Immunologist Dr. Anthony Leonardi speaks on Long COVID and the dangers posed by SARS-CoV-2

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This is Part 2 of a two-part interview. Part 1 can be read here.

Dr. Anthony Leonardi, PhD, a T-cell immunologist who studied at Johns Hopkins University, co-authored an important scientific report published in October in the journal *Pathogens.* Dr. Deepti Gurdasani, an epidemiologist and outspoken advocate for Zero COVID, was also one of the co-authors.

Among other topics, this report notes the complexity of, and long-term complication associated with Long COVID. The authors wrote, "Although COVID-19 has been described as a respiratory syndrome, evidence supports the involvement of multiple organ systems, with fibrosis, and inflammation in the lung, heart, kidneys, central nervous system (CNS), liver, adrenal glands, bone marrow, lymph nodes, and gastrointestinal tract. SARS-CoV-2 infection has also been associated with serious thrombotic complications, including strokes, pulmonary embolism, and cardiac injury."

Dr. Leonardi, who has opposed unsafe school reopening, recently spoke at the World Health Network Summit outlining the dangers posed to children. In response to the dangers posed by in-class instruction, he responded, "There's publication that lists a lowered productive lifespan in kids, and it's more of an attenuation in kids than adults. So, it's a bad idea. We're setting kids up to have chronic illness."

Last week, Dr. Leonardi accepted our invitation to speak on these issues.

[*Note to reader: Hyperlinks have been added to specific issues throughout the interview. Please refer to these as additional resources. Additionally, explanatory notes have been inserted for some of the technical terms employed during the discussion.*]

BM: Having established the complexity of SARS-CoV-2 infection and our immune system, during the recent World Health Network Summit hosted by Professor Yaneer Bar-Yam, you provided a somewhat more comprehensive definition of Long COVID. So how would you define Long COVID and what is the mechanism behind this disease?

AL: I think Long COVID is going to be as diverse a problem as cancer. It's hard to define, because, like cancers, they present as a very different spectrum of diseases depending on where they are and where they came from. Long COVID, I would say, for an easy definition, is a persistent sequela of SARS-COV-2 infection.

BM: And what are those?

AL: It can be anything. We can say it's fibrosis in the lungs or fibrosis in the heart or kidneys or brain fog or there's a brain hypometabolism phenotype. For instance, there is hypometabolism in the brain in depression and people who've been infected with SARS-CoV-2 have a brain hypometabolism that persists for a while. I don't know for how long, but they imaged it. It's just a complete multi-system problem because of how ubiquitous ACE2 is.

[*Hypometabolism is decreased function, in the brain or other organ. ACE2 or angiotensin-converting enzyme is a surface receptor on respiratory cells which is used by the SARS-CoV-2 virus to enter the cells.*]

And not only that, but the immune system also goes haywire.

Now, the immune system is responsible for going into all the tissues in the body, except for a few immune-privileged sites. But SARS-CoV-2 doesn't respect the immune-privileged site whatsoever. It brings T-cells into the brain. So, we can see the impact of the infection across every physiological system. Because if it distorts the immune system and the immune system is responsible for patrolling the body everywhere, then there are going to be problems everywhere.

BM: You mentioned neurodegenerative concerns raised from SARS-CoV-2 infections. Maybe you can discuss these concerns, especially as they pertain to young children and young adults.

AL: The neurodegeneration … there's one that I'm quite worried about. It's a study that is still in pre-print where rhesus macaques ended up having Lewy bodies after being infected with the virus.

BM: What are Lewy bodies? I don't think most people have ever heard that term before, so it would be good to maybe explain what these are.

AL: They're like disaggregates. They're like clumps of alpha-synuclein. And I think they're arranged in a certain way. And there's a certain histopathological means of diagnosing Lewy bodies. From what I understand, it's clumps of basically misfolded alpha-synuclein.

BM: Abnormal proteins.

[*Lewy bodies are abnormal aggregations of misfolded Alpha-synuclein proteins (proteins common to the brains of most mammals) that accumulate in nerve cells in the brain. They can lead to dementia and Parkinson's-like disease. Alpha-synuclein proteins regulate neurons' ability to communicate at their synapses. They also aid in DNA repair processes.*]

AL: Yes, clumps of abnormal proteins. And the problem with this is the disease process is irreversible. It begets an irreversible neurodegenerative process.

BM: And what happened in these macaques monkeys who develop these Lewy bodies after SARS-CoV-2 infection?

AL: They didn't do follow-up of them, but one could imagine that once you kick off this process, you go down a course of neurological degeneration. And that's what the human experiences, at least, they know that Lewy bodies will end up proceeding Lewy body dementia and Parkinson's disease.

