

## HPV — The Most Common Sexually Transmitted Virus

Human papilloma virus (HPV) is a common infection that affects skin and mucous membranes. Some types cause common skin warts in areas such as the hands or feet. Some types cause warts in the genital areas. Certain high-risk types can cause cancers of the cervix, vagina, vulva, penis, and anus. More than 100 viral types of HPV have been identified — approximately 30–40 percent of these are associated with sexually transmitted infections, and people may be infected with more than one type at a time (Schiffman & Castle, 2003; Wiley, et al., 2002). HPV has affected humans for thousands of years — ancient Greek and Roman medical records described genital lesions consistent with genital warts and associated them with sexual activity (Jay & Moscicki, 2000).

Today HPV is one of the most common sexually transmitted infections in the U.S. — yet 70 percent of Americans have never heard of it and 89 percent have never discussed HPV with their health care provider (KFF, 2000). Up to 20 million Americans are currently infected with sexually transmitted HPVs, and approximately 6.2 million Americans acquire sexually transmitted HPV annually (Cates, 1999; CDC, 2006). The highest rates of new genital HPV infections — approximately 74 percent of annual infections — occur among young adults between the ages of 15 and 24 (Weinstock, et al., 2004). In 2000, there were approximately 9.2 million sexually active young adults infected with HPV — this translates to one in four of all young adults in America (Weinstock, et al., 2004). HPV is also prevalent among people with immunosuppressive disorders, such as HIV (Koutsky & Kiviat, 1999). HPV is believed to be widespread across racial groups and to have very little variation in prevalence across regions in the U.S. (CDC, 2000). HPV is so common, in fact, that it is considered a virtual marker for having had sex (Boonstra, 2004). In fact, the

lifetime risk for contracting HPV is at least 50 percent for all sexually active women and men, and, it is estimated that, by the age of 50, at least 80 percent of women will have acquired sexually transmitted HPV (CDC, 2004; CDC, 2006).

### Transmission

HPV is transmitted by direct skin-to-skin contact with an infected individual. Transmission is usually from vaginal, oral, or anal sexual contact, and can occur whether or not warts or other symptoms are present (McDermott-Webster, 1999). Unprotected penetrative intercourse with multiple partners is the greatest behavioral risk for contraction of HPV (Kjaer, et al., 2001; Winer, et al., 2003).

The virus can also be transmitted from mother to infant during childbirth — also known as vertical transmission (Puranen, 1997). In one of the largest studies to look at both oral and genital HPV infections in newborns, research showed that the vertical transmission rate was less than one percent (Smith, et al., 2004). The development of recurrent respiratory papillomatosis (warts in the respiratory tract) is one potential consequence of vertical transmission (Smith, et al., 2004; Kashima, et al., 1996). It is estimated that about 2,000 out of every four million newborns are infected (Jay & Moscicki, 2000). This is a serious, and potentially fatal, condition that may require frequent laser surgery to prevent obstruction of the infant's airways (NIAID, 2004).

Some research also suggests that genital HPV can be transmitted through nonsexual routes, via fomites — inanimate objects such as towels or underwear — but more research must be conducted to examine these modes of transmission (Carson, 1997; Keller,

et al., 1995; Stevens-Simon, et al., 2000).

### Natural History

Although there is currently no “cure” for genital HPV infection, most cases are transient and clear themselves without medical intervention (Brown, et al., 2005; CDC, 2001; Elfgren, et al., 2000; Ho, et al., 1998). It is estimated that approximately 80 percent of all HPV infections in women between the ages of 15 and 25 years are transient (Meijer, et al., 1998). One study designed to determine the natural history of genital HPV infection followed college women for three years (Ho, et al., 1998). HPV was detected using a sensitive DNA test that detects small amounts of HPV, even when there are no symptoms present. While there was a high rate of HPV infection (43 percent tested positive for HPV at some point over the study period), the average duration of HPV infection was eight months. Repeated HPV DNA testing showed that 70 percent of the women cleared their HPV infections within one year through the natural immune process, and only nine percent continued to be infected after two years. Another study conducted in Sweden supported these findings, with a five-year clearance rate of 92 percent (Elfgren, et al., 2000). In these studies, and in more current research, the viral type of HPV was a major determinant in the duration of infection, with types 16, AE7, 61, 18, and 73 having the longest average duration (Elfgren, et al., 2000; Ho, et al., 1998; Muñoz, et al., 2004; Richardson, et al., 2003; Woodman, et al., 2001). Other factors associated with the persistence of HPV infections are age (older than 30 years), infection with multiple HPV types, and a compromised immune system (Hildesheim, et al., 1994; Ho, et al., 1995; Moscicki, et al., 1998).

### Subclinical Manifestations of HPV

Most HPV infections are subclinical (no visible signs or symptoms), and many people with HPV never know they have it (Verdon, 1997). HPV targets the deep, basal level of the skin and most often causes no clinical or microscopic changes in the cells of the skin (Keller, et al., 1995; Verdon, 1997). In some cases, subclinical HPV may cause cellular changes that are only detectable using clinical instruments or the study of cervical cells. These changes may be, in rare instances, the precursor to cancer cells (Lytwyn & Sellors, 1997).

Changes related to HPV infections that cannot be seen with the naked eye may be identified using a variety of clinical tools:

- A hand lens or colposcope may be used to magnify cervical and vaginal tissue (Verdon, 1997).
- Pap tests may reveal precancerous conditions of the cervix that are caused by HPV. (Some experts also recommend anal Pap tests for men at increased risk of anal cancer — men who have sex with men and men who are HIV positive) (Gilden, 2005; Tuller, 2003).
- HPV testing of samples taken with a cervical swab can detect high-risk types of HPV.

