Human Papillomavirus (HPV) in Patients with HIV

Medical Care Criteria Committee, July 2018

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Purpose of This Guideline

This guideline on human papillomavirus (HPV) in individuals with HIV was developed by the New York State (NYS) Department of Health (DOH) AIDS Institute (AI). Its purpose is to inform primary care providers and other practitioners in NYS about HPV-related cervical and anal disease and to identify opportunities for screening and treatment. Accordingly, this guideline addresses the following topics on HPV: prevention, screening methods, diagnosis and presentation, and treatment. This guideline aims to achieve the following goals:

- Increase the numbers of NYS residents with HIV who are screened for HPV-related dysplasia and provided with effective care for HPV-related disease.
- Support the NYSDOH Prevention Agenda 2013-2018 to decrease the burden of HPV by educating providers on the importance of HPV vaccination and increasing the three-dose HPV immunization rate [NYSDOH 2016].
- Reduce the morbidity and mortality associated with HPV in people with HIV through early identification and treatment of precancerous and cancerous lesions, when treatment is most likely to be successful.
- Integrate current evidence-based clinical recommendations into the healthcare-related implementation strategies of the Ending the Epidemic initiative, which seeks to end the AIDS epidemic in New York State by the end of 2020.

The Burden of HPV

There are many HPV types, some of which cause cancer (oncogenic) and others that cause noncancerous disease (non-oncogenic verruca vulgaris and condyloma acuminata). A subgroup of approximately 30 different HPV types infects cells in the anus and genital tract, including the cervix, and may cause asymptomatic infection, condylomata acuminata (genital warts), squamous intraepithelial lesions (SIL), glandular cell abnormalities, and, rarely, anal and cervical cancer or other genital carcinomas. The incidence of HPV-related oropharyngeal cancer is increasing [CDC 2017a, 2017c, 2017b, 2017d]. HPV infection is often asymptomatic, and the time course from initial infection to the presence of lesions has not been determined. These factors prevent a reliable method for determining the source and time of acquisition.

In the general U.S. population, HPV types 16 and 18 are responsible for approximately 70% of cases of cervical and anal SIL and cervical and anal cancers [Steinbrook 2006; Lowy and Schiller 2012] in addition to most oropharyngeal, vaginal, vulvar, and penile cancers [Bouvard, et al. 2009; Grulich, et al. 2010; Forman, et al. 2012; Saraiya, et al. 2015]. Non-oncogenic HPV types 6 and 11 account for approximately 90% of genital warts [Steinbrook 2006]. A wider range and higher prevalence of HPV types responsible for oncogenic and non-oncogenic disease have been documented in people with HIV [Clifford, et al. 2006; Kojic, et al. 2011; Massad, et al. 2016]. HPV-associated cancers occur more often among people with HIV and AIDS than in the general population [Jemal, et al. 2013; Liu, et al. 2018]. The distribution of HPV types responsible for SIL and warts also differs between these two populations [Clifford, et al. 2006]. HPV type 16 is the most common high-risk type associated with cervical, anal, and penile neoplasia. HPV types 58 and 52 also are frequently associated with cervical SIL in women with HIV but are rarely associated with SIL in women without HIV [Clifford, et al. 2006]. Although HPV type 18 is commonly associated with SIL in individuals without HIV, it is much less common in people with HIV [Clifford, et al. 2006]. Infection with more than one HPV type occurs more frequently among individuals with HIV, and these individuals can be at risk of cervical and/or anal SIL and nonmalignant disease simultaneously [Clifford, et al. 2006; Castilho, et al. 2015].

Tobacco use is an established contributor to HPV’s oncogenic potential and is an independent risk factor for acquisition and progression of cervical SIL [Collins, et al. 2010], anal neoplasia [Daling, et al. 2004], oropharyngeal cancer [NCI 2018], and vulvar cancer in individuals with HIV [Kutlubay, et al. 2013; ACS 2018]. Some data suggest that HIV-related immune suppression can contribute to relapse and progression of HPV disease, and antiretroviral therapy-mediated immune reconstitution can lead to regression of SIL associated with HPV infection [Blitz, et al. 2013]. Other studies do not support this finding [Adler 2010; Piketty, et al. 2013].
Cervical cancer rates have decreased due to the benefit of a robust screening system in the United States that has been in place since the 1960s. The incidence of anal cancer persists, particularly among men who have sex with men with and without HIV and among women with HIV [Palefsky, et al. 1998b; Clifford, et al. 2005; Diamond, et al. 2005; Hessol, et al. 2009; Hessol, et al. 2013;Islami, et al. 2017]. Screening for anal HPV disease is a relatively new recommendation, and data on the benefit of screening and immediate treatment interventions are not yet definitive. Based in part on the epidemiological evidence and benefits of the analogous cervical screening, this Committee has recommended anal screening for individuals with HIV since 2007. Studies are underway to clarify the benefit of immediate treatment interventions for anal HPV disease [AMC 2017]. Although screening tests are available for oropharyngeal cancers, the utility and benefits have not been established; therefore screening other than visual inspection, is not yet recommended [see American Dental Association > Oral and Pharyngeal Cancer for more information]. There are no routine screening tests or procedures for vulvar, vaginal, or penile cancers.

