Future Directions – Cervical Cancer

[Announcer] This podcast is presented by the Centers for Disease Control and Prevention. CDC – safer, healthier people.

[Dr. Saraiya] Welcome to this CDC program on cervical cancer screening. I'm your host, Dr. Mona Saraiya. With me today by phone is Dr. Alan Waxman, a professor of obstetrics and gynecology at the University of New Mexico. Dr. Waxman worked for the Indian Health Service for over 25 years, and he has been instrumental in leading colposcopy training of both mid-level and physician providers at the Indian Health Service. He chairs the ACOG Committee for the Underserved, and he serves as an advisor to the National, New Mexico, and the Navajo Breast and Cervical Cancer Early Detection Program. He's going to talk to us about several case studies for cervical cancer screening and management. Welcome to the show, Dr. Waxman.

[Dr. Waxman] Well thank you very much Mona, I'm happy to be here.

[Dr. Saraiya] Thank you. Well, Dr. Waxman, I understand that HPV 16 and HPV 18 are the types that cause the majority of cancers. Can you comment on that and the risk?

[Dr. Waxman] Well, HPV 16 and 18 are responsible, worldwide, for about two-thirds to three-quarters of cervical cancers. One of the spin-offs of this same study that I've been talking about, it would be really neat if we could take this woman who's Pap smear-negative but HPV-positive and say, "Are you positive for HPV 16 or 18?" And in fact, a secondary analysis of that study showed that where as the 10-year risk of a woman who was positive for the generic HPV test, her risk was about 4 percent. If you split out the HPV 16 and 18 group, their risk went up to almost 20 percent over a 10-year period. And in fact, by about three years out, if a woman was positive for HPV 16 or 18, her risk for CIN3 or worse was up in about the 12 percent range. So, if we could take this woman who is Pap-negative and HPV-positive, do an additional test to look for HPV 16 and 18, and if it was positive, then we know that her risk is suddenly very increased and we could preferentially schedule that person for colposcopy. The one whose HPV was found to be positive but was not 16 and18, she could wait another year and then get a repeat Pap plus HPV at that time.

Well, it turns out that in March of 2009, the FDA did approve the first HPV 16 18 assay. This is a test that not all labs will be doing but that many I suspect will. And at the time of this taping, it's not yet on the market, but as soon as it becomes I think we will have a better feel for the cost, the cost-effectiveness and the utility of it. The American Society for Colposcopy and Cervical Pathology (ASCCP) has already put out the clinical guideline that this test might be useful in women who have that scenario - the positive Pap – correction - the negative Pap, positive HPV. The next test that they recommend then, if it's available, would be to do a 16 18 assay. If the 16 18 test is positive, the patient would go to colopscopy; if negative, she would return to screening in another three years. If that test is not available, then the clinician is advised to repeat the Pap and the HPV in one year.

[Dr. Saraiya] Well, you just told us about the Cervista HPV 16 18 test. But isn't there also another one that's coming out called the Cervista High-Risk HPV?

[Dr. Waxman] Well, the Cervista High-Risk HPV test is very comparable to the Hybrid Capture II test that is currently on the market. And the recommendation is that if you are doing Pap plus HPV testing as primary screening, that you use either the Hybrid Capture II or the Cervista High-Risk test. It's recommended that you *not* use the 16 18 assay in that scenario as the initial primary screening test with the Pap test. It's also recommended by ASCCP that you not use the 16 18 assay for reflex HPV testing, which of course is the testing of HPV after a woman has had ASCUS – A-S-C-U-S - on her Pap test.

[Dr. Saraiya] Dr. Waxman, it sure sounds like we should throw out the Pap test and use the HPV DNA as our screening test.

[Dr. Waxman] Mona, you're a few years ahead of the curve on that. Right now, there is no FDA approval to use an HPV DNA test as a primary screening test. This is in part, I suspect, because the company that went to the FDA to get approval went and requested the Pap plus HPV testing as the screening test. There are a lot of researchers in Europe and quite a few in the United States as well who are suggesting that we look seriously at the possibility of switching to the HPV alone as the screening test and scrapping the Pap test. This would need to be done with very strict guidelines because if one was to use the HPV test as a screening test in women under 30, we would find an awful lot of HPV positivity and a very low rate of disease. If you look at many, many studies done around the world, at the age-specific prevalence of HPV DNA, it's extremely common in women from the mid-teens to the early thirties; hence, your HPV would very likely be positive; at the same time, the risk of cancer is extremely low in this age group. So this is a case where you'd spend a lot of buck and not get very much bang for it; it would not be cost-effective. So until good algorithms come out with a suggestion of how to screen the younger women, when to convert to HPV screening, what to do as the next step if the HPV is positive—until we get those algorithms, we're stuck with the current system which is screening with the Pap test from about three years after the onset of intercourse until age 30; at an annual to every-other-year rate, and then extending the interval at or after age 30 to every two to three years in women who had been previously negative. We can certainly add the HPV, as we've mentioned, to the Pap test after age 30, but until we get those algorithms, until we get FDA approval, we're using Pap test, with or without the HPV.

[Dr. Saraiya] Well what about extension of the screening intervals to beyond three years among women who are Pap-normal and HPV-negative?

[Dr. Waxman] Again, there are a number of studies that have been done. One very recent study out of Europe looked at women who were Pap smear-negative and compared them with women who were Pap- or Pap- and HPV-negative and found that the protection offered by a negative HPV test after six years was better than the protection offered by just a negative Pap test after three years, and the combination of the Pap and HPV, again, offers even more protection. So this strongly suggests that we could extend the interval beyond three years, and there are a number of professional organizations that are looking at this - the U.S. Preventive Services Task Force, the American Cancer Society, the American College of Obstetricians and Gynecologists. At present, that's not the current recommendation, but I think that, in the future, we may very well see a recommendation to extend it to four, five, or perhaps even six years. And again, extending the

interval for cervical cancer screening doesn't necessarily translate to extending the interval for other health maintenance exams that we do when we see our patients on a periodic basis.

[Dr. Saraiya] Well, Dr. Waxman, thank you so much for sharing this information with us. Do you have any last minute comments?

[Dr. Waxman] Just that it is a very exciting field. It's a very dynamic field. Things are changing. New studies are coming out all the time. Stay tuned; keep your eyes on the literature.

[Dr. Saraiya] OK, thank you.

[Dr. Waxman] Thank you, Mona.

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