

Treating Children with Autism Using Hyperbaric Oxygen Therapy

Summary:

In more than 7,000 facilities worldwide, hyperbaric oxygen therapy (HBOT) has been used for decades to heal serious infections, non-healing wounds, and to treat divers with the bends. An increasing number of these hyperbaric medical centers are also successfully treating neurological injuries and disease such as autism. Recent studies have suggested that a common link among children with autism is chronic inflammation of areas of the brain and gut, and that the anti-inflammatory effects of HBOT may make it one of the safest and most effective ways to help resolve the debilitating effects of autism.

In Hawaii, according to the most recent Department of Education statistics, nearly 1 in every 74 children with special needs¹ enrolled in public schools in Hawaii are children who fall within the autism spectrum, and direct DOE services for these children are estimated to cost over \$30 million per year. Since 1992, statistics show the prevalence of children in Hawaii diagnosed with autism has increased by over 2700%.² Geneticists researching autism have suggested that this may be related to a genetic pre-disposition among Pacific Islanders and Asians. According to a 2004 US Dept of Education report³, Asian American and Pacific Islander students (who ethnically make up more than 65% of all children enrolled in public school in Hawaii) were also 1.24 times more likely to receive special education and related services for autism than all other racial/ethnic groups combined.

Resources for the evaluation and treatment of autistic children in Hawaii are very limited. For example, there are currently only two registered DAN! doctors (trained specialists in autism) in the entire state, and functional imaging SPECT scans commonly used to understand the ongoing neuropathology are virtually unavailable for children in Hawaii. As the only hyperbaric treatment facility in the state commonly providing therapy to children with autism, we have documented consistently positive reports of improvement in autistic patients following HBOT. In order to provide a more objective basis for the use of HBOT to treat these children, however, a study using less subjective reporting methodology was needed.

This study evaluated the effects of 20 hours of hyperbaric oxygen therapy on the functional outcomes of twenty children (4 females and 16 males) ranging in ages from three to seven years, each with a clinically proven diagnosis of autism, and living in Hawaii. Pre-HBOT baseline and post-HBOT follow up evaluations were performed by experienced autism testing clinicians in the community, independent of the treating facility. Testing outcomes proved statistically significant clinical improvements in 100% of the children in one or more of the following areas: Communications, Social Interaction, Imagination/ Creativity, Stereotyped Behaviors and Global Assessment of Functioning (GAF) scores.

Background:

More than 50 years ago, Dr. Leo Kanner, a psychiatrist at Johns Hopkins University, wrote the first paper using the term 'autism' to describe a group of children who had severe social, behavioral and communication problems. In a review of his original case descriptions, it appears that he was especially interested in these children because their constellation of symptoms was so unusual.

Today, those same symptoms are more commonplace than many other childhood diseases, and are being recognized at an earlier and earlier age by enlightened physicians and well-informed parents who are unassailable advocates on behalf of their children. To put this in perspective, a recent Hawaii Autism Prevalence Report makes the comparison of rates of autism to rates of cancer. This telling comparison, which is based upon figures from the Centers for Disease Control, shows that autism is now more prevalent in the United States than all forms of cancer combined.

Autism is probably most accurately characterized as a neurodevelopmental disorder with a complex etiology. In the science of epidemiology, environmental factors are those determinants of disease that are not transmitted genetically. Environmental factors also may determine the development of disease in those genetically predisposed to a particular condition. Stress, diet, exposure to chemicals, toxins, pathogens, and radiation are common environmental factors that determine a large segment of non-hereditary disease. If a disease process is found to be the result of a combination of genetic and environmental influences, it is considered to be *multifactorial*. Autism is a classic example of a disease with a multifactorial etiology, in that it is believed to manifest itself only in children who have both a genetic predisposition and also an exposure to some kind of environmental trigger.

Although there is great debate among experts about the actual causes of autism, it is accepted among health statisticians that a consistently rising prevalence trend (as we have seen in Hawaii) implicates environmental factors in the causality of autism. A steady prevalence trend over time (which we have not seen) would be more likely to implicate genetic factors in the causality of autism.

The fact that genes, alone, are not a deciding factor in the development of autism was shown in a recent multi-million-dollar genetics study which gathered and studied data on over a thousand families with at least two children diagnosed with autistic spectrum disorder.⁴ Comprehensive genetic screening was used to evaluate each family's genetic makeup, but in the final report, the researchers reported that "None of our linkage results can be interpreted as 'statistically significant'..."

In another recently published study, a percentage of the group studied showed an increased sensitivity to mercury than the general population, thus supporting the hypothesis that autistic children may carry a genetically increased susceptibility to certain environmental toxins, including mercury.⁵ ON a note important to Hawaii, a large 2006 published study found that ***Pacific Islanders, Asian, Native Americans, and multiracial subjects studied had a higher prevalence of elevated blood mercury than all other racial/ethnic participants.***⁶ A five-year study of over 100,000 people found that Asians and Pacific Islanders also have the highest levels of iron in their bloods of all the racial/ethnic groups screened.⁷ Researchers involved in the study have suggested that Asians and Pacific Islanders may carry a genetic mutation which allows their bodies to process heavy metals differently than other races. This is significant in the world of autism research since heavy metal exposure is one of the most often discussed factors as a possible environmental trigger for the disease.⁸

In a remarkable related study just released by researchers from the Harvard Medical School⁹, heavy metal toxicity as a cause of oxidative stress and its effect on children with autism was discussed in detail. This research focused on specific biological “markers” of oxidative stress in the brain. These markers were found to be elevated by 68.2% in patients with autism when compared to tissues from those without autism. The study notes that “Mercury strongly associates with oxidative stress...(Mercury) induced oxidative stress results in oxidative modification of DNA, protein and lipids, as well as inhibition of the enzymes crucial for the brain development. Thus elevated levels of mercury in brain potentially interfere with normal brain development.” Oxidative stress is caused when oxygen-based processes in the body are not adequately supported or balanced (oxidants vs. antioxidants). ***Multiple studies since 2001 have demonstrated the effectiveness of hyperbaric oxygen therapy to decrease oxidative stress overall, and improve the function of proteins (HSB70) in the body which naturally protect against oxidative stress.***¹⁰

As the incidence of autism has increased over the past 20 years, many other important clinical studies have contributed to an increased understanding of how the disease manifests itself and how to define and recognize the symptoms. This has led to earlier identification and assessment in affected children, thereby affording parents and physicians the opportunities to provide earlier interventions. Unfortunately, many of those effective interventions were poorly understood and not readily available until just a few years ago.