The Role of NYS Primary Care Providers

Primary care clinicians have a major role in the prevention, screening, diagnosis, and treatment of sexually transmitted infections in individuals with HIV. The goal of this guideline is to provide standards for clinicians in NYS to prevent and identify HPV disease and to determine appropriate treatment and follow-up in individuals with HIV.

Development of This Guideline

This guideline was developed by the NYSDOH AI Clinical Guidelines Program, which is a collaborative effort between the NYSDOH AI Office of the Medical Director and the Johns Hopkins University School of Medicine, Division of Infectious Diseases.

Established in 1986, the goal of the Clinical Guidelines Program is to develop and disseminate evidence-based, state-of-the-art clinical practice guidelines to improve the quality of care provided to people with HIV, hepatitis C virus, and sexually transmitted infections and to improve drug user health and LGBT health throughout NYS. NYSDOH AI guidelines are developed by committees of clinical experts through a consensus-driven process.

The NYSDOH AI charged the Medical Care Criteria Committee (adult HIV and related guidelines) with developing evidence-based clinical recommendations for primary care clinicians in NYS who provide services to individuals with HIV. The resulting recommendations are based on an extensive review of the medical literature and reflect consensus among this panel of experts in HIV and women’s health. Each recommendation is rated for strength and quality of the evidence (see below). If recommendations are based on expert opinion, the rationale for the opinion is included.

<table>
<thead>
<tr>
<th>AIDS Institute HIV Clinical Guidelines Program Recommendations Rating Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strength of Recommendation</strong></td>
</tr>
<tr>
<td>A = Strong</td>
</tr>
<tr>
<td>B = Moderate</td>
</tr>
<tr>
<td>C = Optional</td>
</tr>
</tbody>
</table>
Transmission and Prevention

Transmission and Prevention of HPV

- Clinicians should recommend the 9-valent human papillomavirus (HPV) vaccine 3-dose series at 0, 2, and 6 months to all individuals who are 9 to 26 years of age with HIV regardless of CD4 cell count, prior cervical or anal cytology (Pap test) results, HPV test results, HPV-related cytologic changes, or other history of HPV-related lesions. (A3)
- Clinicians should engage patients who are 27 to 45 years of age in shared decision-making regarding HPV vaccination. (A3)

a. In October 2018, the U.S. Food and Drug Administration (FDA) changed its HPV vaccination recommendations to include ages 27 to 45. There was no specific mention of HIV [FDA 2017].

HPV Vaccine

The FDA has approved a quadrivalent vaccine that protects against non-oncogenic HPV types 6 and 11 and oncogenic HPV types 16 and 18 (Gardasil) and a 9-valent vaccine that protects against non-oncogenic HPV types 6 and 11 and oncogenic HPV types 16, 18, 31, 33, 45, 52, and 58 (Gardasil 9).

Because it offers broader coverage of HPV types, the 9-valent vaccine is the only HPV vaccine available in the United States (see the Centers for Disease Control and Prevention [CDC] Supplemental information and guidance for vaccination providers regarding use of 9-valent HPV for more information). The HPV vaccine is FDA-approved for preventive but not therapeutic use. There are currently no data to support the use of the HPV vaccine to ameliorate existing anal dysplasia.

Extrapolating data from the demonstrated effectiveness of the quadrivalent HPV vaccine in older individuals [Wilkin, et al. 2016], the FDA expanded the age range for recommended HPV vaccination in the United States from ages 9 to 26 years to include individuals who are 27 to 45 years of age [FDA 2017]. There is no specific mention of HIV infection in the updated FDA recommendation. Although 1 study demonstrated lower efficacy of the quadrivalent vaccine in individuals with HIV [Wilkin, et al. 2016], other research linked HIV viral suppression to vaccine efficacy [Money, et al. 2016].

→ KEY POINTS

- In individuals with HIV, the 9-valent HPV vaccine is administered in 3 doses at months 0, 2, and 6.
- HPV testing is not recommended before administration of the HPV vaccine.

