Episode: Ethics Talk Videocast Transcript – Vaccine Ethics and the Novel Coronavirus (SARS-CoV-2)

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[bright theme music]

TIM HOFF: Welcome to another special edition of *Ethics Talk*, the *American Medical Association Journal of Ethics* podcast on ethics in health and health care. I'm your host, Tim Hoff. This episode is an audio version of a video interview conducted by the Journal's editor in chief, Dr Audiey Kao, with Dr Arthur Caplan. Dr Caplan is the Head of the Division of Medical Ethics at New York University, Grossman School of Medicine, and he joined us to talk about the development, production, and use of potential vaccines against the novel coronavirus, or SARS-CoV-2. To watch the full video interview, head to our site, JournalofEthics.org, or visit our YouTube channel.

DR AUDIEY KAO: Good afternoon, Art, and thank you for being a guest on *Ethics Talk* today. [music fades out]

DR ART CAPLAN: Very happy to be here. Thanks for having me, Audiey.

KAO: So, Art, as you know, creation of a safe and effective vaccine to combat the global health threat posed by SARS-CoV-2 has been characterized by some as a race against time and a competition among companies and countries. To speed creation of this vaccine, you and others have advocated for human challenge vaccine trials. Can you explain to our audience what these trials are and why you think they are appropriate in this case?

CAPLAN: Sure. I think it's a really important discussion to have. The world faces a lot of damage, both in terms of health and destroyed economies, particularly in poorer countries where starvation is the consequence of closing down your economy. So, finding an answer is crucial. And our politicians are telling us that. That's why they talk about things like Operation Warp Speed in the United States, why the British have said they're going to devote billions to vaccine research. The Chinese have said so, too. So, the stakes in terms of vaccinating our way out of this pandemic are huge. The damage, I think, justifies thinking about challenge trials. And the way I sort of explain them to you is to say the first question is, would we ever think about deliberately infecting a subject with a dangerous and sometimes deadly agent? And that's what a challenge trial does. It gives a person something known to be nasty, toxic, unhealthy. Most of the time, historically, it's been something like exposing people to pollutants to see whether they get biochemical changes that indicate trouble. In terms of physiology, you might see challenge studies in programs like the astronaut corps where somebody says, gee, I wonder how long somebody can be centrifuged before they pass out. And they literally—there's no benefit to them—they're just going to do a physiological challenge and see what the answer to that question is.

KAO: Right.

CAPLAN: With the stakes high, with the world in dire straits health wise and economy wise, that puts the question of could we get data more quickly by giving people the COVID-19 virus deliberately on the table? So, the first part of my answer is, I think it's worth considering because the stakes right now are so high. So, what is it exactly? You would try out new vaccines after testing them in animals and in human volunteers, at least for safety, in what's called a Phase 1 study, usually a small number of people: 20, 10. Then you do some dose studies to see what might produce an antibody reaction that you thought, hmm, that might be good enough to help confer immunity. But then you launch the challenge study to say, look, we're going to, having immunized you, we're going to test whether this vaccine works by giving you a purified form of this virus, literally injecting it into you and knowing that what we have to rescue you should you become sick, is pretty poor: remdesivir, maybe some other antiviral agents, way experimental, but we don't really have a rescue therapy for somebody who got sick.

KAO: So, if I can just interrupt you on that point, you mentioned remdesivir. So, that's the only demonstrated treatment for COVID-19 so far, and it's only been shown to shorten hospitalization, not actually reduce mortality. So therefore, should we consider human trials, human challenge trials, at this point before we actually have proven treatments that reduce mortality are available?

CAPLAN: So, certainly, some people have argued no, but I would argue yes. And the reason I say that again is high stakes. Plus, if we're testing vaccines the standard way, what you rely on is natural infection to see how well your vaccine works. But despite some of these optimistic predictions about we'd get an answer in six months, we're not going to get an answer in six months if we're waiting for natural infection in a 30,000-person study, which is what you see in vaccines. So, you're waiting and you're waiting, and the virus ebbs and flows. And that means people are dying all around the world because of the virus. So, it's a dire situation with many deaths. Even though we don't have a rescue, if we properly got informed consent from the subjects and said, "Should you become sick, we don't really have anything that will save you. If you're lucky enough to survive on a ventilator or make it through kidney dialysis, we got this drug that might speed up your recovery a little bit. But we don't have a agent to rescue you." Normally, we wouldn't even consider doing a challenge study without that. We've done them with malaria, but we have different types of interventions we can use there to try and rescue somebody. We've done them with cholera, and we have rehydration, which helps a lot. But here we don't. So, my defense rests on the idea that you understand what you're doing.

