

James A. Neubrandner, MD
USAAA 2007 International Conference

**Hyperbaric Oxygen Therapy for Children with
Autistic Spectrum Disorders**

**Written for the USAAA Annual International Conference
Denver, Colorado, August 2007**

Foreword: The following manuscript demonstrates irrefutably from collective observations of over 100,000 treatment hours by my colleagues and me that hyperbaric oxygen therapy is a valuable treatment option for children with autism. Historically, any positive results seen were reported by clinicians using pressures greater than 1.5 atmospheres with 100% oxygen. However, approximately 80% of the results reported below were obtained by the use of soft chambers with low oxygen concentrations and low pressures. Many of the concepts and explanations you are about to read are shared by my colleagues. On the other hand, as a disclaimer for them, my concept of 3 general mechanisms of action and the protocols I currently use, based on over 20,000 treatment hours in my clinic following this logic, may not be shared by all. Nonetheless, each of us is in agreement that hyperbaric oxygen therapy is a valuable tool for the treatment of autism, that it is safe, that it provides at least some benefit for the majority of the children, that its benefits for children with autism may be due to additional factors not necessarily present in other diseases or disorders, and that treatment should not be delayed while waiting for science and research to catch up with what we see clinically to be a powerful biomedical adjunct to all the other therapies being used.

In my clinic, two of the most powerful treatments now commonly used for children on the autistic spectrum were discovered by accident – methylcobalamin (methyl-B₁₂) and hyperbaric oxygen therapy. This paper focuses on the use of oxygen under pressure as a powerful treatment modality for children on the spectrum. Interestingly, for children with autism, there appears to be a synergistic effect between the two.

Hyperbaric oxygen therapy is *classically defined* as the inhalation of 100% oxygen at greater than 1 atmosphere absolute (ATA) in a pressurized chamber. This definition is now *popularly defined* as the inhalation of varying degrees of oxygen at greater than 1 atmosphere absolute (ATA) in a pressurized chamber. *Conventional wisdom* has stated that unless one receives HBOT in a multi-chamber or hard chamber with 100% oxygen at atmospheric pressures equal to or greater than 1.5 ATA, little or no benefit will be seen. However, as history has

James A. Neubrandner, MD

shown repeatedly throughout the years, ***convention is only convention until challenged, proven wrong, and then changed.*** Such is the case with HBOT and autism where both high and low pressure treatments produce results.

In my practice approximately 80% of children respond to HBOT to some degree, especially if they continue their treatments, and probably because they are also being treated with methyl-B₁₂. I have found that *HBOT is a treatment, not a cure* and that continued *treatment sets* of sessions actually build upon any previous treatment sets of sessions therefore providing a *cumulative beneficial effect*, much like the educational process builds upon what was learned in the past in order to learn even more for the future. Essentially any of the symptoms common to autism have the potential to be helped by HBOT. However, certain benefits seem to be more common than others or more intense when present. Some of the notable “top 20” include language, awareness, independence, self confidence, “presence” (putting action to their new found awareness), self motivation, and improved bowel function. The two most common negative side effects are increased hyperactivity and stimming. Children receiving HBOT also show *positive-negative behavior changes* that are disturbing to parents who do not understand that such changes are *good things, not bad*. Positive-negative behaviors are most commonly the result of a generalized increased awareness whereby the child feels or wants more control in life. The associated positive events are manifested with stronger opinions about life, greater self assertiveness, self assuredness, self confidence, and much more independence. However, the ways a child may express these things are not always positive and often include a host of negative behaviors, a few examples being assertiveness, periods of increased frustration, mood swings, and being uncooperative. As a general rule, these *positive-negative behaviors* are only present when a parent, teacher, or therapist *places a demand* on the child to which the child does not want to comply. A common example is for a child to have a tantrum or become more noncompliant when a parent tells the child to put something down that he is doing because it is time to do something else. Also as a general rule, as the child continues to improve these symptoms lessen or disappear.

