

Genital human papillomavirus infection in women who have sex with women: A review

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Sexual transmission of human papillomavirus between women has been postulated on the basis of reports of abnormal Papanicolaou smears in women who reported no prior sex with men and by studies using amplified deoxyribonucleic acid technology for human papillomavirus detection. To review the current knowledge of the epidemiology of human papillomavirus and the Papanicolaou smear screening practices among women who have sex with women, studies were identified from a search of the MEDLINE database from January 1980–June 1999. Several factors, including prior or concurrent sex with men and sexual behaviors between women, validate the possibility of human papillomavirus infection among women who have sex with women, and data support that human papillomavirus transmission also occurs. Limited data indicate that the frequency of routine Papanicolaou smear screening among women who have sex with women may be suboptimal relative to heterosexual women. Education of women who have sex with women and the providers of their health care should counter any assumptions that sex between women confers no risk of human papillomavirus transmission. Women who have sex with women should receive Papanicolaou smear screening in accord with current guidelines. (Am J Obstet Gynecol 2000;183:770-4.)

Key words: Human papillomavirus, lesbian, homosexuality, cervical neoplasia, cervical cancer, Papanicolaou smear

Human papillomaviruses (HPV) constitute >80 distinct types, some of which are sexually transmitted and predominantly infect genital skin and mucosa. Most genital warts are caused by sexually transmitted HPV types 6 and 11.¹ As is true for all viral sexually transmitted diseases (STD), infection with HPV is chronic; no cure exists, although genital warts (but probably not all of the virus) may be cleared with ablative or immunomodulatory therapies. Specific types of HPV, most commonly types 16 and 18, cause cervical cancer, a disease that is largely preventable with periodic Papanicolaou smear screening. Sexual transmission of HPV between women has recently been postulated on the basis of reports of abnormal Papanicolaou smears in women who reported no prior sex with men.²⁻⁴ Some data suggest, however, that routine Papanicolaou smear screening among women who have sex with women is performed less frequently than national

guidelines advise.^{4,9} This article reviews the current knowledge regarding the epidemiology of HPV among women who have sex with women, as well as data suggesting that HPV is sexually transmitted between female sex partners and that Papanicolaou smear screening may be suboptimal in this group. Throughout this article the term *women who have sex with women* is used as a description of sexual behavior. The term *lesbian* is used only to refer to its use by other authors who are cited, because it implies a designation of self-identity or self-definition that does not always predict or correlate with sexual behavior.^{10, 11}

Is it plausible that HPV is sexually transmissible between women? General assumptions about sexual practices between women have contributed to the general opinion that sex between women confers a relatively low risk of bacterial STD transmission (including gonorrhea and chlamydia).¹² Such assumptions presume absence of the mucosal contact present during vaginal-penile sex. The transmission of HPV, however, requires only skin-to-skin contact, making sexual transmission between women by direct genital-to-genital or digital-genital contact plausible. The potential for transmission by shared sex toys may also exist,¹³ and genital HPV types have recently been identified on human fingers.¹⁴ Perhaps of equal importance, most women who have sex with women (53%-99%) have had sex with men, and many (21%-30%) con-

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tinue to have sex with men.^{12, 15} Among these women, acquisition of chronic viral STD, including HPV, genital herpes, and the human immunodeficiency virus (HIV), from male partners presumably occurs at a rate per contact that is similar to that in heterosexual populations, and women infected by this route could serve as a source for subsequent viral transmission to their female partners. Finally, it is important to note that assumptions about the relative "safety" of sex between women have not been challenged by prospective studies incorporating detailed information on sexual behavior.

Material and methods

Articles that have been published in medical journals were identified from a computerized search of the MEDLINE database from January 1980 through June 1999, including all languages. Additional references identified by articles retrieved through the MEDLINE search were reviewed if relevant. The search terms used were *human papillomavirus*, *lesbian*, *homosexuality*, *Pap smear*, and *cervical cancer*. Any article that reported original research on HPV infection among women who have sex with women was included. Three studies reported the occurrence of grade 2 cervical intraepithelial neoplasia in association with HPV detection by amplified deoxyribonucleic acid (DNA) techniques in women who have sex with women and who had never had sex with a male partner.^{2,4} Three studies reported on HPV-associated conditions, including report or observation of genital warts or abnormal Papanicolaou smears.¹⁵⁻¹⁷ Survey-based self-reports of genital warts and Papanicolaou smear abnormalities were given by 3 sources.¹⁸⁻²⁰ Data on sexual practices among women who have sex with women were discussed in 5 articles.^{18, 21-24} Papanicolaou smear screening practices were assessed in 6 articles.^{5-7, 18, 25, 26} Finally, self-perception of risk for STD transmission between women was addressed in 3 articles.^{8, 9, 15}

