

## Peter Hotez, MD, PhD, on understanding the origins of the pandemic

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In today's COVID-19 Update, a discussion with Peter Hotez, MD, PhD, dean of the National School of Tropical Medicine at Baylor College of Medicine and co-director of the Texas Children's Hospital Center for Vaccine Development about COVID-19's origin story and why it matters.

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#### Speaker

- Peter Hotez, MD, PhD, dean, National School of Tropical Medicine, Baylor College of Medicine

### Transcript

**Unger:** Hello, this is the American Medical Association's COVID-19 Update. Today we're talking with friend of the show, Dr. Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine and co-director of the Texas Children's Hospital Center for vaccine development in Houston, Texas, about COVID-19's origin story and why it matters. I'm Todd Unger, AMA's chief experience officer in Chicago.

Well, Dr. Hotez, thanks for joining us again. Now I know, because I saw the movie 12 Monkeys, that it's very important, even if you have to travel back in time, to find the origin of a virus in a big pandemic. Now that was fiction and so I'm interested if you would share with our audience out there the reality of why it's so important to understand the origin of the COVID-19 virus and kind of what do we do with that?

**Dr. Hotez:** Yeah, absolutely Todd and first of all, thanks for having me back. I always enjoy speaking with you and working with the AMA. I think the reason it's so important is very straightforward. COVID-19 is not our first major coronavirus epidemic. This is our third one in the last 20 years. So, the third one of the 21st century. We had SARS, the original coronavirus pandemic/epidemic, severe acute respiratory syndrome, rose out of Guangdong province in South China in 2002 and then spread to Toronto and caused a lot of deaths and havoc in the city of Toronto, shut down the city for a while in 2003.

Then we had MERS, Middle Eastern respiratory syndrome, in 2012 and that has lasted a few years. It went into South Korea and caused a hospital-associated outbreak there. Again, very high mortality and a lot of deaths. And that's why we started working on coronavirus vaccines. We were mostly working on parasitic disease vaccines but I said to my science co-partner for the last 20 years, Maria Elena Bottazzi, Dr. Bottazzi, I said, "Maria Elena, you know, this isn't going to be the last one. We've had two now. You know, there's a message here. We're going to have a third one and probably it's going to come out of China. We ought to start working on coronavirus vaccines." And guess what? That's what happened right on cue.

And I tell that story for a couple of reasons. One, that we've been working on coronavirus vaccines for 10 years, and that's always useful because people claim the COVID vaccines appeared out of nowhere. They weren't. I mean, we did a lot of work showing that the spike protein was the target of the virus and how you deliver the spike protein and how virus-neutralizing antibodies are so important. But the other is to say that we expected another coronavirus pandemic/epidemic. This was the worst by far. But it's useful because it reminds people that this was not entirely unexpected. And so the reason why it's so important to uncover the origins is because we still don't understand the forces that are in play to make coronaviruses emerge.

We know bats have an important role because coronaviruses are found naturally in bats. And by the way, bats are natural hosts to other catastrophic viruses. Nipah virus for instance, that caused a terrible epidemic in India in 2018. Ebola circulates in bats, so that was important in 2014 and then 2019. And so the point is that understanding how the bat ecology interfaces with other animal reservoirs as a second intermediate host, or how the viruses jump from bats to people or bats to another animal to people. This has become one of the most important themes in understanding the origin of pandemics and that's why it's so absolutely critical to understand because this has become now a new normal of catastrophic epidemics and pandemics often involving bat origins as well. And this has become now a global priority.

**Unger:** Well, first of all, it's a good thing that that research had been underway for a decade, which I'm imagining put us a great deal farther ahead in terms of vaccine development for this novel coronavirus. Second, I want to kind of zero in on some of the ... I guess I'll call them two primary theories around the origin. One is kind of what you talked about before, which is kind of the animal to

human transmission and how that occurs with bats and other animals, and a second being more man-made lab origin. So can you talk about these two ideas just kind of quickly but I want to delve into more about the support on either end for those.