In March 1999, the U.S. Food and Drug Administration (FDA) approved the Hybrid Capture II HPV test — a DNA-based technology that can detect 13 high-risk types of HPV (those associated with an increased risk of cancer) (“HPV DNA Tests”, 2000). Produced by Digene Corporation, this routine test is not recommended for women under the age of 30 unless they have atypical or unclear Pap test results. This is because HPV is very common; cervical cancer is rare at this age; and most HPV infections go away by themselves without causing any health problems. For women age 30 or older, HPV tests can be done at the same time as a Pap test. If both test results are normal, a woman has a very low risk of developing cervical cancer. She will not need a Pap and HPV test for three years. Some women age 30 or older see this choice as more appealing than having a Pap test each year (ACOG, 2003).

### Clinical Manifestations of HPV

In some instances HPV infection can lead to clinical manifestations that can be seen with the “naked” eye. Clinical manifestations can appear as classical warts, or as a variety of lesions on the cervix, vagina, vulva, penis, or anus.

### Genital Warts

Genital warts (condylomata acuminata) are the most common clinical manifestation of genital HPV. In more than 90 percent of cases, they are caused by HPV types 6 and 11, which are considered low-risk

types because they are not associated with increased risk of cancer (Jay & Moscicki, 2000; Moscicki, 2005; Wiley, 2002).

It is estimated that one percent of the sexually active American population has genital warts, and women and men have similar rates of infection (Cockerell, 1995; Jay & Moscicki, 2000; Moscicki, 2005). Between half a million and one million cases are diagnosed annually (Moscicki, 2005).

Genital warts usually start as small bumps that appear in the anogenital area. They may be single or clusters and have a cauliflower-like appearance as they grow larger. In women, genital warts may appear on the vulva, in the vagina, on the cervix, groin, or in the anal area. In men, they appear on the foreskin, head or shaft of the penis, groin and in the anal area, urethra, and scrotum (ASHA, 2006; Cockerell, 1995). Rarely, warts may also develop in the mouth or throat of a person who has had sexual contact with an infected person (Koutsky & Kiviat, 1999).

Genital warts usually are painless, but they may cause itching or irritation (Cockerell, 1995). Genital warts are very contagious, with an estimated rate of infection between 60 and 75 percent from unprotected exposure (NIAID, 2004; Soper, 2002). The incubation period for genital warts is usually between three weeks and six months, but it may last for years after exposure (ASHA, 1998; ASHA, 2006).

### Treating Genital Warts

Because there is no cure for HPV infections, the purpose of treatment is to control outbreaks of warts. Although genital warts often fade away by themselves, they sometimes need to be treated. There are a variety of options to treat warts, including several chemicals that can be applied directly to genital warts:

- biochloroacetic acid (BCA)
- trichloroacetic acid (TCA)
- podofilox
- imiquimod

BCA and TCA are chemicals that must be applied by a clinician. Podofilox and imiquimod are two treatments that can be prescribed for use at home. Podofilox is a self-applied cream or gel that destroys wart tissue. Imiquimod, also a self-applied cream, is an immune system modulator. It works by boosting the immune system to fight HPV infection. Some of

these treatments can cause local discomfort, and some cannot be used during pregnancy (ASHA, 2006).

A clinician can also remove genital warts with cryotherapy (freezing off), electrocautery therapy (burning off), laser therapy, or surgery (ASHA, 2006).

### HPV and Cancer

It is estimated that in 2006 there will be about 9,710 new cases of invasive cervical cancer in the United States, which will result in about 3,700 deaths (ACS, 2006a). Worldwide, nearly 500,000 new cases are diagnosed each year (WHO, 2005). Cervical cancer is the second most common type of cancer among women worldwide and one of the leading causes of cancer-related mortality in women in the developing world (WHO, 2006). The median age of diagnosis for cervical cancer for all races is 48 years (Ries, et al., 2006). Half of all women diagnosed with cervical cancer are between the ages of 35 and 55 (ACS, 2006a).

Due largely to routine screening using Pap tests, the number of deaths attributed to cervical cancer in the United States dropped 74 percent between 1955 and 1992, and the death rate continues to drop nearly four percent annually (ACS, 2006a). The five-year survival rate is virtually 100 percent for pre-invasive cervical cancer, and 91 percent for early invasive cancer. The overall five-year survival rate for all stages of cervical cancer is about 73 percent (ACS, 2006a).

African-Americans experience a disproportionate number of deaths from cervical cancer — due mainly to underscreening in this population. In 2001, the death rate was 4.7 per 100,000 for black women, compared to 2.2 per 100,000 for white women (Ries, et al., 2005). Latinas and Native Americans also have cervical cancer death rates that are above average (NCI, 2005).

Since the late 1800s, researchers have suspected that cervical cancer was sexually transmitted. Medical reports noted that nuns and virgins were not likely to have cervical cancer, and that women who were married to men who traveled a great deal or who had previous wives who died of cervical cancer were more likely to develop cervical cancer ("The Cervical Cancer Virus," 1995). Today, 15–20 types of HPV have been classified as oncogenic, and the DHHS has added HPV to the list of cancer-causing

agents (Janicek & Averette, 2001; Kay, 2005; Muñoz, et al., 2003; Schiffman & Castle, 2003; Wiley, et al., 2002). Large studies have found that HPV is present in more than 99 percent of cervical cancer tumors (Clifford, et al., 2003; Walboomers, et al., 1999). HPV 16 and 18 are responsible for about 70 percent of all cervical cancers. Other HPV types are associated with the remaining 30 percent of cases (Bosch & deSanjosé, 2003; Clifford, 2003; Shah, 1997).

Most HPV infections never lead to the development of cervical cancer — even in the absence of medical intervention — and appropriate management of precancerous cervical lesions detected by Pap tests has greatly reduced the rate of invasive cervical cancer (Ho, et al., 1998; NCI, 1999a). Only one out of 1,000 women with HPV develops invasive cervical cancer (ACOG, 2000).

