

Medical News & Perspectives

Anthony Fauci, MD, on COVID-19 Vaccines, Schools, and Larry Kramer

Jennifer Abbasi

In late May, as coronavirus disease 2019 (COVID-19) stay-at-home orders and closures eased, George Floyd's on-camera death in police custody in Minneapolis sparked antiracist demonstrations across the nation. Some turned violent. With the protests and the pandemic colliding, fears arose that new COVID-19 outbreaks could soon follow.

The possibility of protest-related infections came up when JAMA Editor in Chief Howard Bauchner, MD, [spoke by video with Anthony Fauci, MD](#), director of the National Institute of Allergy and Infectious Diseases

+
Audio and Video

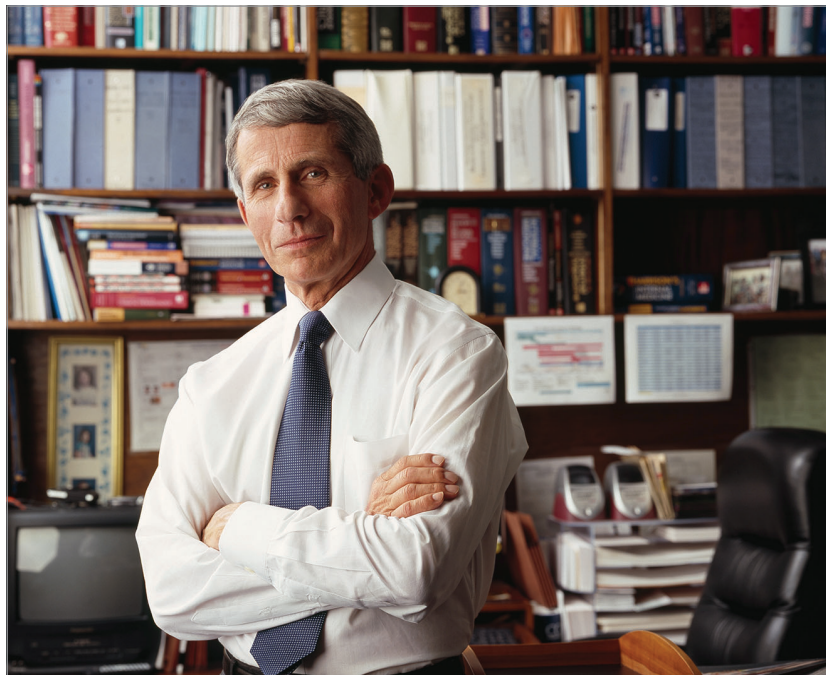
and a member of the White House's coronavirus task

force. Their June 2 discussion ranged from COVID-19 vaccine development to immunity passports to the recent death of prominent AIDS activist Larry Kramer, whose relationship with Fauci evolved over decades. The following is an edited version of the conversation.

DR BAUCHNER: A phase 3 COVID-19 vaccine trial will start in July. Could you talk a little bit about what that will look like?

DR FAUCI: It's going to be a randomized placebo-controlled trial of 30 000 individuals and the first of the candidates, which is the Moderna mRNA [messenger RNA] vaccine that was developed at the NIH [National Institutes of Health] and the Vaccine Research Center. It's now done its [phase 1 study](#). The company started the beginning of a phase 2 study literally a few days ago, and we're preparing the sites now for the phase 3 study, which are [at] both international and national sites. It's going to be a big trial because we want to get as many data points as we possibly can.

Very soon thereafter, or possibly even simultaneously, the AstraZeneca [candidate](#) that was developed in the UK.... That's going to be very closely aligned with the study I just mentioned. And then some of the other studies are going to start maybe toward the



end of the summer. So there's an array of at least 4 and possibly 5 trials that I am aware of and directly or indirectly involved in, either in the development of it or in providing some of the clinical support for the sites.

DR BAUCHNER: How long does a phase 3 trial have to last to know if there's effectiveness? People in the control group need to see disease, as do people in the vaccinated group.

DR FAUCI: If you have dribs and drabs of infection, even though you have 30 000 people, it could take months, and months, and months, and months to get an answer. If you start the phase 3, and then when you're a month or two into it, you happen to get in an area that you highly vaccinated where you've had a big surge of cases, you could get your answer pretty quickly.

DR BAUCHNER: Will the trial be focused on healthy, younger individuals?

DR FAUCI: It will be predominantly people ages 18 to 55, but there also will be those who are elderly and those who have conditions that are underlying and comor-

bidities. So it's going to be the entire spectrum, actually.

DR BAUCHNER: Are you optimistic?

DR FAUCI: I'm cautiously optimistic that, with the multiple candidates that we have with different platforms, we're going to have a vaccine that shows a degree of efficacy that would make it deployable. The reason I think so is that one makes a pretty good immune response against this coronavirus. Even though the deaths are profound for this outbreak—over 105 000 deaths so far—the majority of people make an immune response which clears the virus. If the body is capable of making an immune response to clear the virus and natural infection, that's a pretty good proof of concept to say that you're going to make an immune response to a vaccine.

