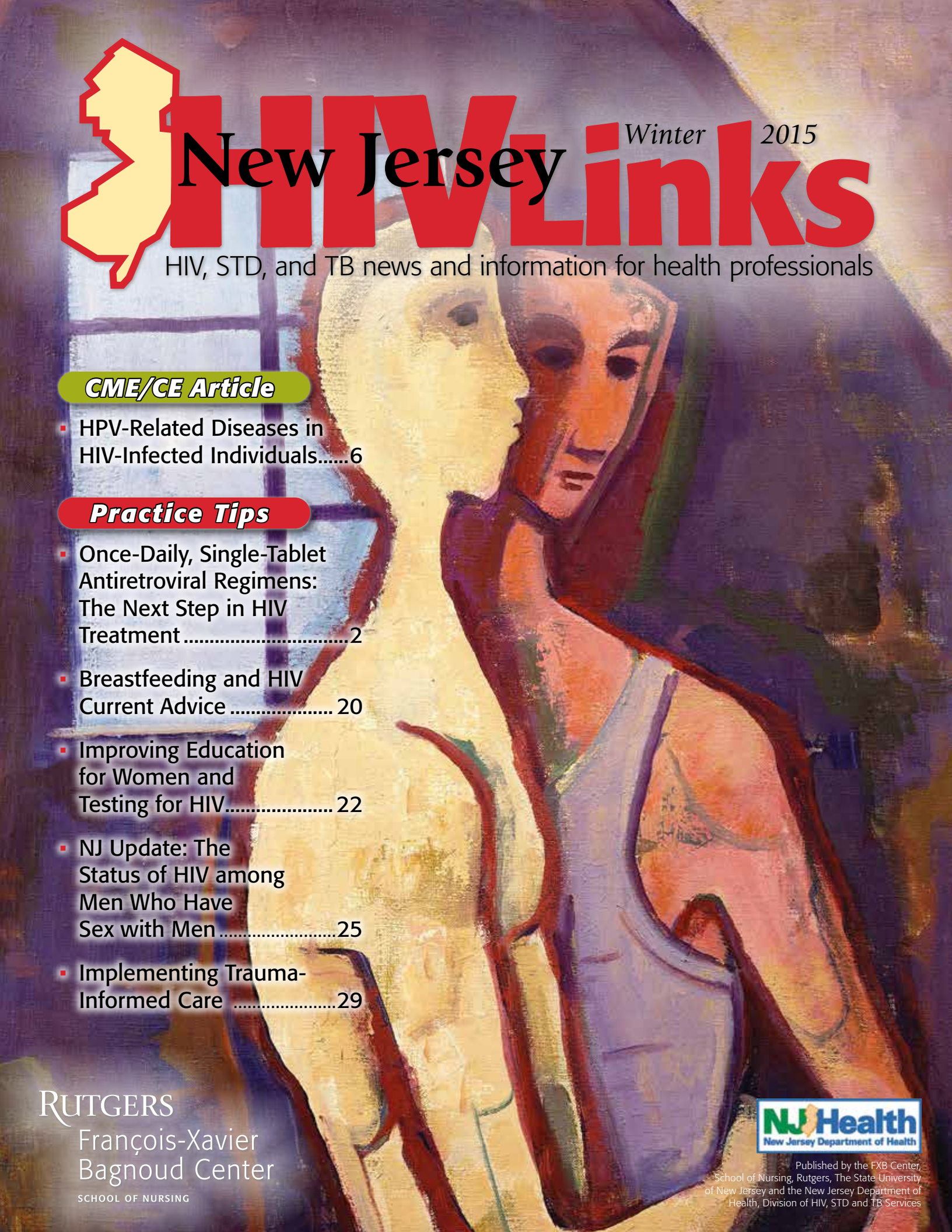

New Jersey HIV Links

Winter 2015

HIV, STD, and TB news and information for health professionals

CME/CE Article

Practice Tips

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Once-Daily, Single-Tablet Antiretroviral Regimens:

The Next Step in HIV Treatment

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Antiretroviral therapy is the cornerstone for management of human immunodeficiency virus (HIV) infection, helping to suppress HIV replication and restore immunologic function in infected patients while preventing HIV transmission to non-infected individuals. Over the past 3 decades, the armamentarium of antiretroviral agents available for HIV treatment has grown substantially, from the single drug zidovudine to over 25 drugs in 6 different antiretroviral classes.[1] In addition to new antiretroviral agents, co-formulated products containing combinations of commercially available antiretroviral agents have also been developed. These co-formulated products provide effective and well-tolerated HIV regimens with a reduced pill burden and more convenient dosing. There are currently 4 once-daily, single-tablet regimens (STRs) approved by the Food and Drug Administration (FDA) for treatment of HIV-1 infection. This article will review the properties of each STR and describe therapeutic considerations for each regimen based on recent guidelines for antiretroviral therapy published by the Department of Health and Human Services (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents.[1]

Efavirenz/Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC)

EFV/TDF/FTC (trade name Atripla®), the first commercially available once-daily STR product, was approved by the FDA in 2006. The product contains the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz along with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), tenofovir disoproxil fumarate and emtricitabine. EFV/TDF/FTC is indicated for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older.[2] Although the NNRTI-based regimen was previously considered a first-line regimen for treatment-naïve HIV-infected patients, it is now considered an alternative regimen in the latest DHHS guidelines published in April 2015 due to concerns regarding tolerability.[1]

EFV/TDF/FTC should be given orally once daily at bedtime on an empty stomach. The NRTI components require dosage adjustment in the setting of renal impairment; therefore, the single-tablet formulation of EFV/TDF/FTC cannot be used in patients with creatinine clearance less than 50 mL/min.[2] While most adverse events reported with EFV/TDF/FTC are mild to moderate in nature, the regimen is associated with higher rates of nervous system and psychiatric adverse effects compared to other HIV regimens.[3] Efavirenz is associated with a wide range of nervous system symptoms, ranging from dizziness to insomnia and/or abdominal dreams to hallucinations. While these side effects usually resolve within 2 to 4 weeks of therapy, they can be moderate to severe in nature and result in discontinuation of therapy.[2,4] Serious psychiatric symptoms, including suicidality, have also been reported with efavirenz-based regimens.[1,5] Virologic resistance is a concern as transmitted NNRTI resistance has been observed in treatment-naïve patients[6] and efavirenz has a low genetic barrier to developing resistance, especially in the setting of nonadherence.[1] Given the availability of other HIV regimens with more tolerable side effect profiles and higher barriers to resistance, EFV/TDF/FTC should only be used as an alternative regimen when first-line regimens are inappropriate.[1]

Efavirenz may cause fetal harm during the first trimester in pregnant women; therefore, women of childbearing potential should take measures to prevent pregnancy. All NRTIs carry a black box warning for lactic acidosis and severe hepatomegaly with steatosis. Tenofovir, both as monotherapy and in combination with emtricitabine, has activity against hepatitis B virus (HBV) and is used for the treatment of hepatitis B infection. In patients co-infected with HBV and HIV, discontinuation of tenofovir and emtricitabine may cause reactivation of HBV and severe acute exacerbations of hepatitis B infection. Tenofovir has also been associated with renal dysfunction and decreased bone mineral density; routine monitoring and preventive measures should be considered. Patients' medication regimens must be carefully reviewed for potential drug-drug interactions, particularly because efavirenz is a substrate and inducer of the cytochrome P450 (CYP) 3A enzyme.[2]

New Jersey HIVLinks Winter 2015
HIV, STD, and TB news and information for health professionals

Rilpivirine/Tenofovir Disoproxil Fumarate/ Emtricitabine (RPV/TDF/FTC)

RPV/TDF/FTC (trade name Complera®) is an STR containing the NNRTI rilpivirine and the NRTIs tenofovir disoproxil fumarate and emtricitabine. The product was FDA approved in 2011 for the treatment of HIV-1 infection in adult patients (18 years or older) with no previous antiretroviral treatment and pre-treatment HIV-1 RNA less than or equal to 100,000 copies/mL. Given concerns for virologic failure in patients with higher HIV viral loads, the DHHS guidelines categorize it as an alternative regimen for treatment-naïve individuals, but only those with baseline HIV RNA less than 100,000 copies/mL and CD4 cell count greater than 200 cells/mm^3.[1,7] RPV/TDF/FTC is also indicated for use in treatment-experienced patients with HIV viral load less than 50 copies/mL on antiretroviral therapy and intending to replace their current regimen with RPV/TDF/FTC.[7] Support for the conversion of existing antiretroviral therapy to RPV/TDF/FTC comes from a clinical trial in HIV-infected patients with at least 6 months of virologic suppression (HIV-1 RNA less than 50 copies/mL) while on a regimen of a ritonavir-boosted protease inhibitor and 2 NRTIs. These patients were receiving either their first or second antiretroviral regimen, had no history of virologic failure, and had no current or past history of resistance to any of the 3 components in the STR.[7] There is limited data evaluating therapy conversion to RPV/TDF/FTC in patients receiving other antiretroviral regimens or those with prior virologic failure and/or resistance.[8,9]

RPV/TDF/FTC should be taken once daily with food. The STR is not recommended in patients with estimated creatinine clearance less than 50 mL/min because both emtricitabine and tenofovir disoproxil fumarate require dosage adjustments for renal insufficiency. Compared to efavirenz, rilpivirine is associated with a lower incidence of treatment-related neuropsychiatric effects, as well as a lower rate of discontinuation due to these adverse effects.[7,10] RPF/TDF/FTC may also be a safer STR option for women of childbearing potential as rilpivirine did not demonstrate any embryonic or fetal toxicity in animal studies.[7] However, in clinical trials comparing RPV/TDF/FTC to efavirenz-based regimens, rilpivirine was associated with a higher rate of virologic failure (defined as HIV RNA greater than or equal to 50 copies/mL) after 96 weeks of treatment in the subsets of patients with baseline HIV-1 RNA exceeding 100,000 copies/mL and/or medication adherence of 95% and lower.[11] The favorable tolerability properties of RPV/TDF/FTC must be considered relative to the potential for virologic failure and antiretroviral resistance in patients with higher baseline viral loads. The E138K substitution is most commonly associated with rilpivirine resistance and confers cross-resistance to other available NNRTIs, including efavirenz and etravirine.[7]

Similar to all co-formulated products containing tenofovir disoproxil fumarate and emtricitabine, RPV/TDF/FTC has black box warnings for lactic acidosis, severe hepatomegaly with steatosis, and acute exacerbations of hepatitis B following discontinuation of the medication in co-infected individuals. Clinically significant drug-drug interactions exist between rilpivirine and acid suppressive therapy, including proton pump inhibitors, H_2-receptor antagonists, and antacids. Use of concomitant proton pump inhibitors (e.g., pantoprazole) is contraindicated because plasma concentrations of rilpivirine can be significantly reduced, leading to increased risk of virologic failure and antiretroviral resistance. RPV/TDF/FTC may be used with antacids and/or H_2-receptor antagonists if administration of each medication is separated per manufacturer recommendations. As a substrate of the CYP3A enzyme, serum concentration of rilpivirine will be affected by concomitant administration with medications that are inducers or inhibitors of this enzyme. Rilpivirine should also be used with caution in patients with conditions and/or medications that may prolong the QTc interval and increase the risk of Torsades de Pointes.[7]

Elvitegravir/Cobicistat/ Tenofovir Disoproxil Fumarate/Emtricitabine (ELV/c/TDF/FTC)

