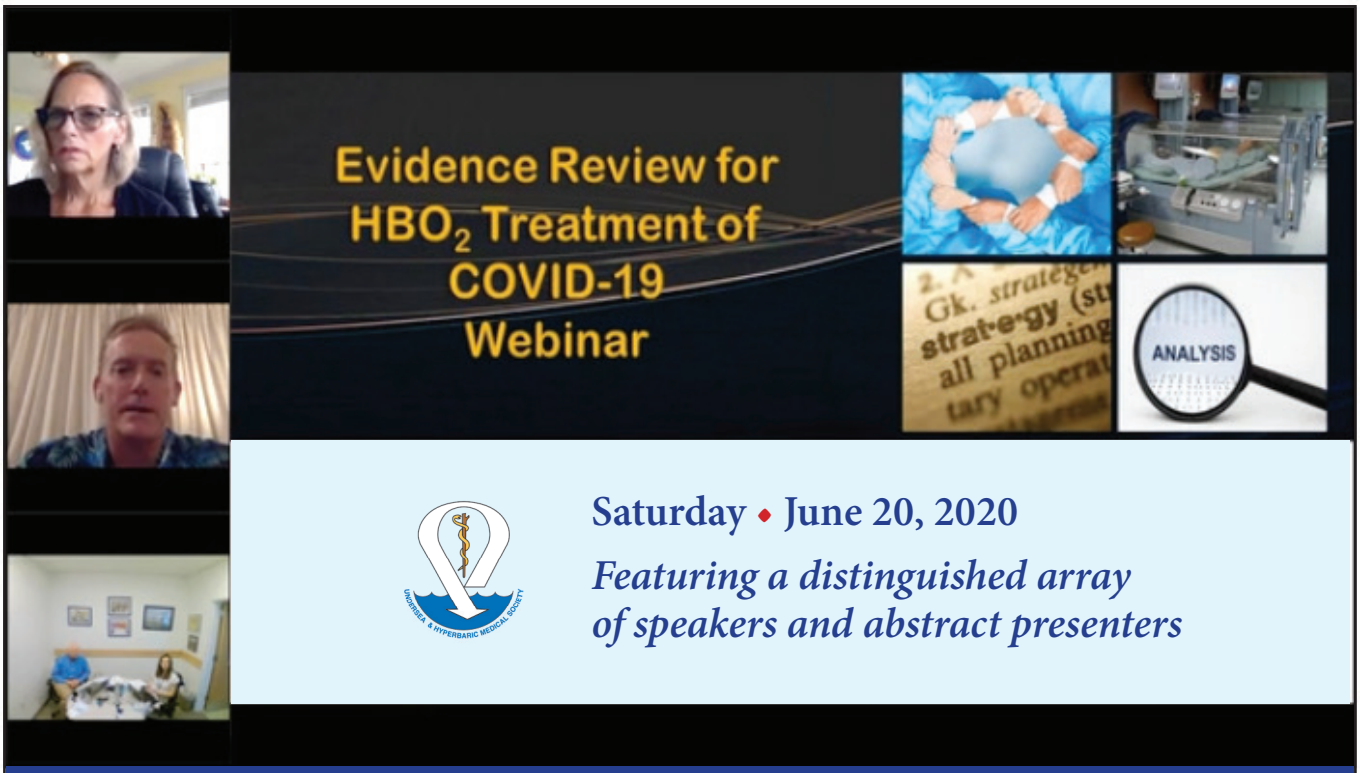

Saturday • June 20, 2020

Featuring a distinguished array of speakers and abstract presenters

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WEBINAR Q&As for ABSTRACT PRESENTERS

SCHEDULE

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11:20 11:25	Q & A
11:25 11:40	**SESSION 2: Clinical course of COVID-19 and the possible role of HBO_2** **Sandra Wainwright, MD** Describes the clinical course of COVID-19 from asymptomatic patients through ventilated patients, identifying any opportunities for intervention using HBO_2. Will summarize the published clinical experience treating COVID-19 patients with HBO_2.
11:40 11:45	Q & A
11:45 12:00	**SESSION 3: Safety concerns for the use of HBO_2 in COVID-19 patients** **Scott Gorenstein, MD** Discusses potential hazards to COVID-19 patients including: pulmonary oxygen toxicity; sick patients leaving ICU to go to HBO_2 department; pulmonary barotrauma.
12:00 12:05	Q & A
12:05 12:20	**SESSION 4: Considerations for use of HBO_2 in COVID-19 patients** **Marcus Speyrer, CHT** Discusses operational considerations for facilities that intend to treat COVID-19 patients including: infection control in the hyperbaric chamber; staff education; adaptation of emergency procedures.
12:20 12:25	Q & A
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16:00 17:00	**Session 7: Synthesis of the data** **John Feldmeier, DO** Synthesizes the presented data into a cohesive document with three general goals: • What questions have we answered? • What questions still need to be answered? • What elements of study design should be incorporated in future studies?
Moderators:	Jay Buckey, MD: Nicole Harlan, MD; Andrew Melnyczenko, CHT

Evidence Review for HBO_2 Treatment of COVID-19 Webinar: Abstracts

Effects of volatile gaseous compounds induced by hyperbaric oxygen, in counteracting the SARS-CoV-2 virus in asymptomatic patients and SARS-CoV-2-positive patients with mild symptoms

Longobardi P [1], Hoxha K [1], Lanza F [2], Milandri M 2, Perreca F [1], Pinton P [3], Poletti G [2], Rubini M [3], Sambri V [2], Tajana G [4], Vezzani G [5], Pelaia P [6]

[1] Centro Iperbarico (Hyperbaric Center) Ravenna; [2] Romagna AUSL (Local Public Health Unit)
[3] University of Ferrara; [4] Full Professor of Histology and Embryology
[5] Honorary President of the Association of Patients Treated in Hyperbarism (As.Pa.T.I.)
[6] Full professor of Anesthesia, Intensive Care and Intensive Care

Presenting Author: Pasquale Longobardi, MD – *direzione@iperbaricoravenna.it*

Hyperbaric oxygen (HBO_2) therapy will be provided at Centro Iperbarico in Ravenna, Italy, to patients as an adjunct to standard therapy for a cohort of 20 SARS-CoV-2-positive patients. These are asymptomatic patients or patients with mild symptoms who have nitric oxide synthase (NOS)genetic polymorphism and two or more comorbidities highly related to the reduced NO synthesis and the mortality rate in COVID-19.

In Italy the median age of patients who died from COVID-19 is 20 years older than asymptomatic positive patients. In addition, 82% of deceased patients have concomitant diseases strongly correlated with NOS genetic polymorphism and reduced synthesis of NO.

HBO_2 therapy significantly increases the production of volatile gas compounds (VOCs) such as nitric oxide (NO), reactive oxygen species (ROS) and reactive nitrogen species (RNS), which in the laboratory has proven capable of inhibiting the replication of SARS-CoV. NO acts by reducing the palmitoylation of the spike glycoprotein (S) on the virus necessary to penetrate human cells. Furthermore, in the early stages of virus replication, NO reduces the reproduction of the genetic structure (viral RNA), altering proteins (cysteine proteases) encoded in the Orf1a genetic site of the SARS-CoV-1 virus, and supposedly it will act the same way on SARS-CoV-2.

HBO_2 upregulates the hypoxia-inducible factor HIF (also induced by oxidative stress), which promotes the expression of human antiviral peptides: defensins and cathelicidins effective to block the coated, positive-sense single-stranded RNA virus (such as SARS-CoV-2).

The pilot study protocol includes five HBO_2 sessions of 76 minutes each, once a day, with control of the nasopharyngeal swab for SARS-CoV-2 after the third and fifth HBO_2 sessions. After the intervention portion of this study, a chart review will be performed to compare the outcomes of intervention patients versus patients who received standard of care (quarantine). ■

Sounding the alarm: An unexpected hyperbaric emergency during the COVID-19 pandemic

Vidafar, MA
Plainview Hospital, Plainview, New York
Presenting Author: Michael A Vidafar, CHT – *mvidafar@gmail.com*

Case description: The impact of increased hospital burden due to COVID-19 extends even to outpatient "COVID-free" units and hospital-based hyperbaric programs not treating COVID populations. While the majority of discussion concerning the impact of COVID-19 is correctly focused on patient outcomes and the role of hyperbaric oxygen (HBO_2) in treatment – as well as staff/HBO_2 patient safety in terms of infection control when/where COVID patients are receiving HBO_2 treatment), there is a potential for an increased burden on bulk O_2 delivery systems that can impact hyperbaric programs. This includes monoplace and multiplace facilities and is a safety concern that is often not frequently drilled or seen. Incidents can occur when oxygen demand from the bulk O_2 delivery (LOX) system is greatly increased, such as in the case of hospitalized and critically ill patients during the COVID-19 pandemic. The author presents a case report outlining a recent high-pressure alarm experienced and resolved at Plainview Hospital's Division of Advanced Wound Healing and Hyperbaric Medicine.

Intervention: Chamber operations were halted until O_2 pressure was satisfactorily controlled by high-pressure power washing of LOX vaporizers by engineering staff.

Outcome: Incoming O_2 pressure was restored; staff gained greater understanding of LOX systems.

Discussion: The primary emphasis of this case is the importance of communication among hospital departments and leadership, the utilization of those resources, and the importance of interdisciplinary problem-solving. ■

Efficacy and safety of hyperbaric oxygen for patients with COVID-19; rationale and protocol of the randomized controlled trial COVID-19-HBO_2

Kjellberg A, Rodriguez-Wallberg K, Lindholm P
Dept. Physiology and Pharmacology, Karolinska Institutet, Biomedicum, Solnavägen 9, 171 65 Solna
Presenting Author: Anders Kjellberg, MD – *anders.kjellberg@ki.se*

Introduction: SARS-CoV-2 affects the innate immune response and activates an inflammatory cascade. Patients with risk factors such as diabetes and hypertension have increased risk of severe disease with inflammation out of control. Hyperbaric oxygen (HBO_2) has proven anti-inflammatory effects. The overall hypothesis to be evaluated is that HBO_2 may reduce mortality, increase hypoxia tolerance and prevent organ failure in patients with COVID-19 pneumonitis by reducing the inflammatory response. The primary objective is to evaluate if HBO_2 reduces the number of ICU admissions compared to best practice for COVID-19. Main secondary objectives are to evaluate if HBO_2 reduces the load on ICU resources, morbidity and mortality in severe cases of COVID-19. Other objectives are to evaluate safety and evaluate and if HBO_2 mitigates the inflammatory reaction in COVID-19.

