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Coping After COVID: How Can We Help Long-Haulers?

Dr. Wilner:
As the number of new COVID-19 infections continues to decrease and the United States begins to open back up, it's important to note that there are patients who have survived COVID but are still suffering. Shortness of breath, brain fog, and fatigue are just a few of the numerous symptoms that just won't seem to go away. So what is the research on discovering the 'why' of these symptoms and what to do about them?

Coming to you from the ReachMD studios, this is *COVID-19: On the Frontlines*. I'm Dr. Andrew Wilner, and joining me today is vascular biologist Dr. William Li. Dr. Li is the president of the Angiogenesis Foundation and author of the New York Times best-selling book, *Eat to Beat Disease*. Dr. Li, it's a pleasure to talk with you again. Welcome to the program.

Dr. Li:
Thank you, Dr. Wilner, it's a pleasure to be back.

Dr. Wilner:
So Dr. Li, the last time we spoke in 2020, we discussed your *New England Journal of Medicine* article that demonstrated the blood vessel damage that COVID can cause. It's more than a year now since we recognized this disease, and we're seeing something new. What has been termed "COVID long-haulers," people who continue to have symptoms even after the acute infection is resolved. Can you tell us what we've learned about COVID-19's long-term effects on our vascular system?

Dr. Li:
Yeah, Dr. Wilner, this is a big topic and it's getting bigger every day. Here's basically what we do know. We know that most people who have been infected by COVID recover, at least in the short-term. And in the very beginning of the pandemic, which seems so long ago because we've all been kind of held in thrall for seemingly forever, we thought it was really only vulnerable people who got very sick. We thought it was the elderly, we thought it was the morbidly obese, we thought it was people with diabetes and other underlying illnesses, but it turns out that pretty much anybody can get COVID. So our appreciation and understanding of the natural history of COVID acute infection has changed. And we know that anybody can get it, children can get it, young people, adolescents, that's the fastest growing group now, adolescents and young adults, and of course, older people. Now with the vaccine, it has altered the landscape, meaning that we've got 50% and growing, more than half of the United States have had adults that are fully vaccinated. We are in a completely different place in this country in terms of acute infection.

However, the lessons from last year, people who were infected and have recovered, which is most of the people, are now starting to come to life in a brand new way. And this is what you're talking about, referring to long COVID, or the patients call themselves 'long-haulers' after the truck drivers that carry a load across the country, driving seemingly forever. These are people who have recovered, many of them actually got COVID back in March of 2020. They got better after a few weeks, maybe after a month, and then three, two, three, four, five, six months, even nine months later, they developed these odd constellation of symptoms that are called, "Long COVID," and in fact, the NIH convened a workshop to examine what's called "post-acute sequalae of COVID," PASC, P-A-S-C.

So what is Long COVID? It is every bit as mysterious now as acute COVID was to the world in March of 2020. We are seeing brain fog, we are seeing tachycardia, racing of the heart. We are seeing abnormalities in the muscles, extreme muscle weakness, fatigue. We are seeing shortness of breath that is not explained by a chest x-ray or even a CT scan. We are seeing gastrointestinal problems, we are seeing endocrine, hormonal differences, including Addison's-like symptoms. And just reported recently, we're beginning to hear about erectile dysfunction and finding virus particles actually in the penis that have actually embedded itself for long-term in patients who have recovered from COVID. So lots of new things, over one hundred symptoms seem to characterize Long COVID. There's no diagnosis,

there's no ICD number, there's no billing code for it. There really isn't even a diagnostic criteria yet for this Long COVID, or PASC, as we're calling it. And there's certainly no treatment.

So what I wanted to share with you is, you started this question by asking what are we finding out from the vascular side. There are three cardinal things that we know, considering we know so little about Long COVID. We know that in people who have Long COVID, over a hundred different symptoms. They have continued microvascular damage, endothelial damage, damage to small blood vessels and the lining of blood vessels. Number two, there's damage to the nerves, both in the brain, in the central nervous system, as well as in the peripheral nervous system. And you're a neurologist, so this is an area of interest to you. And the third is there's chronic inflammation and it can be low-grade, and it seems to be attached to some sort of autoimmune phenomenon. So these are the three legs of the stool. Vascular damage, neurological damage, and chronic inflammation autoimmunity.

Dr. Wilner:
So say I'm a patient, I had COVID three months ago, and I'm just dragging. I can't think straight, and I don't have the energy I used to, maybe I'm better, maybe I'm not better, what do I do? How do I find out if I have this Long COVID or not?

Dr. Li:
Yeah, the thing is that if you had COVID or even some people who weren't able to get a test early on, but still don't feel right, and all you have to do is type "Long COVID" in the internet and look at all the reports. There is an excellent patient advocacy group called Survivor Corp c-o-r-p, that actually has brought together through social media tens of thousands of patients. You can see what other people are reporting. And if you actually have any doubt, you should talk to your regular doctor, your primary care doctor, your GP, and let them know that you are concerned about this.

Now six months ago, physicians were not aware or as aware of Long COVID, or PASC. Now I think increasingly, everybody's radar is on, so we now are trying to look for problems that may be Long COVID. And you may needof course, a regular physical exam blood test, but in case it forks the usual diagnosis, there are Long COVID rehab centers that are being set up. And even though they don't have the exact answers, they are actually gathering expertise on how to diagnose and manage this condition.

