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Cervical Cancer Screening: The Case of the Young Patient

Announcer:
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Dr. Huh:
So I recently saw a patient in my practice that I think is relevant to this podcast. It's a 24-year-old gravida 0 who was coming to see me for routine gynecologic care, and she was inquiring about cervical cancer screening. But what was interesting about her history is that she knew she was vaccinated against HPV and was wondering when she should start her screening practices. And I thought this would be the perfect case for us to talk about cervical cancer screening and related issues in the United States.

This is CME on ReachMD, and I'm Dr. Warner Huh.

Dr. Cantrell:
And I'm Dr. Leigh Cantrell.

Dr. Huh:
So welcome, Dr. Cantrell. I’m really thrilled to have you join me. And I want to dive a little bit deeper into this topic. There is without question, since the ‘50s, that the rates of cervical cancer in the US and mainly worldwide as well have plummeted. I mean, we have decreased the rates by as much as 70% to 75% with mass screening, so there's no question that our widespread screening efforts have had a huge impact. And coupled with that is the impact that HPV vaccination has had, not just only in the US, but most notably other countries that have high vaccination rates like Australia. Yet, even though we've been offering screening for over 50 years at this point, there continues to be considerable confusion in 2022 about how to best screen and who needs to be screened and what's the best test. And I think that with a recent issue of the 2020 American Cancer Society [ACS] Cervical Cancer Screening Guidelines, as well as the American Society of Colposcopy and Cervical Pathology, also known as the ASCCP, management guidelines, I would be interested to know what your thoughts are of these guidelines on our clinical practice today.

Dr. Cantrell:
Well, I think, like you said, there's still a lot of confusion, Warner, and practitioners across the country are baffled by these different guidelines. And the ACS guidelines really focus on screening for HPV and high-risk types. And the American Society for Colposcopy and Cervical Pathology have now shifted their guidelines towards the risk of a patient with the findings that you get whether on Pap or HPV subtype, that you treat based on what those results mean for the patient and their risk of CIN3 or cancer.

And because we know that young patients generally clear HPV, many of them now have been vaccinated, they have recommended that we not start screening until age 25. And I think that's just different for a lot of practitioners. And so we know that age, as far as our response to HPV, matters. And so that's been a change for practitioners, especially ones that lived through Pap smear screening and the success that that's meant, like you were just talking about for cervical cancer rates.

Dr. Huh:
Yeah, and I think that's relevant to this case study. Because, again, we have a 24-year-old, and I think traditionally, we've been very used to starting screening at 21. And, Dr. Cantrell, it seems like yesterday where we were screening women at the age of 18 or within 3 years of sexual activity. But more importantly now, this growing understanding that Pap cytology has probably served its full purpose as a screening modality with a focus concentration on looking at HPV screening as a primary screening test.

And so before we get into that some more, I thought maybe you might want to further comment on the ASCCP guidelines specifically and exactly what has changed and how you think that these guidelines will change practice in the US.

Dr. Cantrell:
So the guidelines really now take your results – so you may have cytology, but hopefully you for sure have a HPV result – and then it takes those data, gives a recommendation for the next steps of care, like colposcopy, et cetera, based on the person's risk of CIN3. It also takes into account the patient's most recent screening. So what was their last Pap? What was their prior HPV screenings? And so it takes that data and gives a risk estimate and gives the practitioner an idea of what to do.

And that's just a complete change. Before, it was if this cytology, then consider all these different things. And I think it's just a completely different model of what to do with patients.

Dr. Huh:
No, I mean you're exactly right. And to kind of articulate further on that, I mean, what is different is, and you went into this, is that our past guidelines were very much algorithm driven. And right now, our recommendations are based on a calculation of a risk percentage. And that risk percentage is tied into a specific form of management. And so for the audience, there are really only 5 options: maybe treatment, colposcopy, follow-up in 1 year, 3 years, and 5 years. And so we have distilled the management options down so that it's easier for providers to understand this because we have so many more tests and it's gotten so much more complicated. But I think for the audience and the clinicians listening to this, this is going to be the foundation for our recommendations for many, many years to come. So to understand the importance and necessity of a risk-based guideline strategy is really, really foundationally important.

So Dr. Cantrell, I thought maybe you could dive into some of the newer approaches that are being used for screening and triage that have been approved in the United States. And again, I think this perfectly ties into our case study.

Dr. Cantrell:
Right. And so the American Cancer Society guidelines promote primary HPV screening and recommend that as the preferred way to screen patients and to start, as in this patient who's 24, the next year at age 25, and to do that screening. And it's the most sensitive test. And so then, if they're HPV is negative, you can feel safe that they are safe from developing CIN3 or cancer. But if it's an HPV high-risk type, there's further tests we can do, which I think we'll get into later, but it allows us to triage HPV-positive patients into the next steps. And that's just a big change from what people are used to.