When to Vaccinate

HPV vaccination may be scheduled at the same time as standard adolescent vaccines offered at age 11 or 12 years. For young people who have experienced sexual abuse or assault or who are immunocompromised, the vaccine series should begin at age 9 [Glidden, et al. 2016]. In the general population, a 2-dose HPV vaccine is recommended for individuals younger than 15 years, and a 3-dose vaccine regimen is recommended for individuals aged 15 and older [CDC 2016]. For individuals with HIV who are 9 to 45 years of age, the 3-dose HPV vaccine remains the recommended approach [Meites, et al. 2016]. The 9-valent HPV vaccine should be administered according to the CDC standard schedule for immunocompromised adults, children, and adolescents (a 3-dose regimen over a 6-month period at 0, 2, and 6 months) [Kojic, et al. 2014] and should be offered regardless of CD4 cell count.

HPV vaccination provides high levels of neutralizing antibody for at least 5 years and is protective in individuals aged 26 years or younger who do not have HIV, regardless of history of sexual activity; however, the full length of its protection has not been established. Although data are limited, the immunogenicity of the quadrivalent HPV vaccine has been demonstrated in individuals with HIV [Wilkin, et al. 2016].

HPV testing and vaccination: HPV testing is not recommended before vaccine administration. It is unlikely that an individual will have been infected with all the HPV types covered by the 9-valent vaccine; therefore, it is expected that the 9-valent HPV vaccine will be effective against any of the 9 HPV types or any HPV types to which the individual has not
been exposed. There also may be beneficial prevention due to cross-reactivity with other HPV types not included in the 9-valent vaccine [Wheeler, et al. 2012].

Revaccination with the 9-valent HPV vaccine is not currently recommended for individuals who previously received the bivalent or quadrivalent HPV vaccine [Petrosky, et al. 2015]. Vaccination with the quadrivalent HPV vaccine has demonstrated cross-protection against other oncogenic HPV types [Kemp, et al. 2011]. Clinicians may consider the benefit of protection against the additional 5 oncogenic HPV types targeted in the 9-valent vaccine for individual patients [CDC 2016]. If a scheduled vaccine dose is missed, there is no need to repeat doses; there is no maximum interval [CDC 2019].

Other Forms of HPV Prevention

HPV infection is the most common sexually transmitted infection (STI) in the United States, and many individuals become infected with multiple types of HPV during their lives [CDC 2013]. HPV is transmitted via skin-to-skin contact, so barrier methods, such as male and female condoms, offer some, but not full protection. Because prior identification of HPV infection in a sexual partner is unlikely, limiting the number of sexual partners may reduce but not eliminate an individual’s exposure to HPV [Winer, et al. 2003].

→ KEY POINTS

- It is important that clinicians inform patients with HIV about the risk of acquiring HPV and other STIs from close physical contact with the external genitalia, anus, cervix, vagina, urethra, mouth and oral cavity, or any other location where HPV lesions are present.
- Consistent and correct condom use remains an effective way to prevent the transmission of most STIs, including HPV. However, it is important that clinicians inform patients that barrier protection such as condoms and dental dams may not fully protect against HPV.

Screening

竖 RECOMMENDATIONS

Screening

- Clinicians should continue to perform cervical and anal Pap smears as recommended for individuals with HIV, regardless of their HPV vaccination status (see the NYSDOH AI guidelines Cervical Screening for Dysplasia and Cancer and Anal Dysplasia and Cancer). (A2)
- Clinicians should examine the neovagina in transgender women who have undergone vaginoplasty to assess for visible HPV lesions at baseline and during the annual comprehensive physical examination. Examination can be done using an anoscope, a small vaginal speculum, or a nasal speculum. (A3)
- Clinicians should ask all patients about sexual behaviors and new sex partners at each routine monitoring visit to assess for risk behaviors that require repeat or ongoing screening. (A3)