ELV/c/TDF/FTC (trade name Stribild®) was the first integrase inhibitor-based STR approved by the FDA in 2012 as initial treatment of HIV-1 infection in treatment-naïve adult patients (18 years or older), or as replacement of existing antiretroviral therapy in those with well-controlled HIV infection (HIV RNA less than 50 copies/mL) and no history of treatment failure or resistance to the product's individual components. The product contains the integrase inhibitor elvitegravir and the 2 NRTIs tenofovir disoproxil fumarate and emtricitabine.[12] The STR was also the first commercially available product to contain the CYP3A inhibitor cobicistat. ELV/c/TDF/FTC is considered a recommended regimen for previously untreated HIV-infected patients based on the recent DHHS guidelines.[1]

The recommended dosage regimen for ELV/c/TDF/FTC is 1 tablet once daily with food. The product should not be initiated in patients with estimated creatinine clearance less than 70 mL/min due to concerns of new onset or worsening renal impairment. In patients with preexisting renal insufficiency, ELV/c/TDF/FTC should be discontinued when the creatinine clearance is below 50 mL/min because renal dosage adjustments for the NTRI components are necessary. ELV/c/TDF/FTC is generally well-tolerated; the most common adverse drug reactions reported in clinical trials included nausea and diarrhea. Both cobicistat and tenofovir disoproxil fumarate may increase serum creatinine, although via different mechanisms. Cobicistat inhibits tubular secretion of creatinine without causing renal injury or affecting glomerular function, while tenofovir can be directly nephrotoxic and damage the proximal renal tubules, potentially causing acute renal insufficiency that can progress to renal failure.[12] With cobicistat, increases in serum creatinine usually range between 0 to 0.2 mg/dL from baseline, present within the first 1-2 weeks of therapy, and stabilize during con-

continued on next page

tinued therapy with no further elevations in creatinine.[12,13] Progressive increases in creatinine exceeding 0.4 mg/dL may require closer monitoring and evaluation for tenofovir-associated nephrotoxicity.[12] The previously described black box warnings and adverse effects associated with the NRTI backbone of tenofovir disoproxil fumarate and emtricitabine also apply to the STR regimen of ELV/c/TDF/FTC.

Cobicistat is used therapeutically to increase the serum concentration of elvitegravir via inhibition of the integrase inhibitor's metabolism by CYP3A. However, as an inhibitor of CYP3A, CYP2D6 and multiple transporters, cobicistat may also increase the concentrations of other medications metabolized via these pathways. Medications that induce or inhibit CYP3A or 2D6 may affect the serum concentrations of both elvitegravir and cobicistat.[12] Thorough review of a patient's medication regimen is needed to minimize the occurrence of clinically significant drug-drug interactions. The effectiveness and safety of ELV/c/TDF/FTC in pregnant women have not been evaluated in clinical studies, but none of the individual components have demonstrated teratogenicity in animal studies. Use of ELV/c/TDF/FTC may be considered if the potential benefit outweighs the potential risk to the fetus.[12]

Dolutegravir/Abacavir/ Lamivudine (DTG/ABC/3TC)

DTG/ABC/3TC (trade name Triumeq®) is the latest integrase inhibitor-based STR approved by the FDA in 2014. Unlike the other commercially available STRs, it is the only product to contain a NRTI backbone using abacavir and lamivudine. It is indicated for the treatment of HIV-1 infection in patients with no current or past history of resistance to integrase inhibitors or the NTRIs included in the formulation.[14] The DHHS guidelines list DTG/ABC/3TC as a first-line regimen for treatment-naïve, HIV-infected adult and adolescent patients.[1] Dolutegravir may have a higher barrier to resistance than the other integrase inhibitors, raltegravir and elvitegravir; therefore, it can be considered as a potential treatment option in treatment-experienced patients (including those with prior integrase inhibitor exposure) depending on the number and type of baseline integrase inhibitor substitutions present.[1,15] It is important to note that dolutegravir must be given twice daily in integrase inhibitor-experienced patients with certain resistance substitutions or clinically suspected integrase inhibitor resistance, which would require the use of additional pills outside of the DTG/ABC/3TC STR.[15]

DTG/ABC/3TC should be taken once daily with or without food. It is not recommended in patients with renal insufficiency (creatinine clearance less than 50 mL/min). Prior to initiating therapy, patients must be screened for the presence of the HLA-B*5701 allele, which has been linked to increased risk of abacavir-related hypersensitivity reactions.[14] While uncommon, signs and symptoms of the hypersensitivity reaction usually occur within the first days to weeks of treatment with abacavir and can potentially become life-threatening. Abacavir-containing regimens should be discontinued immediately and permanently when a hypersensitivity reaction is suspected; abacavir should never be re-introduced due to the risk of severe and potentially fatal reactions.[14,16] In general, DTG/ABC/3TC is very well-tolerated and the most common adverse effects reported are insomnia, headache and fatigue. There are multiple black box warnings for the NTRI components found in this product, including abacavir-associated hypersensitivity reactions, lactic acidosis and severe hepatomegaly with steatosis, and acute exacerbations of hepatitis B in HIV/HBV co-infected patients who discontinue lamivudine.[14] While lamivudine does have activity against HBV, the NRTI should not be used as a single agent for hepatitis B infection treatment due to the high risk of developing lamivudine-resistant HBV.[1]

Dolutegravir is metabolized by CYP3A and UGT1A; therefore, potential drug-drug interactions may exist with inducers and inhibitors of these enzymes. Dolutegravir dosage adjustments are recommended when given concomitantly with rifampin or carbamazepine. Other antiepileptics, such as phenytoin and phenobarbital, should be avoided with dolutegravir because of the lack of guidance on dosing recommendations. Medications containing polyvalent cations, including antacids, laxatives, and vitamins, can decrease serum concentrations of dolutegravir and should be separated from administration of dolutegravir as recommended by the manufacturer. There is limited data supporting the use of DTG/ABC/3TC in pregnant women, and DTG/ABC/3TC should only be used if the potential benefit outweighs the potential risks to the fetus.[14]

There are several factors to consider when selecting the most appropriate regimen for initiation of therapy in a treatment-naïve HIV-infected patient. In addition to guideline recommendations, patient-specific characteristics, such as baseline HIV viral load, HLA-B*5701 status, and co-morbid conditions, as well as a potential regimen's properties (dosing frequency, pill burden, resistance barrier, adverse effect profile, potential drug interactions) must be evaluated.[1,6] Clinical studies have demonstrated improved medication adherence, greater viral suppression, and better patient satisfaction with STRs compared to multi-tablet regimens.[17,18] While these clinical benefits make STRs very attractive treatment options for HIV, the limitations of these products must also be recognized. Patients requiring antiretroviral agents and/or doses that are not included in the fixed-dose STR formulations will need to take multiple tablets to complete their HIV regimens. The effectiveness and safety of many STR products have not been evaluated in certain patient populations, including pediatric patients and pregnant women. Additional studies and clinical experience with the STR products are needed. Furthermore, as additional antiretroviral agents and co-formulated products become available, HIV treatment will advance forward to provide more safe, effective, and convenient regimens for HIV-infected patients.

Commercially Available Once-Daily, Single-Tablet Regimens and Recommendations for Use

Product (Trade Name)	Components	Antiretroviral Classes	DHHS Recommendation
EFV/TDF/FTC (Atripla®) 	Efavirenz 600 mg Tenofovir disoproxil fumarate 300 mg Emtricitabine 200 mg	NNRTI + 2 NRTIs	Alternative Regimen
RPV/TDF/FTC (Complera®) 	Rilpivirine 25 mg Tenofovir disoproxil fumarate 300 mg Emtricitabine 200 mg	NNRTI + 2 NRTIs	Alternative Regimen (only when pre-treatment HIV RNA < 100,000 copies/mL and CD4 cell count > 200 cells/mm^3)
ELV/c/TDF/FTC (Stribild®) 	Elvitegravir 150 mg Cobicistat 150 mg Tenofovir disoproxil fumarate 300 mg Emtricitabine 200 mg	Integrase Inhibitor + CYP 3A Inhibitor + 2 NRTIs	Recommended Regimen
DTG/ABC/3TC (Triumeq®) 	Dolutegravir 50 mg Abacavir 600 mg Lamivudine 150 mg	Integrase Inhibitor + 2 NRTIs	Recommended Regimen

References

1 Panel on Antiretroviral Guidelines for Adults and Adolescents. "Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents." Department of Health and Human Services. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed September 26, 2015.

2 Atripla (efavirenz/emtricitabine/tenofovir disoproxil fumarate) package insert. Bristol-Myers Squibb and Gilead Sciences, LLC.; 2015 Jan.

3 Deeks ED, Perry CM. "Efavirenz/emtricitabine/tenofovir disoproxil fumarate single-tablet regimen (Atripla®): a review of its use in the management of HIV infection." *Drugs* 2010;70(17):2315-2338.

4 Sustiva (efavirenz) package insert. Princeton, NJ. Bristol-Myers Squibb Company; 2015 Mar.

5 Mollan KR, Smurzynski M, Eron JJ, et al. "Association between efavirenz as initial therapy for HIV-1 infection and increased risk for suicidal ideation or attempted or completed suicide: an analysis of trial data." *Ann Intern Med* 2014;161(1):1-10.

6 Huang HY, Dar ES, Sax PE, et al. "The prevalence of transmitted antiretroviral drug resistance in treatment-naïve patients and factors influencing first-line treatment regimen selection." *HIV Med* 2008;9(5):285-93.

7 Complera (emtricitabine, rilpivirine, tenofovir disoproxil fumarate) package insert. Foster City, CA. Gilead Sciences, Inc.; 2015 May.

8 Gantner P, Reinhart S, Partisani M, et al. "Switching to emtricitabine, tenofovir and rilpivirine as single tablet regimen in virologically suppressed HIV-1-infected patients: a cohort study." *HIV Med* 2015;16(2):132-6.

9 Mills AM, Cohen C, Dejesus E, et al. "Efficacy and safety 48 weeks after switching from efavirenz to rilpivirine using emtricitabine/tenofovir disoproxil fumarate-based single-tablet regimens." *HIV Clin Trials* 2013;14(5):216-23.

10 Mills AM, Antinori A, Clotet B, et al. "Neurological and psychiatric tolerability of rilpivirine (TMC278) vs. efavirenz in treatment-naïve, HIV-1-infected patients at 48 weeks." *HIV Med* 2013;14(7):391-400.

11 Cohen CJ, Molina JM, Cassetti I, et al. "Week 96 efficacy and safety of rilpivirine in treatment-naïve, HIV-1 patients in two Phase III randomized trials." *AIDS* 2013;27(6):939-50.

12 Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate) package insert. Foster City, CA. Gilead Sciences, Inc.; 2015 July.

13 German P, Liu HC, Szwarcberg J, et al. "Effect of cobicistat on glomerular filtration rate in subjects with normal and impaired renal function." *J Acquir Immune Defic Syndr* 2012;61(1):32-40.

14 Triumeq (abacavir, dolutegravir, and lamivudine) package insert. Research Triangle Park, NC. ViiV Healthcare; 2015 August.

15 Tivicay (dolutegravir) package insert. Research Triangle Park, NC. ViiV Healthcare; 2015 August.

16 Martin MA, Kroetz DL. "Abacavir pharmacogenetics – from initial reports to standard of care." *Pharmacotherapy* 2013;33(7):765-75.

17 Hodder SL, Mounzer K, Dejesus E, et al. "Patient-reported outcomes in virologically suppressed, HIV-1-infected subjects after switching to a simplified, single-tablet regimen of efavirenz, emtricitabine, and tenofovir DF." *AIDS Patient Care STDS* 2010;24(2):87-96.

18 Bangsberg DR, Ragland K, Monk A, et al. "A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people." *AIDS* 2010;24(18):2835-40.