I recommend HBOT for all my patients because there is scientific evidence that increased pressure, independent of the concentration of oxygen, decreases inflammation and also that any concentration of oxygen under any increased amount of pressure will allow more oxygen to dissolve into the extracellular fluids of the body (plasma, lymph, cerebrospinal fluid, and interstitial fluid) thereby allowing more oxygen to reach the cells and eventually affect the organelles and intracellular biochemical reactions. Because *dissolved oxygen* is not confined to a hemoglobin molecule, it can go wherever “body water goes” and therefore reach “deeper tissues” more easily and more consistently than ever before.

A few of the multiple mechanisms demonstrating how HBOT may work for children with autism was comprehensively described by Dr. Dan Rossignol. A

James A. Neubrandner, MD

summary of these specific mechanisms is shown below along with a couple others that have been suggested. They include:

1. *Angioneogenesis from the addition of oxygen:*
2. *Angioneogenesis from the removal of oxygen:*
3. *Increases in blood flow independent of new blood vessel formation,*
4. *Decreasing levels of inflammatory biochemicals:*
5. *Up-regulation of key antioxidant enzymes and decreasing oxidative stress:*
6. *Increased oxygenation to functioning mitochondria:*
7. *Increased production of new mitochondria from HBOT.*
8. *Bypassing functionally impaired hemoglobin molecules, the result of abnormal porphyrin production, thereby allowing increased delivery of oxygen directly to cells:*
9. *Improvement in immune and autoimmune system disorders:*
10. *Decreases in the bacterial/yeast load found systemically and in the gut:*
11. *Decreases in the viral load found systemically and possibly decreases in a viral presence that may exist in the intestinal mucosa:*
12. *Increases in the production of stem cells in the bone marrow with transfer to the CNS:* Studies have shown that HBOT increases the production of stem cells in the bone marrow and that transfer of stem cells to the central nervous system is possible.
13. (Theoretical only) *Direct production of stem cells by certain areas in the brain.*
14. *Increased production and utilization of serotonin:*
15. (Theoretical only) *The possibility that oxidation may help rid the body of petrochemicals.*
16. (Theoretical only) *The possibility that oxidation may help rid the body of mercury and heavy metals.*

[For a more complete explanation of these mechanisms, refer to and Dr. Rossignol's paper (in press) entitled Hyperbaric Oxygen Therapy Might Improve Certain Pathophysiological Findings In Autism, and the chapter I've written for the 2007 3rd edition of Dr. Jaquelyn McCandless's book, Children with Starving Brains]

In addition to these 16 *specific mechanisms* that may be playing various roles in autism, I suggest that 3 *general mechanisms* of action may also be acting in concert or synergistically. These 3 mechanisms include: a) *increasing the total concentration of oxygen per treatment;* b) *increasing the total time of treatment with lower oxygen concentrations and lower pressures;* c) *increasing pressure independent of oxygen concentration.* Though these three concepts are not new, the way that I suggest they interact and how I apply them are my hypotheses, my opinions, my treatment protocols, and do not necessarily reflect those of my colleagues.

Relatively fewer and fewer oxygen molecules reach their target tissues as the concentration of oxygen molecules originally found in the alveoli of the lungs travels to arteries to arterioles to capillaries to cells to intracellular organelles.

