

The year ahead—exclusive interview with Anthony Fauci, MD, NIAID director

Watch the exclusive interview with Anthony Fauci, MD, during the November 2020 sections' meetings about what lies ahead for physicians and medical students during the COVID-19 pandemic.

Featured topic and speakers

AMA CEO and EVP James Madara, MD, interviews Anthony Fauci, MD, director of the National Institutes of Allergy and Infectious Disease, about the COVID-19 pandemic and what lies ahead for physicians and medical students.

Learn more at the AMA COVID-19 resource center.

Speakers

- Anthony Fauci, MD, director of the National Institutes of Allergy and Infectious Disease
- James Madara, MD, AMA CEO and EVP

Note: This transcript has been edited for brevity and clarity.

COVID-19 vaccine efficacy, safety & future outlook

Dr. Madara: Well, welcome to the 2020 AMA Section Meetings. As always, we use this time to shape policy in the interest of the health of our patients. Now, obviously, the pandemic makes this time unique. So it's fitting that to get this kicked off, we have the privilege of interviewing Dr. Anthony Fauci, someone you know really well. Dr. Fauci, as you know, has served as Director of the National Institute

of Allergy and Infectious Disease since 1984, and has been an extraordinary public servant and also a scientific leader in the field for more than four decades. Most recently, he has been recognized for his depth, scientifically grounded leadership related to the COVID-19 pandemic, and simply put, he has been the reliable source of facts based on the best evidence at the time as this pandemic unfolded with surprising and sometimes nearly astounding twists and turns. He served similar leadership roles in the past during HIV, H1N1, and the challenges related to a bull as well. So Dr. Fauci, thank you very much for being here today and being such an effective voice for reason and science in this difficult time.

The topic today is the year ahead, maybe it should be the two years ahead, and I'd like to begin with what's on the headlines today and the COVID-19 vaccines. And assuming that one or more of the vaccines are shown to be safe and effective and a significant portion of the population is vaccinated, how do you see the next one or two years unfolding? And then part of that question also is I sense almost implicitly when you hear people speak, read media, that there's a sense that once a vaccine is out there, the door is closed and the pandemic's over, which doesn't sound too mathematically possible. So, where do we stand and how should we be looking at this?

Dr. Fauci: Well, I think the issue with vaccines is actually good news in a time of considerable concern and stress about the outbreak. We have six candidates that the United States government is helping out with either in the development of or in the facilitation of the testing of. Five of those six are already in phase three trial, and two of them, the Moderna and the Pfizer product, started phase three trials on July the 27th. They're fully enrolled. And as you and I are speaking right now, data are being collected regarding efficacy and safety. And we hope that as we get into November and maybe in the early December, we will get an answer as to whether or not one or more of these candidates are safe and effective. I'm cautiously optimistic that we will have a safe and effective vaccine and then we'll be able to start distributing doses reasonably soon thereafter in a graded fashion to individuals with the highest priority such as healthcare workers and people on the front lines.

What that's going to mean apropos of your question is that there are two factors that are going to determine the degree to which public health measures are going to be playing an important part in protecting our country and the people in our country. First of all, how effective would the vaccine be? And as importantly, how many individuals are going to opt to take the vaccine? Because there is a considerable degree of reticence skepticism about the vaccine that we need to overcome by transparency and messaging and reaching out to the community. But if we get a reasonably effective, 75% effective vaccine, and a substantial proportion of the population takes the vaccine, I think we're going to be going in the right direction towards approaching some degree of normality as we head into 2021 in the second, third, and fourth quarter of 2021.

So that's good news. Obviously, you can't declare victory until you get the results of whether or not the vaccine is safe and effective. But as I mentioned, I'm cautiously optimistic based on data that we have

from the animal studies, as well as from the phase one trial showing a robust degree of neutralizing antibodies in those early phase one studies. So things are looking good in that regard.

Safety of mRNA vaccines

Dr. Madara: You brought up the issue of safety, and recognizing that some of the vaccines are new platforms, these mRNA vaccines, does it take any extra caution or how do we think about safety in the context of a new platform?

Dr. Fauci: Yeah. Well, we're always focusing on safety, whether it's an old or a new platform, but you're absolutely correct. When you're dealing with a new platform like an mRNA, you want to stay heads up for maybe different types of adverse events that you're not used to seeing in other types of platforms. So you're absolutely correct. There's going to be a real sharp heads up to make sure that we don't miss any unanticipated, severe adverse events. And if they're severe, it's very unlikely that you're going to miss them, but you want to make sure you keep your eye out on them.