HPV testing with cytologic screening enhances the identification of HPV-related cervical disease in individuals with HIV (see the NYSDOH AI guideline Cervical Screening for Dysplasia and Cancer). Clinicians should perform cervical and anal cytologic (i.e., Pap) screening for people with HIV according to the recommended guidelines for this population (see the NYSDOH AI guidelines Cervical Screening for Dysplasia and Cancer and Anal Dysplasia and Cancer). Examination of the anogenital area of patients with HIV to assess for visible HPV lesions is necessary because HPV can also infect the urethra and the external genitalia [Weyers, et al. 2010; Tyerman and Aboulafia 2012; Leeds and Fang 2016; CDC 2017b; Ehrenpreis and Smith 2018]. Speculum examination of the vagina (includes neovagina) and cervix and anoscopic examination of the anus and lower rectum also may reveal lesions. There are currently no data on urethral screening and treatment, but referral to a urologist will facilitate appropriate assessment and management when this is a concern. Asking patients to provide details about all gender-reassignment and gynecologic surgical procedures they have undergone is essential to determine the type of screening needed.
Recent data demonstrate increased risk of anal dysplasia and rising rates of anal cancer among females with HIV [Gaisa, et al. 2017]. Although anal squamous intraepithelial lesions have been associated with concurrent cervical squamous intraepithelial lesions (CSIL), they also occur independently of CSIL. Therefore, anal cytology should be performed for all females with HIV [Kojic, et al. 2011; Hessol, et al. 2013; Stier, et al. 2015; Gaisa, et al. 2017] with and without cervical abnormalities according to guidelines for adults with HIV. In addition, it is important that digital examination of the anus for anal cancer continue at the recommended intervals (see the AI guideline Anal Dysplasia and Cancer), regardless of Pap test results. Although there are no specific data on transgender men or women, the recommendation is extended to also perform anal screening for these populations.

**→ KEY POINTS**

- Assessment for visible HPV lesions in individuals with HIV can be accomplished through baseline and then annual examination of the peri-urethral and anogenital areas and the vagina and cervix.
- Individuals who have received HPV vaccination should still be screened for cervical and anal disease according to the recommended schedules (for more information, see the AI guidelines Cervical Screening for Dysplasia and Cancer and Anal Dysplasia and Cancer).

**Obtaining a Sexual History**

When obtaining a sexual history, questions should focus primarily on the patient’s sexual behavior and not solely on sexual and gender identity (e.g., avoid use of such labels as “lesbian,” “homosexual,” or “gay”) [Lanier, et al. 2014]. A study conducted in New York City found that self-reported sexual identity could not independently establish patients’ risk. Many men who have sex with men in the study did not identify as “gay,” underscoring the importance of assessing sexual behavior when determining a patient’s risk [Pathela, et al. 2006; Bernstein, et al. 2008]. Transgender people differ widely in terms of sexual behavior and anatomy. It is helpful to ask about the type of sex a person is having and the parts of anatomy used for sex, as well as about the anatomy of partners. A patient’s openness to discuss his or her sexual and gender identity may be important for the clinician’s understanding of the patients’ health status, perceived stigma, and risk of acquiring or transmitting sexually transmitted infections (STIs) [Lanier, et al. 2014; CDC 2017a]. Therefore, clinicians should stress the confidential nature of discussions about sexual activities and maintain a nonjudgmental attitude to encourage patients to disclose all sexual behaviors.

For clinicians who are uncomfortable discussing sexual behaviors and STI transmission risk, training may help increase their comfort level and assist them in developing a nonjudgmental approach to educating patients about the importance of STI screening. The New York State (NYS) Department of Health Clinical Education Initiative Line (866-637-2342) enables clinicians in NYS to discuss post-exposure prophylaxis, pre-exposure prophylaxis, HIV, hepatitis C virus, and STI management with a specialist, and the New York City STD/HIV Prevention Training Center provides HIV-related educational resources and training for providers. The Centers for Disease Control and Prevention’s Guide to Taking a Sexual History offers parameters for discussing sexual health issues with patients.

**Presentation and Diagnosis**

**RECOMMENDATIONS**

**Presentation and Diagnosis**

- Clinicians with limited expertise should refer individuals with abnormal anogenital physical findings, such as warts, hypopigmented or hyperpigmented plaques/lesions, lesions that bleed, or any other lesions of uncertain etiology for expert evaluation. This evaluation may include colposcopy, high-resolution anoscopy, and/or biopsy. (A3)
- Clinicians should maintain a low threshold for obtaining biopsies of lesions that are atypical in appearance, condylomatous, that are hyper- or hypopigmented or variegated, or that fail to respond to standard treatment. (A3)
- Clinicians should refer for or perform colposcopy for individuals with HIV who have abnormal cervical cytology (including persistent atypical squamous cells of undetermined significance) and high-risk human papillomavirus (HPV) (see the NYSDOH AI guideline Cervical Screening for Dysplasia and Cancer). (A2)
## RECOMMENDATIONS

