



# Sexual Health Update

## Human Papilloma Virus (HPV)—What Is It?

**H**uman papilloma virus, or HPV, is a common virus that infects the skin and mucous membranes (lining of the vagina, mouth, etc.) of humans. There are approximately 100 serotypes (or strains) of HPV—30 of which cause genital infections.<sup>1</sup> HPV is spread by direct contact with an infected person. Genital HPV infections are spread most often by intimate sexual activity, and potentially, by hand-to-genital contact.<sup>2</sup> When an individual becomes infected with HPV, the body's immune system can often eliminate the infection within 6-12 months, but not in all cases. In one study of U.S. college women, 30 percent of HPV infections were still present after 12 months, and 9 percent of infections were still present after 24 months.<sup>3</sup> The longer an infection persists, the more likely the infection will cause pre-cancerous and even cancerous cell changes.<sup>4</sup>

## Why Is HPV Important?

**S**ince most HPV infections never cause symptoms and resolve spontaneously, some will ask, "Why should we care about HPV?" The answer is simple: HPV infects more people each year than any other STD, resulting in 5.5 million new infections each year.<sup>5</sup> Even though only a small percentage of infected individuals will develop genital warts, abnormal Pap smears or cervical cancer, hundreds of thousands of Americans suffer from these problems each year.

**G**enital warts are the most common clinical manifestation of HPV infection and affect over one million sexually active Americans yearly.<sup>6</sup> Though not usually cancerous, genital warts can be an extremely distressing problem. Treatment of genital warts is often painful and may require multiple physician visits. Some warts are resistant to medical treatments and require surgical removal. Additionally, even when genital warts initially get smaller or disappear, recurrence of the warts is common. Many patients with genital warts also experience emotional suffering knowing that they have become infected with a sexually transmitted infection.

**T**he link between HPV infection and cervical cancer is now well established. A 1995 study reported that HPV infection was present in 93 percent of cervical cancers. This finding supports the premise that the virus is the causative agent in cervical cancer rather than simply an associated condition.<sup>7</sup> In 1999, a re-examination of earlier data led to the conclusion that HPV infection was actually present in over 99 percent of cervical cancers.<sup>8</sup> HPV infection also causes cervical intraepithelial neoplasia (dysplasia or "pre-cancer").

**T**hese diagnoses—made initially by Pap smear and confirmed by colposcopy with biopsy—often require surgical procedures on the cervix in order to prevent the development of cervical cancer.<sup>9</sup> More than any other reason, the association between HPV and cervical cancer explains why HPV is now receiving attention from both the public health and medical communities, and is frequently discussed in the popular media.

**H**PV infection can also lead to vaginal cancer. One study of 71 biopsy specimens from women with vaginal intraepithelial neoplasia ("pre-cancer") revealed that all 71 specimens showed evidence of infection with HPV.<sup>10</sup> While fewer women are diagnosed with vaginal cancer each year (2,300) than with cervical cancer, about 600 women die annually from vaginal cancer.<sup>11</sup>

**V**ulvar cancer is another condition linked to HPV.<sup>12</sup> This form of cancer, which affects the external genitalia of women, is again less common than cervical cancer and affects 3,300 women each year in the U.S.<sup>13</sup> If small, some vulvar cancers can be removed during biopsy, but if larger, surgery (and even, post-operative radiation) may be required.<sup>14</sup> Treatment can result in substantial disfigurement of the external genitalia, particularly when radical vulvectomy (surgical removal of the vulva) is required. Approximately 900 American women die from vulvar cancer each year.<sup>15</sup>

**H**PV infection also precedes cancers that develop in men. Men with HPV infection on the penis are at higher risk to develop penile cancer. About 1,400 American men develop cancer of the penis each year.<sup>16</sup> Early penile cancer is usually treated with local excision of the affected skin, however, removal of all or part of the penis is rarely necessary.<sup>17</sup>

**H**PV infection of the anus can lead to anal cancer in both men and women. The incidence of this cancer has more than doubled in men and increased by 46 percent in women since 1973.<sup>18</sup> Currently, over 3,000 individuals develop anal cancer each year. At-risk individuals include men who have sex with men, and women who have anal sex. Anal carcinoma in women may also be due to "migration" of the infection from the genital area to the anus.<sup>19</sup> Physicians who care for patients at high risk for this disease perform anal "Pap smears" as a screening procedure.<sup>20</sup> Anal cancer is usually treated by excision of the rectum and anus, accompanied by the surgical construction of a colostomy.<sup>21</sup>

Cancer of the oral cavity is another cancer that may be caused by HPV infection. Studies have shown an association between the presence of the HPV virus and the presence of cancers in the mouth.<sup>22</sup> These infections may be transmitted by oral sex.