They didn't follow up in the rhesus macaques. They just sacrificed them and did pathology. We don't know how they would have ended up, but it happened in every monkey and the monkeys had very mild symptomatic illness. It should be said that monkeys are much better at recapitulating diseases than mice are, in terms of what the human experiences is.

So, one big fear is that a lot of people will end up with a dementia or Lewy body dementia …

BM: At a much younger age I'm assuming?

AL: Yes. The alpha-synuclein protein functions as a prion because it causes the aggregates, the accumulation, to keep happening and propagate. And it's not reversible. [A *prion is a type of protein that can trigger normal proteins in the brain to fold abnormally. It has a domino effect causing other proteins to assume the misfolded shape.*]

BM: Have there been autopsies done on humans who had died from COVID to look for such neurodegenerative changes?

AL: There have been such studies, but they only show signatures of acute inflammation. What there has not been is autopsies of people who have died of other causes after recovering from SARS-CoV-2 for some long period.

BM: But we have imaging studies of people with infections … there was a study that looked at brain images before the pandemic and then during it comparing changes between people with and without infection.

AL: You are referring to the UK Biobank study. They saw reductions in size and in the hippocampus and in the gustatory regions. They also saw reductions in the area responsible for memory. And I also think the areas that would imply Parkinson's.

BM: One of the questions that people have frequently asked is, if you have Long COVID, does taking the vaccine help fight the process? And the follow-up question to that would be if you've been vaccinated and you develop a breakthrough infection, can you still develop Long COVID?

AL: There is an excellent immunologist-virologist at Yale, Professor Akiko Iwasaki. She has a theory that would possibly describe some Long COVID experiences where there is some persistent virus somewhere in the body that is being addressed by the vaccination.

She had a recent preprint study where she showed that there is replicating SARS-CoV-2 virus in macrophages and monocytes [*cellular components of the immune system*]. So, there could be a reservoir somewhere in some people's bodies.

BM: In such patients who have a reservoir of viruses replicating at low levels in their macrophages, would they have a positive PCR test if they were swabbed? Or would it be negative?

AL: If the PCR was done on their macrophage, then it would be positive. Because if you take a saliva PCR test or a swab, it's not going to be able to detect a chronic low-level infection. However, we have to say, this is speculation that there is persistent SARS-CoV-2. It's preliminary data. We don't know yet, but it could be there persisting in monocytes and macrophages.

Vaccinating these people would provide a super physiological T-cell and B-cell response and boost antibody titers that will likely address persistent reservoirs. And, so, some people do see an improvement in their symptoms after vaccination. It's very recommended to get vaccinated, even if you've had COVID once and you have Long COVID, because it could be that there is some persistent virus there indefinitely. Recall, COVID infection means that you don't make good immunological memory or have a good number of antibodies. The vaccine is a way of programming your body to have a good T-cell and B-cell response and have good circulating antibodies.

SARS-CoV-2 distorts your immune memory formation. It messes up cell development and it messes up T-cells. Giving yourself a vaccination will give you a level of immunity, especially if you've had the virus once before.

BM: Have you heard of patients developing Long COVID after a breakthrough?

AL: In a recent study in preprint form showed that it's basically the same rate, whether or not you've been vaccinated. This study showed that if you had a clinical reinfection with SARS-CoV-2 that you are at the same risk of developing Long COVID as someone unvaccinated. Meaning that with breakthrough infection, the virus can re-establish itself in the body.

BM: Why aren't the vaccines able to achieve sterilizing (near-permanent) immunity? We may have touched on this earlier. What are the qualities of this virus that that makes it difficult to create sterilizing vaccines?

AL: It's the same answer about mucosal immunity. If we had a mucosal immune response, like the IgA we were talking about, it would be sterilizing immunity. It isn't that there is something wrong with our vaccines per se. It's just that immunity wanes to the extent to leave our mucosal surfaces exposed.

I imagine that there are a few candidates in the pipeline meaning we would eventually see the development of a mucosal vaccine against SARS-CoV-2. There isn't anything preventing us really from developing an inhaled vaccine.

BM: I assume people who get infected develop mucosal immunity?

AL: Correct. But unfortunately, as we are seeing, it doesn't persist greatly. It's just the way our physiology is set up. Remember that the SARS-CoV-2 virus distorts B-cell formation. It will harm the cells that make antibodies. It'll distort their function a bit. You can still make antibodies, but the virus works against it. And those mucosal responses will also wane. Inevitably, we will need a booster vaccine or an inhaled vaccine.

