

Hyperbaric Therapy — A Vastly Underused Treatment Modality

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STORY AT-A-GLANCE

- > Hyperbaric oxygen therapy (HBOT) is indicated for at least 100 different conditions, but only 14 are approved indications by the U.S. Food and Drug Administration, which most insurance companies use for reimbursement
- > HBOT boosts mitochondrial function, decreases systemic inflammation and helps cells generate the required amounts of energy for optimal function. It also stimulates stem cell responses, growth factors, collagen responses and angiogenic responses
- > The main benefits of HBOT are achieved through the cumulative effect and the increasing and decreasing — the wave of hyper-oxygenation back to normal oxygen levels, creating a hyperoxia-hypoxia type paradox
- > Conditions that can benefit from HBOT include tissue wounds, stroke, TBI, heart attack, post ischemic reperfusion injury, neurodegenerative conditions and autoimmune diseases
- > Hyperbaric can also rebalance the immune system and help fight infection, and can be added to longevity and regeneration therapies

Dr. Jason Sonners, author of the book, "Oxygen Under Pressure: Using Hyperbaric Oxygen to Restore Health, Reduce Inflammation, Reverse Aging and Revolutionize Health Care," started out as a chiropractor. His passion, however, is hyperbaric oxygen therapy (HBOT), which is the focus of his Ph.D. studies at the University of Miami.

While commonly used to speed up stubborn wounds and tissue infections, hyperbaric medicine can also be helpful in the treatment of infectious diseases such as COVID. It's also enormously useful for stroke patients. I can't think of a more effective intervention than to get the stroke patient into a series of hyperbaric treatments as quickly as possible.

HBOT for General Health and Disease Reversal

Every cell in your body, with the exception of your red blood cells (which have no mitochondria that require oxygen), requires oxygen to create energy. Many chronic diseases of the modern world involve decreased mitochondrial function, increased systemic inflammation, and an inability of cells to generate the required amounts of energy for optimal function.

"We use hyperbaric oxygen, traditionally, for these terrible and severe conditions," Sonners says. Unfortunately, it's typically a last resort, literally right before an amputation surgery or as a life-saving mechanism for somebody with carbon monoxide poison or air gas embolism.

"So, we only think about it, traditionally, to help save the life or limb of somebody in a really severe condition, but the mechanisms that are working for those folks are very similar to the reasons that you and I might consider using hyperbaric oxygen:

For upregulating the oxygen levels inside your body, which will help reduce inflammation, increase mitochondrial function ... and thereby increasing the energy that those cells are able to generate ..."

HBOT for Chronic Diseases

Sonners' goal is to expand the use of HBOT from the acutely life-threatening issues like gangrene to more chronic conditions, such as autoimmune and neurodegenerative diseases.

"My thought process is that the mechanisms of action of hyperbaric are the same whether we're talking about gangrene, radiation burns and osteonecrosis, or TBI [traumatic brain injury], concussion, maybe MS [multiple sclerosis] and post-stroke.

If we really get a mastery of the mechanisms of action, we can start to apply those mechanisms across the board. Clinically, we've seen hyperbaric work for so many of these other chronic illnesses ...

So, if we could really home in on those mechanisms and understand them better, and then get a better feeling for what time and pressure settings we require in order to get those mechanisms to kick in, then we can really, with more confidence, apply this therapy to these other conditions and have more consistent results in doing so.

A lot of the work I'm proposing to do is tagging onto some of this work in regenerative medicine, where they were looking at the collagen, fibroblast and stem cell response to hyperbaric. A study came out in 2020 on telomeres, and looking at this potential, upwards of 20% increase in telomere length, especially in certain immune system cells.

I want to build on that knowledge base, so what I'm doing is I'm creating a study that's going to have a lower-pressure group and a higher-pressure group, and we're going to be looking at a whole cytokine panel, so we can understand the mechanisms of the anti-inflammatory side.

We're going to have a methylation panel so that we can start looking at the epigenetic effects of hyperbaric. We're going to have a telomere component, similar to the telomere study that was done a year and a half ago.

And we're going to start comparing all of those metrics across roughly a threeto six-month timeframe of treatment, and over two separate pressure settings, to better understand which pressures are getting which effects, and again, what period of time should we be expecting before we get the results that we're looking for?"

Research Underway

On the low end, Sonners will be using 1.3 atmospheres (4.2 PSI) at 100% oxygen, and on the high end, he'll use 2.0 atmospheres (14.7 PSI) at 100% oxygen. Both test groups will use soft chambers. If it turns out that soft chambers can get the job done, it would vastly expand the availability of this type of treatment, as they're far less expensive than the hard chambers required for higher pressures.