Participation in ongoing vaccine trials

Dr. Madara: Do we have any worries once a vaccine is proved and shown to be safe and effective that people in other trials for other vaccines might leave those trials to get something that's approved? How do we think about that possibility? Is there something we should be doing around that?

Dr. Fauci: Well, we're actually prepared for that eventuality that you might see a vaccine to get chose to be safe and effective in December and then there's another trial that's not going to end until March. So what happens to those people in those trials? It's really going to depend on a couple of factors, A, how effective a vaccine is. Now, if a vaccine is shown to be 95% effective, then it's very likely that what you'd have to do besides breaking the blind and giving it to the people who are in the placebo arm of that given trial, you might want to modify. And again, I say might because I don't want to get ahead of the people who are designing the trials, but one of the options would be to make the placebo arm in that second or third trial, the actual vaccine that was just shown to be effective.

So you could do a non-inferiority trial, which would require getting more people enrolled, but you could compare the unproven vaccine with the one that's proven. So if it's as good, well, then you'll know it's as good. It's 90% effective. If it isn't, well, you want to find out how much it isn't. If it's 85%, that's pretty good. If it's 40%, not so good.

Biology of the virus & vaccine development

Dr. Madara: This is maybe a bit of a theoretical question, but it's noted that knowing that what we do about the biology of the virus, the spike protein seems to be something that one would go after. And if one were devising a vaccine toward a surface element, it would be hands down logical to go in that direction. So, every company, you can imagine thinking that way, but when you think of the worldwide portfolio of vaccines, is it wise or not to have the vaccine dominated by one target?

Dr. Fauci: The answer is no, but this target is so clearly important in the binding of the virus to its cellular receptor, which is the ACE2 receptor, that you would have to have the predominant effort being using the spike protein receptor binding domain as the target of the neutralizing antibody. But you're absolutely right. You never want to put all your eggs in one basket. And that's the reason why the next generation of vaccines certainly would include something above and beyond the receptor binding domain of the spike protein. But you would really have to go with that first and predominantly from everything we know in animal studies and even in in vitro physiology.

Pathways to herd immunity

Dr. Madara: So one of the things you brought up was the pathway to herd immunity. And you mentioned a vaccine say could be 75% effective, and then I understand the floor for acceptance is around 50% and you'd even hope for something better than 75%. When one starts playing with numbers and you think that maybe to get to herd immunity, you would have to have 70% of the population have an immune response and maybe 50 or 60 million Americans will have been infected by the virus, you start playing with those numbers a bit and it's hard to get to the 230 million that would be 70% of the 330 when you start altering each of the variables. Is that a worry for us? Or how do we... Do we think that we're just going to have to have more infection than the population in maybe a slow way, so the health system can deal with that, or how should we be thinking about that?

Dr. Fauci: Yeah, I would prefer to look at it in a more positive way. I understand where you're going is to lessen the dependence on infection and heighten the dependence on vaccine. And the way... If you have a vaccine that's 78% effective, you can't make it any more than 78% effective, but what you can do is get more people vaccinated. So there's two parts of the equation. There's the efficacy of the vaccine itself and then there's the number of people who take the vaccine. So what we need to do to really put a lot of the effort on the herd immunity that's vaccine induced, we need to just get a lot more people vaccinated.

Understanding the death rate

Dr. Madara: The death rate now compared with the terrible months of March and April seems attenuated. To what part is that attributed that we just know how to deal with this better versus testing versus we're dealing with a more resilient population now getting infected? How do we put all those things together and understanding that lower death rate?

Dr. Fauci: Well, it's all of the above. First of all, as we've learned with every disease that's new and that we've been challenged with, from HIV to other types of diseases, we just get better at treating people. More experienced. You know what works, you know what doesn't work, including just fundamental non-pharmacological approaches, whether to put people on ventilators or not, whether to make oxygen be much more prevalent than intubation. Those are the kinds of things that we've learned.

Number two, we have treatments now. We know that dexamethasone clearly diminishes the death rate in people requiring mechanical ventilation and/or high flow oxygen. We have Remdesivir for hospitalized patients who have lung involvement. And also we're starting to see a younger population get infected. In fact, if you look at the age range for people getting infected now versus people that were getting infected in the spring, there's almost a decade difference of being younger now, mostly because college kids coming back to school, they're getting infected more. Ultimately, they're going to wind up affecting people in the community, but they're the ones that are driving the infection. So it's age, experience, and better drugs.

