After the Fact | Conversations on Science: In Pursuit of Scientific Discovery

Originally published September 18, 2020

Total runtime: 00:21:50

TRANSCRIPT

[Opening Music]

Dan LeDuc, host: Scientific discovery can be inspiring, and even mind-blowing, and certainly can challenge our perceptions of how we view the world. But ultimately, it's what moves us as a people forward.

Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases: We have decades of experience with coronaviruses, four of which are the cause of about 15% to 30% of the common colds that each of us get multiple times a year. It's a darn confusing virus because of all of the outbreaks that I've been involved with over the last 40 years, I've never really seen a virus that has such a wide breadth of manifestations. That makes messaging really difficult.

Dan LeDuc: That's a voice you've already heard in the first episode of this season—and are probably familiar with over these past several months—it's Doctor Anthony Fauci discussing the complexity of the coronavirus. As we continue our conversations on science, we're going to talk about scientific discovery today, and of course, that includes the race to find a vaccine and better treatment for COVID-19.

And now to our data point: most people, 79 percent of the United States adult population according to a World Values Survey, agree that science has made the world a better place. Each decade shepherds in a new era of scientific discovery, big and small, whether it's robotics for the hospital operating room, the detection of a new species in nature, or finding a cure for a global pandemic. People around the world recognize the importance of science to create a future that is healthier, safer, and better. We asked Mary Woolley, the president and CEO of Research America, about that.

Dan LeDuc: Mary Woolley, welcome. You are the president and CEO of something called Research America, which works to increase awareness of the health and economic benefits of medical research. And that is a noble cause, but I'm slightly disheartened that we have to make that case. It seems so obvious. Why do we have to make that case?

Mary Woolley, CEO of Research America: Well, we have to make the case, Dan, because the Congress, which funds the federal component of medical and health research, has many priorities, and so making the case for medical research is a responsibility of citizens—people who elect members of Congress—and of all of us by exercising our constitutional rights to be advocates for the things that we believe in.

Science, in all of its success, has gotten us much closer to the answers for many diseases and for many problems that are broader than medical. But it hasn't solved everything, and new things come up all the time. At the moment, we're all thinking about COVID, but we were thinking about Ebola not too long ago. We've been thinking about cancer for a long time, and heart disease, and actually getting to cure, and ultimately a prevention for HIV/AIDS, for diabetes.

There's a lot out there. And unfortunately, right now, the big science agencies, and the federal government are not able to fund more than about 1 out of 5 applications for funding that they receive. It gives you an idea that the cutting room floor could be making a difference in people's lives.

Dan LeDuc: Wow. So, 1 out of 5—that means 80 percent basically of what one would assume valid, necessary research out there is going unfunded by the federal government. So, what's filling the gap?

Mary Woolley: Well, sometimes nothing. Sometimes there's just—we're on pause. And I should say, Dan, that it's—depending on the area of science, it might be more than 1 in 5. It could be 2 of 5, but it's rarely above that percentage—at least not in the last several decades. So, what happens is that sometimes some of that work is picked up by foundations–and by foundations, I also mean to include patient groups—the American Heart Association, the American Cancer Society, and we also have industry, I should say. Industry supports quite a lot of research both in academia as well as in-house in their own laboratories. But still, we're not getting all the science that science is capable of delivering.

Dan LeDuc: So, let's talk about some of the public-private partnerships. Is that a good model for trying to advance medical innovation in the country?

Mary Woolley: Well, not only do those of us who've spent their careers associated with it believe it's a good model, but other countries do too. And that's an extraordinary reality, that the United States kind of created the playbook for public investment in discovery science, if you will, which then gets handed off to industry—to the private sector—to develop it and reduce it to practice so that it benefits everyone.

The basic idea is that it takes scientists working in different parts of the enterprise. In addition, it's also informed by the patient community in very important ways, because patients have a better grip on what they need now. And that over the years has become a much more important role in determining what research will be funded, how quickly it will move. The participation of volunteers in the clinical trial aspects of research depends on trust in science and upon it feeling to patients that the research they're being asked to participate in is appropriate. It makes sense. It's good to advance things.