Finally, in 2004 a paradigm-changing study in the world of autism research encouraged researchers to focus less on finding the cause or etiology of autism, and instead to find more effective ways to treat the resulting biological effects of the disease itself. Drs. Vargas, et al. found that although autism manifests itself in a wide variety of symptoms, the common factors among autistic patients studied ***of all ages*** was a chronic inflammatory process which affected both the brain and immune system functioning.¹¹

Shortly thereafter, Dr. Andrew Wakefield, and his colleagues in Texas, published a study of gastrointestinal symptoms in 148 young children with a primary diagnosis of autistic spectrum disorder (ASD). Much like the Johns Hopkins University researchers, they found that chronic inflammation (this time in the gut, manifesting itself as acute and chronic gastrointestinal symptoms) was a “characteristic pathological finding in children with ASD.”¹² A number of related studies with similar findings have since been published supporting this finding.

The Johns Hopkins University researchers were clear in their recommendation that “(b)ecause this neuroinflammatory process appears to be associated with an ongoing and chronic mechanism of CNS dysfunction, potential therapeutic interventions should focus on the *control of its detrimental effects* (while preserving reparative benefits) and thereby eventually modify the clinical course of autism.”

As autism researchers around the globe studied these findings, they began to evaluate available treatments to resolve the chronic inflammation which acts as the basis of so many of the challenges faced by affected children.^{13, 14}

The use of corticosteroids (Prednisone), Minocycline (an antibiotic with antiinflammatory properties), and nonsteroidal anti-inflammatory drugs have all been studied in the treatment of autism^{15, 16, 17}, but all have significant negative side effects and some are even contraindicated for use in children because of the potential for serious complications (e.g., Reye's syndrome).

Further review of available treatments in search of a safer way to address chronic neuroinflammation in autistic children led to evaluations of decades of neuro recovery research in the field of hyperbaric medicine^{18, 19, 20}

Hyperbaric oxygen therapy (HBOT) has a well-known anti-inflammatory effect²¹, and has been shown to measurably improve immune function²². This is important because studies have suggested that there is a genetic relationship between autism and immune system dysregulation.²³ Multiple studies have shown that oxidative stress can be significantly reduced with HBOT through the upregulation of antioxidant enzymes. HBOT increases blood flow in the brain in areas where blood flow is depressed, improves the function of existing mitochondria cells, and increases the production of new cells, as well as improving neurotransmitter abnormalities.²⁴ All of these results are crucial in the comprehensive treatment of a child with autism.

Clearly one of the most important factors to consider when treating these fragile young patients is that hyperbaric oxygen therapy is one of the safest and lowest risk medical treatments available today. One of the best proofs of this fact may be Dr. James Neubrandner's clinic in Edison, New Jersey, through which over 25,000 hours of hyperbaric therapy have been safely and effectively provided to children with autism. The safety factor is widely recognized by those who assign and evaluate medical risk. As Paul Harch, MD notes in his book, *The Oxygen*

Revolution, “Possibly one measure of the (safety of hyperbaric oxygen therapy) is the minimal rate ascribed by malpractice insurance companies to HBOT, which falls into one of their lowest ranking (risk) categories.”²⁵

Perhaps the most comprehensive review of the medical science supporting the use of HBOT to treat autism was performed at the University of Virginia by Daniel Rossignol, MD,²⁶ and was published in 2006. In it, Dr. Rossignol reviewed the effects of hyperbaric oxygen therapy on the most common pathophysiology found in autism, including neuro inflammation, gastrointestinal inflammation, cerebral perfusion, detoxification enzyme function, immune system dysregulation, and six other commonly affected areas. **In all of these areas of pathophysiology critical to the resolution of autism in children, HBOT was found to have a clinically important positive effect.**

Study Objectives:

Examine the effects of hyperbaric oxygen therapy on fifteen key behaviors commonly evaluated in children with autism and autistic spectrum disorder.

Participant Selection:

The study included 20 children with DSM-IV diagnosis of Autistic Disorder, confirmed with Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R) testing. Pre-HBOT and post-HBOT testing was performed by experienced autism testing clinicians in the community, independent of the treating facility.

The children included 4 girls and 16 boys ranging in age from 3-7 years of age, with a median age of 5 years 7 months at the start of treatment. Two of the participating boys were identical twins, and one of the boys had an unaffected fraternal twin brother at home. Fifteen of the children came from either an Asian or Pacific Islander ethnic background. All of the children had been diagnosed for at least a year or longer prior to participation in our study.

The mean age of the biological mothers at the time of birth was 34.6 years, with four of the mothers aged 40 or over. The mean age of the biological fathers at the time of birth was 37 years, with eight of the fathers age 40 or older when their child was born.

Although exact individual childhood immunization schedule information was unavailable for each of these children, the state of Hawaii follows the CDC recommended protocols for childhood vaccinations, and it is believed that each child received immunizations consistent with that protocol, beginning with the Hepatitis B vaccine within 48 hours of birth. Unlike states such as California, Delaware and Iowa, the state of Hawaii does not regulate or restrict the amount of the mercury-based preservative thimerosal used in immunizations.

Two of the children were born as the result of in-vitro fertilization. Eighteen of the children had lived the majority of their lives in Hawaii, with 17 residing on Oahu and one on Maui. Six of the children were from military families, reflecting the high percentage of U.S. military personnel residing on the island of Oahu in Hawaii. There was no placebo or control group.