James A. Neubrandner, MD

Because hemoglobin very quickly reaches its maximum saturation capacity, *any additional oxygen present under pressure is dissolved into plasma, lymph, cerebrospinal fluid, and interstitial fluids*. This is one of the primary reasons that hyperbaric therapy has the potential to work so effectively for so many children. Interestingly, only 0.3% of the oxygen that is presented to the lungs will ever reach the mitochondria! Because parents and most physicians cannot calculate the “millimeters of mercury of oxygen”, the classic way to describe the amount of oxygen that reaches each tissue level within the body, I developed the **concept of POC and EPOC**. This concept allows any person to **visualize** the amount of oxygen that is dissolved into body water – plasma, lymph, CSF, interstitial fluid – and it allows any person to understand that the **relative ratio** of any final concentration of oxygen molecules per unit body water that is detected at any tissue level **changes little**, is *relatively* independent of the starting concentration of oxygen that the lungs breathe, and is *relatively* independent of the initial pressure to which to body is subjected. *Boyles Law* states that the *pressure and gas volume are inversely proportional*. *Henry’s Law* states that *gases can be dissolved into liquids*. Therefore, if we are at sea level, by definition the pressure on our bodies is 1 atmosphere absolute (1 ATA) with an oxygen concentration of 21%. By multiplying these two numbers together, 1 ATA x 21% oxygen, you will see that the amount of oxygen that is dissolved into your body water -- plasma, lymph, CSF, interstitial fluid -- is a *relative* 21%. This is your “physiologic oxygen concentration” (POC). To visualize this *relative* process, picture “21 oxygen marbles floating in a jelly jar”. If we were 16 ½ feet underwater, the pressure would be 1.5 times more than the pressure at sea level. This is one of the pressures that is commonly used in hard chambers or multi-place chambers. If at this depth/pressure we were breathing 100% oxygen instead of 21% oxygen, the amount of oxygen dissolved into our blood would be 1.5 ATA x 100% oxygen or 150% or what I call your “equivalent oxygen concentration” (EPOC). To visualize this *relative* process, picture “150 oxygen marbles floating in the same size jelly jar”. If you were approximately 10 feet underwater, the pressure would be 1.3 times more than the pressure at sea level. This is the same pressure that is commonly used in soft chambers. If at this depth/pressure we were breathing 21% oxygen, the amount of oxygen dissolved into our blood would be 1.3 ATA x 21% oxygen or about 27% EPOC. Depending on multiple factors including rate of air flow exchange through a soft chamber, the amount of oxygen actually delivered by an oxygen concentrator, whether a child uses a mask or not, the distance away from the nose that the tube delivering the oxygen is held if the child will not wear the mask, etc., variable EPOC values will be realized. Common EPOC values that are safe to use and frequently found in soft chambers range from 27% to 70%.

It is important to understand that by increasing or decreasing the oxygen concentration and/or the pressure used, *you can achieve any EPOC value* you want ranging from below 21% to incredibly high numbers that are not physiologically safe! It is also important to understand that the higher the EPOC value, the shorter the treatment time must be to assure safety. *In my clinic for children with autism, EPOC values ranging from 27% to 70% in a soft chamber*

James A. Neubrandner, MD

have been safely used for 1.0 to 1.5 hours twice daily if there is a three to four hour interval between sessions. After 75 to 90 soft chamber treatment hours within a 30 to 45 day period I recommend taking a break for 2 to 4 weeks. If children receive less intense “sets” of mild chamber treatments, the break does not need to be as long. Also in my clinic for children with autism, EPOC values of 150% in a hard chamber have been safely used for 1.0 hour sessions five days per week. I prescribe “treatment sets” of 40 hours over an 8 week period in the hard chamber before recommending a 2 month break. However, if the child receives the 40 treatment hours over a longer period of time with a less intense schedule, the treatment break can be proportionately less. Occasionally I progress from 150% EPOC treatments to 175% EPOC treatments but I never start at this higher level. To date I am not yet convinced that the gains I was hoping to see for children with autism by using 175% EPOC have been substantially greater than the gains I was already observing at the 150% level while the potential for side effects is definitely increased at the higher EPOC levels.

My hypothesis is that high pressure treatments using 100% oxygen with higher pressures have a totally different overall general mechanism of action than do low pressure treatments using oxygen concentrations ranging from 27% to 70% and that both mechanisms may be necessary for a specific child in order to obtain maximum results! In general, high pressure mechanism deals with mass action and concentration whereas low pressure mechanism deals with time. Based on my clinical findings, I hypothesize that high EPOC values may produce more mitochondrial product whereas lower EPOC values used for longer periods of time may result in more cellular product. After reviewing meteorological tables, weather patterns and how related atmospheric pressures affect my patients with inflammatory joint disease, I also hypothesize that pressure products from the pressures able to be obtained from either high or low pressure chambers are enough to produce clinical benefits.

