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HBOT-HYPERBARIC OXYGEN THERAPY FOR AUTISTIC SPECTRUM DISORDERS

Written by Jim Neubrander, MD
Reviewed and edited by Dan Rossignol, MD

Foreword

The following manuscript demonstrates irrefutably from collective observations of over 75,000 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 pressure. 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 10,000 treatment hours by 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 provides at least some benefit for the majority of the children, that the benefits seen for children with autism may be due to additional factors not necessarily present in other diseases or disorders, that much more research is needed to get all the answers, but that treatment should not be delayed while waiting for science to catch up with what we see clinically.

Description

Many of the greatest discoveries in science and medicine have been found by accident. So it was with methylcobalamin and autism. So it is with hyperbaric oxygen therapy and autism.

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. You will hear many terms used interchangeably by lay people and professionals alike: hyperbaric oxygen therapy (HBOT), mild hyperbaric oxygen therapy (mHBOT), hyperbaric therapy (HBT), hyperbaric oxygen (HBO), hyperbaric air therapy (HBAT), hyperbaric enriched air therapy (HBEAT), etc. However, the most common way the term is used by the autism community is to just say "HBOT". Then most parents will state what they are doing, e.g. "we're using 1.5, 1.75, or 2.0 atmospheres in a hard chamber with 100% oxygen, or we're using a soft chamber (also referred to as a mild chamber) at 1.3 atmospheres 'with or without a mask' to which 'concentrated oxygen' is be sup-

plied at concentrations varying from 24% to 70%." *Conventional wisdom* states that unless one receives HBOT in a hard chamber with 100% oxygen at atmospheric pressures greater than 1.5 ATA, little or no benefit will be seen and if parents use a soft chamber with lower pressures and lower oxygen concentrations, they are just wasting their money and cheating their children. However, as history has shown repeatedly throughout the years, ***convention is only convention until challenged, proven wrong, and then changed.*** Such is the case with HBOT and autism! Based on the soon-to-be published studies by Dr. Rossignol, the early work of Dr. Buckley and Dr. Kartzinel, and the tremendous number of children that have been treated by physicians such as Dr. Bradstreet, Dr. Feingold, Dr. Freedenfeld, Dr. Stoller and myself, and a growing number of other physicians who are now using HBOT routinely in their offices, there remains no doubt that HBOT works and that it works well for children with autism. There is also no doubt that it works well at low pressures with varying degrees of oxygen concentrations as well as at varying degrees of high pressures with 100% oxygen. As shown from Rossignol's study, high pressure and low pressure treatments both respond about equally well but high pressure treatments and low pressure treatments may each do better to improve different types of symptoms. It is my opinion that this early research, when considered alongside the three general mechanisms of action I will propose later on in this paper, suggests that most children may need treatment at *high and low pressures with varying oxygen concentrations* in order *to receive the maximum cumulative benefit.*

Hyperbaric oxygen therapy (HBOT) was something I began recommending for my patients approximately 3 years ago. Since beginning this new 'unproven' therapy for autism and after monitoring thousands of hours of treatment, I can state that in my practice approximately 80% of children respond to some degree, especially if they continue their treatments. 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 in the future. Everyone understands that education is *a process, not an endpoint.* So it is with HBOT. *The presence of a response, not*

the intensity of a response is the most important factor that determines HBOT to be a treatment that is needed by the child and a therapy that should be continued long-term in order to achieve maximum results!

Benefits

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. For example, one of the most hoped-for responses parents wish to see is improvement in their child's *language*. In my practice as well as from Dr. Rossignol's study this is one of the most commonly reported benefits. Parents very frequently tell me their child exhibits more conversational language and uses longer sentences with more complete and complex sentence structure that now includes pronouns, prepositions, adjectives, and adverbs. They report an increase in spontaneous speech with initiation of conversation at appropriate times. They report that their child's vocabulary is more complete than ever before and that their child will now *ask* a question, *wait* for their response, and then *respond* appropriately to what they just said. They also report that the words "who, what, where, when, why, and how" and "yes–no" become commonplace whereas before these words were rarely used.

Another very frequently reported category of benefits includes those that occur within the frontal cortex of the brain where executive functioning originates. Dr. Stoller's report in Pediatrics (October 2005) demonstrated that a teenager with a 15 year matured brain injury/poisoning (Fetal Alcohol Syndrome) had sustained and permanent improvements in neurocognitive abilities. Stoller's study demonstrates that the brain is not static and has the ability to heal. Such is definitely the case in autism, a disorder often labeled incorrectly as "static encephalopathy" thereby implying that the brain in an autistic child does not have the ability to heal. Nothing could be further from the truth! In my practice, increased *awareness* with all of its associated findings is almost universal in children treated with HBOT. Children become more "*present*" meaning that they become

more involved and *actively engaged* in what they are now *aware* of. They are much more *attuned* to what is happening on a day-to-day basis and now *understand* their relationship to the world and what is happening around them and how they fit into the scheme of things. With this new level of awareness they become *less fearful* and therefore less rigid, more *flexible*, more *resilient*, less frustrated, and more tolerant to changes that before would upset their world. However, should something now upset them, they are able to bounce back more quickly and recover in a much shorter period of time than they ever did before. Another extremely common occurrence is that the children's *eye contact* becomes markedly improved. They are now very aware that they are being called or spoken to and they respond by looking into their parent's eyes and by holding eye contact for a significant period of time rather than their usual fleeting glance as was typical in the past. They are more aware of what they are to do, when to do it, and how to do it to please others. In addition they will sit still and *tend to tasks* at hand for much longer periods of time, often completing them, something they never did before.