Eligibility Criteria:

- 1) Participants were at least 3 years old at the start of the study, and did not reach their 8th birthday by completion of treatment.
- 2) Both genders were eligible, and we did not seek to balance the number of boys and girls. It was just by chance that our numbers accurately reflect the reported 1:4 ratio of incidence between girls and boys with autism.
- 3) Participants had a DSM-IV diagnosis of Autistic Disorder, confirmed with a complete schedule of testing including Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview - Revised (ADI-R). All pre-study testing was completed within 30 days of each child's first hyperbaric treatment.
- 4) All participants were HBOT naive prior to treatment.
- 5) All participants completed 20 hours of HBOT within 6 weeks of their start.
- 6) Post-study testing was completed within 30 days of the final HBOT session.
- 7) Parents chose the independent testing clinicians from a list of recognized and experienced resources available in the community, and made their own testing appointments. None of the clinicians had any prior experience working with children who had completed a course of HBOT. Although the HBOT sessions were provided without charge, the costs of pre-study testing (ADOS and ADI-R) and post-study testing (same tests plus The Childhood Autism Rating Scale or CARS) were paid for by the participants' families.

Exclusion Criteria:

Our exclusion criteria followed a model suggested by autism research Daniel Rossignol, M.D.:

- 1) DSM-IV diagnosis of Pervasive Developmental Disorder other than Autistic Disorder, including PDD-NOS (Pervasive Developmental Disorder, not otherwise specified) and Asperger's Syndrome
- 2) Chronic ear infections, with last incidence less than 3 months ago
- 3) Uncontrolled asthma, especially anxiety-induced asthma
- 4) Uncontrolled seizures
- 5) Inability to equalize ear pressure
- 6) Fragile X syndrome
- 7) Currently undergoing chelation therapy
- 8) Juvenile diabetes

Methodology:

For this study, all participants received comprehensive ADOS and ADI-R testing no more than 30 days prior to beginning HBOT.

Of the 20 children participating in our study, 60% (12) were on concurrent diet (primarily gluten- and casein-free) therapy, and 55% (11) were taking various forms of supplements. Although several of the children had undergone previous chelation therapy, none were participating in concurrent chelation therapy throughout the course of treatments.

Each child was treated at the Hyperbaric Medicine Center, in Honolulu, Hawaii. Protocols used included 20 hours HBOT at 1.5 ATA of pressure using only 100% oxygen. Each child was treated in the same Fortius 420 hard sided monoplace chamber. Although this chamber is customarily used with hyperbaric hoods, we used tight-fitting pediatric aerosol masks instead because compliance was much greater when compared with the hoods. These masks were sealed (no open holes in the face portion), and had a colorful dinosaur face molded into the mask. Each child chose their own mask at the beginning of their treatment sessions, and used that same mask each time they were treated.

All children were accompanied during treatment sessions by a parent or adult caregiver. In one case where there were identical twin boys participating in the study, they were actually treated at the same time throughout the majority of their sessions. This was made possible because the Fortius 420 has two output connectors for oxygen flow within the same chamber, making it possible to connect two separate masks at the same time.

It should be noted here that we chose to use the hard-sided chamber because the protocols required that we use 100% oxygen and 1.5 ATA of pressure - neither of which are available in the soft inflatable chambers. Soft chambers have been used successfully in both research (Dr. Daniel Rossignol's study) and therapy programs (Dr. James Neubrandner's Center in Edison, New Jersey, uses a prescribed combination of both hard-sided chambers and inflatable chamber protocols for each child). However, soft sided chambers generally cannot be used at pressures above 1.3 ATA, and require the use of oxygen concentrators which produce a lower percentage of therapeutic oxygen than the 100% we needed for this study. Furthermore, our past experience treating children with autism has been most successful using the 100% O₂ and 1.5 ATA protocols recommended by many experts in the field. Therefore, only the hard sided monoplace chamber was used.

Each participant was required to complete their 20 hours of therapy within a six week period. 55% (11) of the children completed at least a portion of their treatments using longer periods of time in chamber per session - 90 to 120 minutes. Of these children, more than half (6) showed a statistically greater improvement than the average, with total ADOS scores improving at least 7 points overall. Of interesting note, the child who showed the most significant improvements in all areas of evaluation completed nearly all of his treatments in 90-minute increments over the course of only 14 days.

Six of our participants completed their therapy in 15 days or less after the first treatment. Of these 6 children, 50% (3) showed a statistically better scoring level of improvements overall than the mean. Based on these results, we would recommend that additional studies investigate whether more significant improvements can be achieved overall if the HBO treatments are completed on accelerated schedules.