BM: I've recently read that there is a correlation between non-communicable diseases and infections with viruses or pathogens. And, for instance, the kidney and lung damage, and other organ system injuries we see with SARS-CoV-2, to what extent are these linked? To what extent do you think, and this is probably a hypothetical question, but diseases like high blood pressure and diabetes, to what extent are previous infections linked to non-communicable diseases?

AL: It depends on the chronic illness. For things like diabetes and hypertension, et cetera, we must lay blame on the Western diet. But they are starting to refine their thinking on neurodegenerative illnesses. They are starting to point the finger at viruses now—many of them.

But here's the thing. Viruses can kick off an inflammation process that can … they say genetics loads the gun and environment pulls the trigger. Viruses are like the environmental factor to your genetics that create disease.

BM: Your comment raised another question for me. Can you possibly expand on previous pandemics and the long-term sequelae that they have caused to human populations? I read that victim of the Russian flu in the 1800s had symptoms analogous to Long COVID.

AL: I will send you a reference that I think will provide a good review on this topic.

[*Encephalitis lethargica was a neurological syndrome that appeared in the winter of 1916, during World War I, and continued into the 1930s. The disease, also known as sleeping sickness,was first described by an Austrian neurologist named Dr. Constantin Von Economo. It appeared to have affected more than a million people, directly leading to the death of 500,000. When researchers began to piece the history of such large-scale neurological disorders, they realized many such outbreaks of this disease had occurred across Europe as far back as 1580. Current theory believe it is a "post-infectious autoimmune" disorder. Most of these victims never completely recovered. They develop brain damage similar to Parkinson's disease.*]

BM: You recently wrote a letter to California school boards which was very powerful. You raised some very important issues. What are your concerns about COVID infections in children?

AL: Well, it does really worry me. We are just assuming that infection won't have long-term consequences in people, and especially in children. And there's almost a systematic exposure of people and children to the

virus before they're vaccinated. I know from what I've read in the studies that have come out that some people are going to definitely be genetically susceptible to very bad outcomes and death. And I think it's not right for kids to be just exposed to this without a fighting chance, without vaccination.

It's very disturbing when I think that we're running the risk for everybody to get something like any Lewy body disease or neurodegeneration and we're systematically exposing generations to this. I was trying to help. My hope is that we take it seriously and we give people protection. If these children have genetic susceptibility or health concerns, or if their family has health concerns, they're given remote options. I was thinking if I were in their position, would I want to be consigned to definite exposure to SARS-CoV-2? No, I wouldn't! And I would want to be protected, with acknowledging that the virus is airborne. So, better ventilation in classrooms, mask wearing and vaccination of children.

There's a terrible assumption that kids are okay with SARS-CoV-2 infection when there's data coming out that they have lost out on a greater number of healthy years than adults. Kids have better immunological response to vaccination than adults as well. And kids are more likely to be infected than adults and kids are more likely to be reinfected than adults.

We're messing up! We're doing this completely wrong only because probably, my assumption is, kids have less agency. Kids don't have the agency adults do. That's fine that they are not like grandma or grandpa when it comes to being infected, it isn't as dangerous. But it's unjust to not protect them and vaccinate them. Infection in children should not be written off.

A lot of people are saying it's endemic and everyone is going to get it. So, they relinquish responsibility of controlling its spread and making these areas safe and just consigning kids to definite inflammation and infection where they're less likely to make immune-competent memory.

BM: In bringing the interview to a close, the *World Socialist Web Site* is calling for global elimination of COVID-19, to get rid of the disease out of all human populations. Is this something you would support? Why would it be important?

AL: Unfortunately, that idea of elimination and how to achieve it is beyond my area of expertise. But I strongly feel that humans should not accept infection just because it's "endemic." We should use our technology to prevent infections, to stop this systematic infection of the youth. And I guarantee you that in 20 years kids in classrooms are not going to be infected with the SARS-CoV-2. We're not going to just allow that to happen. My hope is that we do go for suppression and elimination. And I'm pretty certain with our emerging technologies we're going to be able to achieve this.

The problem is that interest groups just want us to accept where we are at now with mediocre technologies other than just our vaccinations. Right now, we're in a very early phase and the rhetoric is to just accept the level of disease right now when in 10 years or so, we're going to have fantastic technology and all those people harmed and maimed will be for naught.

It's a good idea to suppress the virus as much as you can and prevent infections because in the future our technology is going to be able to deal with it. As far as eradication and elimination strategies go, I'm uncertain. It's beyond my field, but I can tell you from an immunological standpoint the infection is not going to get better for us. It's not going to become a cold virus. It's not going to become like, something benign or light, so I'm, I am in favor of preventing as much, infection as possible.

BM: Dr. Leonardi, thank you so much for your time and the incredible work you have done. I hope we will have a chance to speak again.

AL: Thank you.

Concluded

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