CE Continuing Education

HPV-Related Diseases in HIV-Infected Individuals

Release Date: December 1, 2015 ▪ Expiration Date: November 30, 2017 ▪ Course Code: 18HH01

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Provided by François-Xavier Bagnoud Center, School of Nursing, Rutgers, The State University of New Jersey and the Center for Continuing and Outreach Education at Rutgers Biomedical and Health Sciences.

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STATEMENT OF NEED
HIV-infected individuals are at increased risk for HPV infection, persistent infection and anogenital cancers associated with HPV. In the post-HAART era, cervical cancer incidence among HIV-infected women in US has been unchanged, and anal cancer continues to increase. New treatment options are expanding for anal dysplasia and offer more hope of effective treatment. Though guidelines on routine anal cancer screening have not been established, it may be a reasonable cancer prevention strategy among those with HIV. Data on efficacy studies on prevention of HPV-associated cancers through prophylactic vaccination in HIV individuals are limited and ongoing.

This activity will assist health care providers with implementation of current recommendations for diagnosing and treating HPV infection.

TARGET AUDIENCE
This activity is designed for physicians, physician assistants, advanced practice nurses, nurses, dentists, health educators and other health care professionals in New Jersey who are involved in the care of people infected with HIV and their HIV non-infected partners.

METHOD OF PARTICIPATION
Participants should read the learning objectives, review the activity in its entirety, and then complete the self-assessment test, which consists of a series of multiple-choice questions. Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a letter of credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials. This activity may also be completed online at http://ccoe.rbhs.rutgers.edu/catalog/.

LEARNING OBJECTIVES
Upon completion of this activity, participants should be able to:

1. Describe the prevalence of HPV infection, intra-epithelial neoplasia, and other HPV-associated cancers among HIV-infected individuals.
2. Summarize national guidelines regarding routine cervical cytologic screening of HIV-infected women, and HPV vaccination use in all HIV-infected 11-26 year olds.
3. Discuss guidelines for treatment of cervical intraepithelial neoplasia, and treatment options for the anal intra-epithelial neoplasia in HIV-infected individuals.

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Jihad Slim, MD receives grant/research support from Gilead Sciences and ViiV Healthcare. He also is a member of the Speaker's Bureau for AbbVie, Bristol-Myers Squibb, Janssen Pharmaceuticals and Merck & Co.

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All other authors, planning committee members, peer reviewers and field testers have no relevant financial relationships to disclose.

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Trichloroacetic acid, imiquimod, cidofovir, or 5-fluorouracil topical therapy for small low-grade anal intraepithelial neoplasia lesions; ifrared coagulation or electrocautery/hyfrecation ablation therapy for high-grade or larger anal intraepithelial neoplasia lesions.

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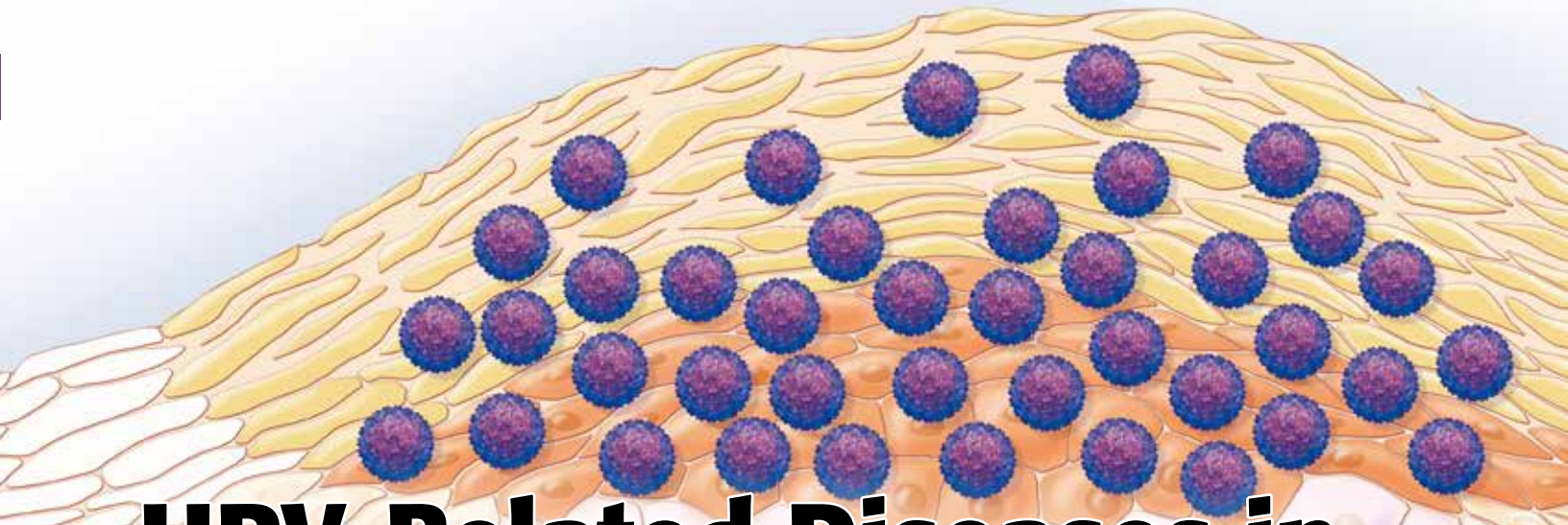

HPV-Related Diseases in HIV-Infected Individuals

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By the end of this activity, participants should be able to:

- Describe the prevalence of HPV infection, intra-epithelial neoplasia, and other HPV-associated cancers among HIV-infected individuals.
- Summarize national guidelines regarding routine cervical cytologic screening of HIV-infected women, and HPV vaccination use in all HIV-infected 11-26 year olds.
- Identify guidelines for treatment of cervical intra-epithelial neoplasia, and treatment options for the anal intraepithelial neoplasia in HIV-infected individuals.

Artist's illustration of a genital wart. The human papillomavirus (HPV) is responsible for the wart. The blue cells represent the immune cells. Credit: JACOPIN / BSIP / BSIP

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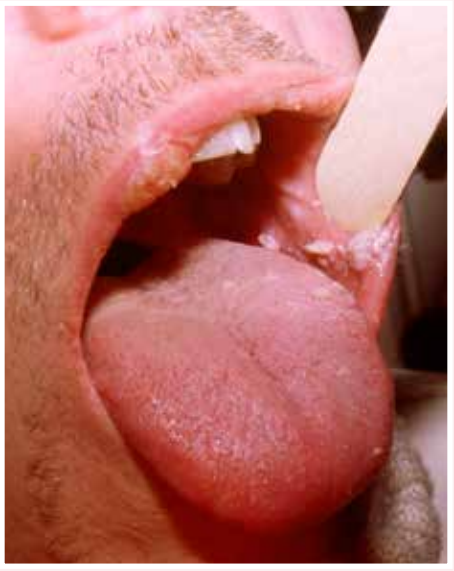
Introduction

Infection with human papillomavirus (HPV), a DNA virus, is the most common sexually transmitted infection in the United States (US).[1] The clinical spectrum of diseases associated with HPV ranges from anogenital and oral warts, anogenital cancer precursors (cervical, anal, vulvar and vaginal squamous intraepithelial neoplasia), and squamous cell cancers of the anogenital tract and oropharynx. HPV causes essentially all cervical cancers, and is linked to about 90% of anal cancers, 60% of oropharyngeal (excluding laryngeal), 35% of penile, 60% of vaginal, and 50% of vulvar cancers in the US.[2] Of these, rates of anal and oropharyngeal cancers continue to rise.[3-4] It is well documented that individuals with HIV/AIDS have higher prevalence of oral and anogenital HPV infection, anogenital cancer and oropharyngeal cancers compared to the general population.[5-7] In this review, we discuss the epidemiology, pathogenesis, and management of HPV-related diseases in HIV-infected individuals, underscoring the need to optimize screening and treatment of HPV-associated precancerous lesions and prevention of HPV-associated cancers among persons living with HIV.



Condyloma. Condyloma acuminatum, wartlike growths on the mucosa of the mouth caused by human papilloma virus (HPV). Credit: Aubert / Phanie

HPV infection in the General Population

It is estimated that up to 80% of sexually active adults will acquire a genital tract HPV infection before the age of 50.[8] Although the incidence of HPV infection is high, the majority of infections, including those caused by high-risk types, are transient and asymptomatic, and up to 90% clear and become undetectable by HPV DNA PCR within 2 years.[9-11] In women, genital HPV infection is most common in young sexually active women, with the highest prevalence among females aged 20-24 years old (45% in the National Health and Nutrition Examination Survey [NHANES]).[12] Among men who have sex with men (MSM), HPV prevalence typically remains high (50-60%) and is constant throughout life, likely from acquisition of other HPV types from new sexual partners over time.[13] Oral HPV infection is much less common than genital infection, but time to clearance of infection appears to be similar.[14-15]

Other than host factors, the major risk factor for persistence and progression to a cancer precursor lesion is HPV type. Twelve HPV types are currently classified as high-risk oncogenic types, and include predominantly types 16 and 18, and less frequently types 31, 33, 35, 39, 45, 51, 52, 56, and 68. HPV 16 and 18 account for approximately 50% and 20% of all cervical cancers in the United States, respectively. Low-risk HPV types (mostly types 6 and 11) are responsible for 90% of benign genital warts or condyloma accuminata.[26] High-risk HPV types have a predilection for mucous membrane infection whereas low-risk types have a predilection for cutaneous epithelium and are found in plantar and nongenital warts.

The oncogenic potential of HPV is attributed to 2 oncoproteins, E6 and E7, expressed during the early stages of the HPV lifecycle, which bind to and inactivate host-tumor suppressor proteins p53 and pRB. Both E6 and E7 are consistently expressed in HPV-carrying anogenital tumors.[17-18]

Cervical HPV infection progresses with increasing dysplasia before invasive cancer develops, and other anogenital HPV infections are presumed to do so as well. Cellular changes associated with cervical or anal HPV infection and dysplasia that are seen on Papanicolaou (Pap) smears are currently classified as squamous intraepithelial lesions (SIL). In cervical and anal HPV infection, low-grade SIL corresponds to histologic diagnoses of flat condylomas and cervical intraepithelial neoplasia (CIN) 1 or anal intraepithelial neoplasia (AIN) 1 whereas high-grade SIL corresponds to the histologic diagnoses of CIN/AIN 2 and 3.[19] In general, low-grade SIL usually does not progress to invasive disease, and often regresses without treatment, whereas high-grade SIL is considered a cancer precursor. High-risk oncogenic types of HPV increase in frequency with severity of histologic lesion. The development of initial HPV infection to CIN 2-3 typically occurs in less than 5 years, whereas progression of CIN 2-3 to invasive cancer may take several decades.[20] The lag between HPV infection and development of invasive cancer allows for routine Pap screening to detect dysplastic changes before significant invasion occurs. Anal cancer progression is assumed to occur similarly to cervical cancer, though data is limited showing direct progression of AIN 2-3 to invasive anal cancer.

HPV-associated cervical and anal cancers typically develop at sites of squamous metaplasia. The transition zones at the cervical and anorectal squamous columnar junction are vulnerable to high-risk HPV infection,[21] and are the areas targeted for cytologic cervical and anal cancer screening.

HPV Infection in HIV-Infected Individuals

HPV is transmitted primarily by close contact, usually through sexual contact. HIV-induced immunosuppression contributes to the greater prevalence and persistence of HPV infection and progressive disease among those infected with HIV. HIV-infected individuals have higher HPV viral loads, more frequent infections with concomitant multiple

It is hoped that universal HPV vaccination among adolescent males and females will reduce the overall burden of HPV disease.

