Vaccine for Human Papillomavirus Prevents Genital Warts, Cervical Ca

BY HEIDI SPLETE
Senior Writer

WASHINGTON — A human papillomavirus vaccine developed by Merck & Co. is 100% effective in preventing genital warts in women in addition to preventing cervical cancer, Dr. John T. Schiller reported at the annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy.

The vaccine, known as Gardasil, includes HPV types 6, 11, 16, and 18. Types 16 and 18 account for about 70% of cervical cancer, and types 6 and 11 account for about 90% of genital warts, said Dr. Schiller, head of the neoplastic disease section of the National Cancer Institute, Bethesda, Md.

At 2 years of follow-up, Gardasil achieved 100% efficacy against genital warts, vulvar neoplasia, and vaginal neoplasia, in addition to the previously reported 100% efficacy against cervical intraepithelial neoplasia (CIN). The phase II Females United to Unilaterally Reduce Endo-Ectocervical Disease study (FUTURE I) included 2,717 women randomized to a vaccine group and 2,725 randomized to a placebo group. Overall, there were no cases of genital warts in the vaccine group, compared with 40 cases in the placebo group.

Dr. Schiller also shared the latest findings from the FUTURE II study, a randomized, double-blind, phase III clinical trial that included about 12,000 women aged 18-25 years. The intent-to-treat numbers in the FUTURE II study showed extremely strong protection at 2 years of follow-up—only two cases of CIN grade 2 or 3—and the vaccine was generally well tolerated. One case of CIN was associated with HPV type 16, and the other was associated with a combination of types 16 and 18. The phase III studies are ongoing, and the data remain under review, but findings similar to those from the phase II study are expected with regard to genital warts and vulvar and vaginal neoplasia.

Merck filed its Gardasil data with the Food and Drug Administration on Dec. 1, 2005, and a vaccine could be available in the United States by late summer in 2006, Dr. Schiller said. GlaxoSmithKline Inc. has stated that it will seek regulatory approval in 2006 for its vaccine, Cervarix, which immunizes against HPV 16 and 18, but that it might seek initial approval in Europe.

Once the vaccine becomes available, the top candidates for immunization will be 10- to 13-year-old girls. "They are the ideal first targets because presumably, they have not yet been exposed to sexually transmitted viruses," Dr. Schiller said at the meeting, sponsored by the American Society for Microbiology.

But before the vaccine becomes standard for young girls, it may be used in young women because of the high demand in that population, he noted. Some adult women may not have been exposed to the oncogenic strains of HPV, and vaccination may reduce transmission to their partners as well. An HPV vaccine has yet to be tested in men, but only 10% of HPV cancers occur in men, and high vaccination coverage of women may result in sufficient herd immunity, Dr. Schiller noted.

The HPV vaccines are based on purified viruslike particles (VLPs) that consist of single proteins. They are noninfectious and nononcogenic, but they can induce high titres of neutralizing antibodies, Dr. Schiller said.

Despite the promising results, several questions about HPV vaccination remain unresolved, including effects on current cancer screening programs, public acceptance, price, and distribution to underserved populations.

"Women might think that they are protected from cervical cancer because they have the vaccine, and abandon their screening programs, which would be a disaster," Dr. Schiller said. Vaccination would not replace the need for a pap test, he emphasized, although it might reduce the incidence of repeat pap tests resulting from unclear results.

Vaccine acceptance is another issue, but preliminary surveys of parents suggest that as many as 75% would agree to vaccination of their adolescent daughters. But the logistics of delivering three intramuscular doses of vaccine to early adolescent girls over a 6-month period may prove challenging, Dr. Schiller added.

The price of the vaccine is critical to how many women and girls receive it. It is likely to be expensive at first, "perhaps as much as $100 per dose," Dr. Schiller said.

Price is a huge barrier to providing the HPV vaccine to the underserved women who need it most. "Cervical cancer is a disease of poverty—80% of cases occur in developing countries where women don't have access to good quality pap screening," Dr. Schiller noted. "This vaccine will not have the impact it should if the only women who are vaccinated are those who already get good cervical cancer screening."

Regional production might be the best way to build up the amount of the vaccine and reduce the cost. In addition, researchers continue to investigate a second-generation vaccine that could be administered orally. ■

Clinicians' HPV Facts Outdated

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — When it comes to human papillomavirus, U.S. clinicians who see the most patients with it are aware of the basics but aren't always up on the latest information, Dr. Nidhi Jain reported in a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The finding comes from a survey of a nationally representative sampling from nine clinical specialties that care for substantial numbers of sexually active patients: The 4,305 respondents (to a total 6,906 mailed surveys) included family/general practice physicians (9%), general internists (7%), adolescent medicine specialists (10%), ob.gyns. (11%), dermatologists (12%), urologists (11%), nurse practitioners (15%), certified nurse midwives (15%), and physician assistants (12%).