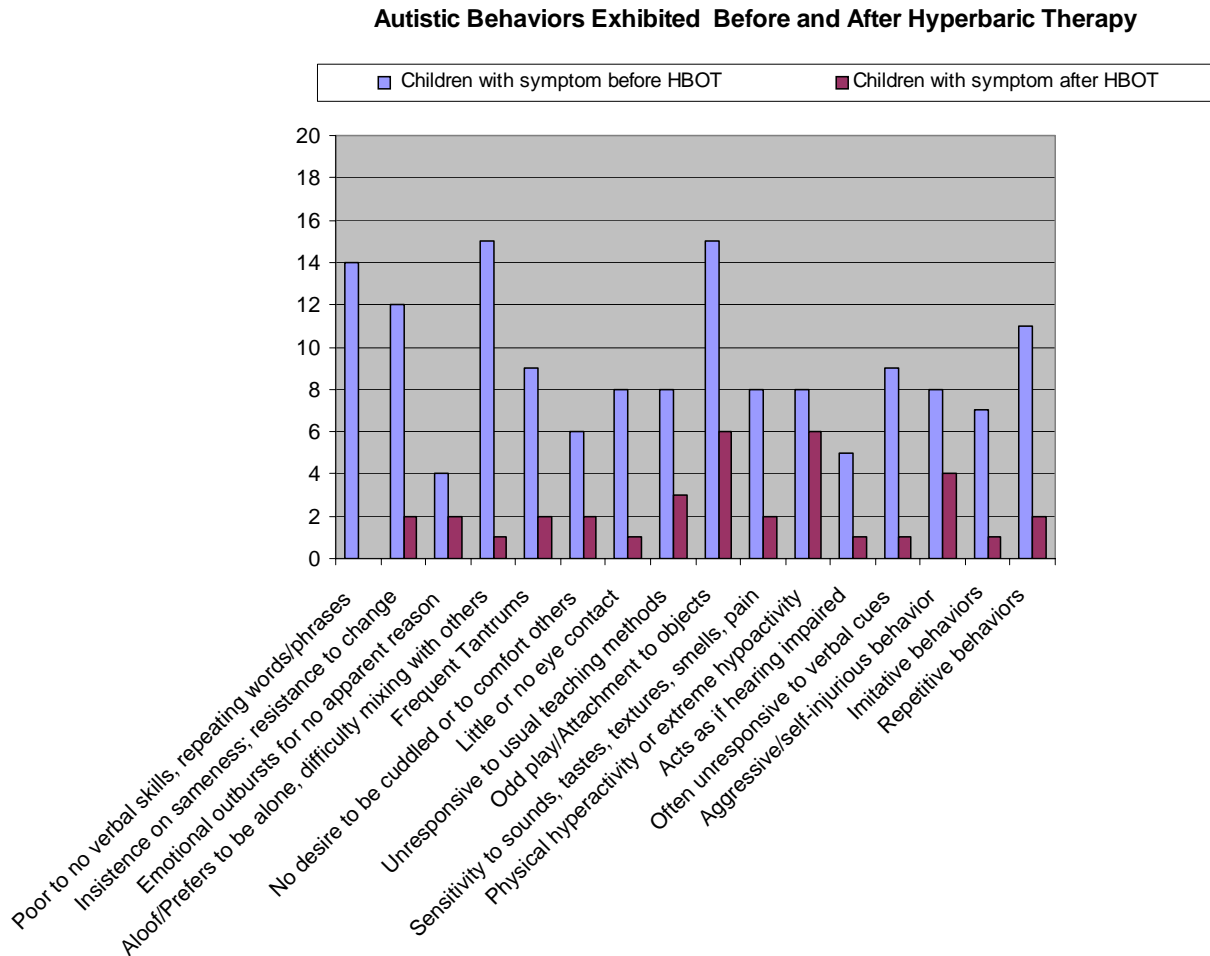
After completion of therapy, the children were retested using the same testing criteria, with the addition of a CARS profile with comments. Results were measured solely based upon those noted in the independent testing reports. No subjective data or clinical observations recorded during the course of treatment by the treating facility's medical staff was included or available to the testing clinicians.

Although the independent testing clinicians knew that the children were receiving hyperbaric therapy, they were purposely given no direct information or instructions as to what specific autism symptoms to evaluate or discuss in their reports, other than to follow traditional ADOS and ADI-R testing criteria and guidelines.

Sixteen common areas of autism symptomology were evaluated and compared using standardized autism testing tools in each of the 20 children before and after HBOT. The 16 specific symptom categories included those found in the areas of communication, social interaction, imagination and creativity, and stereotyped behaviors. Each child was also evaluated using a Global Assessment of Functioning (GAF) scores.

Results:

Results of the study are illustrated on the graph below.



1. Verbal Skills: 70% (14) of the children exhibited impaired to no verbal skills in the pre-treatment testing and/or demonstrated moderate to frequent repetition of words and phrases. 100% (14) of the children exhibiting these symptoms showed significant measurable improvements. 40% (8) of all of the children in our study moved from a strictly “Autistic” rating (the most severe) into the less severe “Autistic Spectrum” category. **20% (4) of all of the children in our study actually improved to a point that where they were no longer on the autistic spectrum in the area of communications and verbal skills.**

2. Insistence on sameness; resistance to change: 60% of the children (12) showed insistence on sameness and a resistance to change in the pre-treatment testing. 83% (10) of those children showed measurable improvements in this common autism symptom area.

3. Emotional outbursts (laughing, crying, etc.) for no apparent reason: 20% (4) of the children exhibited notable challenges with repeated emotional outbursts in the pre-treatment phase. 50% (2) of these children improved as rated in post-therapy testing.

4. Aloof; prefers to be alone; difficulty mixing with others - This was one of the most common symptoms noted among our study group in the pre-therapy testing 75% (15) of the children exhibited these symptoms to a degree that it was specifically notable in the pre-therapy testing phase. 93% (14) of these children showed significant measurable improvements after HBOT. Post-therapy testing noted that improvement in this symptom area affected the childrens' ability to interact with peers in school, relate to siblings better and feel more comfortable in situations where they are exposed to a large number of strangers, such as in recreational and team sport activities.

5. Frequent tantrums: This was an important findings in 45% (9) of the study children prior to their treatments. 77% (7) of these children experienced measurable improvements in this area according to the post-therapy testing. Not unexpectedly, this was one of the most often cited improvements resulting from the therapy by the parents, themselves.

6. No desire to be cuddled or to comfort others: 30% (6)of the children in our study regularly exhibited these symptoms according to the pre-therapy testing reports. 66% (4) of these children exhibited measurable improvements in this area. The development of empathy for others around them and concern for the feelings of others is an area that can fail to develop in children with autism even much later in life, and can result in difficulty functioning in a workplace or in interpersonal relationships. Therefore, improvement in this area can be of vital importance.

7. Little or no eye contact: 40% (8) of the children routinely made little or no eye contact in the pre-therapy testing phase. 87% (7) of these children improved enough after therapy to change their original findings in this area. For the facility staff, this is often one of the earliest subjective symptoms of improvement in the children we treat with autism.

8. Unresponsive to usual teaching methods: 30% (6) of the children exhibited measurable challenges in this area of the pre-treatment evaluations. 83% (5) showed measurable clinical improvement in the post-testing evaluations. This finding is important as improvement often means that the child can be integrated into a more common classroom setting.

9. Sustained odd play; spins objects or self; unusual attachment to objects: 40% (8) of the children exhibited this behavior for scoring purposes in the pre-therapy testing period. 62.5% (5) improved enough to change their scoring related to this common symptom.

10 Apparent over-sensitivity or under-sensitivity to sounds, tastes, textures, smells, fear or pain: 75% (15) of the children in our study exhibited one or more of these areas of increased or decreased sensitivities prior to HBOT. 60% (9) of these children experienced significant measurable improvements as noted in the post-treatment testing evaluations.