- Clinicians should refer for or perform high-resolution anoscopy for individuals with HIV who have abnormal anal cytology, who have visible anal lesions, or if palpable lesions are elicited on digital anorectal examination. (A2)
- Clinicians should refer individuals with visible urethral lesions to a urologist experienced in HPV biopsy and diagnosis. (A3)
- Clinicians should diagnose, treat, and follow-up HPV-related lesions in patients with HIV in consultation with a clinician experienced in the management of HPV and HIV. (A3)

Diagnosis of external condylomata acuminata is often made on the basis of clinical appearance. The appearance of warts varies. Condylomata acuminata (genital warts) can be smooth and skin-colored or hyperpigmented papules or plaques that may be flat, hyperkeratotic, nodular, or exophytic. Symptoms may be absent or may include itching, bleeding, burning, and discomfort. Warts on the external genitalia and the cervix are commonly flat, plaque-like lesions. They also can be exophytic and visible to the naked eye. Cervical lesions are best visualized by colposcopy. Penile lesions can occur along the shaft, but also may be along the penile urethra and hidden from view.

Small external lesions often are treated without biopsy. Lesions that are atypical or variegated in color or shape require biopsy to exclude squamous intraepithelial lesions (SIL) or cancer. Clinicians should maintain a low threshold to obtain biopsy of the following: atypical-appearing lesions; pigmented, internal, or condylomatous lesions; rapidly growing lesions; or lesions that fail to respond to standard treatment, because these may be indicative of precancerous or cancerous lesions.


- Condylomata acuminata, anal SIL/anal intraepithelial neoplasia, and cervical SIL/cervical intraepithelial neoplasia have all been reported to occur more frequently in people with HIV.
- With increased immunosuppression, there is evidence for increased risk of the following:
  - Persistent and recurrent HPV infection and disease of the anal and genital tracts.
  - Decreased rates of spontaneous disease regression.
  - Increased severity of HPV disease.
  - Anal SIL.
  - Cervical SIL.
  - Development of condylomata acuminata.
- HPV may be more difficult to treat and more likely to recur with advanced immunosuppression.
- Patients with more advanced immunosuppression have an increased relative risk of developing HPV-related invasive anogenital cancers.
- See the following sources for images:
  - U.S. Department of Veterans Affairs Image Library > Human Papillomavirus Virus
  - CDC Public Health Image Library > Quick Search > HPV
  - MedicineNet.com > Sexually Transmitted Diseases

Data are mixed regarding the contribution of HIV-related immune suppression to the relapse and progression of HPV disease, and whether antiretroviral therapy (ART)-mediated immune reconstitution can lead to regression of SIL associated with HPV infection [Adler 2010; Blitz, et al. 2013; Piketty, et al. 2013]. Although there are cases of involution of mucocutaneous warts after initiation of ART, the prevalence or course of anogenital HPV disease is not altered significantly by ART [Adler 2010; Lofgren, et al. 2015].
KEY POINTS

- Cervical and anogenital symptoms of HPV-associated disease include itching, bleeding, pain, or spotting after sexual intercourse. HPV-associated disease should be considered in the differential diagnosis when symptoms are present.
- Failure to correctly diagnose precancerous or cancerous HPV-related disease in a timely manner can cause delay of appropriate therapy and possible mortality. Therefore, clinicians should maintain a low threshold for obtaining biopsies of lesions that are atypical in appearance, condylomatous, have variegated pigmentation, or that fail to respond to standard treatment.

Treatment

RECOMMENDATIONS

- Clinicians should use the same therapeutic modalities in patients with and without HIV when treating HPV, with the exception of sinecatechin use; sinecatechins should not be used in immune-compromised individuals. (A3)
- Clinicians should obtain a biopsy to exclude dysplasia or cancer for condyloma that have not responded to treatment. (A3)
- Clinicians should switch treatment modalities if biopsy-confirmed warts/condyloma have not improved substantially within 4 months of therapy. (A3)
- Clinicians should refer patients with lesions that are resistant to topical therapies; that change in appearance; that have ulceration, irregular shape, or variegated pigmentation; or with biopsy-proven dysplasia to clinicians experienced in the management of HPV and HIV. (A3)
- Clinicians should refer patients with visible urethral lesions to a urologist for treatment. (A3)
- Clinicians should refer patients with HIV who have anogenital cancer to an oncologist for treatment. (A3)
- Clinicians should avoid imiquimod during pregnancy unless the benefits outweigh the risk. (A3)
- Clinicians should not use sinecatechins, podophyllin, or podofilox (podophyllotoxin) in pregnant individuals. (A3)

See the Centers for Disease Control and Prevention’s [CDC] guideline on Anogenital Warts.

