

Hyperbaric Oxygen Therapy (HBOT) can destroy harmful bacteria and viruses, while enhancing the body's natural defenses. We propose HBOT for high risk, early stage COVID-19 patients, recommending this novel use of pressure and oxygen based on its low risk and potentially lifesaving benefits, as well as its availability in hospitals and free-standing clinics nationwide.

The effectiveness and feasibility of HBOT has been confirmed by numerous clinical studies over several decades. A 2009 study, conducted by Cassandra A. Godman, found that HBOT regulates approximately 40% of the human genome. Godman identified 8,101 genes mediated through hyperbaric oxygen. Most significant was the upregulation of anti-inflammatory genes, and the down regulation of pro-inflammatory genes. A subsequent 2010 publication states, "Hyperbaric oxygen induces a cytoprotective and angiogenic response in human microvascular endothelial cells." This research opened the door to understanding how HBOT acts as an agent activating antioxidant and cell protecting genes to safeguard against lethal insults like viruses and bacteria.

Principal among HBOT's effects is increased oxygen tension in tissues. Many micro-organisms that cause infections and systemic illnesses do not tolerate oxygen. Increased partial oxygen pressure in the blood destroys these micro-organisms, eliminating infection. The body is defenseless against Anaerobic infections, or infections caused by viruses, bacteria, and fungi that don't need oxygen to live. HBOT elevates oxygen levels in cells to destroy these microbes.

COVID-19 mortality is due to pulmonary infection which leads to respiratory failure. The primary pathology is in the lungs, exactly where hyperbaric oxygen effects begin. Hyperbaric conditions facilitate oxygen diffusion from the alveoli to the blood stream.

Doctor Paul Harch, Director of Hyperbaric Medicine at Charity Hospital adds that "Applied correctly, hyperbaric therapy may have utility in Coronavirus patients like its life-saving history with the Spanish Flu. The publication of a retrospective analysis of lung CT scans on 121 patients infected with coronavirus in four Chinese provinces was announced. The CT scans showed progressive air space disease that radiologically depicted the diffusion barrier to oxygen that Dr. Paul Harch suggested was similar to the lung pathology in Spanish Flu victims of 1918. Harch's team found evidence of successful treatment of a severe case of coronavirus infection in Wuhan, China. This patient managed to successfully traverse the critically ill period and was no longer in jeopardy.

Hyperbaric Oxygen Therapy is effective in treating the cascading challenges associated with the coronavirus immune response. With any infection, the body's immune system responds by attacking the foreign virus or bacteria. While this immune response can rid the body of the infection, it can also cause collateral damage in the body termed a "cytokine storm". The immune cells produce cytokines to fight infection, however, when too many are released, chronic autoimmune problems can result. People most vulnerable to COVID-19 are individuals with pre-existing health challenges associated with chronic cytokine storm syndrome.

Cytokine Storm Syndrome - also termed a "sepsis syndrome" is a diverse set of (autoimmune) conditions unified by a clinical phenotype of systemic inflammation, multi-organ failure, hyperferritinemia which, untreated, can be fatal. This "clinical constellation" (cytokine storm) is caused by the elaboration of extreme amounts of pro-inflammatory cytokine mediators resulting from unchecked feedforward immune activation and amplification. The initiating factors of HBOT have demonstrated effectiveness against the cytokine storm.

The proposed treatment of newly or early diagnosed patients with HBOT before symptoms potentially worsen is supported in the literature; recently (March 2020) the World Health Organization stated that: "Oxygen therapy is the major treatment intervention for patients with severe COVID-19. All countries should work to optimize the availability of pulse oximeters and medical oxygen systems." HBOT is effective at infusing blood plasma and organs safely with oxygen under pressure. HBOT was reported to heal patients in China and South Korea for conditions that define those most at risk. South Korea reported:

https://www.upi.com/Top_News/World-News/2020/02/14/Oxygen-therapy-working-for-coronavirus-patient-Seoul-says/6651581696794/?spt=su&or=btn_fb

As mentioned, hyperbaric oxygen therapy is already used internationally to heal patients in the most-at-risk COVID-19 groups (heart disease, cancer, COPD, stroke, compromised immune systems, etc.). The anti-inflammatory effects of oxygen under pressure are well documented and can be lifesaving even absent the presence of COVID-19.

