

Vaccinating Girls for HPV

A New Horizon of Hope for Cancer Prevention



Clare McLean

Priscilla McElhose, ARNP, health care specialist at the University of Washington Hall Health Primary Care Center Women's Clinic, with her daughter Katherine, who had just received her third and final HPV vaccination.

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Every 14 days, a woman in this country dies of cervical cancer. Other cancers take more lives, but cervical cancer kills at a relatively young age (57 years versus 72 years for other cancers). As a result, the average woman dying of cervical cancer in the US loses more than 26 years of potential life. Among the major causes of mortality in the US, only violent deaths and HIV are associated with similarly high average numbers of years of life lost. Women with lower incomes and education are more likely than other women in the US to die from cervical cancer because they have less access to screening, diagnostic, and treatment services. Cervical cancer is even more of a burden in lower-income nations, where it is the number one or two cause of female cancer death.

HPV-cancer connection

Virtually all cases of cervical cancer are caused by human papillomavirus (HPV), a sexually transmitted viral infection that is frequently acquired in late adolescence or early adulthood. In fact, HPV is so common and communicable that many young women are infected with HPV by their first and only sex partner. Routine Pap testing has reduced the overall rate of invasive cervical cancer in this country by 75 percent during the last 40 years, but the rate of cervical adenocarcinoma, which typically occurs in an area of the cervix that is more difficult to sample for Pap testing, has risen. Furthermore, every year thousands of primarily reproductive-aged women require colposcopy, biopsy, and treatment procedures for a precancerous cervical lesion. Treatment is usually effective, but more frequent Pap testing is recommended for years afterwards, and treated women are at increased risk for cervical stenosis and for premature rupture of membranes and preterm labor during pregnancy. The same HPV types that cause cervical cancer, also cause

vaginal and vulvar cancer in women, penile cancer in men, and anal and oral cancer in both men and women. Other types of HPV cause genital warts and recurrent respiratory papillomatosis (RRP), which are not lethal conditions, but are difficult to clear and sometimes cause more serious secondary consequences. In rare instances, genital warts can cause locally invasive tumors and obstruction of the birth canal, and RRP, which usually requires repeated treatments, can cause life-long vocal pattern changes.

The new vaccine

A new vaccine prevents infection with four clinically important types of HPV: two types that cause 70 percent of cervical cancers (HPV-16 and HPV-18) and two that cause 90 percent of genital warts and cases of recurrent respiratory papillomatosis (HPV-6 and HPV-11). Because this vaccine does not prevent infection with all cancer-causing HPV types and will not clear existing infections, recommendations for Pap screening will remain the same. However, as vaccination becomes more widespread, fewer women will develop Pap test abnormalities that require diagnostic and treatment procedures for precancerous cervical lesions and invasive cancer. Whether boys and young men will benefit from vaccination is not yet known, although it is possible that vaccinating them could have indirect health benefits for women and girls. Results of studies of male adolescents and young men are expected by early 2008.

As with other commonly used vaccines, such as polio, measles, and hepatitis B, the HPV vaccine is preventative, not therapeutic. For this reason, vaccination will offer the most protection if administered before sexual debut or shortly thereafter. According to data from the 2002 National Survey of Family Growth, 40 percent of 16-year-old and 70 percent of 18-year-old

females in the US report having had at least one sex partner. These statistics prompted the Advisory Committee on Immunization Practices (ACIP), American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP), American College of Obstetrics and Gynecologists (ACOG), and the American Cancer Society (ACS) to recommend routine vaccination of 11- to 12-year-old females (and as early as age 9) with catch-up vaccinations through age 18 (ACS) or through age 26 (ACIP, AAP, AAFP, and ACOG). The vaccine is included in the federal Vaccine for Children program, which provides recommended vaccines to states for children and adolescents less than 19 years of age who are Medicaid eligible, uninsured, under-insured, Alaska Native, or American Indian. (Washington State, however, is a “universal coverage” state, which means the state government uses a combination of federal and state funds to provide vaccine to all eligible children and adolescents less than 19 years of age, regardless of private insurance coverage.)

Barriers to vaccine use

Cost and limited access are two barriers that must be addressed in order to realize the full potential of the vaccine. At \$288 to \$360 for the three-dose regimen, the vaccine is expensive relative to most other childhood vaccines.

In December 2006, Washington State Governor Christine Gregoire proposed funding for about 143,000 doses of the HPV vaccine. If approved by the legislature, this allotment would provide three doses of vaccine for more than 50 percent of all 11- to 12-year-old females, or about 14 percent of the estimated 336,000 females 11 to 18 years old in the state. The Centers for Disease Control and Prevention estimates that only 25–36 percent of the recommended age group will be vaccinated in the first year of licensure, which ends in June of 2007. Vaccines are most effective from a public health perspective when coverage of the target population is high (at least 80 percent), but it typically takes at least a few years after licensure for vaccine coverage to reach this level.

Vaccination requirements for school entry have been shown to improve immunization rates, due in part to reducing the opportunity for passive omission by parents and physicians. Unfortunately, laws governing vaccination prior to school entry may generate concerns about loss of parental/guardian autonomy. Washington State, as many other states, has no compulsory school-entry mandates for vaccines. Parents or legal guardians can decline to vaccinate their children based on medical, religious, or personal reasons. Opting out of vaccination is so simple in Washington State that exemption rates for childhood vaccines have been increasing, putting children at risk for serious illness due to vaccine-

HPV Vaccine in the US: Potential Annual Effect

HPV- Related Disease	Estimated Annual Morbidity Prior to HPV Vaccines	Vaccine Preventable HPV 6-, 11-, 16-, or 18- Related Morbidity
Invasive cervical cancer	11,150	7,800 (~70%)
Vulvar, vaginal, penile, and anal cancers	11,560	5,780 (~50%)
Head and neck cancers	34,000	3,400 (~10%)
Recurrent Respiratory papillomatosis (RRP)	1,000	800 (~80%)
Precancerous cervical lesions (CIN 2/3, AIS)	500,000	250,000 (~50%)
Genital warts	500,000	450,000 (~90%)

Sources: American Cancer Society, 2007; Chesson HW. *Persp Repro Health*, 2004; Saslow D. *CA Cancer*, 2007.

preventable infections. Arresting the trend toward larger numbers of parents refusing immunization is a genuine public health challenge that is not limited to HPV vaccine.

Beyond ensuring widespread use of the HPV vaccine, the primary outstanding issue is the duration of vaccine-induced protection. Girls and young women in the research studies were followed for only up to five years after the first dose. No evidence of waning immunity or decreased efficacy for prevention of infection or persistent shedding of virus has been found during five years of follow-up. The possibility of HPV developing mutations that would allow it to escape from vaccine-induced protection is unlikely; the HPV genome is very stable with mutational changes occurring at frequencies similar to those of the human genome. Also, an antigen challenge of the HPV vaccine was shown to stimulate a response that is characteristic of vaccines, such as the hepatitis B vaccine, that provide long-lasting protection. Considered together, these findings suggest that HPV vaccine-induced protection could be durable. However, until there is longer follow-up of vaccinated females, the need for boosters cannot be ruled out.

The HPV vaccine has a good safety profile and high efficacy for preventing HPV6/11/16/18-related precancerous lesions of the uterine cervix, vagina, and external genitalia in female adolescents who have not been infected with one or more of the four targeted HPV types. As with other new vaccines, parents, health care providers, and policy makers should continue to educate themselves about this vaccine. ■

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