"There's nowhere near the amount of research in soft chambers as there are in hard chambers," Sonners says. "The overwhelming majority of research is done at that 2-atmosphere range, which is why I'm choosing that as the upper end of the research that I'm doing in the soft chamber research.

There is definitely some [research] on sports recovery. There's actually some ongoing studies right now on hyperbaric for stem cell use that we're waiting for. In some cases, 1.3 [atmospheres] has been used as the sham group, opposed to a treatment arm in the research. Maybe the study team really thought that 1.3 wasn't going to have an effect and it's a legitimate sham ...

I'm not sure, but there are some great studies. There's a study that was done on cerebral palsy (CP) and 1.3 was used as the sham group ... In this particular study, with 1.3 being the sham group, there was also a ... control group that got no hyperbaric at all.

Within the sham group, there was significant improvement on the metrics they were measuring. Then they had a 1.5 [atmospheres at] 100% oxygen, which also had a good improvement and then, a 1.75 [atmospheres at] 100% oxygen, which had even a greater improvement.

The issue in the study was that while all three of those groups improved, there was no statistical difference or enough of a statistical difference between the

1.3, the 1.5 and the 1.75. So, the conclusion of the study was therefore that hyperbaric does not work for CP, although all three of those groups had significant improvement.

So, because the sham group was not considered a treatment, that was the conclusion of that study. Now, the natural consequence of that should have been redoing the study and creating a different level of what the sham and the treatment arms ought to be, but that was never redone.

So, as a result, there's this study with results that say hyperbaric does not work for CP. Meanwhile, clearly, what it means is we need more studies. It's just that studies are expensive. They're very time consuming and you really have to have a large interest in trying to come up with the right answers to put forth the effort and time and money to get that kind of work done."

Mechanisms of Action

If you breathe 100% oxygen under pressure, it's intuitively obvious that you're going to deliver more oxygen to your tissues. That's one clear mechanism, but it's not the only or even primary reason for most of the benefits of hyperbaric therapy.

Evidence suggests part of the benefit might be related to the degeneration of a molecule called hypoxia-inducible factor alpha (HIF-1 alpha), which is generated when you lower the pressure. The pressure is high inside the chamber, and is lowered when you exit the chamber and enter the normal atmosphere. That means some of the benefit might actually be occurring when you get out of the chamber. Sonners explains:

"We don't have an exact number right now, but roughly half of the treatment is occurring while you're in the chamber, being exposed to the pressure, being exposed to the oxygen and literally accumulating a surplus of oxygen because of the therapy itself.

The other half of the therapy is when you get out of the chamber, as that oxygen can no longer stay in solution. It literally starts trying to bubble out of solution.

As that happens, it's not inert, it's actually very active. So, as it's coming out of solution, it's interacting with all of our cells.

As a result, it's triggering a massive cascade of events, cellular communication that seems to stimulate multiple series of regeneration and anti-inflammatory [events], even within the reactive oxygen species themselves.

When we look at the first part, which is the dosage of oxygen a person is getting, and that's measurable, you could say, 'Here's a person, they were in a chamber, they were at this pressure, breathing this percentage of oxygen for this amount of time,' and you could literally calculate the theoretical dose of oxygen that person was exposed to and should have been able to absorb.

We've kind of just stayed in that mindset for all these years. [However], there was a great paper out of Israel called 'The Hypoxia-Hyperoxia Paradox,' and what they're saying is we know that there's amazing benefits of hypoxia actually."

Benefits of Relative Hypoxia

Some of these benefits include the stimulation of HIF-1 alpha, stem cell responses, collagen responses and the angiogenic responses. For these reasons, Sonners views hyperbaric as an anabolic therapy — a therapy that stimulates vitally important growth and repair, as growth factors such as VEGF (vascular endothelial growth factor), and BDNF (brain derived neurotropic factor) are both stimulated.

Again, these growth factors are not stimulated by the hyper-oxygenation. They're a result from the hypoxic component, the process your body goes through as the oxygen is leaving your body.

"The important thing to note is that once you've accumulated all this extra oxygen, your hyper-oxygenation component, as that oxygen is leaving your body, you're never truly hypoxic," Sonners says, "but the cell signaling factors

that respond to traditional hypoxia are also seemingly responding to this relative hypoxia.

If you look at that paper ['The Hypoxia-Hyperoxia Paradox'] ... it seemed to delineate this. With hypoxia alone, you will still get VEGF, which means you'll still get a lot of angiogenics, the rebuilding of the endothelial lining, the creation of a new micro-circulation bed, all this capillary regrowth will happen from hypoxia.

