Pandemics of the past and future: A conversation with Nobel-winning virologist

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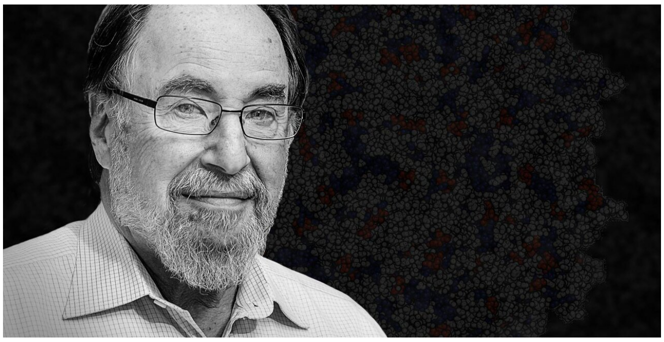

Credit: California Institute of Technology

Though no two pandemics are the same, each one that occurs has lessons to teach us about the next one. David Baltimore, President Emeritus and Robert Andrews Millikan Professor of Biology, is a virologist who studied HIV during the height of the AIDS pandemic in the 1980s and 1990s.

In 1975, Baltimore shared the Nobel Prize in Physiology or Medicine for his discovery of the enzyme that viruses such as HIV use to copy their RNA into DNA. These so-called retroviruses then permanently insert the DNA copy of their genes into a host cell, making it impossible to truly clear an infection. Though the novel coronavirus (severe acute respiratory syndrome coronavirus 2, or SARS-CoV-2) is fortunately not a retrovirus, it is still causing the most destructive global pandemic since the peak of the AIDS pandemic.

We talked over the phone with Baltimore to get his perspective on that pandemic, this one, and how to prepare for the inevitable ones to come.

Can you first walk us through the timeline of the AIDS epidemic?

The AIDS epidemic started, actually, with some observations in Los Angeles of patients who were turning up at doctors' offices with a variety of strange symptoms, all of which suggested a failing immune system. It was a syndrome that had never been seen before. Particular skin diseases and mouth diseases and other things which, together, made no sense. These patients were largely gay men, and were seen by doctors who specialized in treating gay men.

The doctors reported these cases to the Centers for Disease Control in Atlanta, which published this occurrence as an oddity, but other doctors in other places recognized that they were seeing similar problems. It became a syndrome of unknown origin, and it took a while before the cause was recognized to be a virus, called human immunodeficiency virus or HIV.

Once it was clear that it was a virus, then it was able to be thought about as an infectious disease being spread from one person to another. That helped enormously to pinpoint the kind of problem it was, but it was clearly an agent we had never seen before. It turned out to be a virus belonging to a class of viruses that I had worked on 10 years before, called retroviruses. I had discovered that retroviruses had a unique enzyme capacity to make a DNA copy of their RNA. For that, I had won the Nobel Prize in 1975. Now, by the early 1980s, this class of viruses was well established, but no one had ever seen it causing a disease of this sort.

The HIV virus eventually was traced to a virus that's endemic in monkeys in Africa that made its way into chimpanzees, made its way into humans, and was being transmitted—poorly, but effectively—among humans. Poorly in the sense that it's not a very infectious virus. That all became clear over the 1980s and '90s.

Meanwhile, the HIV virus of course spread around the world. It is pretty uniformly lethal, causing a pandemic of disease and deaths. Luckily, people had been studying inhibitors of viruses like this, and there were on the shelf some drugs that immediately got tested for their ability to stop this disease. In fact, one of them, AZT, turned out to be very effective, although short-lived in its effect because the virus mutated against it. But, it gave the clue that this was the direction to go in the development of drugs. Many other drugs of that class were made by different pharmaceutical companies, and ultimately we got pretty good antiviral compounds.

The scientific community studied the nature of the virus and found other weak spots that were targets for drug development. We ended up with a wide spectrum of drugs to treat this disease with. Today, AIDS is maintained as a chronic disease, but its lethality has largely been controlled, at least in the developed world where the drugs are more consistently available. We now live with the AIDS virus, HIV, as part of our world.

