



The Vision and Voice of **Women** in Medicine

Position Paper **Cervical Cancer Prevention**

- I. AMWA advocates public health policy that makes cervical cancer elimination a priority and ensures that all women are educated about cervical cancer and the role of human papillomavirus (HPV) in cervical cancer.
- II. AMWA advocates health initiatives that:
 - Recognize the widespread vulnerability of women to HPV infection;
 - Recognize the role of HPV infection in the development of cervical cancer;
 - Promote regular screening of appropriate women for cervical cancer with the Papanicolaou test to reduce mortality from cervical cancer;
 - Promote access for all women to the most advanced cervical cancer screening and preventive technologies, including Pap (liquid-based) and HPV (human papillomavirus) testing; and
 - Promote the universal protection of women from cervical cancer with vaccines shown to be safe and effective for its prevention.
- III. AMWA advocates public health policy and practice related to prevention of and screening for HPV and cervical cancer that is based on empirical medical evidence — rather than on political, philosophical or religious beliefs — such that all Americans have access to the best disease protections available.
- IV. AMWA advocates continuing research, development and approval of additional safe and effective vaccines to prevent cervical cancer and expansion of the indications for HPV vaccines based on new evidence as it comes available.

Founded in 1915 as the oldest and largest multispecialty association of women physicians, residents and medical students, the American Medical Women's Association (AMWA) today represents a community of professionals working to promote health and encourage the professional and personal development of those in medicine, healthcare and health-related fields. AMWA is dedicated to the promotion of ethical principles of medical practice, particularly as they apply to health care issues involving women and their families. Cervical cancer is an important women's health issue. Current research and development suggests that cervical cancer may be preventable for women in the future.

Background

Worldwide, more than 500,000 women are diagnosed with cervical cancer each year.¹ In 2007, in the United States alone, there will be an estimated 11,150 new cervical cancers diagnosed and 3,670 cervical cancer deaths.²

Annually, an additional 1,250,000 American women are diagnosed with precancers by cytology using the Papanicolaou (Pap) smear. These precancers include a continuum of pathologic changes ranging from atypical squamous cells of undetermined significance to low-grade squamous intraepithelial lesions (LSIL) to high-grade squamous intraepithelial lesions (HSIL) to invasive cancer. The precancerous conditions LSIL and HSIL are also referred to as cervical intraepithelial neoplasia (CIN) 1, 2, and 3. Lesions can regress, persist, or progress to an invasive malignancy, with LSIL (CIN 1) more likely to regress spontaneously and HSIL (CIN 2/CIN 3) more likely to persist or progress. The average time for progression of CIN 3 to invasive cancer has been estimated to be 10 to 15 years.³

Nearly all cases of cervical cancer are associated with human papillomavirus (HPV) infection, which is transmitted during sexual activity.⁴⁻⁶ Although most women with cervical cancer have the human papillomavirus (HPV) infection, not all women with an HPV infection will develop cervical cancer. Many different types of HPV can affect the cervix and only some of them cause abnormal cells that may become cancer. While some HPV infections go away without treatment, the presence of HPV indicates increased vulnerability to cervical cancer and the need for adherence to a regular schedule of screenings. Thus, women who do not have regular Pap and HPV tests are at increased risk of cervical cancer.

Human Papillomavirus

Epidemiologic studies to evaluate risk factors for the development of squamous intraepithelial lesions (SIL) and cervical malignancy demonstrate conclusively a sexual mode of transmission of a carcinogen.⁵ It is now widely accepted that human papillomavirus (HPV) is the primary etiologic infectious agent.⁶⁻⁸ Other sexually transmitted factors, including herpes simplex virus 2, may act as co-factors in causing cervical cancer.⁹ The finding of HPV viral DNA integrated in the majority of cellular genomes of invasive cervical carcinomas supports epidemiologic data linking this agent to cervical cancer.⁵ Direct causation, however, has not been demonstrated. More than 80 distinct types of HPV have been identified, approximately 30 of which infect the human genital tract. HPV types 16 and 18 are most often associated with invasive disease and cause about 70% of all cervical cancers. Characterization of carcinogenic risk associated with HPV types is an important step in the process of developing a combination HPV vaccine for the prevention of cervical neoplasia.

In a population-based study of HPV infection and cervical neoplasia in Costa Rica, 80% of high-grade squamous intraepithelial lesions (HSIL) and invasive lesions were associated with HPV infection by one or more of 13 cancer-associated types.¹⁰ In this study, the risk of about half of HSIL and invasive cervical cancer was attributable to HPV-16. HPV-18 was associated with 15% of invasive disease, but only 5% of HSIL, suggesting that HPV-18 may have a role in more aggressive cases of cervical malignancy.

Given the etiologic role of HPV in the pathogenesis of cervical neoplasia, vaccines to immunize against HPV infection offer a primary prevention strategy for cervical cancer for those women not already infected with HPV types 16 and 18. Vaccines using HPV late protein (L1 and L2) constructs to induce antibody-mediated immunity are in clinical trials.¹¹

Vaccine to Prevent HPV Infection

Persistent infection with oncogenic types of HPV, such as HPV-16 and 18, is associated with the development of cervical cancer.¹² Vaccines to prevent HPV infection with oncogenic-type viruses have the potential to reduce the incidence of cervical cancer. A vaccine against HPV-16 and HPV-18 is effective in preventing persistent infection. A vaccine with HPV-16 and HPV-18 types, the two most common strains, could prevent 71% of cervical cancers worldwide.¹⁴

As of 2006, a vaccine that targets HPV 6, 11, 16, and 18 was approved by the FDA for the prevention of cervical cancer, and another vaccine targeting HPV 16 and 18 is in clinical trials. Despite the promising implications for the future of investigational vaccines, in order to be effective, these vaccines should be administered to women prior to initial sexual contact. Furthermore, the currently approved vaccine and those in the pipeline as of 2007 were developed to be given as a series. Since efficacy depends upon repeated dose administration, adherence will be a challenge to providing full immunity. Moreover, although there are good data indicating that the vaccine will be effective for at least 3 years,¹⁵ actual duration of immunity is unknown as of this posting but follow-up studies are in progress. For these reasons, and because the vast majority of our population is over the age of first sexual contact, it is imperative that women continue to have access to and be encouraged to seek screening through regular Pap testing using the most effective technologies and HPV testing for women age 30 and over to protect them from cervical cancer. AMWA supports access to the most effective methods for cervical cancer and HPV detection including HPV testing when Pap testing results in ASCUS findings and HPV testing of women over age 30 in accordance with recently established guidelines.^{16,17}

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