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Extended HPV Genotyping: Higher Sensitivity to Detect Cervical Cancer

Narrator:

Welcome to CME on ReachMD. This segment, **Extended HPV Genotyping: Higher Sensitivity to Detect Cervical Cancer,** is sponsored by Omnia Education and supported by an educational grant from BD Life Sciences. Your expert joining us today is Dr. Warner Huh, the Margaret Cameron Spain Endowed Chair in Obstetrics and Gynecology, Professor/Division Director of Obstetrics and Gynecology at the University of Alabama at Birmingham, in Birmingham, Alabama.

Dr. Caudle:

While cervical cancer has become less common in the United States, there will still be an estimated 12,990 new cases and 4120 deaths in 2016. Cervical cancer screening is increasingly incorporating HPV genotyping, especially for HPV genotypes 16 and 18; however, extended HPV genotyping, the analysis of additional genotypes, has emerged as a possible means to limit unnecessary testing and potential harm to women compared with current HPV screening approaches. Barriers to adoption of this newer technology in clinical practice must be discussed in an open forum.

I am your host, Dr. Jennifer Caudle, and joining me today is Dr. Warner Huh, the Margaret Cameron Spain Endowed Chair in Obstetrics and Gynecology. He is also Professor and the Division Director of Obstetrics and Gynecology at the University of Alabama at Birmingham. Dr. Huh, welcome to CME on ReachMD.

So, let's first start, cervical cancer screening is increasingly incorporating HPV genotyping, especially for HPV 16, can you explain the rationale for specifically calling out HPV 16 and what you hope to achieve by identifying these in women?

Dr. Huh:

It's really a great question to start off this discussion. So the reason why we're specifically calling out type 16 is that what we know is the majority of, not only cervical cancers, but many pre-cancers of the cervix, what we call CIN 2/3, are associated with type 16. And so, that's one reason. And the second reason which is really the more important reason is, if you follow women who are infected with HPV 16 over time, and I'm talking about over, let's say, a 5-year window, what we know is that an individual's life-time risk of developing pre-cancer or cancer of the cervix with persistent HPV 16, and what I mean by persistent is generally one year or more, their life-time risk is anywhere from 25 to 35%. That's a pretty considerable risk because there are not many things in women's health, when you really look at it, that carries a risk that high, and so that's the reason why we're so interested in 16. So, by identifying 16 in these women, in conjunction with screening and otherwise, we're actually able to triage these women so that: A) we can treat them earlier, or; B) that we can provide an intervention that allows us to determine whether or not the patient has a real problem.

Dr. Caudle:

You know, when we think of genotyping we generally think of type 16 and 18. We are now hearing about the introduction of extended genotyping. Can you explain what this is and how it works?

Dr. Huh:

Right. And so, the genotyping as it exists today, using FDA-approved tests, we look at generally 14 total high-risk types. And when we say high risk, these are types that are associated with the epidemiologic risk of developing cervical cancer. But as we discussed earlier in the first question, so one type is type 16, because it's highly common and it's also a very virulent type. The other type that we look at is type 18. Why? Because it is also another common type and one that's associated with adenocarcinomas of the cervix which occurs in about 20% of women and it's more difficult to detect because those lesions are usually higher up in the cervix and things like Pap smears can frequently miss them. And the other type is type 45, and this is a type that's also somewhat prevalent in the US population, and so, extended genotyping really, as of 2016, is usually restricted to type 16, type 18, and type 45, for the reasons I have discussed.

Dr. Caudle:

I think you might have touched on this a little bit in the answer to that question, but continuing along the spectrum of extended genotyping, in what way can this extended genotyping limit unnecessary testing and potential harm, but still be an effective screening tool?

Dr. Huh:

Right. And so, I think what's interesting about extended genotyping is that it's, let's say a woman gets a co-test, and what I mean by co-test is, a women gets both a Pap smear and one of these HPV tests, and we usually recommend this in women 30 years and older. Well, what happens, let's say, if a woman has a normal Pap test and has an abnormal or positive HPV test? Well, by genotyping, for type 16, type 18, or type 45, what we know is that woman definitely carries a higher risk of having not only a clinically-significant lesion, but is also at risk for developing a clinically-significant lesion like pre-cancer or cancer in the future. So, in that circumstance, we may elect to do something called a colposcopy, which is basically magnification of the cervix, and might take biopsies much earlier than we would otherwise. So, in contradistinction to that, so in the scenario where a woman has a normal Pap and is positive for high-risk HPV, in that scenario without genotyping, we would normally recommend that they just come back in one year. So what extended genotyping provides us is the ability to kind of risk-stratify people so that we can provide earlier intervention and not have to provide: A) a window that's too long, or; B) to over-treat people. And so, it's really about risk stratification.

Dr. Caudle:

Are there any unique methodologies associated with this extended HPV genotyping, and really, how are results obtained in the clinical setting?