So the AIDS pandemic was ultimately slowed with drugs for treatment, but not a vaccine to HIV. Why has there not been an HIV vaccine?

That's a very interesting story, because we assume we will be able to make a vaccine against most viruses when they're first discovered. Historically, we've made vaccines against a very wide range of viruses: smallpox and polio, measles, mumps, rubella, on and on. With that history, we expected to make a vaccine.

I was involved in thinking about this in the '80s, and when we looked at this virus, we saw that it had a characteristic that suggested that it might not be possible to make a vaccine. This characteristic is that the virus can and does mutate freely, so that it is constantly presenting a different immune profile. In spite of work by companies and university scientists around the world, we don't have a vaccine. There really has never been a virus that's been this recalcitrant to control and this lethal. Still, some of my colleagues are working on ways that we ultimately may be able to develop a vaccine.

So this is the background against which COVID-19 has appeared. What are some differences between that pandemic and this one? For example, you mentioned that HIV is transmitted poorly, whereas the COVID-19 virus seems to be transmitting very readily.

Yes, one of the main differences is that SARS-CoV-2 is extremely infectious, whereas HIV is very poorly infectious.

There are many other differences between the two viruses. First of all, they're part of very different families of viruses. SARS-CoV-2 is a coronavirus. HIV we call a retrovirus or lentivirus. They have a completely different evolutionary history and a whole lot of differences in mechanisms. Although they are both viruses—that is they're very small agents that only grow inside cells—they behave in very different ways.

But they're similar in that they both came from animals. For HIV, it was monkeys, and for SARS-CoV-2, we think bats. They're both new to humans. We don't have any drugs to deal with coronaviruses because the coronaviruses have not been a big problem up until now. They were a small focal problem with the viruses that cause SARS and MERS [Middle East respiratory syndrome] which are coronaviruses, but those outbreaks were contained relatively quickly.

How are we tackling this current pandemic? Is the focus on treatment with drugs or development of a vaccine?

For the moment, we have nothing to deal with the virus. We're hoping maybe that drugs that were developed for other purposes might work against coronaviruses, but of course, we have no vaccine. We're starting from scratch. However, we have a huge armamentarium to work on this. We have companies that have made vaccines against many other viruses and that have developed drugs like those for HIV.

The scientific community is hopeful that making a vaccine against COVID-19 will be relatively straightforward. But we don't have experience to go on. We've never made a vaccine against any coronavirus because we haven't had to. We don't have the experience to know whether this class of viruses will be easy to deal with immunologically or difficult. I'm hopeful, but the virus is spreading so incredibly effectively that we don't have much time if we're going to have an impact on its spread.

So we've chosen the only route that we know will work to slow up the spread of the virus, and that is to stop people from congregating. This virus, like any other virus, only exists by spreading from one person to another person to another person. That spreading requires close contact between people, and that's why we're now asking people to stay six feet apart, to wear masks, to stay at home.

We're doing things that we've never done before on this scale to try to block the transmission, without drugs and without a vaccine. We have to accept the disruption of society, disruption of economic activity, disruption of intellectual activity, disruption of all ordinary behaviors.

The common cold is also often caused by a coronavirus; why is it not considered a pandemic?

The common cold is also a pandemic. But it's not lethal. There are hundreds of different kinds of viruses that cause the common cold—some of them being coronaviruses—but we don't usually worry about them because they take care of themselves. They cause a mild cold, often in kids, which then goes away.

Those kinds of coronaviruses are not serious causes of disease and so we don't worry about them. Even if they cause a pandemic—meaning, there are lots and lots of people around the world who are getting the sniffles—we just allow our immune systems to deal with it.

It's probably not a great idea that we ignore the common cold viruses. Public health officials sometimes do study the common cold, to at least understand its natural history and where it's distributed, how infectious it is, other things. But we don't put a lot of resources into that because it's not a real challenge to our society.