Credit: Ton Koene / age fotostock

HPV oncogenic types, and less HPV clearance than HIV-uninfected individuals.[22-27] Considerable data demonstrate that HPV infection and cancer risk are directly related to degree of immunosuppression, as reflected by CD4+ cell count. The degree of immunosuppression also predicts the severity of HPV disease (e.g., extent of lesions and multisite involvement)[26,28-33] and response to treatment.[34-36] Additionally, HIV itself promotes carcinogenesis at the molecular level. It has been shown that HIV-encoded tat protein may enhance expression of the HPV E6 and E7 oncogene proteins.[37] HPV and HIV also interact in a complex bidirectional manner, and several studies have shown that HPV infection, like other sexually transmitted diseases, may be a risk factor for HIV acquisition.[38-40]

Cervical HPV Infection in HIV-Infected Women

Epidemiology

The risk of cervical cancer among HIV-infected women is 5 to 8-fold the risk for HIV-uninfected women,[5-6,41-43] and invasive cervical cancer is a Centers for Disease Control and Prevention (CDC) AIDS defining illness.[44] It is well-established that HPV infection and high-grade CIN are significantly more prevalent among HIV-infected women than HIV-uninfected women.[22-26,31-33,45-46] In the Women's Interagency HIV Study (WIHS), the largest study on cervical-vaginal HPV infection, presence of HPV DNA was 2 times greater among HIV-infected women than HIV-uninfected women, with the highest prevalence of HPV DNA among infected women with a CD4+ count less than 200 cells/μL.[31] The HIV Epidemiologic Research Study (HERS) also found that HPV prevalence was not only greater (64% vs 28%), but HPV persistence was nearly double in those with a CD4+ count less than 200 cells/uL.[33] Ellerbrock et al. found that HIV-infected women were 4.5-fold more likely than HIV-uninfected women to develop CIN at 54 months of follow-up.[24]

Screening for Cervical Neoplasia

Since HPV dysplasia is far greater among HIV-infected women, screening HIV-infected women for cervical cancer is critical. Cervical cytologic screening permits

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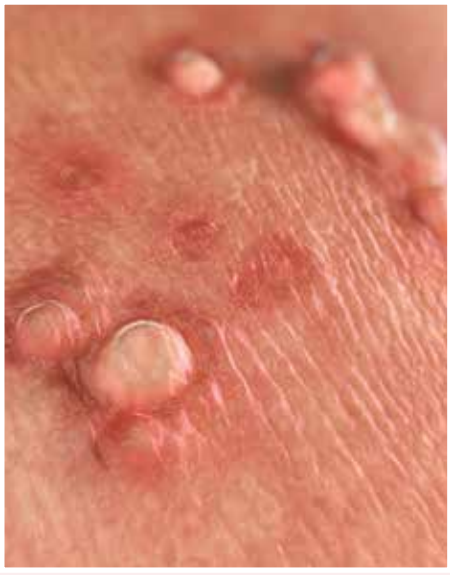
diagnosis at precursor stages often prior to invasive cervical cancer. Pap testing alone or co-testing with Pap and HPV DNA are both acceptable screening methods in HIV-infected women, though consensus guidelines vary on follow-up screening intervals. If screening with Pap tests alone, the American College of Obstetricians and Gynecologists (ACOG) and the US Preventive Services Task Force recommend that HIV-infected women undergo cervical Pap testing at initial evaluation, 6 months after baseline, and annually, as long as both Pap results are normal.[47-48] The CDC and Department of Health and Human Services (DHHS) recently updated follow-up intervals for screening in HIV-infected women. If the results of 3 consecutive Pap smears are normal, the CDC/DHHS recommend that HIV-infected women 30 years and older be followed with Pap smear testing every 3 years throughout life. HIV-infected women who are younger than 30 years old should have Pap smear testing beginning within 1 year of onset of sexual activity but no later than 21 years of age regardless of sexual history.[49]

Co-testing with HPV DNA and HPV genotypic testing in combination with Pap smear testing may also be done at baseline in women 30 years and older, and is now the preferred screening method in this group[50-51] Co-testing is not recommended in women younger than 30 years old in both HIV-infected and HIV-uninfected women because of high HPV prevalence in this age group. As per the CDC/DHHS guidelines, HIV-infected women who co-test negative for both PAP and HPV test may have their next cervical screening in 3 years (as opposed to 5 years in HIV-uninfected women). HIV-infected women with a normal PAP but positive HPV test for low-risk types on HPV genotype test may be followed with repeat co-testing in 1 year. Those with abnormal cytology or positive HPV testing at 1 year follow-up are recommended to have colposcopy. Women with high-risk HPV 16 or 18 identified on HPV genotype should also be referred for colposcopy.[49] Women with cytologic results showing atypical squamous cells of undetermined significance (ASCUS) and positive HPV testing or higher grade of dysplasia (low-grade or high-grade squamous intraepithelial lesions), should be referred for colposcopy. Women with cytologic results showing ASCUS but without HPV testing available, may also have repeat cervical cytology performed in 6-12 months.[52]

Because of the high risk of multifocal disease in HIV-infected women, colposcopic examination should include examination of the vagina and vulva as well as the cervix. Initial and follow-up examinations should include a thorough visual inspection of the anus, vulva, and vagina, as well as the cervix to assess for visible signs of warts, intraepithelial neoplasia or invasive cancer. Biopsy or referral is indicated when inspection or palpation identifies lesions suspicious for intraepithelial neoplasia or cancer.



Close up view of warts. Warts are caused by the human papilloma virus or HPV.
Credit: Science Picture Co/Science Picture Co

Treatment of Cervical Neoplasia

Primary treatment of CIN in HIV-infected women is generally similar to the management in non-infected women. Treatment for CIN 2/3 in the developed world is primarily through excision through loop electrosurgical excision procedure (LEEP) in which a cone of cervical tissue containing the lesion is removed using an electric wire. CIN1/2 in adolescents and young women desiring future fertility is frequently managed conservatively with increased surveillance rather than LEEP. In developing countries where LEEP is not as readily available, ablation through cryotherapy is often used.[52] For CIN 2/3, topical 5-fluorouracil (5-FU) (2 gm of 5% cream biweekly), is recommended as adjunctive therapy to excision or ablation procedures.[53]

HIV-infected women with CIN should be counseled that recurrence is more frequent than in the general population. Recurrence rates have been shown to be as high as 50% at 1 year, and 60% with longer follow-up in some studies.[35-36,46, 54-55] ACOG recommends close follow-up with cervical cytology and colposcopy at 6 month intervals over the first year after treatment.[47]

While studies on the effect of combination antiretroviral therapy (cART) on CIN have yielded conflicting results, recent data suggest that cART may be associated with regression of CIN.[56-63] The WIHS Study found a 12.5% per year overall rate of regression of incident CIN post-cART among HIV-infected women receiving cART. Among 312 women, 45% had lesions that regressed to normal cytology with a median time of regression of 2.7 years. Higher rates of regression were observed in women with higher Cd4+ counts and low-grade incident CIN.[56]

Treatment of invasive cervical cancer is similar in HIV-infected and HIV-uninfected women and should follow National Comprehensive Cancer Network guidelines.[64]

Anal HPV Infection in HIV-Infected Individuals

Epidemiology

While anal cancer incidence is increasing in the general population, it is substantially higher in the HIV-infected population,[3-5] with the highest rates among HIV-infected MSM. In the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) study which combined data from 13 cohort studies, HIV-infected MSM experienced the greatest risk for anal cancer with incidence rates >80 higher than in HIV-uninfected indi-

viduals (131/100,000 person years). Anal cancer incidence rates were also significantly higher among HIV-infected other men (46/100,000) and women (30/100,000) compared to the general population (2/100,000).[65] In a meta-analysis, HIV-infected men had higher prevalence of anal canal HPV of any type (93 vs. 64%), high-risk HPV types (74% vs. 37%), and anal SIL (57% vs 19%) compared to uninfected men. The risk of progression from high-grade SIL to anal cancer among HIV-infected MSM has been estimated to be 1/377 per year.[66] In women, where the prevalence of anal HPV is actually higher than the prevalence of cervical HPV, HIV-infected women have a 7-fold higher incidence of anal cancer than HIV-uninfected women.[5,22,31] The introduction of cART has not altered the prevalence of anal SIL, and may be associated with an increased incidence of progression to anal cancer due to the longer life expectancy of HIV-infected individuals.[65,67-75]

Screening for Anal Neoplasia

National guidelines on anal cancer screening are currently lacking. Given the high risk of invasive anal cancer among HIV-infected men and women, some experts have adopted routine anal screening as a standard intervention in HIV primary care. The approach of anal cancer screening is similar to cervical cancer testing with the goal of identifying precancerous areas that can be ablated to prevent invasive anal cancer. Like cervical screening, anal cytologic examination is the first step, followed by confirmation of the disease stage by high resolution anoscopy and biopsy. Screening is advised, however, only if there is an infrastructure in place for ready access to high resolution anoscopy and treatment.

Screening for AIN should begin with documentation of any history of anogenital warts, anal receptive intercourse, prior cervical or anal squamous intraepithelial lesions, and other sexually transmitted diseases. Symptoms, such as discharge, pain, bleeding, itching, or spotting after intercourse, should be elicited from patients.

Anal cytologic screening with Pap smear may be easily performed, using a Dacron swab moistened with ordinary tap water with the patient in fetal position. The swab should be inserted as far into the anal canal as far as it will comfortably go, to a maximum of 5 cm, and withdrawn slowly while rotated in a spiral fashion. The swab is then swirled in a liquid cytology vial to release cells into the liquid (liquid should change from clear to slightly cloudy). Anal Pap smear should be followed by a digital rectal exam to palpate for nodules, condylomas or abnormal anal skin (e.g., rough or irregular). A thorough examination of the perianal area and genitalia should be performed. High-grade AIN typically appears as grayish, hyperpigmented patches on the perianal area. Any abnormalities on cytology (ASCUS, low-grade, or high-grade dysplasia) should prompt further evaluation with high resolution anoscopy and biopsy.[49,76]

Similar to cervical colposcopy, high resolution anoscopy identifies possible high-grade AIN and condylomas. A lubricated anoscope is inserted into the anus, and a cotton swab wrapped in gauze and soaked in 3% acetic acid is inserted through the anoscope. The acetic acid reacts with the skin and allows visualization of dysplastic epithelium by turning it white, referred to as "acetowhite". Areas suspicious for high-grade AIN, such as those with acetowhitening, or areas showing abnormal vascular patterns, or changes induced by applying Lugol's iodine (dysplastic lesions appear mustard or light yellow instead of mahogany color) should be biopsied.[76]

An anal screening protocol for HIV-infected patients has been proposed by Chin-Hong and Palefsky. They recommend that HIV-infected patients with normal anal cytologic results be screened with an anal Pap annually. Those with any abnormal anal cytologic results (ASCUS or higher grade of dysplasia) should undergo high resolution anoscopy with biopsy. Patients' whose high resolution anoscopy with biopsy show either no lesion or AIN1 (low-grade SIL) may be followed-up every 6 months, whereas those with high-grade SIL or severe dysplasia or carcinoma in situ should be treated and have repeat anoscopy every 4-6 months.[76]

Treatment of Anal Neoplasia

While optimal approach to treatment of AIN has not yet been defined, many experts treat patients with high-grade AIN. Treatment for those with low-grade AIN is optional but may reduce risk of further enlargement or progression to high-grade AIN or reduce AIN-associated symptoms and patient anxiety. The choice of treatment depends on the size of the lesion and the location of the lesion (perianal vs intra-anal). Although treatment with a variety of approaches may result in complete regression, recurrences are frequent with all treatment modalities in HIV-infected individuals, and often require multiple treatments and close post-treatment follow-up.[77-79] The quality of the high resolution anoscopy in detecting and treating all high-grade lesions is key to minimizing disease recurrence.

