Interview with Dr. Paul Harch: the application of hyperbaric oxygen therapy in chronic neurological conditions

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Abstract

Introduction: Hyperbaric oxygen therapy (HBOT) remains a controversial and misunderstood therapy, especially when applied to chronic neurological conditions and autism. This interview explores the science behind these applications. **Methods:** HBOT is defined as a pharmaceutical and its pharmacologic effects are reviewed in the context of the author's historical application of HBOT to neurology, including autism. **Results:** HBOT has a powerful drug effect in acute brain injury through inhibition of the acute inflammatory reaction of reperfusion injury (the injury caused by return of blood flow after blood flow interruption—e.g. cardiac arrest at birth, near-drowning, etc.) The author's successful use of HBOT in divers with delayed treatment of brain decompression sickness led to the application to other types of chronic brain injury, including autism. HBOT is suggested to have common pharmaceutical actions on the pathology of chronic brain injury, including autism, that are reinforced by the author's proof of effectiveness in an animal model of chronic traumatic brain injury. Some of the author's 25 autistic patients seem to have significant birth insults that contributed to the diagnosis of autism. HBOT appears to be effective for these insults years later. Other physicians are now duplicating the author's findings in autism. There appears to be no identifiable body of information on HBOT in combination with chelation therapy. **Conclusions:** HBOT appears to be effective in the treatment of autism. The pathological targets of treatment are unknown at this time.

Keywords: HBOT (hyperbaric oxygen therapy), autism, pharmaceutical, chronic brain injury, chelation therapy

Dr. Paul Harch is a graduate of Johns Hopkins University School of Medicine and is a Diplomate of the Board of Certification in Emergency Medicine and the American Board of Hyperbaric Medicine. His clinical experience spans 20 years of hospital-based emergency medicine and 18 years of hyperbaric and diving medicine. Dr. Harch is a Clinical Assistant Professor and Director of the Louisiana State University, School of Medicine, Hyperbaric Medicine Fellowship Program and Medical Director of the Hyperbaric Medicine Unit at the Medical Center of Louisiana in New Orleans. His first application of hyperbaric oxygen therapy and SPECT brain imaging to the central nervous system began with divers with chronic brain decompression sickness and boxers with dementia pugilistica. He began using hyperbaric oxygen therapy and SPECT brain imaging with chronic traumatic brain injury and stroke in the early 1990s and with cerebral palsy and autistic children in the early and mid-1990s. After improvement in people with chronic brain injury, Dr. Harch's research provided the first ever demonstration of improvement of chronic brain injury in an animal model in the history of science. In 2001, Dr. Harch completed a study on SPECT brain imaging and toxic brain injury. He has made three presentations to the U.S. House of Representatives, Appropriations Sub-Committee on Labor, Health, Human Services and Education and the Government Over-Sight Committee with regard to the application of hyperbaric oxygen therapy in chronic neurological conditions. He has written or contributed to many articles and book chapters. In April 2004, Dr. Harch was nominated for the NIH Directors Pioneer Award.

Dr. Harch it is a privilege to have you with us here today on this most interesting topic.

Thank you. It's a privilege to be here.

Dr. Harch, first of all, what is hyperbaric oxygen therapy?

Hyperbaric oxygen therapy is the use of greater than atmospheric pressure oxygen by enclosing someone in a chamber and using it as a drug to treat basic disease processes and hence the diseases themselves.

So oxygen is considered a drug. What are the indications for use?

Well, there are a number of indications and the absolute number somewhat depends on the country that you live in. In the United States there is a list of typically reimbursed indications. And then there is a list that is reimbursed by Medicare and Medicaid and there's some overlap between those two or there's quite a bit of overlap. Outside the United States however, there is a much larger list—in Europe, in the Far East, and in Russia. So asking about a list is somewhat dependent on where you're practicing. In the Unites States it's fairly narrow and outside the United States it is a much longer list, including many neurological applications.

All right. So let's differentiate between what is reimbursable insurance wise and what conditions hyperbaric oxygen therapy makes sense for. What would be the indications for use then if we weren't worried about who was paying what?

Well if we weren't restricted, you would have likely some additional indications, including the use in acute severe traumatic brain injury, the use in acute cardiac decompensation usually in the setting of acute myocardial infarction, and a use in cerebral palsy.

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So, what's holding up being able to use hyperbaric oxygen therapy for situations where it would really benefit the patient?

That's a great question. It's a combination of what I like to call the culture of medicine and medical politics. The typically reimbursed indications have been compiled by a committee in the Undersea and Hyperbaric Medical Society(UHMS). And unfortunately, that list of indications, at least for probably six of the thirteen indications, does not meet the standard for medical proofing. In other words, there isn't good clinical data to support the use of it. However, the list was compiled by tradition and by the physician members of the Committee who had done maybe some animal research and clinical treatment in that given indication. And trying to get additional indications on that list for reimbursement has a degree of arbitrariness to it. For example, there is more evidence for the use of hyperbaric oxygen in acute severe traumatic brain injury than for most of the indications on the reimbursed list. In cerebral palsy there is more data now showing a benefit of hyperbaric oxygen than there are for a number of the other indications on that list. So, the problem is partly political. And I think it's also rooted in doctor problems. The United States Navy has dominated the field of hyperbaric medicine for years and outsiders have had difficulty having their ideas accepted. In particular, one of the individuals in the United States, Dr. Richard Neubauer, who pioneered the use of hyperbaric oxygen primarily for chronic neurological conditions—how should I say this—has not had his scientific thoughts properly evaluated. And he has been disparaged because he has had the nerve to treat outside of this accepted indications list. So to sum this all up, getting something on the typically reimbursed indications list is a matter of both science and politics and that's what has inhibited some of the applications to neurological conditions.

