Mark Masselli (00:04)
Our guest is co-director of the comprehensive COVID-19 Center at Northwestern University, which has cared for nearly 3000 long haulers from 44 states.

Dr. Igor Koralnik (00:16)
Long COVID patient are still there. we see patient in the clinic who had, let's say, seven episode of COVID-19, and then they picked up long COVID after the third one. There's data being published already out of Canada and other countries that the more episode of COVID-19 people have the higher the risk.

Margaret (00:37)
Dr. Igor Koralnik brings us his insights about the latest on long COVID. This is the second part of our series on this topic.

Dr. Koralnik (00:45)
We saw a lot of patient in televisit from all over the us. and sometime patient told us, well, they may be neurologist in my area in California, Florida, let's say, but nobody is either interested or willing to take care of me. And so that's why I'm coming to, you know, Chicago in televisit.

Margaret (01:03)
This is Conversations on Healthcare.

Mark (01:16)
Dr. Koralnik, welcome to Conversations on Healthcare.

Dr. Koralnik (01:20)
Thank you very much for having me. It's a pleasure to be here.

Mark (01:23)
You know, we understand there are roughly 17 million adults in the US with long COVID, and there are estimates it carries enormous health in economic burdens for patients. I wonder if you could tell our listeners about your center and its mission.

Dr. Koralnik (01:38)
Certainly. So I'm a neuro HIV specialist by training. and then I expanded my interest to all neuro infectious disease. So in December 29 2019, when the pandemic started here in the us I was well placed to try to understand what was going on with this new disease. And actually we started seeing a lot of patients being hospitalized with a horrible pneumonia and a brain alteration, including encephalopathy. We thought that we should open my clinic, my neuro infectious disease clinic for those patients when they would be discharged from the hospital. But in fact, the majority of the people that we saw coming to the clinic were people who were not hospitalized with pneumonia. Had a very mild case of COVID-19 sore throat cough that went away, but then developed those lingering and debilitating complication, including brain fog, fat, fatigue, headache, dizziness, and so on. And so to date, we have seen more than 3000 patients in the clinic with neurologic manifestation of COVID-19. and over the past five years in the clinic opening May, 2020 for those patients, in September, 2020, Northwestern Medicine opened a comprehensive COVID center that counted 12 specialties at the time, including pulmonology, cardiology, gastroenterology, and so on. We added two other specialty recently, gynecology and ophthalmology. Now, we have 14 specialty clinic for the total care of long COVID patients. So when patients come to the center, they don't need a physician referral. They can just call, get an appointment. They are triaged by a nurse to the different clinic that they need to see. So if they say they have brain fog and palpitations and shortness of breath, they will come to neurology, pulmonology, and cardiology in parallel, right? And so they see those different specialists. And in each clinic we establish, we see patients for one hour for new appointment, we establish a differential diagnosis followed by investigation to rule out other disease. And e every patient has a, a specialized plan of treatment.

Margaret (04:04)
Well, that, that is really quite remarkable. And I've learned some things just from your opening comment there. And I think the, the biggest one is then there is no one specific treatment for COVID. You've got 14 different specialty centers operating under one roof, and congratulations on getting that all up by May of 2020 when most of the world was still trying to figure out what was going on. But given that it's very complex, very complicated, it would seem to effectively treat patients with COVID. How, how does your center coordinate the care of

people so that people are not being treated by organ system, but treated with a comprehensive set of problems that they bring to you?

Dr. Koralnik (04:45)
So that's a very excellent question. And long COVID is a multi system, um syndrome that may affect any organ system actually, and some in combination brain, heart, lung, gi, and endocrinology and so on. And so this is because the, all, all this started during the lockdown, right? So we didn't have the time and the possibility to build a brick and mortar, you know, new building on the Northwestern campus downtown. So it was a virtual center that um started from everybody's existing clinic. at the beginning we saw a lot of patient in Televisit, right? So ISO provision televisit from 44 states in the US when we didn't, did not need to be licensed in every state to see patients. And so we formed this comprehensive COVID center where we coordinated the care through this triage system at the beginning. And then patients could be referred from one specialty to the other. We had weekly and or monthly team meeting to try to coordinate the, the, the care of those patients, also try to understand what we were seeing in neurology and what were they were seeing in pulmonology and in GI and the chronology, dermatology and so on, to try to make sense of this new syndrome, right? That that nobody had seen before. And I became the co-direct co-director of the Comprehensive COVID Center to the, together with the pulmonologist, Dr. Mark Sala who is seeing patients himself in the pulmonology clinic. And we try to coordinate or care the best we can and, and try to understand the advances that are, um happening in every specialty. we also have a, a long COVID support group now for our patients who come to the Comprehensive COVID Center. It's meet, it meets on Zoom every month on a fixed schedule. There's always a specialist of the comprehensive COVID center that comes to talk to the patients for 15 minutes about their area of expertise. And then a licensed social worker is there to lead the group after that provide emotional support for the patients, patients can meet each other, understand more about what's going on in you know, other specialties and in other patients and, and move forward. with that.