New treatment options are emerging for the treatment of high-grade AIN. Ablative therapy with infrared coagulation (applying 1.5 second pulse of irradiation in the infrared red directly to dysplastic skin to a depth of approximately 1.5 mm) or electrocautery/hyfrecation offers office-based treatment for high-grade SIL that is effective and well-tolerated.[77,80] For individual intra-anal lesions that are small and that represent less than 50% of the circumference of the anal transformation zone, therapy is suggested with either ablation or provider-applied 80% trichloroacetic acid (particularly if lesions are less than 1 cm^2 at the base). Therapy options for larger intra-anal lesions are either ablation with infrared coagulation or electrocautery/hyfrecation. Alternatively, patient-applied topical 3% or 5% imiquimod (applied 3 times per week) or 5% fluorouracil (4 cycles applied twice daily for 5 days followed by 9 days off) may be used in a staged, step-wise manner to reduce lesion size followed by ablation methods.[79]

None of the current approaches for high-grade AIN are FDA approved, and data on efficacy to reduce or clear high-grade AIN

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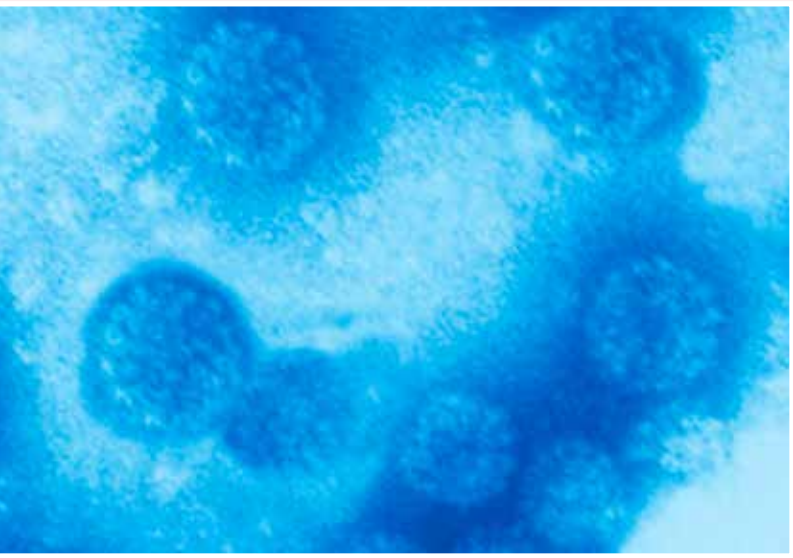


Human papillomavirus, HPV © Estiot Veronique/Oredia

are very limited. In the only randomized trial comparing treatment modalities in men with AIN treated with imiquimod, topical fluorouracil or electrocautery, complete response rates were 24%, 17%, and 39%, respectively. Recurrences were common, with cumulative recurrence rates of 71%, 58%, and 68% respectively by 72 weeks.[81] Ablative therapies are generally well-tolerated and possible complications include mild to moderate post-procedural pain and bleeding for up to 2 weeks; rare complications (<1%) include infection of the treated area and severe bleeding.[77,80-81] A phase III National Institutes of Health trial by the AIDS Malignancy Consortium, the ANCHOR trial, is currently underway to assess not only effectiveness of treatment for high-grade AIN but also whether topical or ablative treatment for high-grade AIN compared to active monitoring through regular examinations is ultimately effective in preventing subsequent development of anal cancer.[82]

The most commonly used treatment for invasive anal cancer is combination radiation and chemotherapy. Treatment is similar in HIV-infected and HIV-uninfected individuals.

Anogenital Warts in HIV-Infected Individuals

Anogenital warts (condyloma accuminata) are more common, severe, and recalcitrant to treatment in HIV-infected individuals compared to non-infected persons.[83-86] Diagnosis of genital warts can usually be made by visual inspection of the affected area, and typically appear as flat, papular, or pedunculated lesions that are skin-colored or pink. Most warts are asymptomatic, but may cause pruritis and discomfort. Advanced immunosuppression is associated with more extensive disease, and depending on size and location of lesions, may cause dyspareunia or dyschezia. The extent of involvement should be determined by further evaluation with high resolution anoscopy, colposcopy and/or vaginal speculum examination as appropriate, and typically appear acetowhite with application of 5% acetic acid. Since high-grade squamous intraepithelial lesions and carcinomas are more common in HIV-infected persons and may arise in or resemble genital warts, biopsy is indicated to confirm diagnosis in suspected lesions. Biopsy should be done also if diagnosis is uncertain, if lesions do not respond to standard therapy, or if lesions are atypical, pigmented, indurated, fixed, bleeding, or ulcerated.[49]

Similar to the uninfected population, small condylomas may be treated with local topical treatment (patient applied podophyllotoxin cycles of 3 days on and 4 days off) or imiquimod or provider-applied liquid nitrogen or trichloroacetic acid), local ablation or surgical excision while more extensive lesions can be approached medically with the application of imiquimod or 5-fluorouracil or surgical intervention.[49] Some studies have found a regression of anogenital warts with cART,[87] whereas other studies have reported increased rates of oral warts following cART initiation.[88-89]

Other HPV-Associated Cancers in HIV-Infected Individuals

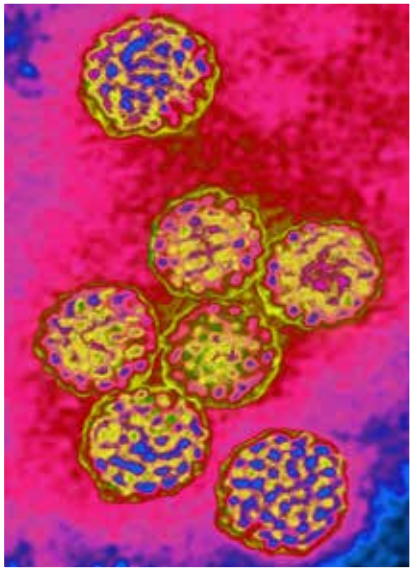
As with other HPV-associated cancers, persons with HIV/AIDS have higher incidence of vulva, vaginal, penile, and oropharyngeal cancers compared to the general population. AIDS cancer registry match studies have found that the risk for oropharyngeal cancer is 1.5-4 fold higher among HIV-infected individuals compared with non-infected persons.[6-7] Chaturvedi et al. found statistically significant increased incidence ratios for cancer of the penis, vagina or vulva, and oropharyngeal cancer among persons with AIDS.[7] Unlike cervical and anal cancers, only a subset of these cancers is associated with HPV. HPV-associated oropharyngeal cancers are primarily found in the oropharynx and base of the tongue and tonsil, and are primarily associated with sexual risk factors as opposed to alcohol and tobacco use, traditionally associated with non-HPV associated oropharyngeal cancers. There are currently no clinically available screening tests for detection of oropharyngeal HPV infection.[90] Penile, vulvar or vaginal neoplasia are recognized through visual inspection, including high resolution anoscopy, colposcopy, and biopsy as needed.

Treatment of low-grade vulvar and vaginal dysplasia can be observed or managed as for anogenital warts. Treatment modalities for vulvar intraneoplasia include local excision, laser vaporization, ablation and imiquimod therapy. Treatment options for vaginal intraneoplasia include topical 5-FU, laser vaporization with CO2 laser, and excision. For cancers of the penis and oropharynx, treatment is similar in HIV-infected and HIV-uninfected men and women. Current data suggest a more favorable prognosis for HPV-associated oropharyngeal cancers compared with non-HPV associated oropharyngeal cancers.[49]

HPV Vaccination in HIV-Infected Individuals

Bi-valent (Ceravix®), quadrivalent (Gardasil®), and 9-valent (Gardasil 9®) HPV vaccines are licensed for use in the US and

available for the prevention of genital HPV infection in men and women.[91-93] Bi-valent HPV vaccine is effective against HPV types 16 and 18. Quadrivalent vaccine targets HPV types 6, 11, 16, and 18, and 9-valent vaccine targets types 6, 11, 16, 18 as well as 31, 33, 45, 52, and 58. The vaccines are composed of type-specific HPV L1 protein, the major capsid protein of HPV. In large clinical trials, bivalent, quadrivalent and 9-valent HPV vaccines have been shown to be nearly 100% efficacious in preventing cervical, vulvar and vaginal intraepithelial neoplasia, and genital warts in healthy women without prior HPV infection[94-98] and 78% and 86% effective, respectively, in reducing anal intraepithelial neoplasia and persistent HPV vaccine types among healthy young men.[99]



Human papilloma virus (HPV). Image produced using high-dynamic-range imaging (HDRI) from an image taken with transmission electron microscopy. Viral diameter around 55 nm. Credit: Cavallini James/BSI /BSIP

However, efficacy of HPV vaccination in the HIV-infected population has not been demonstrated and is currently being evaluated in major clinical trials. Although studies have found bivalent and quadrivalent HPV vaccines to be well tolerated and immunogenic in HIV-infected persons,[100-103] it is possible that immunosuppression may attenuate development of protective titers of HPV antibodies. Some studies have found lower geometric mean titers against HPV virus vaccine types among those infected with HIV compared to those uninfected.[100,102] Additionally since HPV vaccines are most effective when given to recipients without prior HPV infection, vaccine efficacy might be reduced among HIV-infected individuals who are less likely to be HPV-naïve to vaccine types. Ideally HPV vaccine should be given prior to HPV acquisition and sexual debut.

At the current time, CDC recommends routine HPV vaccination for HIV-infected individuals age 11 through 26 years who have not been previously vaccinated.[104] The quadrivalent vaccine and 9-valent vaccines are administered in 3 doses at time zero, and at 2 and 6 months following initial dose. The bivalent vaccine is administered in 3 doses at time zero and at 1 and 6 months following initial dose.[104]

Patients should also be counseled on use of male or female condoms (made of latex or polyurethane) to prevent transmission or acquisition of HPV infection and other sexually transmitted diseases. Studies have shown consistent condom use has been associated with a 70% lower incidence of oncogenic HPV infection among women[105] and a reduced risk of genital warts and CIN in women.[106]

Conclusions

The burden of HPV-related disease is high among HIV-infected individuals and carries increased risk for cervical and other anogenital tract and oral-pharyngeal cancers compared to HIV-uninfected persons. While routine cervical cytologic screening has significantly reduced the incidence of cervical cancer in the US, rates of anal cancer continue to rise in the US in the general and HIV-infected population. Significant gaps still remain in the management of anal dysplasia and in primary HPV prevention in persons with HIV infection. Treatment data on anal dysplasia are limited and more effective treatments are needed. Further studies to determine the effectiveness of routine anal cancer screening, and whether screening will be beneficial in earlier cancer detection and reduce the incidence of anal cancer are also needed. Until such consensus guidelines are established, we should develop the necessary infrastructure to make HRA readily available to perform routine anal cytologic screening in HIV-infected individuals and offer treatment for anal dysplasia. HIV-infected patients should be counseled and educated about HPV and their increased risk for HPV-associated cancers. Providers should adhere to cervical cancer screening and treatment guidelines. While vaccine efficacy among HIV-infected individuals is still being evaluated, HPV vaccine should be given to eligible patients and may potentially prevent vaccine-type HPV-associated anogenital precancers, cancers, and condylomas. It is hoped that universal HPV vaccination among adolescent males and females will reduce the overall burden of HPV disease.

