Covid Musing August 19, 2020 Dr. Francis Collins NSMC Dan Graber

This is long, but a good interview. A good description of science and faith, plus the ongoing research. Thanks to the people who passed this on to me! Remember – I'm open to sharing your resources!

JUST ASKING QUESTIONS JULY 1, 2020

A Long Talk With Anthony Fauci's Boss About the Pandemic, Vaccines, and Faith

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Even before he became the point person in a global effort to find a coronavirus vaccine, Dr. Francis Collins occupied an interesting perch in government. One of the few Obama appointees still serving in a major role in the Trump administration, Collins, who rose to prominence in 1990s as leader of the Human Genome Project, is the head of the National Institutes of Health, the federal government's gargantuan hub for medical research. With an annual budget of $42 billion, the NIH is essentially unrivaled in the world as a research center. Among its 20,000 employees is Dr. Anthony Fauci, who runs the division focused on infectious diseases. Fauci was a mentor to Collins when the latter joined the NIH decades ago, and they remain close, talking at length on the phone most evenings. Intelligencer chatted with Collins about the prospects for a coronavirus vaccine — he's optimistic — and about winning the $1 million Templeton Prize, awarded each year for remarkable work exploring the deepest questions of human existence.

We're obviously at a critical stage in the evolution of this pandemic. What's your perspective on this moment, and what do you feel like we've learned over the past three months?
Well, this is an unprecedented global pandemic in the lifetime of any of us. This virus has the ability to be transmitted even from people with no symptoms, which has made it extremely difficult to manage from a public-health perspective. We have seen now more than 125,000 deaths and millions of people infected just in the United States, and we're not done with it. When you see what's happening in the last few days, the really significant increases in the number of cases, particularly in the Southeast, tells us that any hope that somehow summer weather was going to be an antidote does not seem to have held up.

Until we have a vaccine that can be widely applied and provide immunity, most of our country is still at risk. This is not the time to relax.

What are the big questions that you and the NIH are most focused on unraveling? Obviously there is still a lot of uncertainty about immunity and new mutations.
Well, this virus is still brand new, although it's a member of the coronavirus family that includes SARS and MERS and even some common cold viruses. But it's sufficiently different from all of those that its biology is still not that well understood. There are a lot of mysteries about this virus, particularly why individuals respond so variably to exposure. We know some of the things that are associated with high risk: being older, which might mean your immune system's not quite as vigorous,

or having chronic illnesses — but we still don't understand a lot of the differences between individuals.

Some of that might be genetics. Some of that might be the initial exposure. Did you get a heavy dose or a light dose of the virus? But the variability is really quite striking from person to person in terms of what the consequences are.

A big question is whether somebody who has had COVID-19 is now immune from getting it again. So far we don't see compelling evidence of people getting reinfected, but that's still a bit early to say for sure. That's going to make a huge difference in everything we try to do about this going forward. A vaccine, of course, depends upon the idea that immunity is protective.

The usual way you conclude that is because people who've had the natural illness don't get it again. We *think* that's true for COVID-19, but it would be great to be more sure of that. The other big question mark is if you are immune, how long does that last? Is this going to be a condition where you've had it once and you're protected for the rest of your life? Or will you gradually become susceptible again? That will translate into decisions about whether a vaccine will need to be readministered, whether you'll need to get a booster shot now and then. We don't know. There are lots of uncertainties.

Is there any emergent thinking on that question of how long immunity might last — whether it's months or years, or maybe it will vary by individual? Is there any theory on that that is starting to gather momentum?

It's all pretty hypothetical. There are a couple factors that will relate to whether immunity lasts a long time. One is whether the antibodies that somebody generates after infection are around for years afterward or whether they fade away. There hasn't been enough time yet to be able to say that. The other is whether the virus itself changes its biology and then evades the immune response that people have had. Obviously that's a big deal with influenza, which is why we have to get a flu shot every year. And it's been a horrible deal with HIV — and why we've never been able to get a vaccine for it, because HIV is changing its coat almost hourly.

I think we have reason to be much more optimistic about SARS-CoV-2 [the virus that causes COVID-19]. There doesn't seem to be compelling evidence of it being that highly mutable. It's a typical RNA virus that seems to have a typical mutation rate. It doesn't look like it's doing a lot of changing of its coat proteins. So I'm fairly reassured by what we've learned so far, after looking at the viral genome of thousands of isolates, that this one is not changing that rapidly.

If you had to guess what the next two to three years looks like in terms of vaccine development — how do you see the process shaping up? A first wave of vaccines that are less effective, then working toward a better one?

I am guardedly optimistic that by the end of 2020 we will have at least one vaccine that has been proven safe and effective in a large-scale trial. Nobody should accept it as safe and effective without that large-scale trial. There are at least four vaccines that will be getting into such large trials this summer beginning as early as July. Each one of those trials will involve roughly 30,000 volunteers, half of whom will get the vaccine, half of whom will get a dummy placebo. You have to have that control or you will never know if the vaccine worked or not.