Armed with this knowledge, why can't HBOT be used as a prophylactic treatment for COVID-19 given how HBOT is cytoprotective and expresses growth promoting genes in the endothelial cells? Can these molecular responses induced by HBOT be used to prevent the progression of a patient's COVID-19 and the inflammatory response to pneumonia, ARDS/SIRS and potentially septic shock? Tocilizumab (a DMARD) is one of the current potential treatments being investigated. HBOT similarly modulates the immune response, downregulates IL-6, and subsequently IL-1 and TNFa.

Today, tens of thousands of studies have consistently shown that increased oxygen in the plasma (through increased pressure) aids in the prevention and treatment of inflammatory derived diseases. HBOT has the potential to save lives in fighting the COVID-19 crisis. More than twenty years ago, the US FDA cleared HBOT's use for 14 serious conditions, and today over 1500 hospitals in the US use it in wound care centers to reduce amputations by 40%. The international community expanded HBOT's use to treat many inflammatory propagated diseases, injuries, viruses, accidental drug overdoses and suicidal ideations, considered off-label in the US.

Call to action... If we can show HBOT to be effective at fighting COVID 19, immediate steps could be taken to implement its widespread use in the US. This could be done by mobilizing all HBOT chambers at hospitals and free-standing clinics with effective protocols in the U.S., representing an estimated 5,000 seats (mono and multi place combined).

Separately, once proven, we should consider using the nation's aircraft as pressure chambers. At sea level, today's airliners can reach differential pressures similar to what Cunningham applied successfully during the Spanish flu pandemic (1.6atm +/-).

To this end, I propose opening a single HBOT clinic as the COVID-19 epicenter for treating infected patients. The facility is a free-standing clinic located in RTP with two large multi-place chambers and a 3000 gal. liquid oxygen supply.

To accomplish the best possible outcome and assure the safety of the patients, I propose we join US based HBOT experts with local HBOT physicians to plan a way forward. I have spoken with several NC HBOT wound care Doctors and am aware of the concerns surrounding SOP's, IRB's and off-label use of drugs (oxygen included).

In view of this pandemic's catastrophic threat, time is of the essence. We must address these objections quickly, and clear the way for this potentially lifesaving approach.

Please help us help many.

Sincerely,

Edward R. di Girolamo, PE

CEO, Extivita-RTP office (919) 354-3701

cell (919) 602-5005

Cc: Dr. James Stevens, Medical Director, Extivita-RTP

office (919) 926-3010

cell (919) 215-8300

Included:

Footnote and References (links) Page 4-5

Proposed COVID 19 HBOT Treatment Algorithm Page 6

Attached - Extivita-RTP [HBOT Contraindications Checklist](#)

Footnote* and References:

*The cause of the near 3 million deaths in the US tracked by the CDC in 2017 were initiated or exacerbated by inflammation from hypoxia (which is a lack of oxygen).^{5,6,7} Oxygen is a powerful anti-inflammatory and essential element for life to continue and cells to produce energy.^{8,9} If oxygen is administered under pressure (HBOT) it saturates blood plasma, increases natural stem-cell production and upregulates the bodies reparative and regenerative genes.¹⁰ Furthermore, Oxygen in our plasma acts as a genomic chemical element that positively regulates 40% of our genes, including our anti-inflammatory genes.¹¹ HBOT is used internationally to heal patients for conditions that are in the most-at-risk group widely reported (heart disease, cancer, COPD, Stroke, etc.) often the cause of death reported by the CDC in the US.¹⁴