References

1. Satterwhite CL, Torrone E, Meites E, Dunne EF, Mahajan R, Ocfemia MD et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. *Sex Transm Dis.* 2013; 40(3):187-193.
2. Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. *Cancer.* 2008;113(10suppl):3036-3046.
3. Jemal A, Simard EP, Dorell C, et al. Annual report to the nation on the future" since it is implied].status of cancer, 1975-2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. *J Natl Cancer Inst* 2013;105:175-201.
4. Kurdgelashvili G, Dores GM, Srour SA, Chaturvedi AK, Huycke MM, Devesa SS. Incidence of potentially human papillomavirus-related neoplasms in the United States, 1978to 2007. *Cancer* 2013;119:2291-2299.
5. Frisch M, Biggar RJ, Goedert JJ. Human papillomavirus-associated cancers in patients with human immunodeficiency virus infection and acquired immunodeficiency syndrome. J Natl Cancer Inst. 2000;92(18):1500-1510.
6. Clifford GM, Polesel J, Rickenbach M et al. Cancer risk in the Swiss HIV cohort study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. *J Natl Cancer Inst* 2005;97:425-432.
7. Chaturvedi AK, Madeleine MM, Biggar RJ, Engels EA. Risk of human papillomavirus-associated cancers among persons with AIDS. *J Natl Cancer Inst* 2009;101:1120-1130.
8. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(RR-03):1.

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9. Ho GYF, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med* 1998;338:423-428.
10. Franco EL, Villa LL, Sobrinho JP, Prado JM, Rosseau M-C, Desy M, Rohan TE. Epidemiology of acquisition and clearance of cervical human papillomavirus infection in women from a high-risk area for cervical cancer. *J Infect Dis.*1999;180(5):1415-1423.
11. Molan M, van den Brule A, Plummer M, Weiderpass, E, Posso H, Arslan A et al. Determinants of clearance of human papillomavirus infections in Colombian women with normal cytology: a population-based, 5 year follow-up study. *Am J Epidemiol* 2003;158:486-494.
12. Markowitz LE, Sternberg M, Dunne EF, McQuillan G, Unger ER. Seroprevalence of human papillomavirus types 6,11, 16, and 18 in the United States: National Health and Nutrition Examination Survey 2003-2004. *J Infect Dis* 2009;200:1059-1067.
13. Chin-Hong PV, Vittinghoff E, Cranston RD, Buchbinder S, Cohen D, Colfax G et al. Age-specific prevalence of anal human papillomavirus infection in HIV-negative sexually active men who have sex with men: the EXPLORE study. *J Infect Dis* 2004;190:2070-2076.
14. Gillison ML, Broutian T, Pickard RK, et al. Prevalence of oral HPV infection in the United States, 2009-2010. *JAMA* 2012;307:693.
15. Kreimer AR, Pierce Campbell CM, Lin HY et al. Incidence and clearance of oral human papillomavirus infection in men: the HIM cohort study. *Lancet* 2013;382:877.
16. Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med* 2003;348:518-527.
17. Doorbar J, Quint W, Banks L, Bravo IG, Stoler M, Broker TR et al. The biology and life-cycle of human papillomaviruses. *Vaccine* 2012;30 Suppl5:F55-70.
18. Konopnicki D, DeWit S, Clumeck N. HPV and HIV coinfection: a complex interaction resulting in epidemiological, clinical and therapeutic implications. *Future Virology.* 2013;8(9):903-915.
19. Kurman R, Solomon D. The Bethedsda system for reporting cervical/vaginal cytologic diagnoses: definitions, criteria and explanatory notes for terminology and specimen adequacy. *New York: Springer Verlag;*1994.
20. Pinto A, Crum C. Natural history of cervical neoplasia: defining progression and its consequence. *Clin Obstet Gynecol* 2000;43(2):352-362.
21. Veldhuijzen NJ, Snijders PJF, Reiss P, Meijer CJLM, can de Wijgert J. Factors affecting transmission of mucosal human papillomavirus. *Lancet Infect Dis* 2010;10:862-874.
22. Sun X-W, Kuhn L, Ellerbrock TV Chaisson MA, Bush TJ, Wright TC. Human papillomavirus infection in women infected with the human immunodeficiency virus. *N Eng J Med* 1997;337:1343-1349.
23. Minkoff H, Feldman J, DeHovitz J, Landesman S, Burk R. A longitudinal study of human papillomavirus carriage in human immunodeficiency virus-infected and human immunodeficiency virus-uninfected women. *Am J Obstet Gynecol* 1998;178:982-986.
24. Ellerbrock TV, Chaisson MA, Bush TJ, Sun X-W, Sawo D, Brudney K, Wright TC. Incidence of cervical squamous intraepithelial lesions in HIV-infected women. *JAMA* 2000;283(8):1031-1037.
25. Moscicki A-B, Elenberg JH, Crowle-Nowick P, Darragh TM, Xu J, Fahrat S. Risk of high-grade squamous intraepithelial lesion in HIV-infected adolescents, *J Infect Dis.* 2004;190;1413-1421.
26. Strickler HD, Burk RD, Fazzari M, Anastos K, Minkoff H, Massad S et al. Natural history and possible reactivation of human papillomavirus in human immunodeficiency virus-positive women. *J Nat cancer Instit* 2005;97(8): 577-586.
27. Clifford GM, Goncalves AG, Fransceschi S. Human papillomavirus types among women infected with HIV; a meta-analysis. *AIDS* 2006;20:2337-2344.
28. Palefsky JM, Holly EA, Hogeboom CJ, Ralston ML, DaCosta, MM, Botts, R et al. Virologic, immunologic, and clinical parameters in the incidence and progression of anal squamous intraepithelial lesions in HIV-positive and HIV-negative homosexual men. *J Acquired Immune Def Syndr and Human Retrovirology* 1998;17(4):314-319.
29. Palefsky JM, Holy EA, Ralston, ML, Arthur SP, Jay, N, Berry JM et al. Anal squamous intraepithelial lesions in HIV-positive and HIV-negative homosexual and bisexual men: prevalence and risk factors. *J Acquired Immune Def Syndromes and Human Retrovirology* 1998:17(4):32-326.
30. Palefsky JM, Holy EA, Ralston ML, Jay N, Berry JM and Darragh TM. High incidence of anal high-grade squamous intra-epithelial lesions among HIV-positive and HIV-negative homosexual and bisexual men. *AIDS* 1998; 12:495-503.
31. Palefsky JM, Minkoff H, Kalish LA, Levine A, Sacks HS, Garcia P et al. Cervicovaginal human papillomavirus infection in human immunodeficiency virus-1 (HIV)-positive and high risk HIV-negative women. *J Natl Cancer Inst* 1999;91:226-236.
32. Holly EA, Ralston ML, Darragh TM, Greenblatt RM, Jay N, Palefsky JM. Prevalence and risk factors for anal squamous intraepithelial lesions in women. *J Natl Cancer Inst* 2001;93:843-849.
33. Ahdieh L, Klein RS, Burk R, Cu-Urvin S, Schuman P, Duerr A et al. Prevalence, incidence, and type-specific persistence of human papillomavirus in human immunodeficiency virus (HIV)-positive and HIV-negative women. *J Infect Dis* 2001;184:682-690.
34. Maiman M. Management of cervical neoplasia in human immunodeficiency virus-infected women. *J Natl Cancer Inst* 1998;23:43-49.
35. Robinson WR, Hamilton CA, Michaels SH, Kisinger P. Effect of excisional therapy and highly active antiretroviral therapy on cervical intraepithelial neoplasia in women infected with human immunodeficiency virus. *Am J Obstet Gynecol* 2001;184:538-543.
36. Reimers LL, Sotardi S, Daniel D, Chiu LG, Van Arsdale A, Wieland DL et al. Outcomes after an excisional procedure for cervical intraepithelial neoplasia in HIV-infected women. Gynecol Onc 2010;119:92-97.
37. Vernon SD, Hart CE, Reeves WC, Icenogle JP. The HIV-1 tat protein enhances E2-dependent human papillomavirus 16 transcription. *Virus Res.* 1993;27(2):133-145.
38. Chin-Hong PV, Husnik M, Cranston RD, Colfax G, Buchbinder S, Da Costa M et al. Anal human papillomavirus infection is associated with HIV-acquisition in men who have sex with men. *AIDS* 2009,23:1135-1142.
39. Averbach SH, Gravitt PE, Nowak RG, Celentano DD, Dunbar MS, Morrison CS et al. The association between cervical human papillomavirus infection and HIV acquisition among women in Zimbabwe. *AIDS* 2010;24;1035-1042.
40. Nowak RG, Gravitt PE, Morrison CS, Grange SJ, Kwok C, Oliver AE et al. Increases in human papillomavirus detection during early HIV infection among women in Zimbabwe. *J Infect Dis* 2011;203:1182-1191.
41. Franceschi S, Dal Maso L, Arniani S et al. Risk of cancer other than Kaposi's sarcoma and non Hodgkin's lymphoma in persons with AIDS in Italy. Cancer and AIDS Registry Linkage Study. *Br J Cancer* 1998;78:966.
42. Serraino D, Carrieri P, Pradier C, Bidoli E, Dorrucci, Ghetti E et al. Risk of invasive cervical cancer among women with, or at risk for, HIV infection. *Int J Cancer*;1999;82:334-337.
43. Serraino D, Dal Maso L, La Vecchia C, Franceschi S. Invasive cervical cancer as an AIDS-defining illness in Europe. *AIDS* 2002;16:781.
44. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *JAMA* 1993;269:729.
45. Massad LS, Riester KA, Anastos KM, Fruchter RG, Palefsky JM et al. Prevalence and predictors of squamous cell abnormalities in Papanicolaou smears from women infected with HIV-1. *J Acq*

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Immune Def Syndr. 1998;21:33-41.

