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Long-Term Efficacy & Safety of HPV Vaccination

Announcer:
Welcome to CME on ReachMD.

This activity, titled “Long-term Efficacy and Safety of HPV Vaccination,” is provided in partnership with Prova Education and supported by an independent educational grant from Merck.

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Here’s your faculty, Dr. Warner Huh.

Dr. Huh:
Hello, my name is Warner Huh. I’m a gynecologic oncologist at the University of Alabama at Birmingham in Birmingham, Alabama, and today we’re going to talk about the HPV vaccine and hopefully provide you with an update in terms of where we are with HPV vaccination.

A little bit about HPV, or also known as the human papilloma virus, it’s a virus that I think most women’s health providers are aware of, but the importance of HPV is that we know that through work that has been done over the last 30 to 40 years and has even been the focus of a Nobel Prize in physiology and medicine over 10 years ago, that HPV is a requisite cause for the development of cervical cancer as well as other anogenital malignancies, like vulvar cancer and vaginal cancer. Also what we know is that HPV is associated with other malignancies, including certain oropharyngeal malignancies as well as rectal cancers.

So, when we actually test for HPV, particularly in women, we associate certain types of HPV as high-risk types. There are 14 types that we are most concerned about, and many of our testing platforms that are FDA-approved for HPV testing include these 14 types. To be even more specific beyond that, there are certain types that we know that are not only more prevalent, but they are also bad actors as well, and those types include types like 16 and type 18.

I want to focus a little bit on 16 and 18 mainly because, one, those 2 types are the types that are within the HPV vaccine that is presently available in the United States, but also, more importantly, type 16 is actually probably the most common type, but it’s definitely the most virulent type. And we know that women who are persistently positive for type 16—so they might be positive on 2 separate HPV tests a year apart—those women can have up to about a 40% chance of developing a significant precancerous or cancer lesion in their life, so this is why, not only knowing whether or not a woman is HPV positive is important, but also what specific types they are positive for is going to be relevant as well. But again, focusing on this talk, it’s important to recognize that the vaccine that is currently available, which is the nonavalent HPV vaccine, also known as Gardasil 9, includes type 16 as well as 18, as well as 5 other types, that are relevant for the protection of particularly cervical cancer.

So, historically speaking, we’ve had several vaccines that have been available in the United States as well as being FDA-approved, and originally, back in 2006, the original Gardasil, or the quadrivalent vaccine, was FDA-approved and introduced for clinical use. And then, shortly thereafter, the bivalent vaccine, which the trade name at that time was Cervarix, was introduced and FDA-approved in 2007. And then, most recently, in 2014, the nonavalent vaccine, or Gardasil 9, was introduced to the United States as well as worldwide. Presently,

in 2019, there is only 1 HPV vaccine that is available, and that vaccine is Gardasil 9.

Now, since 2014, we have had a fair or substantial amount of changes in how the vaccine is being utilized and who should be getting the vaccine, so not only are we recommending that girls and boys be vaccinated, but recently, as of last year, and then basically kind of recommended by the CDC and the Advisory Committee on Immunization practices, also known as the ACIP, that the vaccine Gardasil 9 is actually approved all the way up to 45 years of age. And I think, particularly for people who are listening to this, this is important, because up to recently, the vast majority of HPV vaccine in this country was given by pediatricians, which makes perfect sense since the target age is around 11 or 12 years of age. Well, now that the vaccine is not only FDA-approved but generally recommended by the ACIP and the CDC, this is actually a new opportunity for women's healthcare providers to talk about the role of what's known as catch-up vaccination in women particularly between 26 and 45 years of age. So it's an interesting time, and the ACIP and the CDC recommend that there needs to be a shared decision-making and discussion between the patient and the provider, but I hope people listening to this lecture recognize that, again, there is a unique opportunity to offer vaccination, particularly to women between 26 and 45 years of age.

As I mentioned earlier, there are 7 types in Gardasil 9 that are considered to be high-risk types, and that includes the original 16 and 18 that were in Gardasil. And so, when you look, actually, at the expansive protection, particularly in the United States, we're talking about roughly 92% to maybe 93% of all invasive cervical cancers could theoretically be prevented by giving a woman Gardasil 9. When you ask that similar question to other malignancies, like oropharyngeal or head and neck malignancies, the majority of those malignancies are caused by type 16, so in some ways you could argue that Gardasil 9 is really a vaccine that is really more geared toward prevention of cervical cancer, but that shouldn't take away the importance of the fact that both boys and girls should be equally vaccinated in this country.

And as of recently, what we know from basically survey data from the CDC is that we're definitely vaccinating at a much better rate than we did previously. Based on the most recent data, I think that the vaccination rate is up to about 60–65%. In boys it's still lower. We also know that boys and girls who get vaccinated, they more often than not get vaccinated—that vaccination is driven by a recommendation from their provider, so the most important thing to recognize is that if a provider tells a parent and a patient that you need to get vaccinated, that has considerable influence, positive influence, on whether or not the teenager actually winds up getting vaccinated with the HPV vaccine. To this day it's still really critically important that we continue to espouse the importance of HPV vaccination, explain that to the parents and actually children both and understand that this is a legitimate cancer prevention vaccine.