**Dr. Hotez:** Yeah. So, the point is we were expecting to see another major coronavirus pandemic and it happened and, no surprise to us, that it arose out of China. In this case, not south China like SARS, but central China. So I was a little surprised when all of a sudden we started seeing papers or articles pop up saying, "Hey, wait a minute, this didn't happen through natural. This was through a deliberate gain of function research." That people were manipulating coronaviruses in order to cause this pandemic. And I thought, "Well, that didn't make any sense to me," because we've known that these viruses are emerging on a regular basis and then I looked at the evidence being cited for this, one of the things that came out early was they were saying, "Hey look, this virus has a furin cleavage site," which is a cleavage site for a class of proteases known as furins.

And some very prominent scientists were touting that as evidence that there was some type of laboratory manipulation involved. And that didn't make any sense to me either because MERS, Middle Eastern respiratory syndrome, the virus has a furin cleavage site and now we know multiple beta coronaviruses in this family have furin cleavage sites, so there's nothing particularly unique about that.

And so you just saw a lot of talking heads say that they've got the smoking gun, that the SARS II coronavirus is through gain of function and research, and each one I looked at, I said, "That's not a smoking gun at all." I mean, we know a lot about coronaviruses and I just don't see the evidence for gain of function. And then it was the lab leak theory, so then it kind of shifted a bit—although there's still many who want to claim that it's gain of function research, which I'm not convinced about. Then there are those who are saying, "Well, maybe it was leaked from a lab either through gain of function or maybe research was being done on bat coronaviruses and it was maintained in the lab and there was an accidental laboratory leak."

And I said, "Well, what's the evidence for that?" Well, they say there's a well-known coronavirus research institute in Wuhan province and the epicenter of the epidemic initially was in Wuhan. And I said, "Well, Wuhan is a massive city and I don't see necessarily that as a smoking gun either because we know there are bat caves all over central China and Hubei province and Yunan province." And what impressed upon me was the zeal that people had to want to show that it was gain of function or lab leak. And I said, "Look, it's not impossible, but here's what we need to do. The most important thing is to uncover the origins and the only way you are really going to do that, whether it's lab leak or otherwise, is to do an outbreak investigation." And we know how to do this.

We need to bring in a team of scientists that are working Hubei province, international scientists, U.S. scientists, working with Chinese scientists to collect saliva, blood samples from bats, from other potential secondary animal sources, from humans and really trace the origins of COVID-19. And then

I make the statement, "We have to do this because otherwise, if we don't understand it, how are we going to prevent COVID-26 or COVID-32." And that needs to be the priority. Now, during that investigation you might uncover some evidence that there might be a lab leak somewhere. It's not impossible. I doubt it but I can't say it's impossible. But the emphasis has to be on the scientific investigation in cooperation with the Chinese. That would be the ideal situation.

And we could talk about some of the problems associated with that. But instead, what you're getting is so many individuals and some scientists that I have a lot of respect for, so focused on the lab leak and the gain of function. And they talk about how we've got to throw more U.S. intelligence at this. And I said, "Well heck, U.S. intelligence has been all over this for the last year, right?" I mean, you can throw all the intelligence you want at it but it's not a substitute for doing a scientific investigation. And then they say, "Well, we got to look at the lab notebooks." I said, "Well, first of all, Wuhan Institute of Virology is by no means the only institute in China working on coronaviruses. What happened after SARS? There are multiple university labs all over China, probably in Hubei province as well, that began working on coronaviruses. There's no particular reason to focus only on the Wuhan Institute of Virology."

And they say, "Well it's because there was an NIH grant given to the Wuhan Institute of Virology and there was a specific aim and therefore potentially looking at the virus and substituting different spike protein genes." So there was a sort of misunderstanding about how science is done in China. There's this misperception that the labs are underfunded and that they're just sitting around waiting for an NIH grant to provide the funding so they can do the research. In fact, the amount of funding from an NIH grant that was going to China for this kind of research was extremely modest. The Chinese labs are extremely well-funded now. The environment in China has changed dramatically over the last decade or so. In fact, American laboratories are losing a lot of Chinese scientists who are going back to China because they're so well-funded.

