

Ruth Adewuya, MD (host):

Hello. You are listening to Stanford Medcast, Stanford CME's podcast where we bring you insights from the world's leading physicians and scientists. If you're new here, consider subscribing to listen to more free episodes coming your way. I am your host, Dr. Ruth Adewuya. This episode is part of the COVID-19 Mini-series, and today we will be discussing long COVID.

Ruth Adewuya, MD (host):

To help explain what long COVID is, I am joined by Drs. Hector Bonilla and Linda Geng, who are the co-directors of the Post-Acute COVID-19 Syndrome Clinic at Stanford Healthcare, which is a multidisciplinary group of physicians that are tackling this challenging public health problem and advancing the care of patients with persistent symptoms after COVID-19 infection.

Ruth Adewuya, MD (host):

In 2017, Dr. Bonilla joined the Stanford University Myalgic Encephalomyelitis or Chronic Fatigue Syndrome Clinic. His early career as an infectious disease physician focused on the clinical management of HIV-AIDS and HCV. He's currently a clinical associate professor of medicine and infectious diseases. He is a strong patient advocate and believes in the care in which physicians communicate and coordinate efforts to deliver the best medical outcomes for patients.

Ruth Adewuya, MD (host):

Dr. Linda Geng is a clinical assistant professor in the Division of Primary Care and Population Health at Stanford University. She is an internist focusing on puzzling conditions and director of a team-based diagnostic second opinion clinic called Consultative Medicine that evaluates patients with rare, unusual, and complex illnesses. She's also a co-investigator on a long-term follow-up research study looking at post-COVID health and immune response.

Ruth Adewuya, MD (host):

Thank you both for joining me today.

Linda Geng, MD, PhD (guest speaker):

Thank you for having us.

Ruth Adewuya, MD (host):

For some people, the effects of COVID-19 can last well beyond the immediate illness. Patients and clinicians across the United States are reporting long-term effects of COVID, now referred to as long COVID. Can you define long COVID for us or post-COVID syndrome?

Hector Bonilla, MD (guest speaker):

The definition of long COVID has evolved over time. There are two definitions. One definition that the CDC proposed was people who have symptoms after 30 days of the initial infection. The UK have been very active in trying to collect the data, and they came out with definitions of more than 12 weeks of the symptoms. This kind of definitions, I think, was based on the initial evaluation, but now this has been more defined according to the symptoms.

Hector Bonilla, MD (guest speaker):

But it's important for this kind of definitions in the context of the viral infections. And the way we make a diagnosis on this kind of conditions is one, through PCR. The other thing that we use is the culture. We know if the patient has more than 13 days of symptoms, it's very unlikely we are able to make the germ to grow in the culture plate. Also, the PCR could be positive, and the PCR is detection of a piece of the virus. So the PCR positive doesn't mean you're going a positive virus.

Hector Bonilla, MD (guest speaker):

The other thing is the amount of the virus you get at the beginning. So one way we can infer the amount of virus is how quickly the PCR is detected. We call it cycles. The more cycles you need, the less likely you're going to have the virus. The less cycles you have, the most likely you have the virus.

Ruth Adewuya, MD (host):

Since the early months of the pandemic, the media has heavily covered long COVID, but as you mentioned, information emerges really quickly. Dr. Geng, can you briefly give our listeners some background on our current understanding of long COVID? What are its symptoms? How does it arise? And how common is it?

Linda Geng, MD, PhD (guest speaker):

Yes, Great questions. Thank you.

Linda Geng, MD, PhD (guest speaker):

So, in terms of the symptomatology, this is where it can get quite complex. I will say some of the most common and most commonly reported as well, probably in the media as well as by patients, include fatigue and breathlessness, but the list really goes on. I can give some examples, but it can be quite complex and a myriad of symptoms.

Linda Geng, MD, PhD (guest speaker):

Some patients do have a couple of isolated symptoms, but I would say many have a slew or a multisystem symptomatology that manifests. For example, respiratory symptoms, breathlessness, cough. There can be cardiovascular symptoms such as chest pain, palpitations. There can be what we call general or constitutional symptoms, fatigue, but it could be ongoing mild fevers, or just generalized aches and pains, sleep disturbances. There can be more specific neurological symptoms, cognitive impairment, more colloquially known as brain fog. It could be headaches as well as neuropathy type symptoms.