HPV appears to be necessary, but not sufficient, to the development of cervical cancer. Besides HPV type, researchers believe there are several cofactors that may contribute to the development of cervical cancer. These may include alcohol consumption, smoking, diet, familial history, HIV infection, hormonal factors — including multiple pregnancies and the use of both oral contraceptives and DES, low socioeconomic status, the presence of other sexually transmitted infections, such as chlamydia and/or herpes simplex virus 2, and having an uncircumcised male partner (ACS, 2006a; Anttila, et al., 2001; CDC, 1999; Moscicki, 2005; NCI, 1999b).

Certain high risk HPV types are also now considered to be a cause of many cancers of the vagina, vulva, anus, and penis. Although each of these cancers occurs less frequently than cervical cancer, taken together they equal more than the number of cases of cervical cancer in the U.S. (ACS, 2006b). The average age for diagnosis of these cancers is significantly later than for cervical cancer. The median age of diagnosis for vaginal cancer is 68 years and 69 years for vulvar cancer. Anal cancer is typically diagnosed at 63 years of age for women and 58 years for men, and the average age of diagnosis for cancer of the penis is 68 years (Ries, et al., 2006). As is the case with cervical cancer, HPV 16 and HPV 18 are most often associated with vaginal, vulvar, anal, and penile cancers (Eng & Butler, 1997). HPV is also associated with 20 percent of oropharyngeal (primarily the tongue and tonsils) cancers and 90 percent of skin cancers in immunocompromised patients (González, et al., 2002). An association has also been made between HPV and other oral, head, and neck cancers,

although further research needs to be conducted to establish a causal relationship (Mork, et al., 2001; Schwartz, et al., 1998). Men are three times more likely than women to develop head and neck cancers (*HPV Treatment and Prevention Resource*, 2001).

### **Prevention — Vaccination, Safer Sex Practices, and Pap Tests**

Over the last few years, there have been great strides in the development and testing of vaccines against HPV. Prophylactic vaccines that prevent HPV infection and therapeutic vaccines designed to prevent the development of precancerous cells are being developed. Other vaccines in development are both prophylactic and therapeutic in nature (Austell, 2000).

#### **Gardasil®**

Gardasil®, a prophylactic, quadravalent (HPV types 6, 11, 16, and 18) vaccine manufactured by Merck and Co., Inc., was approved June 8, 2006 by the U.S. Food and Drug Administration. Given in three injections over a six month period, clinical trials have shown this vaccine to be both safe and effective (Koutsky, et al., 2000; Mao, et al., 2006; Skjeldestad, et al., 2005; Villa, et al., 2005).

The latest follow-up studies (3.5 years after vaccination) have shown an effectiveness rate of 94 percent against persistent HPV 16 infection (Mao, et al., 2006). These studies have also found a 100 percent effectiveness rate in preventing the development of high-grade (CIN 2–3), pre-cancerous cervical lesions related to HPV 16 and 18 (Koutsky, et al., 2000; Mao, et al., 2006; Villa, et al., 2005). So far, results of the FUTURE II study, a phase III clinical research trial currently underway, find the vaccine to be 100 percent effective in preventing HPV 16 and 18 related pre-cancerous cervical lesions and other genital lesions associated with HPV types 6 and 11 (Skjeldestad, et al., 2005).

Except for local irritation at the injection site, side effects in the study group were similar to the placebo group (Kahn, 2005).

#### **Cervarix™**

GlaxoSmithKline (GSK) is also currently working on the development of a prophylactic HPV vaccine,

Cervarix™. Clinical trials of this three-dose bivalent (HPV types 16 and 18) vaccine have shown Cervarix to be both safe and effective (Harper, et al., 2004). The most recent efficacy studies showed the vaccine to be 100 percent effective in preventing HPV type 16 and 18 infections, and nearly 100 percent immunogenic over a period of 4.5 years that have been measured so far (Harper, et al., 2006). No serious adverse events related to the vaccine were reported during these studies (Kahn, 2005). Preliminary results of phase III clinical trials showed detectable HPV 16 and 18 antibody levels six months following the completion of the vaccination series to be at least 16 to 26 times higher than antibody levels seen after natural infection (GSK, 2006; Schwarz, et al., 2006). GSK filed an application for approval of its vaccine in Australia, Europe, and in parts of Asia and Latin America in March 2006, and expects to submit its request for approval to the FDA by the end of 2006 (GSK, 2006).

### **Social Acceptance of STI Vaccines for the Young**

Because HPV types 16 and 18 are responsible for nearly 70 percent of all cervical cancers, as well as many anal, penile, and some oropharyngeal cancers, the development of these HPV vaccines has the enormous potential to improve the reproductive health and well being of women and men. And because prophylactic HPV vaccines are only effective in individuals not currently infected by the virus, it will be important for the vaccine to be administered to all women *before* they become sexually active.

In 2003, nearly 28 percent of young women in the ninth grade, and more than 37 percent of young men in the ninth grade had had sexual intercourse (Grunbaum, et al., 2004). To reach these young people before they become sexually active, the FDA approved Gardasil for girls and women from nine to 26 years old, and the Center for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) has recommended that the vaccine be *routinely* administered to girls starting at age 11 and 12 and up to age 26 (Associated Press, 2006; FDA, 2006). Initial testing was done mostly on women 15–26 years of age.

Not enough data exists for the FDA to approve either vaccine for young boys. However, many physicians think that young boys should be vaccinated off-label in order to produce a "herd immunity" effect. (When the vast majority of

individuals are immunized, the targeted pathogen is prevented from invading the community — even if only a small number of individuals remain unvaccinated.) A recent study estimated that the vaccination of 12-year-old girls could potentially reduce the number of HPV 16- and 18- related cervical cancer cases by more than 95 percent. The vaccination of both young boys and girls could further reduce the number of cervical cancer cases by an additional three percent (Taira, et al., 2004). Protecting men from genital warts could also potentially break the chain of transmission of genital warts (Bor, 2006).

