

COVID-19 vaccines for kids under 5 with Paul Offit, MD [Podcast]

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UPDATE

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In today's COVID-19 Update, AMA Chief Experience Officer Todd Unger discusses the status of COVID-19 vaccines for kids under 5 with Paul Offit, MD, director of the Vaccine Education Center and an attending physician in the Division of Infectious Diseases at Children's Hospital of Philadelphia. Dr. Offit is also a member of the FDA's vaccine advisory committee.

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Speaker

- Paul Offit, MD, director, Vaccine Education Center and an attending physician, Division of Infectious Diseases, Children's Hospital of Philadelphia

Transcript

Unger: Hello, this is the American Medical Association's COVID-19 Update video and podcast. Today we're discussing the status of COVID vaccines for kids under five with Dr. Paul Offit, director of the Vaccine Education Center and an attending physician in the Division of Infectious Diseases at Children's Hospital of Philadelphia. Dr. Offit is also a member of the FDA's Vaccine Advisory Committee. I'm Todd Unger, AMA's chief experience officer in Chicago. It's great to see you again, Dr. Offit.

Dr. Offit: Thank you.

Unger: A lot of parents out there, anxiously awaiting vaccine authorization, as you probably know, for kids under five. We know that Moderna and Pfizer are both getting closer. Can you talk a little bit about where their applications stand right now?

Dr. Offit: Right. Moderna has a two-dose vaccine with 25 micrograms per dose, given to children between six months and less than six years of age. The dose is given four weeks apart. They've submitted to the FDA for approval through emergency use authorization. Pfizer is in the midst of a three-dose trial, not a two-dose trial like Moderna but a three-dose trial where it's three micrograms per dose. You remember for adults or older adolescents, it was 30 micrograms per dose. For the five to 11-year-old, it was 10 micrograms per dose. For the less than five-year-old, in the case of Pfizer, it's a three microgram dose. I haven't seen preliminary data on that trial but I have seen just preliminary data, meaning top line, press release data from the Moderna trial. My suspicion, if I had to make a guess, and it is a guess, is that probably sometime in mid-June, both of these vaccines will be considered but we'll see.

Unger: Well, that's good news because I think a lot of parents were expecting it to be earlier. Is that kind of what you're advising them on, expect kind of early summer?

Dr. Offit: No, I think that's right. I mean to, if it's true that we, the FDA Vaccine Advisory Committee, does consider this vaccine in mid-June and let's say just for theoretical purposes because you don't know until you see all the data whether you are going to recommend approval, that if the advisory committee recommends approval, usually the FDA then goes along with that within a couple days. Then it goes to the Advisory Committee for Immunization Practices at the CDC. Let's say that for theoretical purposes, they too recommend it. Then it goes to the CDC. That all usually happens within a two-week period of time. If we do meet in mid-June you would think by no later than beginning of July, this vaccine or these vaccines would be available for children less than six years of age.

Unger: If that did work out and given the kind of dose regimens that you talked about earlier, would that mean that kids would be able to have that taken care of before school starts in the fall?

Dr. Offit: Right. That's what it would mean. I think the Moderna vaccine is given as two doses four weeks apart. The Pfizer vaccine, my understanding is the first two doses are three weeks apart. And then I think the third dose is two months after the second dose. Yeah, I think that's the way it would work out.

Unger: That's good news. Obviously, you sit on the FDA's Vaccine Advisory Committee, which it almost feels like a double-edged sword in that if the FDA authorizes quickly, people get concerned and think maybe the review wasn't thorough enough. But if they take the length of time that's necessary to get a EUA for kids under five, then it's too long. How do you balance those competing pressures and messages to parents out there?

Dr. Offit: Well, this is the fastest vaccine ever made. I mean, the virus was isolated and sequenced in January of 2020 and 11 months later, we'd completed two large clinical trials. Pfizer, 40,000, Moderna, 30,000. You can't make a vaccine faster than that. I mean, you do have to go through a series of stages. The hardest for young children is the phase one stage, which is to say dose and dose-ranging.

You have to figure out what dose to give, what interval of dose between doses and how many doses to give. And so you need to because you want to make sure you're getting a consistent, high level of neutralizing antibodies that you think is going to be associated with protection against illness.

I think the biggest challenge here is going to be to remember, that the vaccines that are being given, whether it's Pfizer or Moderna are against that original strain, the original recipe vaccine, if you will, against the ancestral strain. But these studies are being done when Omicron and BA.2 are circulating and protection at least against mild disease with the ancestral strain is not as good with those variants. And you already saw that with the Moderna trial, where you've looked at top-line data where sort of for the six months to two-year-old child protective efficacy was around 51%. For the three, four and five-year-old child, protective efficacy was 37% against mild illness. Now, the good news is that when you look, for example, at the five to 11-year-old child, I mean there, the study was done when Delta was predominant. That vaccine was 91% effective against mild illness but when it got out there and it's been out there since early November and now Omicron is the most common. And then BA.2 is the most common and these sub variants of BA.2 are common.