46. Wright TC Jr, Ellerbrock TV, Chiasson MA et al. Cervical intraepithelial neoplasia in women infected with human immunodeficiency virus: prevalence, risk factors, and validity of Papanicolaou smears. New York Cervical Disease Study. *Obstet Gynecol* 1994;84:591.
47. The American Congress of Obstetricians and Gynecologists. Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 117: Gynecologic care for women with Human Immunodeficiency Virus. 2010:117:1-18.
48. Final Recommendation Statement: Cervical Cancer: Screening. U.S. Preventive Services Task Force. October 2014. Available at http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/cervical-cancer-screening
49. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf. [Section accessed 10/11/15: P-1-P20]
50. The American Congress of Obstetricians and Gynecologists. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists: Screening for Cervical Cancer. November, 2012.
51. US Preventive Services Task Force Final Update Summary: Cervical Cancer: Screening. U.S. Preventive Services Task Force. July 2015. http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening
52. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M et al. 2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. 2013, American Society for Colposcopy and Cervical Pathology. *J Lower Gen Tract Dis* 2013:17(5):S1-S27.
53. Maiman M, Watts H, Anderson J, Clax P, Merino M, Kendall MA. Vaginal 5-fluorouracil for high-grade cervical dysplasia in human immunodeficiency virus infection: a randomized trial. Obstet Gynecol 1999;94:954-961.
54. Maiman M, Fruchter RG, Serur E, Levine PA, Arrastia CD, Sedlis A. Recurrent cervical intraepithelial neoplasia in human immunodeficiency virus-seropositive women. *Obstet Gynecol* 1993;82:170-174.
55. Gilles C, Manigart Y, Konopnicki D, Barlow P, Rozenberg S. Management and outcome of cervical intraepithelial neoplasia lesions: a study of matched cases according to HIV status. *Gyneco Onc* 2005;96:112-118.
56. Ahdieh-Grant L, Li R, Levine AM, Massad LS, Strickler HD, Minkoff H. Highly active antiretroviral therapy and cervical squamous intraepithelial lesions in human immunodeficiency virus-positive women. *J Nat Cancer Inst* 2004;96(14):1070-1076.
57. Minkoff H, Ahdieh L, Massad LS, Anastos K, Watts DH, Melnick S et al. The effect of highly active antiretroviral therapy on cervical cytologic changes associated with oncogenic HPV among HIV-infected women. *AIDS* 2001;15:2157-2164.
58. Adler DH, Kakinami L, Moids enyane T, Tshabangu N, Mohapi LDe Bruyn G et al. Increased regression and decreased incidence of human papillomavirus-related cervical lesions among HIV-infected women on HAART. *AIDS* 2012;26(13):1645-1652.
59. Konopnicki D, Manigart Y, Gilles C, Barolow P, de Marchin J, Feoli F et al. Sustained viral suppression and higher CD4+ T-cell count reduces the risk of persistent cervical high-risk human papillomavirus infection in HIV-positive women. *J Infect Dis* 2013:207;1723-1729.
60. Blitz S, Baxter J, Raboud J, Walmsley S, Rachlis A, Smaill F et al. Evaluation of HIV and highly active antiretroviral therapy on the natural history of human papillomavirus. *J Infect Dis* 2013;208:452-462.
61. Heard I, Tassie J-M, Kazatchkine MD, Orth G. Highly active antiretroviral therapy enhances regression of cervical intraepithelial neoplasia in HIV-seropositive women. *AIDS* 2002;16:1799-1802.
62. Delmas M_C, Larsen, C, van Benthem B, Hamers FF, Bergeron C, Poveda J-D et al. Cervical squamous intraepithelial lesions in HIV-infected women: prevalence, incidence and regression. AIDS 2000;14:1775-1784.
63. Paramsothy P, Jamieson DJ, Heilig CM, Schuman PC, Klein RS Shah KV et al. The effect of highly active antiretroviral therapy on human papillomavirus clearance and cervical cytology. *Obstet & Gynecology* 2009;113(1):26-31.
64. Koh WJ, Greer BE, Abu-Rustum NR, Apte SM, Campos SM, Cho KR et al. Cervical Cancer, Version 2.2015. J Natl Compr Canc Netw 2014;13(4):395-404.
65. Silverberg MJ, Lau B, Justice AC, Engels E, Gill MJ, Goedert JJ et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. *Clin Infect Dis* 2012;54(7):1026-1034.
66. Machalek DA, Poynten M, Jin F, Fairley CK, Farnsworth A, Garland SM et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. *Lancet Oncol* 2012;13:487-500.
67. Bower M, Powles T, Newsom-Davis T, Thirlwell C, Stebbing J, Mandalia S et al. HIV-associated anal cancer: has highly active antiretroviral therapy reduced the incidence or improved the outcome? J *Acquir Immune Defic Syndr* 2004;37(5):1563-1565.
68. Diamond C, Taylor TH, Aboumrad T, Bringman D, Anton-Culver H. Increased incidence of squamous cell anal cancer among men with AIDS in the era of highly active antiretroviral therapy. *Sexually Transmitted Diseases* 2005;32(5):314-320.
69. Piketty C, Selinger-Leneman H, Grabar S, Duvivier C, Bonmarchand M, Abramowitz L et al. Marked increase in the incidence of invasive anal cancer among HIV-infected patients despite treatment with combination antiretroviral therapy. *AIDS* 2008;22:1203-1211.
70. Palefsky JM, Holly EA, Efirdc JT, Da Costa M, Jay Net al. Anal intraepithelial neoplasia in the highly active antiretroviral therapy era among HIV-positive men who have sex with men. *AIDS* 2005;19:1407-1414.
71. D'Souza G, Wiley DJ, Li X, Chmiel JS, Margolick JB, Cranston RD et al. Incidence and epidemiology of anal cancer in the multicenter AIDS cohort study. J *Acquir Immune Defic Syndr* 2008;48:491-499.
72. Patel P, Hanson DL, Sullivan PS, Novak RM, Moorman AC, Tong TC et al. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. *Ann Intern Med* 2008;148:728-736.
73. Crum-Cianflone NF, Hullsiek KH, Marconi VC, Ganesan A, Weintrob A, Barthel RV et al. Anal cancers among HIV-infected persons: HAART is not slowing rising incidence. *AIDS*. 2010;24:535-543.
74. De Pokomandy A, Rouleau D, Ghattas G, Trottier H, Vezina S, Cote P et al. HAART and progression to high-grade anal intraepithelial neoplasia in men who have sex with men and are infected with HIV. *Clin Infect Dis* 2011;52(9);1174-1181.
75. Van der Snoek EM, van der Ende ME, den Hollander JC, Shutten M, Neumann HA, van Doornum GJ. Use of highly active antiretroviral therapy is associated with lower prevalence of anal intraepithelial neoplastic lesions and lower prevalence of human papillomavirus in HIV-infected men who have sex with men. *Sex Transm Dis* 2012;39(7):495-500.
76. Chin-Hong PV, Palefsky JM. Natural history and clinical management of anal human papillomavirus disease in men and women infected with human immunodeficiency virus. Clin Infect Dis 2002;35:1127-1134.
77. Goldstone SE, Kawalek AZ, Huyett JW. Infrared coagulator: a useful tool for treating anal squamous intraepithelial lesions. *Dis Colon Rectum* 2005;48:1042-1054.
78. Marks DK, Goldstone SE. Electrocautery ablation of high-grade anal squamous intraepithelial lesions in HIV-negative and HIV-positive men who have sex with men. J *Acqui Immune Defi Syndr* 2012;59(3):259-265.

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79. Richel O, Wieland U, de Vries HJ, Rokmeyer NH, van Noesel C, Potthoff A et al. Topical 5-fluorouracil treatment of anal intraepithelial neoplasia in human immunodeficiency virus-positive men.*Br J Dermatol* 2010;163(6):1301.

80. Pineda CE, Berry JM, Jay N, Palefsky JM, Welton ML. High-resolution anoscopy targeted surgical destruction of anal high-grade squamous intraepithelial lesions: a ten-year experience. *Dis Colon Rectum.* 2008;15:829-837.

81. Richel O, de Vries HJ, van Noesel CJ et al. Comparison of imiquimod, topical fluorouracil, and electrocautery for the treatment of anal intraepithelial neoplasia in HIV-positive men who have sex with men: an open-label randomized controlled trial. *Lancet Oncol* 2013;14:346.

82. U.S. National Institutes of Health. Topical or ablative treatment in preventing anal cancer in patients with HIV and anal high-grade squamous Intraepithelial lesions; October 2015. Available at https://clinicaltrials.gov/ct2/show/NCT02135419.

83. Beck DE, Jaso RG, Zajac RA. Surgical management of anal condylomata in the HIV-positive patient. *Dis Colon Rectum.* 1990;33(3):180.

84. Conley LJ, Ellerbrock TV, Bush TJ, Chiasson MA, Sawo D, Wright TC. HIV-1 infection and risk of vulvovaginal and perianal conylomata acuminate and intraepithelial neoplasia: a prospective cohort study. *Lancet* 2002;359(9301):108.

85. Piketty C, Darragh TM, Da Costa M, Bruneval P, Heard I, Kazatchkine MD, Palefsky JM. High prevalence of anal human papillomavirus infection and anal cancer precursors among HIV-infected persons in the absence of anal intercourse. *Ann Intern Med.* 2003;138(6):453.

86. Ciobotaru B, Leiman G, St John T, Hyman N, Ramundo M, Grace C. Prevalence and risk factors for anal cytologic abnormalities and human papillomavirus infection in a rural population of HIV-infected males. Dis Colon Rectum. 2007;50(7):1011.

87. Massad LS, Silverberg MJ, Springer G, Minkoff H, Hessol N, Palefsky JM et al. Effect of antiretroviral therapy on the incidence of genital warts and vulvar neoplasia among women with the human immunodeficiency virus. *Am J Obstet Gynecol* 2004;190:1241-1248.

88. Greenspan D, Canchola AJ, MacPhail LA, Cheikh B, Greenspan JS. Effect of highly active antiretroviral therapy on frequency of oral warts. *Lancet* 2001;357 (9266):1411-1412.

89. King MD, Reznik DA, O'Daniels CM, Larsen NJ, Osterhold D, Blumberg HM. Human papillomavirus-associated oral warts among human immunodeficiency virus-seropositive patients in the era of highly active antiretroviral therapy: an emerging infection. *Clin Infect Dis* 2002;34(5):641-648.

90. Beachler DC, D"Souza G. Oral HPV infection and head and neck cancers in HIV-infected individuals. *Curr Opin Oncol.* 2013;25(5):503-510.

91. Food and Drug Administration. Product approval-prescribing information [Package insert]. Cervarix [human papillomavirus bivalent (types 16,18) vaccine, recombinant], Glaxo Smith Kline. Silver Spring, MD:US Department of Health and Human Services, Food and Drug Administration; February 2015. Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UC.

92. Food and Drug Administration. Product approval-prescribing information [Package insert[. Gardasil [human papillomavirus quadrivalent (types 6, 11, 16, and 18) vaccine, recombinant, Merck & Co, In. Silver Spring, MD:US Department of Health and Human Services, Food and Drug Administration; April 2015. Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UC.

93. Food and Drug Administration. Product approval-prescribing information [Package insert]. Gardasil-9 [human papillomavirus 9-valent vaccine, recombinant, Merck & Co, In. Silver Spring, MD:US Department of Health and Human Services, Food and Drug Administration; August 2015. Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UC.

94. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med* 2007;356;1928-1943.

95. Future II study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med* 2007;356:1915-1927.

96. Joura EA, Guilaiano AR, Iverson OE, Bouchar C, Mao CMehlsen J et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *N Engl J Med* 2015:372:711-723.

97. Paavonen J, Naud P, Salmeron J, Wheeler CM, Chow SN, Apter D et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjunvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomized study in young women. *Lancet* 2009;374(9686):301-314.

98. Munoz N, Manalastas R, Pitisuttithum P, Tresukosol D, Monsonego J, Ault K et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24-45 years: a randomized double-blind trial. *Lancet* 2009;373:1949-1957.

99. Guilano AR, Palefsky JM, Goldstone S, Moneira ED, Penny ME, Aranda C et al. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. *N Engl J Med* 2011;364:401-411.

100. Levin MJ, Moscicki A-B, Song L-Y, Fenton T, Meye WA, Read JS. Safety and immunogenicity of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old. *J Acq Immune Def Syndr* 2010;55(2):197-204.

101. Wilkin T, Lee JY, Lensing SY, Stier EA, Goldstone SE, Berry JM et al. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-1-infected men. *J Infect Dis* 2010;202(8):1246-1253.

102. Denny L, Hendricks B, Gordon C, Thomas F, Hezareh M, Dobbelaere K et al. Safety and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine in HIV-positive women in South Africa: a partially-blind randomized placebo-controlled study. *Vaccine* 2013;31:5745-5753.

103. Kahn JA, Xu J, Kapogiannis BG, Rudy B, Gonin R, Liu N et al. Immunogenicity and safety of the human papillomavirus 6, 11, 16, 18 vaccine in HIV-infected young women. *Clin Infect Dis.* 2013;57(5):735-744.

104. Centers for Disease Control and Prevention. Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports.* 2014/63(RR05);1-30

105. Winer RI, Hughes JP, Feng Q et al. Condom use and the risk of genital human papillomavirus infection in young women. *N Engl J Med.* 2006;354(25):2645-2654.

106. Manhart LE, Koutsy LA. Do condoms prevent genital HPV infection, external genital warts, or cervical neoplasia? A meta-analysis. *Sex Transm Dis* 2002;29(11):725-735.