The young target age of vaccination has led many researchers, health care providers, parents, and the patients themselves to consider the unique issues related to the acceptance of an STI, or more specifically an HPV vaccine. Some of the many potential barriers to vaccination include the belief that young children already receive too many vaccinations, concern that immunization might lead to risky sexual behavior, concern about vaccine safety, a reluctance to immunize against an STI, and a reluctance to talk with young children about STIs and sexuality, (Kahn, et al., 2005; Mays, et al., 2004). These potential barriers were very similar to those observed upon the development and approval of Hepatitis B vaccines — the first vaccines developed to reduce the risk of contracting a virus that can cause cancer (Rosenthal, et al., 1995).

When individuals and parents learn about the connection between HPV and cervical cancer their reluctance to vaccinate dissipates. Surveys of young adults have shown HPV and general STI vaccination acceptance rates between 74 and 89 percent (Boehner, et al., 2003; Kahn, et al., 2003). Surveys of parents have shown HPV vaccine acceptance rates between 73 and 84 percent (Davis, et al., 2004; Mays, et al., 2004). Vaccinating young children opens the door to parent-child and provider-child communication. The HPV vaccine presents a unique opportunity to both introduce and educate young children about sexuality education and health sexual expression.

### **Cost**

Parents and providers are also concerned about the costs associated with the HPV vaccines. Gardasil will cost \$360 (Merck & Co., Inc., 2006b). We don't yet know the cost of Cervarix. To help defer the cost of HPV vaccines, ACIP voted to add Gardasil to the government's Vaccine for Children program — a

program that covers the cost of vaccinations for the uninsured and underinsured population (Associated Press, 2006). ACIP's recommendation could also lead to the deferment of costs through insurance companies or state health plans (Bor, 2006). Merck also plans to provide free vaccines to uninsured or low income adults through the development of a new patient assistance program for adult vaccines (Merck & Co., Inc., 2006a).

While the potential cost of the vaccine is high, it is not comparable to the total cost of HPV and cervical cancer in the United States. In 2000, the total cost attributed to HPV among women and men between the ages of 15 and 24 years was approximately \$3 billion (Chesson, et al., 2004). A cost-study analysis of women's health plan enrollees determined that the average per-woman cost associated with the screening and treatment of cervical HPV-related diseases was \$26,415 (Insinga, et al., 2004). Vaccines will not eliminate the total cost of screening or treatment, but they do have the potential to significantly reduce it.

### Ongoing Prevention

Vaccine boosters might be necessary. Until other vaccines are developed that will protect against *all* oncogenic HPV types, women will need to continue to practice safer sex *and* receive regular Pap tests.

Abstinence and lifelong monogamy will continue to be the most effective ways to avoid HPV infection entirely. Even if Gardasil is 100 percent effective, it only prevents HPV types that cause 70 percent of cervical cancers. Women will still need screening to protect themselves against the other 30 percent. For most sexually active women, the most important preventive measure to protect themselves from developing cervical cancer will continue to be regular Pap tests (Janicek & Averette, 2001). Avoiding skin-to-skin contact with someone with HPV is the most effective, but not always practical, strategy to prevent HPV infection. And although condoms may not entirely eliminate the risk of transmitting HPV, they are recommended for risk reduction (ASHA, 2001; Winer, et al., 2006). A recent study published in the *New England Journal of Medicine*, showed that women whose partners used condoms consistently and correctly during vaginal intercourse over a period of eight months were 70 percent less likely to acquire a new HPV infection than women whose partners used condoms less than five percent of the time (Winer, et al., 2006).

Because HPV may shed beyond the covered area, however, condoms do not provide as complete protection as they do for some other pathogens, such as HIV and gonorrhea (Stone, et al., 1999). The claims of condom-use opponents who suggest that condom use leads to increased numbers of HPV infections are false and alarmist. Condom use cannot be blamed for the high prevalence of HPV infection or the incidence of cervical cancer among women in the U.S. In fact, two Dutch studies found that condom use promotes the regression of HPV lesions in women and men, as well as the clearance of HPV in women (Hogewoning, et al., 2003; Bleeker, et al., 2003).

While HPV is endemic among sexually active women and men in the U.S., it is reassuring to know that a vaccine is now available, that these infections most often remain asymptomatic, that their symptoms, if they occur, are usually manageable, and that condom use is likely to reduce the risk of infection. Sexually active women should also be sure to have routine Pap tests as well.

### Additional Resources

American Social Health Association (ASHA)  
P.O. Box 13827  
Research Triangle Park, NC 27709  
(919) 361-8400  
(919) 361-8425 (fax)  
[www.ashastd.org](http://www.ashastd.org)

American Cancer Society (ACS)  
1599 Clifton Road NE  
Atlanta, GA 30329  
800-ACS-2345  
[www.cancer.org](http://www.cancer.org)

National Center for HIV, STD, & TB Prevention  
Centers for Disease Control and Prevention  
1600 Clifton Road NE  
Mailstop E-49  
Atlanta, GA 30333  
[cdcinfo@cdc.gov](mailto:cdcinfo@cdc.gov)  
[www.cdc.gov/nchstp/od/nchstp.html](http://www.cdc.gov/nchstp/od/nchstp.html)  
800-232-4636  
800-311-3435