Well, Dr. Harch, I think I jumped way ahead, but I've got to tell you, that parents of children with autism are well acquainted with the scenario that you have just described, that Dr. Neubauer has faced. So we can commiserate, at least speaking for myself.

Let me just interject one more quick thing. Unfortunately, both the UHMS and another medical society have now issued statements about punitive actions against their members who treat outside their list. And this is contrary to the practice of medicine, historically, and the Hippocratic Oath. It is also what's inhibiting the application to other indications. So what we're developing now is a speak-easy situation with hyperbaric departments where I get phone calls from doctors around the United States asking about how to treat a given patient in their hospital hyperbaric unit, but the doctor is not willing to discuss it or stand up and talk about it for fear of repercussions and recriminations from the medical societies. It's a very big problem. But, we'll go on to the other things. I know you had a lot of questions.

Okay. Let's backtrack. Describe the pathogenesis of brain injury, and the death or idling of neurons.

Any insult to the brain induces a primary immediate injury. And the degree of damage is proportional to the degree of the insult or the force of it such as in traumatic brain injury. You can have a very mild traumatic brain injury or you can have a very severe one. However, regardless of whether it is a traumatic brain injury or a cardiac arrest or an electrocution or a toxin exposure— whatever—the immediate insult damages, or I should say, kills some of the neurons and injures others. After that immediate insult however, the body's typical inflammatory reaction is set in motion and part of that inflammatory reaction, regardless of what the initial insult is, is an elaboration of chemicals in the brain that damage neurons, dilate blood vessels, make them leak, and cause leakage of fluid known as edema or swelling. That swelling, once the liquid has leaked out of the blood vessels, compresses tiny blood vessels and reduces blood flow and hence oxygenation. So you have a secondary insult that occurs and then the later part of the inflammatory reaction is elaboration of white blood cells. In other words, they come in, they are activated, they stick to the vessel walls, cause further leakiness, discharge their enzymes and do further damage. These secondary injury processes cause a stereotypic type of pathology that leaves some cells dead but leaves others in a state of low blood flow and oxygenation or a metabolically injured state that can last for quite some period of time. The specialty of neurology has had the view for years and years and years, if not hundreds of years, that there's no such thing as a stunned or injured neuron that can exist beyond, let's say, hours. In fact a lot of people originally thought it was six minutes. However, other tissues in the body have shown injury that can last much longer and what is becoming apparent with the application of hyperbaric oxygen to all these chronic neurological conditions is that the thinking in neurology was wrong. In fact, injured brain cells can last for a far greater time than what was originally thought.

Is that the idling of neurons?

Correct. Those injured neurons are considered the idling neurons and that was the Letter to the Editor of *Lancet* in 1990 that Dr. Neubauer published, where he described a 14 year post-stroke, 60 year old woman, who was wheelchair bound, couldn't speak, couldn't feed herself, drooled, etc. He did SPECT brain blood flow imaging and was able to show before and after a single hyperbaric treatment an improvement in blood flow to what was thought to be a dead area of the brain. Over the course of about 16 months or so giving hyperbaric oxygen at a lower pressure than typically used and supplementing it with face mask oxygen at a nursing home, they were able to improve the function in this lady. The idea was that they may have activated these idling neurons that had existed in this low blood flow state in the stroked area.

Wow, that is really wonderful and that would be a person who people would typically tend to give up on, too.

Absolutely.

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So let me just go over this and see if I have it right and correct me if I'm wrong. You have a primary or immediate injury to the brain, such as from cardiac arrest or electrocution or toxic injury. So you have an insult, then you have inflammation, then you have chemical reactions in the brain, this dilates blood vessels, this causes edema or swelling which compresses blood vessels, that reduces oxygenation and then you have an elaboration of white blood cells—that causes further damage such as to the cell wall and correct me if I'm wrong and then this results in a chronically, metabolically injured state.

Correct. But I'm going to shorten the time frame there. The white blood cell elaboration, chemical elaboration, and secondary injury is all occurring within minutes to hours of the initial insult and develops simultaneously. The white blood cell injury, chemical injury, and leakage of fluid continues over the next 36 to 48 hours. This stereotypic reaction results in the stereotypic, common pathological injury. That is what hyperbaric oxygen therapy is treating in delayed fashion when we come in a year or two later, as well as if you treat acutely.

Are there many examples or studies of the effectiveness of hyperbaric oxygen therapy in a variety of acute injuries, including acute brain injury?

Yes, but most of them are in animal models (if you limit acute to the first 3-6 hours after injury). There are an increasing number in humans. But for instance, the number of studies now in animal models of acute brain injuries such as what is called global ischemia, meaning you have stopped all the blood flow to the brain or severely reduced it, as in cardiac arrest—the numbers of these studies is multiplying and the results are uniform. What they're showing is that in acute carbon monoxide poisoning and acute global ischemia--even in some of the other acute injuries—a single hyperbaric treatment within the first few hours of injury can markedly reduce the injury and subsequent damage. By markedly I mean upto let's say 90%, almost a 100%, in some cases. The human examples of this, though, have not been as well documented or researched. There have been some in infants dating to 1963 in England and in Brazil in I believe the early '90s. And there have been some reports of coma cases in China and a group of near-hanging patients in northern France, 170 near-hanging patients. So the human examples are not as common yet, but what it appears is that hyperbaric oxygen in the setting of acute brain injury is acting like a generic drug.

Okay, so what is the common problem of all these injuries that hyperbaric oxygen therapy seems to address?

That's a great question. Many of the targets are not identified. But one of the targets is the white blood cells and it appears that the white blood cells are inhibited by the hyperbaric oxygen, such that as they come through the blood vessels in the damaged area, they don't stick to the walls of the blood vessels. As a result, they don't initiate much of the secondary injury.