You'll get these stem cell releases, this potential for increase in the regenerative nature of cells. You'll get this increase in the HIF-1 alpha. But if you're chronically hypoxic, you're also going to get a downregulation of sirtuins [longevity proteins] and you're going to get a downregulation of mitochondrial function.

Sirtuins could play a great role in things like cell cycle life, getting cells out of cellular senescence — kicking them back into active life — or apoptosis, killing that cell so that we can replace it with a new stem cell, or even the genetic and epigenetic repair mechanisms. A lot of that has to do with sirtuins, so we don't want to downregulate those. We want to upregulate those."

So, to clarify, with HBOT, you get the benefits of hypoxia with none of the downsides. Rather than inhibiting sirtuins, which are important for health and longevity, you actually get an upregulation of sirtuin activity. It also upregulates mitochondrial function and boosts mitochondrial replication, which the complete opposite to what happens in true hypoxia.

What About the Free Radical Component?

Without any doubt, HBOT is a type of oxidative stress, but it doesn't have the adverse effects you'd expect. Sonners explains:

"There was a great paper done by Dominic D'Agostino and Angela Poff, back in 2017 or 2018, specifically looking at the reactive oxygen species or the free radical component of hyperbaric oxygen. What are the benefits or consequences as we upregulate, as we increase the amount of oxygen into the body?

As the cells and the mitochondria start to uptake that oxygen, producing more energy, there is a natural consequence where this byproduct of free radicals are released as a part of normal cellular respiration. Excess free radicals is obviously consequential to cell membranes, lipid peroxidation and protein degradation.

It could destroy cell membranes, mitochondrial membranes, nuclear membranes, genetic material ... At the same time, it's a normal response to cellular respiration and our bodies have their own intrinsic mechanisms for dealing with some of this excess free radical, things like the superoxide dismutase, catalase and glutathione pathways.

So, there seems to be a distinction that we should make. One is that some of the free radicals our bodies are exposed to come from the outside world in. Radiation, smoking, air pollution, the list goes on and on. So, we need to have a robust, intrinsic ability to tolerate these free radicals with our own antioxidant system.

But in excess, we could be getting too much free radicals and we could be depleting our own systems, in which case supplementation should certainly be considered and used. On the flip side, we look at hyperbaric oxygen as this tool that theoretically has all these great effects, but one of those consequences would also be this increase in free radical exposure.

There seems to be a very big delineation between a body that's exposed to free radicals from the outside world, versus a body that is exposed to free radicals that it's creating on its own.

One of those distinctions is that through the use of hyperbaric oxygen, even without supplementation, and the increase in free radical production from

mitochondrial ATB production, the body itself — assuming it has the right raw materials — will actually increase its own superoxide dismutase, catalase and glutathione pathways.

This would No. 1, help make you more resilient to hyperbaric oxygen, but No. 2, would also help make you more resilient to all the other free radicals that you're potentially exposed to in your environment.

So, I would say two things. One, especially with patients who are a little bit more fragile when it comes to oxidative stress, those people, I would tend to not over oxidize to begin with, so I might start at a gentler hyperbaric protocol with them, and I'm likely to want to start quickly upregulating their own system, getting the right supplementation for improving their intrinsic antioxidant systems ...

Then, as their system improves their tolerance for reactive oxygen species, we may not need as much of that, or if we're going to be using high dose hyperbaric oxygen for a period of time, we might use things like certain SOD precursors, or molecular hydrogen.

Through conversations with you, it has become one my favorite antioxidants that we use. Between 45 minutes to an hour before [hyperbaric treatment], we'll start loading people with the molecular hydrogen as a mechanism to reduce the consequences. There are benefits, in other words. Reactive oxygen species on its own also helps stimulate hormone balance and helps stimulate cell repair by themselves. So, there has to be this balance.

We don't want to quelch all the free radicals because free radicals are a very important signaling molecule for so much cellular activity and at the same time, we want to be aware of the fact that hyperbaric does increase that, and we want to make sure that we're not over-exposing somebody."

HBOT Functional Medicine Course Now Available

Sonners also reviews the curriculum he developed for the International Board of Undersea Medicine. The IBUM has been certifying people in hyperbaric medicine for 25 years, and the curriculum Sonners created has been taught as a functional medicine hyperbaric course for clinicians for the past year.

"A big push for me, and even for the research I'm doing, is to help create awareness that gets more doctors excited about [HBOT], that want to actually use it in their practice," Sonners says. "So, this has been an attempt to really improve the education so that people aren't just going to hyperbaric courses to learn about wound care.

We needed courses to help practitioners like myself or other people interested in the regenerative side to be able to learn how to apply it that way. So, we now have a course that I teach a few times a year to get people on the same page.