Materials and Methods: The trial *A Randomized, Controlled, Open-Label, Multicenter Clinical Trial to explore Safety and Efficacy of Hyperbaric Oxygen for preventing ICU admission, Morbidity and Mortality in Adult Patients With COVID-19* was initiated in Karlskrona, Sweden, on May 20, 2020. Additional centers are invited. An online eCRF (SmartTrial®) and online randomization tool (Randomize.NET) will be used.

Study design: Prospective randomized open label multictr.

Study population: 200 adults with moderately severe COVID-19 admitted to hospital and who require oxygen and have at least two risk factors for increased morbidity/mortality

Intervention: HBO_2 1.6-2.4 ATA, 30-60 minutes, with a maximum five treatments within seven days

Control: Best practice for COVID-19 pneumonitis

Primary endpoint: ICU admission

Main secondary endpoints: 30-day mortality, time to intubation, time to ICU, mean change in inflammatory response.

Results: Ethics and dissemination – The trial was approved by Swedish Ethical Review Authority (2020-01705) and Swedish Medicinal Products Agency (EudraCT 2020-001349-37). Results will be published in peer-reviewed scientific journals (OA).

Trial registration: NCT04327505.

Grants: Swedish Research Council.

Summary/Conclusion: A positive result from an RCT would make a strong argument in convincing health care systems to scale this treatment for general use against COVID-19 pneumonitis. ■

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Discussion: The primary emphasis of this case is the importance of communication among hospital departments and leadership, the utilization of those resources, and the importance of interdisciplinary problem-solving. ■

Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a multicenter case series

Serena TE, Thibodeaux KT, Speyrer, M, Raza A, Mayhugh TA
SerenaGroup Research Foundation Cambridge, Massachusetts
Presenting Author: Kerry T. Thibodeaux, MD – *kerrythibodeaux1960@gmail.com*

Introduction: The highly contagious SARS-CoV-2 virus is responsible for the deaths of more than 100,000 Americans at this writing. Infected patients present with symptoms that range from minimal complaints to life-threatening respiratory failure. Elderly patients and those with comorbidities are at greatest risk for severe acute respiratory syndrome (SARS) requiring mechanical ventilation. Once on a ventilator, mortality rates skyrocket. In April 2020 Dr. Thibodeaux treated five patients with severe COVID-19 at the Wound Treatment Center in Opelousas, Louisiana. The case series published in the *Journal of Wound Care* in May 2020 detailed the use of hyperbaric oxygen (HBO_2) therapy to reduce the need for mechanical ventilation. These results prompted further investigation.

Materials and Methods: An IRB-approved protocol and informed consent for the collection of de-identified information on COVID-19 patients treated with HBO_2 to reduce the need mechanical ventilation was provided to interested clinicians across the globe. Once registered on the SerenaGroup Research Foundation website, the investigational sites were provided with and trained to use a data collection app (Tissue Analytics, Baltimore, Md.). Investigators obtained separate approval for the off-label use of HBO_2 therapy for COVID-19.

Results: At this writing, three sites have entered information on 12 patients treated with HBO_2 to prevent the need for mechanical ventilation. To date, 11/12 (91%) patients avoided mechanical ventilation. In addition, in the majority of patients, oxygen saturation increased, tachypnea resolved, and D-dimer levels and inflammatory markers fell. Ten sites have registered on the website. Further data is being uploaded at the time of this writing. No adverse events directly related to HBO_2 have been reported.

Summary/Conclusion: In this small sample of patients HBO_2 therapy appeared to reduce the need for mechanical ventilation in patients with severe COVID-19. Data collection is ongoing. However, the results thus far suggest that HBO_2 may be a safe and effective treatment of symptomatic COVID-19 disease. ■

Hyperbaric oxygen therapy for COVID-19 patients with respiratory distress: Treated cases versus propensity-matched controls

Gorenstein SA, Castellano ML, Slone ES, Gillette B, Liu H, Alsamarraie C, Jacobson AM, Wall SP, Adhikari S, Swartz JL, McMullen JJ, Osorio, M, Koziatek, CA, Lee DC

NYU Winthrop Hospital, NYU School of Medicine

Presenting Authors: Scott Gorenstein, MD, and David Lee, MD – david.lee@nyumc.org

Objective: Given the high mortality and prolonged duration of mechanical ventilation of COVID-19 patients, we evaluated the safety and efficacy of hyperbaric oxygen for COVID-19 patients with respiratory distress.

Methods: This was a single-center clinical trial of COVID-19 patients at NYU Winthrop Hospital from March 31 to April 28, 2020. Cases received hyperbaric oxygen therapy at 2.0 atmospheres of pressure in monoplace hyperbaric chambers for 90 minutes daily for a maximum of five total treatments. Controls were identified using propensity score matching among COVID-19 patients admitted during the same time period. Using competing-risks regression to perform a survival analysis, we studied our primary outcome of inpatient mortality and secondary outcome of mechanical ventilation.

Results: We treated 20 COVID-19 patients aged 30 to 79 with hyperbaric oxygen, with an oxygen requirement ranging from 2 to 15 liters on hospital days 0 to 14. Of the 20 patients, two (10%) were intubated and died, and none remain hospitalized. Among 60 propensity-matched controls based on age, sex, body mass index, coronary artery disease, troponin, D-dimer, hospital day, and oxygen requirement, 18 (30%) were intubated, 13 (22%) have died, and five (8%) remain hospitalized (two of whom are still on mechanical ventilation). Assuming no further deaths or intubations among controls, we estimate that the adjusted subdistribution hazard ratios were 0.37 for inpatient mortality (p=0.132, 95% CI of 0.10 to 1.37) and 0.26 for mechanical ventilation (p=0.046, 95% CI of 0.07 to 0.98).

Conclusions: Though limited by its study design, our results demonstrate the safety and possible efficacy of hyperbaric oxygen among COVID-19 patients and strongly suggests the need for a well-designed multicenter randomized control trial. ■

The role of hyperbaric oxygen treatment for COVID-19

Paganini M [1], Bosco G [1], Paolocci N [1], Kohlscheen E [2], Bassetto F [2], Giacomo G [3], Camporesi EM [4], Thom S [R 5]

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[5] Emergency Medicine, University of Maryland, Baltimore

Presenting Author: Gerardo Bosco, MD, PhD – *gerardo.bosco@unipd.it*

Introduction: The recent COVID-19 pandemic produced extreme demands for hospitalizations and equipment, with depletion of critical care resources. Current therapies provide limited clinical relief, and a robust vaccination program is not yet available. Therefore, several empirical investigations were initiated with intermittent hyperbaric oxygen (HBO_2) therapy to overcome the relentless and progressive hypoxemia that is often refractory to maximal ventilator support of intubated patients. However, more recently, less severe patients at the edge of impending hypoxemia were exposed to HBO_2, which prevented intubation and obtained the rapid resolution of symptoms. With this summary we illustrate the possible biological mechanisms of action of HBO_2 in COVID-19 patients.

Materials and Methods: We performed a scoping review, gathering the most valuable evidence supporting mechanisms of action of HBO_2 and possible overlaps with COVID-19 pathophysiology.

Results and Discussion: First, HBO_2 acts by increasing the amount of oxygen in the plasma and peripheral tissues. Possible direct effects of HBO_2 on viruses are still uncertain, but in COVID-19 patients, hyperoxia could mobilize stem cells, block the inflammatory cascade, interfere with interstitial fibrosis development in the lungs, delay the onset of severe interstitial pneumonia, and reduce the risk of multisystem organ failure due to an overall abated SARS-CoV-2 viral load. HBO_2 proved able to reduce interleukins levels, specifically of IL-1 beta, IL-6, IL-8, and TNF-alfa, all involved in the development of pulmonary fibrosis. Moreover, the increased production of nitrogen oxide during HBO_2 therapy can increase vasodilation and reduce platelet activation, potentially hampering the procoagulant state encountered by COVID-19 patients. HBO_2 also seems to preserve the antioxidant capacity of lymphocytes, thus protecting the resilience of the immune system that is known to be impaired in COVID-19 cases. Potential, known adverse effects of HBO_2 – such as oxygen pulmonary toxicity, hyperoxic seizures, or transient visual impairment – are preventable and rare at pressures currently used.

Conclusion: In this period it seems reasonable to take every possible method into account to take care of COVID-19 patients. Despite its possible beneficial effects, the role of HBO_2 in COVID-19 patients still needs to be demonstrated with properly designed trials. Therefore, when using HBO_2, clinicians should weigh possible benefits with potential damages and risks. ■

Evidence Review for HBO_2 Treatment of COVID-19 Webinar: Q&As for speakers

Note: Meeting organizers have amended some of the questions and responses for clarification.

GENERAL QUESTIONS – answered by DR. JOHN FELDMEIER

1. Q: We did not see thus far a study that could prove different outcome with the use of HBO_2. It is all about trying HBO_2. What about ECMO (extracorporeal membrane oxygenation) compared to HBO_2?

A: There is no definitive evidence for the value of HBO_2. The reports of Gorenstein, Thibodeaux and the Chinese are all suggestive of a positive response. There are no comparisons of HBO_2 to ECMO as yet. As reported by Dr. Wainwright in her case report, ECMO has not proven to be a panacea.

2. Q: What's the shallowest treatment that attains satisfactory oxygen saturation? *~ Fitzroy Armour*

A: There is no answer to your question as yet, and this would be highly dependent on the severity of the pathology for each individual patient. If the patients are monitored by pulse oximetry or transcutaneous O_2 while in the chamber their pressure could be titrated to hopefully achieve a pulse oximetry reading of 90% or better.

3. Q: What about chest PT? When not on a vent? Awake for prone patients? *~ Debbie Ravel*

A: I don't know of any evidence that addresses the benefits of chest PT as yet.

4. Q: The goal is to improve tissue oxygenation: We do not need PO_2 of 5, 6 or 600, so what about using less ATA for more extended dives/treatments? *~ Mohamedaouf Khaznadar*

A: That issue is more the point of HBO_2 rather than ground-level O_2. It is extremely difficult to oxygenate these patients in spite of high FiO_2s (fractions of inspired oxygen) and mechanical ventilation with positive end-expiratory pressure (PEEP). As experience with protocols using different pressures and times are accumulated, we may know the answer to your question.