11. Physical hyperactivity or extreme hypoactivity: 40% (8) of our study participants exhibited significant measurable symptoms in these areas prior to treatment. 75% (6) of those children showed substantial improvements in the post-therapy testing following their hyperbaric therapy. It is important to note here that anecdotally, we have sometimes seen a temporary increase in hyperactivity between the 15th and 20th hour of therapy in the children we have treated for a full 40 hour course of therapy outside of this study. In the study children, however, only 10% (2) of the children showed any increase in hyperactivity and that increase was characterized as moderate. In addition, one of the children actually showed a measurable improvement in this area as compared to her pre-therapy evaluation.

12. Acts as if hearing impaired; often unresponsive to verbal cues: 45% (9) of our study children were shown to have measurable challenges in these areas prior to taking part in the hyperbaric therapy protocol. 88% (8) of these children tested at improved levels after treatment, with better responses overall.

13. Aggressive/self-injurious behavior: 40% (8) of our participants had either a demonstrated habit or significant history of aggressive or self-injurious behaviors in the pre-therapy testing period. This included skin scratching and scraping, biting, hitting, kicking with the intent to harm another, and similar destructive or injurious behaviors. 50% (4) of these children showed significant improvements or a complete cessation of these behaviors after completing their therapy.

14. Imitative behaviors: 35% (7) of the children participating in our study exhibited “frequent imitative behaviors” in their pre-therapy testing evaluations. 85% (6) of these children showed significant, measurable reduction in their most common imitative behaviors following hyperbaric therapy.

15. Repetitive behaviors: As one of the most recognizable symptoms of autism, it wasn't surprising that 55% (11) of the children participating in the study revealed typical repetitive behaviors in their pre-therapy testing evaluations. 81% (9) showed a marked reduction in these behaviors after therapy.

16. GAF: The Global Assessment of Functioning scale is a common psychological evaluation tool which measures the patient's overall social, psychological and (when appropriate) occupational functioning and coping skills against that of society at large. Fully 70% (14) of the children participating in our study showed increases in their GAF scores between the pre- and post-therapy testing. The remaining 6 children were all noted to have shown improvements, but not enough to change their overall Global Assessment of Functioning score.

Conclusions:

This study was conducted at the Hyperbaric Medicine Center located in Honolulu, Hawaii. Our interest in working with children with autism is long-standing, beginning with a play therapy and respite program which began nearly ten years ago. When hyperbaric therapy was added to the rehabilitative programs in 1992, one of the program's earliest patients was a child with autism.

To date, we have provided HBOT to more than 60 children with a primary diagnosis of autism or autistic spectrum disorder. Based upon very positive clinical experiences, we have come to expect generally good recovery results in children with symptoms similar to those who participated in our study. The detailed clinical testing performed before and after the course of treatment, however, provided significantly greater evaluation data than we have ever been able to observe previously, and the results have been deeply encouraging.

Communication: Of the children in our study, 70% (14) of the children exhibited improved scoring in the area of communication skills as tested with the Autism Diagnostic Observation Scale (ADOS). Of the remaining six children, five showed improvements during testing, but not enough to change their overall score. Although one child did not specifically show improvements which could be verified with testing, it was noted that the child was already high functioning with good verbal skills prior to treatment. *Perhaps most importantly, 4 of the 20 children in our study scored well enough to move out of the autistic spectrum in the area of communication after HBOT, and 8 of the children improved enough to move from strictly autistic (as scored in the ADOS) to autistic spectrum.*

Social Interaction: 80% (16) of the children showed improved scoring in the area of social interaction. 30% (6) of these children showed remarkably significant improvements of 4 or more ADOS scoring points. Of the remaining four children, two showed positive changes, but not enough to change their overall score. One of the children showed a negative scoring change in the area of reciprocal social interactions, but the testing clinician also noted that this child had recently lost two Skills Trainers with whom he had an emotional attachment, and that this may have affected his social interactions.

A second child also tested slightly lower in this one category, but the evaluating physician attributed this to the fact that the child did not want to engage in the ADOS activities when he was being observed rather than an actual negative change in symptoms. The physician notes that although the scoring did not reflect an overall improvement in the child's reciprocal social interaction skills, measurable improvements were noted in other important areas including interest in other children, interest in group play, sharing enjoyment, pointing and gesturing.

Overall in the area of reciprocal social interaction, 10% (2) of our study children improved enough to move out of the autism spectrum in this area altogether; and 25% (5) of the children moved from autistic into the autistic spectrum scoring realm.

Imagination & Creativity: In the area of imagination and creativity, 30% (6) of the children showed obvious improvements in scoring. 70% (14) of the children's overall scores remained unchanged in this area. *Anecdotally, it has been our experience outside of this study that when children go on to complete the usually recommended protocol of 40 hours of HBOT, we see the greatest improvements in imagination and creativity occurring somewhere after their 30th hour of treatment .*

Stereotyped Behaviors: In the area of stereotyped behaviors, 55% (11) of the children show measurable clinical improvements which was reflected in their scoring. 30% (6) of the children were reported to have shown improvements, but not enough to change their score in this area. 15% (3) of the children showed a slight (1 point) increase in stereotypical behaviors after HBOT. Two of the three children, however, improved to the point overall that they moved to the next lower level of impairment in all other categories. One of the three remaining children exhibited improvements in all other areas of evaluation except stereotyped behaviors, but not enough to change his overall scoring.

In summary, 100% (20) of the children involved in this study exhibited statistically significant measurable improvements in one or more of the ADOS scoring areas noted above and/or their Global Assessment of Functioning scale. The testing clinicians noted again and again that these areas of improved symptoms all represent important day-to-day, quality of life changes including: (1) better ability to cope with and participate in classroom settings, (2) better control of, or even in some cases, a complete cessation of tantrums, (3) less sensory challenges which resulted in, for example, a willingness to eat a wider variety of foods, less sensitivity to unexpected noises, (4) greater ability to focus (for example, one of the children sat through an entire school assembly for the very first time after treatment), (5) more interest in being cuddled, and in comforting others, (6) improvements in sleep habits, (7) accelerated learning and retainment of skills, and (8) improved levels of anxiety overall.