The majority of this last year, other than getting through school and writing the thesis, has been developing and promoting that course. I think we've certified about 125 to 150 practitioners and technicians specifically on the functional medicine side of hyperbaric use ...

At this time, I still see a pretty big mix between soft chamber use and hard chamber use. A lot of those doctors are either Dos, MDs, chiropractors or naturopaths, getting into more of a functional medicine base, just looking for other natural approaches to the things they are treating.

Hyperbaric supplies the body with a fundamental ingredient and it's so necessary for cellular performance. It just seems to make sense to start implementing a tool and a modality like that into a setting where you're trying to reduce inflammation, you're trying to improve energy production cellularly."

HBOT Has at Least 100 Indications for Use

While the list of potential uses for HBOT is extremely long, in the U.S., the Food and Drug Administration has approved and most insurance will pay for HBOT for the following 14

conditions:1

Air or gas embolism	Carbon monoxide poisoning
Clostridial myositis and myonecrosis (gas gangrene)	Crush injuries, compartment syndrome and other acute traumatic ischemia
Decompression sickness	Arterial insufficiencies, such as central retinal artery occlusion
Severe anemia	Intracranial abscess
Necrotizing soft tissue infections	Osteomyelitis
Delayed radiation injury (soft tissue and bone necrosis)	Compromised grafts and flaps
Acute thermal burn injury	Idiopathic sudden sensorineural hearing loss

In terms of conditions that can benefit from HBOT, I would certainly add stroke, TBI, heart attack, anytime there's post ischemic reperfusion injury, and most neurodegenerative conditions. Internationally, there are about 100 recognized indications. While that might make it sound like a magical cure-all, it's important to remember that it doesn't cure anything directly.

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What it does is provide your body with a foundational nutrient, oxygen, that virtually all cells require. HBOT supplies your body oxygen in a surplus, creating an excess reservoir of oxygen to improve that function. That's why it can help improve such a wide variety of health conditions.

Even autoimmune diseases such as MS, lupus and rheumatoid arthritis, just to name a few, may benefit, Sonners says. A whole other category of potential use would be wellness, longevity and regenerative-type therapies.

"We're just applying the tools slightly differently to help match the intensity of the therapy to the severity of the condition. We can utilize the principles of gas exchange in various ways to help so many different types and various types of conditions," Sonners says.

"One condition or subclass that we talked about it in the beginning is, from the immune system standpoint, upregulating your ability to fight infection by increasing white blood cell activation through the reactive oxygen species mechanisms. We use it for anaerobic infection, bacterial infections all the time.

One of the main reasons that hyperbaric works in those severe conditions is those bacteria are anaerobic. They don't live in high oxygen environments.

So, we know that putting a patient in a high oxygen environment massively decreases bacteria's ability to function, potentially helps to kill that infection, helps to block the toxicity of that infection and helps to break down the biofilms around that infection. So, hyperbaric becomes an amazing tool in the capacity of immune system balancing and/or ability to help fight infection."

More Information

As a general guidance, Sonners recommends doing hyperbaric for about two hours a week on a regular basis. That's his personal routine. In addition to that, three times a year he does a 30- to 40-hour protocol over the course of six to eight weeks. He explains why:

"We know that in general ... three or four sessions is not going to ever cut it.

The main effect of hyperbaric is really achieved through the cumulative effect and the increasing and decreasing — the wave of hyper-oxygenation back to normal oxygen levels — creating that hyperoxia-hypoxia type paradox ...

When you do a protocol similar to like what I would do for a patient, let's say four to six hours a week for eight weeks, the frequency of those ... the space in between them, really shrinks and you get far more signaling to occur ...

If all we cared about was the physical dose, we would stay at 100% oxygen as long as we possibly could, at the highest pressure we could tolerate to get the most oxygen absorption. I don't think that that's where the majority of benefit exists.

Every time your pressure changes or your percentage of oxygen changes, you're stimulating HIF-1 alpha, the reactive oxygen species load, sirtuins, you're signaling a hormetic effect. I picture them as switches. You're flipping that switch on, off, on, off, on, off. I think it's the amount of times that you stimulate that switch that will create the benefits we're looking for, more than the physical dose of oxygen over time."

To learn more about HBOT in general, be sure to pick up Sonners' book, "Oxygen Under Pressure: Using Hyperbaric Oxygen to Restore Health, Reduce Inflammation, Reverse Aging and Revolutionize Health Care."

In the interview, we also discuss how you can incorporate HBOT in your fitness routine, along with fasting, to augment and upregulate cellular performance, recovery and regeneration. So, if that's of interest to you, be sure to listen to the interview in its entirety, or read through the transcript.

Sources and References