Results

Natural history of HPV. HPV is probably the most common STD, with up to 75% of sexually active adults in the United States demonstrating clinical or serologic evidence of infection by a genital HPV type.²⁷ Among women with negative Papanicolaou smears, the prevalence of HPV infection as detected by amplified DNA assays (generally, polymerase chain reaction) has ranged from 4%-48%.²⁸⁻³⁰ Younger age (<25 years) is strongly associated with a higher prevalence of HPV. The large, prospective studies assessing the natural history of HPV have evaluated only heterosexual women or have not reported information on same-sex behavior of participants.^{31, 32} These studies indicate that among college-aged women the acquisition of HPV from male partners is common, occurring in 39% to 43% of subjects during the study periods.^{31, 32} After acquisition, HPV remains detectable by polymerase chain reaction in the genital tract

for 8 to 16 months; after 2 years, it is difficult to detect even with highly sensitive techniques such as polymerase chain reaction. Systemic antibodies to HPV types 6 and 16 have been assessed and generally do not become detectable until a mean of 8 months after infection.³³

Many HPV infections of the cervix result in cellular changes that spontaneously resolve (low-grade squamous intraepithelial lesions; see subsequent text). Even for those infections that do not resolve, a relatively long time (15-20 years) is required for invasive cervical cancer to become evident, and it is possible that other cofactors (such as cigarette smoking, other cervical infections, and multiple vaginal births) promote its development.³⁴ This "lag time" between HPV infection and invasive cancer allows periodic Papanicolaou smear screening to detect neoplastic change before significant invasion occurs.

Relationship between HPV and cervical cancer. The association between HPV infection and cervical cancer is well established.³⁵⁻³⁹ More than 90% of cervical cancer specimens contain HPV DNA. The HPV types more frequently detected in cancers include HPV 16, 18, 45, and 31. HPV DNA is detected in <20% of cervical specimens obtained from women with normal Papanicolaou smears. Cellular changes associated with cervical HPV infection and dysplasia that are seen in Papanicolaou smears are currently classified as squamous intraepithelial lesions.⁴⁰ Squamous intraepithelial lesions correspond to the histologic finding of cervical intraepithelial neoplasia. Low-grade squamous intraepithelial lesions or grade 1 cervical intraepithelial neoplasia usually does not progress to invasive disease and often spontaneously regresses. High-grade squamous intraepithelial lesions, or grades 2 and 3 cervical intraepithelial neoplasia, include moderate and severe dysplasia and carcinoma in situ.⁴¹ Prospective studies have validated the association between HPV infection and development of high-grade squamous intraepithelial lesions. Among 615 STD clinic clients assessed with unamplified HPV DNA probes, grades 2 and 3 cervical intraepithelial neoplasia developed in 18%, and at least one positive unamplified test result was found in 89% for any type of HPV DNA, in 41% for HPV 16 or 18 DNA, and in 31% for HPV 31, 33, or 35 DNA. Among the women in whom grades 2 and 3 cervical intraepithelial neoplasia developed, this occurred in 91% within 2 years of the first detection of HPV DNA. In this study the presence of unclassified types of HPV also conferred a significant risk of subsequent development of grades 2 and 3 cervical intraepithelial neoplasia (relative risk, 2.1; 95% confidence interval, 1.2-3.8). Young age (<25 years) was the only significant predictor of new or persistent HPV infection.³⁷

Current knowledge of HPV epidemiology among women who have sex with women. Because genital warts, cervical squamous intraepithelial lesions, and molecular evidence of HPV infection (that is, detection of HPV DNA) are not reportable conditions, defining the epi-

demographic characteristics of HPV in any population is difficult and often requires extrapolating from studies performed in specified populations, such as STD clinic clients. Accordingly, very few data exist on the epidemiologic features of HPV infections among women who have sex with women. Some studies of women who have sex with women have reported low prevalences of genital warts and cervical neoplasia.^{5, 16, 17} Among 27 women who reported sex with women evaluated at an STD clinic in London, United Kingdom, all except 3 of whom had prior heterosexual contact, 6 women (17%) had genital warts; 2 of these 6 subjects denied prior sex with men. Of 25 evaluable women, 4 (16%) had "dyskaryosis" (corresponding to squamous intraepithelial lesions) and 6 (24%) had inflammatory Papanicolaou smears.¹⁶ A retrospective case-control study comparing 241 lesbians with 241 heterosexual women attending an STD clinic in London found that, whereas genital warts were more common among heterosexuals, all of the 4 abnormal cervical cytology results occurred in lesbians; 2 of these were high-grade squamous intraepithelial lesions and occurred in women whose last sexual experience with men was 16 or 20 years previously, respectively.¹⁷ Among 148 subjects seen in a study clinic that recruited women who have sex with women in San Francisco, California, in the early 1980s, 3% had cervical dysplasia; none of these women had had sex with men in the preceding 2 years.⁵