Parents frequently report that their child now has a new level of *understanding for cause and effect* and that they *understand new concepts* and follow through with the appropriate actions. For example, one child who was previously unaware that he could fall and hurt himself whenever he was high up in the air suddenly turned to his mother when he saw her near the edge of a ledge and said, "Mommy, no fall – back!" Parents report that *cognition* becomes more complex, more consistent, and that their children handle *age-appropriate* problem solving of all types much more accurately and in far less time than ever before. Parents report that their children's *comprehension* becomes greater, that the child understands more complex thoughts and concepts, and that s/he understands those more quickly allowing parents and teachers to not have to repeat or re-teach as much as they needed to do before. The children become far more *inquisitive* asking, "What's this – what's that?" Parents report it is if their children are *seeing the world* for the first time and are finally taking the *initiative* to do innovative things and explore new things that they never would do on their own before.

Another major set of symptom improvements that are commonly seen include the area of socialization and emotion. Very fre-

quently parents report that their child will *initiate play* with a peer or adult whereas before such an event was uncommon or rare. Parents report that for the first time their child *makes his/her needs known* to family, friends, or playmates and actually expects the family, friends, or playmates to respond and do something about it. The children frequently become *engaged* or are engaging. Parents often report that for the first time they observe out of the corner of their eye that their child is watching them closely, studying everything they are doing, and then later they find their child trying to *imitate* or duplicate what the child observed them doing. Many parents report that for the first time their child finally *understands facial expressions and body language and the feelings of others*. They are thrilled when they see their child respond to an emotional situation with the appropriate reaction, e.g. when a mother was sad her son said, "No sad, Mommy", or when a father was angry his daughter responded by taking her father's hand and tried to pull him out of the yard where he was arguing with a neighbor saying, "No mad; no mad – go home."

Two other wonderful benefits are frequently reported by parents. The first is that children suddenly have an *increased appetite* and are willing *to try new foods* without putting up a fight with their parents. Many parents report that for the first time in over 2 years their child is finally *gaining weight*! *One of the other most consistent responses in the top 20 most frequently reported benefits* is that a child's *bowel function improves, often remarkably so*! It is not uncommon for a child who has had typical autistic-like loose "mashed potatoey" unformed stools for years, many of whom have even been taking major GI medications, after starting HBOT their stools become "picture perfect" for the first time in their life! Several parents have reported that their child self-potty trained over a weekend when prior to HBOT they had struggled with this issue for years.

Side Effects

All is not perfect with HBOT and children who have autism. The HBOT textbooks state that the most common side effects include barotrauma (2%), sinus squeeze, serous otitis, claustrophobia, reversible myopia, and seizures (0.01–0.03%). Side effects do exist

in my practice but most often are what I call positive-negative side effects rather than negative-negative side effects and tolerable side effects rather than intolerable side effects. The most common negative-negative side effect is hyperactivity though there are some physicians who consider this a positive-negative side effect. According to Rossignol's study, the hyperactivity diminishes over time. Increased stimming is also a fairly common negative-negative side effect. By contrast, most of the behavior problems parents commonly see are *positive-negative responses* by their child and *indicate that HBOT is actually working* and that it is a good thing being manifested in a bad way. Frequently children may become more frustrated, more aggressive, less compliant, tantrum more, become less cooperative, follow directives or commands less, become more irritable, have more mood swings, and show less flexibility. The most common reason for this set of unwanted behavior reactions is that the child's brain is "coming back" and the child is therefore more aware in general, therefore allowing the child to be more self-assured, more self-confident, more independent, more opinionated, and a child who wants and expects more control of his/her own situation in life. Therefore, when unchallenged and/or no demands are being placed on the child, the parents see many of "the good things" mentioned above. However, when the parents make a request or put a demand on the child, the child often responds in these negative and unpleasant ways. For example, when a parent tells their child that she will need to take a bath, put the Gameboy away, eat dinner now, come inside from playing, the child sees it as a challenge to her right to control her life and therefore may respond by kicking, crying, screaming, or having a meltdown. Likewise when a child now becomes more aware of what he wants to communicate to his parents and is now more aware that he can't because of the language barrier, once again the same negative reactions may occur because he is either frustrated at himself or frustrated that you have a problem—not him—and don't understand what it is he wants. Therefore the key to knowing whether an action/reaction is a positive-negative behavior or a negative-negative behavior is to note whether the majority of the times such unwanted behaviors occur when followed by a request or demand that the child doesn't want to do at the time or when a child makes a request or demand that you cannot accommodate.