Current COVID-19 treatments

Dr. Madara: And when we think of those drugs and the therapeutics that are coming out, it sounds like the dexamethasone is cheap. Something we can take to the bank now. Remdesivir, it seems like you hear one thing from WHO, another thing in terms of the FDA approvals, how should we be thinking about that compound?

Dr. Fauci: Well, it's not a knockout drug for sure. It's a drug that has a beneficial effect in diminishing the time to recovery, but it isn't a blockbuster in the sense of it really makes things dramatically different, but it does have a beneficial effect. You don't want to discount that, but you don't want to expect it to do something that it's not doing.

Dr. Madara: And when we think of anticoagulant use, are they used in very specific subpopulations? And how do we think about that?

Dr. Fauci: Well, usually with advanced patients who have beginning of organ system function, we're starting to do it prophylactically now. We're starting to see that... We're not starting, we know now for sure that it's the case that there is a degree of hypercoagulability that's associated with advanced disease. You see that in curious microthrombi in small vessels of different organs, kidney, heart, even nervous system, but you also see more dramatic thromboembolic phenomenon sometimes leading to strokes in otherwise relatively normal people. So there's no doubt that there's hypercoagulability and either treatment or prophylaxis with a variety of anticoagulants is something that is now common practice with COVID-19.

Role of secretory IgA & COVID-19

Dr. Madara: There are some people that work in the innate immunity and mucosal surfaces are wondering what is the role of secretory IgA? There's such a big defense factor in GI and airway and I don't hear much about it. Do we know much at all about the role of secretory IgA?

Dr. Fauci: No, we don't know specifically with regard to COVID-19, but given the history and our knowledge over many, many years of secretory IgA, I cannot imagine that it doesn't play a role when you have a respiratory borne illness that enters and resides in the upper airway and then goes to the lung, as well as the fact that you have a considerable degree of GI involvement in some individuals. So I can't imagine it's not playing a significant role.

Long-term side effects of COVID-19

Dr. Madara: So the sections that are meeting now are part of our House of Delegates, 180 medical societies, all state and specialty branches of military medicine, and the leadership of those societies are part of the recipients of this knowledge. And in medicine, as you know, in the last half century, we've moved from episodic to more chronic disease. And now with COVID, we find these very odd symptoms and effects in a longer period of time. So how should physicians be thinking about that? On one hand, do we have to prepare for yet another source of chronic disease or are these side effects uncommon? And how do we in our practices, when we see patients with a history of COVID that seemingly have recovered, how do we think about odd things that seem to manifest themselves that just strike you as maybe not usual for this particular patient?

Dr. Fauci: Well, you're hitting on something that is a work in progress and that it's evolving. We do know for absolutely certain that there is a post-COVID-19 syndrome, referred to sometimes as long COVID, chronic COVID, long haulers. It's got different names. I think we better get an appropriate medically reasonable name for them soon. And what it is is that variable percentages, and we're

studying a number of cohorts now that the NIH is funding. And in fact, we have a program right here in Bethesda, in which we're looking at a large cohort of post-COVID survivors. And we're seeing variable percentages in anywhere from 25% to 35% or more have lingering symptoms well beyond what you'd expect post any viral syndrome like influenza and others. It's fatigue, shortness of breath, muscle aches, dysautonomia, sleep disturbances, and what people refer to as brain fog, which is a non-medical way of describing a lack of ability to concentrate or to focus.

So there's no doubt that that is going on. That can last anywhere from weeks to months. And it might even be longer. And the reason we don't know it's longer because we've only been involved with this syndrome for about 10 months right now. So it could be even longer than that. The other thing we're seeing that's really quite curious and somewhat disturbing is that there have been a number of studies of people who have recovered virologically from either moderate disease or maybe severe disease, which required hospitalization. You didn't have to be hospitalized to get this, but when a bunch of cardiologists did MRI scans of the heart, they found that even in asymptomatic people, about 60% of them had indication of inflammation in the heart.

Now, that could be of no ultimate clinical consequence, which would be fine, or it could down the pike lead to things like premature atherosclerotic cardiovascular disease, unexplained arrhythmias, cardiomyopathies. We don't know what it's going to mean. Hopefully, it won't mean much. But the findings there are real, and that's one of the things we really want to keep an eye on.