So again, there's this kind of misunderstanding I think about the science ecosystem that goes on in China as well. So again, not impossible that there's a lab leak involved. I don't think so. I don't see any smoking gun for deliberate kinds of gain of function research.

**Unger:** Well, two follow-up questions. First, you said something earlier, you said understanding the origin of COVID-19 will help us prevent COVID-23. What do you mean by that? What specifically does having the origin story for COVID-19 nailed down do to help you prevent future versions of it?

**Dr. Hotez:** Well, for instance, one of the things that I'd like to know is are coronaviruses jumping from bats to humans all the time. For instance, when we read about the history of HIV/AIDS, it wasn't a one-time jump from non-human primates to people. It probably happened multiple times over many years, maybe decades, before it finally sort of took hold and got critical mass and whatever metaphor you want to use and ignited and it really took off. It's probably the same with coronavirus as well. One hypothesis is that they're jumping from bats to people, or bats to people through an intermediate

animal host on multiple occasions.

I think we need to know that. I think we need to know if there are secondary animals involved, what are the characteristics of it? It's often said that it's because of the unique types of animals found in the Chinese wet markets. Possibly, but we need to know that. That doesn't explain what happened for instance with MERS, Middle Eastern respiratory syndrome, and the involvement of camels for instance. So I think there's so much we don't know and I don't see how you could think about designing prevention strategies without having some understanding of that.

**Unger:** Well, the term that you also used is this one called gain of function research, which to the lay person like me sounds very scary, let's just put it that way. Is this a common thing? Does it apply to coronavirus research right now? And is this research, the potential risks of it, kind of outweigh the benefits?

**Dr. Hotez:** Yeah. I mean, this has been hotly debated under by bioethicists and scientists. And it usually refers to taking a human pathogen and making it more virulent so that it's better at infecting people and making people sicker. As far as I know, that kind of research was never in the cards for coronaviruses—at least anything that's in the public domain. I think looking at that NIH grant, that looked more like taking animal coronaviruses and seeing if there are things that make it more efficient at binding to different cell types. So it's just not really quite the same as gain of function research, although many call it that.

But the point is, true, true and unrelated—whatever kind of research was going on to understand coronaviruses, I just haven't seen any strong evidence that it was linked to the origins of COVID-19, and recognizing that it probably was jumping from animals to humans for quite a while.

Let me give you an example. With SARS in 2003, the first outbreak I think was February 2003 but now they've traced it back to an individual for four or five months prior to that. And that is not an uncommon timeframe. So for instance, John Brownstein at Harvard Medical School has done some nice work looking at satellite images and doing Google searches and seeing that there was an uptake in hospital activity in central China four or five months before COVID-19 hit. That would make some sense to me. But there's enough uncertainty that we really need to do that kind of outbreak investigation.

And if all you do are hurl threats at the government of China and all you do is say, "We're going to go through your notebooks until we find something that we want to look for," you know that's just not going to go anywhere. And then I even say, "What are you going to do?" I mean, let's say you have access to the notebooks. First of all, if you were to add up all the notebooks on coronavirus research in central China, we're talking about hundreds of thousands of pages, which all would have to be translated into English or some other language. And then what are you going to do? Search term for the word "whoops" with an exclamation point? This is easier said than done.

So I think the focus right now needs to be on sending an envoy to China, meeting with leadership and Chinese scientists and convincing them to do a proper international outbreak investigation. And that's not quick work, right? That's going to be a year at least in the field of virologists, of epidemiologists, of bat ecologists to really do a deep dive in understanding how coronaviruses are emerging. And we have to do this. Otherwise we're going to be again shooting blind in understanding how coronaviruses emerge. In the course of it, it may come out that in talking and interviewing with scientists that maybe there was a lab leak involved. I think probably not but that's the only way you're going to do it. If you simply point accusatory fingers and demand an FBI-style investigation, one it's not going to happen, and second, it won't be very productive.