5. Q: Ultraviolet (UV) lights are not recommended around chamber acrylic (Perry chambers)? ~ Robert Lambertsen

A: UV light as a type of ionizing radiation is likely to weaken the chemical bonds keeping the acrylic intact. This can lead to the acrylic becoming brittle, subject to explosion and rapid decompression, as was seen in the era of radiating patients for cancer through an acrylic-hulled chamber.

6. Q: Can we consider treating a pregnant patient who is COVID-19-positive?

A: Yes. We don't see that there are any contraindications.

7. Q: How close do the chambers need to be to the ICU? I'm thinking chambers would have to be in hospital. *~ Susan Millan*

A: This is a clinical judgment. It depends on availability of support during transport and the severity of the patient's symptoms.

8. Q: Can HBO_2 therapy open collapsed alveoli? Which is more effective: HBO_2 or ventilation?

A: PEEP is more effective in that regard. HBO_2 works by delivering more O_2 across the pulmonary membrane and dissolving additional amounts in the plasma (Dr. Wainwright).

9. Q: What about treating non-COVID HBO_2 indications in this pandemic? *~ Hassan Alqartoobi*

A: Dr. Thibodeaux answered this question. He indicated that they treat patients with the usual indications for one-half of the day and COVID-19 patients the other half. Disinfecting the chamber after the COVID patients adequately is absolutely necessary.

QUESTIONS FOR DR. SANDRA WAINWRIGHT

Clinical course of COVID-19 and the possible role of HBO_2

1. Q: If mechanical ventilation was initially thought to be so critical in the treatment of patients with severe symptoms but then found not be as effective as hoped, why would HBO_2 therapy not have been almost automatically considered as a superior therapy? *~ Barry Argroves*

A: At the time we had COVID patients HBO_2 therapy was just emerging in the literature from Wuhan. I'm the only HBO_2 doc [at my facility] and was overwhelmed with critically ill patients. Plus, we had to consider the infection control measures and staffing to do HBO_2 therapy: Staff had all been pulled to the front line to support the overwhelming number of sick patients who were hospitalized. There are many factors and permissions that have to be implemented before we do HBO_2 therapy in COVID patients, so at the time we couldn't do it.

2. Q: Should you consider MMR vaccination to help reduce symptoms and progression to severe disease? *~ J. Nicholas Vandemoer*

A: Sorry, I do not know how the MMR would help reduce COVID symptoms. We were grasping at straws in the middle of the battle with COVID and were throwing everything we could at it. Plus, vaccination takes weeks to develop immunity. The patients were progressing and dying within days to a few weeks.

3. Q: An FDA official took some pains to comment that removing the emergency indication status of HCQ (hydroxychloroquine) for the treatment of COVID-19 changes the status of the drug to that of any other medication ... i.e., can be used off-label (including for COVID-19) at physician discretion ... true? *~ Williams Palko-Schraa*

A: I believe that is true. We were giving HCQ based on the French article that showed better recovery when given with zithromax; then more information came out later.

4. Q: (on viewing the 33-year-old, March 27 slide): Why? Aggressive intubation? That's a right mainstem [bronchus] *~ H. Leo Tanaka*

A: Massachusetts General Hospital and other entities were saying we should intubate early so patients don't desaturate while anesthesia is trying to intubate the patient. We quickly realized if we intubated everyone by this criterion we'd have 130 intubated patients; many were doing "OK" on 100% oxygen. Yes, regarding mainstem intubation, we pulled it back.

5. Q: What is ECMO? *~ Jill Baron*

A: Extracorporeal membrane oxygenation – heart-lung bypass.

6. Q: Did the ECMO patient survive? *~ Susan Churchill*

A: Unfortunately no. Very sad.

7. Q: Does awake proning improve non-ventilated patients? *~ Ibrahim Shehata Hussin*

A: Yes. Awake and nocturnal proning on non-intubated patients coupled with incentive spirometry really helped. I think we were able to avoid intubations as a result.

8. Q: Great presentation. Didn't hear anything about PEEP levels. Any pneumothorax (PTX) on high PEEP? *~ H. Leo Tanaka*

A: PEEP ranged 8-12 for my pneumothorax patients, which made me scratch my head because we were trying to come down on PEEP as quickly as we could. We were using PEEPs as high as 28 to 30! But no PTX on those.

9. Q: Rate of pneumothorax in these patients? *~ Hassan Alqartoobi*

A: Four patients and five pneumothoraces of 60 ventilated patients in one week. One of the four patients had both lungs with pneumothorax.

10. Q: Can general practitioners give prophylactic fraxiparine? *~ Albert Van den Brink*

A: I can't comment on that, sorry.

11. Q: For informed consent, what did you tell patients about the known superior form of oxygenation – hyperbaric oxygenation? *~ Brian Lynch*

A: (I'm in favor) How do we give good consent to Spanish-only speaking patients; how do we provide a service that isn't staffed? In a pandemic you get OVERWHELMED by the volume of critically ill patients. Each hyperbaric unit will have made a decision on whether to treat or not off clinical trial. Others will have launched an IRB-approved clinical trial While we know that hyperbaric oxygen can increase oxygenation in patients with COVID, there is insufficient evidence to conclude definitively that it affects overall morbidity and mortality. A discussion of both potential advantages and toxicities are necessary for an informed consent.

12. Q: Could you please address pulmonary compliance in COVID 19 patients? *~ Bruce Voss*

A: Driving pressures ranged from 10-30; some had stiffer lungs than others. The less stiff hypoxic lungs were probably microthrombi or PE. I think the high PEEPs we had to give to keep them alive with tolerable oxygenation did injure the alveoli over time and lead to stiffer lungs. We had to tolerate peak pressures in the high 30s and 40s, PEEPs of 20-24, but when we proned them, oxygenation would improve; then we could take PEEPs down to the teens sometimes.

13. Q: I've heard that the ARDS (acute respiratory distress) that COVID-19 patients get may act differently than "regular" ARDS. Is there anything to that? *~ Ronald Devine*

A: We saw both. Some "usual" ARDS, with stiff lungs, some with hypoxemia, but better lung compliance with better ABGs (arterial blood gas) on more normal tidal volume measures (Vts).

14. Q: Can you talk a bit about the timing of dexamethasone and duration? ~ *David Lambert*

A: We used methylprednisolone 40mg every eight hours for three days.

15. Q: How long is recovery of ICU patients in general? Any information of long-term sequelae beyond the typical ones with intubation?

A: Our lucky patients spent about 30 days in ICU. We are now seeing some patients back with tracheostomies and PEG tubes, and it is around day #65 for these patients (about five of them).

16. Q: Do you think that HBO_2 therapy will be helpful for all patients with moderate illness (pre-ventilation stage)? ~ *Mohab Shafei*

A: I personally do not have enough evidence yet to make a conclusion. Based on some anecdotal evidence from colleagues who have done this, it seems that in the "not yet intubated" hypoxic hospitalized patients, hyperbaric treatment seems to be helpful.

17. Q: Did you try CPAP (continuous positive airway pressure) and NIV (non-invasive ventilation) prior to intubation? ~ *Pieter Bothma*

A: In the beginning we were concerned about using NIPPV (non-invasive positive pressure ventilation) because of the aerosolization risk. In the few patients we were willing to do this, they should have been intubated. However, NIPPV was being widely used in NYC and it seems that it was helpful. The little bit of positive pressure, I think, can be helpful. We were also slow to adopt high-flow nasal cannula, again because of the aerosolization risk and not enough equipment.

QUESTIONS FOR DR. SCOTT GORENSTEIN

Safety concerns for the use of HBO_2 in COVID-19 patients

1. Q: What are the chances of damage to acrylic of monoplace chamber with bleach. Is it recommended? Will it lead to erosion if used regularly? ~ *Manoj Gupta*

A: I am not sure, but we did not notice any deterioration of the acrylic. I suggest checking with your chamber manufacturer.

2. Q: What is PPE? ~ *Gerardo Roblero*

A: Personal protective equipment.

3. Q: How many sessions [for] each patient? ~ *Rita Araujo*

A: Each patient could get up to five treatments.

4. Q: Would there be a practical advantage in using a twin-lock multiplace chamber in case medical intervention is required? ~ *Troy Gessner*

A: The advantage would be the ability to intervene. However there would be increased risk to the inside tenders.

5. Q: How did you decide the number of HBO_2 treatments. Was there an endpoint? ~ *Sharad Patel*

A: The number of treatments was decided by consensus panel and based on immunomodulation modeling.

6. Q: Any inflammatory markers measured pre- and post-HBO_2? *~ Leonardo Profenna*

A: We had no additional lab tests for this study.

7. Q: Were the areas between the HBO_2 facility to the ward or ICU cleaned after transporting patients? *~ Daniel Gericke*

A: The hallways were not cleaned, but the chamber and chamber area were cleaned daily.

8. Q: How is infection control managed with patient transport? *~ Daniel Gericke*

A: All transport staff wore full PPE; patient had mask over oxygen.

9. Q: Can the patient remain alone during HBO_2 treatment? *~ Gerardo Roblero*

A: NO. Patients absolutely must be supervised.

10. Q: Is there any risk for a non-COVID hyperbaric patient to contact COVID in the chamber even after the unit was "cleaned"? (i.e., the same chamber that previously treated a COVID-positive patient)? *~ Scott Anderson*

A: We were treating COVID patients only.

11. Q: I heard the doctor state that five HBO_2 sessions were given. Is that correct, and were they daily or twice daily? *~ Leslie Wagenberg Gella*

A: Treatments were daily.

QUESTIONS FOR MARCUS SPEYRER

Considerations for use of HBO_2 in COVID-19 patients

1. Q: What was the main cause of death in the three patients who expired? *~ Sharad Patel*

A: One had pulmonary embolus after two dives/treatments; two had confinement issues and refused further dives.

2. Q: Why a month treatment lapse between patients 12 and 13? *~ Noah Rosen*

A: COVID cases admitted were very few. We have seen an uptick the last couple of weeks.