Discussion:

Hyperbaric oxygen is not a new treatment for children with neuro dysfunction. A review of the scientific literature shows that as early as the 1960s, studies have been published (Lancet, 1964)²⁷ demonstrating the positive effects of hyperbaric oxygenation on oxygen-deprived infants. More recently there have been very large research projects evaluating the use of HBOT to treat children with cerebral palsy. One of the largest (nearly 100 children) has been funded by the U.S. military, is a multi-year, randomized double blind study that is currently underway in Dayton, Ohio.²⁸ .

In simple terms, hyperbaric oxygen therapy is a medical treatment that helps the body heal itself by making oxygen available to tissues which are not receiving an adequate supply. In the case of children with autism, this appears to be due to a chronic inflammatory process which interferes with many complex brain functions that would normally occur without the inflammation. An analogy would be to imagine trying to focus and make decisions when one has a severe headache or upset stomach. It is difficult for most of us to function under these conditions. In children with the symptoms of autism, the frequent inability of their brain and digestive system to function properly causes a wide constellation of interrelated challenges which are difficult to overcome without intervention at the root level - improving the underlying inflammatory process.

Hyperbaric oxygen has a multilevel effect on the central nervous system: it reduces swelling of the inflamed tissues; it repairs the blood-brain barrier and stabilizes cell membranes. It also increases the ability of white blood cells to stabilize or “clean up” damaged areas and - perhaps most importantly - creates new blood vessels in areas where they are needed. This is a process called angiogenesis, and is vitally important to the resolution of the neurological symptoms manifested in children with autism. This is also important to maintain the long-term improvements gained though HBOT, because once the new blood vessels have grown into the damaged tissue areas of the brain, they are believed to become a permanent improvement. It is primarily why the resolution of symptoms seen during treatment tend to consistently remain after HBOT is completed.

The potential for permanent improvements is also a key factor in figuring the overall cost effectiveness of HBOT. According to Fighting Autism (www.fightingautism.org) a group that tracks autism prevalence and costs statistics, the annual cost of education, medical care and related services for a child with autism ranges from \$30,000 to \$65,000 a year, and these costs are generally borne by parents, health insurers, school systems, as well as state and federal government stake holders. The one time cost of 40 hours of HBOT in Hawaii is between \$6,000 and \$9,000, and since the effects are thought to be permanent, lasting throughout the child’s lifetime, it is expected that the one-time cost of therapy may be far offset by the savings in costs of current and future care.

Hyperbaric oxygen therapy is also important in the treatment of children with autism because it is effective in helping the body rid itself of excess heavy metals such as mercury. It is theorized that children with autism may have a genetic abnormality that causes a reduction in the normal levels of glutathione which is an important mercury-detoxifying agent in the body.²⁹ This makes it more difficult for their bodies to get rid of excess mercury such as that found in vaccines containing thimerosal.³⁰

Thimerosal is a preservative which contains nearly 50% ethyl mercury by weight. The FDA estimates that throughout the 1990s it was used in more than thirty licensed vaccines and other medications marketed in the US. During this time the vaccine schedule for infants included as much as 187 mcg of mercury in the first six months of life--far exceeding levels accepted as safe. Scientists have often noted that many symptoms of autism closely resemble those of mercury poisoning. Reportedly, thimerosal is no longer being added to most vaccines, and states which have taken the added step to ban its use (e.g., California) are, interestingly enough, beginning to see a drop in their state's autism rate.³¹

Although our study included only children in the 3-8 year age range, studies have shown that biomedical interventions (including HBOT) may be helpful even in older autistic individuals.³² Harvard's Martha Herbert, MD, PhD writes that "... *the awareness that the brain as well as medical conditions of children with autism may be conditioned by chronic biomedical abnormalities such as inflammation opens the possibility that **meaningful biomedical interventions may be possible well past the window of maximal neuroplasticity in early childhood because the basis for assuming that all deficits can be attributed to fixed early developmental alterations in neural architecture has now been undermined.***" [emphasis added] In simple terms, this means that even older children or autistic adults may be improved with treatment.

In Hyperbaric therapy, the baseline recommended protocols for treating an autistic child is 40 hours of treatment at 1.5 ATA of pressure using 100% medical grade oxygen. Even though our study was only able to treat each child for half (20 hours) of the protocol recommended number of treatments, the resulting improvements in symptoms were clearly apparent in all levels of testing. It should be noted that the protocol pressure used in the study - 1.5 ATA - was chosen because studies tracking glucose utilization and metabolic activity have shown it to be a pressure which is optimal for most brain support and repair.

Based upon prior experience treating children with autism, we expected that children who were most severely affected by their symptoms would see the most significant improvements. Instead, we found that the distribution of improved scores were fairly consistent among all of the children.

We also expected that our younger study patients (5.5 yrs and younger) would respond faster and show more significant improvements in their evaluation scores overall than our older (5.6 years and older) children. Although the testing results showed this to be true in most cases in the area of communication skills, our scores showed improvements consistently throughout all age ranges in the areas of social interaction, imagination & creativity.

In the area of stereotyped behaviors, two of the youngest children exhibited a slight increase in stereotypical behaviors, but in both cases the increase in minor stereotypical behaviors also accompanied an increased interest in a variety of important areas. The testing clinician noted that this increase interest "...provides the motivation for further development, and therefore the overall prognosis is greatly improved."

Early Diagnosis

Experts agree that early diagnosis is still the key to best recoveries overall for these children.^{33, 34, 35, 36, 37} Unfortunately, there are many practical obstacles to recognizing autism in a child at a very early age. It is important to understand that traditionally, the three behavioral domains of autism are not considered a medical problem (such as an infection or a wound would be), and may easily be overlooked for months or years. For example, social interaction problems can appear to be related to hearing impairments, and delays in language development can be written off as just a "late-talker." Several of the children in our study came from multi-lingual families, so initially there was a concern that this slowed their recognition of words. Consequently, the slow development of language skills may not have been reported as early as it otherwise might have been.