Linda Geng, MD, PhD (guest speaker):

So you can see that it really is a complex multi system, multi organ type of manifestations that occur. Now, in some patients, they may have a few of these, but in some others, they may have multiple, even 10 or a dozen of these different symptoms that all manifest in one individual.

Linda Geng, MD, PhD (guest speaker):

And why does this happen? In terms of the pathophysiology, it's unfortunately not very clear yet. This is an active area of research collectively across the world. We're trying to understand better the mechanisms driving persistent long COVID or post COVID syndrome.

Linda Geng, MD, PhD (guest speaker):

But given the complexity and the variability, my suspicion is there is likely multiple mechanisms that contribute to the pathogenesis. A couple of the leading ideas have been that there are persistent inflammatory damage and immune dysregulation in response to the initial infection. There have also been proposed ideas about virus specific effects and maybe even long term virus persistence. But I think this remains to be seen and further research is really imperative to elucidate the underlying mechanism.

Linda Geng, MD, PhD (guest speaker):

In terms of the third component to your question about the prevalence or how common long COVID is, the conservative estimates are around 10 to 20% of patients with acute COVID-19 infection will get long COVID. But there are studies reporting as high as in the 70s and 80s. And so there's some variability there, which we noted is that some of these may not be bothersome enough or severe enough to be brought to clinical attentions. It may be under diagnosing long COVID as well.

Linda Geng, MD, PhD (guest speaker):

There was a New England Journal of Medicine that was published in August. Their conservative estimate in that paper was that we expect more than 15 million cases of long COVID resulting from this pandemic.

Ruth Adewuya, MD (host):

Dr. Bonilla, with a condition like long COVID, for which so much is still unknown, misinformation can arise. What are some common misconceptions about long COVID that you hear from your patients or in the media?

Hector Bonilla, MD (guest speaker):

This is nothing new. When you're looking for the old coronavirus, like the SARS and the MERS, the one happened in Southeast Asia and the one happened in the Middle East. After those people recovered from those infections, they experienced similar symptoms like we describe now in patients with post-COVID syndrome.

Hector Bonilla, MD (guest speaker):

The other misconception for many physicians and the media, is many people will have only symptoms. There's no clear evidence of, okay, you have the liver enlarged, you have a heart murmur, like how we can pinpoint specific problems. Most of the time, we order labs in those patients and we don't find, in the routine labs, any findings. There's a kind of misconception about this is no real disease, it's something manufactured or created. But when the people experience those symptoms and symptoms that have been reported before in other post-viral infections, something maybe is going to bring us attention [inaudible 00:08:16] viral syndromes are real conditions.

Ruth Adewuya, MD (host):

Dr. Geng, take us back to when the pandemic first started. When in the pandemic did you first realize that COVID-19 would create an unprecedented medical need to address long term complications?

Linda Geng, MD, PhD (guest speaker):

Following up with what Dr. Bonilla was just mentioning about the known post-viral syndromes that already existed prior to COVID, I think it was something that some of us had expected in terms of looking

out for as well as considering that patients could have lingering symptoms after initial viral and coronavirus infections. However, I think in terms of following the pandemic, fairly early on, there were multiple research studies going on. And in following patients over time afterwards, it was clear that people still had lingering symptoms. And as you recall in about the spring and early in the pandemic in the United States, at least New York City had been the epicenter of the pandemic, by May of 2020, Mount Sinai, a leading academic institution, had already announced one of the first post-COVID centers, specifically dedicated to the care for patients with long-term complications from acute COVID infection, as an example, recognizing this medical need and emerging public health problem.

Linda Geng, MD, PhD (guest speaker):

Then as we roll around to early summer of 2020, a number of papers were getting published in academic journals describing the long-term symptoms and the complications from COVID acute infection. In addition, of course, to the lay press news articles that were accumulating over time.

Linda Geng, MD, PhD (guest speaker):

So I would say relatively early on, but evidence and media reports were accumulating and started to gain traction around the summertime as well.

Ruth Adewuya, MD (host):

Dr. Bonilla, you alluded to this earlier with your background in chronic fatigue syndrome. How have your academic and clinical backgrounds from prior to the pandemic informed your work in the PACS clinic?