The standard therapeutic approach to treating HPV-related nonmalignant lesions (condyloma/warts) and dysplasia (squamous intraepithelial lesion or above) in individuals with HIV is the same as that for individuals without HIV. Treatment of condyloma is aimed at removing symptomatic visible warts. However, some untreated warts may resolve spontaneously. To date, there has been no evidence that any available treatment regimen eradicates infection. Comparative efficacy trials of the different treatment options for patients with HIV have not been conducted. Treatment of precancerous lesions includes ablation using cryotherapy or laser, and surgical or laser excision. These procedures should be performed only by experienced clinicians (see the AIDS Institute guideline Cervical Screening for Dysplasia and Cancer for more information).

Cryotherapy, electrocautery, podophyllotoxin, interferon, imiquimod, cidofovir gel, trichloroacetic acid, and bichloracetic acid have all demonstrated efficacy treating anogenital warts in patients without HIV. In a systematic review and meta-analysis, electrocautery and imiquimod were shown to be efficacious in the treatment of anogenital warts in people with HIV [Werner, et al. 2017]. Controlled studies of other HPV interventions in people with HIV have not been done. Interferon, 5-fluorouracil, and podophyllotoxin are no longer preferred HPV treatments in the primary care setting because of low efficacy and toxicity that may limit their routine use [Lacey, et al. 2013]. The safety and efficacy of sinecatechins has not been evaluated in individuals with HIV and therefore should not be used [FDA 2007].

There are limited data on imiquimod use in pregnancy, but animal data suggest low risk of harm. This drug can be used during pregnancy if no other options, including waiting until after delivery, are available. Due to a lack of safety data, podophyllin should not be used during pregnancy. Podofilox (podophyllotoxin) is contraindicated in pregnancy [Briggs, et al. 2017].
Data for the treatment of HPV lesions of the neovagina, whether penile or colonic in origin, are limited to case reports and small case series. Standard, provider-applied approaches to treatment should be used [Fiumara and Di Mattia 1973; Liguori, et al. 2004; Wasef, et al. 2005; Matsuki, et al. 2015; van der Sluis, et al. 2016; Labanca and Mañero 2017].

Clinicians often report poor clearance rates after therapy in patients with HIV [Richel, et al. 2013]. More than one application of therapy, more than one method of treatment (e.g., topical imiquimod followed by cryotherapy), or longer duration of treatment is often needed. Treatment length may vary and frequent visits (as often as biweekly) are necessary to assess lesion regression and side effects. Topical treatments may cause side effects such as irritation and a burning sensation, which may affect treatment adherence. The response to treatment and its side effects should be evaluated throughout the course of therapy. The treatment approach may need to be changed if a patient has not improved substantially after standard therapy. There are no data available regarding effects of HPV treatment on HPV transmissibility.

Clinical judgment should inform a clinician’s decisions about whether to treat a patient with HIV for anogenital warts or refer the patient to a specialist. The following factors should be considered when making this decision: clinician experience and available resources, diagnostic certainty, anatomic site of lesions, potential adverse effects of treatment, and patient ability to adhere to treatment.

Table 1, below, lists available treatment options for condyloma for patients with HIV.

<table>
<thead>
<tr>
<th>Condyloma Types</th>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anogenital Condyloma</td>
<td>• Cryotherapy</td>
<td>• Extra-genital warts, including warts on penis, groin, scrotum, vulva, perineum, external anus, and peri-anus</td>
</tr>
<tr>
<td></td>
<td>• Podophyllin resin 10%–25% in a compound tincture of benzoin*</td>
<td>• Weaken condoms and vaginal diaphragms</td>
</tr>
<tr>
<td></td>
<td>• Surgical excision</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Trichloroacetic acid (TCA) or bichloracetic acid (BCA) 80%–90%*</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Patient self-administered treatments:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Imiquimod 3.75% or 5% cream (may decrease likelihood of recurrences)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Podofilox 0.5% solution or gel*</td>
<td></td>
</tr>
<tr>
<td>Urethral Meatus Condyloma</td>
<td>• Cryotherapy with liquid nitrogen</td>
<td>−</td>
</tr>
<tr>
<td>Vaginal Condyloma</td>
<td>• Cryotherapy with liquid nitrogen</td>
<td>−</td>
</tr>
<tr>
<td></td>
<td>• Surgical excision</td>
<td></td>
</tr>
<tr>
<td>Cervical Condyloma</td>
<td>• Cryotherapy with liquid nitrogen</td>
<td>• Management of cervical warts should include consultation with a specialist</td>
</tr>
<tr>
<td></td>
<td>• Surgical excision</td>
<td>• For those who have exophytic cervical warts, a biopsy evaluation to exclude high-grade squamous intraepithelial lesions must be performed before treatment is initiated</td>
</tr>
<tr>
<td></td>
<td>• TCA or BCA 80%–90% solution</td>
<td></td>
</tr>
</tbody>
</table>
### Table 1: Available Treatment Options for Anogenital Condyloma for Patients with HIV (adapted from CDC 2015, unless otherwise noted)