Dr. Huh:

Right. And so, there are really, I think there are two main tests. There are really four FDA-approved HPV tests out there but there are really two main tests that provide extended genotyping. The Cobas 4800 platform. It's a PCR-based test. It's FDA approved for primary screening, and that genotypes for types 16 and 18. And there's another test called Aptima that is an mRNA-type test. It's a test that looks at really more of what we call the integration of HPV into the host genome and that test type tests for type 16, type 18, and type 45. And so, normally, we will request those tests when anyone orders an HPV result. Again, we're asking labs and clinicians to use extended genotyping for our guidelines, because where it gets tricky is if you start extending genotyping even past those genotypes, we really don't know what the clinical relevance are, and I think that we have to kind of weigh the balance between getting the right amount of information and too much information, because the problem is if we provide our clinicians with too much information, i.e. give them even more data on these other genotypes, beyond 16, 18, 45, it becomes really confusing really, really quickly. But that

kind of gives you just sort of a general view of how we use this genotyping and how it's ordered.

Dr. Caudle:

Cervical cancer screening seems to be undergoing rapid advancements in technology. What barriers exist in facilitating the adoption of such new technologies, and really, how can they be overcome?

Dr. Huh:

I think that one of the rapid advancements that we have been talking about for the last 10 minutes is really about using HPV-type testing and extended genotyping, and I think some of the greater barriers is really getting the clinicians to work with the laboratories to make them understand what's the value of this type of testing, what's the value to an individual woman, and how does it benefit not only detection, but the thing that we have not talked about yet is, what if women test HPV negative? I mean, when women test HPV negative, it's one of the strongest predicators in the future for women not developing cervical cancer or pre-cancer. And so, I think the best way to overcome this is to analyze the data, look at the research; talk to your laboratory directors. The clinicians need to have some skin in the game and be able to recognize the clinical value of this type of testing and to talk to the labs as to why they should roll it out. Some of this testing is very expensive, but in terms of the actual value to the healthcare system and to the patient, it could be enormous. But then I think there needs to be a very clear dialogue between the clinician and the lab.

Dr. Caudle:

So, that's really interesting, you're talking about, for example, a woman who might test negative. There are other questions I think that do come up. What impact do you think extended HPV genotyping will have in the triage setting? You're talking about risk stratification, and especially, maybe, for a woman who initially tests positive. And do you think this new information will allow us to reduce more invasive testing along the way and reduce harm?

Dr. Huh:

Yes, absolutely. And so, what I'm going to present to you is a clinical scenario that's commonly encountered by a lot of OB/GYNs, internists, primary care doctors, but I also want the audience to recognize that this is not really a society rec, or a professional society recommendation, but I think we're headed in this direction. So for many years, we have recognized, really since the late 1990s, that the use of HPV testing, or high-risk HPV testing for women with ascus cytology, this is basically women that have equivocal cytology results. If those women are HPV positive then we are currently recommending that those women go to colposcopy and that they get biopsies. Well, those women roughly have about a 15% rate of having a pre-cancer in that setting. So what that ultimately means is that there are a lot of women out there who have no abnormalities whatsoever, abnormalities are not detected. So, what if we used extended genotyping, as an example? So, what we know from some of the Roche data is that if we used extended genotyping like type 16 and 18 for those women that had these equivocal Pap smears and they were positive for 16 or 18, then the detection rate goes from, let's say, 15% to perhaps as high as 25 or 30%. And I think this is what you're seeing. You're seeing us basically reduce the variance and narrow our risk, basically parameters, and have a much better idea of what kind of testing we legitimately need to do. But to your point, is how can we reduce unnecessary tests? So, what we might be able to say down the road is that if women were negative for a certain panel of HPV genotypes, then we could just say that she just needs to come back and having testing back in one year. If she has another set of genotypes that are positive, then we might go on and say that maybe, perhaps, that woman needs an immediate colposcopy. And then, the third scenario, which I think it's going to take some time to figure this out is, if you have a certain set of genotypes, perhaps that woman needs to be treated right away, not just get a biopsy. So, I see there being great value in extended genotyping in terms of risk stratification, and to your point, reducing the number of unnecessary procedures for women.

Dr. Caudle:

Dr. Huh, are there any other points that you'd like to discuss for our learners today that we haven't already discussed or addressed during our discussion?

Dr. Huh:

I think a couple of things. I mean, to your point earlier, it's hard for clinicians because our screening and treatment guidelines have gotten so complicated. I mean, there are multiple algorithms for multiple different scenarios and when you look at the history of this, this has just gotten literally exponentially more challenging, to the point where we have to even use an app. And it's the American Society of Colposcopy and Cervical Pathology, or ASCCP, has this wonderful app that you can download on your iPhone or android device to help you kind of navigate through that. But what I'm concerned about is, as we make it more challenging, that perhaps clinicians get frustrated and they do the wrong thing. And so, this is definitely not an excuse to over-test women and you have to use HPV testing carefully because there's a lot of stigma to an individual woman when you tell them that they're HPV positive. And if you're going to do HPV testing, you should use that testing to really guide your decisions. That's true for any lab test. So I think, really, my concerns going forward are that: 1) we need to continue to screen. This is not going to obviate the obvious need to screen women, but 2) is to understand the algorithms and you might need some assistance with that. But there's no question that there is a clear role of HPV testing and genotyping in the world of screening and treatment for women with abnormalities.

Dr. Caudle:

Well, thank you for that. That's very helpful. I definitely want to thank you, Dr. Huh, for your time today and for sharing your insights on extended HPV genotyping.

Dr. Huh:

Thank you for having me.

Narrator:

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