CONVERSATIONS WITH MIKE MILKEN

David Baltimore

President Emeritus, Professor of Biology at the California Institute of Technology; Nobel Laureate

April 6, 2020

Mike Milken: Good morning David, and thank you for joining us.

David Baltimore: Good morning.

David, when we think back many, many years ago to the 1980s, it's vivid in my mind this television show of Oprah Winfrey when she said she heard it on good advice that up to 20% of all Americans might die of AIDS in the next three years. As you know, probably better than anyone in the world, after 35 years in the AIDS epidemic we still don't have a vaccine. However, antivirals and other things have dramatically reduced the death rate and controlled it. What is the difference between AIDS and the coronavirus in developing treatments or a vaccine?

Each virus that we encounter is its own problem. Some viruses we have found it very easy to make vaccines against; other viruses, very difficult. The most difficult one is the AIDS virus, HIV, and it's because of the nature of the interaction between the virus and the susceptible cells in the body. That is idiosyncratic to the AIDS virus, and there's nothing else like it. It presents a challenge that we have not figured out how to meet in spite of the fact that since the 1980s, we've had teams working on this problem all

---

This interview has been lightly edited for clarity and readability.

around the world. So it's not that it hasn't received attention – it's that it is a unique and extremely difficult problem. Compare it to flu, influenza virus – that's as difficult but for other reasons. And so we can make a yearly vaccine against influenza because it's constantly shifting its structure and we have to meet those shifts with new vaccines every year. But if we do that, we can control influenza.

We don't know what we're going to find as we try to make a vaccine against coronavirus. It may be straightforward. It may be a rife with difficulties that we have not seen before. But we will try to do that. And the very best brains in the country – in the world – are focused on that issue today.

We would love to have a vaccine that we could use to stop the progression of the virus, and that would ultimately allow us to control the infection and bring our world back into kilter.

David, we have brought AIDS and HIV relatively under control. As you know, a woman at one time had more than a 90% chance of passing AIDS onto her children and today with proper treatment, she has less than a 2% chance. People are living with HIV and AIDS today. How did we do it? What happened?

Well, we had a hint of the kind of chemicals that would control the virus, and we used that hint as a lever to build new molecules that got better and better and better. And today we can treat an infected person with a single pill a day and they can keep their virus under control. It's never cured, but it does keep it under control. But that's particular to HIV, and we don't control any other virus in that way.

"We don't know what we're going to find as we try to make a vaccine against coronavirus. It may be straightforward. It may be a rife with difficulties that we have not seen before."

You know, I think back as a child, David, my father had polio and when I was in school, it was declared an epidemic in 1952. Three years later on April 15, 1955, you started giving these shots to us in school, whether it was a Salk or the Saban vaccines. Today's technologies are light years ahead of the 1950s. Does that make you optimistic that we're going to solve this in a short period of time or at least make it chronic, not life threatening?

It does make me optimistic, but I was optimistic about being able to deal with HIV and it turned out to present so many unique kinds of problems that, as we've been saying, it's not really under control even today – although the disease is in the United States, in the developed world. We should know that we're still getting some 50,000 infections a year with HIV in the United States. So we don't really have it stopped.

I think we will find soft spots in the coronavirus that we can attack with antibodies, with small molecule drugs, and bring it under control. I don't know about a short time because we really only have a very short time right now, and developing new vaccines, developing new drugs is generally a long-time operation. We're estimating a year to a year and a half for a decent vaccine. We could be surprised and it could be longer. We could be surprised and it could be shorter.

Scientists around the world are coming together to work collaboratively to solve this problem. There has never been a larger international effort to try to deal with infection. That alone makes me optimistic.

When we think about many of these issues, David – and I think about Caltech and other universities that are dominant in science, and obviously you have number of your Nobel Prize colleagues at Caltech – one of the thoughts is that by bringing people together who maybe haven't exactly worked in a field, they sometimes approach a problem differently and think of novel ideas. Do you think convening a group – whether they were in computer science or mathematicians or physics, besides for biology and chemistry et cetera – would be helpful here? Would it give us new, novel ways of looking at this?