There are other effects that are likely occurring on the cells and in particular the DNA. During a low blood flow, low oxygen insult there is a type of injury to the DNA and it appears that hyperbaric oxygen may be reducing or preventing that injury if it's delivered early enough.

Okay. Is the impact of a lack of blood flow and the impact of a lack of oxygen equal?

No. It appears that low blood flow is a more severe injury. In other words, low oxygen by itself, as a purely individual form of brain insult is fairly well tolerated for a certain period of time. But eventually, with low enough oxygen you affect the heart and you will decrease the heart's pumping ability and so you eventually end up with low blood flow. So low blood flow has the insult of not only low oxygen, but you deprive the tissue of all of the other nutrients, and especially for the brain that's glucose or sugar. It appears that the insult of low oxygen, low glucose, and low nutrients is a more damaging form of injury.

How does this relate to what happens to children with autism? Is the brain injury in autism considered chronic or acute and does the hyperbaric oxygen therapy fit both?

Well, that is more difficult to answer because no one knows with certainty the exact cause of autism. It appears that autism has many different causes and if you could pinpoint the cause at the time the cause was elaborated, then hyperbaric oxygen rendered immediately may have some impact on the insult that's going to generate the autism injury or diagnosis. But most of the children that we're seeing we are unable to couple the hyperbaric oxygen with the insult, unless it occurs at birth. So for instance a number of the autistic children that I have treated have had very obvious birth insult with low blood flow, low oxygen insults, very poor APGARs, resuscitation, etc. Hyperbaric oxygen therapy potentially delivered at that time may have a big benefit. But most of the children we're seeing are two years and beyond and of course by that time it is a chronic brain injury. What you're treating at that point is a little bit more speculative because the exact pathology has not been identified.

Okay. Are there birthing events that can cause or act as a set-up for autism?

It appears so. Part of the problem is the inexactness or I should say the non-reproducability of the diagnosis. In other words, a lot of different pediatric neurologists will give a diagnosis of autism or autism-spectrum and some of the time it may not be completely along the guidelines of certain rating scales. But the children nevertheless are called autistic based on a predominance of certain behaviors. Many of the children I've seen or, I should say, a good number of the children have deficits in addition to the typical autistic ones that may be motor, sensory or appear to be sensory, coordination problems and so on which suggests that there is a global brain injury such as would occur with low blood flow at birth.

Okay. So are you saying that the mechanics of certain birthing injuries are consistent with symptoms displayed by some children who have autism such as it looks like it happened to a

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trauma site in the brain or they're displaying emotions or behaviors that are consistent with birthing injuries?

What I'm saying is that birthing injuries can result in a pattern of injury to the brain that gives you the constellation of signs and symptoms that result in a diagnosis of autism. Essentially, in some autistic children you can't implicate necessarily a vaccine problem or let's say another toxin because from day one of birth these children are abnormal after the birth insult. And yet later they are given a diagnosis of autism. So it appears that that insult is causing an injury to the brain that is mechanistically different from a toxic injury, but may injure the same areas of the brain and, hence, give you the same constellation of signs and symptoms that result in the diagnosis.

Okay, so let's talk about these children for a moment. What can you do about this, and how effective might hyperbaric be if it's started days or years after the injury?

Well, it can be very effective and it has a range of effectiveness. For some children it's a small effect. For others it's a fairly dramatic effect. I can't say that we have cured any of these children. What we're doing is correcting, or I should say, repairing a chronic wound in their brain with hyperbaric oxygen much like we do for chronic extremity wounds in diabetics or chronic radiation wounds or any of the other chronic indications that hyperbaric oxygen has typically been applied to.

All right. Now let's talk about the children who have documented toxicity issues such as mercury poisoning. I think we've already mentioned the fact that hyperbaric oxygen therapy can help with toxic brain injury. How does it do that?

It's unclear in the case of mercury.

Okay, well, all right. What kinds of results have been seen with those children?

The same range of results, a variable range. Some of them, again presuming that those children have a toxic injury and that's very hard to prove at least in the individual patient, but assuming that they do, they have a range of responses also. See, I think that the key that needs to be understood here is that the discovery I made in the late 1980s and 1990s was in our divers with brain decompression sickness and in the boxers in whom my partners had started a program attempting to treat. These were boxers who had brain damage from boxing and of course all of these cases of the boxers were chronic. The divers were acute, subacute and then we had some chronic cases. What appeared to me is that when we were treating the time-honored, traditional HBO application, i.e., decompression sickness, that we were not treating bubbles in these patients, especially the farther we got out from the injury. It rang a bell and alerted me to the fact that possibly we were just treating chronic brain injury that could be treated in other patients with other diagnoses. So I started extending a lower dose protocol of HBO to patients with old stroke, old trauma, etc. and in the process got referred in 1992 what was to become the first cerebral palsy child treated in North America with hyperbaric oxygen. And then what followed were more children, including autistic children What I started doing was applying in a very stereotypic manner SPECT brain imaging to document the changes seen with low pressure hyperbaric oxygen and running a fairly rigid protocol. What I found was these autistic children were responding just like all of the other diagnoses we were treating. Basicly, the 23 or so children with autism, autism spectrum, Asperger's Syndrome, and children with neurological abnormalities and strong autistic traits or behaviors, improved just like the adults and other pediatric diagnoses. Some of them I'm sure are due to toxins, some clearly were due to birth injuries. and some due to causes that we don't know. But the great majority were responding fairly similarly. And now what's happened is two other sites in the United States have duplicated this. One in Los Angeles (the physician there is now retired), treated nine of these children in the late 1990's and early 2,000's. In New York there are approximately 20 children that have also been treated. Both of these doctors were claiming an improvement very similar to what I was seeing.

Okay. So those are studies, right?

