Papillomavirus Common in HIV-Positive Women

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.

In one study, researchers found that 23% of HIV-positive participants had two or more human papillomavirus types present.

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 said, "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," he said. Determining which one of these patients will benefit from vaccine prophylaxis is "a study we want to get started on here at the University of Miami." ■

Sepsis Protocol Helps Minimize Adverse Effects of High BMI

BY MARY ELLEN SCHNEIDER
New York Bureau

ORLANDO — The use of a standardized therapeutic approach for treating severe sepsis may help to mitigate the increased mortality associated with a high body mass index, according to research presented at the annual congress of the Society of Critical Care Medicine.

Dr. Puneet S. Garcha and his colleagues at Drexel University, Philadelphia, performed a retrospective review of 62 patients with severe sepsis who were treated under a standardized therapeutic sepsis guideline based on early goal-directed therapy. The patients were admitted to a tertiary care unit medical ICU over a 15-month period between December 2004 and March 2006.

Patients with a body mass index (BMI) of 30 kg/m^2 or greater had a 28-day mortality rate similar to patients with a lower BMI, Dr. Garcha and his colleagues wrote in a study presented as a poster at the meeting.

The researchers compared 41 patients with a BMI of 29.9 or less to 21 patients with a BMI of 30 or greater. Patients in both groups had similar mean Acute Physiology and Chronic Health Evaluation (APACHE II) scores (25.8 in the lower BMI group, compared with 25.3 in the higher BMI group). In addition, the time to achievement of resuscitation goals and time from onset of severe sepsis to antibiotic administration was similar in both groups.

The researchers analyzed 28-day mortality, number of days on a ventilator, days spent in the ICU, and days in the hospital in an effort to see the impact of higher BMI on outcomes. None of the factors was statistically significant.

The 28-day mortality among patients with a BMI of 29.9 or less was 32.7%, compared with 34% among those with a BMI of 30 or greater.

While higher BMI was not associated with an increase in 28-day mortality, the researchers did observe a trend in the data indicating increased resource use in that group. For example, patients in the higher BMI group seemed to spend more time in the hospital. Among survivors, those with a BMI of 29.9 or less spent 48 days in the hospital on average, compared with 59 days on average among survivors in the higher BMI group. The difference approached statistical significance ($P = .06$).

Long-term follow-up will be necessary to determine if the mortality benefit seen at 28 days continues over time despite the morbidity and risk of complications seen in higher BMI patients, the researchers wrote. ■

Vasopressin Reduces Deaths In Less Severe Septic Shock

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Added to norepinephrine, low-dose vasopressin decreased mortality in one group of patients with septic shock, Dr. James Russell reported at the International Conference of the American Thoracic Society.

In a multicenter, randomized controlled trial, vasopressin at a dose of 0.03 U/min decreased mortality at 28 days and at 90 days in patients with less severe septic shock, but not in patients with more severe septic shock.

The reduction in mortality did not come at the expense of additional serious adverse events, said Dr. Russell of the University of British Columbia, Vancouver.

For the purposes of the trial, patients with more severe septic shock were defined as those needing more than 15 mcg/min of norepinephrine in the hour before randomization. Patients needing 5-15 mcg/min of norepinephrine formed the less severe group.

A total of 779 patients participated in the trial, all of whom were very ill, with Acute Physiology and Chronic Health Evaluation II (APACHE II) scores averaging 27. About half of the patients were in the less severe subgroup.

The less severe patients receiving vasopressin in addition to norepinephrine had a 9% absolute reduction in the risk of death at 28 days (36% to 27%), and a 10% absolute reduction in the risk of death at 90 days (46% to 36%), when compared with patients taking norepinephrine alone.

In the patients in the more severe subgroup, vasopressin was not associated with significant decreases in mortality at either 28 days or 90 days.

Physicians conducting the study were blinded as to whether they were administering vasopressin or norepinephrine. Patients were started at a steady infusion rate of 5 mL/min, corresponding to 0.01 U/min of vasopressin or 5 mcg/min of norepinephrine. The study drug was titrated from 5 to 15 mL/min over the course of 40 minutes in order to reach a mean arterial pressure of 65-75 mm Hg.

Once the patients were stable for 8 hours and receiving open-label vasopressors, they were weaned off the study drug. ■