Mark (07:20)
You know, Margaret, we've had the opportunity to talk to a number of long COVID specialists at Yale and NYU. And I'm, I guess I shouldn't be surprised by anything that we've heard about long COVID, but one of the more surprising findings is that there are patients who've never tested positive for COVID, but now find themselves with long COVID. I'm wondering if you can shine a light on that for some of our listeners out there, doctor.

Dr. Koralnik (07:43)
Certainly. And that was a big problem at the beginning. You remember, during the lockdown especially, you could not get a test if you are not seriously sick with pneumonia in the hospital, intubated, you know, because of COVID pneumonia. And a lot of our patients at the beginning, actually half of the patient during the first six months probably of the clinic were in this predicament. They had symptoms consistent with COVID-19, but they, you know, they could stay at home. They did not have to be hospitalized, and therefore they were not tested on time or tests were not available in their geographic area. And they ended up having, you know, survive a mild case of COVID-19, but then develop those debilitating long COVID symptoms. Yet they were rejected by, you know, medical professionals and other centers because they didn't have a diagnostic diagnosis of SARS-CoV-2 infection in the first place. So, because we understood those limitations, and we wanted to be, as, you know, inclusive as possible, we deliberately decided not to require a positive SARS-CoV-2 test, either, you know PCR home test or a serological test for patient to be evaluated in the clinic. And so we saw a number of patients at the beginning who had exactly the same long COVID symptoms, yet they were not diagnosed formally with the COVID-19 at the time. And we decided we just to treat them just the same with supportive measures different child diagnosis, ruling out other other condition. And we've done this ever since in every clinic of this, the comprehensive COVID Center at Northwestern.

Margaret (09:32)
Well, it's so important to be having this conversation now when I think, you know, people have turned away somewhat from COVID, but for the people with long COVID, of course, there's no turning away, right? Until you improve you're in Chicago. Sounds like you were a center of all of this going on during the COVID pandemic, I assume, at medical centers and healthcare facilities around the country. Now, there's some common approaches to treating long COVID. But as you talk about, again, the multiplicity of organ systems involved in the different clinical presentations, have we gotten to a place where we have common agreement on treatment protocols, even if it's for different manifestations of the same disease, or are we still figuring it out?

Dr. Koralnik (10:21)
So I wish it was as you said, that now we have common protocols and you know, treatment that we know work for patients. Unfortunately, it's not the case. You know, we had the long COVID Awareness Day, the first long COVID Awareness Day on March 30 March 15th, 2025 marking the first five years of the pandemic obviously different geographic area were struck differently by the first wave of COVID to 19. Obviously in New York, it was worse than every anywhere else in the country. It came to Chicago a little bit after that they are different centers that were created out of shared need, you know, to take care of those patients. and at some point, I counted about 60 around the country for a publication that we put together. But unfortunately, I've heard that many have actually started to close down for the reason that you mentioned that people now have moved, moved on from the height of the pandemic. Nobody is dying anymore from COVID-19 pneumonia. We are not talking about, you know, how many respiratory we can get, you know, for those patient, and that's great. But COVID long COVID patient are still there. we see patient in the clinic who had, let's say, seven episode of COVID-19, and then they picked up non COVID after the third one. There's data being published already out of Canada and other countries that the more episode of COVID-19 people have the higher the risk for them to develop long COVID. And so since vaccination boosters are not preventing new infections, then I think that the number of patients is con is going to continue to increase. Uh epidemiologists have estimated that worldwide there is more than 400 million people who have long COVID costing the economy, about a trillion dollars per year, about 1% of the global economy. So it is really significant problem. We, since I'm a global neurologist, we have started collaboration in Nigeria, in Colombia, and in India started neuro COVID program there as well and published on those patient populations. So long COVID is not an American invention. It, it exists everywhere in know in the world. here we started to be deluged with patients, and then we did the research to try to figure out in those other countries you have to do the research first to show that the disease is there and to try to justify that those patient need to have clinical care as well. So, going back to your initial question about protocol and understanding I think that the, the more people publish about their experience, the better. You know other people get informed about their you know, the the options that we have to take care of the those patient. There is no uniform protocol, you know, for treating those manifestations. we have published what we've been doing in 2022 here at Northwestern for the Nordic manifestation, both in patients and outpatients. Other have published also on their experience in other centers. there are uh clinical trials that have been ongoing for the treatment of long COVID, let's say, with Paxlovid, this antiviral medication. there are two trials that have been independently done in other places in the US, and showed no benefit from Paxlovid in a smaller sample. There's a, a trial from the recover initiative sponsored by NIH that is close to enrollment now, and it's being analyzed. but unfortunately there is still no diagnostic tests for long COVID and no specific treatment for the root cause of long COVID.