They are not true studies, really. They are children who were referred and were clinically treated. Many of mine were actually treated on a protocol that was approved by the Human Experimentation Committee (Institutional Review Board-IRB) of our local hospital. So mine was a formal study, initially. But now we don't have that protocol and I'm back to treating the children clinically. What I'm saying is that all of the results are very similar .

Tell us about SPECT imaging and how the computer develops the pictures.

All right. SPECT is an acronym for Single Photon Emission Computed Tomography. It is CT scanning technology applied to nuclear medicine. SPECT measures brain blood flow and indirectly gives you information on metabolism. What happens is, instead of shooting the x-rays through the tissue like you do with a CT scan, you inject a very small amount of a radioactive material, 5% of which is taken up into the brain. And it stays in the brain for hours. It is distributed and taken up in brain proportional to blood flow. So you're able to measure blood flow. As it gives off these radioactive counts you lay underneath what's a sophisticated Geiger counter, if you will, and the best of these machines have three Geiger counter-like cameras around the head that rotate around over the course of about 16 minutes. They collect all of the counts and then the computer reconstructs it and a technologist processes it to give you a picture of brain blood flow. What you're able to see is each area of the brain's blood flow or function in relation to the other areas in the brain. So the way the computer does this is it takes the brightest spot in the brain where the highest amount of radioactive counts are, which means the highest amount of blood flow, and gives it a relative value of a 100. All the rest of the areas of the brain are then scaled to that and you get a picture showing on this type of scale how much blood flow there is in all of these areas in a relative fashion. What it allows you to do is see

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how the brain is working as opposed to looking at just a road map of the brain like CT or MRI gives you.

Wow. So you do a SPECT scan and then you perform hyperbaric oxygen therapy and repeat scan.

Yes. And the way this began was in it's application to the divers. What we would do is image them as soon after they had their initial treatment to see what their brain looked like. Then we either treated them another time and repeated the imaging right afterwards to see if we were further improving the brain and it matched them clinically, or we would repeat the imaging once the diver said, okay I'm feeling pretty good, I'm not getting any better with successive treatments. At that point we we'd see how the imaging looked. What we found was it correlated very highly and strongly with the diver's clinical reports of his improvement and our demonstration of that on our physical exam.

Excellent.

So we then took that sequence of SPECT, one HBOT, repeat SPECT, and thought well maybe we could use this as a test in the divers, like Dr. Neubauer had done in the Lancet with the stroke patient. We decided to look at it in a very rigid fashion for anyone with a chronic brain injury and we chose chronic brain injury because we didn't want anybody to say that the cases had improved on they're own because they were only three weeks out from an injury. So we made people wait a minimum of one year and then I would examine them, video examine them, take a detailed history from them, and do a SPECT brain scan. The following day or two days later they would go in the chamber a single time and then within hours we would repeat the brain scan and look to see if there were improvements. Whether or not we did, we went ahead and offered the patient treatment and at the end of treatment we sat down and I repeated all the exams, history, videos, etc. and we repeated the SPECT scans. What we found was that second SPECT scan after a single treatment was predicting and showing injured brain that would cause clinical improvement with repetitive treatment. Furthermore, the clinical improvements were documented by improvements on SPECT brain imaging after a course of treatment. And so the autistic children, the cerebral palsy children, the adults with trauma, stroke, and toxic brain injury were all put in there, or I should say, were all part of this study, which ran for nearly six years and involved a couple hundred patients.

Wow. That is really exciting.

Now what we found though is that we didn't need the imaging. It was a leverage tool. Statistically, if you looked at all the patients the vast majority of them showed some improvement with repetitive low pressure hyperbaric oxygen treatment. Eventually, the imaging was only necessary if people wanted to try to see what their brain looked like, the dysfunction, or see the injury in their child and/or use it as evidence in application for insurance reimbursement of hyperbaric oxygen. Or they needed it for documentation in litigation when there was some question about whether there was a brain injury or not. In these instances if you have the imaging showing an abnormality and then after treatment an improvement and simultaneously improved patient, you knew that there was an injury there in fact to begin with.

Okay but you're feeling that the scan wasn't absolutely mandatory is that because of your previous work showing that when someone said they had improved clinically it was evidenced by their scans.

Yes.

But I'm saying the imaging, now because of the large experience between 1993 and 2000, is optional. We're no longer on a rigid protocol by a hospital experimental committee and an experimental protocol mandating the imaging. We now know that we have a very good chance of improving a patient clinically without having to prove it on the imaging. But if people want the imaging I'm happy to do it.

Okay. So I think I heard you say that you have a way, and I'm not telling people that this is 100% reliable (that's not up to me,) but you can prognosticate or test the amount of recoverable tissue in the brain of an autistic patient by scanning?

Yes.

By scanning.

Correct.

By that sequence. Interestingly, something very important happened in here. When I was showing the imaging around the country and even internationally at meetings and lectures I ended up in contact with a very, highly respected nuclear radiologist who offered to take the imaging on a number of the children I had treated and analyze it by a very sophisticated method. I sent him all of the imaging on the first 18 children that I had treated beginning in 1992 through I guess it was 1998 or so. What he did was take all of the first scans, baseline scans, average them, take all of the scans after a single treatment and average them, and then all of the scans after a course of treatment and average them. And then we subtracted. We took the second scan which is after that first treatment that was trying to look at injured brain's responsiveness to hyperbaric oxygen and we subtracted it from the final scan after a course of treatment. What we found was the areas of the second scan that had showed improvement were some very important areas of the brain that had to do with memory or cognition, vision, emotion, aggressivity, etc. And those areas that showed up on that second scan were the same areas that showed improvement after a course of treatment so that when you subtracted the second one from the final scan there were almost no changes. The subset of patients where it was really proven was the cerebral palsy children. So, when we looked at a homogeneous diagnosis, cerebral palsy, we found this very tight correlation which proved that what Dr. Neubauer had shown in that idling neuron letter was true. In other words, like Dr. Neubauer, we proved that you

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could identify damaged areas in the brain with SPECT brain imaging before and after a single treatment that would respond to repetitive hyperbaric oxygen.