<table>
<thead>
<tr>
<th>Condyloma Types</th>
<th>Treatment</th>
<th>Comments</th>
</tr>
</thead>
</table>
• Imiquimod 3.75% or 5% cream (may decrease likelihood of recurrences)  
• Podofilox 0.5% solution or gel*  
• Podophyllin resin 10%–25% in a compound tincture of benzoin*  
• Surgical excision  
• TCA or BCA 80%–90%*  | • Weakens condoms and vaginal diaphragms |

*Imiquimod, podophyllin, and podofilox (podophyllotoxin), and sinecatechins should not be used in pregnant individuals [Briggs, et al. 2017]. TCA or BCA can be used to treat small external warts during pregnancy but may not be as effective. Sinecatechins should not be used in any individual with HIV because safety and efficacy data do not exist [FDA 2007].

### Partner Exposure to HIV and HPV

#### ☑ RECOMMENDATIONS

**Partner Exposure to HIV and HPV**

- **NYS Public Health Law** requires that medical providers talk with individuals with HIV about their options for informing their sex partners that they may have been exposed to HIV, including the free, confidential partner notification assistance offered by New York State Department of Health (NYSDOH) and New York City Department of Health and Mental Hygiene.

- When a patient with HIV is diagnosed with human papillomavirus (HPV), clinicians should advise the patient to encourage sex partners to seek evaluation for possible exposure to both HPV and HIV. (A3)

Treatment of lesions solely for the prevention of future transmission cannot be recommended because the value of treatment in reducing infectivity is not known. However, sex partners of patients who have genital lesions might benefit from counseling and examination to assess the presence of genital warts and HPV-related dysplasia. Sex partners should also be evaluated for the presence of other sexually transmitted infections (STIs), including HIV, because HPV disease is transmitted sexually [Workowski and Bolan 2015].

Clinicians should inform patients that any sex partner who does not have confirmed HIV infection should have routine HIV testing for early identification of HIV acquisition. If a patient with an HIV exposure presents within 36 hours, evaluation for non-occupational post-exposure prophylaxis (PEP) should occur. When possible, onsite availability of HIV testing and STI treatment for partners is ideal because it may increase the likelihood that partners will receive timely access to HIV testing and appropriate treatment, including HIV post-exposure prophylaxis and treatment for the STI as needed (see NYSDOH AIDS Institute [AI] guideline [PEP for Non-Occupational Exposure to HIV]). Such strategies may also increase identification of individuals who require ongoing medical care. Partner education about reducing high-risk behaviors, including counseling about the use of barriers, such as male/insertive and female/receptive condoms, and making condoms visibly available in the clinic, may further decrease the risk of transmission of both HIV and other STIs. Patients who remain at high risk of exposure after completing a course of nPEP and who are negative for HIV at the time of the 4-week test should be offered pre-exposure prophylaxis (PrEP), to begin immediately after the last dose of nPEP (see NYSDOH AI guideline [PrEP to Prevent HIV and Promote Sexual Health]). Patient education about *Undetectable=Untransmittable* (U=U) as an HIV prevention strategy should stress that an undetectable HIV viral load prevents only the sexual transmission of HIV. Consistent and correct condom use remains the best method for preventing pregnancy and the transmission of STIs other than HIV.
The NYSDOH Partner Services program provides assistance to individuals with HIV and to care providers who would like help notifying a patient’s sex partner(s) of possible exposure to HIV, chlamydia, gonorrhea, or syphilis. Available options for partner notification include anonymous notification from the local health department, dual disclosure (patient disclosure with the help of Partner Services staff), and self-disclosure. Partner Services staff within local health departments work with patients to develop a plan to notify their partners, whether that plan includes staff notifying potentially exposed partners anonymously or helping patients who choose to tell their partners on their own develop a notification plan and strategy.

→ KEY POINTS

- When a patient with HIV is diagnosed with a new STI, the clinician should inform the patient about the implications of the diagnosis for his/her sex partner(s):
  - A new STI diagnosis signals that the patient was engaging in sexual behaviors that place sex partners at increased risk of acquiring HIV infection.
  - The local health department may contact a sex partner confidentially about the potential exposure and treatment options.
- Clinicians should provide patients with information and counseling about notifying partners, risk reduction, and safer sex practices.