It is important to note that an autistic child's neuronal cells are programmed a certain way, that their cell's programming may be different than other children's programming, and that this programming results in both the good things as well as bad things we presently see them doing every day. Therefore when oxygen "wakes up" cells that have been lying dormant and were just idling, it is common sense that the gap between the positive reactions and negative reactions will widen. Think of it this way. If prior to HBOT a child's brain was only using 100 neurons and these neurons were doing 10 good things with a moderate intensity and 3 bad things with a mild intensity, once HBOT wakes up 1000 neurons in the child's brain, the child now has 10 times more cells working to produce "neuronal product"—both the good neuronal products as well as the bad ones. Therefore the child may now do 20 good things with a marked intensity and 6 bad things with a moderate intensity! This is the *expected response* that may often occur during the healing process though it is never the desired one!

When deciding whether to continue or discontinue HBOT when side effects occur to more than a mild degree, a couple of rules will usually help parents and clinicians make the best decision how to proceed. *Rule 1*: Side effects that disrupt the life or safety of the child or others, or that disrupt the child's ability to learn are considered "intolerable" and the treatment should always be discontinued or the protocol altered significantly. *Rule 2*: If the child's gains are *undeniably* present and the side effects are "tolerable", though very much a nuisance and undesirable, the total number of hours used per treatment and the frequency of treatments may remain the same or be varied only slightly. However, usually the child will be able to continue the treatments without protocol changes and the side effects will typically pass if given enough time.

The reason I recommend HBOT for all my patients is because there is scientific evidence that pressure, independent of the concentration of oxygen, decreases inflammation and 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. 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. Because no test is able to predict which child may and which child may not respond to *extra pressure and/or extra oxygen (in contrast to excessive oxygen)*, I let nature take its course and prescribe a clinical trial of HBOT for all my children. Though I let "nature take its course", I would not consider prescribing or administering HBOT to children with autism unless there was good scientific evidence to support its use. Fortunately such evidence does exist, the body of which continues to accumulate, and the mechanisms of action by which HBOT may work for children with autism, as described below, will probably already be outdated by the time this manuscript is published.

Multiple Mechanisms

A few of the multiple mechanisms demonstrating how HBOT may work for children with autism was originally and thoroughly researched over many months time by Dr. Rossignol. These mechanisms are shown below along with a couple others that have been suggested. They include:

1. *Angioneogenesis from the addition of oxygen*: The growth of new blood vessels has been shown to occur from soft chambers as well as from hard, and is a process that may continue to increase subsequent to discontinuing therapy for a period of time after oxygen loading. Though it has been stated often on the internet boards that angioneogenesis does not occur unless pressures are 1.5 ATA or greater, the South American physician Dr. Efrain Olszewer has pre- and post-angiograms documenting collateral circulation beginning as early as ten to twenty hours after initiating hyperbaric therapy for cerebral vascular disease and peripheral arteriosclerosis at pressures lower than 1.3 ATA. It is known that one of the problems children with autism have is decreased blood flow to the brain (cerebral hypoperfusion) Therefore is has been speculated that angioneogenesis is the way that HBOT helps autism. However, though angioneogenesis may be one mechanism by which children with autism are helped by HBOT, angioneogenesis may not be the primary mechanism by

which HBOT works. The amount of cerebral hypoperfusion in autistics compared to controls is about 8%, so a small increase in oxygen delivery may be all that is needed to overcome this deficit and show clinical benefit. The small amount of increased oxygen that is needed by the cells to improve their function does not necessarily require new blood vessel formation to be accomplished because with HBOT free oxygen molecules are dissolved directly into the cerebrospinal fluid. Therefore these cells are no longer dependent on increased oxygen delivery from increased blood vessel formation that secondarily delivers a greater oxygen load because it carries more hemoglobin.

2. *Angioneogenesis from the removal of oxygen*: At times it may actually be the sudden removal of higher than normal oxygen concentrations that the body has adapted to rather than the higher levels of oxygen itself that may stimulate angioneogenesis. There are reports that the new vessel formation in the retinas of premature infants who were on high doses of oxygen was stimulated by the rapid removal of oxygen and not from the oxygen itself.
3. *Increases in blood flow independent of new blood vessel formation*, not only due to the competing mechanisms of vasodilation and vasoconstriction, but also due to decreasing the inflammation that secondarily constricts blood vessel lumens in a closed space. Because inflammation is accompanied by swelling, tissue expansion or compression will occur. Therefore, whenever inflammation brings more fluid to a region of the body that is comprised of solid tissue and hollow blood vessels, the first thing to happen is that the hollow blood vessel lumens will be compressed and deliver fewer red cells carrying oxygen to the area. Once inflammation is reduced the secondary vascular narrowing is improved allowing increasing amounts of red blood cells carrying oxygen to reach the hypoxic areas and SPECT scans will once again "light up" turning from blue to yellow. SPECT scans demonstrate the relative amount of blood that is able to reach the different areas in the brain. Color coding allows easy visualization of what is occurring with blue areas representing little blood flow and yellow areas indicating normal blood flow.