Dan LeDuc: In your world of science and public policy, what are the areas where you see potential for breakthroughs based on all these groups coming together with funding, support, policymakers jumping behind something? Where are the areas of promise that are coming our way?

Mary Woolley: Oh, Dan, there's so many. And the sad reality is that the COVID threat has put many things on hold that just had to be for the safety of the researchers themselves. Labs had to be shut down. Long-running experiments involving animals and cultures had to be terminated. That means delays in finding—first, in discovery, and then in reducing that via development to cures, treatments, preventions. So, the backlog is immense.

But I think the silver lining here is the appetite for more has never been stronger. And the realization that we've shortchanged the science enterprise for way too long—getting back to that funding 1 in 5 grant proposals—we've got to up our game here.

[Transition music]

Dan LeDuc: COVID-19 has put a lot of scientific research in other subjects on hold, but it's also shown how the scientific community worldwide can quickly band together to take on an immediate health crisis. One scientist doing just that is Pamela Bjorkman. At her lab at Caltech, Bjorkman and her team usually study immune recognition of viral pathogens, with a focus on HIV. But since the coronavirus outbreak she has shifted her work to concentrate on COVID-19, which in our conversation she refers to as SARS-COVID-2.

Pamela Bjorkman, biochemist at Caltech and Pew biomedical scholar: Most of the infections that we're exposed to, we don't know anything about because our body got rid of them.

Dan LeDuc: All the time our bodies are fighting like these many assaults of infections, right?

Pamela Bjorkman: Absolutely, yeah. All of us are filled with viruses. Just most of them don't do anything to us.

Dan LeDuc: So, like right now, I mean something is going on in our body probably fighting off a virus.

Pamela Bjorkman: Probably. But sometimes you wouldn't even call it fighting off. I mean, there's several ways you have to protect yourself from pathogens. One of them is just like your skin. And if the pathogen breaks the skin, then it goes to the first line of defense, which is called the innate immune system. And then that recognizes things that don't look right.

And so, it's very good at recognizing that bacteria do not have the same sort of carbohydrates as our own cells. And so, the innate immune system says, "nope, there's something wrong with this. I'm going to get rid of it." They recognize something weird about it. And they just get rid of it immediately. But if that doesn't work, you go to the adaptive immune system, which takes longer to get activated. If you're infected with SARS-COVID-2, it takes about a week at least before you can see if you've made antibodies or not.

Dan LeDuc: Media reports have raised concerns about how the virus mutates and how contagious it is. So, I asked Pamela about this and what she's seen in her research.

Pamela Bjorkman: All viruses mutate. So, as the virus copies its genetic material, it will make mistakes and mutations will accumulate, but they don't mean the virus is more transmissible necessarily, and they don't mean that the virus is more virulent necessarily.

So, the more dangerous form of a virus is exactly what we have right now. You don't even know you're sick. You're young, you're out there, you're infecting all kinds of other people. And you just spread it all over the place. So, it has evolved for just in an amazing way of being transmitted. And that's why it's more successful than, let's say, SARS. Because with SARS, it was transmitted only after the person knew that he or she was sick and was probably hospitalized. And so, people were very careful not to allow further spread.

Dan LeDuc: The speed and collaboration that is marking the response to the coronavirus represents a turning point in the scientific community. Most of the time, medical research can be slow and bureaucratic barriers to progress can be high. Esther Krofah directs a project called FasterCures at the Milken Institute.

Esther Krofah, executive director of FasterCures at the Milken Institute: FasterCures was started over 20 years ago, really took a look across biomedical innovation. So, when we look across the system that develops medicines, develops treatments, and hopefully cures, what we see is a lot of silos across that end-to-end system. We see people who are focused on their own individual areas, very focused on their own research, and many times, to the neglect of looking at the ecosystem as a whole.

