 1978; Lyne 1978; Palmquist et al. 1984; Ross et al. 1996). These effects are thought to be caused by oxidative free-radical damage to the lens of the eye, resulting in changes to its refractive index. It must be noted again that there is minimal risk of free-radical formation during low-pressure HBOT (see protocol in section 3). The myopic changes observed in these studies were as follows:

- Anderson et al: 1.6 dioptres (mean), observed in all seven subjects, after 40 120-minute sessions at 2.0 ATA.
- Lyne: 0.5 to 5.5 dioptres, observed in 18 of 26 subjects, after 4-52 weeks (mean 16) of daily treatment at 2.5 ATA for 90 minutes.
- Palmquist et al: 3.0 dioptres (mean), observed in all 25 subjects, but in 23 subjects only after 100 hours of HBO at 2.0 to 2.5 ATA.
- Ross: degree unknown, observed in only 2 of 8 subjects, after 20 120-minute sessions at 2.0 ATA.

Note that HBOT was administered at high pressures (≥ 2.0 ATA) in all four of these studies, and in three of the studies the sessions were quite long (90 or 120 minutes, not 60).

HBOT investigators disagree about the reversibility of HBOT-induced myopia. Most report that any changes reverse themselves after the cessation of treatment, within six weeks (Kindwall), three months (Lyne), or six months (Jain). However, Ross et al. claim that any changes are reversed more slowly. All investigators concur that HBOT-induced myopia is not fully reversible in a small minority of patients. An additional finding by Palmquist (1984) was that of the 15 subjects who had clear lens nuclei prior to treatment, 7 developed nuclear cataracts with reduced visual acuity during treatment. However, these effects were noted only after at least 150 hours of HBOT at 2.0 to 2.5 ATA. In the Lyne study, no subject who started with a clear lens developed cataracts, and in those subjects who had pre-existing cataracts, no worsening was seen during treatment or at long-term follow-ups. Kindwall reports that he has never seen new cataracts arise during HBOT treatment.

[24] See article and references at http://www.focusnewsletter.org/hperbari.htm.

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D7. Auditory side effects

Barotrauma. The most common side effect of HBOT is barotrauma to the middle ear (Kindwall 1995c). Barotrauma is a familiar experience to anyone who has felt discomfort during descent in an airplane due to an inability to "clear one's ears." Barotrauma can also occur in blocked cranial sinuses, or in dental work containing an air bubble. In general, the term refers to pain caused by a difference in pressure between any sealed air-containing cavity in the body and the ambient pressure outside the body.

Under ordinary circumstances, pressure differentials between the middle ear and outside air are equalized through the Eustachian tubes, which connect the middle ear to the mouth. The Eustachian tubes are ordinarily closed, but can be opened briefly by yawning, swallowing, or using one of several "ear clearing" methods such as the Frenzel maneuver (closing the mouth, pinching the nostrils shut, and "blowing").[25] Pressure must be equalized continuously in both ears during a dive or compression, because the openings to the Eustachian tubes are squeezed shut and cannot be opened when the pressure differential exceeds about 0.25 ATA (equivalent to diving about four feet in sea water).

Barotrauma is avoidable in almost all cases by using a very slow rate of compression and carefully monitoring the patient for signs of discomfort. In a multiplace hyperbaric chamber, an adult can help a child clear their ears easily by drinking water. The slow compression rate is particularly important when the patient is unable to communicate verbally, as is the case with infants and many developmentally disabled children. If discomfort becomes apparent, the pressure can be temporarily decreased, equivalent to a short "ascent", which allows the patient to clear their ears before compression resumes. The standard practice used by Neubauer and most private clinics is to compress from 1.0 ATA to 1.5 or 1.75 ATA over the course of 15 minutes (see section 3). This compression rate is equivalent to diving in sea water at the very slow rate of about one foot per minute. If mild barotrauma does occur and lead to crying, Neubauer and several clinic operators report that the crying quickly leads to pressure equalization (personal communication).

Barotitis. If a pressure differential inside the middle ear continues to increase and is not equalized, pain increases and the patient can develop barotitis. Barotitis is marked initially by irritation of the eardrum (tympanic membrane), and can progress to symptoms including free blood in the middle ear and rupture of the eardrum (usually via a small perforation which heals spontaneously within 10 to 14 days, according to Kindwall (1995c)). Beuerlein et al. (1997) conducted a prospective study of 30 patients undergoing HBOT, 19 of whom were able to clear their ears ("autoinflaters") and 11 of whom were comatose or intubated and therefore could not clear their ears ("non-inflaters"). Autoinflaters underwent a mean of 19 HBOT treatments and noninflaters underwent a mean of 11 HBOT treatments, at either 2.0 ATA for 120 minutes or 2.4 ATA for 90 minutes. Noninflaters showed a higher incidence of barotrauma (91%) compared to autoinflaters (37%). Patients were also examined before and after treatment to check for possible hearing loss. No patient showed any significant changes in extended high-frequency audiometry tests. Some changes in distortion product otoacoustic emission (DPOAE) tests were observed in 4 of 15 autoinflaters and 2 of 7 noninflaters, but these changes did not correlate with any extended high-frequency

[25] For an excellent guide to these earl-clearing methods, see http://weber.u.washington.edu/~ekay/MEbaro.html.

audiometry changes and were of unknown significance. Note again that the HBOT pressures and durations used in this study substantially exceeded the protocol in section 3.