Okay. So you're not saying there wasn't any change in the amount of restoration between the second scan and the final scan. You're saying that the areas that were improved in the final scan were those areas that were improved in the second scan, is that correct?

Yes. it's not quantitative, really. I mean you can't correlate the exact amount of change on the scan with exact amount of change in functions. All we saw was that by this statistical and mathematical method that the areas that showed significant improvements in blood flow after a single hyperbaric treatment were the same areas showing significant improvement in blood flow after a full course of hyperbaric oxygen.

Okay.

Simultaneously the children were improving.

Were improving in clinically from the second to the final scan.

Correct.

Okay. Good enough. And some of the areas that you said had improved in those patients were memory, cognition, vision, emotion and aggressivity.

Yes, well in more general sense, areas that control emotion and behavior, irritability, this type of thing.

Tell me the difference between low and high dose and whether you use the same dose of hyperbaric oxygen therapy for chronic illness as you do for acute injury.

The difference is somewhat arbitrary. You'll have a hard time finding people who will define it. But in the K.K. Jain Textbook of Hyperbaric Medicine, in one of the chapters I wrote, I defined low pressure HBOT and we have talked about it in terms of being less than two atmospheres of absolute pressure. .So generally two atmospheres of pressure and greater is considered higher pressure hyperbaric oxygen or traditional hyperbaric oxygen. Less than two atmospheres is considered low pressure. And then what's crept in also is this term "mild hyperbaric" which they've used to describe treatment in the portable chambers where hyperbaric air or oxygen supplemented hyperbaric air is pressurized to 1.3 atmospheres. But generally, when we talk about low pressure hyperbaric oxygen it is less that two atmospheres and it's generally in the range of an atmosphere and a half.

Okay. So what do you use?

I'm in that low pressure range for the chronic conditions. For acute conditions it is different; the responsiveness of tissue is mainly at higher pressures, but you can't usually treat as much at these higher pressures acutely. Meaning you can't go on for many, many treatments like we can at lower pressure.

So for acute injuries do you switch from higher to lower or do you just stop?

Well you have to adjust the dose based on the patient's response. Often though if you get to patients quick enough, for instance with decompression sickness, you only need the first treatment. When they did a review of the world Navy's experience with HBOT in decompression sickness, they found that, the first treatment was curative in 90% of cases if they delivered it within one to two hours. And that's a generally high pressure treatment. So, if you get someone quick enough a high pressure treatment can be curative on the first treatment and you don't need a lot more additional treatments.

Okay. And speaking of you mentioned the word "mild" and you talked about portable chambers. Now are portable chambers as efficacious as going to a center that does not have portable chambers or is there a safety concern?

Well, the first part of that nobody knows. The safety concern is always there and depends on the knowledge and experience of whomever is delivering the treatment and using the chambers. We know from the Collet Study in 2001 of the Montreal cerebral palsy children, where they made a mistake in the design of the experiment and they gave the control group of children 1.3 atmospheres of air, that this had a beneficial effect. In fact it was equivalent to and in some cognitive measures a little bit better than the hyperbaric oxygen group that got 1.75 atmospheres. The 1.75 I felt was too much so there may have been both an overdose effect with the 1.75 and who knows, maybe the proper dose or even an under dose at 1.3 atmospheres of air. But what happened is it appears that 1.3 atmospheres of compressed air or 30% increase in oxygen was enough to cause a very measurable benefit in those children. So that is the one study we know that has some evidence for "mild hyperbaric air." Beyond that there's claimed widespread use, especially in the Far East but there's very little data on this. Dr. Heuser out in California had some SPECT imaging and other data that he showed in children and sent as a letter to the Lancet that followed the Collette article, but beyond these instances there's very little published information on the "mild hyperbaric" to make a really solid statement about effectiveness in many conditions.

And I guess the other part of my question was: is it safer to go for hyperbaric oxygen therapy in a center rather than using a portable unit?

Well, we always think it's safer to go to a center where you've got medically knowledgeable people. What people forget is that hyperbaric oxygen therapy is a medical treatment. It always has been and it always will be. It's just that in this neurological field now, it's pushed underground partly by these punitive statements or threatening statements that have been made by medical societies and some of their doctors so that we have people forced to be their own doctors, buy portable cham-

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bers and so on. But you can have problems with any medical treatment and especially with pure oxygen. So we recommend that this be done at a facility where there are medically trained people. In fact if you go back to I believe 2001 there was an article published in the online edition of Pediatrics and it was the doctors from the hospital-based facility in Vancouver reporting on two complications that occurred at a free-standing facility delivering low-pressure hyperbaric oxygen in Vancouver. We wrote a rebuttal to that article because it just was scientifically inaccurate. The point is though, they had some complications at this facility and the level of medical expertise and care there may not have been adequate. In other words, they had to send the patients to the hospital and these children were treated for pretty severe conditions, some of which may have been preventable. So we recommend that it be done in a facility where there are medically knowledgeable people because accidents and side effects occur, untoward effects of hyperbaric oxygen, complications etc., like with any medical treatments.

Okay. So it's not that this is a particularly or even as risky procedure but it just needs to be done right, is that correct?

Absolutely correct. This is one of the lowest risk procedures in all of medicine.

Okay. In an autistic child with mercury-induced brain damage, will hyperbaric oxygen therapy produce any lasting growth and restoration of function without chelation also being administered?