It will require well designed research studies to validate my hypotheses. Unfortunately this will *take many years* to happen and we have *children to save now*. Therefore, no matter what my hypotheses may be, only one thing really matters and that is how *children respond to treatment* as long as what we are doing *is safe*. Therefore I would like to share just a few *typical examples* of the hundreds of cases that I now have accumulating in my files.

Steven was a 5 year old who presented to my clinic with the diagnosis of PDD-NOS and a very skeptical father who was a physician. In a progressive and stepwise fashion I had the parents begin many of the biomedical therapies you have been reading about in other chapters in this book. Those that were shown to benefit Steven the most prior to HBOT included methyl-B₁₂, the CFGF diet, and supplements. Though Steven did very well with these treatments, he still had a long way to go. In May of 2007 Steven began using a soft chamber with a mask. Within 10 days his father reported that his language was increasing at a noticeable and unexpected rate. In addition his eye contact began to improve as

James A. Neubrandner, MD

did his ability to start interacting with his peers and he became much more responsive. Steven continued to progress rapidly and only 6 months later his father told me that Steven had lost all services because he was considered by his neurologist to be 95% recovered!

Cole's story did not have as marvelous an ending though his family is thrilled. Cole was 8 years old and severely autistic when he began doing HBOT last spring. Prior to HBOT treatments Cole could not go into public places because he would become extremely aggressive, agitated, scream, and run away. Soon after starting soft chamber treatments Cole's speech increased in all areas and he became much more aware of everything in general. His eye contact improved significantly and he became much less aggressive and calmer. However, what was the most important benefit to Cole and his family was that by 27 hours of treatment he could now do new things that he could never do before. There are no words that can completely capture what Cole's parents were feeling when they *tearfully expressed* to me, "It's like *we've been in prison* for eight long years and finally *we've been released!* For the first time in our lives we can now sit in a restaurant like a normal family and have a meal together! We can now go to a theme park from the minute it opens and be the last ones to leave and no one can tell there is anything different with our child when before Cole would have run out screaming and holding his ears within the first few minutes after we arrived. This has been truly amazing! For the first time we feel like *we have a real family!*" Cole is still severely autistic but HBOT has given a quality of life to him and his family they never before even imagined!

Six year old Andrew presented with autism and colitis. He responded to methyl-B₁₂, the CFGF diet, chelation, and desensitization for environmental allergies. Soft chamber HBOT began in January 2006 and showed undeniable benefits including improvement in his bowels and fine motor skills. His language became much more conversational and he became engaging and social. After doing soft chamber treatments one hour daily several times per week his previously uninterpretable handwriting was readable. His handwriting then progressed from readable to easily readable to almost age appropriate after continuing soft chamber treatments but after increasing the treatment time from 1.0 hour daily to 1.0 to 1.5 hours twice daily and increasing the treatment frequency from several times per week to daily. What you see pictured below occurred over a 4 month period of time while using this more intense soft chamber treatment schedule! Since that time Andrew has taken the recommended breaks that I require between HBOT treatment sets. In addition I have moved him to the hard chamber using 150% EPOC and Andrew has continued to progress even more, especially in language, awareness, and fine motor skills.

James A. Neubrandner, MD

June 2006



September 2006



When Jack came to me he was 3 years old with the diagnosis of PDD and colitis. To those who knew him he was described as *The Silent Shy Child*. Prior to HBOT his major improvements came from methyl-B₁₂ and sulfasalazine. However, once he started HBOT his communication went beyond age appropriate to significantly advanced. Within a few months he officially lost his diagnosis from his neurologist and today, less than one year later Jack is considered a normal child who is far advanced of his peers in many areas, the most surprising one being that the once silent and nonsocial child is now described as *Mr. Never-Shuts-Up Socialite!*

Matthew was 4 years old when he came to me with the diagnosis of autism, colitis, and immune deficiency. Though methyl-B₁₂ and major GI medications helped him significantly, he still had chronic diarrhea and severe autism. After just a few weeks of mild HBOT sessions the parents saw a new level of spontaneous language and a noticeable increase in vocabulary. For the first time in his life Matthew could follow commands and his teachers said his personality literally exploded! However what impressed his parents the most was what they described as "*picture perfect poops*" instead of chronic diarrhea, something he had never experienced before in his entire life!

