CONVERSATIONS WITH MIKE MILKEN

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Mike Milken: Richard, thank you for joining us.

Richard Hatchett: Mike, thank you for having me. It's a real pleasure.

Richard, we all have plans when we're young as to what we want to do, but then some event changes the course of your life. For me, the Watts riots occurred in Los Angeles, and I was home from Berkeley on August 11th, 1965. And I met a young African American man who told me he would never have access to capital because of his race, nor did his father. No one would ever loan them money to build a business. And it caused me to rethink this concept of the American Dream and that it wasn't just a chance to succeed based on your ability, but also that someone would invest in you. And then in the early '70s and mid-'70s a number of life-threatening health challenges faced my family – my father, my mother-in-law, our own children. Cancer eventually took my mother-in-law and father's life, and I now had another journey besides access to capital. And lastly I began to focus heavily on education. So education, healthcare, and finance have dominated my life and medical research and accelerating medical research. Let's talk a little bit about your career that eventually brings you to lead the Coalition for Epidemic Preparedness Innovations, or CEPI. Richard, you're probably the

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This interview has been lightly edited for clarity and readability.

best prepared person in the world to lead it as it was formed three years ago, but let's go back in your history and talk about the things that changed the course of your life.

Sure. Thanks, Mike. Thanks for telling your own story. I hadn't been aware of all of that and it does speak to how lives intersect – with fate or destiny or just what happens – and go in unpredictable directions.

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I trained as a physician and actually did have an interest in infectious diseases. While I was a medical resident, I worked on an Ebola project in central Africa, in Gabon, shortly after a series of outbreaks had occurred there. I ultimately elected not to do an infectious diseases fellowship, but went into emergency medicine and was living in New York City working at Memorial Sloan Kettering Cancer Center, which has a very specialized emergency room that takes care of cancer emergencies, and was on my way to being an oncologist when September 11th happened. I happened to be running the emergency room at Sloan Kettering that day. I spent the entire day – stayed until 11:00 PM – preparing for an onslaught of patients who didn't arrive. People either made it home or they perished.

Late that evening I went and stayed at a friend's in the city and I woke up the next morning to hear that there had been a call for medical volunteers, so I went down and presented myself as a medical volunteer. I found literally hundreds of medical volunteers, but no system for incorporating them into the response at all. I don't know why they put the call out. They didn't know what to do with the volunteers. But to make a long story short, a group of us made our way down to ground zero, and because I happened to be an emergency room physician, the person who had been taking care of the search-and-rescue workers since the night before tapped me on the shoulder and said "you're in charge." For the next roughly 48 hours, we help build what became very, very rapidly a four-story field hospital providing medical support to the thousands of search and rescue workers who were combing over the rubble and searching for survivors and searching for their compatriots.

Coming out of that experience, I had the presence of mind to know who was leading different parts of this field hospital. We got together to think about what civilian medical workers could do. We knew that we were entering what was going to be a long war on terrorism, and we came with the concept to create something called the Civilian Medical Reserve. As we began to shop that idea around, we originally thought of it as being for New York City, but pretty soon I found myself in Washington talking to the Office of the Vice President and to the Department of Health and Human Services that were running

the emergency preparedness programs, and I was asked to come down to Washington to help install that program. And my life took a right turn that I never anticipated. I have stayed in public health preparedness essentially ever since and had the privilege of working in the Bush White House and was called back to the Obama White House when the 2009 pandemic began. Then I moved over to an organization called BARDA – the Biomedical Advanced Research and Development Authority – which focuses on developing vaccines and drugs and diagnostics against agents of terrorism where I stayed for five or six years until I was asked to come and lead CEPI in early 2017.

Richard, let's talk about BARDA's mission, the Biomedical Advanced Research and Development Authority, which you led prior to CEPI.

BARDA itself wasn't established till 2006, but the predecessor office was established right after the anthrax attacks in late 2001. It was set up to basically fill a hole in the development pathway for products against agents of bioterrorism, chemical terrorism, radiological/nuclear terrorism, and to help address our very clear gaps on pandemic influenza with the idea that there really is no commercial driver for the development of treatments for anthrax or treatments for smallpox. I mean smallpox as a disease doesn't even exist in nature anymore. And if the U.S. government wanted to have products to prevent these diseases or wanted to have capabilities to prepare for pandemics which only happen every 10 to 40 years, they were going to have to make significant public sector investments.

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Over time BARDA developed a very interesting model for supporting the development of these products and overcoming that so-called "valley of death" where private-sector capital is not going to step in and see that products are developed because there's no commercial return. BARDA has its own institutional capabilities, clinical research capabilities, ability to manufacture material or to fill and finish vaccines, and it can bring all of that to bear in support of developing these products, and it's had a remarkable track record. Since its establishment almost 15 years ago, they've brought over 50 products to the point of FDA approval, clearance or licensure, and it's really set a gold standard for the world about how to conduct public-private partnerships to overcome barriers where the market isn't going to generate products that we need. The BARDA model has been very much in my mind and I think is one that I've tried to bring to addressing emerging infectious diseases epidemic and now pandemic threats.