3. Q: You don't use ultraviolet light for disinfection? *~ Rita Araujo*

4. UV light should be unsafe for the acrylic. *~ Anthony Johnston*

5. Q: If used in monoplace chambers wouldn't the UV light disinfection potentiate yellowing or crazing of the acrylic? *~ William Palko-Schraa*

6. Q: One point about UV cleaning in the HBO_2 unit: UV light can damage the acrylic so there has to be some care taken when using this for chamber room sanitizing. *~ Brian Pruss*

A: For questions 3-6 immediately above: We do not use UV lights for disinfection purposes, nor do we have fluorescent lights over the chambers.

7. Q: What is the reason for pressurizing the chambers to 3 ATA after cleaning? And the 20-minute sit time? *~ Daniel Gericke*

A: I felt pressurizing it to 3 ATA and holding it for 20 minutes then venting added another layer of protection.

8. Q: What type of disinfectant should be used in the chamber? *~ Gerardo Roblero*

A: We use LPH se cleanser.

9. Q: How was 2.0 ATA decided upon and not 2.4 ATA? *~ Leslie Wagenberg Grella*

A: 2.0 ATA is what our physicians felt would suffice. That is the profile we use for the majority of our indications.

10. Q: Why do you pressurize to 3 ATA when empty after cleaning? *~ Clair Ashford*

A: It's our protocol to pressurize and vent our chambers after cleaning for pressure verification and ensure vent function works properly.

QUESTIONS FOR DR. MICHAEL BENNETT

Translation of research into practice

1. Q: Has anyone been treating COVID in multiplace chambers? How is PPE for the inside attendant handled? *~ David Wakely*

A: Anders Kjellberg, MD, from Karolinska Institute, who presented at the webinar, is treating patients in a multiplace facility and many of his participating centers in Europe do so as well. Europe has very few monoplace sites. The considerations for the use of PPE for hyperbaric staff in the chamber would be the same as for attendants and caregivers in the ICU environment.

2. Q: Have HBO_2 trials using animals been considered? *~ John Garvin*

A: There are no animal models for COVID-19 because in part viruses are very specific to certain species. If possible, it would take some time to develop an animal model.

3. Q: What does DCI/DFU mean? *~ Jill Baron*

A: DCI means decompression illness (bends); DFU means diabetic foot ulcer.

4. Q: How much money does one session of HBO_2 cost? *~ Ertugal Kerimoglu*

A: Costs vary by country and location within the U.S. The national Medicare-allowed billing for its beneficiaries is $550 U.S. per treatment (technical and professional components), but costs for commercially insured patients can be more than twice that.

5. This comment does not apply to our awesome speakers per se but to the apparent change in institutional reliability in an age in which politicization of medical decision-making has invaded public policy and institutional behavior, dare I say trustworthiness (review the Lancet article on HCQ retraction and related scandal as only one of many recent examples). In the future speakers will need to comment on the potential conflict of interest existent for the institutions they are affiliated with relative to study outcomes or even the balance of the nature of information presented. We need a global medical professional conversation on this sad and onerous subject.
~ *William Palko-Schraa* (Comment only.)

6. Q: It would be interesting to study HBO_2 effects on recovery duration and how it affects different patient populations in a non-emergency context. ~ *Fabian Cuntze*

A: We agree. The UHMS Research Committee has recommended short-term, intermediate-term and long-term follow-up in study designs so that these issues can be addressed.

7. Q: A few reports exist stating that patients living at high altitudes are significantly less susceptible to the COVID-19 illness. Since barometric pressure is significantly lower, and therefore PaO_2 is lower as well, how do we reconcile this finding with the benefits due to significantly higher PaO_2 levels achieved through HBO_2 therapy? ~ *Thilo Hanisch Luque*

A: No explanation is readily available. If indeed this experience is a consistent finding, we can only postulate that those living at high altitude have physiologically adapted to hypoxic circumstances in some fashion or fashions.

8. Q: What is the role of the multiplace HBO_2 chamber in regard to COVID-19 treatment?
~ *Mohamedaouf Khaznadar*

A: This discussion continues in regard to a potential advantage for multiplace chamber treatments, especially for potentially unstable patients suffering from any disease. On the other hand, chamber disinfection and infectious disease control issues are much easier to deal with in the monoplace environment. The vast majority of hyperbaric facilities in the U.S. are monoplace. Availability would therefore necessitate treatment in monoplace units.

9. Q: What is the survival rate for the ones who go on to ventilation? ~ *Daniel Gericke*

A: Mortality rates in early series of ventilator patients have varied from about 60% to 80%.

10. Q: Observation of higher altitude patients less susceptible to COVID-19 illness … Are you saying less susceptible to becoming infected or less susceptible to severe sequelae from infection?
~ *Phi-Nga Jeannie Le*

A: Reports in the lay press suggest that both incidence and death rate are reduced for those who live at altitudes higher than 3,000 meters. The suggestion without supporting evidence is that those who live at these altitudes are more likely to be adapted to hypoxia because of conditioning at altitude. This result has been reported in Bolivia, Peru, Ecuador, Tibet and China.

Evidence Review for HBO_2 Treatment of COVID-19
Webinar: Q&As for abstract presenters

Note: Meeting organizers have amended some of the questions and responses for clarification.

QUESTIONS FOR DR. PASQUALE LONGOBARDI

1. Q: How does the provision of HBO_2 therapy result in modulated NO levels?
~ Brion von Herzen

A: Hyperbaric oxygen (HBO_2) accelerates the reaction of L-arginine + oxygen (O_2) catalyzed by the enzyme nitric oxide synthase in the three endothelial (eNOS), inducible (iNOS), and neurological (nNOS) variants.

Reference: Allen BW, Demchenko IT, Piantadosi CA. Two faces of nitric oxide: implications for cellular mechanisms of oxygen toxicity. J Appl Physiol 106: 662–667, 2009. doi:10.1152/japplphysiol.91109.2008

2. Q: If chamber treatment pressure is limited to 1.5 hours at 2 ATA, wouldn't it be beneficial to use it for a longer time at a lower ATA of maybe 1.5 ATA if the chamber availability could be resolved? If larger chambers could be used at a lower ATA of 1.5, would you be able to treat more patients with the necessary attendants present with less risk to the attendants? *~ Dan Shonka* (also intended as a general question to the speakers in general for consideration.)

A: Your hypothesis is clear, but it should be verified. There are no dose / effect studies for HBO_2 treatment in contrast to the SARS-CoV-2 virus. I think that the right absolute pressure is 2 ATA, alternating the breathing in oxygen and medical air to stimulate the messengers that activate the antiviral defenses. Higher pressure would create excessive oxidative stress which could favor the mutation of the virus (making it resistant to therapies). Lower pressure may be unable to produce reactive oxygen and nitrogen species useful for inhibiting the virus. I repeat: Clinical studies are needed to evaluate the most effective HBO_2 dose.

3. Q: Have you treated anyone yet; and if so, have you been able to measure NO in patients?
~ Kent McLaughlin

A: We haven't measured NO yet. The Italian Medicines Agency has expressed an unfavorable opinion because it believes that the project, although scientifically valid, is not easily applicable uniformly throughout the Italian territory. The study does not include the measurement of nitric oxide (NO) in patients though the genetic test that demonstrates a polymorphism of nitric oxide synthase (reduced NO synthesis) is an inclusion criterion. The design idea is based on the study already carried out for SARS-CoV-1 (see Åkerström S, et al).

References

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Åkerström S, Gunalan V, Tat Keng C, Tan Y-J, Mirazimi A. Dual effect of nitric oxide on SARS-CoV replication: Viral RNA production and palmitoylation of the S protein are affected. Virology 395 (2009) 1–9. doi:10.1016/j.virol.2009.09.007

4. Q: The nasopharyngeal swab is an RNA test and could be positive even if the dead virus is in the nose. RNA does not equal infection. Is measuring RNA in the nose a good endpoint for study?
~ Noah Rosen

A: I agree that the nasopharyngeal swab could be positive even if dead viruses are in the nose, but the pilot study protocol provides for the inclusion of patients with symptoms in progress and the swab is performed at the same time as the diagnosis (with a tolerance of one day). So it is reasonable to assume that the swab is positive for viable viruses as symptoms are associated with infection.
If the test is positive for dead viruses at the check after three and five HBO_2 sessions, in the absence of symptoms, this could be a bias only in case of study failure.

5. Q: Very interesting NO effects. Multiplace chambers with multiple patients aren't more effective than individual [monoplace chambers for] patients? *~ Fitzroy Armour*

A: In Italy the legislation currently exists only for multiplace hyperbaric chambers, so I have no personal experience with monoplace chambers. I believe that multiplace chambers, respecting some rules to avoid cross-contamination (fireproof polycarbonate panels to separate patients, mask breathing for the whole HBO_2 session with the switch from oxygen to medical air controlled outside the hyperbaric chamber, sanification of the gas lines at the end of the session) allow treatment of a greater number of patients with a better cost / utility indicator. You can ask for detailed information from the engineer Sergio Cappelletti (LINK: https://www.drass.tech/ • E-mail: sergio.cappelletti@drass.it)

Figure 1: Fireproof polycarbonate panels to separate patients

Figure 2: Medical device controlled outside the hyperbaric chamber to switch from oxygen to medical air in order to permit mask breathing for the whole HBO_2 session

Hyperbaric Centre - Centro Iperbarico, Ravenna, Italy

6. Q: It has been stated by a few reports that smokers induce nitric oxide and therefore are less prone to die from COVID-19. In fact, in China smokers were less affected than non-smokers according to stats. This would reaffirm your own data. What is your opinion on this?
[LINK: https://www.medpagetoday.com/infectiousdisease/covid19/86144] ~ *Thilo Hanisch Luque*

A: I like what is reported in the article you cited:
"One possible explanation is that smoking results in increased production of nitric oxide within the nasal passages, which have the important role of cleaning and filtering the air prior to it being pulled down to the lungs. This gas has been shown to block the ability of SARS-CoV-2 from entering cells as well as impair the ability of the virus to replicate once inside the cell. On the other hand, if the infection ensues, the systemic effect of smoking breaks down the body's ability to defend itself. The same inflammation that potentially protects against initial infection suddenly becomes the body's Achilles heel."

