[Music]

Mark Masselli: Our guest is a renowned epidemiologist and innovator who serves as the chair of the advisory board of Ending Pandemics, non-profit working to fight outbreaks faster around the world. His expertise is a result of his success in helping the World Health Organization eradicates smallpox in the 1970s, the only disease the human race has eliminated.

Margaret Flinter: Dr. Larry Brilliant has a very appropriate last name. He is often referred to as brilliant and by many other complimentary adjectives. He's been recognized by Time Magazine as one of the 100 Most Influential People. He's led public companies and startups. He is an author, received four honorary doctorates and currently serves on a number of foundation boards of directors.

Mark Masselli: Dr. Brilliant, welcome to Conversations on Health Care.

Dr. Larry Brilliant: Thank you so much for inviting me. I am very happy to be with you.

Mark Masselli: You know it's Immunization Awareness Month and we have a lot to go over on that topic. You have praised the WHO for declaring monkeypox a global health emergency and you believe ring vaccination approach is needed as New York State, San Francisco, where you're nearby, have declared it as an emergency situation. I'm wondering if you could unpack that for our listeners and give us the details of how a ring vaccination strategy could work.

Dr. Larry Brilliant: I think my praise was tempered. My exact comment was better late than never, which might be WHO's nickname, better late than never. We should have taken action when there were 100 cases or 1,000 cases. Today, there are over 20,000 cases. We now sadly have three deaths to report, two in Spain, one an immunocompromised person, we don't know the state of the second one, one in Brazil. During this period, there have also been five deaths from monkeypox in the two endemic regions in Africa. That alone should make us say that this is an emergency, a disease of international concern.

What I'm most worried about, however, is that these two spots of endemicity, one in Congo, one in West Africa, the two different clades of the virus, what I'm most concerned about is that those two areas of endemicity could balloon up to 100 or 1,000, and in every large city we might have endemic monkeypox. Let me explain why that is.

First of all, smallpox is not a disease of smalls and monkeypox is not a disease of monkeys. There are hundreds, if not thousands, of different orthopoxviruses, many of them like cowpox infect dozens of different species and the virus, which is called monkeypox, is probably dominantly a rodent infection. We don't really know what its original host animal is, but it is certainly capable of infecting hamsters, prairie

dogs, giant Gambian, house rodents and regular urban rats. If we have so many cases of human monkeypox virus and we allow it to allow unchecked, that's like giving Steph Curry unlimited shots on gold, and he will make most of them. What I worry about is that number of replications will lead to so many mutations that the virus may take on much worse clinical characteristics might become endemic in our urban sewers and urban rodent population, squirrel population, and as it bounces back and forth, spilling over and spilling back, we don't know what this virus will do.

I have a small group of friends that I am part of the Smallpox Warriors, we call ourselves. Unfortunately, it's a dwindling group but there is a lot of concern, could this virus over time, with enough shots on goal, mutate into something that resembles smallpox, heaven forbid, and that's where the ring vaccination comes from, Mark. The original vaccine against smallpox is extremely effective against monkeypox. I've seen numbers of 85% or 90%. In the case of that vaccine against smallpox, it was close to 95% to 100%. It's a very effective vaccine. Because it was so effective, because the world feared smallpox so much in the immediate period before it was eradicated, smallpox killed half a billion people, 300 million to 500 million in the 20th century alone. One out of three people who contracted it died from it and the way that we were able to eradicate it was by following a unique strategy conceived by Bill Foege who then was working on the smallpox program, became the head of CDC, and that was to find every case of smallpox in the world at the same time, and to draw a ring of immunity around each case, and that ring was not just geographic, it was sociometric, investing the index case by doing forward and backward tracing, words that we've come to learn about from COVID, but in reality they have a much deeper meaning than the simple way of thinking about just contact tracing.

We were able to immunize all those people who might next get smallpox until there were no more susceptible hosts around, and that's how we eradicated smallpox. We could do the same thing with monkeypox now. If we wait much longer, it will be too late. Once it's endemic in rodents all over the world, I'd not like to believe that we would bequeath our children and our grandchildren a world like that, Mark.

Margaret Flinter: Dr. Brilliant, I think you just gave our listeners a lot to think about there and I wonder if I can ask you, what's your assessment of how ready and capable we are throughout the country, either states operating independently or as part of a coordinated strategy with CDC to implement this ring approach? I'll put that in the context in our own state of Connecticut, certainly one of the smaller states but as of today, I think, Mark, 15 or 20 community clinics of which we have six of them, have vaccine on hand to be used in the appropriate

situations, and certainly very much tied to Public Health Department, really, identifying the positive cases and making sure that they do contact tracing, and that those vaccines are pretty readily available in facilities and organizations that people are likely to be able to access. Do you think that's part of the state health departments already having watched this ring approach? What do you see happening across the country in the US right now?