All Recommendations

☑ All RECOMMENDATIONS: Human Papillomavirus (HPV) in Patients with HIV

Transmission and Prevention of HPV

- Clinicians should recommend the 9-valent human papillomavirus (HPV) vaccine 3-dose series at 0, 2, and 6 months to all individuals who are 9 to 26 [a] years of age with HIV regardless of CD4 cell count, prior cervical or anal cytology (Pap test) results, HPV test results, HPV-related cytologic changes, or other history of HPV-related lesions. (A3)
- Clinicians should engage patients who are 27 to 45 years of age in shared decision-making regarding HPV vaccination. (A3)

a. In October 2018, the U.S. Food and Drug Administration (FDA) changed its HPV vaccination recommendations to include ages 27 to 45. There was no specific mention of HIV [FDA 2017].

Screening

- Clinicians should continue to perform cervical and anal Pap smears as recommended for individuals with HIV, regardless of their HPV vaccination status (see the NYSDOH AI guidelines Cervical Screening for Dysplasia and Cancer and Anal Dysplasia and Cancer). (A2)
- Clinicians should examine the neovagina in transgender women who have undergone vaginoplasty to assess for visible HPV lesions at baseline and during the annual comprehensive physical examination. Examination can be done using an anoscope, a small vaginal speculum, or a nasal speculum. (A3)
- Clinicians should ask all patients about sexual behaviors and new sex partners at each routine monitoring visit to assess for risk behaviors that require repeat or ongoing screening. (A3)

Presentation and Diagnosis

- Clinicians with limited expertise should refer individuals with abnormal anogenital physical findings, such as warts, hypopigmented or hyperpigmented plaques/lesions, lesions that bleed, or any other lesions of uncertain etiology for expert evaluation. This evaluation may include colposcopy, high-resolution anoscopy, and/or biopsy. (A3)
- Clinicians should maintain a low threshold for obtaining biopsies of lesions that are atypical in appearance, condylomatous, that are hyper- or hypopigmented or variegated, or that fail to respond to standard treatment. (A3)
- Clinicians should refer for or perform colposcopy for individuals with HIV who have abnormal cervical cytology (including persistent atypical squamous cells of undetermined significance) and high-risk human papillomavirus (HPV) (see the NYSDOH AI guideline Cervical Screening for Dysplasia and Cancer). (A2)
All RECOMMENDATIONS: Human Papillomavirus (HPV) in Patients with HIV

- Clinicians should refer for or perform high-resolution anoscopy for individuals with HIV who have abnormal anal cytology, who have visible anal lesions, or if palpable lesions are elicited on digital anorectal examination. (A2)
- Clinicians should refer individuals with visible urethral lesions to a urologist experienced in HPV biopsy and diagnosis. (A3)
- Clinicians should diagnose, treat, and follow-up HPV-related lesions in patients with HIV in consultation with a clinician experienced in the management of HPV and HIV. (A3)

Treatment

- Clinicians should use the same therapeutic modalities in patients with and without HIV when treating HPV, with the exception of sinecatechin use; sinecatechins should not be used in immune-compromised individuals. (A3)
- Clinicians should obtain a biopsy to exclude dysplasia or cancer for condyloma that have not responded to treatment. (A3)
- Clinicians should switch treatment modalities if biopsy-confirmed warts/condyloma have not improved substantially within 4 months of therapy. (A3)
- Clinicians should refer patients with visible urethral lesions to a urologist for treatment. (A3)
- Clinicians should refer patients with visible urethral lesions to a urologist for treatment. (A3)
- Clinicians should refer patients with HIV who have anogenital cancer to an oncologist for treatment. (A3)
- Clinicians should avoid imiquimod during pregnancy unless the benefits outweigh the risk. (A3)
- Clinicians should not use sinecatechins, podophyllin, or podofilox (podophyllotoxin) in pregnant individuals. (A3)
  - See the Centers for Disease Control and Prevention’s [CDC] guideline on Anogenital Warts.

Partner Exposure to HIV and HPV

- NYS Public Health Law requires that medical providers talk with individuals with HIV about their options for informing their sex partners that they may have been exposed to HIV, including the free, confidential partner notification assistance offered by New York State Department of Health (NYSDOH) and New York City Department of Health and Mental Hygiene.
- When a patient with HIV is diagnosed with human papillomavirus (HPV), clinicians should advise the patient to encourage sex partners to seek evaluation for possible exposure to both HPV and HIV. (A3)

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