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ANOGENITAL PAPILLOMAVIRUS INFECTIONS

IF YOU'RE LIKE most people, unless you've already read the headline you probably wouldn't be able to guess which sexually transmitted disease:

- is the most common in the U.S., affecting >20,000,000 people
- infects at least 500,000 Americans each year
- leads to over 2,000,000 physician visits annually.

In 1997, the same infection caused an estimated 18,000 new cases of invasive cancer of the cervix or anus and some 5,300 deaths. Today's mystery agent: the human papillomavirus (HPV).

For many reasons, the public health importance of HPV anogenital infections is often overlooked. Most infections are asymptomatic and undetected. Accurate diagnostic tests are not readily available. Infections are not reportable. In general, the epidemiology of HPV infections is poorly understood, in part because few population-based studies have been done.

More than 70 different HPV types have been characterized by gene sequencing. Most types are associated with a characteristic histopathologic process and anatomic site of infection. For example, HPV types 1 and 2 are commonly associated with plantar and common warts, while types 6, 11, 16, 18, and 31 commonly cause genital warts and neoplastic processes of the cervix and anogenital area.

TRANSMISSION AND EPIDEMIOLOGY

HPV infections of all sites result from skin-to-skin contact. For those types associated with anogenital warts, cervical cancer, and anal cancer, transmission is almost always sexual. Infection is often unsuspected, because carriers may have no warts or no visible warts. Even after treatment or spontaneous regression of anogenital warts, normal-appearing epithelium can contain HPV DNA that can be infectious or can lead to recurrence. The only proven method of prevention is abstinence, which studies suggest may also make the heart grow fonder. Although the efficacy of barrier contraceptives (e.g., condoms) in preventing transmission is not well established, they are probably somewhat to considerably better than nothing.

Nonsexual transmission of anogenital warts among children can occur but is not common.[1] Approximately 20% of prepubertal children with warts have HPV types 1 or 2 in their lesions — HPV types more commonly associated with cutaneous warts. In addition, DNA of HPV type 6 (more commonly associated with anogenital warts) has been identified in cutaneous warts of family contacts of children with anogenital warts. Although these examples of nonsexually transmitted HPV infections do occur, anogenital warts in children should always raise suspicion of sexual abuse.

Because of a dearth of population-based studies and sensitive diagnostic tests, there are no good measures of overall population prevalence. Not surprisingly for an STD, the highest prevalence is among sexual partners of HPV-infected people; 50-80% of the partners of those with anogenital warts have evidence of HPV infection.[2] In one STD clinic survey that used three diagnostic methods, 52% of women were infected.[3] Overall estimates of infection prevalence among college-age women are in the 15-35% ballpark.

The prevalence of infection has apparently increased sharply over the past 30 years. By one estimate, based on data from a regular survey of private physicians' office-based practices in the U.S, the number of physician visits for anogenital warts increased 680% from 1966 to 1984. "First visits" (a rough surrogate measure of incidence) for anogenital warts increased to more than 300,000 annual visits in the mid-1980's and remains more than 200,000 per year.[4]

Data about incidence are harder to come by, but studies suggest that young, sexually active women have the highest incidence of HPV infection, and the risk of infection rises with number of sexual partners. In a study of female university students, 20% of women with a single lifetime sexual partner had demonstrable HPV DNA in cervical swabs, compared with 70% of women with more than 10 sexual partners.

DISEASE

As far back as 1842, it was observed that cervical cancer behaved epidemiologically like an STD.[5] Cervical cancer is rare among celibates (e.g., nuns), and there is an increased risk associated with having a male sexual partner whose previous partners developed cervical cancer. HPV infection is now recognized to be the major risk factor for cervical intraepithelial neoplasia (CIN) and invasive cervical cancer. Although HPV's capacity for latency, reactivation, and malignant transformation is still unclear, HPV DNA can be found in up to 90% of advanced CIN lesions and cervical cancers.[6,7] Only a few HPV types are associated with more malignant potential, however. HPV types 6 and 11 have a low risk of transforming cervical epithelium but are commonly associated with anogenital warts. In contrast, HPV types 16, 18, 31, 33, and 35 are less frequently associated with anogenital warts but have greater malignant potential and are often seen in CIN and the majority of cervical cancers. There are risk factors and there are Risk Factors; HPV is one of the latter. Women with HPV type 16 infections have a risk 10-20 times greater than women without HPVof developing advanced CIN.

The time between infection and development of cervical neoplasia can be very short. When a cohort of women with unremarkable Pap smears and no evidence of HPV infection were tested every four months for HPV DNA and given cytologic and colposcopic cervical examinations, 28% of the women developed advanced grades of biopsy-proven CIN within two years of a documented HPV infection.[8]

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HPV has also been implicated in the development of some vaginal, vulvar, anal, and penile squamous cell cancers. Receptive anal intercourse among men who have sex with men (MSM) and people with a history of anogenital warts have a greatly increased risk of anorectal cancer compared to control populations—presumably due to HPV. Although malignant transformation of anal condylomata has been described, only recently has a specific association between anorectal dysplastic lesions or cancer and HPV infection been recognized, primarily in MSM (infra).[9,10]

The incidence of anorectal cancer is increasing among both women and men in the U.S., as is the incidence of anogenital warts. From 1973 to 1989, the incidence of anal cancer in women and men in the U.S. increased by over 35% and 68%, respectively.[11]

HIV AND HPV

HPV coinfection is common among HIV-infected persons. Prior to the AIDS epidemic, anal condylomata were one of the most common STDs among gay men, and they remain so today. In one study, 30% of HIV-negative MSM had a history of anal warts; 13% had visible anal warts. Currently, there is little information on the proportion of these lesions that progress to invasive cancer among HIV-negative men.[12]

A history of anal warts or detection of HPV DNA in the anus is independently associated with HIV infection. HPV and HIV coinfections are also noted among women. In an STD clinic study, women with anogenital warts were three to four times more likely to be HIV-infected than those without warts. Prospective studies have failed to show that anogenital warts increase one's susceptibility for HIV infection, so it is likely that these infections independently resulted from transmission during unprotected sex.

HPV infections are more likely to progress to dysplasia and malignancy in HIV-infected individuals, although it is unclear if that simply reflects more rapid progression of disease. Therapy of genital warts in men and women with HIV infection appears to be more difficult and recurrence following local therapy may occur in up to half of HIV-infected individuals.

BENEDICTORY COMMENTS

Patients are often devastated to learn they have an STD, and practitioners must recognize both the physical and psychosocial effects of infection.[13] Comprehensive care includes not only a medical assessment but the counseling, education, and support that can help clients negotiate a difficult time in their lives. Some patients may react with shame or embarrassment that can block their ability to assimilate more information about the infection. If so, another appointment just for counseling and education may be necessary. Patients must be educated about treatment, long-term effects, and transmission, including information about condom use. Great emphasis should be placed on the role of routine pelvic examinations with annual Pap smears to reduce the possible morbidity and mortality of cervical cancer.

As with other STDs, we recommend that sexual partners be informed. This is not easy, but for many people it is a learnable skill—and one that they may have a lifelong need for. Recent data suggest that even many of those who do inform their partners soon after diagnosis get out of the habit within 6 months. Reeducation may be helpful.

Treatment of HPV infections is complicated, controversial, and not very effective. Revised STD treatment guidelines from CDC are expected within the next month and will be publicized in these pages.

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