4. *Decreasing levels of inflammatory biochemicals*: Recent studies have demonstrated that children with autism frequently have neuro-inflammatory and gastrointestinal inflammatory conditions occurring. Multiple studies demonstrate the beneficial effect of hyperbaric oxygen therapy in inflammatory conditions. C-reactive protein and high levels of cytokines have been shown to decrease with HBOT. One study demonstrates that the anti-inflammatory effect from HBOT is probably due to pressure effects and not necessarily increased oxygen tension.
5. *Up-regulation of key antioxidant enzymes and decreasing oxidative stress*: Children with autism have been shown to have increased oxidative stress and less reduced (active) glutathione. HBOT, especially when using pressures less than 2.0 atmospheres, can up-regulate these antioxidant enzymes and afford antioxidant protection against oxidative stress.
6. *Increased oxygenation to functioning mitochondria*: Mitochondria are the energy producing organelles of the body. A growing number of studies are focusing on the mitochondria and its relationship to many disorders. The possibility exists that some autistic symptoms may occur if these organelles are dysfunctional or fewer in number than the number found in children without autism. HBOT may have the potential to activate dysfunctional mitochondria and/or to activate "dormant/idling cells" thereby allowing more "mitochondrial product" to be appreciated by the body.
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*: A recent study documented impaired production and abnormal ratios of porphyrins in children with autism. Because porphyrin is involved in the production of functional heme/hemoglobin, and because this appears to be disordered in autism, the impaired delivery of oxygen to cells will be improved when HBOT bypasses hemoglobin-dependent oxygenation.

9. *Improvement in immune and autoimmune system disorders*: HBOT has been shown to benefit the immune system and multiple studies have shown that autism is frequently associated with various types of immune and autoimmune system biomarkers.
10. *Decreases in the bacterial/yeast load found systemically and in the gut*: Many children with autism have increased amounts of abnormal bacteria and yeast in their gastrointestinal tracts. These same children have shown clinical improvements when this overgrowth phenomenon is treated with antibiotics, either by natural agents or pharmaceuticals. HBOT has been shown to decrease abnormal bacteria/yeast 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*: Children with autism have difficulty handling viral infections, most likely due to immune dysfunction. It has been postulated many times that children with autism have a chronic low grade viral gastroenteritis and viral encephalitits. HBOT has been shown to decrease HIV viral loads. I speculate that one of the primary reasons HBOT works so well for so many children whose abnormal stools improve once they start HBOT is because the chronic, low-grade, smoldering live viral load harbored in the intestinal mucosa (Wakefield/Krigsman hypothesis) does poorly when surrounded by higher oxygen concentrations. The literature states that in order to kill viruses 100% oxygen at 2.7 ATA or above is required. However, there is no reason to believe that even mildly increased oxygen tensions may inhibit viral activity and/or make the host less hospitable to chronic viral inhabitation. This explanation is in keeping with the clinical results I see. In my clinic improved bowel function is in the top 20 most commonly seen benefits. I explain to my patients that to get cockroaches out of the kitchen, I can either kill them with my shoe or turn on the light. Interestingly it only takes a little bit of light for them to leave the room. Likewise it is my theory that it only takes a little bit of increased oxygen tension for viruses to leave.
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*: Studies have shown abnormities in the autistic brain whereby it does not produce and subsequently does not use serotonin properly. Newer studies have shown that HBOT can work like an anti-depressant by increasing brain serotonin levels.
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.*

Safety Concerns

Because a few, many, or all of these multiple mechanisms can be operative in autism at any point in time and vary significantly from child to child, and because no one mechanism seems to "answer all the questions" for any given child, as was so elegantly stated by Dr. Bernie Rimland, "Do what works!" Once again this argues for the use of combination high pressure/low pressure HBOT sessions that not only work because of the *specific* mechanisms discussed above but also work more comprehensively by considering three important *general* mechanisms, those mechanisms being: a) *increasing total concentration of oxygen per treatment; b) increasing total time of treatment with lower oxygen concentrations and lower pressures; c) increasing pressure independent of oxygen concentration.* Though these three general mechanisms of action (effects of concentration; effects of time; effects of pressure) affect all 16 specific mechanisms of action, whichever general mechanism is dominant at the time has the potential to enhance or inhibit the rate and intensity of the clinical responses. Though these three concepts are not new, the way that I interpret them and how I apply them are my hypotheses, my opinions, and do not necessarily reflect those of my colleagues. I offer them to you, not for you to agree with, but rather to explain what I am doing and the reasons why I have created new protocols by which to treat my patients, and why I believe I am seeing the very positive clinical results that I am seeing.