Regarding the fact that the severity of the infection is greater in smokers, the epidemiological data is that 82% of the patients who died from COVID-19 had two or more comorbidities. The main comorbidities are cardiovascular, brain, dysmetabolic diseases, organ complications (liver, kidney, lung), cancer in the past five years. These comorbidities are very frequent in smokers.
LINK: https://www.epicentro.iss.it/en/coronavirus/bollettino/Report-COVID-2019_25_june_2020.pdf (Page 3, Table 2)

7. Q: Do you need regular air breaks to stimulate production of hypoxia-inducible factors (HIF)? (This isn't the usual treatment table that we'd use in the UK) ~ *Liam Hudson*

A: Although the term *HIF* refers to hypoxia, it is actually oxidative stress that stimulates the mitochondria to produce HIF. Oxidative stress occurs due to frequent variations between high and low oxygen partial pressure [1-5]. Sunkari (2015) has shown that HBO_2 increases HIF-α, which induces the expression of iNOS and virucidal peptides (defensins, cathelicidines) [1]. An elevated partial pressure of oxygen for a prolonged period appears to be deleterious in infections (sepsis). The increased mortalities observed with excessive oxygen treatment is a result of increased inflammation, oxidative stress on cardiovascular, pulmonary and neurological systems and vasoconstriction in the patient [6-7] (See Figure from Vanderhaeghen, Page 1485, Figure 3: Dual role of HIF in sepsis [6])

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8. Q: For Drs Longobardi or Kjellberg: What capabilities must a multiplace chamber have in place before committing to treating COVID-19 patients? [SEE QUESTION #5 above for illustrations]

A: I believe that multiplace chambers have to respect some rules avoid cross-contamination (fire-proof polycarbonate panels to separate patients, mask breathing for the whole HBO_2 session with the switch from oxygen to medical air controlled outside the hyperbaric chamber, sanification of the gas lines at the end of the session) allow treatment of a greater number of patients with a better cost / utility indicator. You can ask for detailed information from the engineer Sergio Cappelletti (LINK: https://www.drass.tech/ • E-mail: sergio.cappelletti@drass.it)

QUESTIONS FOR DR. ANDERS KJELLBERG

1. Q: Sickle cell disease and trait would be at higher risk of COVID-19 complications. How would this be useful? *~ Fitzroy Armour*

A: Chronic inflammation as a risk factor seems to correlate with inflammation out of control in COVID-19. Whether sickle cell anemia has a similar correlation I do not know.

2. Q: Any preliminary results at this stage? *~ Daniel Reynolds*

A: No. Only one subject was included.

3. Q: If patient was improving, would you consider going beyond five treatments? *~ V. Pinnamaneni*

A: For our trial, no. Only five treatments were allowed, according to protocol.

4. Q: How soon do you expect results? *~ Brian von Herzen*

A: Depends on how many centers can be recruited to the trial.

5. Q: This presentation is discussing an RCT (randomized controlled trial), but since there is no placebo arm would it not be an observational trial? *~ Leslie Wagenberg Grella*

A: A randomized controlled trial does not necessarily need a placebo: The control is standard care. This is a weakness, though, because you can always argue that there is only the placebo effect that makes subjects better.

6. Q: Is this going to be a multicenter study? *~ Daniel Gericke*

A: Yes, it is a multicenter trial – so far three centers. We hope to have at least 10 centers involved for quick results.

7. Despite the weakness mentioned by Dr. Kjellberg, this is the best, well designed study, which could be taken as base for further studies. *~ Mohamedaouf Khaznadar* (Comment only.)

8. Q: For any of the presenters who have treated patients: Of the patients you treated who got better, did any of them get worse, and did you have to treat them again? Also, would it be an option to treat them again? *~ Dana Hahn*

A: For our trial, no. Only five treatments were allowed according to protocol.

9. Q: At what point is it ideal to start treating patients to expect the best results with HBO_2? ~ *Yury Salinas*

A: The Research Committee of the UHMS addressed this question in their guidelines on study design (see https://www.uhms.org/covid-19-information.html). Based on theoretical considerations and experience to date, the Committee recommended that patients be considered for treatment at the point their respiratory status has begun to deteriorate but they have not yet required intubation.

10. Q: For Drs. Longobardi or Kjellberg: What capabilities must a multiplace chamber have in place before committing to treat COVID-19 patients? ~ *Phil Frazier*

A: Depending on the location of the chamber within the hospital, the physicians and nursing staff caring for the patient must be versed in critical care – probably minimally ACLS-certified. Laryngoscopes and other equipment for intubation should be readily available. "Crash cart" medications should also be immediately available. Suction, EKG monitoring, pulse oximetry or $TCPO_2$ (transcutaneous oximetry) capabilities should also be available.

QUESTIONS FOR DR. KERRY THIBODEAUX

1. Q: What are your stopping parameters? ~ *Joseph Nevarez*

A: Stopping parameters: $FiO_2 < 50\%$, tachypnea resolved, O_2 saturation holding steady.

2. Q: For those whose D-dimers were elevated and decreased, what anticoagulants were used? Were they still fully anticoagulated? ~ *Daphne Denham*

A: Heparin was the most common anticoagulant. The hospitalist and critical care pulmonologists handled the patients medically.

3. Q: If these patients are receiving multimodal therapy, how do you attribute their improvements to HBO_2? ~ *Monique Abner*

A: The patients all subjectively felt better and breathing was very much less labored after HBO_2.

4. Q: From your cases do you think HBO_2 therapy is particularly useful for African American patients? ~ *Julian Eden*

A: Yes.

5. Q: Any thoughts about bid (twice daily) HBO_2 vs. daily? ~ *Judith Nolan*

A: We did daily because we still operated at full capacity with non-COVID HBO_2 patients and a wound center.

6. Q: No one has commented on smoking history in the patients reported in the case studies. Can we ask some of the presenters on this? ~ *Leslie Wagenberg Grella*

A: Three of the 14 patients we treated had a history of smoking.

7. Q: Was any PaO_2 taken for each patient and day of infection when HBO_2 started? ~ *Hooi Geok See*

A: They all had decreased PaO_2 levels and increased inflammatory markers.

8. Q: Have inclusion criteria evolved over time? *~ Anthony Johnston*

A: Our protocol to treat has remained FiO_2 > 50%, tachypnea and patient's ability to cooperate with HBO_2.

9. Q: Claustrophobia aside, what is the subjective patient experience with HBO_2 therapy in terms of symptomatic relief? *~ Brian von Herzen*

A: All patients reported breathing was easier, and they felt markedly better while in the chamber. Most of them slept during the dive/treatment.

10. Q: Did the patients receive antithrombotic therapy as well – especially for those patients who died of pulmonary embolism? *~ Selin Sumen*

A: Yes. They were treated with heparin.

11. Q: What were the findings of the follow-ups with arterial blood gas analysis post-HBO_2? *~ Thilo Hanisch Luque*

A: ABGs were improved post HBO_2.

12. Q: Did you use monoplace or multiplace chambers? *~ Raghib Manzoor*

A: Monoplace chambers.

13. Q: Were the radiographic findings of the patients in this series similar? Were any changes noted? *~ Josh Bezanson*

A: They all had similar chest X-rays, as was shown during webinar. After a few treatments the chest X-rays did show some improvement.

14. Q: What were the PF ratios pre-treatment and how changed after the treatment course? *~ Bruce Voxx*

A: PF ratios were not looked at when compiling this data.

15. Q: Were you able to compare outcomes with any patients at your hospital who did not receive HBO_2 therapy? *~ Daniel Reynolds*

A: Patients treated with HBO_2 had shorter lengths of stay and did not require mechanical ventilation.

16. Q: So all three female African American > 65 years old died: Any concerns that age/gender/race could contribute to outcome? Any concerns that tobacco smoking status influences clinical response? *~ Olayinka Ajayi*

A: Two were African American and one was Caucasian. One died of PE, one had encephalopathy and became a non-candidate. The Caucasian had confinement issues and made herself a DNR.

17. Q: What would be the time/hours between BID (twice-daily) treatments, if needed? *~ Keith Ly*

A: If you had to do BID treatments it would be optimal to do them every 12 hours. Challenge would be staffing.

QUESTIONS FOR DR. DAVID LEE

1. Q: Could you please speak more to what matching method was used for determining the propensity scores and if there was any weighting done? *~ Josh Bezanson*

A: These topics have addressed in our paper available at: https://www.uhms.org/publications/uhm-journal/uhm-journal-ahead-of-print-public/hyperbaric-oxygen-therapy-for-covid-19-patients-with-respiratory-distress-treated-cases-versus-propensity-matched-controls/viewdocument/4695.html

2. Q: Now that dexamethasone has been shown to be effective therapy for COVID-19, every patient will be receiving it. Outcomes in all series will need to take into account use of systemic steroids. Are there any medicators of inflammation that are suppressed by HBO_2 and not dexamethasone? *~ Neil Hampson*

A: This was addressed in Q&A, I think. Some on the webinar who know better than I think that the suppression by HBO_2 might be different.

3. Q: On O2 requirements can you please define low, moderate and high needs? Never mind. I found 1-5, 6-11 and 12-15. *~ V Pinnamaneni*

A: That is correct.

4. Q: Good study but lacking numbers. *~ Mohamedaouf Khaz*

A: That's right. We need a larger study, but if the effect size is approximately right, then there wouldn't necessarily need to be a lot of patients.

5. Q: Has dexamethasone been used in New York? USA? *~ Pieter Bothma*

A: In some hospitals, but not all. Before the recent study, there were reasons for and against.

6. Q: What is the thought of installing a monoplace chamber in or closer to the ICU? *~ Robert Lambertsen*

A: In general, our experience has been decreased transit time is probably better.

7. Q: Did you use any neck seals and hoods to either hook up the patient to air and O_2 or when transporting patients? Italy was using this, and it appeared effective. *~ Debbie Ravel*

A: We used standard hospital guidelines to transport patients. We had thought about oxygen hoods, but since we didn't have the direct experience we didn't pursue.

8. Q: Not saying I could convince my facility to do this, but how would a center that is interested in participating volunteer for a multisite study; and is there a prerequisite checklist of resources and personnel available? *~ Anthony Johnston*

A: As I mentioned, funding is the key issue in getting a multicenter randomized controlled trial since we will have to pay for HBO_2 with research dollars if it's going to be studied.

9. Q: The cases who died, died in hyperbaric chamber or in ICU? *~ Paula Burchard Senoret*

A: In my presentation none died in the hyperbaric chamber.