### How Big Is the Problem?

HPV is the most prevalent viral STD in the United States. In fact, current estimates suggest that 5.5 million Americans acquire the infection each year. Nearly 20 million Americans are currently infected with the virus.<sup>23</sup> Perhaps the most astounding statistic is that 80 million Americans between 15 and 49 years of age have been infected by genital HPV at some point in their lives! This means that approximately 75 percent of sexually active individuals are now, or have previously been, infected with HPV.<sup>24</sup>

These estimates are supported by numerous scientific reports. In 1998, an article in the *New England Journal of Medicine* reported the number of sexually active females who tested positive for HPV infection during a 3-year study at Rutgers University. Twenty-six percent of the women tested were HPV-positive at the beginning of the study, and another 43 percent of participants tested positive for HPV at some point during the 36-month follow-up period.<sup>25</sup> When the researchers included those participants with pre-existing infections with those who became infected (or re-infected) during the course of the study, they concluded that 60 percent of the young women tested showed evidence of HPV infection at some point during the study. Other studies confirm that HPV is the most common sexually transmitted infection among adolescent girls.<sup>26</sup>

Available evidence clearly demonstrates that the burden of disease caused by HPV infection is huge. Last year in the United States, 14,000 women developed cervical cancer, and each year, approximately 5,000 die from this disease.<sup>27</sup> To put these numbers in perspective, cervical cancer caused by HPV infection kills more American women each year than does AIDS/HIV.<sup>28</sup> Additionally, another 2.5 million women who receive Pap smears are diagnosed with CIN (pre-cancer) and require additional diagnostic and treatment procedures.<sup>29</sup> Internationally, 400,000 to 500,000 cases of cervical cancer occur annually, and about 300,000 individuals die.<sup>30</sup> These problems are especially severe in developing countries where access to Pap smears and medical care is limited.

### Testing for HPV

Since HPV infection is not a reportable disease in the United States, routine screening for infection is not currently recommended, and until recently, tests to detect actual HPV infection were not available. Though screening for HPV infection is not routine, Pap smears screen for the pre-cancerous and cancerous cell changes caused by the infection.

The HPV Prevention workgroup of the Centers for Disease Control and Prevention states, "Additional studies should be performed in U.S. populations to evaluate HPV testing as an adjunct to the Pap smear in primary screening for cervical cancer as a method

of enhancing sensitivity and lengthening screening intervals. These should involve evaluation of self-collected samples for HPV testing as a means of increasing coverage of screening programs in difficult-to-access populations and should be supplemented by modeling studies to assess cost-effectiveness".<sup>31</sup>

Currently, the United States Preventive Services Task Force recommends that every sexually active woman should have a Pap smear to screen for cervical cancer at least once every three years.<sup>32</sup>

In practice, most clinicians suggest that, since HPV is so common and cancer often develops in less than three years, every woman who has ever had sexual intercourse should have a yearly Pap smear. Screening should be performed more frequently if Pap smear abnormalities are detected.

Screening for cervical cancer is important, because early detection impacts the treatment, course and chance of cure of the disease. If CIN (pre-cancer) is discovered, treatments can usually prevent the progression of the pre-cancerous condition to invasive cervical cancer. Individuals diagnosed with localized cervical cancer (early stage) have a 90 percent probability of surviving for at least five years.<sup>33</sup> Those with more advanced cancerous lesions at the time of detection have only a 14 percent probability of being alive in five years.<sup>34</sup>

### How Is HPV treated?

There is no cure for HPV. Genital warts, a common manifestation of HPV infection, can be treated in several ways. The chemical, podophyllin, is commonly the first treatment attempted. Podophyllin is usually applied in the physician's office, and the patient is instructed to wash after 8-12 hours. If podophyllin is unsuccessful, freezing the wart may be attempted. If freezing is unsuccessful, additional topical treatment, surgery, injection or laser treatment may be attempted. For continued recurrences, a series of injections with interferon may be attempted. Even when treatment is "successful" and the wart gets smaller (or disappears) genital warts often recur.

### Do Condoms Prevent the Spread of HPV?

We don't know to what extent, if any, condoms prevent the spread of HPV. Few studies looking specifically at this question have been completed, and the results of these studies are not consistent. The scientific community is currently debating how to accurately state what we know about condoms and HPV transmission.

### Condoms, HPV and Women

Most experts do agree that existing data on condoms and HPV transmission do not support the notion that condoms prevent the transmission of HPV infection from an infected man to an uninfected woman. After a review of available data, the National Institutes of Health stated, "The data on the use of barrier methods of contraception to prevent the spread of HPV are controversial but do not support this as an effective method of prevention."<sup>35</sup>

Similarly, the Centers for Disease Control and Prevention (CDC) recently convened an expert panel to discuss HPV prevention. The report from this meeting states:

*Theoretically, barrier contraceptives such as condoms are less likely to be effective in preventing infections such as genital HPV, which can involve the external genital skin, than they are for infections which are limited to specific mucosal areas and spread by semen (e.g., chlamydia or gonorrhea), although estimation of potential benefit of condoms for HPV is hindered by absence of measures of infectivity. Studies which have attempted to assess male condom benefit for women have generally found no evidence of protection against infection. Existing reports, however, have not adequately assessed consistency and correctness of condom use, and, in cross-sectional studies, HPV infection may have preceded condom use.*<sup>36</sup>

While absolute conclusions cannot be made from the results of existing research, one can confidently say that there is no substantive evidence that condoms significantly reduce the risk of HPV transmission from infected men to their female sexual partners.