Because *safety* must be our first concern, to understand why I am doing what I do, consider the following principles and *two new terms* I have coined—*POC and EPOC.* For any given volume of room air at sea level (1 atmosphere absolute—1 ATA) the concentration of oxygen is 21%, the tension/partial pressure of the oxygen equals 0.21 ATA, the concentration of nitrogen is 79%, and the tension/partial pressure of the nitrogen equals 0.79 ATA. For this discussion we will focus on the oxygen concentration only. The POC—physiologic oxygen concentration—we are exposed to at 1 ATA with 21% oxygen is defined as 21% (1.0 ATA x 21% O_2 = 21% POC). You can easily visualize what is happening when you remember that Henry's gas law proves gases will dissolve into liquids, the reason we have carbonated beverages like Coca Cola, Pepsi Cola, Seltzer water, etc. In your mind picture 21 molecules of oxygen dissolved into one unit body water where *body water is plasma, lymph, cerebral spinal fluid, and interstitial fluid.* Boyle's gas law teaches that any oxygen concentration and tension/partial pressure can be achieved by adjusting either the pressure used and/or the concentration of the oxygen. Therefore, when using a pressure of 1.5 ATA with 100% oxygen, the EPOC—*equivalent* physiologic oxygen concentration —as compared to the physiologic oxygen concentration (POC) of room air at sea level is 150% (1.5 ATA x 100% O_2 = 150% EPOC vs. 1.0 ATA x 21% O_2 = 21% POC). Now picture 150 molecules of oxygen instead of 21 molecules of oxygen dissolved into the *exact same* unit of body water you were previously picturing—plasma, lymph, CSF, and interstitial fluid. It is important to understand that by increasing or decreasing the oxygen concentration and/or increasing or decreasing the pressure used, *you can achieve <u>any</u> EPOC value* you want ranging from below 21% to incredibly high numbers that are not physiologically safe.

The actual number of molecules of oxygen suspended in the alveoli in the lungs, transferred to the red cells in the lung capillaries, dissolved into lung plasma, and then passed from arteries to veins and to non-plasma body water compartments, and then to cells and eventually to cellular organelles like the mitochondria becomes less and less the further along the pathway the oxygen travels. Interestingly the mitochondria only see 0.3% of the oxygen presented to the lungs! Therefore, because parents and most physicians cannot calcu-

late the "millimeters of mercury of oxygen", the classic way to describe the amount of oxygen that reaches each tissue level within the body, the ***concept of POC and EPOC*** was developed. This concept allows you to ***visualize*** the amount of oxygen that is dissolved into body water—plasma, lymph, CSF, interstitial fluid—and it allows you to understand that the ***relative ratio*** of the final concentration of oxygen molecules per unit body water that is detected at any tissue level is unchanged, is independent of the starting concentration of oxygen that the lungs breathe, and is independent of the initial pressure to which to body is subjected. For example, the *relative ratio* of oxygen molecules present in the lungs as compared to the number of oxygen molecules that will remain by the time they travel to the arteries, veins, cells, and organelles *remains the same* no matter what the starting pressure and starting oxygen concentration happened to be. Therefore, by being able to create in your mind a *relative picture* of what is taking place in your child's body water, it then becomes much easier to understand the principles of safety, effectiveness, and how the different general mechanisms of action—effects of concentration; effects of time; effects of pressure—each have there own reasons to be used. A *better term* than EPOC is ***relative EPOC (R-EPOC)***—the relative amount of oxygen that is detected at any body tissue when compared to what is normally detected by that tissue when breathing room air at sea level.

Unfortunately, the higher the concentration of oxygen dissolved into body water (R-EPOC), the shorter the treatment time must be before oxygen toxicity, CNS toxicity, and pulmonary toxicity become a concern. The opposite is also true whereby the lower the concentration of oxygen dissolved into body water (R-EPOC), the longer one may safely continue treatment. Oxygen "oxidizes" and oxidation must be controlled so that it produces good things, not bad. Bleach oxidizes and makes clothes look whiter and brighter as long as a dilute solution is used. However, if clothes were put directly into pure bleach, they would be "chemically burned" and be ruined. Should one use varying *concentrations* of bleach solutions, the *time* that the clothes could stay in each solution before being burned and ruined would depend on how strong or how weak the final concentration was of the bleach solution. Therefore the importance of Boyle's law *for your child* is that by adjusting the oxygen-

oxidizing concentration and the pressure used, any range of oxygen concentration per unit body water can be achieved varying between slight, moderate, marked, or excessive. Common examples of *safe soft chamber R-EPOC values are 28%, 32%, 36%, 45%, and 60%.* Such concentrations can be used for *many hours without toxicity* issues. Concentrations commonly used in hard chambers for children with autism are 150%, 175%, and 200%. These R-EPOC values are also used safely but must be used for less total time during a 24 hour period.

My hypothesis is that high pressure treatments using 100% oxygen have a totally different *overall general mechanism of action* than do low pressure treatments using oxygen concentrations ranging between 24% to 60% 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*. High pressure mechanism allows more molecules of oxygen to be dissolved into the same volume of "body water", whether that body water is plasma, lymph, cerebral spinal fluid, or interstitial fluid. Because we are not mummies, only our fingernails, toenails, and hair are dry allowing the rest of our now *relatively more* highly oxygenated body water to be able to touch almost every cell in our body. Possibly some cells need higher concentrations of oxygen than is normally delivered to them, especially for children with autism. An excellent example may be mitochondria and other organelles due to the fact that 99.7% of oxygen has been consumed by the time it reaches them. However, to only consider or use the mechanism of high pressure high oxygen concentration overlooks the fact that other cells in the body may be damaged by too much oxygen (R-EPOC) if one is using the *mechanism of concentration* to deliver a "total load" of oxygen to these cells rather than using the *mechanism of time*. Therefore it is important to *consider using both* high pressure high oxygen concentrations as well as low pressure low oxygen concentrations *in each child* in order to receive those benefits associated with the general mechanism that requires more oxygen and those benefits associated with the general mechanism that requires more treatment time in order to be maximally effective.