I can't answer that exactly. That's not known. Of the 23 children that I have treated a good number of them have had chelation therapy either before, during or after hyperbaric oxygen. And because the numbers are small it's hard to dissect out enough patients in each little group to make a statement such as that. It seems to me, and it makes good sense, that if you have a toxin that's embedded in tissues that is inhibiting tissue growth that you would want to remove it to get lasting changes. However, hyperbaric oxygen therapy may be able to induce some of the changes in the absence of removing it or may even stimulate removal of it. We don't know for sure.

How much may the efficiency and effectiveness of either therapy (and I understand that this may be educated speculation)—chelation or hyperbaric oxygen therapy—be increased? By using both, may it shorten the overall time of therapy?

Nobody knows that answer. That was the projected thought and that was the protocol that we were wanting to design and set up at the University of Oklahoma. And it was the thought that stimulated me to make some very, very positive statements about the potential for this at the Congressional Hearing in 2004. In other words, we had taken Dr. Buttar's reports of improvement in the autistic children he had chelated and coupled them with the reports of improvement in these children by myself and other hyperbaric oxygen practitioners to make the statement that combining the therapies made the most sense and potentially could have the greatest benefits. And what we were hoping to do and what I was hoping to do by making what maybe even a little hyperbolic statement was to stimulate interest and funding to get this whole process rolling at the University of Oklahoma. We wanted to put it in an online format and be able to collect massive amounts of data from patients all over the country who are getting chelation therapy, hyperbaric oxygen, or a combination of both and allow them to sign up on a formal protocol where we would put them in one arm or another. It make sense. I think it would be the best way to do it, in other words, chelation plus hyperbaric in some combination, but we don't have solid proof that it would work. It's more a theoretical possibility.

So is the International Hyperbaric Medical Association still collaborating with the American Board of Clinical Metal Toxicology under the supervision of Oklahoma University Health Science Center to study this? What is the status of this project?

Well, yes, but it's gotten mired in some administrative delays in trying to set it up. Part of it is a funding issue. It takes a number of thousands of dollars to actually set up the Institutional Review Board application, get all of the online programming done and roll this out as a formal program. So it is awaiting funding and some more administrative maneuvering.

So let's talk about the exact mechanisms—I'm backtracking a little bit again—the exact mechanisms which hyperbaric oxygen therapy actually helps, restores and cleans up the areas of the brain. Thinking back on what you said earlier, does it do things like restore the brain tissue metabolism of oxygen and nutrients or you know you said it woke up the idling neurons?

Yes, well if we go back to my definition, it is the use of high pressure oxygen as a drug to treat basic disease processes and hence the disease itself. In acute situations as I talked about we're affecting that inflammatory reaction. We're also able to oxygenate these low oxygen areas and that seems to have some kind of metabolic benefit, acutely and some type of effect on reversing the abnormal or injury physiology. In a chronic situation with a chronic wound what has become apparent is that hyperbaric oxygen is acting as a DNA signaling drug. And there are now multiple molecular biochemical experiments showing this in animals. Even in the acute situation actually hyperbaric oxygen is acting on the DNA to stimulate the DNA to begin elaboration—the process actually is called "transcription," of gene sequences that code for repair hormones. And this has now been measured. Various hormone levels have been elevated with hyperbaric oxygen and they're measuring those transcription products— called messenger RNA—and also showing up-regulation of certain types of growth hormone receptors on the cells. So in the chronic situation what we're doing is we are repairing the wound. And to my knowledge, except for Regranex the isolated platelet-derived growth factor that's available for application to diabetic foot wounds, HBO is the only prescription repair drug that we know of. In other words, we are stimulating the repair process through hormonal elaboration and the eventual result is growth and replication of healing tissue cells and of new blood vessels.

Wow.

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Yes. And that's what we were able to show indirectly in an animal model. In the early '90s as I started showing this at various types of meetings in the chronic patients that we were treating, the complaint was that I didn't have an animal model. And so we went to a well-known acute animal model and we just let the injury mature until it was a chronic one. Then I went and applied the human protocol to the animals (it was a trauma model) and what we found was an increase in blood vessel density in the damaged area of the brain that was causing the behavioral or the cognitive defects in memory and a simultaneous improvement in that memory function in the hyperbaric treated rats. Importantly, the two of those, the blood vessel density and the improvement in cognition, were highly correlated. This manuscript is done and it's been a long time in the making and we're very near to submitting it.

Wow. That is just dynamite.

Well it is and that's what has allowed me to make some of the bold statements that I have made in the textbook chapters and in public appearances, namely, that we have a treatment for chronic brain injury. I mean normally the FDA drug approval process is that you do test tube work, small animals, large animals, then the foreign human trials and finally in the United States they do the clinical trials. What we had done is found this worked, just serendipitously if you will, in the treatment of the age old indication for hyperbaric oxygen—divers' disease or decompression sickness—and then extended the findings to a variety of different human clinical situations and then go backward and apply the human protocol to animals and prove that it worked. What it suggests is what I talked about earlier in the application of hyperbaric oxygen to the acute animal situation, that HBO is acting as a somewhat generic drug on generic pathology in animals and humans.

Can you please repeat what you said about transcription gene sequences, messenger RNA, regulation of growth hormone, etc.?

Okay. Hyperbaric oxygen in both acute, but especially in chronic situations, is acting as a DNA signaling drug to turn on the transcription process of DNA and specifically the genes that are coding for growth and repair hormones. The transcription process, which means taking the DNA to messenger RNA, proceeds to translation where the messenger RNA gets translated into proteins. It's those proteins that are growth and repair hormones. Simultaneously, there is a stimulation and up-regulation of the surface receptors on the cells that accept some of these growth hormones. So you're making more hormones and you're also having the cell be able to respond to these hormones better. The net result is growth of tissue—in particular blood vessels.