KAO: Yeah. You mentioned a couple of times now that obviously, this infectious disease outbreak is a global pandemic. And so, that brings into the question of where human challenge trials are conducted as being a very important consideration. As you know, prior to the current pandemic, some called for conducting human challenge trials in low-and middle-income countries where many relevant diseases are endemic. But this raises many issues about who bears the risk and who reap the benefits. Can you speak to these concerns?

CAPLAN: Yeah, that's a great question. During Ebola, what you said, Audiey, was proposed: a challenge trial for an Ebola vaccine. Weirdly enough, we got on top of Ebola with therapeutic drugs, and we didn't really actually get a vaccine trial. However, you may remember some vaccines were tried without any Phase 3 studies on an emergency basis. So, that was about as risky and as ethically controversial as you could get. I was on the Ebola WHO Ethics Committee at the time. I did not like the idea of just vaccinating without

anything. So, we've seen desperation. It also creates distrust in some parts of the world. People just say, "Look, they're going to use us as guinea pigs."

KAO: Yeah.

CAPLAN: They wouldn't run that in Britain, or they wouldn't try that in Connecticut. So, sure, they're happy to do it in Sierra Leone or Tanzania or Myanmar or someplace like that. But the reality is, I think the first challenge studies will have to be done in facilities that can at least have good hospitals, at least have the best standard of care, such as it is. I don't think you're going to see it done initially in lower-, middle-income countries. I think they just don't have the infrastructure to support it. There will be an issue, though, which we can get to later: let's say we got a vaccine. If the U.S. spends a lot of money to develop one in Operation Warp Speed, or China says, we got one, are they going to share it? And are they going to make it available to these poorer countries? I think justice says you should. Even epidemiology may say you should, if that's where the flare ups are. I don't know that we have the power in place that will say you must do it.

KAO: Yeah, I think we'll touch on that a little bit later. But to switch gears from the development of a potential vaccine to its production and distribution. As you know, to encourage the development and deployment of medical countermeasures during a public health emergency, the Public Readiness and Emergency Preparedness Act, or PREP Act, authorizes the Secretary of Health and Human Services to limit legal liability related to the administration of countermeasures such as vaccines. In February, the HHS Secretary invoked the PREP Act and declared COVID-19 to be a public health emergency. On the face of it, these liability protections seem necessary to facilitate the needed widespread production and distribution of SARS-CoV-2 vaccines. That said, Art, what potential risks are posed by these legal safe harbors, and what should be done to minimize harms?

CAPLAN: Huge issue. Not getting the attention it deserves, I don't think. One issue is, if you have immunity, are you encouraging people to move forward with vaccine candidates with less data than they might have otherwise? Are they going to take more risk because they think, mm, I'm insured. I'm protected. It's not that they would do crazy things, but maybe at the margins you might see people saying, "We got to go faster. We got to speed up. We have to get this thing out there. Plus, we have immunity." So, that makes me nervous. Historically, whether it's been polio vaccine or in 1976 swine flu vaccine, we saw manufacturing mistakes trying to go quickly.

KAO: Right.

CAPLAN: And we can't do that. I also worry what anti-vaccine people are going to say if they say, "Well, they've issued immunity." There are a lot of people up on the Internet trying to stoke up resistance to vaccination. They've been there long before COVID, and they're growing in their voice trying to make alliances with other people they think might be nervous about government assurance that everything's okay. If you come out and say, "Oh, well, look what they did. They created immunity. There's no legal recourse if something goes wrong. How safe can those things be," I think public trust might not be there to take the vaccines. So, at a minimum, Audiey, I'm going to say you must set up a compensation program or extend the existing one we have—the Vaccine Compensation Fund—to pay people who claim to be harmed, who can establish that they were harmed. Otherwise, the immunity may keep the manufacturers there, but it may not keep the customers there!

KAO: Sure. Yeah. And I think you make a good point because, it may be an imperfect comparison, but currently in some states, the capacity to test right now is actually outstripping demand for the testing capacity. So, whether or not that is a manifestation of people's distrust or a lack of acute concern about the COVID-19 pandemic certainly will be aggravated if people perceive that companies will not be held accountable if vaccines prove to be harmful to people.

CAPLAN: It's a huge, huge problem. And it doesn't take big numbers to undermine one of the key advantages of vaccines, which is herd immunity.

KAO: Sure.

CAPLAN: So, even if we got a vaccine, which, again, people aren't saying so clearly, none of them have ever been 100 percent effective in the history of vaccines. I think the best one I've ever seen is measles, probably comes in about 94 percent. Whooping cough might be at 85 percent. But the advantages, I mean, getting ready to take the darn thing, then you get herd immunity on top of the effectiveness of the vaccine. If we don't have that, we have more trouble because then you have pockets that flare up and flare up.