**Unger:** Well, that lab leak theory, I would say, originally was kind of brushed off kind of a little bit as a conspiracy theory but for whatever reason, in recent kind of months, it seemed to gain back a little traction. There are all sorts of questions.

**Dr. Hotez:** Let me make a comment on that because I've seen that, especially on the conservative news networks, they say, "We were saying this all along and the scientists brushed us off and saying it's not possible." That's not what happened. That's revisionist history. I know what happened because I was being interviewed on the cable news networks when a person from the White House, from the west wing—not connected with the COVID-19 coronavirus task force—came out and said that they feel that the "Chinese communist party is taking infected Chinese citizens and sending them abroad to deliberately ignite the epidemic." That's what they were saying. And that's when I said this is nonsense. There's no evidence for that and it's totally irresponsible and it's deflecting from really trying to battle COVID-19.

That's what I went up against. It was never about the lab leak. And then over time, the right wing media kind of revised that to say that we were discounting lab leaks. That's not what I pushed back against. I pushed back from these outrageous conspiracy theories of sending infected Chinese abroad and that's that.

**Unger:** I guess there was a report in the New York Times not long ago about kind of missing sequences of the virus and then online databases. This just, again, central to the story, not central to the story, or is it really—

**Dr. Hotez:** Well, it wasn't all that hidden because my understanding is somebody picked it right up in another file, so I don't know what to make of that. It seemed to me if people were ... I actually didn't follow that story very closely but it seems to me if somebody were deliberately trying to hide things, it wouldn't be so easy to recover those sequences.

**Unger:** So, I think what you're saying comes through loud and clear is that we do need to investigate this and we do need a scientifically based look at how this is because just like you said, 10 years ago, we could be facing another version of this years from now and probably that's likely given the

experience to date. Are there any other kind of lessons that we should learn from what we've gone through that would apply to the situation we're facing now?

**Dr. Hotez:** Well, it's not that the Chinese government gets a total free pass on this either, right? I mean, I didn't learn about COVID-19 until New Year's Eve of 2019, 2020. But this outbreak epidemic was well underway and it would have been really helpful if we had known that all through the month of December because once we had the sequence, we were able to move pretty quickly. The sequence came online January 14 and that's when I said to my science partner, "Yeah, I think we can we can make a vaccine." We contacted the NIH and we were off to the races but there should have been more of a heads up. I mean, the South China Morning Post put out an article saying that at least the original known patient was in early mid-November.

And so not having that transparency with all of the things that we had put in place, it's not like the world hadn't learned from previous pandemics. After SARS in 2003, the WHO put in place international health regulations and a global health security agenda after H1N1, and then CEPI, the Coalition for Epidemic Preparedness [Innovations].

So we have built infrastructure that's made a difference after each epidemic, so the fact that things did not go as smoothly in November and December, that needs to be looked out as well. Because again, otherwise we're just not going to be able to manage this. And we saw quickly this epidemic spread. I mean, if you remember President Trump, one of the first things he spoke about was the travel ban on China and that was I think in February or March, I think it was. And now we know that by the time that travel ban in China was in place, the virus had already entered New York City from southern Europe and ignited that first wave of the terrible epidemic.

So it looked like that hit southern Europe pretty quickly and that wasn't even the Delta variant. That was the original lineage. If it was Delta, we know it's a much more transmissible. So I think the other lesson is these viral outbreaks can move very, very quickly, maybe far faster than many of us are aware, so really being on top of it is going to be absolutely critical.

**Unger:** Dr. Hotez, its always so fascinating to talk to you. I really, really appreciate you being on our update today and we'll look forward to getting more perspective from you down the road. That's it for today's COVID-19 Update. We'll be back soon with another segment. In the meantime, for resources on COVID-19, visit [ama-assn.org/COVID-19](https://ama-assn.org/COVID-19). Thanks for joining us. Please take care.

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