I think it would, and I think it's happening. I know that scientists of all kinds of backgrounds – engineers as well as basic scientists – are putting their minds, their laboratories to finding unique ways of approaching this problem. And I think the more we encourage people to come together, the more likely it is that there will be a surprising solution to this problem.

"I think we will find soft spots in the coronavirus that we can attack with antibodies, with small molecule drugs, and bring it under control."

As you know, David, being on the board of directors of FasterCures, we put out every day and update this list of vaccines, antivirals, antibodies, immunology, agents that are being worked on and where they stand. And there's more than a hundred of them. There are so many potential options to treating the virus from antibodies to new repurposed drugs to these anti-malaria cocktails we've heard so much about. What is your take on these different options.

Most of them are very early, in their development. Some of them are going to not pan out. Many of them are not going to pan out. That's the nature of the beast. But, again, hopeful that with all these various approaches, one or another will break through.

> ***"If we had a good test for whether an individual is making those antibodies, we could know that that individual is protected."***

In particular, there are some approaches being made by big companies that use the skills that these companies have developed for other viruses, particularly Ebola virus, to attack the coronavirus. That could bear fruit in months, and I know that those companies are moving forward and they can bring hundreds of people to the problem. They can bring manufacturing skills as well as scientific skills. There's a wide range of problems that have to be solved to make a vaccine, some of them just logistic. That's where you'll find the expertise to deal with those problems.

We're going to develop a large cohort of people who've been infected and have cleared of symptoms or are asymptomatic – they don't have any symptoms. Is there a safe way we can begin reestablishing our economy or work in the healthcare system by identifying those individuals that might have antibodies and get them back to work?

Absolutely. To my mind, that is the right route to bringing the economy back and to getting through to the other side of this problem. We should take advantage of the fact that once you've had a virus infection, that you then make antibodies that protect you against further encounters with that agent. That's how vaccines actually work. If we had a good test for whether an individual is making those antibodies, we could know that that individual is protected well enough so that even without gowns and masks that individual could help in dealing with the health of newly infected people; can work in hospitals safely; could work with the virus safely in research laboratories.

Identifying that group of people is extremely important, and we're not doing it today very effectively. What we need is fast, effective tests for antibody. We need to have enough experience to know what level of antibody is necessary for an individual to be protected. And then we've got to mobilize the skills of those individuals and put them to work. I think if we did that, we would find that there's a vast number of people already who are protected and more and more each day. And those people could be the backbone for rebuilding our economy and our health system.

David, we hear people talk about the herd. If enough people have these antibodies in a community, things change. What is meant by that? I've never quite understood how that works. How does that work?

Actually, it's very simple. Right now the virus is being transmitted from one infected person to another uninfected person, and on average one person is infecting two people so that the infection is spreading exponentially. If half of the people in the country had antibody, then when the virus was passed on from one person to two others, one of those people would be protected. And so actually the transmission would go from two people to one person. As soon as that happens, or just slightly lower than one person, the epidemic would burn itself out. What we want to do is to have a large fraction of the population be resistant. It doesn't have to be everybody by any means. And then the infection will burn itself out. That's herd immunity.

Let's talk about it at a personal level, how are you and Alice coping with this? You're both scientists. You're both doctors. You fully understand the issues. How are you dealing with this?

Well, by isolation. We have spent a lot of time already and look forward to a lot more together in our home. We go out only when we absolutely need to. We walk the dog daily, which gives us a little exercise. My wife was just out shopping very early in the morning when there aren't many people in the stores, and actually the stores are full of goods, so it's great time to go shopping.

I'm assuming you've become an expert on Zoom or all of these platforms for your board meetings, for trustee meetings, et cetera. How has your life changed digitally?

I'm focused on my machines, and I interact with people through those machines. Luckily, I know a lot of people from earlier in my life, and so when I connect to them electronically now we're comfortable with each other because we do have a history of knowing each other. If you deal with complete strangers, it's a little more difficult because you don't have that shared history.

Well, as Lori and I watch our young grandchildren go to school online, one of the cute stories we had the other day, David, was our five-year-old granddaughter when her father walked in the room, told him he has to leave because she's in a meeting with her other classmates right now. We're going to get a whole new generation with a different view of schooling. I wish you and Alice good health, and I appreciate you joining us today, David.

Thank you, and I appreciate what you're doing.