

Women May Resist Pap + HPV Testing

Clinical staff should discuss testing before patient is seen by the doctor.

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VANCOUVER, B.C. — Incorporating testing for human papillomavirus into cervical screening practices for women older than 30 years may take more effort than one would think, Walter Kinney, M.D., said at the 22nd International Papillomavirus Conference.

He described the first 123,909 HPV tests performed within the Kaiser Permanente system on women over age 30 who also had satisfactory results from cytology performed at the same time. Kaiser announced its "cotesting" policy for women over age 30 in 2002.

"We told the lab to anticipate a tidal wave of specimens. That didn't happen," said Dr. Kinney of the Permanente Medical Group, Sacramento. "You can't just buy the reagent, announce the guidelines, turn on the machine, and expect this to happen."

Kaiser officials set about figuring out what to do to get clinicians and patients to accept HPV testing.

"This was a humbling process that went on for a couple of years" but led to excellent acceptance rates by physicians and patients, he said at the meeting, sponsored by the University of California, San Francisco.

Between May 2003 and August 2004, 85%-93% of appropriate patients underwent cotesting at Kaiser facilities, with the exception of one facility that posted a 70% cotesting rate.

This compares with results of a 2005 survey of 185 ob.gyns. randomly selected from the American Medical Association database in which only 33% said they would offer cotesting, despite recommendations for its use by the American College of Obstetricians and Gynecologists and the American Cancer Society (Am. J. Obstet. Gynecol. 2005;192:414-21).

Kaiser gained wider acceptance of cotesting by addressing issues related to staff, patients, and physicians. For staff, training on how and why to do HPV testing is critical. "They have to think it's something they would

choose for themselves," and they need to know how to talk with patients about it, Dr. Kinney said. "Sometimes the patients believe the staff a lot more than they believe you."

Kaiser created a specimen handling policy and flow charts for cotesting, posted summary sheets, obtained new color-coded order forms and color-coded specimen bins, and redesigned its "Pap books" to track results and patient responses.

Patients should be informed about cotesting before the physician arrives in the exam room, he said.

One way to do this is to have a medical assistant give the patient written materials after taking her blood pressure. Have information sheets as well as brochures handy. For patients with abnormal test results, have available brochures explaining their condition.

What the physician says to the patient about cotesting is important too. A poll of 350 Kaiser patients and 37 physicians asking why the patient did or did not have cotesting found that physicians believed both their words and printed materials were important. Patients, on the other hand, felt that what mattered most was whether physicians said cotesting is a good idea and that they would choose testing themselves.

Give physicians the education and tools they need to know what to say to patients about cotesting, and how to say it. Steps include conferences and guidelines, sample messages or scripts, and handouts on frequently asked questions.

In the Kaiser study, only 5.3% of the first 123,909 cotests were HPV positive. Of these, 3.7% had negative Pap tests.

The rate of HPV positivity dropped by half after age 39, from 9% in 30- to 39-year-olds to 5% of 40- to 49-year-olds. HPV positivity rates decreased with age to a low of 3% in women in their 60s, then crept up a bit over time, he said.

The lead investigator in studying the HPV data was Barbara Fetterman, Ph.D., of the Permanente Medical Group, Oakland, Calif. ■

Dietary Carotenoids May Defend Women Against HPV Infection

VANCOUVER, B.C. — Women who eat their vegetables and take vitamins may have a better chance of avoiding or clearing human papillomavirus infection, Marc T. Goodman, Ph.D., said at the 22nd International Papillomavirus Conference.

Low serum levels of tocopherol (vitamin E) or retinol (vitamin A) may increase the risk for acquiring human papillomavirus (HPV) infection, according to preliminary data from a controlled study of micronutrients and HPV.

High serum levels of carotenoids may enhance clearance of HPV infection and avoid persistent infection, said Dr. Goodman of the University of Hawaii, Manoa.