Dr. Larry Brilliant: I don't think we are very well-prepared. I don't think that CDC has mounted as energetic a response as I would like to see. Scott Gottlieb by the former head of the FDA has an op-ed in today's New York Times, I believe, saying that if we don't act quickly this would become the most abysmal public health failure in memory. There is a lot of other competitions for that throne, so that would be something.

You know, I think that part of the reticence, and I attended a couple of WHO advisory meetings on monkeypox, part of the reticence is that we have an approved vaccine that works against smallpox and monkeypox that works both before you're exposed and after. I likened it back to that something we called PEP, post-exposure prophylaxis. If you're using it as a post-exposure prophylaxis, the question you might ask, should it be regulated as a vaccine or should it be regulated as a therapeutic, and I would like to come back to that because a big difference in the amount of vaccine we have available to us if we regulate it as a treatment, as a post-expo prophylaxis, but the… I think I said prophylaxis, I meant therapeutic.

So, if we think of this as something we are vaccinating people and the risk is low, like the vaccines that we use for childhood immunization, then the bar has got to be very high and no side effects of any real consequence, rare side effects, if at all. If you're using this as something in the middle of an epidemic or a pandemic that's going to save lives immediately, then the bar is a little bit lower. The vaccines that we have that are specific for monkeypox, they are mostly without many side effects. The old smallpox vaccine, which we're calling dry vax that we used to use by distributing it almost like freeze-dried coffee in little vials, and then reconstituting it in the field, and then using a bifurcated needle and a couple of … I'll show you my arm here, and a couple of intradermal pokes with a bifurcated needle, that vaccine has to me a very low number of side effects, but it is true that that would be an unacceptably high number of side effects, were it not that this was an emergency, and those are the things that WHO has been wrestling with and because I'm concerned about this long-term possibility of monkeypox becoming endemic in the animal populations all over the world, I would be in favor of using more vaccine more quickly, and we just don't have enough of it right now to vaccinate everybody.

I think in fairness to WHO and CDC, those are the things that they've been wrestling with. I think I would've taken a much more aggressive position but I may be in the minority, because I've seen so much death from smallpox.

Mark Masselli: You give low grades to WHO, Gottlieb criticizes Congress maybe around the CDC and implicitly, the CDC. Just trying to think back over the last couple of decades, we've had SARS and swine flu and MERS, COVID-19, now monkeypox. Maybe Marburg is on the horizon there, who knows. What's your global sense of this early warning system, is it just building on these two organizations? Obviously, the Europeans and others do it. What's the larger strategy, because we were talking and been interviewing people during the COVID-19, something else is coming, something else is coming, be ready. Everyone should be forewarned. Don't be casual about what's around the corner. What's our state of readiness in your mind?

Dr. Larry Brilliant: First of all, I give very high grades to WHO for doing what it's supposed to do as a regulatory agency, as an agency that sets standards, despite having the world's worst organizational structure, not the fault of the current administration of WHO, but the idea that WHO has to rule by consensus of 100 countries meeting once a year has a regional structure, with all the power and monies in the regions, but the responsibility is at the center. Both of these agencies, WHO and CDC are a bit long in the tooth from their original structures.

You know I've written a lot about entering an age of pandemics. My colleagues and I in foreign affaires couple of years ago wrote an article about COVID, we called it the Forever Virus. Those sound like very pessimistic titles for articles, but they are actually quite optimistic because if you identify those problems, then you can do something about it, Mark and Margaret, and if you don't identify them and you don't name them for what they are, COVID is a forever virus. We are in an age of pandemic. That doesn't mean that we should hide or live in fear. I think there is something like 1,400 recognized zoonotic viruses that can infect human beings, maybe it's more than that now, it doesn't mean we live in fear of the environment that we're in. It means we understand what we need to do to identify those pathogens that are in animals that will jump or can jump to humans, that do create illness or death and we prioritize that part of our health system. It's not the cancer control part of a health system or the stroke part of a health system, but this part of our health system and it needs to be permanent.

In the middle of a huge forest like we have in California right now is not the time to start thinking about what the paint on the fire engine should look like or how many people should be sitting in the fire department, it has to be there all the time. That's what Benjamin

Franklin taught us, the fire department has got to be there all the time and we are in the midst of a fire of new pandemic potential diseases, more so than ever. I think a sweet interlude between the Spanish flu of 1918 and COVID, we had two other small pandemics, each with a million deaths, which is small in the pandemic world, but that doesn't mean it's going to be another 100 years before we have another catastrophic pandemic, and why is that?