Myringotomy. In patients who are unable to clear their ears by the methods described above, a myringotomy (also called tympanostomy) is sometimes performed prior to HBOT (Kidder 1995; Riley et al. 1997). This procedure is conducted by an otolaryngologist using local anesthetic. In the procedure, a small incision is made in each eardrum with a myringotomy knife, or a small tube ("T-tube") is inserted through each eardrum (T-tubes are also commonly used in some children with chronic ear infections, to allow fluid drainage from the middle ear). Ordinarily, T-tubes are expelled within a few weeks, and the eardrum perforation heals completely without complication. In a recently developed variation of the myringotomy procedure, the incision can be made with a laser (Vrabec et al. 1998).

The myringotomy procedure has several risks and side effects, in addition to the possibility of direct damage to the inner ear if the procedure is not performed properly by a trained otolaryngologist. In a study of 45 patients who received bilateral myringotomies prior to HBOT, Clements et al. (1998) found that 17 patients (38%) experienced complications, with most having more than one complication. Otorrhea occurred in 13 patients (29%), and persistent tympanic membrane perforations occurred in 7 patients (16%). Earlier studies have shown slightly lower complication rates, with otorrhea occurring in 5-20% of cases and persistent tympanic membrane perforations in less than 5% of cases (Luxford and Sheehy 1982; McLelland 1980). If myringotomy is performed with incision only (no placement of T-tubes), there is a risk that the perforations will close prematurely and pressure will no longer be automatically equalized.

Due to the potentially significant risks from barotrauma coupled with the risks and side effects of myringotomy, there is substantial variation in clinical practice about whether myringotomy should be performed routinely before HBOT (Capes and Tomaszewski 1996). Many medical centers use topical nasal decongestants as an alternative to routine myringotomy, but Carlson et al. (1992) have shown that topical nasal decongestants are not effective against middle ear barotrauma.

The consensus among Neubauer and several clinic operators (personal communication) is that in the absence of specific indications of Eustachian tube dysfunction, myringotomy should not be performed routinely before HBOT. Instead, treatment should begin with very slow compression rates and careful monitoring, as described earlier in this section. If the patient shows signs of discomfort and/or symptoms of barotitis, treatments should be halted until T-tube myringotomies can be performed. This protocol was also recommended in the "Ask the Expert" column of a recent issue of the newsletter of the Undersea and Hyperbaric Medical Society (Farmer 1998).

Another possible alternative to myringotomy is a commercial product called "Earplanes," manufactured by Cirrus Air Technologies and distributed by Mellen Medical Products.[26] Earplanes are special earplugs containing a ceramic pressure regulator. This regulator approximately halves the rate at which the eardrum is exposed to pressure changes, thereby allowing additional time for pressure in the middle ear to equalize.

[26] For more information, see http://www.earplanes.com/earplane.htm or call 1-800-649-4372.

D8. SPECT scan risks

SPECT scans (see Appendix B) are now a widely accepted diagnostic tool in neurology, and are believed to have no significant risks or side effects. The radioactive tracer used in the procedure has a half-life of only a few hours, and therefore stays in the body only briefly. As with magnetic resonance imaging (MRI) the patient must remain motionless for the duration of the scan, so most children undergoing the procedure require sedation. The risks of sedation depend on the particular sedative used, and should be discussed with an anesthesiologist.

D9. HBOT and cancer

Feldmeier et al. (1994) concluded that the available data do not support the idea that HBOT has a cancer-causing or cancer-promoting effect.[27] Their review article counters the suggestion that the formation of new blood vessels stimulated by HBOT might have a cancer-causing or cancer-promoting effect in patients with a pre-existing tumor or propensity for cancer.

If anything, HBOT may actually have a cancer-protective effect. HBOT is commonly used with cancer patients to treat osteoradionecrosis and other treatment-related tissue damage. A few studies have followed such cancer patients and looked at their tumor recurrence rates (Granstrom 1996; Marx 1995). Recurrence rates were consistently lower in patients who received HBOT than in those who did not.[28] This is certainly not conclusive evidence that HBOT has anti-cancer properties, but it is interesting nonetheless.

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[27] This review is also discussed at http://www.baromedical.com/newsletter/97q105.html.
[28] These studies are also discussed at http://www.baromedical.com/newsletter/97q106.html.

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