FACT SHEET

Cervical Cancer

NATIONAL INSTITUTES OF HEALTH

Yesterday

- As recently as the 1940s, cervical cancer was a major cause of death among women of childbearing age in the United States. However, with the introduction in the 1950s of the Papanicolaou (Pap) smear – a simple test in which a sample of cervical cells is examined under a microscope to detect cellular abnormalities – the incidence of invasive cervical cancer declined dramatically. Between 1955 and 1992, U.S. cervical cancer incidence and death rates declined by more than 60%.
- Epidemiologic evidence had long suggested that cervical cancer might be caused by a sexually transmitted agent, but the nature of this agent was not known until the 1980s.
- In the early 1970s, the mainstays of treatment for cervical cancer and precancerous cervical lesions (growths) were cone biopsy and hysterectomy.
- Clinical researchers were only beginning to develop and test less invasive procedures, such as cryosurgery, laser surgery, and LEEP (loop electrosurgical excision procedure), for treating precancerous cervical lesions.

Today

- Cervical cancer – once one of the most common cancers affecting U.S. women – now ranks 14th in frequency. Because precancerous lesions found by Pap smears can be treated and cured before they develop into cancer, and because cervical cancer is often detected before it becomes advanced, the incidence and death rates for this disease are relatively low. According to the most recent data (for the period from 2003 through 2007), the incidence rate for cervical cancer was 8.1 cases per 100,000 women per year in the United States. The mortality rate was 2.4 deaths per 100,000 women per year. In 2010, an estimated 12,200 women in the United States will be diagnosed with cervical cancer, and an estimated 4,210 will die of the disease.
- In certain populations and geographic areas of the United States, cervical cancer incidence and death rates are still high, due in large part to limited access to cervical cancer screening. Rates are also high in developing nations, where more than 80% of cervical cancer cases occur. Worldwide, cervical cancer is the third most common cancer among women and the second most frequent cause of cancer-related death, accounting for nearly 300,000 deaths annually. In developing nations, it is often the most common cause of cancer-related death among women and a leading cause of death overall.
- Virtually all cases of cervical cancer are caused by specific types of human papillomavirus (HPV). There are more than 100 types of HPV, of which more than 40 can be sexually transmitted. Among these, about 15 are considered to be cancer-causing, or high-risk, types. Two of these high-risk types, HPV-16 and HPV-18, cause about 70% of cervical cancers worldwide. HPV infection is very common, but it usually goes away on its own. Persistent HPV infections, however, can cause cellular abnormalities that sometimes develop into cervical cancer if not treated.
- Highly sensitive and specific molecular tests are now available to identify DNA from high-risk HPV types in cervical specimens. HPV DNA testing can help to determine whether a woman needs further medical attention following a borderline or ambiguous Pap test result. In addition, the FDA has approved HPV DNA testing in conjunction with cervical cytology (i.e., Pap smears) for routine cervical screening of women 30 years of age and older. Pap tests have a relatively high percentage of false-negative results and are, therefore, often repeated annually to maximize their effectiveness. However, if the results on both a Pap smear and an HPV DNA test are normal, a false negative is less likely. Therefore, the screening interval can be extended (to 3 or more years).
- The FDA has approved two vaccines, Gardasil® and Cervarix®, which are highly effective in preventing persistent infections with HPV types 16 and 18, the two high-risk HPV types that cause the majority of cervical cancers. Gardasil also protects against infection with HPV types 6 and 11, which cause about 90% of genital

warts. The vaccine is based on technology developed by NIH scientists and others, whose work laid the foundation for the production of HPV "virus-like particles," or VLPs. These non-infectious agents trigger a robust antibody response that prevents persistent infection with the HPV type from which the VLP is derived. Gardasil is a mixture of VLPs for HPV types 6, 11, 16, and 18, and Cervarix is a mixture of VLPs for HPV types 16 and 18. The vaccines are approved for use in girls and young women for the prevention of cervical cancer but have been proven effective only if given before infection.

- Treatment of cervical cancer has improved considerably. The 5-year relative survival rate for women diagnosed with cervical cancer is close to 75%. Most cervical cancer patients receive radiation plus concurrent chemotherapy as part of their treatment. Cisplatin is the most common chemotherapy agent used for cervical cancer.

Tomorrow

- Research on HPV vaccines is continuing. Although Cervarix and Gardasil protect against infection with HPV types 16 and 18, these vaccines do not protect against HPV types found in approximately 30% of cervical cancers. Consequently, women who have been vaccinated need to continue to have regular Pap smears. Including VLPs for other high-risk HPV types in vaccines is one approach to increase protection against the other viruses. Researchers at NIH and elsewhere are also working to develop a vaccine that induces the production of antibodies against a broad range of HPV types. Such a vaccine may have the potential to prevent infection by many high-risk HPV types.

- Carrageenan, a compound that is extracted from a type of seaweed, has been found to inhibit HPV infection in laboratory studies. This compound, a type of sulfated polysaccharide, is used widely as a food additive and in many other products. Clinical trials are under way to test whether a topical microbicide that contains carrageenan can prevent genital HPV infection.

- Scientists are striving to better understand why HPV infections go away on their own in most people but persist in others and lead to cervical cancer in only some women who have persistent infections. For example, NIH scientists are studying a large population of women in Costa Rica, where the HPV infection rate is high, to identify factors associated with persistent infection and cancer development.

- Screening tests are being developed that will allow clinicians to examine additional markers of HPV infection. Some of these tests, such as ones that assess HPV messenger RNA, may be more specific for disease than the current tests. Other new technologies under development may allow women to collect samples at home, may yield results on the same day as the test, and may be done at low cost. These "rapid" tests may be of particular value in developing nations and medically underserved populations in developed nations.

- NIH is also supporting efforts to make cervical cancer prevention, screening, and treatment more affordable to help reduce cervical cancer incidence and mortality in developing nations and to make interventions more cost-effective in the United States. NIH scientists are also helping to introduce low-cost HPV testing for public health use in low-resource countries. In addition, researchers at NIH and elsewhere are analyzing computer models to identify the most cost effective approaches to both screening and treatment.

- Colposcopy, a magnified examination of the cervix in which biopsy samples are taken, is usually recommended for women who have certain abnormal Pap smear results. However, several factors can influence the accuracy of the results from this procedure. NIH scientists are collaborating with other researchers to develop more sensitive approaches to detect and diagnose cervical abnormalities.

- HPV infections cause not only cervical cancer but also some other genital cancers (vulvar, vaginal, anal, and penile cancers) as well as some head and neck cancers. Overall, HPV infections account for about 5% of all cancers worldwide. Advances in understanding the relationship between HPV infection and cervical cancer will have important implications for developing approaches to prevent and treat other HPV-associated cancers.

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