Paradoxically, the "insistence on sameness" of autistic children can also make them appear to be "easy" children, since they may make few demands. Further delays can occur once concerned parents have recognized that their child has serious developmental issues because the process of scheduling a formal clinical assessment can take months.³⁸

Over the years, many key definitions of autism specified the time for the onset of symptoms as 30 - 36 months.³⁹ Several of the children in our study were exhibiting alarming symptoms as young as 12 months of age. Of the 20 children participating in our study, all were clearly exhibiting classic autistic symptoms by age 27 months, with a median age of clearly recognized symptoms by 15.5 months.

Hyperbaric oxygen therapy is not a cure for autism. It may be, however, a way of ensuring the most complete recovery possible. Hyperbaric oxygen takes the "stress" off all the cells in the body by providing oxygen, a necessary component of every chemical and healing process, and allows the body to recover. Although the brain makes up less than 2% of the body's physical mass, about 20-30% of the body's consumption of oxygen occurs within the brain and

spinal cord. These areas are extremely sensitive and responsive to oxygen increases and support.⁴⁰ HBOT is generally considered the simplest, safest and most effective way known in the field of medicine to provide substantial extra oxygen support when needed.

The use of HBOT to treat children with autism has been somewhat hampered by a medical community perception that there is a lack of studies available to show how hyperbaric therapy works. In fact, over the years there have been over 30,000 studies worldwide relating to hyperbaric therapy, and many of them - especially in recent years - have been related to the treatment of neurological disorders.

Unfortunately, it is difficult to find the funding for large scale efficacy studies. Oxygen is considered a drug, and most drug studies in the United States are funded by major pharmaceutical companies. Since oxygen cannot be patented (thereby achieving some basis for future payments or reimbursement for costs), there is no financial incentive for these companies to invest in continuing hyperbaric research. This fact has made it difficult for parents and physicians to find the detailed study information they need. Fortunately, this is beginning to change as evidenced by Dr. Daniel Rossignol's studies and those of Dr. Paul Harch, Dr. Pierre Marois in Canada, Dr. Daniel Lacey's Dayton Study, Dr. Richard Neubauer, and many, many notable others.

One important result of these recent studies is a reminder that substantial improvements can be achieved most easily (1) by children within the autism spectrum when the children are young and (2) the behavioral and bio-medical issues are addressed through a comprehensive intervention program. ***This study - as well as practical clinical experience from other hyperbaric facilities around the world who treat children with autism - suggests that HBOT is an important component to a comprehensive intervention program in order to achieve fullest and most expeditious recovery for children with autism.***

Acknowledgment:

This study would not have been possible without the support of the owners and staff of the Hyperbaric Medicine Center, donations of oxygen from AirGas in Honolulu, and a generous private donation of a special monoplace chamber specifically used to treat our children.

1. Hawaii Department of Education's 17th Annual Superintendent's Report. 51% of Hawaii's children in public school (approx. 96,533) are considered "special needs" for DOE purposes. 1306 of these children are within the autistic spectrum requiring special education services. 96,533 special needs students divided by 1306 children with autism enrolled in public school equals a prevalence of 1 in 74 children with special needs in public school in Hawaii are listed as autistic.

2. Hawaii Public School Autism Prevalence Report School Years 1992 - 2003. *FightingAutism*, November 2004 - 59 children with autism were identified in 1992 as compared to 1306 children enrolled in Hawaii public schools, at least 87 in private schools, and 70 in the Department of Health's "Zero to Three" program today. Total in 2007 - 1463 children with autism identified as enrolled in public school, private school and pre-school programs.
3. U.S. Dept. Of Education, Office of Speical Education and Rehabilitative Services, 2004. Twenty-sixth annual report to Congress on the implementation of the Individuals with Disabilities Education Act, 2004, Vol. 1. Washington, D.C.
4. Mapping Autism Risk Loci Using Genetic Linkage and Chromosomal Rearrangements, The Autism Genome Project Consortium 2007, (18 February 2007) *Nature Genetics*, pp.39, 319-328
5. Geier, D., & Geier, M.; (2007). A Prospective Study of Mercury Toxicity Biomarkers in Autistic Spectrum Disorders. *Journal of Toxicology and Environmental Health, Part A* (Vol. 70, Issue 20, pgs. 1723 - 1730)
6. Hightower JM, O'Hare A, Hernandez GT, Blood Mercury Reporting in NHANES: Identifying Asian, Pacific Islander, Native American and Multiracial Groups. *Environ Health Perspect* 2006;114(2):173-5
7. Adams PC, Reboussin DM, Barton JC, McLauren CE, Eckfeldt JH, McLauren GD, et. al., (2005) Hemochromatosis and Iron-Overload Screening in a Racially Diverse Population, *New Engl J Med*. 2005;352:1769-1778
8. Holloway CE, Margolis M, George F. (2003, October 3-5) Heavy Metal Esposures, Developmental Milestones, and Physical Symptoms in Children with Autism. Fall Defeat Autism Now! Conference. Portland, OR
9. Sajdel-Sulkowska EM, Lipinsky B, Windom H, Audhya T, McGinnis W, Oxidative Stress in Autism: Elevated Cerebellar 3-nitrotyrosine levels. *Amer J Biochemistry Biotechnology* 2008; 4(2):73-84
10. Shyu WC, Lin SZ, Saeki K, Kubosaki A, Matsumoto Y, Onodera T, Chiang M, et al., Hyperbaric oxygen enhances the expression of prion protein and heat shock protein 70 in a mouse neuroblastoma cell line. *Cell Mol Neurobiol*. 2004 Apr;24(2):257-68
11. Vargas, DL, Nascimbene C, Krishnan C, Zimmerman AW, Pardo CA. Neuroglial activation and neuroinflammation in the brain of patients with autism. *Ann Neurol* 2005;57(1):67-81
12. Wakefield, AJ, et al., The Significance of Ileo-colonic lymphoid Nodular Hyperplasia in Children with Autistic Spectrum Disorder, *Eur j Gastroenterol Hepatol* 2006 May: 18(5):569-71
13. Al-Waili NS, Butler GJ, Effects of hyperbaric oxygen on inflammatory response to wound and trauma: possible mechanism of action. *Scientific World J* 2006; 6:425-41