Then there's four year old Jonathan who is what I call a *delayed responder*. Though his autism responded well to methyl-B₁₂ therapy, he still had *almost nonexistent speech*, socialization, and showed very little evidence of awareness and cognition. He started HBOT in his home July, 2006. After 50+ hours of soft chamber HBOT prescribed at two 1.5 hour sessions daily, Jonathan showed absolutely no positive response to the treatments. His parents were devastated! However, at the 58th treatment hour Jonathan said his first meaningful word and by the 85th hour he was *singing entire songs*. He became engaged, social and interactive. His awareness and ability to reason became unmistakable. Benefits have been cumulative and steady. By January 2007, after having completed more than 200 treatment hours, Jonathan's language became *conversational and almost as good as his peers* and at that time he was considered to be 85% recovered. During our latest follow-up June, 2007 Jonathan's mother told me that Jonathan's Peabody Developmental Motor Scales test went from the profound delay category in June 2006 to the no delay category in June 2007! For over an hour while I talked to Jonathan's mother, Jonathan never quit talking. He was able to walk in and out of his imaginary play world appropriately the entire time and he interacted with Lisa, my physician assistant in ways appropriate to advanced for his age, especially with vocabulary. Neither of us would have ever dreamed less than one year ago that what we were witnessing

James A. Neubrandner, MD

that day could have ever been possible! Therefore the probing question that needs to be asked is, *“If Jonathan’s parents had stopped HBOT after 50 discouraging hours without benefit, where would Jonathan be today?”*

Seven year old David presented with severe autism, chromosome deletion 18q syndrome, and growth hormone deficiency. He had been taking growth hormone shots since he was 2 years old and until he was 5 years old he was not even on the growth charts. It was not until his fifth year of life that his height and weight finally reached the 1st and 5th percentiles. After starting methyl-B₁₂ in November 2005 David made progress within the first six weeks in many areas, primarily awareness, socialization, and motor skills but it was not until he started mild HBOT on June 24, 2006 that he began to retain language, something he never had been able to do before. In addition he showed the ability to comprehend new and more difficult concepts. David became independent and wanted autonomy for the first time in his life. But what was most surprising to all of us was that between June 24th and September 10th while David was doing HBOT he grew 3 inches taller and his weight went from 46 to 50 pounds! This was incredible because David had not grown in the previous 2 years. He has continued HBOT treatments and by March 2007 his height and weight are recorded at the 58th and 62nd percentiles!

Many parents are concerned that HBOT will only work for younger children. This is not true because HBOT does work for *older children and it works in powerful ways!* I would like to introduce you to Andrew and Victor, just two of the numerous older children from my practice who respond to HBOT.

Andrew was 19 years old when he first presented to me with PDD and severe obsessive compulsive disorder (OCD). Though methyl-B₁₂ helped him with many of his PDD symptoms, his OCD remained severe and untouched. His main obsession was with fans. He talked about them incessantly from the time he woke up in the morning until the time he went to bed at night and this had been going on for 17 long years! Surprisingly, after only 23 hours of mild HBOT his obsession with fans had decreased by more than 90%. He was then able to go to places that would previously trigger him to talk for hours about fans -- places like stores, certain rooms at school, and other people’s homes -- and for the first time since he was 2 years old, to the relief of everyone around him he would not say the word “fan” for hours at a time! Unfortunately, due to a tragic illness in another family member’s life, Andrew was forced to stop hyperbaric treatments. Just as tragically was that within 3 months Andrew again started talking about fans, but just a little bit at first. The slowly but progressively his obsession increased until by the 6th month his OCD symptoms were as severe as ever.