To date, the use of amplified DNA probes to detect HPV among women who have sex with women has been limited. Two cases of grade 2 cervical intraepithelial neoplasia have been reported in women who have sex with women and had never had a male partner.^{2, 3} In both, HPV types conferring high oncogenic risk (HPV 16 in one² and not further typed in the other³) were found with a polymerase chain reaction–based detection method. With the polymerase chain reaction assay for HPV DNA in a pilot study performed among volunteer subjects in Seattle, Washington, we found that infection with HPV was common among women who have sex with women (prevalence, 35%), including infection by cancer-associated HPV types.⁴ Also, HPV DNA was present among women who reported no prior sex with men. For most of the women with HPV detectable by polymerase chain reaction who had a history of sex with men, the last sexual encounter with a man was >2 years ago (median time, 2 years; range, up to 18 years). We also found that the prevalence of squamous intraepithelial lesions among women who have sex with women in this study was similar to that reported for heterosexual women.⁴

Whereas they are less precise than clinic-based data and often plagued by low response rates and poor characterizations of responders, survey-based self-reports of genital warts and Papanicolaou smear abnormalities provide another estimate of the magnitude of HPV infection among women who have sex with women. The National

Lesbian and Bi Women's Health Survey found that 16% of 6146 respondents currently had sex with both women and men, and 100 women reported contracting genital warts from a female partner.¹⁸ Among 1921 self-defined lesbians surveyed in 1980, 12% reported ever having had an abnormal Papanicolaou smear (not further specified).¹⁹ Among 421 of 1523 women who have sex with women responding to an STD supplement of the Western Massachusetts Lesbian Health Needs Assessment Survey, 9.3% and 10.5%, respectively, reported genital warts or abnormal Papanicolaou smears.²⁰

Finally, data on sexual history suggest that women who have sex with women are not necessarily "low risk" for acquisition of HPV. As noted here, the large majority of women who have sex with women have also had male sex partners in the past, allowing for acquisition of HPV during heterosexual intercourse.^{12, 15} Many women who have sex with women continue to have male sex partners as well.^{12, 15} The sexual practices between female partners that could account for HPV transmission are common (digital-vaginal sex, oral sex, and use of insertive sex toys).^{4, 21-24} One recent study reported detection of genital HPV on the fingertips of subjects, substantiating the hypothesis that HPV could be introduced intravaginally with digital-vaginal contact between female partners.¹⁴

Routine Papanicolaou smear screening practices among women who have sex with women. Several guidelines exist for routine Papanicolaou smear screening. A consensus recommendation adopted by the American Cancer Society, National Cancer Institute, American College of Obstetricians and Gynecologists (ACOG), American Medical Association, American Academy of Family Physicians, and others recommends that routine Papanicolaou smears be done annually for women who are or have been sexually active or have reached the age of 18 years until 3 normal smears have been documented, at which time the duration between tests may be increased to 2 years "at the discretion of the physician."⁴² The recommendation permits Papanicolaou testing less frequently after ≥ 3 annual smears have been normal, at the discretion of the physician. Guidelines for determining frequency on the basis of risk factors have been issued by ACOG.⁴³ The US Preventive Services Task Force recommends screening at least every 3 years.⁴⁴

Data suggesting that women who have sex with women receive routine Papanicolaou smear screening less frequently than heterosexual women of similar age come from two sources—clinic-based studies and surveys. Unfortunately, the number of clinic-based studies is small and is often limited by incomplete data on sexual history. In the San Francisco, California, study of Robertson and Schachter,⁵ the mean interval between routine Papanicolaou smears was longer among women who have sex with women than for age-matched heterosexual women attending the same clinic (21 months vs 8 months). Data from our

pilot study in Seattle, Washington, suggest that the tendency of women who have sex with women to undergo routine Papanicolaou smear screening may be affected by a history of prior sex with men—57% of our subjects who had never had sex with a male partner (14 women; 14% of all subjects) reported having ≤ 2 routine Papanicolaou smears in the preceding 5 years, compared with 21% of women who had ever had sex with a male partner ($P = .01$).⁴