10. Q: If the problem is hypoxia why do we not treat these patients three sessions per 24 hours? ~ *Selin Sumen*

A: We decided on this protocol given prior experience and the logistics of daily procedures seemed easier to deploy. But these are good questions should we find HBO_2 to be effective.

11. Q: From a safety point view and efficacy to alleviate hypoxia, what about the use of a helmet over the use of facial mask to deliver oxygen in ICU and during HBO_2 treatment?
~ *Hassan Alqartoobi*

A: Our hospitals did not use helmet CPAP or the hyperbaric helmets. Other institutions are looking into these issues. I'm not sure that they should be used while in the hyperbaric chamber as you're setting up a barrier between the pressure of the chamber and the helmet in the chamber.

12. Q: Moving a chamber and setting it up closer [to the ICU] isn't a simple thing due to gas input and exhaust requirements. Not to say it can't be done. but it's certainly not easy. ~ *Brian Pruss*

A: Agree these are not simple issues, and mechanical engineers will be needed should HBO_2 be found to be a viable treatment.

13. Q: Any estimates of resources required (cost) per patient treated? ~ *Daniel Reynolds*

A: For five treatments, the cost would be somewhere around $2,500-$3,000 U.S.

14. Q: What is "double oxygen"? ~ *Johan Douglas*

A: I think this refers to when a patient is not only on high-flow oxygen via nasal cannula but also has a non-rebreather face mask delivering oxygen.

15. Q: Will cost effectiveness be measured in any of the up and coming studies HBO_2 versus control (cost saved possibly less hospital time using HBO_2)? ~ *Daniel Gericke*

A: Given the cost of HBO_2 and the cost of even one ICU day, if HBO_2 is found to be effective, then I don't think there will be any comparison needed.

16. Q: Any observed non-pulmonary manifestation of COVID that got better on HBO_2?
~ *Ziad Mirza*

A: We did not formally track these events, and in general they are less common.

17. Q: Have there been any of these individuals who were scuba / commercial divers who have had better worse outcomes due to their physical experience with underwater compressions?
~ *Justin Kantor*

A: We are not aware of any data for this.

18. Q: Did you use standard depressurization rates or a slow ascent? Did any patients find it harder to breathe during HBO_2 treatment?
~ Kenneth LeDez

A: Addressed by Dr. Gorenstein's presentation.

19. Q: What do you think about the paper of HBO_2 in rehabilitation in COVID-19 patients séquelas? (Sorry for Spanglish) *~ Paula Burchard Senoret*

A: We think probably given that HBO_2 is not as simple as giving a medication that it should probably be used only if it decreases mortality. However, we have hypothesized that it would have benefit in the long run for morbidity if it reduces mortality.

20. Q: Why is treatment for most patients limited to only five treatments? *~ Mohammad Suleman*

A: That was the protocol that we had established, thinking that patients needed to bridged for several days until their cytokine storm had resolved. But it is a good question as to whether additional treatments are better among patients with more severe disease.

21. Q: Theoretically speaking, using dexamethasone during HBO_2 treatments increases the risk of oxygen toxicity. What is your take on that in these COVID patients? *~ Hassan Alqartoobi*

A: I would defer this comment to one of the hyperbaric experts but would say that COVID patients have such severe oxygen debt, I'm not certain how likely they are to have oxygen toxicity.

22. Just a comment: Perhaps HBO_2 therapy is the solution to the ventilation part of the V/Q mismatch, but we still would need some antithrombotic therapy. Perhaps in that scenario improved outcomes would rise even higher. *~ Thilo Hanisch Luque*

A: Absolutely, in the absence of antithrombotic therapy I think that HBO_2 treatment outcomes may not be so good.

23. Q: Are there any extra risks we need to consider when we nurse these patients in the prone position inside the HBO_2 chamber? *~ Hassan Alqartoobi*

A: We did not prone patients in the chambers, but this may be a better question for Dr. Denham, who did.

24. In addition, re cost-effectiveness: You are discharging a much healthier patient. We had many who were able to eat "for the first time in days" after their first treatment. *~ Daphne Denham* (Comment only.)

25. Q: Have your patients had issues with barotrauma more or less than you typically see? *~ Susan Churchill*

A: We did not have any patients with a pneumothorax. In addition, the patient who unfortunately had the hypoxic arrest did have a chest CT after the event, who did not show any evidence of pneumothorax.

26. Q: In a multiplace chamber would it not be more cost effective to keep the main chamber at depth and use the outer lock to put patients in and out while on hoods? *~ Fitzroy Armour*

A: Recommend discussing with those who have more experience with a multiplace chamber.

27. Q: We are less than a half mile from the hospital. What's your feeling on transporting a patient to be treated with HBO_2? *~ Karen Wilson*

A: As discussed, these COVID patients are very ill and tenuous. Transport of these patients with severe respiratory distress can be challenging in itself. We would need to think through the risk and benefit very carefully before even considering. At this time until we have more experience it is our opinion that this is an inpatient procedure only.

28. Apparently neurological symptoms appear with COVID before respiratory symptoms, so I would try to invite Neuro consults for these studies. (Comment) *~ Kurt Laipple*

A: Agree that some of the neurologic issues may be due to severe hypoxia, and HBO_2 may play some role.

29. Q: The risk of pulmonary edema: Has it been a concern and increased risk with treating COVID patients with HBO_2? *~ Daniel Gericke*

A: This is why in this first study of ours we had added the exclusion of negative troponin. We are not suggesting that this is an absolute contraindication, but more data is needed.

30. Q: Would home chambers be advised for patients in self-quarantine? *~ Fitzroy Armour*

A: As we discussed, we believe this is an inpatient procedure and do not recommend that anyone try to self-treat on their own.

31. Q: Should the hyperbaric chamber have ventilator capability? *~ Phil Frazier*

A: We did not evaluate its use among intubated patients as we are not able to do so in our monoplace chambers. We may need to consider risk of pneumothorax even more so among patients who have been on mechanical ventilation.

31. Q: This is an open question for the group. Has anyone decontaminated a chamber with an aerosolized product like hydrogen peroxide or other agent due to its being able to have greater penetration? *~ Pat McCabe*

A: Aerosolized H_2O_2 is corrosive to metal. Eric Hexdall. (Comment)

AFTERNOON Q&AS *(with all faculty on)*

1. Q: Is there any data on treating vented patients in chamber? *~ Lisa Wykoff*

A: As discussed above, our study was only on patients who were not intubated (Dr. Lee).

2. Q: Should patients not being treated for COVID be tested prior to starting treatments? *~ Karen Wilson*

A: This is a difficult question because of the poor sensitivity of the COVID-19 test. There should be some consideration as to whether patients with a clear clinical diagnosis should also be treated if labs, chest X-ray and clinical symptoms and signs are all highly consistent with COVID.

3. Once a patient needs to be on a vent the situation tends to become a different animal: We could with our mono, but the risks are certainly greater. Plus, vent settings tend to be a bit high, and typical monoplace vents are somewhat limited in their capabilities. *~ Brian Pruss* (Comment only)

4. Q: What was the average time frame from completing a treatment to symptoms returning? *~ David Meyer*

A: Almost immediately (Dr. Lee).

5. Please comment on oxygen debt parameters: e.g., lactic acid, acidosis, $ETCO_2$ (end-tidal carbon dioxide) with/without HBO_2. *~ Michael Strauss*

A: Oxygen debt is the minimum requirement for tissue/organ consumption minus the oxygen supply available. Van Meter states that survival is not possible if the oxygen debt exceeds 33 L/m^2. Multiorgan failure occurs at a debt of 22L/m^2, whereas those whose debt is no more than 9L/m^2 typically survive without residual organ dysfunction or injury.

It has been reported that intermittent hyperbaric oxygen may satisfy this "debt" in the setting of severe anemia until hemoglobin levels can be restored. The repayment of oxygen debt has not been demonstrated specifically as yet in COVID-19. The restoration of this oxygen debt may be a valuable effect of hyperbaric oxygen in COVID patients.

On the other hand, tissue hypoxia is an uncommon cause of elevated blood lactate levels (a potential marker of "oxygen debt") in sepsis, particularly after adequate initial resuscitation [1,2]. Other sepsis-related reasons for elevated lactate include impaired oxygen use due to mitochondrial dysfunction [3]. This dysfunction and stress-related increase in glucose metabolism with resultant impaired lactate clearance [1,2,4] are not likely to respond to hyperbaric oxygen. Further study is necessary to determine whether the payment of "oxygen debt" is a key mechanism for HBO_2 in COVID-19 (Dr. John Feldmeier).

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6. Q: What type of oxygen tank would you have prepared for transportation of patients to and from the hyperbaric department?

A: We always made sure we had a full tank each leg of the transport (Daphne Denham). Agree (Dr. Lee).

7. On a side note, a Swiffer-type device using your sanitizing product on a cloth (not using the Swiffer product) does work well for reaching in to clean, especially when using a bleach product. *~ Brian Pruss* (Comment)

QUESTIONS FOR DR. JOHN FELDMEIER

Synthesis of the data

1. Q: Post COVID, what would be patient safety concerns in treating outpatient HBO_2 patients for non-COVID-related diagnoses? These patients would have tested positive and have had a complicated recovery, with respiratory-related problems. *~ Michelle Carrion*

A: We don't know, really. Those who have treated these patients indicate that survivors of severe disease are likely to have significant pulmonary complications permanently. I would recommend a pulmonary consult and pulmonary function tests. I think the issue would be to rule out air-trapping.

2. Q: What do you tell the patient for informed consent if you do not treat? *~ Brian Lynch*

A: Not sure I entirely understand the question. If the patient is enrolled in a randomized controlled trial, you must tell them that they have a chance (usually a 50-50 chance) that they will not be assigned to the treatment group. If it is a one-armed trial, they would probably not receive treatment because they failed to meet eligibility requirements. While we know that hyperbaric oxygen can increase oxygenation in patients with COVID, there is insufficient evidence to conclude definitively that it affects overall morbidity and mortality. A discussion of both potential advantages and toxicities are necessary for an informed consent.