Wow. Now the results you saw in your animal model with improved memory, etc. are, is that the same type of result that an autistic child might experience?

Yes. Or cerebral palsy. Now granted the mechanisms may be different. As we talked about we could be treating all sorts of different things and many different causes in an autistic child. But if we just look at it in the setting and with the perspective that I was treating 40 to 50 different neurological diagnoses over these years and we were seeing the patients—some diagnoses more than others—respond in a similar fashion it implies that we may be inducing the same effect in all of these different diagnoses. In other words, the patients were showing improvement in their injury and when we took that same protocol and applied it to an animal with an injury, we got the same response. So what it suggested was that at least some of the mechanisms that were active in the humans or I should say, some of the mechanisms of hyperbaric oxygen that were in the humans we were treating were the same mechanisms in the animal model. And vice versa.

What kinds of functional areas do autistic children show improvement in? What kind of reports do you hear from parents?

Well, we hear reports of improvements in their autistic features, in other words the socialization, the language, and the repetitive behaviors. We see the children making eye contact, we'll see them advance some in speech where they'll either start to say some words or make sentences. And this is not all of them, I'm just saying there's a range of them. The general one is you have improvement in some or all of these functions. And the third thing is that we'll see improvement in their repetitive behaviors, their "stemming".

And other countries are using hyperbaric oxygen therapy with success it sounds like?

Yes, but I don't know how much or how many of them have applied it to autistic children. What we saw at a number of the International Symposia were doctors applying this to children with cerebral palsy after the reports here in the United States and Canada. And what those doctors were reporting was a general positive experience in those cerebral palsy children. Now how many are treating autism and other pediatric neurological diagnoses is not clear because the information hasn't been published. And what is in the symposia are often some more acute types of studies.

Dr. Harch what are the different kinds of chambers and facilities. I know we talked about having a portable unit in your driveway or going to a center. How many children are allowed in a chamber? Are there any safety risks to having too many people in a chamber?

Well, yes. There are safety risks. There are a number of different types of chambers. There are the single person ones, both the portable and the more hard shell, actually they're divided into the soft chambers with the canvas-like exteriors and then most of those are considered portable and collapsable. Then there are the hard shell chambers, the typical single person ones. And actually these single person ones can have more than one person in them; you don't like to do that but it's been a

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habit. In other words a lot of times the mother or parent may want to go in the chamber with the child so you will have two of them in there at once. Those chambers are also portable even though they're hard shell. Typically I mean they are portable—you can put them on a truck, they're on rollers and you can roll them around. The bigger ones of those however are not so portable. One of them in particular weighs 5,000 pounds. The next level up are the "multi-place chambers that can accommodate multiple persons because of the size of them and they can be 30, 40, 50 feet long. In the 1920s Cunningham's Chamber I think was nearly 100 feet long. They can make, you can make them as big as you want to. But those multi-place chambers are usually so heavy they are fixed, they're not really portable except with a crane and a big truck and they can accommodate a fairly large number of patients. Those, because of their size, are not economical to pressurize with oxygen so they're pressurized with air and then you breath oxygen from a mask or a little hood tent that's placed over the head. Whether or not you are in a portable chamber or a hard shell monoplace chamber or the larger multi-place one, as long as you're at the given pressure, at the same pressure and getting oxygen at that pressure or the same mix of oxygen and air, you're getting the same hyperbaric oxygen.

You don't have to worry about too many people being in a chamber and breathing out gases?

No, well that's another issue. In the air chambers that have hood tents or face masks there is an exhaust line so that when you breathe out you're not breathing into the chamber. You don't want elevated levels of oxygen in an air chamber; that's in fact how many of the fires have occurred. Normally it is exhausted outside the chamber. But the chamber fires that have occurred have been in air chambers where they have oxygen leaks and simultaneously someone brought in some type of fire hazard, hand-warmers, or something that had a spark to them and it started to burn. Of course once you're above about 23 and a half percent oxygen, fire rate is accelerated. The other risk regarding having too many people in a chamber you talked about is if you should have problems. I mean if you had 20 people in a chamber and no inside attendant or one inside attendant and had some kind of problem you may be under-manned to take care of it.

Right, but generally I hear that the risks are minimal., I've heard some children have problems with their ears. Are any problems to any children's eyes or anything?

The main problem is ear clearing, in other words adjusting the pressure like you do when you go up on an airline flight. And there are ways to minimize that, but that's the most common one. In children with seizure disorders you have to be careful. You have to adjust the dose with that because they are more sensitive to the oxygen. Beyond that the risks are really minimal and in the hundreds of cases we've treated at least half of which are children, we have treated extremely ill children, and the complication and problem rate is very, very low. I mean you need to select your patients and be careful and make accommodations when they have airway problems in particular.

Well I guess that's another good reason to have knowledgeable medical providers on hand and doing an evaluation and assessment as with any significant therapy for your child.

Yes. I mean we've had aspirations in children who were very ill. And that was one of the cases up in Vancouver also. So again it's a medical treatment. You like to have people who are medically knowledgeable and adept, who are delivering it. And since we are dosing a drug, you want to carefully be following the patients. You could have too much, other times you're not doing enough.

Yes, I would want to be really careful when I was doing things that would change my child's brain for the better, but still I'd want to be careful.

Yes.

Let's come full circle around to the beginning of the interview and tell us why is this protocol more fiscally logical for government than not using this protocol—in a utopian world?

In a utopian world if you could treat sooner than later, you have a better chance of reversing, correcting or ameliorating a problem. The second reason is, if we can improve these children and if by all indications we are, the long-term economic impact will be far less. In other words, children that require one-on-one attention for their entire adult life are a massive problem in the United States. And not only from just the manpower necessary to accommodate them, but it's a big financial problem from lost productivity in society. And we haven't even talked about the very personal damage to that individual.