Hector Bonilla, MD (guest speaker):

I started working in chronic fatigue, that is, more post-viral syndromes. This gave me the grounds to address this problem of post-COVID.

Hector Bonilla, MD (guest speaker):

During the pandemic, I participated very actively in different clinical trials in COVID patients, and that gave me even more experience, trying to understand what happened and see patients after, within the clinical trials. Still, people had lingering symptoms that interfere with their life.

Hector Bonilla, MD (guest speaker):

For me, working in chronic fatigue syndrome shows me what the people experience. And I see patients in the clinic. They come here with post-COVID. For me, I feel like it's the same patients I see in my routine, the post-viral syndrome. They come with the same kind of symptoms and they are very familiar to me. People present in many ways: cardiac symptoms, other people with autonomic dysfunctions. And I see people present the phenotype or chronic fatigue syndrome.

Linda Geng, MD, PhD (guest speaker):

I had a [inaudible 00:11:15] background, so I'm an internist. And I focus my work on puzzling conditions, and medical mysteries, and complex conditions. And a significant portion of these patients who come to our clinic for a diagnostic second opinion, or have puzzling symptoms that their providers are seeking second opinions for, have often had a triggering viral or some type of infectious illness at the beginning. And then they end up having these poorly-understood symptoms and unexplained complex and puzzling manifestations.

Linda Geng, MD, PhD (guest speaker):

And when the pandemic hit, and it was clear that post-COVID syndrome was becoming recognized, it was very reminiscent and it made me very passionate to say, this is something that we need to address, bring to the limelight, and hopefully also be able to shed light on other post-viral syndromes. And hence, the synergistic collaboration with Dr. Bonilla as well as our other faculty members here as well.

Ruth Adewuya, MD (host):

Dr. Bonilla, how do you process the tremendous amount of new medical information to inform your practice in a field where best practices and the evidence changes daily?

Hector Bonilla, MD (guest speaker):

This information comes, and sometimes we have no time to digest. Today we say something and tomorrow, the thing changes completely. So we have multiple sources of information. The internet is one of them. We receive emails for many groups. We have a meeting with all clinics in the country and we exchange some information. We look at the different kinds of publications, my colleagues. So all these multiple sources of information. And it helps me try to keep up to date, but sometimes it's very difficult.

Ruth Adewuya, MD (host):

I'm glad you mentioned how overwhelming it can be for a clinician. And so I imagine that for the patients, this could also be overwhelming and could be anxiety-inducing. How do you address the anxiety that long-COVID patients feel due to the uncertainty surrounding their condition?

Linda Geng, MD, PhD (guest speaker):

That's such a great question. As physicians, I think acknowledging the uncertainty, being upfront and honest with our patients, and saying, we're dealing with this too, and then modeling how to cope with it, how to digest that information. What is reliable information? There's so many things out there on the internet that could scare somebody, medical profession or not.

Linda Geng, MD, PhD (guest speaker):

I actually start all my new patient visits with my post-COVID patients with an introduction about our clinic. And that introduction includes a very upfront and honest statement about how our collective medical knowledge about post-acute COVID syndrome is new and growing and rapidly growing. We try our best to brainstorm strategies to help manage their symptoms and provide up to day expertise because things are changing on a daily basis sometimes.

Linda Geng, MD, PhD (guest speaker):

But I think it's very important for us as the physicians to be able to be humble and say, sometimes we reach the limits of our current medical knowledge, although it is actively growing on this topic. But then to talk them through what we do know. And even if we don't know all the answers yet, I think imparting what knowledge we do have, and helping guide them about how to obtain reliable resources of information, and addressing their misconceptions and fears can help mitigate some of that anxiety.

Ruth Adewuya, MD (host):

Yeah. And I appreciate you saying that starting the conversation with an acknowledgement of the unknown, because next question that I was going to ask you was the notion that some long haulers, or people with long COVID, have reported that doctors have dismissed their symptoms earlier in the pandemic. How do you practice humility and learn from your patients when patients themselves may have a better understanding of their condition than most doctors?