Operational Hypotheses

Though we do not know for sure the effects of oxygen on plasma membranes, it is my opinion that high pressure, high oxygen concentrations will not directly "push more oxygen across the cell membrane" though greater amounts of diffusion, an indirect process, may actually occur. It is also my opinion that higher pressures with higher oxygen concentrations will probably not increase cell membrane permeability nor transport oxygen from extracellular to intracellular compartments more rapidly. It is my belief that the primary factor that will allow more oxygen to be transported across the cell membrane is *time of exposure* as long as adequate amounts—not excessive amounts—of oxygen are detected by the cell. "More" is not always better when "results" are what one is looking for. Consider a smorgasbord. Though the *concentration* of food is immense, *time* is the limiting factor because only so much of the food can be eaten during a finite period of time by any one person. The mouth only chews so fast, the stomach only holds so much, the rate of absorption is limited, and the digestive processes that pass the waste can only go so fast to make room for more. Similarly, the majority of biochemical reactions are not sped up to any significant degree by higher concentrations of oxygen because each biochemical reaction has its own finite speed of reaction. The analogy I use is that humans run at human speed and are only able to run a little faster if they are being chased by a tiger. Therefore the majority of biochemical intracellular reactions each have their own *fixed* rates of reaction—"how fast they run"—limiting how fast they can make their specific biochemical endproducts. With that fact in mind, one of the things we believe we can change is how many dormant/idling cells we activate with HBOT and how long we keep them turning biochemical substrate into biochemical product. Remember that for every organelle or mitochondrion present in the body there are thousands of intra- and extracellular reactions that occur. Therefore, though the general mechanism of increased oxygen concentrations may be the primary mechanism needed to affect the mitochondria because 99.7% of the oxygen has been lost by the time it reaches them, the general mechanism that may be the most important one to affect intra- and extracellular reactions may be the mechanism of *increased treatment*

time in order to make *more cellular product. This can be done safely the lower the R-EPOC value is.* However, as the R-EPOC value increases, the less time one can safely use to treat the child. Therefore one must not confuse the overall mechanism of *total concentration of oxygen per treatment*—extremely valuable in certain disease states, e.g. some mitochondrial and certain enzymatic disorders—with the overall mechanism of *total time of treatment with oxygen*—extremely valuable for maintenance and to maximize the total amount of cellular product produced and final outcomes of many biochemical reactions! *Theoretically*, the general mechanism of longer treatment sessions at lower pressures *may* prove to be the more valuable of the two mechanisms for the majority of cellular functions and the mechanism that *may* eventually be found to be the predominant one that helps children with autism.

The third general mechanism demonstrates that pressure, independent of oxygen concentrations may be one of the primary mechanisms to decrease inflammation. One study showed that when oxygen concentrations were adjusted so the final R-EPOC concentration remained at 21% while the atmospheric pressure was increased (10.5% O_2 x 2.0 ATA = 21% R-EPOC), laboratory markers for inflammation decreased! Unfortunately at this time we do not know if low pressures will have the same effect as did the high pressure used in this study. Because low pressure treatments have been working so well for a high percentage of the children, many parents have elected to not follow through with a set of high pressure, high oxygen treatments. This could be a mistake if the general mechanism of pressure independent of oxygen concentration is found to need higher pressures than can be obtained in a soft chamber. Therefore, until science can answer this question, my protocol includes both hard and soft chamber treatments though I always start with soft chamber sessions for the reasons that I will discuss below.

How the *three general mechanisms of action* are affecting children with autism are my hypotheses. Applying them as I do is working very well in my clinic. However, much more research is needed before any definitive answers can be made and broad generalizations should not be made until good scientific studies document and confirm what I have seen clinically. Therefore I recommend that parents follow what their doctor advises them to do for their children. I

also *warn parents* who have home chambers to never use extended treatment times or modified pressures or oxygen concentrations or flow rates unless they are under the direct supervision of a clinician knowledgeable in manipulating R-EPOC values with time and pressure variables! Under the care of such a clinician and based on the tables produced by National Oceanic and Atmospheric Administration (NOAA), R-EPOC values from 28% to 60% appear to be safe and very effective when used 1.5 to 2.0 hours once or twice daily several times per week up to 30 days at a time. *Preliminary data* suggest earlier benefits, more benefits, and benefits of greater intensity. Early data also show that most children are holding their results and are not losing the benefits gained whether from longer or shorter sessions if after finishing a *treatment set of sessions* they follow a maintenance schedule consisting of two to four hours monthly. Early data also suggest that the speed one reaches some arbitrary "goal number like the famous 40" is not as important as previously suggested. However, early data also suggest that the more treatments one receives using a greater frequency schedule, the better the cumulative effects. Practically speaking, the earlier parents notice benefits and the stronger these benefits are the more likely parents are to continue this valuable therapy.

