HPV Likely but Etiology Uncertain in HIV Positive

Coinfection often includes a higher prevalence of high-risk strains; is it persistence or reinfection?

BY DAMIAN McNAMARA
Miami Bureau

MIAMI BEACH — Human papillomavirus is often present in women who are HIV positive, but it remains unknown whether affected women are experiencing HPV reactivations, reinfections, or both, Dr. Matthew Pearson said at an ob.gyn. conference sponsored by the University of Miami.

Clinicians who treat women infected with HIV also are likely to see human papillomavirus (HPV) infection, including a higher prevalence of high-risk strains, compared with the general population.

Progression and persistence of HPV are associated with poorer HIV infection status, indicated by either low CD4 counts and/or high viral loads in most studies.

An estimated 50 million people are infected with HIV worldwide, including more than 1 million in the United States, according to the Centers for Disease Control and Prevention.

Also, there are an estimated 256 million people infected with HPV worldwide. In 1993, the CDC defined cervical cancer as an AIDS-defining illness.

"So is this a function of persistence or reinfection? Does the HPV go away and then the person gets reinfected?" asked Dr. Pearson, of the division of gynecologic oncology, University of Miami.

To try to answer this question, researchers looked at the natural history of coinfection in 2,362 women at a mean follow-up of 3 years (J. Natl. Cancer Inst. 2005;97:577-86).

The participants included 1,848 HIV-positive and 514 HIV-negative women enrolled in the longitudinal Women's Interagency HIV Study in 1994 or 1995 (http://statepiaps.jhsph.edu/wihs).

They found the rate of HPV clearance was lower among HIV-positive women (hazard ratio, 0.67), which suggested that persistence is a factor. However, the researchers also found that condom use decreased new HPV infections in women who had three or more partners.

"This is consistent with the idea of reinfection from new partners," Dr. Pearson said.

In 2001 and 2002, investigators for the Women's Interagency HIV Study enrolled an additional 1,144 women to assess the impact of highly active antiretroviral therapy (HAART). These additional participants included 406 HIV-negative women, 254 HIV-positive and HAART-naive women, and 484 HIV-positive HAART-treated women.

An estimated 13% of women treated with HAART had regression of their cervical squamous intraepithelial lesions each year, compared with no regression in the non-HAART group (J. Natl. Cancer Inst. 2004;96:1070-6). After a median of 2.7 years, 45% had lesions that regressed to normal cytology in the HAART group, compared with 59% in HIV-negative women.

There is no consensus about whether routine testing for HPV should be done to screen for abnormalities, Dr. Pearson said. However, HPV screening can guide the frequency of subsequent cancer screening.

For example, when a new HIV-positive patient presents and HAART is prescribed, monitor the patient with a Pap test and HPV DNA analysis at 6 months and 1 year, Dr. Pearson suggested.

If the Pap test results are negative and no high-risk HPV strain is detected, schedule an annual Pap/HPV test. If the patient is Pap negative but HPV positive for high-risk strains, schedule for a follow-up Pap test every 6 months.

If no HAART is prescribed and the CD4 count is greater than 500 cells per microliter, monitor the patient with a Pap test and HPV DNA analysis at 6 months and 1 year, Dr. Pearson suggested. However, if the patient has a CD4 count of 500 cells per microliter or below, schedule a follow-up Pap test every 6 months.

Each HPV type in the quadrivalent vaccine (Gardasil, Merck) is more prevalent among HIV-positive women than in the general population (J. Natl. Cancer Inst. 1999;91:226-36). These researchers concluded that prevalence of oncogenic HPV strains increases as CD4 counts decrease. Also, they found HIV-positive participants are more likely to be infected with multiple HPV strains; 23% of HIV-positive participants had two or more HPV types present.

Multiple HPV types also were more prevalent in HIV-positive women than in the general population (41% vs. 7%, odds ratio 9.3) in a meta-analysis of 20 studies with a total of 5,578 women (AIDS 2006; 20:2337-44).

These researchers also found multiple HPV types increasingly often as grade or abnormality on the Pap test increased. And, Dr. Pearson noted, "HPV 16 nearly tripled from low-grade to high-grade Pap smears."

"The question still remains if we should be vaccinating immunocompromised or HIV-positive women," Dr. Pearson said. "The CDC thinks it is worthwhile." Regarding the HPV vaccine, the CDC stated: "Immunocompromised females, either from disease or medication, can receive this vaccine; however, the immune response to vaccination and vaccine efficacy might be less than in immunocompetent females."

This view is shared by the Society of Gynecologic Oncology in their Statement on the Cervical Cancer Vaccine and the American College of Obstetricians and Gynecologists in their Committee Opinion #344, Dr. Pearson added.