One question that I often get is—even though there have been a litany of clinical trials that clearly demonstrate impressive protection with the HPV vaccine—do we have data that looks at sort of worldwide protection or protection at a population level? And the answer to that is absolutely yes. And I think that the one country that has best demonstrated this over the last decade is Australia. Australia was really one of the original countries that really had a significant vaccination campaign, one that was both school-mandated and one that was community-based as well. Presently, their program is largely basically school-mandated for both boys and girls. But when they looked at the effect of the vaccine on HPV-related diseases, as an example, they looked at the rate of genital warts, which is an HPV-related disease, happens to be protected by the HPV vaccine because many of the genital warts cases are caused by 6 and 11. In one Australian study that was published I think almost about 5 years ago, 4 or 5 years ago at this point, they saw about a 93% reduction in the incidence of genital warts in girls that had been vaccinated over a 4-year period of time. When you actually think about that and step back, that is truly impressive. And my understanding, speaking to other surveillance experts in Australia, is that number is even much higher now.

What's fascinating to me about that study is that only girls were vaccinated between 2007 and 2011, and the question is: Was there any protection seen in boys or men? And the answer to that question is absolutely yes. And what they saw is protection rates as high as 80% in boys, and this is basically passive protection, or what's known as herd immunity. And so, for me, it really speaks to the impressive protection that's afforded not only to girls and women, but protection that's passed on to boys. And in some ways that's irrelevant because in Australia boys are currently vaccinated. Similarly, what they're starting to see is a decrease in the rate of severely abnormal Pap smears in the country of Australia as well, particularly in girls and women who have been vaccinated. And then lastly, the vaccination rates and the disease rates are so impressive in the country of Australia that their public health experts and surveillance experts have basically claimed that they will largely eradicate cervical cancer from the country of Australia in the next 20 years.

I think in regards to one common question that I get all the time is: How long does the protection last related to the HPV vaccine? And there have been numerous studies that have looked at this. I think the most important study out there that has addressed this issue is a publication that was published by Susanne Kjaer, who's from Denmark, in 2018, and this is what is famously known as the Nordic Study or the Nordic Registry. And what she published was basically 12 years of follow-up in Nordic countries, which include Denmark, Sweden, Norway, etc., to see whether or not there were any cases of breakthrough disease in women that had been vaccinated basically 12 years ago, and what they saw, which was probably the single-most important finding, was that they did not see any cases of breakthrough disease, particularly related to HPV type 16 and 18. And we're talking about almost 10,000 years, person years, of follow-

up, so this registry has an incredible power to tell us really whether or not the protection is waning in this population.
So, based on that study, what we know is that the protection lasts through at least 10 years with a trend for continued protection through 12 years of follow-up.

And so, again, the question that begs to be asked is: Women or men, will they need a booster at some point? Unfortunately, we don't have that answer right now, but what we do know is that protection lasts for at least a decade, and it may last much longer than that, so there is a possibility that women and men won't need a booster, but we know right now that the protection is actually quite durable and extends for quite a long period of time.

The one last thing… There are a couple things I want to talk about more, which is the issue of vaccine safety. So this is actually something that has come up many, many times since the HPV vaccine was FDA-approved in 2006, and it's amazing to me that we've had already over 10 years of clinical experience with the vaccine. I would honestly say, and I think that many of my vaccine experts would agree, that the HPV vaccine may be the most heavily scrutinized vaccine, not only by the scientific community but also by the lay community as well. And, unfortunately, I think there is a lot of misinformation that has spread about the vaccine and its safety. Unfortunately, we have countries in the world like Japan who have largely stopped vaccinating their population based on information that I don't think is quite—not quite the right way to look at the information. But I want the audience to know that there have been multiple, multiple studies going back from an original study that was published by Barbara Slade back in 2009 in JAMA at the adverse events or really the toxicities that are related to the HPV vaccine, and I'm here to tell you that when you look at many of these studies—we're talking about an aggregate of about 6, about a half dozen studies—that the safety of the HPV vaccine is actually quite impressive.

Lastly, I think the things that I think are interesting for the audience to listen to is recently we went up to—we went from a 3-dose schedule to a 2-dose schedule, particularly for girls under 15 years of age, and we know now that at least with antibody titers that we can actually effectively vaccinate children with just 2 doses versus 3 doses. But what's really exciting to me is some preliminary evidence to indicate that maybe 1 dose itself may be protective. There was some original work that was done in Costa Rica that demonstrated an impressive level of protection with just 1 dose. It was sort of an exploratory analysis, so I don't think anyone is quite ready to say that we should get away with 1 dose, but there is a study that's being sponsored by the NCI, also being done in Costa Rica, that will hopefully have a definitive answer to this question by, hopefully, the early 2020s, and if that study is positive, I think that will totally be a game-changer for how we offer HPV vaccination not only in this country but worldwide.

So, again, I hope this update was helpful to this audience. I think you're going to be hearing about the vaccine more, particularly from your patients.

Thank you.

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