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

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

Dr. Anthony Leonardi, Ph.D., 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.

They summarized the uncertainties surrounding the long-term implications of living with COVID-19, highlighting the dangers associated with viral evolution and the immune dysregulation that SARS-CoV-2 infections can cause in the human body. They provide insight into the concerns being raised by reinfection and the concept of herd immunity threshold. Additionally, they note the complexity of and long-term complications associated with Long COVID.

They 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 reopenings, 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 readers: 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.

Benjamin Mateus (BM): Good afternoon, Dr. Leonardi. Thank you for speaking with us at the *World Socialist Web Site (*WSWS*).*

Anthony Leonardi (AL): Hello. It is actually evening for me. I'm currently in Europe.

BM: Can you briefly tell us who you are and what you do? You have also been very active on social media. How is that professionally?

AL: My name is Anthony Leonardi. I'm currently a student doing my master's in public health. I previously did research in T-cell immunity and T-cell memory. I have a Ph.D. in T-cell memory.

[*T-cells are specialized white blood cells which play a central role in immune response. T-cells include CD8+ cells, also known as "killer" cells, which destroy pathogens invading the body. The process by which T-cells identify pathogens and direct CD8+ cells against them is known as cellular immunity. Memory T-cells are part of the immune system's adaptive response to pathogens. Once naïve CD8+ T-cells encounter a particular antigen, such as the SARS-CoV-2 virus, they undergo molecular changes being placed in an activated state and developing along different subpopulations, one being the development of memory against future infections with the same pathogen. In general, memory CD8+ T-cells are long lived and respond to repeat infections through an enhanced protective response.*]

That's essentially my background. I'm currently on break. I was a medical student in the UK, and I put that on hold because it's not very safe to be in London right now. I figured I'd stay in Spain and Portugal for a while until I fly back to the US, probably after I get my third dose.

With regards to the social media … I have people that are constantly trying to cancel me that are constantly just emailing up my affiliated institutions.

BM: Why?

AL: They're very angry because they want to have us admit that T-cell immunity is going to confer "natural immunity" and "natural protection." You might have seen Dr. Monica Gandhi constantly refer to this. And then a lot of Republicans are also going on about T-cell immunity and stuff.

My research was in T-cell memory. I found how to control T-cell memory when I worked at the NIH (National Institutes of Health) and in a T-cell immunotherapy lab. I knew back in May [2020] when I saw the first publication in *The Lancet* about this virus. I was in London at the time, and there was a virologist and an oncologist that I knew. Unfortunately, he's very conservative. He's part of the UKIP (UK Independence Party) in the UK. I spoke with him about my concerns about this virus. The immune system doesn't look like it's doing very well at all. I basically understood that the vaccines would be better than infection in conferring immunity.

And obviously that went against what all the corporate interests wanted, like the AIER (American Institute for Economic Research). They want the economy completely open, and they want consumption to be full. They're trying to convince everybody that you didn't necessarily need the vaccines for safety and that immunity will be long lived, but it just wasn't the case.

BM: One of the things I think that we lack in our understanding is how immunity to the virus really works and the interplay between the virus and our immune system. I think that is a very critical piece of the puzzle that you bring to this discussion. If you can briefly address this and how you became involved in COVID-19 advocacy?

AL: To answer the second part of your question on COVID-19 advocacy, I think it's an exciting area of study because it goes directly into what we do. I got into COVID-19 just by being concerned from an immunological standpoint, because I saw the first publication out of *The*

Lancet in January 2020, where the patients demonstrated profound lymphopenia [*a reduced level of the white blood cells that help fight infections*]. That was very significant, and the people were very ill and it looked to me like there was some sort of a sepsis [*infection in blood and tissue that can lead to organ failure, shock and even death*] going on and these usually happen in super antigenic infections [*super antigens, molecules that trigger an immune response, resulting in excessive activation of the immune system as seen with our body's response to COVID-19*]. Reading the paper set off alarm bells in my mind. I thought I knew what I was looking at, from an immunity standpoint that our natural immunity would be harmed and distorted by this pathogen.

It was only out of scientific interest and obligation that I went towards COVID-19. As an immunologist, I also knew the ramifications of it. I knew that we weren't going to have any durable or competent memory from [SARS-CoV-2] infection. So, I drafted letters to disseminate that information providing my opinion on these findings. I also made statements regarding immunity wherever I could, in public.

BM: What does durable competent immunity mean, and what does the term superantigen mean? It would help to define these for our readers.

AL: I would define durable competent immunity as immunity that prevents you from getting sick from a virus the second time you catch it. It's like your one-off infections, where you get it once and then you're good for the rest of the time. For instance, things that don't normally re-infect you, like the chicken pox. It may remain latent inside you, but your immune memory controls it. You don't get sick again unless you get a bout of shingles. That would be a durable competent immunity.