Mark (14:32)
Well, Margaret, I think that's what our listeners probably wanted to ask, is what, what, what have we seen out there anything that's promising on the horizon as you sort of look at research across the globe? It sounded like Paxlovid might work, some cases might not. We also heard that in this first six or eight months for a subset of the population, the symptoms diminish. but I think that's not true for everyone who has it. But what, what do you think is promising out there? What line of research are you keeping an eye on?

Dr. Koralnik (15:06)
Alright, so excellent question. Different, um etiologies have been entertained for the root cause of long COVID, and they're not mutually exclusive. They may, you know, be together at the same time. So viral persistence is one, the virus remains hidden or dormant in some places in the body and needs to be treated with antiviral medication. The treatment of Paxlovid, at least in these two smaller studies for 14 to 20 days I was not efficient. We will await for the result of this larger study that is now we, we enrolled patient at Northwestern in many sites in the country, and we will wait for the result of this study. That's one thing. Another is autoimmunity. The virus comes and confuse the immune system, that there's something abnormal, abnormal in the body that needs to be attacked. We see that in our clinic and in every post COVID clinic, actually, there is a a predominance of women. So two third of the patients are women, and we know that women are more likely than men to develop other autoimmune disease like multiple sclerosis, rheumatic arthritis, lupus, and so on. And we see also an enrichment in the patient population of people who had prior autoimmune disease before COVID-19. So there probably is an autoimmune predisposition. we are working on this in my lab, although labs are also looking at this so far there is no medication or immunomodulatory medication that has come out of this research, which is still ongoing. Third possibility is that long COVID is caused by a microvascular disease. And you know, that the spike protein of the virus can bind the ACE two receptor on the surface of endothelial cells, for example, lining the blood vessel and can trigger some inflammation or even infection of these cells. And we are have published recently a study looking at the microvascular, um a structure of the retina in the back of the eye using a ophthalmological technique called optical coherence tomography angiography with, um lead ophthalmologists

here at Northwestern, Dr. Manchu Gil. and we have seen a decrease in the caliber of very small vessel in the retina in patients with neurologic complication of COVID-19. And so it is possible that this decreased perfusion that we see in the eye is actually a window on the brain and other organs and could, could cause some of the symptomatology that the patients have. And so that may be treatable with different, different modalities, but we need to follow those patients over time to see if it's actually a, a real physical biomarker of long COVID. And this is what we're doing currently in, in, in my lab.

Margaret (18:19)
Wow. Well, fascinating work going on. Dr. Koralnik and I, at risk of getting the acronym wrong, I'm going to ask you about a session I sat in on at the National Academy of Science Engineering and Medicine a few weeks ago, participated virtually it was focused on Lyme disease and long-term Lyme. But they talked about what they called infection associated chronic illness. I think IACI, am I correct on that? That that's the, the acronym?

Dr. Koralnik (18:47)
Yes. It's an, it's an acronym. Yes.