So FasterCures looks across that ecosystem to identify, what are the barriers? What's slowing things down?

Dan LeDuc: How would you view the current state of discovery? It feels like when you read about individual things happening in the biomedical field, it's astonishing what we're able to do right now. Are we in a golden age of discovery in some ways?

Esther Krofah: I think we are. I mean, the human genome was sequenced, and we were able to understand the interrelationship of literally all the genes in our body. We can do things in science that were science fiction maybe 30 years ago like cell and gene therapies—being able to edit a gene and then take that and put it back into an individual to correct for an illness, that's incredible. We have the opportunity to be able to sequence things quickly, use the technologies that we have built over many decades, and have a potential to change health care outcomes, to change treatments, and potentially to have cures.

Dan LeDuc: So, you also look at barriers. And in the modern age, that includes government regulation. And not that those are barriers, necessarily, because they're

necessary. But what are some of the things you've identified that are slowing the pace? And I'm assuming you think they're slow, because your organization is called Faster.

Esther Krofah: Yes. Exactly. And in many cases, when we think about, "well, what is slower" it's not the pace of science, because I just talked about how science is moving faster than it has ever before. What I actually mean are issues around collaboration, patient engagement, very specific regulatory issues, we look at, because regulatory issues really incentivize companies to behave in certain ways. The hope is that if we can eliminate those challenges, then we can really create a smoother pathway for treatments and products to get to patients faster.

Dan LeDuc: When we talk about needing something faster, needing a vaccine right now for the coronavirus seems to be maybe one of our fastest needs. We can look at the numbers of the people who have been infected and who have had serious cases often are people who are minorities or have access issues to the health care system. And we're looking at scientists right now, moving at a rapid pace. So, everything we've been talking about, apply it to what's happening now to the virus. Let's start with the scientists. How we doing? You guys are tracking a lot of the research. How are we doing?

Esther Krofah: We have seen unprecedented levels of collaboration with response to COVID-19. I think, primarily, because it's captured the entire world's attention. We're all experiencing the same shutdown and quarantine and social distance, etc. So, for anyone to move past this, everyone's looking to see, what can I contribute for us to move forward? So, collaboration is actually being addressed. I talked about data sharing. Data sharing is happening in unprecedented ways. Scientists are meeting over Zoom. They're creating different platforms to share data in real time. When we look at what's happening with treatments and cures, potentially a vaccine for COVID-19. Scientists and companies that are working on these technologies are able to share their data in real time with the FDA, so they can align on the design for the next phase of that clinical trial. So, the silos I talked about earlier are breaking down.

Pamela Bjorkman: I think nobody really thought about it except for the scientists who were telling everyone this was going to happen.

Dan LeDuc: One of those scientists who is seeing a breakdown in those silos Esther mentioned is Pamela Bjorkman, who we heard from earlier.

Pamela Bjorkman: I used to read some of the coronavirus literature, just because it was interesting to me prior to COVID-19. And every single paper said this is going to be a problem.

Coronaviruses are enveloped viruses, meaning they have a membrane derived from the host cell, and they have a spike protein that is involved in fusing with the host cell membrane. And so, that's in common with HIV.

Dan LeDuc: For a number of years now, you have been running a lab at Caltech working on this stuff. HIV remains a horrendous problem in the world. But now the world's been gripped by yet a new virus that is taking over things. When did that enter your consciousness as a scientist to say, "huh, don't like the looks of this one?"

Pamela Bjorkman: I think it was in February or so, it looked like the news from China was that this could be very, very bad. And so, my collaborator—Michel Nussenzweig at Rockefeller University—we decided to put in a supplement to one of our National Institutes of Health grants. So, in February, we requested funding to look at SARS-CoV-2 antibodies.

Dan LeDuc: And as a scientist, when you see this, obviously there's the pure science approach, how do I deal with this? But is there, for you as a scientist, any sort of sense of mission as well that says, "hey, this is bad stuff. It's happening really fast and we've got to work on it right away." I'm just curious on what the sentiment is like in the scientific community when something like this happens.