Dr. Huh:
No, I mean, you're exactly right. And what will be very interesting is the United States Preventive Services Task Force, as Dr. Cantrell is in the middle of revising their cervical cancer screening guidelines. And the last iteration of that, the initial draft was one that very much centrally focused on primary HPV screening, not even co-testing, which is the combination of Pap and HPV, but they were pretty much doubling down on primary HPV screening then; that was about 5 years ago. I think we are all fully expecting that the recommendations are going to look very similar to the American Cancer Society. And so that's why this podcast is preemptively important for the audience to understand, because I think that the science is so overwhelmingly in favor of primary HPV testing in lieu of cytology as the screening modality, particularly in a patient like this who's been vaccinated against HPV.

Dr. Cantrell:
Exactly. I think that that's where we're headed. And we just need to figure out the places in the country that don't have access to that primary HPV screening, how do we get it to them? And maybe the doctors need to ask for it as well.

Dr. Huh:
Yeah, I agree. I mean, I think that HPV testing is highly commonly used across the United States, so we didn't have quite the same challenges that we did about 15 years ago.

Dr. Cantrell:
Agree fully. Yep.

Dr. Huh:
So for those tuning in, you're listening to ReachMD. My name is Dr. Warner Huh, and with me today is Dr. Leigh Cantrell from the

University of Virginia. And we're just about to discuss cervical cancer testing and how to conduct risk-based management.

So, Dr. Cantrell, you were about to get into this. So this is the perfect time to ask this question. I thought you might want to just talk about currently available FDA-approved tests as they relate to risk-based management. Perhaps more specifically, how do we best optimize triage testing in women who are positive for HPV under this primary screening algorithm? And, you know, I thought maybe you might want to go ahead and just dive into the role of extended genotyping and something called dual staining, which is staining against p16 and Ki-67.

Dr. Cantrell:
Right. So in a model where we test patients for HPV primarily, then you're going to get a result, and it could be HPV 16, 18, or another high-risk type. And so to further genotype what the HPV type is that the patient has will then tell you what their risk of a high-grade lesion or a cancer could become. And then dual staining, which I'm the most excited about, tells you what the patient's cells are doing in response to the HPV type that they have and whether or not the HPV is actually affecting their protooncogenes and oncogenes and actually having a cellular response, which of all the tests, I think, that we have coming up in the future, that's going to be able to tell us what is this patient's real risk. And I think that we know that HPV causes the majority, over 99%, of cervical cancer, and so it's just so much better at predicting a patient's risk of cancer and high-grade precancers.

Dr. Huh:
That's exactly how I feel. And part of screening is obviously optimizing disease detection. And obviously, you don't want to miss disease. That's the one side of screening. But the other side of screening is not to have too many false positives. So putting patients through multiple procedures, biopsies, and tests that really aren't necessary. I think the interesting thing and the important thing about dual staining and, to a certain degree, extended genotyping is about raising what we call that specificity. In other words, reducing the false positive rate and being able to optimize the detection of disease. And so that's why this is an important concept for our audience to understand is to improve disease detection.

Dr. Cantrell:
Right, and to not do harm. Here we're – in our case today, we're talking about a 24-year-old G0, someone that if we did lots of procedures to her cervix, we could impact her ability to carry a pregnancy to term. And that's what we want to avoid while also protecting her from cancer.

Dr. Huh:
No, that's right. But for our audience to understand dual staining and extended genotyping are not a part of the ASCCP management guidelines. When we created those guidelines, we didn't have the full access to the data to dual staining and extended genotyping, nor was it FDA-approved at that point. But I am pretty sure that the guideline committee is going to deliberate this as there is a plethora of data in favor of this type of testing. But again, it's important to recognize that what we're doing, again, is calculating a risk of disease. And by calculating that risk and stratifying it, it fits actually quite nicely to the current guidelines that have been created. And so I think the audience should fully expect that to be in place, hopefully in the near future.

Okay, well, before we wrap up, Dr. Cantrell, any take-home messages for our audience today?

Dr. Cantrell:
Sure. I think for me, the take-home is that we have switched, should be switching, and will be screening for HPV primarily as a detection for precancer and cervical cancer, both now and in the future. And that that's really been the pivot, that we're now looking for a patient's risk of developing cancer and acting upon that risk, not just a cytology result.

Dr. Huh:
I think that's perfectly stated. I think from my perspective, going back to this case of the 24-year-old, is that primary HPV screening is fantastic as a screening modality for 2 reasons. One is for disease detection. And what we know is that women who are screened with primary HPV screening have up to a 70% lifetime risk reduction from dying from cancer, cervical cancer specifically; that's the first thing. And second thing, and I know Dr. Cantrell has heard me say this before, is the powerful message of what it means to have a negative HPV test. Because again, for our listeners, keep in mind that the majority of people that we screen, screen negative. But the reassurance that you will have, and you can provide to your patient, that her risk of developing cervical cancer with a negative HPV test is really, really small. And I think that's important for our providers and clinicians that are listening to this to understand that when passing that on to our patients.

Well, unfortunately, that's all the time we have today. So I want to thank our audience for taking the time to listen in. And thank you again, Dr. Leigh Cantrell, for your expertise and insight, as always. You're always so articulate and smart about your commentary about the data. And it's always been great speaking with you and particularly today, so thank you so much.

Dr. Cantrell:
Thank you, Warner, it was great being here.

Announcer:
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