Margaret (18:49)
It's an acronym that's being used. And I, I thought of long COVID in this sense, and the struggle that people have and the struggle that entire populations have in this instance of trying to prove a disability or a limitation in their energy, their ability to work, their ability to function without the usual markers of positive tests or positive treatment protocols. What's your sense of where we are as a country? You, you talked about an enormous number of people that are sufferers of long COVID. how well do you think the country has responded in terms of support for people recognizing it as a disability making sure that we can take care of people, provide the emotional support if we don't have treatments, treatments where we can, you're, you're in the bird's eye view of this. What are you seeing?

Margaret (19:37)
Well, it was unexpected occurrence, obviously in 2019 and early 2020 to see all those patients coming down with this new syndrome affecting them so much in their quality of life, cognitive function, ability to work. it was during the lockdown, so there was not a lot of possibilities to move around. we saw a lot of patient in televisit from all over the us. and sometime patient told us, well, they may be neurologist in my area in California, Florida, let's say, but nobody is either interested or willing to take care of me. And so that's why I'm coming to, you know, Chicago in televisit. so I think that people responded as best they could in their, you know, area in their geographic area. Um the, the, the, the fact of the matter is that the, the entire world was consumed with COVID-19 at some point with a, a, a lot of death from pneumonia. Now that that phase fortunately is over people tend to move on, as you said, and then maybe not pay as much attention as they should to the plight of long COVID patients. Even we have patients coming to see us. They only have probably the smell and taste, right? They're, you know, cognition is fine. They're not fatigued, they can run the marathon, yet their quality of life is severely affected because everything that they smell smells like rancid fish, right? and so unfortunately there's no specific treatment for that in time. Patients tend to improve to some extent. And so the question about disability is always a tough one because we know that some patient will improve in weeks and months and be back to normal after that. But there are some patients who still suffer from the same cognitive problem despite cognitive rehabilitation that we, we give them actually around ability Lab across the street from Northwestern despite other, you know, stimulant medication that they may take, they still suffer from fatigue. And so it is not clear yet if those patients will have this chronic condition that will la will last four years or decades, or if they are going to, you know, get better at some point. We have developed an app actually that, um has been adapted by Northwestern medicine IT department to be integrated into the patient's interface called MyChart for our patients to be able to log in their daily symptom, brain fog, yes, no fatigue, yes, no, and also what their percent recovered subjective impression of recovery compared to pre COVID baseline in percent every day, so that we can track their, and, and they can also track their own road to recovery, um on long COVID. And these patients are enrolled in the study. we also measured their blood biomarkers. we measured their capillary micro vessels by optical coherence tomography angiography. and so hopefully by doing this longitudinal fund story study, hopefully will be funded by NIH we will be able to have a better sense of what is the, what, how long is the road to recovery from non COVID and what distinguished people who are the improvers compared to those who are actually stable or even worsen over time.

Mark (23:17)
Margaret, we're not surprised it's a long road. We had Dr. Fauci on four or five times during the pandemic. We had him on January, 2020. And the one thing he reminded us that Coronavirus mutates right all the time. It's very hard to sort of nail down and it will continue to be a problem.

Dr. Koralnik (23:32)
There's a National Center for Health Statistics together with the US Census Bureau that has carried out a household pulse study on long COVID over the past couple of years. The last data point was in September, 2024, and you had data from every state, every age group, every sexual orientation, you know, a lot of other information about the patients who the, the people who took this study and the estimates. it's always obviously an estimate, but that 17.9% of all US adult ever had long COVID. And if you take a population of adult, about 260 million people in the us, so it's about 47 million people, 5.3% of all adults currently suffered from long COVID at the time of the last time point. So it's about 13 million people. And of those 80% has any activity limitation of long COVID. So it's about 11 million people. So it's like the population of New York plus Chicago put together. so I think this is the best data that we have from the national center for Health statistic in the US Census Bureau. Certainly very serious outlets, you know for, for measuring the number of people who have a typical disease in the, in the country. If you would just google long COVID household pulse study It's housed on the CDC website. You can click on the link, go on the table and see all the data for yourself. I think that's a, a, a very interesting exercise.

Margaret (25:22)
I know our time is running a little bit short, but I have to ask you certainly we've seen some research that found no significant, significant differences in long COVID symptom severity between patients who were vaccinated or not vaccinated or vaccinated after a preceding course of COVID infection. Is that accurate to say? Is that what your research bears out? Did being vaccinated make a difference in whether or not you developed long COVID if you did get infected?

