

Long COVID: New research, common symptoms, long-term effects and treatments with Akiko Iwasaki, PhD

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Featured topic and speakers

Akiko Iwasaki, PhD, returns to AMA Update to share the latest science behind long COVID, including how many people are still suffering, most common symptoms and what we know about treatments like Paxlovid. She also shares guidance for physicians on diagnosing and treating post-COVID and new research to watch. AMA Chief Experience Officer Todd Unger hosts.

Watch Dr. Iwasaki's previous episode.

Speaker

- Akiko Iwasaki, PhD, Sterling professor of immunobiology, Yale University

Transcript

Unger: Hello and welcome to the AMA Update video and podcast series. Today, we're talking about long COVID, what we've learned and how it's still impacting patients. Here to discuss the latest research is Dr. Akiko Iwasaki, the Sterling Professor of Immunobiology at Yale University in New Haven, Connecticut. I'm Todd Unger, AMA's chief experience officer in Chicago. Dr. Iwasaki, it's a pleasure to have you back.

Dr. Iwasaki: Thank you for having me back on your program, Todd.

Unger: It seems like a long time ago, but it was about just about a year ago that we talked, and a lot has changed since then. For one, the end of the public health emergency just happened and, also, that's just the general emergence from crisis mode. But, unfortunately, that's not true for everyone.

Dr. Iwasaki, let's just talk a little bit for now about how many people out there are still suffering from long COVID.

Dr. Iwasaki: So long COVID is estimated to affect 65 million people worldwide. This number is likely an underestimate since there is no active surveillance to count the number with long COVID. We don't have a true grasp of how many people are suffering, but it's likely in the tens of millions. Even though the emergency measures have been ended in many countries, long COVID is not going away.

Unger: Now we've had a lot of new variants that have emerged and we've seen the virus itself evolve. In some cases, we've seen different symptoms associated with new variants. Is that the same in terms of long COVID? Or are there still the symptoms we think about, fatigue and brain fog, things of that nature?

Dr. Iwasaki: It is true that the variants of concern have distinct characteristics of immune escape, cellular tropism, spread, as well as clinical outcomes. So it may be that people are suffering from distinct symptoms after acquiring different variants of concern. However, very common symptoms like fatigue and neurocognitive issues still remain to be the dominant symptoms reported for different variants of concern.

Unger: Have you found that treatments like Paxlovid have either helped to prevent or relieve symptoms of long COVID?

Dr. Iwasaki: That's a great question. There is a nice study by the Veterans Affairs that showed that based on medical health records, that people who were given Paxlovid within the first five days of symptom onset during the acute phase of the COVID did reduce the risk for developing long COVID about 26% over a six-month period. Whether Paxlovid can treat an existing long COVID is currently unclear. We've actually started a clinical trial with Paxlovid to see if that can relieve symptoms in an already existing long COVID patients.

Unger: Now in terms of understanding the causes of long COVID, there have been multiple theories that have been circulating. Last time we talked to you, you believe that long COVID was composed of perhaps multiple diseases. Has your thinking changed on that? Or have we learned anything new about the underlying causes?

Dr. Iwasaki: So, we have learned quite a bit since we talked last time. I still think that long COVID is a blanket term that describes multiple diseases. In terms of what diseases are there within the long COVID and what are the driving factors for long COVID is still unclear.

We are still investigating for possible root causes of long COVID, including persistent virus infection as well as autoimmunity and reactivation of latent viruses, like the Epstein-Barr virus, as well as chronic changes that happen in tissues due to inflammation. And so all of these theories still exist. And there are some evidences that we and others are getting that suggest that the persistent virus and the reactivation of herpes virus family, such as Epstein-Barr virus, may be happening more commonly in people with long COVID than those who recover from COVID.

Unger: Now in terms of long COVID, we talked about the two of the top symptoms. But there are actually more than 200 possible symptoms, and I'm sure that it's quite a challenge for physicians to diagnose and treat those especially as we move out of this acute phase, they may not be looking for something in that realm.

How should physicians stay informed about something that's still, we don't know all that much about it and the news, of course, continues to evolve?

Dr. Iwasaki: Indeed, long COVID has over 200 symptoms reported to be associated. However, as we discussed, there are common symptoms that are reported, such as extreme fatigue, post-exertional malaise, cognitive dysfunction, tachycardia, loss of smell and taste. These are some of the common features associated with long COVID. So physicians could be looking at these features as a potential sign of long COVID.

It is also now understood that new onset conditions can happen as a result of COVID infection, such as myalgic encephalomyelitis, dysautonomia, small fiber neuropathy, diabetes, heart conditions, stroke and many others. So these are also potential sequela of acute COVID infection.

Unger: Now in terms of guidance for physicians on the diagnosis and treatment front, and I'm sure many people might show up with one of those 200 symptoms, maybe not even be aware that they had COVID at this point. What advice do you have?

Dr. Iwasaki: There really isn't a one-size-fits-all answer to this question. But in terms of how best to approach this, I think physicians need to familiarize themselves with some of the common symptoms as well as potentially rare but certainly reported symptoms like hair loss and reproductive issues.

The first thing the doctor can do is to familiarize and perhaps remember some of these common ones that we've already discussed as well as they can ask the patients questions about symptoms and their medical history. If the patient is experiencing these issues within the first three months of getting COVID that lasts for over two months, that would fit the WHO definition of long COVID. So that's one big clue about when this happens and how long the symptoms persist. And the doctors can also perform physical exams to rule out other possible causes.