Duration of immunity

Dr. Madara: What do we know now about the duration of immunity and the immune response after infection or after vaccination or either one? And to the degree that we don't have complete knowledge, is it fair or not to transpose the length of immune response in other coronavirus family members or not? How do we think about that?

Dr. Fauci: Yeah. Well, another good question, but unfortunately, an incomplete answer, because we don't know the answer. Let me tell you what we do know. Well, let me tell you what we don't know first. We don't know the durability of antibody responses which may be strictly correlated with protection or not, because it may be that the antibody level goes down, but your memory B cells and your T cells can also provide protection. But we don't know how long the serum antibody titers last because we just started the vaccine trials. From what we know about the common cold coronavirus, the four viruses that are human coronaviruses that cause the repetitive common cold that we all experience every year, usually during the winter months, is that the duration of immunity to that is not lifetime immunity. It's measured in several months to a year or more, unlike measles, which as you know, is like it lasts forever with a 98% protection.

We don't see that with common cold coronavirus as what we don't know is that when someone gets sick with a systemic component of COVID-19, not just an upper airway, we don't know how long the antibody protection is going to last. It might actually be significantly longer due to the systemic nature of the infection, because if you get just an upper airway infection, you're not eliciting the systemic immune response, it's mostly a local immune response. But when you get enough disease to put you in the hospital with acute respiratory distress syndrome or other manifestations, it could be that the immune response is going to last significantly longer under those circumstances.

Physicians' responsibilities during a pandemic

Dr. Madara: You've been immersed in this pandemic, as you have been in others. Are there observations related to what the physicians', whether the physician is in government or outside of government, responsibilities and duties should be during a pandemic? Is it working pretty well or do you see gaps?

Dr. Fauci: No, I think it's working very well. What we all should be very proud of is what our physician population at the local level is doing. People in the towns, the counties, the cities who are in the hospitals, be they local hospitals or big city tertiary care centers, we're seeing our healthcare workers, our physicians, our nurses, and other healthcare providers really putting their lives and their safety at risk continually by taking care of individuals with a disease that has the potential to kill you and that is highly transmissible. So I think that this is a proud moment for the medical profession. And I think that we should be really aware of that.

Patients' hesitation about vaccines

Dr. Madara: How should physicians deal with patients that are hesitant to get vaccines when they come out? Do you have advice there?

Dr. Fauci: Yeah, one thing is you shouldn't criticize them for that because that's going to get you nowhere. If you have somebody that's an anti-vax approach, you don't want to ridicule them for being, but you want to try and explain to them what the reason is for getting vaccines and why the risk benefit ratio it weighs so heavily towards benefits. Some people... Well, there's going to be a hard core group of people who are not going to want to get vaccinated no matter what you tell them, but there's also a larger proportion and group of people who've because of misinformation, they shy away from getting vaccinated.

And the easiest way is in a non-pejorative, instructive way to try and educate them to what the facts are concerning the vaccine. Go over the data with them and explain why it's important for them and their families to get vaccinated. I have found that to be very effective. I think when you start getting frustrated with people who don't want to be vaccinated and you have a tone of blaming them for that, that's not going to win anybody over.

Advice for physician leaders

Dr. Madara: That's very helpful. Thank you. We want to be respectful of your time, but I can't end without asking you something about your own service. You've served with six presidents. And when you do the calculation, it's astonishing that it's almost 15% of the totality of presidents of the United States. So you've seen, I'm sure that folks have had very different styles, the parties at different times have had very different styles, and you've had to adapt successfully and pivot, I'm sure, in many circumstances where the environment around you changes. What makes you effective across this long period of time? What kind of advice can you give physicians as leaders based on your own experience?

Dr. Fauci: Well, I think you just need to stick purely to the science and evidence and data and any recommendations, discussions, guidelines that you're involved with. Opinions that you give have to be based purely on the science. And just stay completely apolitical. Don't get involved in any of the political aspects and just focus on what your job is as a scientist and as a physician. You do that, you'll be fine.

Dr. Madara: We've been focused on that. It's sometimes hard to do, but it is a really important piece of advice. I really want to thank you on behalf of the AMA and House of Delegates for this time. It's very insightful. We've all learned a lot. And we all... So it would be wrong not to recognize our gratitude for your leadership at this time. Thank you very much, Dr. Fauci.

Dr. Fauci: Thank you. It's a pleasure to be with you. Thank you for having me.