## Cited References

- ACOG — American College of Obstetricians and Gynecologists. (2000, accessed 2001, May 23). "Make Decisions about Human Papillomavirus Based on Sound Medicine, Rather than Politics." [Online]. [http://www.acog.org/from\\_home/departments/dept\\_notice.cfm?recno=11&bulletin=1083](http://www.acog.org/from_home/departments/dept_notice.cfm?recno=11&bulletin=1083).
- \_\_\_\_\_. (2003, August). "Cervical Cytology Screening." *ACOG Practice Bulletin*, 45, 1–11.
- ACS — American Cancer Society. (2006a, February 9, accessed 2006, May 17). *Cervical Cancer*. Atlanta, GA: American Cancer Society, Inc. [Online]. <http://documents.cancer.org/115.00/115.00.pdf>.
- \_\_\_\_\_. (2006b). *Cancer Facts and Figures 2006*. Atlanta, GA: American Cancer Society, Inc.
- Anttila, Tarja, et al. (2001). "Serotypes of *Chlamydia trachomatis* and Risk for Development of Cervical Squamous Cell Carcinoma." *The Journal of the American Medical Association*, 285(1), 47–51.
- ASHA — American Social Health Association. (1998). *HPV in Perspective*. Research Park Triangle, NC: American Social Health Association.
- \_\_\_\_\_. (2001, accessed 2004, April 19). *HPV: Get the Facts: HPV and Abnormal Cell Changes*. [Online]. <http://ashastd.org/hpvccrc/abcell.html>
- \_\_\_\_\_. (2006, accessed 2006, May 17). *Learn About HPV: Genital Warts Questions & Answers*. [Online]. [http://www.ashastd.org/hpv/hpv\\_learn\\_warts.cfm](http://www.ashastd.org/hpv/hpv_learn_warts.cfm).
- The Associated Press. (2006, June 29, accessed 2006, July 12). "Panel Backs HPV Vaccine for Young Girls." *The New York Times*. [Online]. <http://www.nytimes.com/aponline/us/AP-Cervical-Cancer-Vaccine.html>.
- Austell, Amy, ed. (2000, Winter). "The Vaccine Marathon." *HPV News*, 10, 1–5.
- Bleeker, Maaikje C.G., et al. (2003). "Condom Use Promotes Regression of Human Papillomavirus-Associated Penile Lesions in Male Sexual Partners of Women with Cervical Intraepithelial Neoplasia." *International Journal of Cancer*, 107, 804–10.
- Boehner, Constance W., et al. (2003). "Viral Sexually Transmitted Disease Vaccine Acceptability Among College Students." *Sexually Transmitted Diseases*, 30(10), 774–8.
- Boonstra, Heather. (2004). "Comprehensive Approach Needed to Combat Sexually Transmitted Infections Among Youth." *The Guttmacher Report on Public Policy*, 7(1), 3–4, 13.
- Bor, Jonathan. (2006, May 11). "HPV Vaccine Nearing Approval; FDA Likely to OK Immunizer That May Eliminate Most Cases of Cervical Cancer." *Baltimore Sun*, p. 1A.
- Bosch, F. Xavier, and Silvia de Sanjosé. (2003). "Chapter 1: Human Papillomavirus and Cervical Cancer — Burden and Assessment of Causality." *Journal of the National Cancer Institute Monograph*, 31, 3–13.
- Brown, Darron R., et al. (2005). "A Longitudinal Study of Genital Human Papillomavirus Infection in a Cohort of Closely Followed Adolescent Women." *Journal of Infectious Diseases*, 191, 182–92.
- Carson, Sylvia. (1997). "Human Papillomavirus Infection Update: Impact on Women's Health." *The Nurse Practitioner*, 22(4), 24–37.
- Cates, Willard. (1999). "Estimates of the Incidence and Prevalence of Sexually Transmitted Diseases in the United States." *Sexually Transmitted Diseases*, 26(4), s2–s7.
- CDC — Centers for Disease Control and Prevention. (1999, accessed 1999, October 1). *STD Trends*. [Online]. [http://www.cdc.gov/nchstp/dstd/Stats\\_Trends/STD\\_Trends/pdf](http://www.cdc.gov/nchstp/dstd/Stats_Trends/STD_Trends/pdf).