Several surveys have attempted to assess the use of the health care system, and specifically the use of routine Papanicolaou smear screening, by women who have sex with women.^{6, 7, 25, 26, 45, 46} All have focused on women who have sex with women in social, political, or health-related venues, thereby requiring some degree of self-selection for subjects' willingness to disclose same-sex behavior, and all are limited by the absence of a control population for comparison. Twenty-three percent of the 1925 respondents in the National Lesbian Health Care Survey had had their last Papanicolaou smear > 2 years previously; 5% of all women and 23% of women aged 17 to 24 years had never had a Papanicolaou smear.⁷ Of 104 women who have sex with women described in a report from a Lesbian Health Clinic in Washington, D.C., the mean interval since last Papanicolaou smear was 34 months and 9% had had an abnormal Papanicolaou smear at a clinic visit (abnormality not specified).⁶

Several factors have been identified as possible reasons for the reduced use of general health care by women who have sex with women, including alienating behavior on the part of health care providers,^{7, 12, 45-48} inability to pay for care (because of lack of health care coverage or overall lower earnings in households without versus with at least 1 male subject),^{7, 25} and perception of low risk for STD and cervical cancer on the part of women who have sex with women and their providers.^{8, 9, 15} Among respondents to the National Lesbian Health Care Survey, 16% stated that they did not receive health care because they could not afford it; 27% of respondents had health providers who assumed heterosexuality, and 16% would not feel comfortable disclosing their lesbianism to providers.⁷ Other studies have noted that the majority of lesbians (53%-72%) do not disclose their sexual behavior to physicians when they seek medical care^{26, 45} and that a substantial proportion of such disclosures (30%) elicits negative reactions from providers.⁴⁸ Similar perceptions on the part of gay medical students have been reported.⁴⁹ Few data are available on economic barriers to routine health care among women who have sex with women, but in a survey of 1681 lesbians attending a music festival in Michigan the respondents' reported income was \$10,000 lower than the Michigan average for women.⁶ Finally, one study reported a direct relationship between the quality of subjects' experience with health care providers and the likelihood of a recent Papanicolaou smear being performed.⁴⁶

Among women who have sex with women, self-perception

of low risk for STD and cervical cancer may also play a role in the reduced frequency of routine Papanicolaou smear screening.^{8, 9, 15} In one survey of 1086 women who have sex with women, the risk perception for HIV acquisition was not as high as has been suggested by the proportion of risk behaviors reported: Only 43% of the women with a verified history of an HIV risk factor perceived themselves to be at risk for HIV acquisition.¹⁵ Because data indicate that HPV is sexually transmitted between female partners and may not require prior or recent sex with men, erroneous assumptions about HPV acquisition from female partners may place women who have sex with women at increased risk for delayed detection of cervical cancer by less frequent Papanicolaou smear screening or none. Finally, women who have sex with women and do not have male sex partners are not likely to access venues providing reproductive health care for the sole purpose of obtaining contraceptive methods; this effectively eliminates another "routine" opportunity for Papanicolaou smear screening to be sought or offered.

Comment

Taken together, the data summarized here strongly suggest that HPV is sexually transmitted between women and thus that recommendations for Papanicolaou smear screening among women who have sex with women should not differ from those for heterosexual women. Women who have sex with women—especially those who have not had sex with men—currently receive less frequent routine Papanicolaou smears. Of critical importance will be the elucidation of reasons for the latter phenomenon and better education of women who have sex with women to counter any assumptions that sex between women confers no, or little, risk of HPV transmission. The type-specific prevalence of HPV infection among women who have sex with women requires further study, and very few data exist on the sexual practices that result in HPV transmission between female sex partners. The presence of high-risk HPV types and squamous intraepithelial lesions among women who have sex with women and report no prior sex with men supports the need for investigation in a larger number of women (particularly younger women, in whom HPV prevalence is likely to be highest). Whether Papanicolaou smear screening is indeed less frequent among women who have sex with women, particularly those who have not had sex with men, should be investigated. The conditions that could contribute to more infrequent Papanicolaou smear screening, including perception of low risk for cervical cancer or barriers to health care, should be defined. Such information would have great implications for counseling women who have sex with women about their risk of cervical cancer, Papanicolaou smear screening, and protective sexual practices. A recent report issued by the Institute of Medicine on research priorities in lesbian health strongly supports the need for more extensive data in these areas.⁵⁰

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