3. Q: Have there been any facilities conducting these studies of HBO_2 therapy with COVID-positive patients treating more than once in a 24-hour period? Also, are patients' lactate values being followed throughout their therapy trial? *~ Vicki Landau*

A: The treatment protocols as I understand them have sometimes allowed for more than one treatment per day. Most have been a single daily treatment. In the suggested study design guidance document (see https://www.uhms.org/covid-19-information.html) we suggest that some investigators may treat more than once daily. Obviously, if one treatment appears to be adequate, it makes sense to do only one treatment per patient daily to allow other patients to be treated and reduce chances of pulmonary oxygen toxicity.

4. Tylenol affects the reticular activating system, so why not bettering the ability to breathe and sleep? *~ Lauren Romeo*

A: This appears to be a comment. In that case we thank you for your explanation.

5. Q: I do not have a series. Our IRB application was approved by the IRB pending hospital approval. The hospital administration blocked our study. Our protocol at 1.6 ATA was based on the Chinese experience after extensive interaction with the Chinese hyperbaric physicians, information from Dr. Orval Cunningham's dose of HBA (hyperbaric air) in dying Spanish flu patients, and the doses used for ARDS in blunt chest trauma patients by Rogatsky. At those doses the chance of pulmonary oxygen toxicity was highly unlikely. *~ Paul Harch*

A: Thanks, Paul. We have seen the paper by Rogatsky and its effect on ARDS patients secondary to blunt chest trauma. In our guidance for study design we note that some individual researchers may opt for pressures lower than 2.0 ATA. If you get to complete your study, your results will be of much interest. As in most interventions we advocate the lowest effective dose to reduce complications.

6. Q: Can we discuss reimbursements vs. DRGs (diagnosis-related groups) of inpatients and HBO_2? *~ Michael Strauss*

A: Mike, thank you for reminding us of this issue. How the payment would sort itself out if the HBO_2 intervention proves to be effective is not known, but as you say for now it would be subject to DRGs. For other interventions, I understand there are considerations for special payments.

7. Q: My administration focused on the cost of doing compassionate use therapy. Has there been any positive discussion of reimbursement for hyperbaric therapy in COVID-19 patients? For as much success as initial trials have gained, why has HBO_2 therapy not received the recognition as others? *~ Gregg Morris*

A: No, to my knowledge there has been no discussion of reimbursement. We will have to make the case if it is shown to be effective. Since these are all in-patients, as things stand now, payment would be subject to diagnosis-related groups.

8. Q: Maybe it is too late to ask the NYU group but curious if any patients treated were febrile; if so, were they treated while having fever, as this could increase seizure risk. *~ Noah Rosen*

A: This would be a question for Drs. Gorenstein and Lee. Since fever is a typical part of the disease spectrum, I would have to think that there were febrile patients. Since it is so hard to oxygenate these patients, oxygen levels achieved in the brain are likely to be lower than those that are seen in central nervous system O_2 toxicity. To date, none of the investigators have to my knowledge reported an O_2-induced seizure in spite of fevers.

GENERAL QUESTIONS AND COMMENTS

1. We started proning patients very, very early – basically as they hit the door and saw very similar results. Can't stress need to prone enough. It does help in many cases. *~ Brian Pruss* (Comment)

2. Q: Is it possible that higher altitude patients have less presentation of inflammatory reaction? *~ Phi-Nga Jeannie Le*

A: My personal hypothesis is that patients at very high altitude are possibly more acclimated to low oxygen and therefore are protected (Dr. Lee).

3. I think we have more questions regarding the effects of HBO_2. I'm not sure once a day will be very effective for what turns out to be a chronic-type disease. If we're talking about buying time, and I can see them multiple times a day I can see some benefit, similar to an acute anemia patient. Be interesting to see how this plays out and what others are seeing and reporting.
~ Brian Pruss (Comment)

A: Just a talking point in response to this: Keep in mind when you're in a pandemic, the entire hospital and staff are being overwhelmed. At the peak of the COVID-19 outbreak for us in Connecticut, we had 70 patients who would have met criteria for severe hypoxemia who were not yet intubated (Dr. Wainwright).

4. Q: Where was the [HBO_2 and COVID] editorial published?
~ Josh Bezanson

A: The editorial by Drs. Moon and Weaver was published in *Undersea and Hyperbaric Medicine*'s most recent edition, Volume 47, Issue 2. This and the accompanying paper from China are both posted on the COVID-19 page of the website at:

Main header
https://www.uhms.org/covid-19-information.html

Editorial
https://www.uhms.org/images/01_edit_-_HBO2_for_COVID_47-2_SECOND_QUARTER_2020_print_version_version_47-2.pdf

Guo et al. paper
https://www.uhms.org/images/02_HBO2_for_COVID_hypoxemia_-_47-2_SECOND_QUARTER_2020_print_version_version_47-2.pdf

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The faculty:

Evidence Review for HBO_2 Treatment of COVID-19 Webinar

Dr. Scott Gorenstein is a board-certified Emergency Medicine Physician and board-certified in Undersea and Hyperbaric Medicine. Dr. Gorenstein has been involved with clinical research in wound care and regenerative medicine at NYU Winthrop. During the height of the pandemic in NYC Dr. Gorenstein and his team treated 20-plus patients in an IRB-approved case controlled study looking at hyperbaric oxygen for COVID-19.

He is a past president of the Northeast Chapter of the UHMS and serves as a peer reviewer for several journals.

Objectives:

1. Understand how unstable the COVID-19 patient is.
2. Learn about best practices for safely treating COVID-19 patients with HBO2.

Dr. John Feldmeier is a 1970 graduate of Duquesne University in Pittsburgh. Dr. Feldmeier initially served as a meteorologist in the USAF Weather Service until 1975. He received his D.O. degree from The Philadelphia College of Osteopathic Medicine in 1979 with USAF sponsorship and completed residency training in Radiation Oncology at the University of Texas Health Science Center at San Antonio, Texas. He received a fellowship certificate from the USAF Hyperbaric Medicine Fellowship Training Program at Brooks Air Force Base in San Antonio, Texas and was a staff physician there from 1980 to 1982. Dr. Feldmeier then served as the Chief of Radiation Oncology from 1985 to 1987 and ultimately simultaneous Chairman of the Hyperbaric Medicine Department at Wright-Patterson Air Force Base Medical Center in Dayton, Ohio. He returned to the University of Texas Health Science Center as faculty in 1987 and ultimately became Chief of Radiation Oncology there. He was also the Radiation Oncology Residency Program Director there before leaving to join the faculty at Wayne State University. He became Division Chief and Clinical Chief of Radiation Oncology at Grace Hospital in Detroit, Michigan in 1993. In 1997 he joined the University of Toledo and served as Department Chairman of Radiation Oncology there until his retirement from that position in 2013. He was named Professor Emeritus upon his retirement.

Dr. Feldmeier has authored numerous publications in both radiation oncology and hyperbaric medicine. He has been the editor of the Undersea & Hyperbaric Medical

Society (UHMS) Hyperbaric Oxygen Therapy Committee Report which provided the rationale for the UHMS accepted indications for HBO_2. He served a review editor of the UHMS scientific journal, *Undersea and Hyperbaric Medicine*. He is a Fellow of Undersea and Hyperbaric Medicine and continues on the UHMS Board of Directors as Past President of the UHMS. He is a Fellow of the American College of Radiation Oncology and has been recognized as one of "The Best Doctors in America" since 2007 until his retirement. He was honored to be selected to deliver one of two keynote addresses for the 2017 UHMS 50th Anniversary Meeting.

Objectives:

1. The attendee will be able to state concerns related to applying HBO_2 to the treatment of COVID-19 patients.
2. The attendee will be able to state potential benefits of HBO_2 to the COVID-19 patient.

Professor Michael Bennett is a Diving and Hyperbaric Medicine physician and anaesthetist at Prince of Wales Hospital and the Prince of Wales Clinical School in Sydney, Australia and has been a member of the UHMS since 1993. He has a specific interest in clinical epidemiology, research methodology and evidence-based medicine. He is an experienced clinician and researcher, and the author of a chapter concerning randomized controlled trials in the UHMS Indications book. Bennett is a staunch advocate of evidence-based practice in hyperbaric medicine.

Objectives:

1. Outline the purposes of peer review, open publication and IRB approval in the context of bridging research and practice.
2. Discuss the ethics of using 'off label' therapies.
3. Outline a rational balance between expediency and protocol in a health crisis.

Marcus S. Speyrer, RN, CWS, DAPWCA is the Chief Operating Officer and Partner in The Wound Treatment Center, LLC & The Wound Treatment Center Consulting, LLC @ Opelousas General Health System in Opelousas, Louisiana. He began in wound care in 1993. He is a Registered Nurse and Certified Wound Specialist. He received his Associate Degree in Nursing at the University of New York Regents College in 1995. He has participated in numerous research trials and has several publications. He is a member of the editorial advisory board for the peer-reviewed journal, *Wounds*. He has served on numerous advisory panels and is a consultant with 3M™/KCI and Organogenesis Speakers' Bureau. Member of Undersea Hyperbaric Medical Society, Association for the Advancement of Wound Care and American Professional Wound Care Association.

Objectives:

1. Review process for HBO2 therapy and COVID-19.
2. Review transporting process for Covid-19 patients.
3. Review disinfecting process.

Dr. Nicholas Bird currently works in the Marshall Islands supporting the U.S .Army missile defense garrison on Kwajalein. He is a regional medical director for Duke Urgent Care and is board-certified in both family medicine and undersea and hyperbaric medicine. Bird splits his time between clinical practice and administrative responsibilities, and has a passion for improving health care delivery to optimize patient access, education and outcomes. Prior to joining the Duke medical staff, he was the chief medical officer and CEO of Divers Alert Network and an internationally recognized expert on diving injuries, accidents and medical treatment. Outside of work, he enjoy traveling, and diving the warm waters of the world. He has been a PADI scuba instructor for more than 25 years. He also enjoys reading Clive Cussler novels, cooking and golfing, when time permits. He lives in Durham, North Carolina, with his wife, Kim. They have three children, a grandson, and a crazy Jack Russell terrier.

Dr. Sandra Wainwright earned her medical degree from St. George's University School of Medicine in Grenada, West Indies. In 2000, Dr. Wainwright began her internship and residency training at Norwalk Hospital – a Yale University School of Medicine affiliate. She was asked to stay on as Chief Resident and was awarded the Samuel Floch award, presented by resident peers to the individual who most exemplified excellence and collegiality among colleagues.