However, having said that, there's never a guarantee, ever, that you're going to get an effective vaccine. I'm concerned a little bit more about the [durability of response](#) than I am about whether you're going to get a protective response. Because if

you look at the duration of protection, when you recover from one of the several benign coronaviruses that cause the common cold, the durability of protection is only measured in a year or less, as opposed to some of the other infections where you could have [a] 10-, 15-, 20-year degree of protection.

DR BAUCHNER: If we get to the fall and there's a good vaccine candidate, what happens with the production of that candidate?

DR FAUCI: That's what's going on right now that's very unique in [vaccine development](#). We and the companies, and the federal government predominantly, are doing this at risk. We're going to start manufacturing doses of the vaccines way before we even know that the vaccine works. We may know whether it's effective by maybe November, December. By that time, we hopefully would have close to 100 million doses, and by the beginning of 2021, we hope to have a couple of hundred million doses. So it isn't as if we're going to have to wait a year to rev up to millions and millions and millions of doses. That's going to be done as we're testing the vaccine. That's what *at risk* means.

DR BAUCHNER: Can you see a role for monoclonal antibodies as we try to sort out schools and colleges and protecting the elderly and nursing home people?

DR FAUCI: Right now we have a major push on a program to develop monoclonal antibodies, [convalescent plasma](#), and hyperimmune globulin, all of which are founded on the same principle of using an antibody that is directed against the virus for either prophylaxis or treatment. And I think you're going to see it's going to be for both. We'd like to have available for those who are at risk—the elderly and those with underlying conditions—either monoclonal antibodies or convalescent plasma. That's a very, very high priority.

DR BAUCHNER: People always raise the issue about vitamin D and whether or not it could be helpful in treatment. Do you have a sense of vitamin D and its role with COVID-19?

DR FAUCI: I think it really relates to the importance of vitamin D in host defense against infection. There's no doubt that if you are vitamin D deficient, you might have a poor outcome or a greater chance of getting into trouble with an infection. Most people in the developed world are not vitamin D deficient, so adding additional vitamin D may not

actually have a substantial clinical effect. That doesn't lessen the importance of a normal level of vitamin D. In some of the developing countries, there have been studies with tuberculosis and other diseases. Those who are vitamin deficient, including vitamin D and vitamin A, they do worse.

DR BAUCHNER: Azithromycin has come up repeatedly. Some people have said, "Well, the reason azithromycin isn't working is because you're not combining it with zinc." I'm not sure if there's much of a basis for that argument. Do you have a sense of zinc and azithromycin?

DR FAUCI: I don't think there's enough data at all to give you any firm conclusion as to the benefit of azithromycin alone vs the benefit of azithromycin plus zinc. There's anecdotal stuff all over the place, as you well know. There are studies now that are looking at a combination of hydroxychloroquine and azithromycin compared to a placebo to see if there's any effect there. That's what we need, as you well know, and you and I have both said that many times.

DR BAUCHNER: Both you and I are strong believers in a randomized clinical trial.

DR FAUCI: And, unfortunately, there's a paucity of that.

DR BAUCHNER: It's been a difficult week for the United States. The death of Mr Floyd has been painful and has clearly moved the pandemic to below the fold in many of the newspapers—rightfully so. States have opened up more aggressively and less aggressively. Do you have a sense of what's happening in the states that have opened up early, and whether or not there's been an increase in disease that is of great concern?

DR FAUCI: There has been a great deal of variability in the states and their opening. Some have leapfrogged over the benchmarks—the gateway from phase 1 to phase 2. We've seen pictures and TV clips of people with no masks very closely congregated on a boardwalk, on a beach, in a pool. That has been and continues to be a concern to me. We're not going to know what the effect of that is for at least a couple of more weeks because in order to determine whether a particular behavioral change has an effect on the incidence of a particular infection, like the coronavirus, it likely is 3 weeks or more. We're only a week-and-a-half to 2 into that, so we need to wait and see.

DR BAUCHNER: Do you have a sense of immunity passports?

DR FAUCI: An [immunity passport](#) I think would be an appropriate thing, possibly, if we knew how long the duration of antibody protection was, and whether or not a certain titer does or does not protect. If someone is infected and they're antibody positive, there is not a lot of data to say how well protected they are against reinfection. Given the fact that coronaviruses in general have a durability of infection that is not measured in multiple years, I think there's a lot of questions about the utility of immunity passports. I'm not ruling it out. There's a possibility that we'll be using them, but it's not a perfect solution.

DR BAUCHNER: Can we get to a way in which the [schools open](#) in the fall? It's going to become a huge issue. I worry about the decisions that mayors and governors are going to have to make. It's 55 million children.