An incompetent immunity, or not durable immunity, is the kind of immunity you usually get from a coronavirus infection, such as the common cold. You can get reinfected, and it'll be as bad as the other times. And even for older people, when older people get reinfected with influenza virus types, they might have it more severely. Just because they've had the vaccine or have been infected in the past, the influenza virus mutates a bit, and that's possibly why the reinfections can be bad, but it could also just be the waning of immunity.

Cellular immunity [*Immune response that does not involve antibodies. Instead, various types of white blood cells, including previously sensitized T-cells, are recruited in response to an infection. Cellular immunity is very effective against cells infected with viruses, intracellular bacteria, as well as cancer cells. It also mediates transplant rejection.*], in some cases, usually it can react quick enough to prevent disease, but for some conditions it's not quick enough to prevent illness again.

Notably, when Delta came along, which is very fast at infecting, it fuses with cells so quickly and replicates so quickly and transmits so quickly, it outpaces our natural cellular immunity because our cellular immunity takes time to ramp up.

What happens is you have an infection, and you stimulate some T-cells that recognize the infection and B-cells get stimulated and they proliferate, and they control the infection. And it takes some time for these cells to grow in numbers and phenotype to address the infection.

Then after the infection is addressed, the numbers dwindle, you get what's called memory formation. And the numbers of the cells that dealt with the infection go down, and they go in like a quiescent state. And when the pathogen comes around again, those cells will recognize the pathogen and then grow in numbers.

The second time around all this happens faster because your body has made cellular memory. But the problem with some viruses though, like the Delta strain of the coronavirus, is that it can outpace our cellular immunity. So, that's what I think is happening with SARS-CoV-2. So, our cellular immunity might be durable enough to let's say prevent some severe illness and in healthy immunocompetent people. But for mild and moderate illness everybody might be rolling the dice if they don't have antibodies that can address it.

Basically, what we're going to need is boosting, to make sure antibody levels are high enough to deal with the pathogen if we encounter it. And then there's the issue also of a mucosal protection, which is a hot topic right now, and the way these vaccines are made…

[*Mucosal immunology is the study of immune responses that occur at the mucous membranes of the respiratory system, as well as at the gastrointestinal and urogenital tracts. In a healthy organism, the mucosal immune system protects against various pathogens, including viruses, while maintaining tolerance towards beneficial microbes and benign substances in the environment. Because of its interface with the environment, the mucosal immune system, mediated by the IgA antibodies, is the largest component in the entire immune system. The current COVID-19 vaccines function to provide systemic immunity, after the virus has passed mucosal defenses in the nose, mouth, eyes and upper airways. Clinical research is currently underway to develop mucosal vaccines, which could have the capacity to prevent infections from becoming established in the first place.*]

There is an immunologist over at MIT that is looking at mucosal immunity as it's conferred from the mRNA vaccines, such as Pfizer and Moderna. She's seen that there's this sort of hybrid antibody that's produced briefly after vaccination that gives a sort of mucosal protection.

This study is still in pre-print form but looks very promising. That will give us clues how it confers better mucosal immunity, meaning a lot of people are now talking about intra-nasal vaccination or mucosal vaccination, and that sort of vaccination may bring immune memory like B-cell and T-cell memory into those mucosal surfaces to deal with SARS-CoV-2 reinfection more quickly. But as it stands now, we're going to need boosters.

There's going to be a waning protection, certainly for mild and moderate illness and possibly even severe illness. So, people are going to need vaccinations, at least yearly, I think.

BM: That raises two questions. I think you've answered partly one and that is that most likely we will need annual COVID-19 vaccinations. First, what's the difference between mucosal immunity and the systemic immunity we get from an intramuscular injection, and why is it important? And, perhaps after answering this question it will lead to the issue, what would happen if this virus became endemic? Some are claiming that SARS-CoV-2 will become less virulent, akin to a "common cold." Or will the virus continue to devastate populations like we are seeing now?

AL: The predominant difference between mucosal immunities and the immunity conferred by the current vaccines is the antibodies that you're generating, as far as the functional difference that we want to see.

We want to see IgA, which is a mucosal antibody, an antibody that's on our mucosal surfaces that's going to be able to neutralize SARS-CoV-2 quickly when it's on our mucosal surfaces to prevent it from establishing itself. Ultimately, that is a very good goal for us to get, because we'd be able to address the virus more quickly.

The immunity that we get in terms of antibodies from our intramuscular vaccination is from IgG. And that's a type of systemic immunity that circulates through our blood. Sometimes it can cross just as Michal Tal, Ph.D., has shown at MIT (Massachusetts Institute of Technology). She's shown that there can be this hybrid that will cross into the saliva and coat the mucosal surfaces to confer some protection.

But the goal that we want is a good amount of IgA, a good amount of mucosal neutralization, or at the very least a mucosal or resident mucosal immune memory cells that can very quickly respond, but that's not, they're not going to respond as quickly as an antibody.

And then your second question: What happens if we allow SARS-CoV-2 to become endemic, what's going to happen to us and what's going to happen to the virus? So, if we allow it to become endemic—and some would argue that it is already endemic—this does not mean that it is going to attenuate, not whatsoever.