Why did you leave BARDA for CEPI?

One, it was a good time for me personally to do so. Moments in your life when it's a good time to make a career change don't come along all that often. But I had been very involved in providing technical advice when CEPI was being established. CEPI was an organization that emerged from a series of conversations among global public health leaders after the Ebola epidemic in West Africa. I think there was great regret among those public health leaders when the Merck recombinant VSV vaccine was shown to be nearly 100% effective – great regret that that vaccine had not been advanced more rapidly and had not been available at the beginning of the epidemic. It had been under development for over a decade, but had never even been in humans before, and they had to accelerate the development process and do phase 1 clinical trials and sort out the manufacturing. And they were able to get it into the field, but right at the end of the epidemic, so it really didn't have any impact in terms of saving lives or preventing damage to the economies of Guinea, Liberia, Sierra Leone. The global public health leaders realized that we could do better as a world. When it came time for the interim board that had been set up for the organization to recruit a CEO, I was one of the people they spoke to. And ultimately I guess they liked me and I was asked to come and lead the organization, which was incredibly gratifying for me because I had always felt that emerging infectious diseases presented a more likely threat to human populations than some of the concerns about bioterrorism that I had focused on previously, and so it was a great honor to be asked to lead the organization.

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We want a vaccine tomorrow, and now you are tasked with analyzing all these different opportunities and can we accelerate vaccine development. As you know, at milkeninstitute.org we have been tracking more than 200 vaccines, antivirals, antibodies, immunology strategies, new testing ideas. But the goal was to accelerate. One of the vaccines that you supported – the Moderna vaccine – from the time that the molecular makeup of the virus was distributed to the time that the vaccine went into a human being was nine weeks – 63 days. Unheard of. What has changed this time versus the past?

Thank you for that tracking work that the Milken Institute is doing. I mean you mentioned over 200 products, and this is over 200 development efforts for disease that we did not know existed five months ago. That's extraordinary. But it's also I think our increasing awareness of emerging infectious diseases as a potential existential threat to society. We have been making investments for a couple of decades now looking for technologies that have the ability to move very rapidly to deliver candidate therapeutics and vaccines in these kinds of timeframes.

How Moderna got that vaccine into clinical trials in nine weeks is a combination of (a) the fact that a fellow named Barney Graham, who's the deputy director at the Vaccine Research Center at NIH, had been working on coronaviruses for a couple of years and (b) a technology platform, the Moderna MRNA vaccine approach that can allow – once you have those genetic sequences – for the rapid development of vaccine candidates meeting each other. Dr. Graham was able to take what he had learned studying other coronaviruses, and to bring that immediately – literally the day the sequence was released –to this new coronavirus and start thinking about how to optimize the presentation of the part of the virus that the immune system sees and to work immediately with Moderna to start developing a vaccine construct. And boom – off to the races. Nine weeks later they're putting injections into people. It's an extraordinary story. I think one of the signal successes that we've seen in the response to date.

Richard, you have limited resources. Gates Foundation, Wellcome trust, Norway and others have been major contributors. You've picked, to my knowledge, seven or eight vaccines to back. How did you break them down? If there's 70, if there's 80, if we're going to track over a hundred around the world – how did you decide which ones that you're going to back from that group?

We have also been keeping eyes on what's happening globally. We had a number of vaccine platforms and a number of actually MERS vaccines – MERS is another coronavirus that we were already supporting – so we had some partners who were already working on coronaviruses when this new one emerged. And we had some partners who were working on these rapid-response platforms, and so we were able to draw from that pool. We also put out a call for proposals to invite any interested vaccine developers to submit proposals. And we had about 50 proposals, less than half of the ones that we know about today, but this was early February.

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Then we had three goals in setting up our portfolio of candidates. One, we knew we wanted a lot of shots on goal because at this stage of development, the failure rates are really high and we can't pick winners in advance. We wanted speed, we wanted vaccines that could scale, and we wanted to be able to ensure global access to those vaccines. And so what we've ended up with is a deliberately diversified portfolio. We have an array of different technologies in the portfolio. We have RNA vaccines, DNA vaccines, viral vector vaccines, recombinant subunit protein vaccines. We've got performers who are located globally. We've got three in Asia, three in Europe and three in North America. And we're hoping to expand that global footprint even beyond that. And we were very careful to select candidates that we believe could be scaled to

hundreds of millions or even billions of doses a year within a relatively short timeframe. That's how we selected.

We have actually just very recently reissued our call for proposals because we know there now 70 or 80 additional programs out there that we haven't had the opportunity to review. We'd like to take a look at those and we're now working under something called the Access to COVID-19 Tools Accelerator, or the ACT Accelerator, which is a global effort with more than 30 countries to bring the partners in – bring industry in, bring governments in, nongovernmental organizations – to work together to develop a collective response to overcome this pandemic.