- \_\_\_\_\_. (2000, accessed 2001, January 25). *Tracking the Hidden Epidemic: Trends in STDs in the United States, 2000*. [Online]. [http://www.cdc.gov/nchstp/dstd/Stats\\_Trends/Trends2000.pdf](http://www.cdc.gov/nchstp/dstd/Stats_Trends/Trends2000.pdf)
- \_\_\_\_\_. (2001, accessed 2001, May 25). *Genital HPV Infection*. [Online]. [http://www.cdc.gov/nchstp/dstd/Fact\\_Sheets/FactsHPV.htm](http://www.cdc.gov/nchstp/dstd/Fact_Sheets/FactsHPV.htm).
- \_\_\_\_\_. (2004, accessed 2006, May 17). *Genital HPV Infection*. [Online]. <http://www.cdc.gov/std/HPV/hpv.pdf>.
- \_\_\_\_\_. (2006, accessed 2006, May 17). *STD Facts: HPV Vaccine*. [Online]. <http://www.cdc.gov/std/hpv/STDFact-HPV-vaccine.htm>.
- "The Cervical Cancer Virus." (1995). *Discover*, 16, 24–6.
- Chesson, Harrell W., et al. (2004). "The Estimated Direct Medical Cost of Sexually Transmitted Diseases Among American Youth, 2000." *Perspectives on Sexual and Reproductive Health*, 36(1), 11–9.
- Clifford, G.M., et al. (2003). "Human Papillomavirus Types in Invasive Cervical Cancer Worldwide: A Meta-Analysis." *British Journal of Cancer*, 88(1), 63–73.
- Cockerell, Clay J. (1995, accessed 1999, October 1). Human Papillomavirus Infections. International Association of Physicians in AIDS Care. [Online]. <http://www.iapac.org/clinmgmt/diseases/cm/cm6.html#1>
- Crabb, Kenneth. (1997, accessed May 5, 2001). "Anogenital Human Papillomavirus Infection." *The Medical Journal of Allina*, 6(3). [Online]. [http://www.allina.com/Allina\\_Journal/Summer1997.crabb.html](http://www.allina.com/Allina_Journal/Summer1997.crabb.html).
- Cuzick, Jack. (2000, January 5). "Human Papillomavirus Testing for Primary Screening." *Journal of the American Medical Association*, 283(1), 108–9.
- Davis, Kristin, et al. (2004). "Human Papillomavirus Vaccine Acceptability Among Parents of 10- to 15- Year Old Adolescents." *Journal of Lower Genital Tract Disease*, 8(3), 188–94.
- Elfgren, Kristina, et al. (2000). "A Population-Based Five-Year Follow-Up Study of Cervical Human Papillomavirus Infection." *American Journal of Obstetrics and Gynecology*, 183(3), 561–7.
- Eng, Thomas, and William Butler, eds. (1997). *The Hidden Epidemic: Confronting Sexually Transmitted Diseases*. Washington, DC: National Academy Press.
- FDA — Food and Drug Administration. (2006, June 8, accessed 2006, July 12). *FDA News: FDA Licenses New Vaccine for Prevention of Cervical Cancer and Other Diseases in Females Caused by Human Papillomavirus*. [Online]. <http://www.fda.gov/bbs/topics/NEWS/2006/NEW01385.html/>.
- Gilden, David. (2005, accessed 2006, August 10). "Protecting Against HPV." *GMHC Treatment Issues*, 19(5/6). [Online]. <http://www.gmhc.org/health/treatment/ti/ti1956.html>.
- Gingrich, Pat Mahaffee. (2004). "Management and Follow-up of Abnormal Papanicolaou Tests." *Journal of the American Medical Women's Association*, 59(1), 54–9.
- GlaxoSmithKline (GSK). (2006, June 5, accessed 2006, July 7). *Press Release: New Data Show Cervarix™, GSK's HPV 16/18 Cervical Cancer Candidate Vaccine, Is Highly Immunogenic and Well-Tolerated in Women Over 25 Years of Age*. [Online]. [http://www.gsk.ca/en/media\\_room/news/20060605.pdf](http://www.gsk.ca/en/media_room/news/20060605.pdf).
- Goldberg, Carey. (2006, May 29 accessed 2006, May 31). "A Fresh Shot: Soon-To-Be Approved Vaccine Can Prevent Cervical Cancer; The Question Is, Are People Ready to Accept It?" *The Boston Globe*.
- González Intxaurreaga, M.A., et al. (2002). "HPV and Carcinogenesis." *Acta Dermatol Venereol*, 11(3), 1–8.
- Grunbaum, Jo Anne, et al. (2004). "Youth Risk Behavior Surveillance — United States, 2003." *Morbidity and Mortality Weekly Report*, 53 (SS-2), 1–96.