The efficacy definitely dropped off against mild disease but was still good against serious illness. You would have to assume that what you're seeing then with these less than six-year-old data where protective efficacy is likely not to be as good against mild illness that it would also be highly protective against serious illness because that's been the story. I mean, ever since the first variant came out of China, the so-called D614G strain that was replaced by Alpha, that was replaced by Delta. That's now replaced Omicron ... I mean the Omicron, the line that was crossed with Omicron is it's more immune evasive and that's for mild illness. But those original vaccines have always been protective against serious illness, which is really the goal of these vaccines.

Unger: And you kind of just outlined, I guess, what I would consider the complication set. One is there's a lot of different regimens to test right now. And then you're doing that in a shifting environment where you've got new variants. Is there any other kind of complicating factor? Are those pretty much the main features there?

Dr. Offit: Well, you're right. I mean, it's like you're building the plane while it's still in the air. And I think you do learn as you go, I mean, there's invariably a human price paid for knowledge. That's true for any medical innovation ever. I mean, we've learned this certainly with the mRNA vaccines, which are a rare but real cause of myocarditis and sometimes serious myocarditis, but typically sort of mild, transient self-limiting myocarditis but it can be serious. That's just true with any disease. You learn with the J&J vaccine, that it was a rare cause of the so-called thrombosis with thrombocytopenia syndrome, which is a fancy way of saying blood clots, including blood clots in the brain, including occasionally fatal blood clots in the brain. And, again, rare but there have been about 10 cases of fatalities associated with that vaccine.

Invariably, anything that does good has the possibility of doing harm. You do learn as you go. The good news is with a five to 11-year-old, about a third of those children, about 30% or so, have been vaccinated in a population of 28 million. You already have about 9 million children or so who have been vaccinated in the five to 11-year-old age group. That's instructive and reassuring because at least the as the most recent date I've seen is that you hadn't seen myocarditis because that was the fear, right?

You knew that it was highest in that sort of 16 to 17-year-old age group, especially boys four days after dose two. And so you really worried as you got to younger groups, it might even be higher but the opposite's been true. With the 12 to 15-year-old, it appears to be lower. With the five to 11-year-old, you're not really seeing myocarditis yet. Again, got to keep our eyes open. That is reassuring. And the reason is that this is for the most part a killer of older people. 80% of the deaths from people over 65, 93% of the deaths from people over 55. This isn't a virus that typically kills children. Although a thousand children have died but it's a thousand of a million, which is 0.1%.

Unger: Well, kind of on that topic of risk, and I got a lot of background from reading someone's book out there. I think it was yours, called *You Bet Your Life*. Parents are concerned right now, numbers are going up. We are hoping for kind of a return to normalcy. What do you advise parents to do who want to keep their kids safe until we have an authorized vaccine but at the same time, we're just eager to get back to some level of normalcy.

Dr. Offit: It's an interesting time right now. I mean, what we have in our heads is the carnage that has been caused by this virus. And it's a bad virus. I mean, it's not a typical respiratory virus like influenza or para flu or RSV or the human coronavirus. And what makes it atypical is its capacity to cause vasculitis. And therefore, because all organ systems have a blood supply, all organ systems can, can be affected, like kidneys, liver, heart, in addition to the lung. That's what makes this virus so heinous. On the other hand, we probably right now are at about 95% population immunity from either a vaccination or natural infection or both. And you're seeing evidence of that.

And the evidence that you see is when you see an increase in cases ... For example, recently in Philadelphia, we had a clear increase in cases. And as a consequence, the health commissioner got nervous and said, "Okay, indoor mask mandates. We're reestablishing indoor mask mandates." Because what she feared is what we've seen in the past when there's an increase in cases. That usually is followed weeks later by an increase in hospitalizations, an increase in ICU admissions and an increase in deaths. Didn't happen. And the reason it didn't happen is that for the most part, we're protected against serious illness now.

You'll see an increase in cases because these strains, Omicron, BA.2 are immune evasive. Even if you've been vaccinated or naturally affected or both, you can get mild illness but that's what you're seeing now. You're seeing a lot of mild illness and we'll see how that plays out over time, because I would argue right now we're not in a pandemic anymore, that we have achieved what we wanted to

achieve, which is protect the health care system, make sure people don't get hospitalized. And hospitalizations are definitely weighed down. I think as we approach winter, that's what people worry about.

