WILLIAM L. HENRICH, M.D., M.A.C.P.
PRESIDENT AND PROFESSOR OF MEDICINE
JOHN P. HOWE, III, M.D., DISTINGUISHED CHAIR IN HEALTH POLICY
The University of Texas Health Science Center at San Antonio

July 28, 2022

The Honorable James E. Clyburn
Chairman, Select Subcommittee on the Coronavirus Crisis
2157 Rayburn House Office Building
Washington, D.C. 20515-6143

Dear Chairman Clyburn,

UT Health San Antonio is one of six health institutions under the umbrella of The University of Texas System, and I am honored to have served as its President since 2009. UT Health San Antonio works collaboratively with our area Congressional delegation continuing to have a direct positive impact on our region. I extend our expert resources to you and the Select Subcommittee, along with our South Texas Congressional delegation, to further investments in healthcare research and services that will continue to provide beneficial results for our constituencies. I would like to thank you for your service as Chairman of the Select Subcommittee on the Coronavirus Crisis. The work led by the members of this Select Subcommittee will continue to help our nation as we move forward through the COVID-19 pandemic.

Please accept my sincere appreciation for inviting UT Health San Antonio Professor and Distinguished Chair for the Department of Physical Medicine and Rehabilitation, Monica Verduzco-Gutierrez, M.D., who provided testimony before the U.S. House of Representatives Select Subcommittee on the Coronavirus Crisis, to provide insight during the hearing on "Understanding and Addressing Long COVID and its Consequences."

As we continue to work through the effects of the COVID-19 pandemic and continue to gain perspective on the impact Long COVID will continue to have on our communities, we must continue to maintain a focus on the work through regional resources, such as the COVID-19 Multidisciplinary Recovery Clinic, which Dr. Verduzco-Gutierrez leads. Continued legislative vehicles and federal resources will be vital to ensuring Long COVID patients obtain the proper long-term care needed. Congressional action will provide a tremendous boost that will help our patients/your constituents rebound from these post-viral complications.

Once again, thank you for inviting Dr. Verduzco-Gutierrez to provide testimony to your Subcommittee hearing. Please do not hesitate to call me if I can assist you, your staff, and the Subcommittee.

Sincerely,

William L. Henrich, M.D., M.A.C.P.

WLH/lca

7703 FLOYD CURL DRIVE • MAIL CODE 7834 • SAN ANTONIO, TX • 78229-3900
210-567-2050 • UTHSCSA.EDU

UT Health San Antonio
The University of Texas Health Science Center at San Antonio

Joe R. & Teresa Lozano Long School of Medicine

July 28, 2022

Re: July 19, 2022, Hearing: "Understanding and Addressing Long COVID and Its Consequences"

Chairman Clyburn, Ranking Member Scalise, and Members of the Select Subcommittee on the Coronavirus Crisis,

The following is my **response to Representative Foster (IL-11):**

Q1. Please elaborate on what research has shown thus far regarding who is likely to develop Long COVID and why—and what knowledge gaps remain.

Data from the CDC as well as from initial research has shown that people who have experienced more severe COVID-19 illness, especially if hospitalized or were in the ICU will have more risk for post-COVID conditions[1]. Other risk factors are people who had underlying health conditions (asthma, obesity, type 2 diabetes mellitus) and those who are unvaccinated. There has been additional research illustrating number of initial symptoms (5 or more[2]) or certain symptoms during primary infection (hair loss, headache, sore throat)[3]. Finally, SARS-CoV-2 viral load is another risk factor and immune response[4].

Knowledge gaps remain in who will develop Long COVID. Previously mentioned studies sample only hundreds of patients, not the millions living with Long COVID. Furthermore, the studies are often on hospitalized patients and not on the more common patient who had mild COVID-19. We need also to figure out which subgroup of COVID survivors will develop myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) subtype as they are significantly more disabled.

---

[1] https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html
[2] Cervia C, Zurbuchen Y, Taeschler P, et al. Immunoglobulin signature predicts risk of post-acute COVID-19 syndrome. *Nat Commun*. 2022;13(1):446. Published 2022 Jan 25. doi:10.1038/s41467-021-27797-1
[3] Wu Q, Ailshire JA, Crimmins EM. Long COVID and symptom trajectory in a representative sample of Americans in the first year of the pandemic. *Sci Rep*. 2022;12(1):11647. Published 2022 Jul 8. doi:10.1038/s41598-022-15727-0
[4] Su Y, Yuan D, Chen DG, et al. Multiple early factors anticipate post-acute COVID-19 sequelae. *Cell*. 2022;185(5):881-895.e20. doi:10.1016/j.cell.2022.01.014

Q2. Please explain why accelerating research into Long COVID is important and what more can be done to ensure we can get the answers needed to help patients as quickly as possible.

