



Human Papillomavirus (HPV) in Patients with HIV

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Purpose of the Guideline

- Increase the numbers of NYS residents with HIV who are screened for HPV-related dysplasia and managed effectively.
- 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.
- 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.

Burden of HPV

- Approximately 30 different HPV subtypes can infect cells in the anus and genital tract, including the cervix, and may cause asymptomatic infection, genital warts, SIL, glandular cell abnormalities, and anal and cervical cancer or other genital carcinomas.
- HPV-associated cancers occur more often in people with HIV than in the general U.S. population.
 - HPV types 16 and 18: Most common high-risk type associated with cervical, anal, and penile neoplasias.
 - HPV types 58 and 52: Frequently associated with cervical SIL.
 - Infection with more than one HPV type occurs more frequently in people with HIV, and these individuals can be at risk of cervical and/or anal SIL and nonmalignant disease simultaneously.
- Some data suggest that HIV-related immune suppression can contribute to relapse and progression of HPV disease, and ART-mediated immune suppression can lead to regression of SIL associated with HPV infection.
- Because screening for anal HPV disease is a relatively new recommendation, anal cancer rates are on the rise, particularly among MSM with and without HIV and among women with HIV.

Tobacco Use and HPV

- Tobacco use is an independent risk factor for acquisition of and progression of cervical SIL, anal neoplasia, oropharyngeal cancer, and vulvar cancer in people with HIV.

Transmission and Prevention

✓ RECOMMENDATIONS

- Clinicians should recommend the 9-valent HPV vaccine three-dose series at 0, 2, and 6 months to all individuals aged 9 to 26 years with HIV regardless of CD4 cell count, prior cervical or anal Pap test results, HPV-related cytologic changes, or history of HPV lesions. (A3)
- Clinicians should 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. (A3)

Transmission and Prevention

→ KEY POINTS

- The 9-valent HPV vaccine is the current formulation for immunization in people with HIV in the United States.
- HPV vaccination may be given at the same time as the standard adolescent vaccines offered at age 11 to 12 years. For young people who have experienced sexual abuse or assault or are immune compromised, the vaccine series should begin at age 9 years. HPV testing before administration of the HPV vaccine is not recommended.
- Although HPV vaccination is highly effective in preventing HPV-related warts, dysplasia, and cancer, it does not protect against all HPV types, and it may not fully protect every person who is vaccinated; therefore, clinicians should continue to perform full anogenital evaluations at the recommended intervals for all individuals with HIV who have received the HPV vaccine (see Screening section in the full guideline).
- Consistent and correct condom use remains the best method for preventing the transmission of STIs, including HPV and HIV.

Rationale for HPV Vaccination

- Nearly 100% of cervical cancers are associated with HPV infections.
- The 9-valent HPV vaccine protects against non-oncogenic HPV subtypes 6 and 11 and oncogenic HPV subtypes 16, 18, 31, 33, 45, 52, and 58.
- Although the HPV infection subtypes most commonly associated with cervical cancer are HPV 16 and HPV 18 in the general population, in females with HIV, a broader range of HPV oncogenic subtypes are associated with cervical dysplasia.
- In females with HIV, the risk of HPV-related cervical disease is greater than in those who do not have HIV, and cervical cancer is the leading cause of cancer death among this population.
- HPV vaccination coupled with regular cervical cytologic screening to identify precancerous lesions, treatment, and follow-up is an effective intervention for decreasing the incidence of cervical cancer.

Screening

✓ RECOMMENDATIONS

- 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 continue to perform cervical and anal Pap smears as recommended for individuals with HIV, regardless of their HPV vaccination status (A2)
 - See the NYSDOH AI guidelines on Cervical Screening and Anal Screening for Dysplasia and Cancer in Patients with HIV.

Screening

→ 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 NYSDOH AI guideline on Cervical Screening for Dysplasia and Cancer in Patients with HIV.

Obtaining a Sexual History

✓ RECOMMENDATION

- 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

✓ RECOMMENDATIONS

- 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 or 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 cytology (including persistent ASCUS) and high-risk HPV. (A2)
 - See the NYSDOH AI guideline Cervical Screening for Dysplasia and Cancer in Patients with HIV.

Presentation and Diagnosis (cont.)

✓ RECOMMENDATIONS

- Clinicians should refer for or perform high-resolution anoscopy for individuals with HIV who have abnormal anal cytology or 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)

Presentation and Diagnosis

→ 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, with the exception of sinecatechins, as in patients without HIV when treating human papillomavirus (HPV) in patients with HIV. 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)

Treatment (cont.)

✓ RECOMMENDATIONS

- 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 and not use sinecatechins, podophyllin, or podofilox (podophyllotoxin) in pregnant individuals.
 - See the CDC guideline on Anogenital Warts.

Available Treatment Options for Anogenital Condyloma in Patients with HIV

Condyloma Type	Treatment	Comments
Anogenital Condyloma	<ul style="list-style-type: none"> • Cryotherapy • Podophyllin resin 10%-25% in a compound tincture of benzoin* • Surgical excision • Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%* <p>Patient self-administered treatments:</p> <ul style="list-style-type: none"> • Imiquimod 3.75% or 5% (may decrease likelihood of recurrences; may weaken condoms and vaginal diagrams)* • Podofilox 0.5% solution or gel* 	Extragenital warts, including warts on penis, groin, scrotum, vulva, perineum, external anus, and peri-anus

Adapted from CDC 2015.

*Imiquimod, podophyllin, and podofilox (podophyllotoxin) should not be used in pregnant individuals. 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 individuals with HIV safety and efficacy data do not exist.

Available Treatment Options for Anogenital Condyloma (cont.)

Condyloma Type	Treatment	Comments
Urethral Meatus Condyloma	<ul style="list-style-type: none"> • Cryotherapy with liquid nitrogen • Surgical excision 	--
Vaginal Condyloma	<ul style="list-style-type: none"> • Cryotherapy with liquid nitrogen • Surgical excision 	--
Cervical Condyloma	<ul style="list-style-type: none"> • Cryotherapy with liquid nitrogen • Surgical excision • TCA or BCA 80%-90% solution 	<ul style="list-style-type: none"> • Management of cervical warts should include consultation with a specialist • For those who have exophytic cervical warts, a biopsy evaluation to exclude high-grade SIL must be performed before treatment is initiated.

Adapted from CDC 2015.

Available Treatment Options for Anogenital Condyloma (cont.)

Condyloma Type	Treatment	Comments
Neovaginal Condyloma	<ul style="list-style-type: none"> • Cryotherapy • Imiquimod 3.75% or 5% (may decrease likelihood of recurrences; may weaken condoms and vaginal diaphragms)* • Podofilox 0.5% solution or gel* • Podophyllin resin 10%-25% in a compound tincture of benzoin* • Surgical excision • TCA or BCA 80%-90%* 	--

*Imiquimod, podophyllin, and podofilox (podophyllotoxin) should not be used in pregnant individuals. 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 individuals with HIV safety and efficacy data do not exist.

Sex Partner Exposure to HPV and HIV

✓ NEW YORK STATE REQUIREMENT

- 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 the NYSDOH and NYC Department of Health and Mental Hygiene.

✓ RECOMMENDATION

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

Sex Partner Exposure to HIV

→ 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.