The COVID-19 virus is lethal in something like 1-5% of infections, unlike the common cold coronavirus, which is virtually never lethal. We had no pre-existing immunity to COVID-19 because it's never been seen in humans before, as far as we know. Now we are mobilizing to try to block its spread because it's killing people and its level of disruption of the ordinary functioning of our society is absolutely extraordinary. We've never seen anything like this since the flu epidemic of 1918—and very few of us saw that.

In hindsight, is there anything that you think epidemiologists and public health officials should have done differently to handle the AIDS pandemic, and anything that you think we should be doing differently now to handle this pandemic?

Well, the AIDS pandemic was handled very poorly. At the time, in the early 1980s, it seemed to be a disease that mainly affected gay men. At that time, homosexuality was treated as a deviance. President Reagan didn't even want to use the word AIDS, the word HIV, the word gay. So we were very slow in developing a response to the HIV epidemic because of homophobia. It really took a decade or two before we recognized that, first of all, this was a virus that was found in the homosexual community very extensively, but also outside of it, and particularly in Africa.

We had to realize that we needed to treat it as a threat to our society, not just as a disease of a particular class of people. We then were much more effective in preventing it by preventing contact and by treating it with the drugs that came along. But it took a long time.

In 1986, I was co-chair of a committee of the National Academy of Sciences that issued a report called Confronting AIDS. This was an activity that should have been undertaken by the federal government, but the federal government was afraid of touching it. So, it was done by the National Academy of Sciences and it laid out a plan for the country to study the virus, to respond to the virus, and act. Money was appropriated by Congress, and we started a serious research program. But that was five years after we knew the nature of the virus.

The start of our response to COVID-19 was very similar to our response to HIV. We tried to pigeonhole it as a disease of only certain people, Chinese people for COVID-19 or homosexuals for AIDS. We tried to ignore it. We knew, in the scientific community, that viruses don't only affect one group of people, that they spread to everybody. As soon as we knew COVID-19 was infectious, we knew it was going to spread everywhere in the world. We're now discovering that the terrible epidemic in New York City actually started in February, but nobody was paying attention to it. And it came from Europe, it didn't come from China.

The scientific community understands that a new pandemic is a part of the history of pandemics and that what happened once before is going to happen again.

What can we, as a society, do to be preparing for the next viral pandemic?

We must put the resources into protecting ourselves and build up our capabilities in the areas of epidemiology, public health, vaccines, rapid responses, and virus science in general.

We should have a cadre of public health people who are studying these problems continually, looking at all of the viruses in the natural world and saying one by one, "If this one got loose, what would we do?" and prepare ourselves. We can do all of that. It's not actually enormously expensive. But it means, first of all, we can't depend on our industries to do it because it's not economically attractive.

It's something that has to be done by the public and that means there has to be money put aside for it. Over my whole lifetime, what I have seen is that every time there is an epidemic, we say, "Now we've got to study this and prepare ourselves for the next one." But within a couple of years, that impetus is gone, the money has been reassigned to other problems and we're not maintaining our surveillance of the natural world. We're not maintaining our capabilities in vaccine and drug development, so we have to start all over again when the next disease comes along. That's shortsighted. It is the reality of politics, however.

Now that researchers are working on drugs and vaccines, and the rest of society seems to be mobilized in our own ways with the stay-at-home directives and protective measures, is there anything in particular that you think we can be doing better?

Well, I'm actually very impressed with what's going on. Some companies have simply said, "We're going to devote our expertise to this problem and we're not going to worry about the economics of it." I think we will have a response to this problem, but the response is already too late. What we've seen with this epidemic is that once the genie's out of the bottle, so to speak, it spreads so widely and so quickly that unless we have all of our defenses ready to go, we're going to be too late. We are now too late.

We should learn from this. We should already have a national program to make sure that the next time this happens, we're not so defenseless.

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