- 1) <https://www.cdc.gov/nchs/fastats/deaths.htm> In 2017, a total of 2,813,503 resident deaths were registered in the United States, yielding a crude death rate of 863.8 per 100,000 population.
- 2) Otto Warburg hypothesized that cancer growth is caused by tumor cells generating energy (as, e.g., adenosine triphosphate/ATP) mainly by anaerobic breakdown of glucose (known as fermentation, or anaerobic respiration). This is in contrast to healthy cells, which mainly generate energy from oxidative breakdown of pyruvate. Pyruvate is an end product of glycolysis and is oxidized within the mitochondria. Hence, according to Warburg, cancer should be interpreted as a mitochondrial dysfunction.
- 3) Glucose is a crucial molecule in energy production and produces different end products in non-tumourigenic and tumourigenic tissue metabolism. <https://link.springer.com/article/10.1007%2Fs12272-019-01185-2>
- 4) At standard temperature and pressure, two atoms of the element bind to form dioxygen, a colorless and odorless diatomic gas with the formula O₂. Diatomic oxygen gas constitutes 20.8% of the Earth's atmosphere. As compounds including oxides, the element makes up almost half of the Earth's crust. Another form (allotrope) of oxygen, ozone (O₃, strongly absorbs ultraviolet UVB radiation and the high-altitude ozone layer helps protect the biosphere from ultraviolet radiation.
- 5) The inflammation theory of disease - PubMed Central (PMC) · Oct 09, 2012 Inflammation has long been a well-known symptom of many infectious diseases, but molecular and epidemiological research increasingly suggests that it is also intimately linked with a broad range of non-infectious diseases, perhaps all. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3492709>
- 6) Hypoxia and inflammation are two sides of the same coin | PNAS Nov 12, 2013 · Hypoxia and inflammation share an interdependent relationship (1). Many recent publications implicate hypoxia-elicited inflammation, or inflammation during hypoxic conditions in the outcomes of a wide array of human diseases (2). On the one hand, inflammatory disease states are frequently characterized by tissue hypoxia, or stabilization of hypoxia-dependent transcription ... <https://www.pnas.org/content/110/46/18351>
- 7) The concept that hypoxia can induce inflammation has gained general acceptance from studies of the hypoxia signaling pathway. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3930928/>
- 8) Hyperbaric oxygen therapy ameliorates osteonecrosis in ... This study shows that HBOT results in an anti-inflammatory action in patients with AVNFB. In AVNFB, HBOT results in a decreased amount of

- circulating TNF- α and IL-6 (Figure 2). HBOT acting on IL-1 β , TNF- α , and IL-6, key bone-resorbing cytokines and their synergistic effects, could ultimately lead to beneficial resolution for the patient. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6171420>
- 9) Hyperbaric oxygen treatment (HBO) promotes rapid recovery from soft tissue injuries. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5778072/>
 - 10) Non-Toxic Metabolic Management of ... - PubMed Central (PMC) Hyperbaric oxygen therapy (HBOT) is the administration of 100% oxygen at elevated pressure. In vivo, HBOT saturates blood plasma with oxygen, allowing it to diffuse further into the tissues and oxygenate hypoxic tumor regions [43–45]. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4464523>
 - 11) Hyperbaric oxygen induces a cytoprotective and angiogenic ... Hyperbaric oxygen therapy (HBOT) involves the administration of 100% O₂ at pressures above 1 atm (Thom 2009). Currently, the Undersea and Hyperbaric Medical Society has defined 13 indications for which HBOT is approved including air/gas embolisms, CO poisoning, acute traumatic ischemias, and chronic wounds (Gesell 2008). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3082642>
 - 12) HBOT is a treatment procedure that involves breathing 100% O₂ for a certain time and under a certain pressure. <https://www.sciencedirect.com/science/article/pii/S0753332218354829>
Hyperbaric oxygen therapy
 - 13) Hyperbaric therapy was first documented in 1662, when Henshaw built the first hyperbaric chamber, or 'domicilium'.² Since this time, reports of beneficial effects from increased pressure have increased. In 1879, the surgical application of hyperbaric therapy in prolonging safe anesthesia was realized and explored. <https://academic.oup.com/qjmed/article/97/7/385/1605756>
 - 14) Globally, HBOT is used to extend life by augmenting the treatment of all injuries, diseases and infections as well as to improve overall wellness and the physical performance of athletes. <https://www.hbotnews.org/international-hbot-indications/>
 - 15) Over the years we have seen HBOT used in treatment of many conditions such as various immune disorders, Lyme Disease, Autism, Stroke, Cancer, and the list goes on and on. <https://www.woundsource.com/blog/fda-approved-uses-hyperbaric-oxygen-therapy> HBOT (Hyperbaric Oxygen Therapy) has now been used for many years.
 - 16) https://www.upi.com/Top_News/World-News/2020/02/14/Oxygen-therapy-working-for-coronavirus-patient-Seoul-says/6651581696794/?spt=su&or=btn_fb
 - 17) Cytokine Storm Syndrome: Looking Toward the Precision Medicine Era <https://onlinelibrary.wiley.com/doi/full/10.1002/art.40071>

A series of publications demonstrate the importance of applying HBOT to understand its potential in fighting COVID 19.

<https://www.sciencedirect.com/science/article/pii/S0140673663900114>

http://hyperbaricireland.com/?page_id=9

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3058327/>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6690284/>

<https://www.ncbi.nlm.nih.gov/pubmed/10985915>

COVID 19 HBOT Treatment Algorithm