Based on the above hypotheses and clinical observations after ten thousand hours of treatment, I believe it is important to use both hard and soft chambers in order to activate the mechanisms of action that are potentially different. I also believe that a patient should *first complete a series of soft chamber sessions* in order to see if they are "soft chamber responders" so that I can obtain a better baseline by which to design future treatment sets or maintenance protocols for both hard and soft chamber follow-ups. If a child is a moderate to strong soft chamber responder, for this family I would more likely recommend home chamber maintenance than I would for a family whose child showed little to no response, as long as the child had completed enough sessions for me to fairly evaluate the child's response. Please note that *I never recommend home chambers to anyone unless they are carefully and continuously monitored* by a clinician qualified to follow their treatments and adjust protocols accordingly. I feel strongly that HBOT home therapy can be one of the most valuable ongoing biomedical treatments a child may

receive, but that parents are likely to over-treat or under-treat their children because they do not understand the concept of R-EPOC and how this relates to total treatment times, frequency of treatments, consistency of therapy, and the timing of scheduled breaks in therapy, all of which are critical to achieve maximum success!

Once I have determined that a patient is or is not a soft chamber responder, I recommend a series of hard chamber sessions. As stated above, I believe that high pressure treatments may effectively treat a different set of mechanisms than may low pressure treatments. Partially in support of this theory is the study by Dr. Rossignol showing that most benefits in children with autism could be seen with both the hard and the soft chambers but that some of the benefits were better with hard and some of the benefits were better with soft. However, because the sample size was small, more studies are needed prior to drawing strong conclusions. Whenever doing hard or soft chamber dives I always recommend a break. One of the reasons this may be important is because at least one mechanism of action may not be initiated until there is a *sudden decrease* in the average oxygen concentration that the body has adapted to while doing HBOT treatments. At times the *rapid removal* of increased oxygen tensions may be the stimulus needed for the body to produce more new blood vessels as a *compensatory mechanism*. This mechanism suggesting the need for periodic breaks is more important when frequent hard chamber dives are being done and/or when a child is subjected to frequent longer total hour soft chamber dives in home chambers or when the treatments are concentrated using 3 or 4 hour sessions in a clinic over a 10 to 15 day period of time. In general I recommend breaks ranging from 2 to 6 weeks, the interval based on the pressure of the dives, the oxygen concentration that was used, and the frequency of the dives per week. The more aggressive or sustained the treatment has been, the longer the interval recommended before starting the next sets of dives or initiating the maintenance protocol.

Maintenance Protocol and Word of Caution

After observing my patients closely and subsequent to thousands of treatment hours, it is now my bias (one that needs further study to validate and one not necessarily shared by my colleagues) that possibly *the most important protocol* all parents should be aware of is the *maintenance protocol.* Many parents will complete a set of HBOT sessions, the most common number being 40 hours of treatment. What is unfortunate is that this number has been viewed by many as the goal, not as the first evaluation point along a *continuum* of treatment sets, the total number of treatment sets depending on each child's individual needs and overall response. Therefore, what is important for every parent to realize is that a maintenance protocol should be established and adhered to *between treatment sets* of therapy. By following such a maintenance protocol for a child, the parents should be able to maintain the child's currently acquired gains or lose fewer of them more slowly and to a lesser degree prior to initiating the *next treatment set* of sessions. This rule applies not only to those who have seen improvements but it is just as important for those who have not. The reason for this is because many gains are biochemical, physiological, and anatomical and may not be recognized within the first 40 to 100 treatment hours as external clinical observations though internally changes are actually occurring at the cellular level. Therefore prior sets of sessions have established the foundation upon which further treatment sets can build. In either case, whether parents have or have not seen gains, the maintenance protocol will allow the child to *retain* many or most of the benefits of HBOT and *not have to start over* at zero when sessions are resumed. Depending whether a patient is "maintaining" at a clinic in a hard or soft chamber determines the minimum amount of time I recommend per treatment. As a general rule for soft chamber dives I recommend a 1.5 to 2.0 hour session every 2 weeks if a child wears the mask and every week to 10 days if the child does not. As a general rule for hard chamber dives I recommend an hour session every 10 to 14 days. Parents with home chambers are advised to follow the break schedule and then resume another *treatment set* of sessions and continue to repeat the process. It should be noted that both

my *maintenance schedule and break schedule recommendations are constantly being reevaluated and revised* whenever necessary.

A STRONG WORD OF CAUTION IS IN ORDER due to the fact that some parents are modifying chambers to reach 1.5 ATA (7 psi gauge pressure) and using oxygen concentrators that are able to deliver higher flow volumes in order to achieve greater total oxygen concentrations. This can be ***catastrophic*** because when chambers are modified, the R-EPOC can become almost as high as that achieved in a hard chamber at 1.5 ATA with 100% oxygen. To do this is ***extremely dangerous*** for many reasons, especially if used for more than one hour a day! As discussed in detail above, an R-EPOC between 28% to 60% is safe for home use and may actually produce more cellular product and more clinical benefits than higher oxygen concentrations and higher pressures do, especially when under the direct supervision of a clinician using some of the longer treatment protocols described above. However, the ***R-EPOC values attainable from modified chambers can be disastrous***! It is my opinion and the opinion of many of my colleagues that when using higher R-EPOC values ***the potential benefit is not worth the probable risk!*** In addition, should a seam fail and the chamber rupture at 1.3 ATA, all that happens is that the chamber deflates. Should the same thing happen at 1.5 ATA, ceiling tiles can come down!