I will end by telling you about Victor, a truly amazing story! When I first saw him he was 23 years old and severely autistic. The first treatment I recommended was methyl-B₁₂. To this he responded very well within the first 6 weeks. Next I added supplements and he continued to improve even more, though only to a mild degree. It was not until the addition of soft chamber HBOT at the age of 24 that

James A. Neubrandner, MD

Victor's previously nonexistent eye contact and severely robotic speech changed in a remarkable way! In the past Victor would never look at me in the eye; instead he would always look to one side or to the other at a 45° to 60° angle, all the while either staring up at the ceiling or down at the floor. If his eyes ever met mine by accident he would quickly jerk his head away almost snapping his neck. Previously his sentences had uncontrollable fluctuations in tone and intensity. The volume would vary within the same sentence from screams to whispers in a very uneven staccato jackhammer manner. Then, after approximately 85 soft chamber treatment hours, his speech became fluid and smooth and almost normal in tone and intensity. No longer did he look away while going from whispers to screams because he could now look at me directly in the eye and carry on a meaningful and almost normal conversation for 2 to 3 minutes! However, the most incredible and unforgettable part of Victor's story happened one bright sunny Saturday morning last summer when his father sat in my office and told me the following story while big tears rolled freely down his cheeks. He said to me, "My son did not receive his diagnosis until he was more than 4 years old. Until that time my wife had hope that Victor was just delayed and would be alright someday. However, from the moment she heard the word autism, the beautiful smile that she gave to world everyday, all the time, to everyone she saw was wiped off her face and I never saw it again for 20 years until HBOT gave it back to her! Now my wife smiles again, all the time, everywhere! If I got nothing else from HBOT other than that, it has been the most valuable gift I ever received in my life!"

In my practice, based on over 20,000 treatment hours I have monitored and based on the patterns of response that I have documented, I can now say with full confidence that the best soft chamber protocol I have seen for the majority of children is what I call my "bite the bullet diagnostic month". This protocol has parents spend 30 consecutive days diving 1.0 to 1.5 hours twice daily for a total of 2.5 to 3.0 hours per day. (Occasionally I will allow the parents an uninterrupted 2 hour session as long as there has been at least a 4 hour break in between sessions.) The family's goal is to achieve 75 to 90 hours in their "*diagnostic month*" and to follow-up with me using the *HBOT-specific* Parent Designed Report Form. *When parents follow this protocol exactly*, very rarely will I not see a response if the child really has the ability to respond to low pressure HBOT. Once a child has completed this treatment set and is found to be responder, some parents will want to continue this type of therapy at home in order to obtain the *cumulative benefits* that we see. Presently my home chamber maintenance protocol is 45 to 60 hours (upwards to 75 hours with my more aggressive parents) in a 30 day period followed by a minimum 1 to 2 week break relative to the intensity of their dives – the more dives within the 30 day period, the longer the scheduled break period must be. The good news is that this maintenance protocol is also a treatment protocol that is not too intense for most families to achieve. Regardless of whether parents continue soft chamber treatments or not, I always recommend sets of hard chamber treatments after I have established their soft chamber baseline because hard chamber mechanism of response can offer some benefits that soft chamber mechanism of response does not (refer to

James A. Neubrandner, MD

the 3 general mechanisms described above). I believe that *it is important to do a soft chamber diagnostic set of treatments before doing hard chamber high pressure high oxygen concentration sessions in order to establish soft chamber baseline*. The reason I say this is because it is extremely difficult to know what to say to the parents whose child has done very well in a hard chamber when they then come to me and ask, “Do you think we should get a home chamber?” The only answer I can give is, “I don’t know because I do not have a baseline to know how your child may respond in a soft chamber!” I freely admit that I am biased that my best responders are those who are doing soft chamber dives at home in order to get cumulative benefits that increase month after month while they periodically do hard chamber dives at a center to add to soft chamber benefits those things that need higher pressures and higher oxygen concentrations.