As you are aware, significant long-term disability has now been seen in a growing population of patients who have survived COVID-19, but people have been suffering with chronic post-viral conditions for decades. Enhanced capacity is necessary for health systems to address the needs of individuals with complex and chronic conditions overall, especially inclusive of Long COVID. Overall, 1 in 13 adults in the US have Long COVID symptoms[5]. Long COVID has been described as a "mass disabling event" that is economically impacting the United States, however, research is not keeping up with the pace of Long COVID diagnoses. Amazingly, research into mRNA vaccine technology and anti-viral treatments in the hospital setting happened at record pace, but the research into its devastating consequences that people must live with long-term has not. A recent independent review published by the Rockefeller Foundation found that the NIH had funded just 8 of 200 Long COVID trials listed in the US ClinicalTrials.gov database as of February[6].

Admittedly, the exact mechanisms and pathophysiology need to be worked out, but there is already enough research to start clinical trials now. For example, there is research showing there are viral remnants in people's bodies with Long COVID. And we have antiviral pills now such as Paxlovid. This trial should be started expeditiously. These trials can be done in Multi-Disciplinary Long COVID Clinics. The American Academy of Physical Medicine and Rehabilitation (AAPM&R) has a PASC Collaborative of 40+ clinics treating patients across the country[7]. New policies would further enhance new and existing clinics to bolster successful clinical trials for people with Long COVID to help patients optimize their health and function in the near term.

---

[5]CDC, National Center for Health Statistics. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm#:~:text=NCHS%20Home-,Nearly%20One%20in%20Five%20American%20Adults%20Who%20Have%20Had,19%20Still%20Have%20%E2%80%9CLong%20COVID%E2%80%9D&text=New%20data%20from%20the%20Household,symptoms%20of%20%E2%80%9Clong%20COVID.%E2%80%9D

[6] Getting and Sustaining the Next Normal. A Roadmap for Living with COVID. https://www.rockefellerfoundation.org/wp-content/uploads/2022/03/Getting-to-and-Sustaining-the-Next-Normal-A-Roadmap-for-Living-with-Covid-Report-Final.pdf

[7] https://www.aapmr.org/members-publications/covid-19/multidisciplinary-quality-improvement-initiative

Historically, post-viral conditions and ME/CFS have been underfunded. There is a vast need for research on PASC to be conducted rapidly and translated to providers. This population is suffering, and their symptoms and disease-state need to be more easily recognized and addressed, and cannot be dismissed for not fitting within existing medical paradigms.

Q3. Based on your clinical expertise, please explain how an intranasal vaccine might be effective in preventing both coronavirus infections and Long COVID, and the extent to which we should pursue additional research into this delivery method.

It is not my medical expertise in delivery of vaccines, but I did communicate with our own local expert Guangming Zhong, MD, PhD who is Professor and Dielmann Endowed Chair of Genetic and Environmental Risk, Department of Microbiology, Immunology & Molecular Genetics at UT Health San Antonio. His response is:

The major difference between intranasally delivered COVID vaccine and intramuscularly injected COVID vaccines is that the former can induce strong (or stronger) mucosal immunity in the airway (and also systemic immunity) to prevent SARS-CoV-2 virus infection locally while the latter mainly induces systemic immunity that is insufficient for blocking local infection in the airway by SARS-CoV-2 but enough for blocking SARS-CoV-2 spreading (hence preventing diseases).

Theoretically, both routes can induce both local and systemic immunity, but the intranasal route induces stronger local immunity (strong enough for blocking local infection) while the local immunity in the airway induced by intramuscular route is not strong enough for blocking local infection.

Since local infection or airway infection with SARS-CoV-2 may contribute to Long COVID, medically, you can say that intranasal COVID vaccine can prevent Long COVID.

Another potential benefit of the intranasal vaccine is that it may prevent SARS-CoV-2 from accumulating new mutations since the virus does not have much chance to replicate in our airway and the vaccine significantly limits the spreading between individuals.

Mechanistically, intranasal vaccine may induce more memory B cells that secrete neutralizing SIgA antibodies in the airway mucosal tissues. These mucosal IgAs may effectively prevent the virus from amplifying itself locally.

Besides airway B cell-secreted IgA antibodies, intranasal vaccine may induce more tissue-resident memory T cells (or Trms) in the airway that can rapidly respond to SARS-CoV-2 virus infection by releasing cytokines. These local cytokines can quickly enhance the resistance of all airway cells to coronavirus infection. On the contrary, intramuscular immunization may not be efficient in inducing Trms in the airway mucosal tissue.

In summary, intranasal vaccine-induced IgA antibodies may neutralize the viruses before the viruses enter our airway cells while the vaccine-induced Trms may quickly ramp up the airway cell resistance to corona viral invasion. The double breaks formed by B and T cells may effectively prevent coronavirus infection in the airway.