Yes.

If you're really looking at just cost-effectiveness, the cost of caring for this entire generation of damaged children is phenomenal. If we can reverse this early on or ameliorate it, it will pay a long term dividend.

Yes and even more important than the money is the health of the child so in a utopian world this wouldn't even have happened to our children.

True.

So, why isn't there more widespread use of hyperbaric oxygen therapy by the medical profession?

That's the million dollar question.

Well it really sounds like this is an exciting and viable road to look into for the field of neurology.

It is. I'll tell you where the problem lies. It gets back to the culture of medicine issue and the problems with medical societies and doctors and so on. A lot of this is also rooted in an inadequate definition of hyperbaric oxygen. Traditionally hyperbaric oxygen was defined as a therapy used for intractable, in-

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curable and otherwise hopeless medical conditions. Of course that definition which went through to as far as almost 2003. Today, it's still in much of that original form except for the addition of the verb "is". The inadequacy of this definition has been responsible for a misunderstanding of what hyperbaric oxygen is. The definition I gave you at the start, in other words, its existence as a drug is very different from what the traditional concept has been. So it has been an unknown therapy that's been used for hopeless medical conditions. Well, that list of accepted indications or typically reimbursed indications put together by the medical society is a group of disjointed diagnoses. Decompression sickness, chronic bone infection, compromised flaps and grafts, carbon monoxide poisoning, brain abscess. When practitioners look at this, they look at it and say this makes no sense. Why this list of seemingly unconnected diagnoses? When you look at hyperbaric oxygen in terms of a drug that acts on basic disease processes common to many different diagnoses you now can go back and look at each diagnosis and say, oh wow it is effective on the hypoxia and the reperfusion injury in this one and this one and this one, it's effective on growing new blood vessels in this one and this one. And pretty soon the list starts to make sense. Then the obvious question comes about, why not many other diagnoses with similar disease processes?

Yes.

Well what happened in the 1970s was Dr. Richard Neubauer said, guess what guys? I applied a lower dose of this than what was traditionally used in chronic wounding and treatment of divers by the U.S. Navy to a few multiple sclerosis (MS) patients and they got better. Next thing you know it got politicized. The MS Society was apparently very upset over claims that this worked on MS.

They funded a study done in New York City which was published in the *New England Journal of Medicine* that proved that hyperbaric oxygen was effective in MS. However, due to various political problems coupled with the fact that the hyperbaric physicians could not explain and defend how this worked—what the mechanisms of action maybe--and they couldn't give an adequate definition that might explain it, i.e., acting like a drug—it was criticized. In the face of unchallenged and unanswered criticism, it became discredited. And then reports surfaced that doctors were applying it to a variety of other conditions much like Dr. Cunningham did in the 1920's when he found it was effective for his initial indication. He thought, the pathology in this condition is such, and here is the same pathology or pathophysiology in another condition, therefore, it should work in this other condition. When he applied this thinking and the HBOT, he got in trouble with the AMA because he didn't report his results. Similarly, in the 1970s and '80s doctors expansively began to apply HBOT to a variety of other conditions. When criticisms were leveled at them they couldn't explain why it was effective. So in this wave of criticism, hyperbaric oxygen was suppressed and died back. A good example of this was in 1978 in medical school, when I was at Johns Hopkins and asked one of our fellows or one of our residents when I had heard of hyperbaric oxygen, "Well what is hyperbaric oxygen?" He said, "Oh, it's a fraudulent, snake oil treatment that is worthless—don't even give it another thought." And I didn't give it another thought until diving medicine—my introduction to this in 1985 and '86. So the point is, there is this massive, misperception and misunderstanding of hyperbaric oxygen from the '70s and '80s which has poisoned the whole generation of doctors. That is now what we we're fighting against as people are realizing that this is a drug with very profound and far-reaching effects on human pathophysiology, acute and chronic. As the experiments are showing this, it's a matter of disseminating the information, applying it appropriately, and explaining the best we can how this is working.. And that's where we are.

Very, very well put. And parents of children who have autism are well acquainted with logic not being well accepted by mainstream entities. So we can again commiserate with that situation. Where should a parent look for more general information about hyperbaric oxygen therapy and to contact an experienced provider?

I'm going to have to tell you that some of the best general information is probably on the internet. There are various books that are for sale on the subject and Best Publishing Company out of Flagstaff, Arizona is a good source of HBO books. For a wide-ranging, open-minded, scientific view of the literature of hyperbaric oxygen the textbook of *Hyperbaric Medicine* which is edited by Dr. K.K. Jain and published by Hogrefe & Huber Publishers out of Germany and the United States is an excellent source. And beyond that the medical societies provide some information but you're going to get a very narrow view with some of them. And so I don't think they're the best source.

So where can a parent find information about an experienced provider?

Well experienced providers—that is another good question. Julie Gordon with the MUMS network maintains a list of providers without offering opinions on the given site. And she encourages people to do their own homework. *Cerebral Palsy Magazine* has just come out with a list of recommended providers for their readership and children with cerebral palsy; that was just published in the June issue. Beyond that it is very difficult to find information on the best place to get hyperbaric oxygen for let's say a neurological application, just as it is trying to find information on the best medical care for any condition in the United States. It involves a lot of homework and research and talking to other patients. I encourage patients to access their support groups. *Autism One*, and the *DAN* People. Also, the various autism conferences are becoming excellent sites for exchange of information and identification of providers of services who appear to be operating in an ethical and appropriate medical fashion.

Dr. Harch I'd like to thank you for providing us with all of this most interesting information and for researching this area that shows promise for helping to move our children forward on the road towards recovery.

Well thank you very much. It's been my pleasure and I appreciate the opportunity.

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