A majority (89%) knew that "genital HPV [human papillomavirus] infection is fairly common in sexually active adults," that infected individuals often lack signs or symptoms (95%), that an HPV infection increases the risk for cervical dysplasia and cancer (98%), and that treatment of external anogenital warts and cervical dysplasia/cancer does not always eliminate the infection (92% warts; 91% dysplasia/cancer).

But only 35% were aware of recent scientific evidence showing that most HPV infections clear without medical intervention, that anogenital warts do not increase the risk of cancer at the same site where the warts are located (38%), and that the HPV types associated with warts are not the same as the types associated with cervical dysplasia (47%).

Of all the specialists, ob. gyns. had the best overall knowledge of HPV. In the group as a whole, clinicians who use HPV testing gave more correct responses than did those who don't use the tests, Dr. Jain said at the conference, sponsored by the American Society for Microbiology.

"However, even the highest percentages were sometimes very low," said Dr. Jain, a medical officer at the Centers for Disease Control and Prevention, Atlanta.

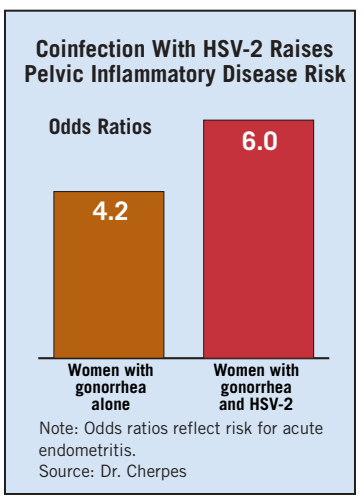
HSV-2 Linked to Higher Risk of Pelvic Inflammatory Disease

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Herpes simplex virus type 2 infection in women may be associated with an increased risk of pelvic inflammatory disease, Dr. Thomas L. Cherpes reported in a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

The role of chronic genital viral infections in the pathogenesis of pelvic inflammatory disease (PID) may be more significant than currently recognized, although no etiologic link has as yet been defined, noted Dr. Cherpes and his associates at the University of Pittsburgh.

A total of 725 nonpregnant women aged 15-30 years who were either diagnosed with a lower bacterial genital tract infection (purulent cervical discharge, untreated *Neisseria gonorrhoeae* or *Chlamydia trachomatis* infection, symptomatic bacterial vaginosis) or were at risk for such an infection (sexual contact with a male diagnosed with gonorrheal, chlamydial, or nongonococcal urethritis) were recruited from sexually transmitted disease clinics and gynecology clinics. Of those, 43% (309) were seropositive for herpes simplex virus type 2 (HSV-2).



Of the 86 women with acute endometritis, 55% (47) were HSV-2 seropositive, as were 51% (70) of the 136 women found to have plasma cell endometritis. Acute endometritis was independently associated with black race (odds ratio 1.7) as well as infections with *C. trachomatis* (3.3), *N. gonorrhoeae* (2.8), *Trichomonas vaginalis* (2.4), and HSV-2 (2.2). Black race also was associated with plasma cell endometritis (odds ratio 1.9), but HSV-2 was the only reproductive tract infection significantly associated with that condition (odds ratio 1.5), they reported.

Coinfection with HSV-2 and a genital tract bacterial pathogen significantly increased the likelihood of PID, compared with having one or the other alone. For example, the odds ratio for acute endometritis was 5.0 for women with chlamydia and 2.6 for those with HSV-2, compared with women who did not have those conditions. However, the odds ratio jumped to 7.3 for women coinfected with both. Similarly, women with gonorrhea alone had a 4.2-fold increased risk for acute endometritis, which rose to 6.0 if they were also infected with HSV-2.

In 471 of the women who underwent hysterosalpingography, 8.1% (38) had both HSV-2 infection and evidence of fallopian tube obstruction: Those 38 accounted for 19% of the 199 women who were HSV-2 positive and 54% of the 71 with fallopian tube blockage.

These data do not exclude the possibility that the higher prevalence of HSV-2 in women with PID may simply reflect a marker for sexual activity and/or the coacquisition of a PID-associated bacterial pathogen, the investigators wrote.

The conference was sponsored by the American Society for Microbiology. ■

Pages 26a—26b