Dr. Koralnik (25:55)
So the question is, does vaccine do vaccine alter you know, the presentation of long COVID? And at the beginning of the pandemic there, there were a lot of urban legends. That vaccine either cured long COVID or vaccine made long COVID worse. we looked at this in our patient population at the beginning, and we didn't see any effect. And more recently, we published a paper on, in brain communications on 1300 patients seen in the clinic the first 1300 patients in, in the clinic including 200 who had previously been hospitalized for pneumonia and 1100 who were never hospitalized. And we looked at patient who got COVID, got vaccinated, and then developed long COVID compared to those who got vaccinated, got COVID after that, and then developed long COVID. And those two population were almost identical. Right. So in, in the, in this study based on my clinic population and we did not see any effect of the vaccine on the subsequent development of long COVID some data comes from large epidemiological studies for, for example, from the VA hospitals and others, where they saw that patients who got vaccinated had a decrease incidence of long COVID after the fact. but a, a mild decrease, maybe 15 to 30% at best. but when we see them coming in the clinic, whether they had COVID before or after the vaccination, if they developed long COVID, it's really the same disease

Mark (27:41)
You know at our health system here, what we focus in on the under-served and uninsured throughout the country. And one of the programs that we're very excited about and really aligns with something that you're doing is to provide e consults to providing access to primary care providers through a specialist. and we've done a couple hundred thousand of these, and high on that list is neurology. And I know you've been focusing on neurology residents in Zambia because you're thinking more globally and which is a real shortfall, obviously neurology for so many population groups. I'm wondering if you could share with the audience what insights about the current international health situation that they're facing with all the budget cuts that are happening in Washington.

Dr. Koralnik (28:33)
Alright, so it is a very large question to answer, but since you're talking about Zambia I've been fortunate to help a young than neurology resident called Dr. Omar Siddiqi, when I was still at Beth Israel Deaconess Medical Center in Boston, to establish himself actually as the second neurologist in Zambia, a country just about the size of Texas. It happened about 2010. He trained at Harvard in neurology, was interested in global health, global neurology. We had the connection with the one neurologist who was in Zambia. And by getting a one year grant and another one year grant, and then a five year grant from NIH was able to establish himself full time. from there in Zambia from there are other people have joined, including Dr. Deanna Sailor from Johns Hopkins, and others who have expanded this program. Finally formed the first neurology residency program in Zambia in 2018. and then the first graduates became attending that in that program. And one of the proudest moment of my career was one year ago at the American Academia of Neurology, when I saw the first graduate of this program chairing a session of global, nor in global neurology in the American academia of um neurology. so Dr. Macina Tromba actually is is this brilliant young neurologist. So this, this started, you know, from the, the one person

effort really. And then other people came and created the, the critical mass, you know, for that to continue. And now the Zambians are training Zambians to become neurologists which is obviously very good for them. we have been sending trainees, residents and fellows you know, almost every year for a rotation in resource limited setting and heavy infectious neuro infectious disease setting also for their own training. And when they come back oftentimes they say that it was really a life altering experience to, to be able to, to you know, to, to go there and, and see and, and learn from, from the, the people who are seeing those patients. Now, obviously there is a lot of limitations based on NIH funding. the, the program initially was not created through NIH. it was created through other foundations, but obviously all the, the, the, the salaries of the people who are on the ground need to be supported one way or another. And so, NIH was a big, big part of that. I truly hope that, um we will be able to continue to do that. I currently collaborate in Nigeria, in Colombia, Latin America, and in India. I think we can definitely learn from them as much as they can learn from us. and infectious disease are, you know, don't know any borders. they don't know any ideology or political, political orientation. Everybody's fair game. And so if we understand that we are really all in it together, then we need to continue to, to work together to fend off those infectious disease that can affect us in the US just the same as in Africa or in Asia, Latin America.

Mark (32:19)
That's a great Message

Margaret (32:21)
A great note to end on. Congratulations for that accomplishment. I'm sure that was a very high moment, not the last high moment, a very high moment in your career. So thank you, Dr. Koralnik, for joining us. Thank you to our audience for being here. And just a reminder to be sure to subscribe to our videos on YouTube, find us on Facebook and x, and please share your thoughts and your comments about this program. Take care, and be well.

(32:48)