Those trials will have to be conducted in areas where the virus is actively spreading because that's the only way you're going to know whether it was protective. With four different vaccines with four different approaches, we've kind of hedged our bets against putting too much emphasis on one particular strategy. That's good — because vaccines are really interesting science, but every new virus presents surprises in terms of how the vaccine turns out to work. So I'd be very worried right now if we had one platform that everybody was counting on. Having four makes me feel a lot better.

Maybe all four of them will work. As long as one of them works, we'll be in a far better position by the end of the year to see our way out of this global pandemic mess. But there will be, then, a time of having to do the scale-up to have billions of doses, which might be what the world needs. So there will still be some time involved, even though we are doing everything possible to prepare for that by manufacturing millions of doses of each of those vaccines even before we know if they would work, so that the highest-risk people can get access right away. So I'm guardedly optimistic that we will see all that happen. But again — this is uncharted territory.

We've got the best scientists in the world working on this. We have incredible resources being put into it. People are working 24/7 to make sure that no mistakes get made and no obstacles are left that might slow this down. But also, everybody is committed to cutting no corners when it comes to the safety part. I know people might be worried about that because this is going so fast compared to the traditional five-year period to develop a vaccine. We will not compromise on the safety. We'll speed up a lot of other parts, but we will not compromise on that.

So you're feeling good about the fast-track process and how it's taking shape?
I am. The things that are making it possible to go so much more quickly are more the strategies and the way in which the regulatory process kicks in. Normally, when you're testing a vaccine, you start with a phase-one trial. Then you stop and examine the data. If it looks like maybe things are okay, then you have to set up a phase-two trial of maybe 1,000 people, which takes a while since you have to find a location and get all the mechanics going. And then after you run that trial, which may take many months, you analyze that data and decide, *Okay, it's time to go for the big 30,000-person trial.*

That takes you a long time to set up. After the trial is run, there then has to be a regulatory decision, which often takes several months. You can see why it can add up to five years — all those steps that are not really part of determining whether it worked, and the mechanics are being shortened up here in a very substantial way. There is this investment in manufacturing tens of millions of doses of these vaccines, even before we know if they're going to work, to prevent long delay at the end. It would be really sad if we were celebrating in December, saying, "Hey, we've got a vaccine that works," and there were no doses left to offer to the people who need it.

So that has to be planned for, even if it means throwing out the doses of the vaccines that failed. We're prepared to do that.

So we're hitting all the key steps — just reducing the in-between periods to as close to zero as we can?
Exactly. All of the vaccines that are starting into the large-scale trial in the next couple of weeks are those for which the manufacturing is already getting underway, even before we know whether they are going to work. The first vaccine to reach phase 3 also depends on a scientific strategy that is particularly amenable to rapid development, because this is the one which only needs to know the genome sequence of the virus to be able to design the vaccine. That sequence was released by the

Chinese on January 10. The vaccine was getting designed by our Vaccine Research Center that very night. That is the very first one that then was possible to put into phase-one trials in just 63 days. Normally, between when you decide you're going to make a vaccine and when you'd have your first phase-one trial would be a year, year and a half.

63 days is a world record. That one looks really good. The phase-one data looks very promising. It will need to go though into this big trial before we'll really know whether it's safe and effective. If it isn't, well, we'll throw it out.

How would you describe the NIH's role in this entire process?
The NIH is the largest supporter of biomedical research in the world. It has research going on from basic science to clinical trials, from rare diseases to common conditions like diabetes, cancer, and heart disease. But it has a particular institute focused on infectious disease which is poised, when there's an outbreak of this sort, to bring all kinds of scientific talent and resources to tackle the problem and put together an effort to design vaccines, but also clinical trials to test them. That same institute has been, in just the last ten years, leading the effort against Ebola, against Zika, and now against COVID-19.

On top of that, the NIH works particularly well in this situation by linking up with our colleagues in the private sector, because the industry has a huge investment in this area that we want to be sure is tightly coordinated. So back in April, I formed a partnership called ACTIV, which stands for Accelerating COVID-19 Therapeutic Interventions and Vaccines, that is now comprised of 18 pharmaceutical companies, multiple parts of NIH, the FDA, the CDC, the Department of Defense, the Veterans Administration, and part of HHS called BARDA [the Biomedical Advanced Research and Development Authority] — bringing all hands on deck to coordinate everything we're doing, both for vaccines and also for therapeutics.

That kind of partnership has been really crucial to make progress, but it's happened at an unprecedented pace. Usually partnerships like that between private and public sectors take a couple of years and a lot of lawyers to work out. This was basically set up in two weeks. Paul Stoffels, who's the head of R&D at Johnson & Johnson, and I are the co-chairs of the executive committee of that group — which now involves about 100 people who are literally working 24/7 to try to move all of this agenda forward. That has been astounding.