Of course, fatigue and cognitive issues are not unique to long COVID. But if you assemble all this information together, it's easier to diagnose long COVID. And running some tests may involve blood tests or imaging tests. That can also help the physician determine if the patients may have any damages to different organs and tissues.

And so based on these results, the doctor can refer patients to specialists and whether it be pulmonologists or cardiologists, neurologists. These specialists can then alleviate some of the symptoms that they might be feeling. Of course, there is no proven therapeutics that are effective currently. But symptomatically they can be treated.

And, lastly, I would say that there are multidisciplinary and multispecialty centers that are dedicated to treating long COVID patients. At Yale, we started one in March. And these centers are great for patients to visit because the physicians are well aware of the different symptoms that are associated as well as one center that can refer the patients to the appropriate specialists.

Unger: Now in terms of research, I know you're involved in a study that is looking at distinguishing features of long COVID that you've identified through immune profiling. Can you share something about what you've learned so far?

Dr. Iwasaki: I'd love to. So we are learning a lot. The first study we're doing is with Dr. David Putrino at Mount Sinai School of Medicine, where he treats thousands of long COVID patients. So his team recruited patients who have had long COVID for over a year, and we are comparing immune responses in people with long COVID and those who recovered from long COVID, who were also infected around the same time. And we're finding four salient features from these studies.

The first is that people with long COVID had reduced circulating levels of cortisol. The second is that we detected recent reactivation of Epstein-Barr virus in people who have long COVID compared to those who recover. EBV may or may not be directly responsible for the symptoms, but this is a feature we're detecting. Third, we found that the immune cells are differentially activated. We see more activated B cells and T cells, and T cells in particular, that secrete type 2 cytokines that are elevated in the people with long COVID.

And, finally, we find that antibody levels to the SARS-CoV-2 viral antigens are elevated in people with long COVID. This may indicate a persistent antigen for which these people are developing more and more antibodies against. So we're currently doing many follow-up studies to investigate each of these findings.

Unger: Now I know you're also involved in something called the Yale LISTEN study. Tell us more about that and what you're hoping to discover.

Dr. Iwasaki: Thank you. So the Yale LISTEN study is done in collaboration with Dr. Harlan Krumholz, who is a renowned cardiologist at Yale University School of Medicine. LISTEN stands for Listen to Immune, Symptom and Treatment Experiences Now. As the name suggests, we are listening to patients and learning from them and, at the same time, trying to investigate the underlying causes of long COVID.

We are also including post-vaccine adverse events in order to learn what the underlying causes there are also. First, we're collecting information about their symptoms and medical records, history from participants. And then we are also inviting some of these participants to provide blood and saliva for immune phenotyping, just as what we're doing with the Mount Sinai cohort. We are applying this deep immune phenotyping to both groups of patients in order to better understand the underlying disease pathogenesis.

So far, we are finding some similarities between long COVID and post-vaccine adverse events. But we've just begun analysis. So this is something to look forward to in the future.

Unger: Any other promising clinical trials that are on your radar that physicians and patients should know about?

Dr. Iwasaki: So as I mentioned already, the Yale LISTEN study is also carrying out the Paxlovid trial. This Paxlovid is an antiviral agent that can hopefully remove the persistent virus reservoir if there is such a reservoir in people with COVID. So we are doing this phase II trial, which is decentralized and it's a one-to-one, randomized, double blind, placebo-controlled trial.

So 50 people are going to be recruited into the placebo arm and then 50 to be in the Paxlovid arm. We're looking at efficacy, safety and tolerability in the 15-day course of Paxlovid compared to the placebo drug.

So we are not expecting everyone to respond to Paxlovid but we're hoping to learn who responds positively to Paxlovid and what are their biomarkers before the treatment so that we can potentially enroll people with such biomarkers for Paxlovid treatment who might benefit more than, say, those without the biomarkers. And it's going to help us also understand the underlying mechanisms from people who benefit versus people who don't benefit from Paxlovid and see what are the features that are associated with these two groups.

Unger: Last question for you, a year ago when we talked about long COVID, you mentioned that it might be a, quote, "pandemic after the pandemic." I know as much as we're hoping all collectively to move on from this, it sounds like that may be the reality. Are we equipped to deal with the situation?

Dr. Iwasaki: Unfortunately, that prediction did come true, that the long COVID is pandemic after the pandemic. I mean, the pandemic is still not over. We still have COVID circulating around and there are

people still getting long COVID from infection and potentially reinfection.

We are nowhere near equipped to deal with this. We urgently need several things. First, we need accurate diagnosis and treatment. This is very, an urgent situation. Doctors and researchers are still learning about the disease. There's need for more research and development of treatments.

Second, long COVID patients need financial assistance. Because long COVID can be a very expensive condition and debilitating, many people are struggling to pay for medical care and lost wages and other expenses. There needs to be more financial assistance to support these people with long COVID.

We also need social support. People with long COVID often feel isolated and are suffering alone. There's a need for more social support programs and resources for people with long COVID.

And, finally, I would say that we also need more public awareness. Many people are still not aware of long COVID. And there is a need for physicians as well as patients so that they can get the best treatment and best therapy possible and to support them through this process.

Unger: Dr. Iwasaki, thank you so much for being here and all your continuing work to help us better understand long COVID. That's it for today's episode. We'll be back soon with another AMA Update. You can find all our videos and podcasts at ama-assn.org/podcasts. Thanks so much for joining us today. Please take care.

Dr. Iwasaki: Thank you.

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