So in summary I can emphatically state that HBOT – hard or soft – is one of the most valuable tools I have ever added to my tool chest to treat children with autism. It is important to point out that in my practice HBOT seems to work better when methyl-B₁₂ is already being used to create a synergistic effect. I can give you hundreds of examples of children improving with HBOT therapy varying all the way from high EPOC values of 150%, moderate EPOC values of 50% to 70%, and low EPOC values of 27% to 36%. It is exciting to report that 80% of children respond to some degree. When I look at this “responder group” as its own group, about 20% of the children show significant responses, about 20% show moderate responses, while the remaining 60% initially show only mild responses. However, these mild responses can become quite impressive over time as you have read from stories like Stephen’s or Jonathan’s or Victor’s. Their stories prove that HBOT provides cumulative effects and that over time even mild responders may show significant responses *relative to* their starting point. ***HBOT is not the magic bullet*** that we are all looking for, a bullet that does not exist. ***However, HBOT has the potential to be a powerful adjunct to all the other therapies that a child is using.*** When done consistently and with realistic expectations being the parent’s guide, and when parents use the HBOT Parent Designed Report Form evaluation tool that they themselves have created, more than 80% of them will be expected to say that HBOT works for their child too! I invite you to explore its potential.

References:

Hundreds of references have been used in the process of writing this paper. Due to space constraints, only the following have been cited:

1. 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.
2. Vlodavsky E, Palzur E, Soustiel JF. Hyperbaric oxygen therapy reduces neuroinflammation and expression of matrix metalloproteinase-9 in the rat model of traumatic brain injury. *Neuropathol Appl Neurobiol* 2006;32(1):40-50.
3. Stoller KP. Quantification of neurocognitive changes before, during, and after hyperbaric oxygen therapy in a case of fetal alcohol syndrome. *Pediatrics* 2005;116(4):e586-91.

4. Collet JP, Vanasse M, Marois P, et al. Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. *Lancet* 2001;357(9256):582-6.
5. Heuser G, Heuser SA, Rodelander D, Aguilera O, Uszler M. Treatment of neurologically impaired adults and children with “mild” hyperbaric oxygenation (1.3 ATM and 24% oxygen). In *Hyperbaric oxygenation for cerebral palsy and the brain-injured child*. Edited by Joiner JT. Flagstaff Arizona: Best Publications; 2002:109-15.
6. Golden ZL, Neubauer R, Golden CJ, Greene L, Marsh J, Mleko A. Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy. *Int J Neurosci* 2002;112(2):119-31.
7. Wilson HD, Wilson JR, Fuchs PN. Hyperbaric oxygen treatment decreases inflammation and mechanical hypersensitivity in an animal model of inflammatory pain. *Brain Res* 2006;1098(1):126-8.
8. Lavy A, Weisz G, Adir Y, Ramon Y, Melamed Y, Eidelman S. Hyperbaric oxygen for perianal Crohn’s disease. *J Clin Gastroenterol* 1994;19(3):202-5.
9. Granowitz EV, Skulsky EJ, Benson RM, et al. Exposure to increased pressure or hyperbaric oxygen suppresses interferon- γ secretion in whole blood cultures of health humans. *Undersea Hyperb Med* 2002;29(3):216-25.
10. 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.
11. Nie H, Xiong L, Lao N, Chen S, Xu N, Zhu Z. Hyperbaric oxygen preconditioning induces tolerance against spinal cord ischemia by upregulation of antioxidant enzymes in rabbits. *J Cereb Blood Flow Metab* 2006;26(5):666-74.
12. Gutsaeva DR, Suliman HB, Carraway MS, Demchenko IT, Piantadosi CA. Oxygen-induced mitochondrial biogenesis in the rat hippocampus. *Neuroscience* 2006;137(2):493-504.
13. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. The effect of inspired oxygen on infection. *Arch Surg* 1984;119(2):199-204.
14. Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol* 2006;290(4):H1378-86.
15. Rossignol DA, Rossignol LW. Hyperbaric oxygen therapy may improve symptoms in autistic children. *Med Hypotheses* 2006;67(2):216-28.
16. Rossignol DA. Hyperbaric oxygen therapy might improve certain pathophysiological findings in autism. *Med Hypotheses* (in press).
17. McCandless, J. *Children with starving brains*, 3rd edition. Bramble books, 2007.