And what has you feeling best on the therapeutics front right now?
Well, we have made some progress. The antiviral drug Remdesivir, in a rigorously designed, NIH-managed clinical trial, did show benefit in terms of reducing hospitalization time and probably improving survival — although statistically that was not quite at the level of significance we generally consider proof. Ten days ago, our colleagues in the U.K., which is a group we've been working closely with, announced that their rigorous trial of dexamethasone, a steroid, showed that it improved survival, particularly for patients on ventilators. So those are two significant steps forward.

Right now, I think one of the things we're most hopeful about is to utilize the antibodies that are being made by people who have survived COVID-19. They got over it. Their antibodies apparently worked. Could we utilize that in a way that would help people who are really sick? That means trying such things as convalescent plasma — getting units of plasma from survivors and giving those to sick people. It's been done now on a fairly large scale, and we're just looking at the data to try to see how much benefit it provided. But an even more powerful way to approach this is to purify antibodies that

you know bind tightly to the virus and inactivate it, so-called monoclonal antibodies, and make those in an industrial format.

There will be trials of those, from about six companies that have been pushing that forward, starting in the next few weeks — again managed through this ACTIV partnership that I've mentioned, trying them on both outpatients and inpatients who have been infected by COVID-19 to see what benefit they might provide. I'm pretty optimistic about those. We know those antibodies have contributed to people getting better from this virus. So giving them to people who are currently ill ought to help.

All of the sudden you have arguably the most famous doctor in the world, Anthony Fauci, now reporting to you. What's the emergence of Fauci as a global celebrity been like from inside the NIH?
Well, Tony's been a hero within the NIH for a long time. I guess the rest of the world knows about him now. As the head of the Infectious Diseases Institute since 1984, he has certainly been through an incredible number of these frightening outbreaks of infectious diseases, starting with HIV and working through all the various influenza episodes, Ebola, Zika, and now COVID-19. Tony is a physician of enormous credibility. He is a doc who still takes care of patients, so he knows everything there is to know about what it's like at the bedside. But he is also one of the most knowledgeable and highly regarded experts in the science of infectious disease.

He's also just an incredibly effective communicator and has been playing that role brilliantly, as a member of the White House Coronavirus Task Force, to speak to the American public.

I've known Tony for 27 years. Initially, he was kind of a mentor to me when I first got to NIH and didn't know what the heck that was going on around this government facility. Now I'm his boss. But he and I, I think, have a very effective relationship. We talk virtually every night to catch up on what happened that day and what each of us is trying to accomplish the next day. I think that partnership has been extremely helpful, and it's very satisfying for me to work with somebody with such remarkable skills.

What's your broad assessment of the American response to this pandemic — spanning federal government, state governments, local governments, and just us as a society?
I think, for the most part, Americans have been willing to sacrifice a lot to try to address this issue. I think most Americans have understood that's not just for themselves; it's for other people around them, because we can't really put a stop to such a rapidly infectious pandemic unless we all take responsibility for that. The consequences have been quite severe for people who have lost their livelihood. The economic strain that has happened to many families has been totally unexpected and incredibly painful.

I especially look at the way in which this disease has hit underserved populations that were already suffering from health disparities and have now been hit even harder by COVID-19. I'm particularly thinking of African-Americans and Hispanics, but also anybody who's in a lower socioeconomic state and can't afford to sequester themselves at home because they've got to be out there in order to put food on the table. Those folks have been hit very hard.

I think for the most part Americans have been willing to say, "We've got to do everything we can to try to protect the vulnerable people around us." I am concerned, however, that the willingness to sustain this individual behavior seems to have been slipping a bit and maybe, in some instances, has

been encouraged as if we're now past this pandemic. We are not past this now. In fact, when you see what's happening just in the last week or so, it's clear that we are at risk for a surge of more cases and ultimately more serious consequences as people have gotten more relaxed. I think most Americans are still being careful, but it doesn't take a huge proportion of those being careless to give the virus its chance. We may be tired of COVID-19, but the virus doesn't care. It's out there, and 90 percent of Americans haven't yet developed any immunity to it and are still totally vulnerable. The chance of having major consequences is just as significant as it was back in February.

Again, I think most Americans have been appropriately sacrificial, but it's time to renew our attention to how you need to wear a mask because you might be the person who has the virus and is spreading it around without realizing it. That mask is not for you. That's for everybody around you. If you care about your neighbors, your family, the people that you encounter in the store — wear that mask. Social distancing is an important part of this, not gathering indoors — especially without masks — packed together. That's the worst thing you can do right now.