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About 30 years ago, part of my efforts were really focused on how do we accelerate cooperation. We focused on collaboration, sharing of data, and I think as you've just mentioned, Richard, I have never seen this level of cooperation. Would you maybe talk about the type of cooperation and partnership that you're seeing?

In talking about this, I have to reflect back. My career took the right turn into public health preparedness. When I was working at ground zero, I saw a level of cooperation and willingness for everybody to check their egos at the door because we knew that we were all facing an external threat. And that's exactly what we're seeing today. Companies are willing to work together in ways that they certainly wouldn't do under normal circumstances or if they were engaged in normal commercial competition. But we're all in this together and every organization that we have approached, they want to know how can we help? What can we do to advance our response to this pandemic?

The way CEPI partners with organizations, certainly what we do is take the funds that our investors provide, and that creates an aggregate pool of funding. And then we find the best partners and we provide that funding. But we also provide both technical support – we have highly competent, very experienced staff coming out of the pharmaceutical industry. But we also, because of our investors who are countries – they have institutions and capabilities that they've invested in – and because of their interest in working together as a coalition, they can bring those capabilities, whether that's a clinical trial network or manufacturing facility or special insight on a particular aspect of product development. And we bring those together and in record time.

As people are analyzing the data today – and you worked in West Africa – they're looking at the Caribbean and not seeing a lot of cases; they're looking at parts of Africa

and saying, even if there was no testing, if large numbers of people were getting this virus, they would be complaining about breathing, coughing, other side effects that we would see. Is there anything in your history and your personal experience that makes you think that maybe the weather has something to do here with this issue?

We know for other respiratory viruses that we've had longer time to study that there is the phenomenon called seasonal forcing, where you see seasonal patterns, particularly in the higher latitudes. Respiratory viruses – not just influenza, but RSV and other respiratory viruses – go up in the winter and they subside in the spring. They still circulate, but you tend to get a lull during the summer.

Other coronaviruses for which it's been studied, there does seem to be some of that, but maybe not as much as there is with flu where you have a very defined season in the winter. The other challenge, of course, is even for flu where you have that pattern, how it manifests at different latitudes is quite different. I don't think we would be surprised to discover that there is some degree of seasonality, and whether that's due to social factors like schools being out and people being outside and maybe more dispersed or due to climate factors, humidity or as you mentioned temperature, we don't know how all of those things fold together. But this appears to be an extremely infectious virus with high rates of transmission and you might anticipate that for a virus with those characteristics that it could overcome some of these weak environmental factors. I think we'll have to see. Everybody's holding their breath as we begin to come out of the lockdowns to see what happens.

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What we do know from the historical studies that we did of the use of these interventions in 1918 with flu is that when the communities emerged from what amounted to lockdowns in the day, many of them did see sometimes even larger than the initial wave. And so you had a second wave effect that was commented upon at the time and it was really quite a striking feature of the 1918 pandemic. I think most epidemiologists, whatever they think about the seasonal patterns of transmission, they're anticipating additional waves. Now, whether that additional wave comes in the summer or it comes when things begin in the northern hemisphere to get cooler in the fall remains to be seen, but I think we can expect continued disease transmission. This disease is not going away.

Richard, a vaccine is the ultimate solution here. In the interim, we have been very focused on antivirals, antibodies, immunology. But one of the things that we're seeing here is what we might call failures from the past. As you're thinking through the portfolio at CEPI that you might invest in, what role have things that didn't work in the past that might work here play?

SARS as you probably know of course is another coronavirus. There were significant efforts to develop vaccines against SARS immediately after its emergence. And one of the things that was observed about some of those vaccines in preclinical models – so these are animal models of SARS – was something called immune enhancement. And basically what that meant was that an animal that was vaccinated ended up having worse disease when exposed to SARS than an animal that was not vaccinated. And this is a phenomenon that has been seen with some vaccines and with some diseases – it happened famously with an RSV vaccine back in the 1960s.

What that means for us in terms of developing vaccines is this is at least a theoretical concern, and if we're rushing to develop vaccines, we have to be focused like a laser on ensuring that those vaccines are safe. We are drawing on our prior experience – these roadblocks that we ran into with previous coronavirus vaccine efforts – because we're going to be giving these vaccines literally to hundreds of millions or even billions of people. We have to know that they're safe and of course that they're effective.

One other aspect, we are trying to use approaches to vaccine development where we have some prior experience if not with licensed vaccines, at least with approaches to vaccine development that have developed similar vaccines for different diseases that have been in human clinical trials where we know that the approach that we're adopting is probably essentially safe. That's an important filter that we're using to think about which candidates to advance.

Well, Richard, I want to thank you for your service to the world. You are probably the most prepared person in the world to lead CEPI today. We want to wish you Godspeed in finding solutions and I'm looking forward to what our partnership together can do to bring the COVID-19 crisis to an end. Thank you for joining us today.

Mike, thank you. And I just want to thank you and the Milken Institute for all the work and contributions that you're making. These are really critical. Thanks so much.