There was a recent study that came out, I think it was 20,000 years ago that that an ancient coronavirus etched its imprint into our DNA. And what I mean by that is it selected traits in us that we're better at surviving the infection. So, basically it selected us, it exerted a selection pressure on us. [*The study was published in the journal* Current Biology *in June 2021. The ancient viral epidemic is believed to have ravaged East Asia 25,000 years ago, lasting for almost 20,000 years. The scientists found evidence that there were genetic mutations in the human genome due to the interaction with the ancient coronavirus.*]

SARS-CoV-2 is a very virulent pathogen, and it's gotten worse since its introduction. It's mutated to be more severe and aggressive, such as Delta. The transmissibility that Delta has come with has shown it to have grown more transmissible and more severe. It is certainly not true that more transmissible versions of SARS-CoV-2 will be more benign. What we are seeing is more aggressive, more transmissible versions which are creating more severe illness. And the virus is still adapting to our physiology. It's doing it at a fantastic rate because the number of virions [*infective form of the virus outside the host cell*] that it produces when it is inside a person is massive, and it's so transmissible. What we're going to see is that it will continue to work against our immune systems, meaning become more immune evasive. It's going to become more chronic as an infection.

A big problem with SARS-CoV-2 two is that in its transmissibility the furin cleavage site gives it a huge advantage, allowing it to fuse with cells and be very infectious in our tissues once it's in our tissues. The area spanning outward near the furin cleavage site has a superantigen site that really hits our immune system hard. Okay. Right now, our body of literature is around the superantigen and MIS-C [*Multisystem Inflammatory Syndrome in Children is a disease process associated with COVID-19 where it is associated with multi-organ system failure and shock, having proved fatal in approximately 2 percent of cases.*]

MIS-C is causing kids to go into the hospital because they're having very strong immune reactions from the superantigen that stimulates T-cells. So that super antigenic stimulation, it's still happening in adults as well. And it's, I would posit, responsible for the profound lymphopenia [*low white blood cell levels*] that's happening in adults, and this is being brought about, I would imagine, from the CD8+ T-cell hyperactivity.

SARS-CoV-2 also distorts B-cell memory formation, the cells that produce your antibodies. It uses a member of the TNF family [*Tumor Necrosis Factor superfamily are special signaling proteins that regulate the diverse functions of immune response and inflammation*], but it makes it so there's a lot of extra-follicular development and subpar B-cell response.

Much of the B-cell response is also an auto-antibody response. And I'm not certain as to the determinant that is causing all this auto-antibody B-cell formation, but from the T-cell side, I know that it's causing auto immunity from what's called a hyperactivated T-cell, which has never been seen before.

These are T-cells that were once T regulatory cells expressing Foxp3. For some reason, SARS-CoV-2—and somebody told me that it was mediated by IL-6—but somehow SARS-CoV-2 was causing the T regulatory cells that are responsible for preventing autoimmunity to become auto-immune licensers to start licensing autoimmunity.

[*T-regulatory cells are a specialized subpopulation of T-cells that act to suppress the immune response. They play a critical role in preventing autoimmunity. Foxp3, also known as scurfin, is a protein that functions as a master regulator in the development and function of the T regulatory cells. Dysfunctions in the gene for foxp3 lead to immune system dysregulation.*]

For this virus to become endemic, we would see a lot of maimed people with autoimmunity. And with immune memory, that is not able to fully prevent mild and moderate infections again. In my opinion, the damage could be cumulative. The virus can also cause vascular injury like what we see with feline coronavirus in a disease called *feline infectious peritonitis,* which is fatal for cats where it causes very small capillaries to become what's called "string vessels" and get blocked. Additionally, it can potentially "kill off" parts of the vascular system, especially in the brain. [*String vessels are thin connective tissue strands that were remnants of capillaries that cannot carry blood flow.*]

For this thing to become endemic also means these disease-causing mechanisms are not going away. We have seen decreases in life expectancy versus our modern medicine. So, what we can mitigate with modern medicine will be to oppose these mechanisms. This will be a tremendous burden on health care globally.

BM: Just to be clear, If I were to try to summarize what you just said, when we talk about the immune-evading capability of SARS-CoV-2, we're not just talking about cloaking itself from the antibodies. We're also saying that the virus is causing severe immune dysregulation, meaning the ability for B-cells and T-cells to communicate and provide an appropriate response is being severely impacted. And, additionally, the dysregulation is causing T-cells that don't routinely attack your own body to now create the potential for an autoimmune disorder to develop in people who have been infected by this virus.

AL: We can't say that it's a clinical diagnosis of an autoimmune disorder because that would be a clinical diagnosis, of course. But what it's doing is turning the cells responsible for quelling autoimmunity into causing autoimmunity, and that's the T regulatory cells. And then as far as the B-cells go, it's stimulating B-cells to create auto antibodies.

BM: And these pose significant potential health hazards for the future. Is that correct?

AL: Absolutely. I imagine that's why we see so much vasculitis or vascular inflammation.

To be continued