- Harper, Diane M., et al. (2004). "Efficacy of a Bivalent L1 Virus-Like Particle Vaccine in Prevention of Infection with Human Papillomavirus Types 16 and 18 in Young Women: A Randomised Controlled Trial." *Lancet*, 364, 1757–65.
- Harper, Diane M., et al. (2006). "Sustained Efficacy Up to 4.5 Years of a Bivalent L1 Virus-Like Particle Vaccine Against Human Papillomavirus Types 16 and 18: Follow-Up From a Randomised Control Trial." *Lancet*. DOI: 10.1016/S0140-6736(06)68439-0.
- Hildesheim, A., et al. (1994). "Persistence of Type-Specific Human Papillomavirus Infection Among Cytologically Normal Women." *Journal of Infectious Diseases*, 169(2), 235–40.
- Ho, Gloria Y.F., et al. (1995). "Persistent Genital Human Papillomavirus Infection as a Risk Factor for Persistent Cervical Dysplasia." *Journal of the National Cancer Institute*, 87(18), 1365–71.
- Ho, Gloria Y.F., et al. (1998). "Natural History of Cervicovaginal Papillomavirus Infection in Young Women." *New England Journal of Medicine*, 338(7), 423–8.
- Hogewoning, Cornelis J.A., et al. (2003). "Condom Use Promotes Regression of Cervical Intraepithelial Neoplasia and Clearance of Human Papillomavirus: A Randomized Trial." *International Journal of Cancer*, 107, 811–6.
- "HPV DNA Tests: Studies Target Use for Cancer Screening." (2000, May). *STD Quarterly*, 1–3.
- HPV Treatment and Prevention Resource: New Opportunities, New Challenges*. (2001). Decatur, GA: Flynn Publications.
- Insinga, Ralph P., et al. (2003). "The Health and Economic Burden of Genital Warts in a Set of Private Health Plans in the United States." *Clinical Infectious Diseases*, 36, 1397–403.
- Insinga, Ralph P., et al. (2004). "The Health Care Costs of Cervical Human Papillomavirus-Related Disease." *American Journal of Obstetrics & Gynecology*, 191, 114–20.
- Janicek, Mike, and Hervy Averette. (2001). "Cervical Cancer: Prevention, Diagnosis, and Therapeutics." *CA: A Cancer Journal for Clinicians*, 51(2), 92–114.
- Jay, Naomi, and Anna-Barbara Moscicki. (2000). "Human Papilloma Virus Infection in Women." In Marlene Goldman & Maureen Hatch, eds., *Women and Health*. San Diego, CA: Academic Press.
- Kahn, Jessica A. (2005). "Vaccination As A Prevention Strategy for Human Papillomavirus-Related Diseases." *Journal of Adolescent Health*, 37, S10–6.
- Kahn, Jessica A., et al. (2003). "Attitudes About Human Papillomavirus Vaccine in Young Women." *International Journal of STD & AIDS*, 14, 300–6.
- Kahn, Jessica A., et al. (2005). "Pediatricians' Intention to Administer Human Papillomavirus Vaccine: The Role of Practice Characteristics, Knowledge, and Attitudes." *Journal of Adolescent Health*, 37, 502–10.
- Kashima, H.K., et al. (1996). "Recurrent Respiratory Papillomatosis." *Obstetrics and Gynecologic Clinics of North America*, 23(3), 699–706.
- Kay, Jane. (2005, February 1, accessed 2006, May 19). "X-Rays Added To Cancer List; Some Viruses Also Among Carcinogens on Federal Registry." *San Francisco Chronicle*, p. A1.
- Keller, Mary L., et al. (1995). "Genital Human Papillomavirus Infection: Common But Not Trivial." *Health Care for Women International*, 16, 351–64.
- KFF — Kaiser Family Foundation. (2000, accessed 2001, May 23). *National Survey of Public Knowledge of HPV, the Human Papillomavirus*. [Online]. <http://www.kff.org/content/2000/20000217a/HPVChartpack2.PDF>
- Kjaer, Susanne Krüger, et al. (2001). "High-Risk Human Papillomavirus Is Sexually Transmitted: Evidence From a Follow-Up Study of Virgins Starting Sexual Activity (Intercourse)." *Cancer Epidemiology, Biomarkers & Prevention*, 10(2), 101–6.
- Koutsky, Laura, and Nancy Kiviat. (1999). "Genital Human Papillomavirus." In King Holmes, et al., eds., *Sexually Transmitted Diseases*, 3<sup>rd</sup> ed. New York: McGraw-Hill.
- Koutsky, Laura A., et al. (2002). "A Controlled Trial of a Human Papillomavirus Type 16 Vaccine." *New England Journal of Medicine*, 347(21), 1645–51.
- Lamb, Steven. (2001, accessed 2001, May 21). *Imiquimod*. [Online]. <http://www.dermnet.org.nz/dna.imiquimod/info.html>.
- Lewis, Ricki. (1995). "New Choices for Coping with Genital Warts." *FDA Consumer*, 29(4), 17–21.
- Lytwyn, Alice, and John W. Sellors. (1997). "Sexually Transmitted Human Papillomaviruses: Current Concepts and Control Issues." *The Canadian Journal of Human Sexuality*, 6(2), 113–26.
- Mao, Constance, et al. (2006). "Efficacy of Human Papillomavirus-16 Vaccine to Prevent Cervical Intraepithelial Neoplasia: A Randomized Controlled Trial." *Obstetrics & Gynecology*, 107(1), 18–27.
- Mays, Rose M., et al. (2004). "Parental Perspectives on Vaccinating Children Against Sexually Transmitted Infections." *Social Science & Medicine*, 58, 1405–13.
- McDermott-Webster, Marian. (1999). "The HPV Epidemic." *American Journal of Nursing*, 99, 24L–24N.
- Meijer, C.J., et al. (1998). "HPV Typing and Testing in Gynaecological Pathology: Has the Time Come?" *Histopathology*, 33(1), 83–6.
- Merck & Co., Inc. (2006a, May 26, accessed 2006, May 26). *Merck to Create New Patient Assistance Program for Vaccines*. [Online]. [www.merck.com/newsroom/press\\_releases/corporate/2006\\_0526.html](http://www.merck.com/newsroom/press_releases/corporate/2006_0526.html).
- \_\_\_\_\_. (2006b, June 8, accessed 2006, July 12). *Product News: FDA Approves Merck's GARDASIL<sup>®</sup>, the World's First and Only Cervical Cancer*. [Online]. [http://www.merck.com/newsroom/press\\_releases/product/2006\\_0608.html](http://www.merck.com/newsroom/press_releases/product/2006_0608.html)
- Mork, Jon, et al. (2001). "Human Papillomavirus Infection as a Risk Factor for Squamous-Cell Carcinoma of the Head and Neck." *New England Journal of Medicine*, 344(15), 1125–31.
- Moscicki, Anna-Barbara. (2005). "Impact of HPV Infection in Adolescent Populations." *Journal of Adolescent Health*, 37, S3–9.
- Moscicki, A.B., et al. (1998). "The Natural History of Human Papillomavirus Infection As Measured By Repeated DNA Testing in Adolescent and Young Women." *Journal of Pediatrics*, 132(2), 277–84.
- Muñoz, Nubia, et al. (2003). "Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer." *New England Journal of Medicine*, 348(6), 518–27.
- Muñoz, Nubia, et al. (2004). "Incidence, Duration, and Determinants of Cervical Human Papillomavirus Infection in a Cohort of Colombian Women with Normal Cytological Results." *Journal of Infectious Diseases*, 190, 2077–87.
- NCI — National Cancer Institute. (1999a, accessed 2001, May 21). *Cervical Cancer: Background*. [Online]. <http://rex.nci.nih.gov/massmedia/backgrounders/cervical.html>.
- \_\_\_\_\_. (1999b, accessed November 9). *Prevention of Cervical Cancer*. [Online]. <http://imsdd.med.uni-bonn.de/cancernet/304734.html>.
- \_\_\_\_\_. (2005, accessed 2006, May 17). *A Snapshot of Cervical Cancer*. [online]. <http://planning.cancer.gov/disease/Cervical-Snapshot.pdf>
- NIAID — National Institute of Allergy and Infectious Diseases. National Institutes of Health. Public Health Service. (2004, accessed 2006, May 23). *Human Papillomavirus and Genital Warts*. [Online]. <http://www.niaid.nih.gov/factsheets/stdhpv.htm>.