DR FAUCI: I think we can, but we've got to remember that we have a very large country. It's a diversified country. The difference between the New York metropolitan area and Casper, Wyoming, the difference between New Orleans and Des Moines, Iowa, is very different, particularly when you have many, many counties where there is almost no infection at all. Under those circumstances, I think it's much easier to make a decision about opening the schools.

If you're in an area that has a considerable degree of active, ongoing infection, you might have to make a tough decision. It may be either delay or do a modified schooling. You can do something as distant as online teaching, or teaching morning vs afternoon session with different cohorts in each, with a much, much diminished crowd. You could have the seats further apart. You could do outdoor to a certain degree.

It depends on where in the United States you are and the status of infections in the region. So the answer is yes for some and caution for others.

DR BAUCHNER: Anything new on asymptomatic spread and PCR [polymerase chain reaction] testing? Say someone is PCR positive and then they get well. How long are they potentially infectious if their [PCR test](#) lingers to be positive for a week or 2. Is there anything new that's crossed your desk?

DR FAUCI: No, but let's just review very quickly. The percentage of asymptomatic carriers was first felt to be less than 5%. It's more likely 25% and, in some [estimates](#), even as high as 50%. We know for sure that when people recover, they may be positive for PCR for days and days and days, even though they're not infected. We're starting to get a feel that it depends on the cycle threshold, which means how many times it takes you to do the PCR cycle to get a positive hit. If it's 35 or more, even though it's technically positive, the chances of that being replication competent are extremely low. In other words, you could have a PCR-positive test and yet still not be contagious.

DR BAUCHNER: Are most people developing IgG and IgM [antibodies](#)?

DR FAUCI: They are, but the titers really, really vary. I have examples of people who clearly were infected who are antibody negative. They probably have such a low titer of antibody that it's below the level of the cut-off. And then there are others that have very robust antibody responses. It isn't a uniformly robust antibody response, which may be a reason why, when you look at the history of the common coronaviruses that cause the common cold, the reports in the literature are that the durability of immunity that's protective ranges from 3 to 6 months to almost always less than a year. That's not a lot of durability of protection. It may be completely different with this coronavirus, SARS-CoV-2 [severe acute respiratory syndrome coronavirus 2]. It may be that people induce a response that's quite durable. But if it acts like common coronavi-

ruses, it likely is not going to be a very long duration of immunity.

DR BAUCHNER: Tony, a very close friend of yours last week passed away, Larry Kramer. You had a very interesting personal and public relationship with him over many years. Can you say a bit about Larry?

DR FAUCI: He was truly an iconic figure. He demanded a seat at the table beginning with the very early years of HIV/AIDS. In order to get the attention, he became extremely iconoclastic, and very abrasive, and very outlandish. At the time, back in the '80s, I was the face of the federal government with HIV. So he decided he was going to viciously attack me, call me a murderer, call me incompetent, call me the enemy. So that was the beginning of our relationship.

But then I did something that I'm proud that I did. I said, "Let me listen and see if I can empathize with what's going on." Not only with Larry, but with the entire activist community. So I reached out to him and we went from being adversaries to being really good friends. I wound up helping to take care of him. When he got seriously ill, I arranged for his liver transplant.

Even though after maybe 20 years of knowing each other, he still used the opportunity to publicly criticize me as representative of the federal government. I'll give you an example. He came down to Washington for a reunion or something like that. And we had dinner, we had a great time. Then a week later, Ted Koppel on *Nightline* invites us to be on the show together. So I thought we would have a warm kind of conversation. He gets on the show and he starts saying, "Tony Fauci,

you're a disgrace. You're an embarrassment. You're not doing enough. You're terrible. You're just a government shill." And I'm sitting there saying, "What's going on?"

After I got home, like 10 minutes later, he gets on the phone and he says, "Hey, Tony, that was great, wasn't it? We did wonderful." And I said, "Larry, you just trashed me in front of 10 million people. What do you mean it was wonderful?" He says, "Oh no, but we made a point. We made a point."

He was an amazing guy who was totally devoted to the welfare and the good of the gay community. When a disease afflicted them that he felt people weren't doing enough about, that's when he unleashed all his fury.

DR BAUCHNER: Your equanimity, does it come from your parents? Does it come from your Jesuit education? It's extraordinary under the face of remarkable criticism, almost always unfair.

DR FAUCI: I think it does come a lot from my parents. My father was very much of a tolerant person who would accept people for what they are and very rarely ever criticized anybody. I went to a Jesuit high school in Manhattan, and from there I went to a Jesuit college. I think it was just right for me because I had always been interested in public service and not being somebody that ever attacks anybody, that accepts them for who they are and what they are. So it was kind of the perfect atmosphere to me to be educated in, and I just carried it along with me. ■

Note: Source references are available through embedded hyperlinks in the article text online.