KAO: Yeah. So, you mentioned people's willingness to take vaccines. Now, that's obviously the 180-degree opposite of mandatory vaccinations. And currently, the most top-read article in the *AMA Journal of Ethics* is on mandatory vaccinations during epidemics. It's generally accepted as settled law that the state has the authority to mandate vaccinations with certain exceptions, including medical exemptions for people who, for example, are immunocompromised. Even if mandating vaccinations are legal, a recent survey found that about a quarter of individuals would refuse to get a SARS-CoV-2 vaccine. And as you just mentioned about herd immunity, experts think that at least 70 percent and probably closer to 80 and 90 percent of Americans need to develop immunity to COVID-19, either naturally or through a vaccine, in order to halt the community spread of the virus. So, what do you think should be done, first of all, to ensure that a potential SARS-CoV-2 vaccine is available to everyone, regardless of where you live or ability to pay? Also, what do you think health professionals and policymakers should do to address vaccine refusals, including and especially among minority populations who are disproportionately affected by COVID-19?

CAPLAN: Well, another good set of questions, and ones that I think we really should be discussing more widely than just listening to forecasts that we're going to be out of this in six months because someone's going to invent a vaccine. Look, to distribute 330 million vaccines [chuckles] in refrigerated trucks to doctors' offices must take six months alone! I can't even imagine how that would be done, much less three billion doses worldwide, even if you were a country that was on the ball like a South Korea or a Singapore. I don't know. That's a challenge. So, I think we're going to see vaccines come out slowly. And so, the first question is to who first. To me, it's health care workers, people who are exposed in essential jobs, probably need food handlers, probably got to do truckers, probably get to, I don't think bioethicists will make it high up on the list.

KAO: [chuckles]

CAPLAN: But there are essential workforce people with high exposure that you want to get the vaccine to first. And I think initially, we'll see kind of an odd situation [clears throat] excuse me, with people saying, "I want the vaccine." We'll see a black market in the vaccine! People will be desperate to get the vaccine. That's as the first batch rolls out.

Then people start to say, “Hmm. I’m not sure I want that vaccine. I’m not sure I believe it’s safe. I saw on the Internet that Bill Gates is just selling it because he wants to make money, and he probably is responsible for this entire pandemic.” Yes, that’s actually out there on the Internet. And so, you then start to see exemptions, resistance, “I’m not going to take it.”

I’m going to say three things. One response will be, what do we do with kids? So, kids historically have had the mandates, the toughest mandates, and they’ve usually been because of diseases that you catch at school. Measles is the classic, and states have been pretty good about saying, you know, we’re going to require vaccinations for school entry. A couple of problems there. One is, what if the schools haven’t opened? There’s no school entry; there’s no way to move either COVID vaccine or any vaccine toward kids. You can get measles outbreaks and COVID outbreaks. So, we need to prepare now not just for what’s the school mandate, but what’s the situation if a year from now we still don’t have the schools or the daycare running the way they ought to be?

KAO: Right.

CAPLAN: I favored, in my own arguments, few exceptions because I think putting others at risk is not something that parents should be able to choose for their kids. So, I’ve argued over the years that we should do away with everything except medical exemptions: no personal belief exemptions, no religious exemptions. By the way, religions, every one I’ve looked at, do not object to vaccination. Most of them have nothing to say about it because their holy texts, if you will, [chuckling] were all written before vaccinations. So, they don’t give you an opinion. But I’ve talked to Christian Scientists, for example—a pretty ardent, small group—and they leave that to conscience. They don’t even say that that is something that can’t be done. So, in any event, it’s maybe tough. The difficulty there is—and I think you know this, Audiey—we’re starting to see these weird syndromes break out in kids who’ve had a COVID infection.

KAO: Yeah. Right.

CAPLAN: You have to really be sure that exposing them to a vaccine doesn’t cause the same sort of syndrome.

KAO: Yeah.

CAPLAN: So, that means a little bit more testing in kids before you can roll a mandate. I’m all for a mandate, but I’m not going to do it till I’ve tried it, if you will, maybe in kids that are high exposure for various reasons, and seen that that’s going to work. Next group might be those at-risk people, health care workers. And as I said, I’m happy to mandate there. You’re talking to the guy who was the proponent of mandatory [laughing] flu shots in hospitals, and they don’t even work that well. I’ll concede that. But it seemed to me if you want to stand for health and you don’t want to lose time at work or infect your patients, you ought to be required to take that shot. And a lot of places have moved in that direction, and I think we’ll see that.

KAO: Yeah.

CAPLAN: The third step, and this is interesting, is I don’t think— Let’s say we are still looking at a Trump administration. I don’t think they’re going to push for mandates. They’ve always been more liberty-oriented in their approaches. It may be that where we

see mandates is coming from your employer, your airline, your recreational, you know, I want to go to the theater. Someone's going to say, "Oh yeah? Show me the vaccine app that you've been vaccinated."