### Condoms, HPV and Men

Men (especially heterosexual men) experience fewer complications from HPV infection than do women, and even fewer studies have been done to assess condom effectiveness in preventing HPV infection or genital warts in men. After reviewing the small amount of available data from these studies, the CDC states, “There are data suggesting a benefit of condom use for men, although the studies are limited. . . .”<sup>37</sup> Such studies appear to demonstrate partial risk reduction from condoms for uninfected men who have sex with HPV-infected women.<sup>38</sup>

Studies from other countries have attempted to examine the protective effect of condoms used by married men who regularly visit prostitutes or have multiple sexual partners. The outcome measured in these studies was whether cervical cancer developed in the man’s wife.<sup>39</sup> These studies are indirectly measuring condom effectiveness in *men* rather than women, since condom use with the spouse is not being measured—only condom use with prostitutes. Though the risk of cervical cancer in the condom-user’s wives was less than in the wives of non-condom-users, there is still appreciable risk of infection even in those who regularly used condoms.

Proponents of condom use for HPV prevention argue that laboratory tests have shown condoms to be impervious to HPV particles.<sup>40</sup> The knowledge accumulated in this type of laboratory study may not have any meaning in the non-laboratory situation, i.e. “the real world.” First, most individuals do not use condoms consistently and correctly.<sup>41</sup> Inconsistent condom users are unlikely to receive benefit from condom use because HPV is both very common and very infectious. Second, even if condoms are used consistently and correctly, there is a legitimate scientific reason for them to be less than effective in the case of HPV infection. As the CDC statement points out, HPV is a *regional*

infection rather than a *local* one.<sup>42</sup> An individual with a regional genital HPV infection likely has viral particles throughout the urogenital region and also on their fingers. Since a condom only covers the penis, it cannot prevent spread of infection from these adjacent areas. This “regional infection” concept is why condoms lack effectiveness.

We will not know what degree of risk reduction condoms may provide until a large prospective study is conducted. Nonetheless, we feel comfortable with these statements: First, condoms probably provide some degree of protection against infection for uninfected men, but that protection is incomplete and very limited. Second, the degree of protection, if any, for women is controversial. There may be some risk reduction, but research has not convincingly demonstrated that as fact. If a protective benefit exists for women, the benefit is likely small and almost certainly less than that afforded men.

Finally, given the limited risk reduction of condoms and the large proportion of the population infected with HPV, sexually active individuals cannot rely on condoms for protection from HPV. If they remain sexually active, their likelihood of being infected with HPV is very high, even with consistent and correct condom use. And given that few people use condoms consistently and correctly, especially with established partners, the risk is probably even higher than anticipated.

### Will a Vaccine Prevent HPV?

Scientists have been working for some time to develop a vaccine that protects against HPV. Because HPV cannot be grown in culture, research into the development of a vaccine has been difficult. Additionally, HPV has many strains, each with different immunologic characteristics. Developing a single vaccine that can prevent all HPV infections is virtually impossible. The most concerted vaccine development efforts are now focused on creating a vaccine for the HPV serotypes that cause most cervical cancers. Some vaccine trials are being conducted, but even if the vaccine is found to offer protection, it will be some time before such a vaccine becomes widely available. And should the vaccine be protective and widely available, sexually active individuals will remain susceptible to infection by other HPV strains.<sup>43</sup>

### What Should Be Done?

The data regarding HPV highlight the health benefits of refraining from sexual activity before marriage and maintaining sexual fidelity within marriage. The risk of becoming infected with a sexually transmitted infection is much higher today than it was two or three decades ago, due to the increased numbers of infected persons. The most effective way to reduce the number of infected Americans is to help young people delay the onset of sexual activity until marriage while encouraging married individuals to practice monogamy.

### HPV and Abstinence

The only way for non-married individuals to achieve adequate protection from HPV is to be sexually abstinent. Fortunately, more young people are now choosing to remain abstinent than in recent years, and other markers of sexual activity, like teen pregnancy rates, are also declining.<sup>44</sup> Other strategies—delaying the onset of sexual



activity, decreasing the number of lifetime sexual partners, or using condoms during every sexual encounter—may at best decrease, but cannot eliminate one's infection risk. With the high prevalence of HPV in our country and the high incidence of new HPV infections, non-married sexually active Americans are at substantial risk of HPV infection. And while many individuals and even health professionals say HPV is "a minor inconvenience," hundreds of thousands of individuals are being hurt by HPV, making the avoidance of this sexually transmitted infection a vital public health message—especially for young women.



## Footnotes

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