Dr. Wilner:

Now you're an expert in blood vessels, which go everywhere in the body. Most people are familiar with atherosclerosis, hardening of the arteries. It's a risk factor for heart attack, and stroke, and death. Now you mentioned that COVID can affect the blood vessels; could that add to atherosclerosis as a risk factor for these kinds of diseases?

Dr. Li:
It's a great question, Dr. Wilner, and it's something that I'm actually working on now. What is the long-term consequences of having been infected by the coronavirus and developing COVID? We know there's vascular damage. One of the questions is, "Does the body repair that vascular damage?" We know that blood vessels will repair themselves. We have stem cells that actually repair blood vessels over time. But to the extent that people are having long-haulers syndrome, Long COVID, this might be chronic endothelial damage over a long period of time. And that's very similar to atherosclerosis, hyperlipidemia; those lead to calcification of the plaques in the arteries, which lead to dangerous plaque rupture, which can cause heart attack and strokes.

And the other things that is of concern, is actually endothelial damage and chronic inflammation are setups for cancer, and another question is now being raised as a specter. So we don't know this yet, but it's a research question, is "What are the consequences of long-term endothelial damage and long-term chronic inflammation in terms of cancer risk?" Or maybe a cancer patient who actually also got COVID and is recovered from it, is there any risk that this could provoke the malignancy to come back or for new malignancies to grow? We don't know this yet, we've only had fourteen or fifteen months of experience with this disease, so we are really early. We're still in the infancy of understanding this condition.

Dr. Wilner:
For those just tuning in, you're listening to *COVID-19: On The Frontlines* on ReachMD. I'm Dr. Andrew Wilner and I'm speaking with Dr. William Li about COVID-19 long-haulers.

So, Dr. Li, looking beyond the vascular system, we know COVID-19 affects many organs. Now as a neurologist, I'm aware of the brain fog symptom and people having trouble concentrating, and of course, strokes and it's a little bit of a mystery. And every sub-specialist has their own view on this, their own particular lens. So how does the healthcare community get together and try and figure out you know what to do about COVID-19 long-haul symptoms?

Dr. Li:

You know, our experience last year has united the medical community and the medical research community in a way that I haven't seen in twenty or thirty years. And I think that we are now realizing that there's no single specialty that owns COVID. We have to collaborate together and share experiences. And so although medicine itself is highly specialized and there is so many silos and specialties that historically haven't really communicated with one another, I think that the management of Long COVID is going to require that we link arms and really begin sharing experiences and sharing data.

I'll tell you something really interesting: of all the organs that have been infected from head-to-toe, brain, nose, smell organ, throat, lungs, heart, gut, muscles, even bone, skin, have all been affected by COVID. The one organ that does not seem to have been affected by COVID is the retina, the back of the eye, the neuro-retina and the retina, even though there's plenty of blood vessels feeding the back of the eye, it seems to have somehow been exempt from acute damage when you first get infected and there hasn't been any reports of Long COVID affecting the back of the eye. I work with ophthalmologists and neuroophthalmologists and retinal specialists and I think there's something really interesting about an organ that doesn't seem to have suffered damage when all the rest of the body seems to have. And this is an example of where we need to actually come together and compare notes.

Dr. Wilner:
Lastly, Dr. Li, if we bring all this together, what are some key points you'd like our listeners to take away from this discussion?

Dr. Li:
Well, we're both physicians, I think we have a pledge that we made while we entered the field of medicine to really do the best for our patients. And so number one, I think that if you're listening to this, and you have been fully vaccinated, congratulations, you know, you're on the other end of the line now, and now we can start to get back to figuring out how to reclaim our lives. If anybody who is listening to this hasn't gotten vaccinated yet, I will tell you as a researcher, the vaccine is something that is very important to consider getting. Everybody had their own decisions to make, but really crossing that line puts you onto the side of being able to move forward and not be afraid of this disease. There are so many things about this disease we don't know. So I think that that's one thing I want people to recognize is the value that the vaccine is uncontestable in terms of being able to move forward.

Number two, I think that we've learned lessons from this that we never learned before, which is how vulnerable our body is. And I wrote a book called *Eat to Beat Disease*, and food is our medicine that we do take and during the last year, when there were no medicines, no treatments, no vaccines, no anti-virals for COVID, we all had our food to be able to eat at home. And so my book, *Eat to Beat Disease*, just scratches the tip of the iceberg, but worth people to read to understand how we can actually use food to enhance our immunity, lower inflammation, protect our blood vessels, these are all the cardinal things that are important for our health going forward.

And the third thing is that we are gonna go regain our lives. We're not going backwards; we're going forwards. Somebody once said to me, you know, after the 1918 flu, nobody said in 2020 how do we get back to 1912? Everybody said, how do we go forward into the roaring 20s. And after World War II, nobody said how do we get back to 1930; everybody said, how do we move forward into the 1950s. And so I think this is where we are as well. What have we learned in the in the last, year? Is that, you know, we have the science to be able to confront a threat that we haven't seen before, take it apart, find out what it's doing to the body, quickly pivot to figure out how we can protect ourselves in the best way possible, and I think because this is not the last pandemic that we're gonna have, we are now in a position to be able to protect ourselves better for the next one that could come down the pike.

Dr. Wilner:
Well I want to thank you, Dr. Li for joining me today and sharing what we currently know and where research is headed. Dr. Li, it was great having you on the program.

Dr. Li:
Always a pleasure, Dr. Wilner.

Dr. Wilner:
I'm Dr. Andrew Wilner, to access this and other episodes in our series, visit ReachMD.com/COVID19, where you can Be Part of the Knowledge. Thanks for listening.