The investigators analyzed data on 242 women who had complete records from at least four clinical

visits, part of a larger longitudinal study at three clinics and two university-based health services. They categorized serum micronutrient levels as either low or high.

Women with low serum levels of vitamins E or A were twice as likely to develop incident HPV infection, compared with women with high levels of these nutrients, he said at the meeting, sponsored by the University of California, San Francisco.

A new HPV infection was found in 18% of women with low serum levels of β -tocopherol and α -tocopherol combined, compared with 9% of women with high levels of these nutrients.

HPV test results went from negative to positive from one visit to the next in 19% of women with low levels of retinol and

10% of those with high serum levels.

Incident HPV infection at one visit persisted in a positive HPV test at the next clinical visit in 20% of women with high serum levels of lutein or zeaxanthin, carotenoids that are abundant in green, leafy vegetables.

HPV persisted in 31% of women with low levels of these carotenoids, a 60% increased risk with low serum levels.

HPV persisted in 22% of women with high levels of β -cryptoxanthin (a carotenoid found in a variety of tropical fruits and nectarines), compared with 38% of women with low levels of this nutrient, who had a 70% increased risk for persistence.

The risk for HPV persistence doubled with low levels of α -carotene and was 60% higher with low levels of lycopene, compared with having high levels of these nutrients.

Dr. Goodman speculated that the differences might be related to the antioxidant functions of these nutrients, or to the interface between cytokine levels and local levels of antibodies.

"We know that the micronutrient levels do enhance the immune response," he said.

Intracellular signaling might play a role. A variety of nutrients affect the genes associated with transcription. It's also possible that antioxidants could directly affect HPV viral load and cell proliferation, he added. ■



High serum levels of carotenoids acted to enhance clearance of HPV infection and prevent persistent infection in women.

HPV Typing May Ease Cervical Lesion Angst

VANCOUVER, B.C. — Low-grade squamous intraepithelial lesions were likely to regress in women older than 30 years who were not infected with types of human papillomavirus associated with a high risk for cervical cancer, a longitudinal study found.

Of 412 women with untreated low-grade cervical intraepithelial lesions (LSIL), only women who tested positive for high-risk human papillomavirus (HPV) developed cervical intraepithelial neoplasia grades 2 or 3 (CIN 2/3) during 2 years of follow-up, Christine C. Clavel, Ph.D., said at the 22nd International Papillomavirus Conference.

HPV testing is approved in the United States to help triage women with Pap results showing atypical squamous cells of undetermined significance, or as an adjunct to Pap smears for screening women older than age 30.

The study suggests that it also

might be helpful by allowing a longer interval between follow-ups in women with LSIL and a negative HPV test, said Dr. Clavel of the University of Reims (France) Hospital Center.

At baseline, 87% of the 412 women and 80% of those older than 35 years tested positive for high-risk HPV types.

Colposcopy and biopsies found 21 cases of CIN 2/3 at baseline and an additional 12 cases during the 2-year follow-up, all in women who initially tested positive for high-risk HPV, she said at the conference, sponsored by the University of California, San Francisco.

Half of the high-risk HPV infections cleared over a median of 9 months in the cohort as a whole and in the subset of women older than 35 years.

Cytologic lesions cleared over time in 66% of the total cohort and in 68% of women older than

35. "There was a significant correlation observed between an initial negative high-risk HPV test, the regression of cytologic lesions, and the absence of CIN 2/3 in follow-up," she said.

Women with LSIL who test negative for high-risk HPV might safely be followed 12 months later by repeat cytology and HPV testing, she said. This would include approximately 13% of all women with LSIL, 20% over age 35 with LSIL, or 24% of women over age 45 with LSIL.

In women older than 45 years, misclassification of LSIL increases and leads to a decrease in detection of LSIL at colposcopy, she noted.

Using HPV testing plus Pap smears to follow HPV-negative women with LSIL could significantly decrease the number of women sent to colposcopy, compared with follow-up using cytology alone, Dr. Clavel said. ■