- Puranen, Mirja, et al. (1997). "Exposure of an Infant to Cervical Human Papillomavirus Infection of the Mother is Common." *American Journal of Obstetrics and Gynecology*, 176(5), 1039–45.
- Richardson, Harriet, et al. (2003). "The Natural History of Type-Specific Human Papillomavirus Infections in Female University Students." *Cancer Epidemiology, Biomarkers & Prevention*, 12, 485–90.
- Ries, L.A.G., et al., eds. (2005, posted 2006, accessed 2006, May 19). *SEER Cancer Statistics Review, 1975–2003*. Bethesda, MD: National Cancer Institute. [Online]. <http://seer.cancer.gov/csr/19752003/>.
- Rosenthal, Susan L., et al. (1995). "Hepatitis B Vaccine Acceptance Among Adolescents and Their Parents." *Journal of Adolescent Health*, 17, 248–54.
- Schiffman, Mark, and Philip E. Castle. (2003). "Human Papillomavirus: Epidemiology and Public Health." *Archives of Pathology and Laboratory Medicine*, 127, 930–4.
- Schwarz, T.F., et al. (2006). "An AS04-containing human papillomavirus (HPV) 16/18 vaccine for prevention of cervical cancer is immunogenic and well-tolerated in women 15-55 years old." *Journal of Clinical Oncology*, 24(18S), abstract 1008.
- Schwartz, Stephen, et al. (1998, November 4). "Oral Cancer Risk in Relation to Sexual History and Evidence of Human Papillomavirus Infection." *Journal of the National Cancer Institute*, 90(21), 1626–36.
- Shah, Keerti V. (1997). "Human Papillomaviruses and Anogenital Cancers." *The New England Journal of Medicine*, 337(19), 1386–8.
- Skjeldestad, Finn Egil, et al. (2005, accessed 2006, May 26). "Prophylactic Quadrivalent Human Papillomavirus (HPV) (Types 6, 11, 16, 18) L1 Virus-Like Particle (VLP) Vaccine (Gardasil™) Reduced Cervical Intraepithelial Neoplasia (CIN) 2/3 Risk." Presented at: Infectious Disease Society of America 43<sup>rd</sup> Annual Meeting; October 7, 2005; San Francisco, California. Abstract LB-8a. [Online]. <http://www.idsociety.org/Template.cfm?Section=Program2&CONTENTID=14108&TEMPLATE=/ContentManagement/ContentDisplay.cfm>.
- Smith, Elaine M., et al. (2004). "Human Papillomavirus Prevalence and Types in Newborns and Parents: Concordance and Modes of Transmission." *Sexually Transmitted Diseases*, 31(1), 57–62.
- Soper, David E. (2002). "Genitourinary Infections and Sexually Transmitted Diseases." In Jonathan S. Berek, ed., *Novak's Gynecology*, 13<sup>th</sup> ed. Philadelphia, PA: Lippincott Williams & Williams.
- Stevens-Simon, Catherine, et al. (2000). "The Prevalence of Genital Human Papillomavirus Infections in Abused and Nonabused Preadolescent Girls." *Pediatrics*, 106(4), 645–49.
- Stone, Katherine, et al. (1999). "Barrier Methods for the Prevention of Sexually Transmitted Diseases." In King Holmes, et al., eds., *Sexually Transmitted Diseases*, 3<sup>rd</sup> ed. New York: McGraw-Hill.
- Taira, Al V., et al. (2004). "Evaluating Human Papillomavirus Vaccination Programs." *Emerging Infectious Diseases*, 10(11), 1915–23.
- Tuller, David. (2003, February 18). "Some Urge Type of Pap Test To Find Cancer in Gay Men." *The New York Times*, p. F7.
- Verdon, Mary. (1997). "Issues in the Management of Human Papillomavirus Genital Disease." *American Family Physician*, 55, 1813–20.
- Villa, Luisa L., et al. (2005). "Prophylactic Quadrivalent Human Papillomavirus (Types 6, 11, 16, and 18) L1 Virus-Like Particle Vaccine in Young Women: A Randomised Double-Blind Placebo-Controlled Multicentre Phase II Efficacy Trial." *Lancet Oncology*, 6, 271–8.
- Walboomers, J.M., et al. (1999). "Human Papillomavirus Is a Necessary Cause of Invasive Cervical Cancer Worldwide." *Journal of Pathology*, 189(1), 12–9.
- Weinstock, Hillard, et al. (2004). "Sexually Transmitted Diseases Among American Youth: Incidence and Prevalence Estimates, 2000." *Perspectives on Sexual and Reproductive Health*, 36(1), 6–10.
- WHO — World Health Organization, Initiative for Vaccine Research. (2005, January). *State of the Art of Vaccine Research and Development*. Geneva, Switzerland: World Health Organization. [Online]. [http://http://www.who.int/vaccine\\_research/documents/Dip%20814.pdf](http://http://www.who.int/vaccine_research/documents/Dip%20814.pdf).
- \_\_\_\_\_. (2006). *Comprehensive Cervical Cancer Control: A Guide to Essential Practice*. Geneva, Switzerland: World Health Organization. [Online]. [http://www.who.int/reproductive-health/publications/cervical\\_cancer\\_gcp/text.pdf](http://www.who.int/reproductive-health/publications/cervical_cancer_gcp/text.pdf).
- Wiley, D.J., et al. (2002). "External Genital Warts: Diagnosis, Treatment, and Prevention." *Clinical Infectious Diseases*, 35(Suppl 2), S210–24.
- Winer, Rachel L., et al. (2003). "Genital Human Papillomavirus Infection: Incidence and Risk Factors in a Cohort of Female University Students." *American Journal of Epidemiology*, 157(3), 218–26.
- Winer, Rachel L., et al. (2006). "Condom Use and the Risk of Genital Human Papillomavirus Infection of Young Women." *New England Journal of Medicine*, 354(25), 2645–54.
- Woodman, Ciaran B.J., et al. (2001). "Natural History of Cervical Human Papillomavirus Infection In Young Women: A Longitudinal Cohort Study." *Lancet*, 357, 1831–6.
- Wright, Tracy. (1998). "Genital Warts: Their Etiology and Treatment." *Nursing Times*, 94, 52–4.

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