Pamela Bjorkman: Despite all the really horrible things that COVID-19 has caused, it has tightened up and strengthened the scientific community because people are working together in ways that I have not seen before. So, there's been a great sense of urgency that we absolutely must get a vaccine that works. Because I don't think we can return to a normal life until people have that in hand.

Dan LeDuc: Esther Krofah is keeping a close eye on the progress.

Esther Krofah: We're tracking now over 260 different treatment compounds that fall under antivirals and antibodies and cell therapies, etc., over 170 vaccine programs that are underway. That is fantastic. We need everything explored that could potentially be beneficial. However, this is the big caveat, is that there are close to almost 2,000 ongoing clinical trials worldwide related to COVID-19. They're not enrolling enough patients. Thirty-five percent of these trials have not yet recruited. When I looked at clinicaltrials.gov recently, 50% of these trials are still recruiting patients.

What we're now seeing is a competition, in some ways, for patients being recruited into these clinical trials. What I think could be helpful here are platform clinical trials. These are trials where you have a master protocol, if you will, alignment around the kind of data that you're collecting, around the design, the endpoints of these trials. You can enroll a higher number of patients. You have an adaptive design, so you can really go through many different compounds and learn from those compounds very quickly to give us answers faster.

So, in some ways, I want everyone to pursue whatever is possible. I do think we can get there, but we do need to align all of these different efforts in a way that is much more efficient.

Dan LeDuc: Obviously, lots of work is going in to develop a vaccine. But once a vaccine is developed, that's only the first step. What happens next?

Esther Krofah: Fantastic question. After a vaccine is developed, we need a framework around equitable access and distribution of that vaccine. And of course, as much more than the vaccine, we have the actual issues around manufacturing and the supply. And in real time, we are developing the vials and the syringes. So that's all very important. Who does that go to and how that is determined, I think needs to be very well laid out for the public.

Dan LeDuc: Based on what you know now, what are some of the takeaways that will have lingering effects on both how science is conducted and how the interaction with science and policy will maybe change, we hope for the better, as we move forward?

Esther Krofah: We're not at the end of this pandemic in any way, shape or form, so we'll continue to learn, but there already are some great things that have emerged.

We have learned, which we already knew, that depending on where you live and how much you make and, potentially, the color of your skin, you're not going to have the same access to health care. We're seeing this live in the number of people, disproportionately minorities, who are dying as a result of COVID. And of course, that's all compounded by underlying health conditions and systemically not having access to care. That's already a learning through COVID.

We need to address that in real and fundamental ways. From a science perspective, we're learning, as we knew, that having these, what I called earlier, platform trials, is an efficient way in order for us to do medical research. And it may be easier right now, in the midst of a pandemic, because we're all aligned. It's not about competitive forces.

We've also learned about virtual clinical trial, incredible. The ability for us to be able to conduct a clinical trial, enroll individuals remotely. You can go through consent forms remotely. Your medicine can be shipped to you remotely. You can self-assess based on questionnaires remotely, and then share that data back in real time.

That could allow us to really involve many more patients in clinical trials. Right now, 5% of oncology patients participate in clinical trials. Can we significantly expand that? So, they're going to be more learnings along the way.

The question is, what do we sustain that's not under the authority of a public health mandate? Because all of that is written, if you read any of the guidance documents, it's all because of the public health emergency. When that goes away, do those policies sunset? We want those to continue.

We can't go back to normal after things are said and done. There is a lot for us to be hopeful about, even the pace of scientific discovery as it relates to the vaccine.

[Transition music]

Dan LeDuc: The collaboration between scientists and the urgency they feel is providing new lessons to the scientific community—and as Esther Krofah says, hope to the rest of us. But often scientific discovery can mean little unless it informs public health decisions. In our next episode we'll discuss how research can—and can't—make for good public policy.

Until next time, for The Pew Charitable Trusts, I'm Dan LeDuc and this is After the Fact.