Well, because human population is going all over the globe, because we're cutting down rain forests, because we have created climate change that have made animals from the south move to the north and spread their viruses and mingle their viruses with other like species. It's because the human-animal interface has been broken and when you live in the same eco-system as animals, you'll share viruses with them, and we're seeing with monkeypox a virus that can spread over, spill over from animal to an animal to a human, and then spill back, as we saw in 2003 with an epidemic of monkeypox in Minnesota that began in Texas with the importation of exotic animals, and led to a small but important epidemic of monkeypox in prairie dogs which were being kept as pets and humans got it from prairie dogs. We've seen it with mink in Denmark that mink farmers were able to give COVID to the mink, and then mink give it to humans, so much so that we had to wipe out that industry. I think that we sacrificed, which means killed, 17,000 – 20,000 mink.

So, we are living in that world in part, in large part because of modernity. Modernity means we have rapid transportation, a virus that jumps from an animal to a human. A bird flu epidemic that begins in Laos or Cambodia among chickens, among ducks that is transferred and humans contract that disease. That disease can be around the world in hours. So we need to rethink what we're doing.

There is a good conversation going on in the world about a pandemic treaty that would elevate the requirements on how to deal with pandemics to the level of a treaty organization. There have been very good conversations of lots of scientists putting a ring around the world of high-performance sequencing labs that help with the early detection or early specification of virus. I'm optimistic that there is enough interest beyond just WHO and CDC, but certainly including them, if you had GAVI and if you add the FAO, and you look at CORDS. I can give you an alphabet soup of acronyms, of really good organizations that are working very hard, but we need Congress to take this seriously. There has been a bill that was stalled for $18 billion to go to pandemic preparedness. Now, the Biden administration, which we all want to have succeed wants to take away these duties from CDC and bring it into an office. That's what's Gottlieb's article is hinting at and taking the assistant-secretary for convention Esper and turn that into an agency like CDC. We need to

have a national conversation about how important these communicable diseases are that are primarily but not exclusively jumping from animals.

Don't forget, we've got antibiotic-resistant organisms that have been held [inaudible 00:18:35] for antibiotics and these antibiotics are not working anymore, and there is very few new ones in the pipeline, but this is not to scare people, this is just to say we can do anything we want if there is public will, but there can't be public will without public trust, and there can't be public trust without a conversation like this.

Margaret Flinter: Dr. Brilliant, I think what you've just said should be mandatory listening or reading for people to understand this world that we're living in, how we're responding to it and how we want to think about the response going forward. We do have this sense as we go about the work of health care and public health of community fatigue, listening fatigue, if you will, to some of this, and in the midst of all that we now have as our next little hurdle on the landscape the announcement by the Biden administration that next month, we expect to have reformulated COVID booster shots available that are expected to hold up better against the now dominant Omicron sub-variant BA.5. I wonder what your view on this is. Is this a big step forward? Is it possible to avoid a winter surge as people grapple with the big issues, this next one seems right in front of us?

Dr. Larry Brilliant: As much a fan as I am of the miracle of the mRNA vaccines, they are not the right vaccines to stop people from getting COVID or to stop people from giving COVID. They don't produce very much mucosal immunity or IgA. We need intranasal vaccines for that. Because they require such deep refrigeration, they don't travel very well. It's hard to get to the two billion or three billion human beings to WHO classify as being outside of the reach of public health systems around the world. I'm cheered by hearing about work being done now to prioritize these intranasal vaccines.

The mRNA vaccine new iterations that are coming out are improvements at the margin but they are not dramatic improvements. I'm not so sure that the new vaccines that will come out in September or October, or whenever they are, by the FDA when they are made available, I'm not so sure that they will be that effective against BA.4 and BA.5. I hope they will be. From what I understand, they are going to have two different antigens, one for the original COVID and one for Omicron, but the Omicron that they targeted against can't possibly be BA.5, because we haven't had it long enough. So, what I've heard at least is that it's just going to be the original Omicron. If that's the case, I hope they are going to be effective. I'd rather see a BA.5-specific vaccine, but if you do that, you're going to play whack-a-mole, because of what's going to

happen with the next variant. Much better, I think, would be to work on intranasal vaccines that prevent you from getting the whole family of COVID, not just on vaccines that try to catch up with the next variant.

That being said, I am going to stand in line to get it because it's certainly an improvement than an incremental one.

Mark Masselli: Dr. Brilliant, let me turn to the environment. The Senate over the weekend announced, one would hope, an historic environment between the Schumer and Manchin, and it would make about $400 billion-worth of investments towards combatting climate change and you're senior counsel at Skoll Foundation, which has a very strong focus on mobilizing climate action, what difference will this law, if it passes the Senate and House, gain for the health of Americans and how can it deliver on its promise?