14. James SJ, Cutler P, Melnyk S, et al. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism. *Am J Clin Nutr* 2004;80(6):1611-7.
15. Singh VK, Autism, Autoimmunity and Immunotherapy: a Commentary. AAPN, The Autism Autoimmunity Project Newsletter, vol.1, no.2, (Dec 1999)
16. Treatment of Childhood Regressive Autism with Minocycline: An Anti-Inflammatory Agent Active Within the CNS. National Institutes of Health Clinical Center, May 2007, sponsored by NIMH ClinicalTrials.gov Identifier: NCT00409747
17. Sangha S, Oviedo J, (2003) Over-the-counter nonsteroidal anti-inflammatory drugs and risk of gastrointestinal symptoms. *The American Journal of Gastroenterology* 98 (5), 1203–1204.
18. Harch PG, Neubauer RA, Hyperbaric oxygen therapy in global cerebral ischemia/anoxia and coma. In: Jain KK ed. *Textbook of Hyperbaric Medicine 3d Revised Edition* Seattle: Hogrefe & Huber Publishers; 1999:319-349.
19. Neubauer RA, James P, Cerebral oxygenation and the recoverable brain. *Neurol Res.* 1998;20 Suppl 1:S 33-36
20. Rossignol DA, A Prospective, Randomized, Double-Blind, Controlled Study on the Clinical Effects of Hyperbaric Therapy in Autistic Children, ClinicalTrials.gov Identifier: NCT00335790
21. Akin ML, Gulluoglu BM, Uluutku H, Erenoglu C, Elbuken E, Yildirim S, Celenk T, Hyperbaric oxygen improves healing in experimental rat colitis. *Undersea Hyperb Med* 2002;29(4):279-85
22. Saito K, Tanaka Y, Ota T, Eto S, Yamashita U. Suppressive effect of hyperbaric oxygenation on immune responses of normal and autoimmune mice. *Clin Exp Immunol* 1991;86(2):322-7
23. Becker KG, Freidlin B, Simon RM, Comparative Genomics of Autism, Tourette syndrome and autoimmune inflammatory disorders. [Http://www.grc.nia.nih.gov/branches/trb/dna/pubs/cgoatad.pdf](http://www.grc.nia.nih.gov/branches/trb/dna/pubs/cgoatad.pdf). 4/23/2003 (accessed 10/27/2007)
24. Veltkamp R, Siebing DA, Heiland S, Schoenfeldt-Varas P, et al. (March 2005) Hyperbaric oxygen induces rapid protection against focal cerebral ischemia. *Brain Research* 1037;1-2:134-138 doi:10.1016/j.brainres.2005.01.006
25. Harch, P.G., McCullough V, (2007) *The Oxygen Revolution*. New York, Hatherleigh Press
26. Rossignol DA, Hyperbaric oxygen therapy might improve certain pathophysiological findings in autism, *Med Hypotheses* (2006), doi:10.1016/j.mehy.2006.09.064
27. Hutchison JH, Kerr MM, Williams KG, Hopkinson WI. (1963) Hyperbaric Oxygen in the resuscitation of the newborn. *Lancet* Nov 16;2:1019-22

28. "An Evaluation of the Therapeutic Effectiveness of Hyperbaric Oxygen Treatments on Children with Cerebral Palsy, A randomized, double blind, study to determine if hyperbaric oxygen treatments (HBOT), using 100% oxygen at 1.5 ATA of pressure can improve the physical condition of children (ages 3 to 8 years) who have cerebral palsy (CP). Study involves 94 children diagnosed with spastic cerebral palsy from the Cerebral Palsy Clinic and Departments of Neurology at The Children's Medical Center and Wright-Patterson Medical Center. Study funded by DOD \$1,775,175.00. Completion date expected to be November 2009. Principal Investigator, Dr. Daniel J. Lacey, The Children's Medical Center, Dayton, Ohio. Contact: Ronald G. Gfell M.A., QMRP ResCare Western Ohio at rgfell@rescare.com
29. Hornig M, Chian D, Lipkin WI (2004) Neurotoxic effects of postnatal thimerosal are mouse strain dependent. *Molecular Psychiatry* June 2004:1-13
30. James SJ, Slikker III W, Melnyk S, New E, Pogribna M, Jernigan S. Thimerosal Neurotoxicity is associated with glutathione depletion: protection with glutathione precursors. *Neuro/Toxicology* 26 (2005) 1-8
31. Geier MR, Geier DA, (2003) Thimerosal in childhood vaccines, neurodevelopmental disorders, and heart disease in the United States. *J Am Physicians Surg* 8;1:6-11
32. Herbert M, Large Brains in Autism: The challenge of pervasive abnormality. *The Neuroscientist*, Vol. 11, No. 5, 2005
33. Dawson G, Osterling J. Early intervention in autism. In: Guralnick MJ, ed. *The Effectiveness of Early Intervention*. Baltimore, MD: Paul H. Brookes Publishing Co; 1997:307-326
34. Hurth J, Shaw E, Izeman SG, Whaley K, Rogers SJ. Areas of agreement among effective practices among programs serving young children with autism spectrum disorders. *Infants Young Child*. 1999;12:17-26
35. Lovaas OI. Behavioral treatment and normal education and intellectual functioning in young autistic children. *J Consult Clin Psychol*. 1987;55:3-9
36. McEachin JJ, Smith T, Lovaas OI. Long-term outcome for children with autism who received early intensive behavioral treatment. *Am J Ment Retard* 1993;97:359-372
37. Smith T, Lovaas OI. Intensive and early behavioral intervention with autism: the UCLA young autism project. *Infants Young Child*. 1998;10:67-78
38. Blaxill MF, (2004) What's going on? The question of time trends in Autism. *Public Health Reports* (Nov-Dec 2004) 119:536-551
39. Rapin I, (1997) Autism. *N Engl J Med* 1997;337:97-104
40. Jain, K. & Fischer, B. Oxygen in physiology and medicine, C.C. Thomas, Springfield, IL. 1989, 376 pages.