Linda Geng, MD, PhD (guest speaker):

Oh, I could talk an hour about this. I work in a diagnostic dilemma clinic and my passion is in this area of puzzling conditions. And I think that's definitely something, when we don't understand something well as medical professionals or as a medical profession, it's very easy, I think, to jump to conclusions when we shouldn't, or to be biased in certain ways that unfortunately occur, and especially to certain populations and certain clinical circumstances when there are puzzling or subjective symptoms without a clear diagnostic test or a clear objective finding to figure out what is exactly going on.

Linda Geng, MD, PhD (guest speaker):

One thing that really helps me, too, is during the pandemic, there have been lay articles, media articles about patient experiences. And what I find really poignant are actually articles from physicians who have expressed their own perspective pieces about suffering from long COVID. It really brings a different lens, and I think helps create that empathy for us as medical professionals to realize anyone could suffer from this. And we need to keep an open mind.

Linda Geng, MD, PhD (guest speaker):

This is the reminder that I give myself, at least, is that although we, as physicians, may be experts in our subspecialties, our medical domains, our area of expertise in terms of our medical knowledge, our patients are experts in their own bodies and lived experiences. To me, it's the merging of that synergistic expertise that really allows us to build those powerful therapeutic relationships, and work together to solve difficult problems like long COVID. And it's really important that we validate their personal experiences. Not making assumptions about the etiology is really crucial to building that trust and approaching puzzling or enigmatic clinical conditions in an unbiased manner.

Ruth Adewuya, MD (host):

Yeah. Such a powerful statement that you made. Thank you for sharing that.

Ruth Adewuya, MD (host):

So, Dr. Bonilla, I have a question for you around vaccines. We know that vaccines have been celebrated for seeing the severity of acute COVID infections, but what is their impact on the development of long COVID?

Hector Bonilla, MD (guest speaker):

Another reason why the people need to get vaccinated. There's a study that just came out not too long ago from the UK. It's interesting because they have a huge population. The data includes over a million patients. And they found out, after the doses, around 6,000 people got infected with COVID, around 0.5% of that population. And after the second doses, they followed up what happened with the people who got the vaccine compared with the controls. And they found in the people that got the vaccine, all the symptoms were either non-symptomatic or the people had very mild symptoms.

Hector Bonilla, MD (guest speaker):

And then they tried to see what happened to the instance of the problems of post-COVID syndrome. They used the definition of more than 30 days of symptoms. They found the people who got the vaccine who had more than 30 days of symptoms was half of the people that did not get the vaccine. The vaccine most likely decreased the prevalence of post-COVID syndromes. So please get vaccinated.

Ruth Adewuya, MD (host):

Do children experience long COVID at the same rate as adults?

Hector Bonilla, MD (guest speaker):

The data is coming in kids, but we don't know, because we are not following details. Sometimes the kids have some symptoms. They don't complain as an adult, not able to express their feelings. But there's something interesting in kids. They develop the multi-inflammatory syndrome. They are normal kids have no [inaudible 00:18:33] underlying medical conditions. They develop COVID [inaudible 00:18:37] was a mild COVID. In four to six weeks, they develop this super inflammatory syndrome [inaudible 00:18:43] what had been called Kawasaki syndrome. And in those patients, they experience fevers, chills, rashes, myalgias, arthritis. And some, they are very sick. They resemble a sepsis.

Hector Bonilla, MD (guest speaker):

This probably needs to be studied more in detail in kids, now that we have no vaccination approved for the younger population. To the patients or the people who have kids, please protect them until we have them vaccinated. Don't overlook, because most of the people that we see in our clinic, the initial event was people have COVID, but no one of them went to the hospital or ICU.

Ruth Adewuya, MD (host):

As we wrap up, what is your perception of the attention that the medical community and the broader media have given to long COVID compared to acute COVID-19 infection? And do you feel that long COVID is reshaping discussions about chronic illness in the medical community?

Linda Geng, MD, PhD (guest speaker):

Yes. Of course, at the very beginning of the pandemic, a lot of the media attention was, appropriately so, on the severity, the death toll, and the absolute devastation of acute COVID infection. As we saw the long COVID cases emerge, and the recognition of long COVID and post-COVID syndrome, I think it has... And this is one silver lining, is bringing attention to a neglected area, post-viral syndrome and post-COVID syndrome.