Dr. Wainwright was accepted for the combined Pulmonary and Critical Care Fellowship at Norwalk and Yale in 2004. She completed her training in 2007 and is boarded in internal medicine, pulmonary and critical care. She declined a teaching position at Yale, when she was offered

the opportunity to become the Medical Director of the Norwalk Hospital Wound Care and Hyperbaric Center in 2007.

Under her leadership the Norwalk Hospital Hyperbaric facility was awarded a generous donation to purchase and become the first department in the hospital to acquire an electronic medical record. Although the center was the first hyperbaric center in the Northeast, established in 1976, Dr. Wainwright successfully led the center to its accreditation with the UHMS in 2013.

Wainwright has been working at Norwalk Hospital since 2007 and is fully clinical in the fields of wound care and hyperbaric medicine as well as Pulmonary and Critical Care. She is currently a faculty member for both the Pulmonary fellowship and Internal Medicine residency programs as well as an associate professor at the Norwalk Respiratory Therapy School and New York Medical College, School of Medicine. She has published an eclectic selection of topics including a chapter in Braunwald's *Primary Cardiology* textbook on heart disease in the pregnant woman. As a Fellow her abstract 'Use of Exhaled Nitric Oxide in Assessment of Adherence in an Inner City Asthma Clinic' was accepted for presentation at the American Thoracic Society in 2006. She presented an abstract to the Symposium on Advanced Wound Care in 2009 on a case series of patients with calcific uremic arteriolopathy and the role of hyperbaric medicine in wound healing and mortality rates. She has co-authored a paper that was just accepted for publication in the *Journal of the American Podiatric Medical Association* on healing venous disease with advanced surgical and wound healing modalities. Dr Wainwright has also participated in the peer evaluation process for authors seeking submission to the *Undersea and Hyperbaric Medicine* Journal.

Dr. Wainwright has recently engaged in regional and national continuing medical education and scientific meetings and has lectured in a variety of topics including calciphylaxis, venous disease, necrotizing fasciitis, carbon monoxide evaluation, management and literature review, the human microbiome, limb salvage and an introductory course in hyperbaric medicine.

Objectives:

1. Participant will be familiar with the physiology of hypoxia
2. Participant will be familiar with pulmonary lung mechanics
3. Review a case presentation of the continuum of COVID focusing on pulmonary sequelae.

Dr. Kialing Perez is currently an infectious disease specialist for PeaceHealth since 2009. He is a hyperbaric physician in a monoplace environment and board-certified in infectious diseases by the American Board of Internal Medicine and a Diving Medical Examiner.

Objectives:

1. The participant will learn current epidemiology for the COVID-19 outbreak.
2. The participant will learn current testing technology.
3. The participant will get an update on vaccines and treatments for COVID-19 in clinical trials.

The moderators:

Evidence Review for HBO_2 Treatment of COVID-19 Webinar

Nicole P. Harlan, MD, MS, is an assistant professor of medicine at the Geisel School of Medicine at Dartmouth. She is board-certified in pulmonary, critical care, and undersea and hyperbaric medicine and has a special interest in the effects of hyperbaric oxygen therapy on the lung.

Jay C. Buckey, MD, is a professor of medicine at the Geisel School of Medicine at Dartmouth and the medical director of the Center for Hyperbaric Medicine at Dartmouth-Hitchcock Medical Center. He is board certified in undersea and hyperbaric medicine, internal medicine, and aerospace medicine. His research interests include hyperbaric registry development, emerging uses of hyperbaric oxygen (particularly inflammatory bowel disease), and decompression sickness. ■

The abstract presenters:
Evidence Review for HBO_2 Treatment of COVID-19 Webinar

Dr. Kerry T. Thibodeaux, a nationally recognized wound care advocate, is a board-certified general surgeon, vascular surgeon and Wound care specialist. He is a Fellow of the American College of Surgeons.

Dr. Thibodeaux graduated *magna cum laude* in 1982 from the University of Southwestern Louisiana with a Bachelor of Science in a dual major of Biology and Chemistry. He underwent his medical training at and graduated from the LSU School of Medicine in New Orleans in 1986. He then completed a five-year general surgery residency at the LSU School of Medicine in New Orleans. While in his residency program Dr. Thibodeaux was the 1990 Surgical Teaching Resident and the Clinical Instructor of Surgery from 1989-1991. During the course of his studies at LSU School of Medicine he received an NIH Grant for Wound Healing Research in 1987, which resulted in the publication of a wound healing article in the *Southern Medical Association Journal*.

Thibodeaux is the founder and Medical Director of The Wound Treatment Center, located within Opelousas General Health System. Dr. Thibodeaux serves as the Corporate Medical Director of Wound Care for LHC Group, Inc. Additionally, he serves as an inaugural member of the Clinical Advisory Board of Molnlycke Health Care. He is also a member of the editorial advisory board for the peer-reviewed journal, *Wounds*, in addition to being a member of a variety of national and international advisory boards and speakers' bureaus related to advanced wound care.

He presented an abstract and poster entitled 'Combined Therapy for Venous Leg Ulcers Using Hyperbaric Oxygen Therapy and Apligraf' at the 1999 International Undersea & Hyperbaric Medical Society Meeting in Boston, Massachusetts. Dr. Thibodeaux presented a poster entitled "Sepaderm for the Management of Acute and Chronic Wounds" at the Symposium on Advanced Wound Care meeting in April of 2010 in Orlando, Florida. Dr. Thibodeaux, along with co-author S. William Tam, PhD, published a case series entitled "Sepaderm for the Management of Acute and Chronic Wounds" in the October 2010 edition of *Wounds*.

Since 1992 Dr. Thibodeaux has been in private practice specializing in general, thoracic, vascular, endoscopic and trauma surgery in Opelousas, Louisiana.

Dr. David C. Lee is a board-certified emergency medicine physician and NIH-funded academic researcher at the NYU School of Medicine. His prior research experience includes mathematical modeling of infectious diseases, analyzing patterns of emergency department use during disasters, and geospatial analyses of chronic disease burden. He has currently been leading several emergency department based projects related to COVID-19. With Dr. Scott Gorenstein, he helped to perform the safety study of hyperbaric oxygen therapy for COVID-19 patients at NYU Winthrop Hospital.

Objectives:

1. Understand the preliminary results of the NYU study of hyperbaric oxygen therapy for COVID-19 patients.
2. Comprehend the limitations of the data and what the implications of the study are for COVID-19 patients.

Dr. Pasquale Longobardi

- ECHM Level 3 in Hyperbaric and Diving Medicine and Fellow of the European College of Baromedicine
- Affiliate Researcher Institute for Life Sciences, Scuola Superiore Sant'Anna (SSSA) Pisa (I)
- WUWHS Executive Board External Advisor (as supervisor for North America)
- President of the Italian Diving and Hyperbaric Medicine Society (SIMSI)
- Medical Director Centro Iperbarico Ravenna (I)

Objectives:

1. In nature, coated positive-sense single-stranded RNA virus, such as SARS-CoV-2, are inhibited by volatile gas compounds (VOCs) and, some of them, derive from oxygen.
2. In vitro single-strand RNA antiviral response is effective in a range of 30 μM and 50 μM while it is ineffective for values <15 μM.

3. Most of the deceased patients (82% in general, 71% of those under the age of 40) have nitric oxide synthase (NOS) genetic polymorphism and two or more comorbidities highly correlated to the reduced nitric oxide (NO) synthesis.
4. HBO_2 therapy can increase the partial pressure of NO if deficient.

Dr. Cong He

• From Sept. 1989 to July 1994: Studied at Hubei University of Medicine.
• From Sept. 1994 to Now: Working at Sinopharm Dongfeng General Hospital.

Dr. Anders Kjellberg

PhD Student/ICU Consultant, Head of Hyperbaric unit, Perioperative Medicine and Intensive Care, Karolinska University Hospital, Stockholm, Sweden.

Medical examinations

• 2013 European Diploma of Intensive Care Medicine (EDIC)
• 2009 Diplomate of European Society of Anaesthesiology (DESA)
• 2009 Specialist, Anaesthesia and Intensive Care
• 2001 Licence to practice
• 1999 Medical School, Göteborg University

Relevant academic education and research education

• 2018-2020 KI Clinical Research school (molecular medicine),18HEC, Karolinska Institutet
• 2017 Laboratory Animal Science Function A- Rodents and lagomorphs, 3HEC, KI

Positions and assignments

• 2019 PhD Student, Dept Physiology and Pharmacology, Karolinska Institutet, Stockholm
• 2017 Consultant ICU/Head of Hyperbaric unit, Perioperative medicine and Intensive Care, Karolinska University Hospital, Stockholm
• 2013-2016 Specialist ICU, ANOPIVA, Karolinska University Hospital, Stockholm
• 2011-2013 Senior Registrar ICU, Flinders Medical Centre, Adelaide, Australia
• 2009-2011 Specialist Anaesthesia/ICU, VO Anaesthesia and Intensive Care, South Hospital
• 2005-2009 Resident, VO Anaesthesia and Intensive Care, South Hospital, Stockholm
• 2002-2010 Diving physician, Swedish Armed Forces (part time)
• 1991-1993 Communications officer, HM Submarine Näcken, Swedish Armed Forces

Publications:

1. Oscarsson N, Müller B, Rosén A, Lodding P, Mölne J, Giglio D, Hjelle K, Vaagbø G, Hyldegaard O, Vangedal M, Salling L, Kjellberg A, Lind F, Ettala O, Arola O, Seeman-Lodding H. Radiation-induced cystitis treated with hyperbaric oxygen therapy (RICH-ART): a randomised, controlled, phase 2-3 trial. Lancet Oncol. 2019.
2. Kjellberg A, Nystrom H, Soderberg M, Dlugosz A, Jornvall H, Steinberg A. Massive air embolism as a complication of upper gastrointestinal endoscopy: A case report illustrating a stroke mimic, literature review, and suggested management. Clin Case Rep. 2018;6(9):1862-1867.

About this program:

VIEWS expressed by contributors are not necessarily those advocated by the UHMS and are distinct from the peer-reviewed scientific papers that appear in the *Undersea and Hyperbaric Medicine* Journal.

THIS WEBINAR provides a forum for ideas and information to the undersea and hyperbaric medical community and welcomes ideas, commentary and support from its readers.

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