At its heart, it's still a winter virus and people gather together in the winter and they're much closer. And so you worry that there is going to be an increase, but ... And there certainly will be an increase in mild cases. The question is, will that be also associated with an increase in hospitalization and death? CDC recently had data showing that there's now an increase in people who, despite being vaccinated, are being hospitalized or dying. But look at those people. Those people for the most part are ... And they're arguing that, see, even vaccination is not protecting these people. But this is a three-dose vaccine for people who are over 65. This is a three-dose vaccine for people who are over 12 who have comorbidities. And that's who you see die for the most part is those people who didn't get that third dose who were in those two groups. I really wish we'd stop using the word booster. This is a three-dose vaccine for certain groups.

Unger: That's interesting. Could you just spent a little bit more time on that? Why do you say that? We shouldn't use the word booster. That's because you're saying that those folks out there in those two groups that you named, they just really need three shots. Let's just call it what it is.

Dr. Offit: Right. Let's call it three-dose primary series because I think what it is. What's the goal? The goal of the vaccine is to prevent serious illness. The immunological correlate of protection against serious illness are memory cells, memory B cells, memory T helper cells, memory cytotoxic T cells. Historically, if you look, for example, at the inactivated vaccines like polio vaccine, hepatitis A vaccine or the purified protein vaccines, which you could argue this is close to, like the human papillomavirus vaccine, the hepatitis B vaccine. To induce high frequencies of memory B cells and memory T cells, you need a four to six-month interval between doses.

When this vaccine launched back in December of 2020, this was a two-dose vaccine with those doses being given three or four weeks apart. There were people at that time that said, "This is a three-dose vaccine," for the reasons I just mentioned. If you're going to induce adequate memory responses, you're going to have to have that four to six-month interval with that third dose. And I think that has held up to be true for certain groups but not all groups. I think it has held up to be true for those who are over 65. I think it's held up to be true for those who are over 12 who have multiple comorbidities. I would still argue that for people who are less than 50, who are otherwise healthy, two doses does appear to continue to hold up for protection against serious illness. Nonetheless, we have a three-dose recommendation, really for everyone right now over 12. And I think probably in the next week or two, you're going to hear a third dose recommendation for the five to 12-year-old.

Unger: Well, last question. You kind of mentioned the fall and big question marks around that. One thing we do know is the virus has mutated more quickly than I think maybe scientists would've predicted. As we think about our vaccine approach for both kids and adults and thinking about the fall,

what do you think the future holds there? How is this going to affect the approach?

Dr. Offit: That's a great question. And I think what's going to happen is in the end of June, June 28, the FDA Vaccine Advisory Committee is going to meet to decide or discuss what we think about giving a fall vaccine, in much the same manner that we give a vaccine for influenza. I mean, every year the FDA Vaccine Advisory Committee gets together in March. We pick the strains of influenza for September because it's a six-month production cycle. I think that's the thinking now. At the end of June, let's pick strains for the fall but do we really need a variant-specific vaccine?

See, I would argue that, and again, I'm just one voting member of the committee but I would argue that we cross a line to need a variant-specific vaccine if there is a variant that arises that despite being naturally affected or vaccinated or both, you are still not protected against serious illness. That's why we give a flu vaccine every year because even if you've been naturally affected or vaccinated the year before, you still might not be protected against serious illness, hence the need for a yearly flu vaccine but coronaviruses aren't flu. And although this virus has mutated, and as you note, has drifted in a manner I don't think anybody would predicted with Omicron or with this BA.2 or these BA.2 sub-variants, there now is immune invasiveness.

You could argue these are drifted strains but you're still protected against serious illness. And so that's why I don't really see a compelling need right now for a variant-specific vaccine. Also, you should note that when you get that, if you look for example, at people who get three doses of the current mRNA vaccine, meaning the ancestral strain vaccine, and compare them to people who get two doses of the ancestral strain vaccine and then the third dose is an Omicron specific variant, there's no difference in Omicron specific neutralizing antibodies because that third dose with the ancestral strain does broaden immunity to include Omicron, hence the advantage of having that third dose. If there is or data there presented at the end of June that shows a compelling reason for either a yearly vaccine or for a variant-specific vaccine, great. But right now, frankly, I don't see those data.

Unger: Well, we will stay tuned and look forward to more information from you. Dr. Offit, it is always so informative to talk to you. Thanks so much for being here today. That's it for today's COVID-19 Update video and podcast. We'll be back soon with another segment. For resources on COVID 19, visit ama-assn.org/COVID-19. Thanks again for joining us, everyone. Please take care.

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