Linda Geng, MD, PhD (guest speaker):

I would say long COVID is now well recognized in the medical community, in the lay press, due to the attention from health authorities, as well as the broader media. And thanks to, also, patients in the advocacy groups, in bringing this to attention and being there in the front lines and grassroots efforts to publicize as well as recognize this. Hopefully this momentum will continue so we can promote the necessary resources investment and infrastructure building and policy changes that really need to be implemented so that we can continue to advance the care and knowledge of this condition collectively across the globe.

Hector Bonilla, MD (guest speaker):

I'm optimistic. Chronic fatigue syndrome has been neglected. The support by NIH has been very minimal. Now, with this kind of condition that is similar to chronic fatigue, the funding for NIH has been increased. And the interest is not only from NIH for example, it's many places in the country that are interested in this kind of condition. In this way, we are able to understand this kind of condition better. I want this momentum to keep on increasing because long term [inaudible 00:21:19] patients are unable to work, people are unable to live their lives. The people who have been infected with this kind of condition are the people in the front lines, the people to work. They are the people with lower economical resources.

Hector Bonilla, MD (guest speaker):

So it's very important we pay attention about this condition, understand better, and try to look for therapeutics, how to help these populations.

Ruth Adewuya, MD (host):

Lastly, for both of you, what is a key takeaway for clinicians on long COVID?

Linda Geng, MD, PhD (guest speaker):

I think there are a couple of key takeaways. If a patient has had COVID initial infection, because of our knowledge about when we follow patients long term in our research studies, there are some who report their symptoms but have not brought it up to the attention of their doctors. And I mentioned a little bit earlier about potential under-diagnosis of long COVID. If we really want to understand and help patients, we really need to be able to solicit that.

Linda Geng, MD, PhD (guest speaker):

And some patients may not be as forthcoming and may not attribute it to their initial acute COVID infection, because some of these symptoms are very nonspecific, like fatigue. Well, I could be tired from X, Y, and Z, and maybe I'm just busy with work, etc. Engage with your patient about it. And raise that question and say, "Has this been new since your COVID infection and is it persistent since then?" I think that definitely warrants further attention and consideration for long COVID syndrome. And there are so many symptoms. So keeping an open mind about what might be correlating with the initial COVID infection, and it could be multisystem and it could be quite complex.

Linda Geng, MD, PhD (guest speaker):

And the other one, of course, is also that we're still an active area where there's new research coming out. And I think a lot of the studies which have been phenomenal in establishing some of the symptomatology, it's also important, as physicians and clinicians taking care of these patients, to do a very thorough investigation into alternative causes for their symptoms. We don't know if there could be comorbidities or other things that are coincidentally happening at the same time. And so a very thorough, comprehensive clinical evaluation from a general perspective is really key and important to exclude and rule out other things which could be dangerous. Some of the symptoms we mentioned, like pulmonary and cardiovascular... If you have shortness of breath and chest pain, you have to make sure other things that are crucial that are excluded in their clinical evaluation.

Linda Geng, MD, PhD (guest speaker):

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[inaudible 00:23:43] definition of post-COVID syndrome. I think it's more than 30 days of symptoms after the illness resolves. Second thing is that multiorgan involvement. We see people for COVID with the lungs, and the lungs could be from [inaudible 00:23:59] inflammation, scar tissue, fibrosis, to pulmonary embolism or clots, they're compromised with the heart, the involvement of the liver and the kidneys, and, most likely, the central nervous system. I want them to know this condition is real and they are showing evidence of persistent inflammation, even months after the initial presentation.

Linda Geng, MD, PhD (guest speaker):

The other thing that is important is listen to your patients and believe what they say. They are not here in your office to see you to waste your time. And always, I tell my students, the patient, they tell you what they have. Always listen to them. The best teacher we have is our patients.

Ruth Adewuya, MD (host):

Thank you both for sharing your insights with us on this topic.

Hector Bonilla, MD (guest speaker):

Thank you so much.

Linda Geng, MD, PhD (guest speaker):

Thank you so much for having us. It's been a privilege and a pleasure.

Ruth Adewuya, MD (host):

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Ruth Adewuya, MD (host):

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