KAO: Yeah.

CAPLAN: "I want to go to a sports event, and I want to sit in the stands. I want to play sports." I have a feeling that the way mandates are going to unfold is not so much—the U.S., and it may be different in other countries—but in the U.S., I think it's going to be where you want to go or to eat in restaurants, like the idea of going to the cinema, you think it's a whole lot of fun to fly to Hawaii or go somewhere on a vacation trip or take a cruise. We all know what risks they were there. You're going to have to show vaccination.

KAO: Right. Yeah, I think you may be right that the mandates may be coming more from the private sector for a variety of reasons.

CAPLAN: By the way, I hate to say it, but it's so American. In some parts of the world, the government's going to say, you can see them, you know, say in Germany or Singapore, "We're just doing the vaccination. The absolute American response is, "Okay, we'll leave it to the private sector."

KAO: Sure. Now, you alluded to already at several points the importance of public confidence and trust in the scientific enterprise is critical at this juncture. And there are many intersections of that, including the long distrust of minority populations of the health care system. So, as you know, there are few business truisms as popular as under promise and over deliver. Given that this pandemic where billions of people are counting on the global biomedical research community to deliver on a safe and effective vaccine, the conventional wisdom right now is that it's just a matter of time before SARS-CoV-2 vaccine is developed. And we just learned today, on May 18th, that Phase 1 results from a Massachusetts biotechnology company appear quite promising. Despite this welcome news, how should we communicate and engage the public so that the scientific community doesn't end up overpromising, underdelivering, and undermining public trust?

CAPLAN: Yeah, I'm very worried about this because the promising has been pretty lofty and loud: six months, 12 months, 18 months. And even if you don't do the challenge studies that I was talking about to try and speed things up, you're still looking at huge manufacturing challenges. I've been looking at vaccines for decades. I can't think of a year in which one vaccine plant didn't go offline just due to production troubles. And I would expect we're going to see that happen here. Let's say you had a vaccine that required two shots.

KAO: Right.

CAPLAN: HPV vaccine does, cholera does, hep B, I think, does. So, you've got a situation where you might need to make in the U.S. [laughing] 600 million vaccines and distribute them. So, if you over promise, the public's sort of like, "Where's my magic bullet? You guys all said you'd have this done in six months or 12 months. And now, I can't even get a truck in my state. What are you talking about?"

KAO: Yeah.

CAPLAN: So, I do think we have to look for realism, not spreading false hope. I also think there's a page to be taken from vaccine critics. Look, part of this is an ethics argument. It's not just facts. If you want to respect your neighbor, if you want to be a good community member, if you want to prevent death to your grandmother, you need to vaccinate. And we've got to take on the idea that I'm free to do what I want. Even the great proponent of liberty, John Stuart Mill, to paraphrase him, said you could swing your arm all you want. It just ends at the other guy's nose. You can't do things that hurt others. And I think Americans should hear the counterargument to what's being out there now at demonstrations and a lot on the Internet, which is liberty. Is, "I'm free to do what I want, and you can't make me do otherwise." We make people do otherwise all the time. You've got to have a car seat. You can't drive drunk. Maybe I want to speed home. I can't do it if I'm putting other people at risk. So, you get where I'm going. We got to make the moral case.

And then in terms of communities of color, minorities that don't trust, we must identify credible spokespersons. People have had great success, for example, with hypertension programs—my colleagues at NYU have done it—in using churches and barbershops to get out messages. Sounds mundane, sounds boring. It works. [chuckles]

KAO: Yeah.

CAPLAN: It's the place where you get solid information into the community. And I think, whether it's Oprah or local people who are trusted, we need those voices, and we need to involve them. After all, that's what the anti-vaxxers do. They get the celebrities out there, and the Jenny McCarthys of the world that are sort of like, "Well, I don't know. Not sure I'm going to do this." It may seem corny and it may seem almost beneath some scientists, but winning the war on the Internet is crucial.

KAO: Yeah, I think you make some excellent points. And on that note, I want to thank you for sharing your expertise and insights with our audience today. Thanks, Art, again for being a guest on *Ethics Talk*.

CAPLAN: Thank you for having me, Audiey. I wish we had a little bit more upbeat news, and maybe we'll get that vaccine in six months! I hope so.

KAO: Yeah. Fingers crossed.

CAPLAN: Fingers crossed.

KAO: Yeah. So, for more COVID ethics resources, please visit the *AMA Journal of Ethics* at JournalofEthics.org. And to our viewing audience out there, be safe and be well. We'll see you next time on *Ethics Talk*. [bright theme music plays]