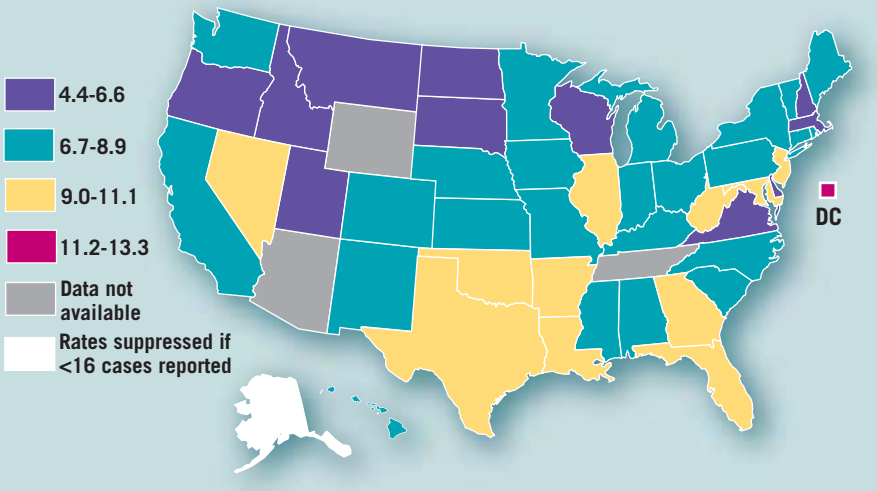
"The types in the octavalent vaccine [Cervarix, GlaxoSmithKline] will be more appropriate in my population, HIV-positive women infected with multiple strains of HPV," Dr. Pearson said.

"Which one of my patients will really benefit from vaccine prophylaxis?" Dr. Pearson asked. "That is really a study we want to get started on here at the University of Miami." ■

DATA WATCH

Lower Rates of Invasive Cervical Cancer in the Northwest

(per 100,000 persons)



Source: 2003 data, Centers for Disease Control and Prevention

Elsevier Global Medical News

Gardasil Efficacy Is Looking Good at Nearly 3 Years' Follow-Up

BY MIRIAM E. TUCKER
Senior Writer

ATLANTA — The efficacy of Gardasil is becoming more apparent over time, Dr. Eliav Barr said at a meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.

Merck is continuing to follow subjects post marketing, with nearly 3 years of data now available from three of the premarketing trials involving more than 18,000 young women.

Among those are 2.4 years for the group that was naive to all four vaccine strains of human papillomavirus (6, 11, 16, and 18) at baseline, 2.9 years for another group that was naive to 14 HPV types, and 2.8 years for a combined group of uninfected and infected women at baseline, said Dr. Barr, program head of HPV Vaccines for Merck Research Laboratories, Blue Bell, Pa.

In the per-protocol investigation comprising only those naive to the vaccine HPV strains, efficacy of the vaccine against HPV 16/18–related cervical intraepithelial neoplasia (CIN) 2/3 or adenocarcinoma in situ (AIS) is 99%, down from 100% at the time of licensure. The drop was the result of just one case of HPV 16/18–related CIN3 in a Gardasil recipient (versus 73 cases in the placebo group). An investigation into that one case determined that it was likely caused by contamination, Dr. Barr said.

Efficacy continues to increase over time as more cases of HPV 16/18–related disease occur in placebo recipients. Against all vulvar and vaginal lesions, including warts, the vaccine has stayed 99% effective.

Efficacy against HPV 16/18–related vulvar and vaginal intraepithelial neoplasia 2/3 remains at 100%, as it was at licensure. Efficacy against any grade of HPV 16/18–related CIN or AIS is now at 96%, compared with 95% at licensure.

Efficacy continues to increase over time as more cases of HPV 16/18–related disease occur in placebo recipients. Against all vulvar and vaginal lesions, including warts, the vaccine has stayed 99% effective.

It's possible that the few vaccine recipients who did develop lesions—6 CIN/AIS and 2 vulvar/vaginal lesions, compared with 148 and 189, respectively, among placebo recipients—were already infected at baseline, he noted.

In the combined group of those infected and uninfected at baseline, vaccine efficacy is now 41% against CIN 2/3 or AIS (versus 34% at licensure), 71% against vaginal or vulvar intraepithelial neoplasia 2/3 (69% at licensure), 54% against CIN of any grade (46% at licensure), and 78% against vulvar/vaginal lesions including warts, up from 70%.

Preliminary data also suggest cross-protection of the vaccine against lesions caused by non-vaccine strains of HPV. The company plans to present those data later this year.

"The preliminary results are quite encouraging," Dr. Barr commented. ■

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