Dr. Larry Brilliant: It's huge. Mark, you probably feel as I do, if there is a category of modern risks that are difficult to articulate, the climate change is odorless, invisible, tasteless gas in the air and people can't believe that it's changing the climate, and so long as we did nothing in the United States, the rest of the world will still look to us. They are not going to do things. India is not going to do things to stop climate. China is going to do less, unless we play our role.

There are so many people around the world who say the industrial countries have created this mess, let them clean it up, and if we were absent at the table, if we were not part of the Paris Agreement, if we were not working on cutting carbon emissions, having targets that we meet, that leadership would be gone and then I think what we do is we all sit around and say this is inevitable, maybe it'll happen in 50 years. For god's sakes, just look around you, it's happening today. Look at the floods in Virginia, the historic floods in Virginia. Look at the wildfires all over the West. Look at the great drought in the West. Look at hurricanes last season, gathering much more steam because of the super-heated water that creates these super-storms. We are in the middle of climate change right now, we're not early, we're in the middle of it right now, and this law, while it's a small amount of money compared to what we need, it is catalytic. I can't overstate how important that is, and how reeled and surprised I was to see it.

By the way, there is a similar bill that Pat Leahy, Senator Pat Leahy of your neck of the woods has proffered and asked specifically for stopping and for creating agencies to work on pandemic preparedness, and I hope that that bill gets the same attention, because we need that just as much.

Margaret Flinter: It was a bit of good news after a seemingly endless not so good news, but I am going to ask you to look into your futurist ball maybe for a

moment. You are known for the development of the Well, a virtual community that you started way back, in the ancient days of 1985 that's been called the precursor of every online business from Amazon to eBay. I'd like to look into your futurist crystal ball and say what's in the future for health care in terms of the metaverse. Is there a purposefulness there that can be captured for the betterment of people and health care?

Dr. Larry Brilliant: I haven't thought very much about that. I do think there is some things that you can do virtually as training programs that are extraordinarily helpful but I actually wish that we wouldn't spend so much time thinking about the metaverse and we'd think much more about the universe that we live in. There is so much more work to do, Margaret, and the fundamentals are honesty and transparency, and trust, and dare I say love that we've forgotten about. You can't get good at the metaverse if you're not good at the universe, and I think all of us, if we're honest, the last couple of years have forced us to do some soul-searching and we failed a lot.

My friend Bill Foege, who I spoke about earlier, my mentor, is working on a program called How to Be a Great Ancestor. I think just thinking about that, how do we become a great ancestor, whether you're dealing with bequeathing a health care system that's functional and working, and we don't have anyone who's not covered by health insurance, or whether you're thinking about how do we put in place the stopgaps to prevent the worst excesses of climate change or pandemics, or drought, or famine, which we are in the cusp of in so many places around the world. If we could focus on that and not the metaverse, I'd be happier.

Mark Masselli: Let me shift gears a little. You know the Biden administration has announced plans for legal psychedelic therapies within two years and you've been talking about this for years. Why do you think it's taking so long and what do you think about the prospects of its approval?

Dr. Larry Brilliant: I'd like to pay some homage to my friend, Dr. Richard Rockefeller who passed away a couple of years ago. He was really the progenitor of a lot of this research and he was also the chairman of the Rockefeller Foundation and the chairman of Doctors without Borders, a psychiatrist who gave so much to the world, and one of the things he did, helping to create MAPS and all these other organizations and having the actual peer-reviewed prospective cohort studies done that have allowed the FDA to approve some psychedelics for use in individual clinical care, I think that's a big step forward. I don't know where it will go.

I know I came out of the '60s when psychedelics had a very different meaning and purpose, and were much more intertwined with our youthful life, but I personally know a lot of people who have been

treated in a psychiatric session with legal psychedelics and they report tremendous results. I've heard that some people have been treated for PTSD, coming out of the Iraq war in a single session and have achieved great insight. So, it's not my area of specialty. I'm an epidemiologist and I'm looking to the data that will come out of it, but I guess I am a cheerleader for anything that can work with the … Jon Stewart reminds me with our wounded veterans who gave everything to fight in Iraq and Afghanistan and have come back wounded with PTSD and in that sense, I am really optimistic and hopeful.

Margaret Flinter: Dr. Brilliant, we can see why past company stated there are few who have had more impact on the world than you have. Thank you so much for being with us. Thanks to our audience as well. You can learn more about Conversations on Health Care or sign up for our updates at www.chcradio.com. Dr. Brilliant, thank you so much for being with us and sharing your thoughts today.

Dr. Larry Brilliant: Thank you for inviting me and thanks so much for your patience and for the good work that you guys do. Thank you so much.

Mark Masselli: And you're well inspiration. We'll continue to follow your work, and again, thanks for taking the time.

Dr. Larry Brilliant: Bye-bye.

Margaret Flinter: Bye-bye.

Mark Masselli: Ciao.

[Music]