We Americans tend to be pioneers in individual behavior, but this is a time for individuals to moderate their behavior.

Yeah, this has unfortunately emerged as a new front in the culture war. As someone who is both an acclaimed scientist and a public Christian, what's your perspective on the pandemic as a cultural issue? Do you see any clear way around that?
It's one of the great tragedies of this current moment that scientifically based public-health measures have somehow been captured as cultural or political phenomena. Your chance of spreading the coronavirus to a vulnerable person has nothing to do with what culture you come from or what political party you belong to. Your responsibility is to try to prevent that from happening to vulnerable people around you. But our country's polarization is so extreme that it even seems to extend into a place like this — where it absolutely doesn't belong. That is really troubling because it's putting people at risk who shouldn't be.

On a happier note, what was it like to recently win the Templeton Prize, the prestigious annual award recognizing individuals for their efforts to bridge the gap between science and faith? That must have been a nice surprise.
It was stunning to get that phone call and to look at the list of previous winners and try to imagine how this could possibly have happened — the first prize winner being Mother Teresa, and other prize winners along the way people I have incredible respect for, like Billy Graham and Archbishop Desmond Tutu. I could only conclude the committee must have made a terrible mistake. I'm really grateful, just the same, because I'm an amateur theologian. I'm a pretty good scientist. But to be put on this roster with those heroic figures was beyond any expectation I ever could have had.

You have worked, in your capacity as a scientist, to fund a fair amount of brain research, and you've also written a book called *The Language of God: A Scientist Presents Evidence for Belief*. Before taking over at NIH, you started a foundation called BioLogos, which makes the case for a harmony between science and Christianity. What's your perspective, at this point in your career, on what consciousness is?
That's the big question in all of neuroscience. In terms of the scientific basis of consciousness, we really don't have a clue. In terms of the spiritual significance, obviously it's pretty important that we human beings seem to be special in our awareness of ourselves and our ability to imagine what other people are feeling at a given moment. All that is part of consciousness. I was an atheist when I entered

medical school. I was a Christian when I left — and it was much driven by this experience of trying to integrate the reductionist aspects of science into the much more fundamental issues I saw my patients wrestling with, like is there a God and does God care about me and what happens after I die?

Those are uncomfortable questions for an atheist 23-year-old, but ultimately they became totally compelling and required some investigation and some answers. Ultimately, out of that, it came to me that it makes a lot more sense to believe in God than to deny God's existence. A scientist isn't supposed to make assertions that you would call universal negatives, because you can never have enough evidence to do that, and yet that's what atheism calls you to do.

I surprised myself as I began to look at the pros and cons of belief versus nonbelief — that actually through science there seem to be a fair number of pointers, not proofs, but pointers toward the idea of a creator and a creator who was not only interested in creating something out of nothing, but also in having that something ultimately give rise to creatures with big brains who would have consciousness, who would have self-awareness, and who would have curiosity not just about nature, but also about who they are and what kind of spiritual creatures they might be.

It took me a couple of years to get through those many thickets of intellectual debate, but it led me then at that point in my life to see science and spirituality as not in conflict but actually quite compatible, quite harmonious, quite self- and co-reinforcing. People said my head was going to explode, that it would not be possible to both study genetics and read the Bible. I've never found a problem with this at all, despite the way in which some scientists have caricatured faith to make it seem incompatible. Most of those caricatures don't resemble my faith.

Similarly, the way that some people have caricatured science as a threat to God, that doesn't resemble the science that I'm doing. It's been a terrible, I think, consequence of our last century or so that this polarization has been accepted as inevitable when I see it not at all in that light. There are many interesting scientific questions that tap into the kind of area that you're asking about, like what is the neuroscientific basis of consciousness? What is the neuroscientific basis of a spiritual experience? If there is such a neuroscientific basis, does that make this spiritual experience less meaningful or more so? Those are fun conversations to have.

Very few people seem to stand publicly and effectively at the juncture of those two worlds. There are certainly some, but not as many as one might expect. From your perspective as head of the NIH, and someone who has also won the Templeton Prize — when you lie in bed at night, what gives you hope about the next 50 or 100 years for humanity? What are the really hard problems that test your optimism and your faith?

Boy, that's a big one. What is our future? I don't want to see a future where this science-versus-faith conflict leads to a winner and a loser. If science wins and faith loses, we end up with a purely technological society that has lost its moorings and foundation for morality. I think that could be a very harsh and potentially violent outcome. But I don't want to see a society either where the argument that science is not to be trusted because it doesn't agree with somebody's interpretation of a Bible verse wins out. That forces us back into a circumstance where many of the gifts that God has given us through intellectual curiosity and the tools of science have to be put away.

So I want to see a society that flourishes by bringing these worldviews together by being careful about which worldview is most likely to give you the truth, depending on the question you're asking.

This interview has been edited and condensed for clarity