The most common concern parents have is that HBOT may not work for their child and that it is an expensive experiment if it doesn't. To answer this concern, most of us who have treated large numbers of autistic children with HBOT agree that approximately 80% of the children will respond within the first 40 hours of treatment using either hard or soft chambers. I estimate that an additional 5% to 10% of children respond when an additional 40 hours of treatment follow. Some of my colleagues believe even more children than this will respond if no limit is put on the number of hours one completes. At this point in time, my bias agrees with that belief. I have one 4 year old boy who had essentially no language who was being treated at home diving 3 to 4 hours per day under my supervision and who was not allowed to make any changes to his treatment protocol other than HBOT until we completed his initial HBOT evaluation phase. His parents saw no benefit of any kind until after 55 treatment hours at which time he said his first

word. Before he reached 100 hours he was singing the entire Blue's Clues and has continued to make even greater progress with more treatment hours!

The second most common concern parents have is that their child will not go in the chamber. To date I have only had two children who did not like the chamber after they got used to it so this concern is usually not a problem. In fact, many of the children run down the hall and cannot wait to get inside, some even banging on the chamber to get the other child out!

The third most common concern parents have is that HBOT may cause problems with their child's ears, either due to pain or due to sound sensitivity. Sound sensitivity is something that can be dealt with for most of the children by using sound muffling devices or other tricks so it is usually not a problem, especially after the child gets used to the chamber. That leaves the issue of pain. Pain is the result of barotrauma. Barotrauma is the most common side effect of hyperbaric therapy and is usually associated with pain in the ears, teeth, or other "closed spaces" and varies in degree from mild to extreme. *Baro* means pressure and *trauma* means damage. Therefore barotrauma of the ears is damage to the eardrums (tympanic membranes) due to pressure effects. Well-trained chamber operators know how to avoid ever getting barotrauma in the first place and well-trained chamber operators learn how to differentiate the signs and symptoms that occur from barotrauma, from sound sensitivity, and from child anxiety. Well-trained chamber operators also learn how to differentiate primary child anxiety that occurs because the child is scared because HBOT is an unfamiliar new procedure, or secondary anxiety that is initiated when the child senses a parent is anxious and unsure about things as well!

Hyperbaric oxygen therapy is only approved for reimbursement by insurance companies or Medicare for the following conditions: a) Blood loss, extensive, including *severe* anemia; b) burns, thermal; c) carbon monoxide poisoning; d) compartment syndrome; e) crush injury; f) decompression sickness; g) embolism, air/gas; h) gangrene, gas; i) infections, necrotizing soft tissue; j) ischemia, acute traumatic (some, not all); k) osteomyelitis, refractory; l) osteoradionecrosis; m) skin grafts and flaps (compromised); n) smoke inhalation, severe, acute; o) wounds, problem type (not all).

All other diagnoses including autism, PDD-NOS, and encephalopathy are what is called "off-label" and do not qualify for insurance reimbursement. However, some insurance companies are now starting to pay for hyperbaric oxygen therapy for the diagnosis of autism, especially when supporting studies and clinical benefit of a child can be documented. In my practice I give patients seeking consideration for insurance reimbursement a letter stating why I believe the child qualifies for hyperbaric oxygen therapy along with a packet of supporting peer reviewed studies to document my reasoning. The soon-to-be published *Rossignol studies* will be the *key supporting documents that every parent should have.*

With all the good things that I've described—things that every parent wants to hear about for any treatment they hope may also work for their child—I must offer a *strong word of caution*! During all the years that I have been refining my skills, *no skill has become more important* than the one by which I teach parents how to be *patient* with their wants, and at the same time *accurate and comprehensive in their observations*. Therefore I tell every parent that the more inconvenient, the more costly, and the more 'hype' that surrounds any given treatment, HBOT or anything else, the more parents demand to see bigger changes than they would normally require to see before saying that that treatment is valuable enough to continue. Though this is unfortunate with any treatment, because of the high cost of HBOT, because HBOT is not yet paid for by most insurance companies, and because HBOT can be inconvenient, with HBOT this demand by parents to "get what they want to get or call it quits" becomes even more of a problem! Therefore it is more imperative than ever before that parents know what they should be looking for and for parents and clinicians to be able to compare the results they are seeing in a specific child with the results that other parents are seeing in general. In my practice *the parents have created an evaluation tool that is stated in their own words the way they see things.* This *HBOT Parent Designed Report Form* has been able to pick up on small, subtle changes that parents tell me they would have otherwise missed. The PDRF, their evaluation tool, not mine, is *more sensitive* and *more specific* for the common symptoms seen when children use HBOT. Its use does not mean that other more standardized evaluation tools should not be used at the same time. However, it has been

the parent's experience that the exercise *they require of themselves* to document in great detail all "*undeniable changes*" they observed enables them to see positive changes sooner than they would have seen them if they had not taken the time to do this. They admit that by seeing these changes earlier and when allowed to compare what they see with what other parents "just like them" are seeing and saying, it encourages them to continue treatment when they confess they would have otherwise quit because the intensity or numbers of "obvious responses" were so few in comparison to the "subtle but yet present changes" that were in reality quite common.

Summary

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. ***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 with realistic expectations being the parent's guide, and when parents use the 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!