Photo used as background image on pages 14-16 is a micrograph showing a low-grade squamous intraepithelial lesion (LSIL). Pap test. Pap stain. LSIL is an abnormality found on a pap test that consists of cells that are abnormal and may develop into cervical cancer. Abnormal cells have an enlarged nucleus, irregular chromatin and relatively abundant cytoplasm. Binucleation (two nuclei in one cell) and peri-nuclear glycogen are commonly seen. Related images LSIL. HSIL. Adenocarcinoma. Credit: Nephron CC BY-SA 3.0

HPV Related Diseases in HIV-Infected Individuals

CE Continuing Education

POST TEST — Page 1 of 1

Questions refer to article content. To receive CME/CNE/CEU credit, complete the post test, registration and evaluation forms on-line at *http://ccoe.rbhs.rutgers.edu/catalog/* or fill in the forms below and on the following pages and mail or fax to CCOE at the address on the registration form.

1. Which of the following statements regarding the epidemiology of HPV-associated cancers is correct?
   a. HPV causes a subset of cervical cancers
   b. HPV is associated with almost all oropharyngeal cancers
   c. Anal cancer incidence is highest amongst HIV-infected MSM
   d. The incidence of anal cancer among HIV- infected persons is declining since cART has been introduced

2. Which of the following statements is correct regarding HPV infection in HIV-infected persons compared to HIV-uninfected persons?
   a. HPV infections are more persistent but prevalence of HPV precancers is similar
   b. HPV DNA clearance is related to degree of immunosuppression
   c. Concomitant high-risk HPV types
   d. Treatment outcomes are similar

3. A 33 year old woman, newly diagnosed with HIV, comes to you for initial evaluation. Which of the following are acceptable for cervical cancer screening?
   a. Perform PAP now, repeat in 6 months, and then annually if Pap is normal
   b. Perform Pap now, repeat in 1 year, and then annually if Pap is normal
   c. Perform Pap along with HPV DNA testing and HPV genotype. If both are negative, then repeat Pap in a year
   d. Perform Pap along with HPV DNA testing and HPV genotype. If both are negative, then repeat Pap in 3 years
   e. B or C
   f. A or D

4. You perform a Pap smear, HPV DNA testing and HPV genotype on the above patient. Pap smear results come back showing ASCUS. You refer her for colposcopy based on the following:
   a. If HPV genotype is positive for type 6
   b. If HPV genotype positive for type 16
   c. If HPV genotype positive for type 18
   d. B and C
   e. A, B, and C

5. A 45 year old MSM with HIV infection comes to you for evaluation. All of the following would be appropriate for initial anal cancer screening EXCEPT:
   a. Inquire about symptoms of rectal bleeding, discharge, and pain
   b. Perform a digital rectal exam
   c. Perform anal Pap smear now and refer for high resolution anoscopy if PAP shows ASCUS or higher
   d. Perform anal PAP smear now and refer for high resolution anoscopy only if PAP shows low-grade AIN or higher

6. True or False: Patients with low-grade SIL on cervical or anal biopsy require treatment.
   a. True
   b. False

7. All of the following would make you suspect high-grade SIL EXCEPT:
   a. Normal vascular patterns are seen on high resolution anoscopy
   b. Acetowhitening with 3% acetic acid is seen on high resolution anoscopy
   c. Hyperpigmented patches are seen in the perianal area on exam
   d. Patient has a history of high-grade SIL lesions that were previously treated

8. A 28 year old HIV-infected MSM comes to see you for treatment of a large anal wart that is pigmented and indurated on exam. What is your next step?
   a. Treat with imiquimod
   b. Treat with podophyllotoxin
   c. Perform HRA and biopsy of the wart
   d. Treat with sitz baths

9. Which of the following is a true statement about HPV-associated oropharyngeal cancers?
   a. HPV is associated with almost all oropharyngeal cancers
   b. Cancers are mostly found in the tongue and tonsil
   c. Cancers are usually associated with a history of smoking and alcohol use
   d. There is a worse prognosis compared to non-HPV associated oropharyngeal cancers
   e. Screening for precancerous oral lesions improve treatment outcomes

10. Who of the following would you vaccinate with Gardasil HPV vaccine?
    a. 19 year old HIV-infected MSM with a history of anogenital warts
    b. 26 year old HIV-infected MSM without a history of anogenital warts
    c. 22 year old HIV-infected female with CD4 cell count below 200
    d. 22 year old HIV-infected female with CD4 cell count above 200
    e. All of the above

CE Continuing Education

HPV Related Diseases in HIV-Infected Individuals

REGISTRATION FORM

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In order to obtain continuing education credit, participants are required to:

(1) Read the learning objectives, review the activity, and complete the post-test.

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SELF-ASSESSMENT TEST *Circle the best answer for each question.*	**1.** A B C D	**2.** A B C D	**3.** A B C D E F	**4.** A B C D E	**5.** A B C D
	6. A B	**7.** A B C D	**8.** A B C D	**9.** A B C D E	**10.** A B C D E

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HPV Related Diseases in HIV-Infected Individuals

EVALUATION FORM

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The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants.

Please note: CE credit letters will only be issued upon receipt of completed evaluation form.

PROGRAM OBJECTIVES: Having completed this activity, you are better able to:	Strongly Agree				Strongly Disagree
Objective 1: Describe the prevalence of HPV infection, intraepithelial neoplasia, and other HPV-associated cancers among HIV-infected individuals	5	4	3	2	1
Objective 2: Summarize national guidelines regarding routine cervical cytologic screening of HIV-infected women, and HPV vaccination use in all HIV-infected 11-26 years old	5	4	3	2	1
Objective 3: Discuss guidelines for treatment of cervical intraepithelial neoplasia, and treatment options for the anal intraepithelial neoplasia in HIV-infected individuals	5	4	3	2	1

OVERALL EVALUATION: This activity:	Strongly Agree				Strongly Disagree
Increased my understanding of the subject	5	4	3	2	1
Will influence how I do my job	5	4	3	2	1
Will help me improve my performance	5	4	3	2	1
Will help me collaborate with other healthcare professionals	5	4	3	2	1
Was evidence based and scientifically balanced	5	4	3	2	1
Was free of commercial bias or influence	5	4	3	2	1
Met my expectations	5	4	3	2	1

Based on the content of the activity, what will you do differently in the care of your patients and/or regarding your professional responsibilities?

☐ Implement a change in my practice/workplace

☐ Seek additional information on this topic

☐ Do nothing differently; current practice/job responsibilities reflects activity recommendations

☐ Do nothing differently; Content was not convincing

☐ Do nothing differently; System barriers prevent change

If you anticipate changing one or more aspects of your practice and/or professional responsibilities please briefly describe how you plan to do so.

If you plan to change your practice and/or professional responsibilities, you may be contacted within six (6) months. Please provide your email address so we may follow up with you:

What issues are you experiencing in your practice and/or professional responsibilities that could be addressed in future programming?

CE Activity Code: 18HH01 — This form may be photocopied.

Breastfeeding and HIV: Current Advice

Joanne Phillips, RN, MS, Senior Education Specialist, and **Deborah Storm, MSN, PhD,** Director, Research and Evaluation, François Xavier Bagnoud Center

The decision to breastfeed is a deeply personal choice that most women must make following the delivery of a newborn. However, women living with HIV (WLWH) receive instructions to abstain from breastfeeding to prevent HIV transmission to infants. In fact, the latest guidelines, "Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States," published August, 2015 continue to reinforce that in the United States (US), as in other developed countries, breastfeeding is NOT recommended because maternal antiretroviral therapy dramatically reduces, but does not eliminate breast milk transmission. This strong recommendation is based on one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes.[1] Rates of HIV transmission from breastfeeding range from a low of 1.1%[2] with antiretroviral intervention to 16%[3] without any intervention.

However, many people recognize that this recommendation may present challenges in the life of a woman living with HIV. Her desire to protect her child from HIV infection may conflict with her general knowledge about the health benefits of breastfeeding and strong public health messages to breastfeed; desire to experience the maternal-child bonding through breastfeeding; knowledge or experience that breastfeeding is in fact recommended for some WLWH in parts of the world where formula feeding is not acceptable, feasible, affordable, sustainable or safe; concerns about unintended disclosure of HIV status by abstaining from breastfeeding; and familial, community or cultural pressures to engage in the practice of breastfeeding.[4,5]

While the latest recommendations do not waiver on abstention from breastfeeding, they have changed to recognize the tension that may arise for some mothers around this topic and encourage clinicians to begin addressing possible barriers to formula feeding during pregnancy and continue to support women after delivery.[6] Asking a WLWH how she feels about the recommendation to formula feed in an open-ended and non-judgmental manner (e.g., "Will not breastfeeding pose a problem for you?") can help clinicians to identify patients who may need more support to develop strategies for problem-solving around her individual concerns.[4] Interventions may include simple counseling about the risks associated with breastfeeding, assistance developing a plausible rationale to provide to family members on why the infant is formula feeding, guidance on lactation suppression techniques, referral for Women, Infants and Children (WIC) services, or support for disclosure of her diagnosis.

In cases where a WLWH maintains an intention to breastfeed after counseling and education, a harm reduction model may be preferable to avoid unmonitored, unsupported breastfeeding practices. A recent article by Levison et al., describes a harm reduction model that includes achievement and maintenance of an undetectable maternal viral load through provision of combined antiretroviral therapy (cART), frequent viral load monitoring, exclusive breastfeeding, recognition and prompt management of mastitis. Pre- and post-natal coordination with pediatrics with possible continued infant antiretroviral prophylaxis until after termination of breastfeeding along with infant HIV testing and monitoring is also recommended.[4] Clinicians considering a harm reduction model should weigh the ethical considerations between the rights of the mother to choose breastfeeding versus the right of the child to live without HIV infection given the lack of adequate data about the safety of this

practice.[7]

While many advances have been made in HIV care and treatment, the recommendation to abstain from breastfeeding remains the gold standard for the prevention of perinatal HIV transmission in the US. However, clinicians should be aware of the pressures that many WLWH feel to breastfeed their newborns and should address the topic in order to identify and resolve any barriers to formula feeding and support the needs of WLWH.

Case Study

MO is a 30-year-old woman living with HIV for 5 years. She emigrated from Cameroon last year and is pregnant with her second child. She breast fed her first child as per her healthcare worker's advice in Cameroon and he is HIV-negative. She lives with her husband's family here in the US. They are unaware of MO's HIV status and she is fearful of what they would do if they found out. You advise her of the recommendation in the US to formula feed and ask her if this will be a problem for her.

- What barriers to breastfeeding do you identify?
- What are some possible strategies to support MO around infant feeding?

References

1. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. "Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States." Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed October 9, 2015.
2. Shapiro et al. "Anitretroviral Regimens in Pregnancy and Breast-Feeding in Botswana." *NEJM*. 2010: 362:22281-94.
3. Nduati R, Mbori-Ngacha J, Richardson B et al. "Effect of breastfeeding and formula feeding on transmission of HIV-1: A randomized clinical trial." *JAMA*. 2000; 28(9):1167-74.
4. Levison J, Weber S and Cohan D. "Breastfeeding and HIV-infected women in the United States: Harm reduction counseling strategies." *CID*. 2014; 59:304-9.
5. Greene S, Ion A, Elston D et al. "Why Aren't You Breastfeeding?": How Mothers Living With HIV Talk About Infant Feeding in a "Breast Is Best" World. *Health Care for Women International.* 2015; 36(8): 883-901.
6. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. "Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States." Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed October 9, 2015.
7. Kennedy V, Loutfy M, Brophy J. "Issues in applying a harm reduction approach to breastfeeding in the context of maternal HIV." *CID*. 2015; 60:672-4.

Improving Education for Women and Testing for HIV

Judith Lightfoot, D.O., F.A.C.O.I

Introduction

As we approach our 26th Annual HIV Medical Update, I couldn't help but reflect about the impact HIV has had among women here in the United States. At the dawn of the domestic epidemic, the earliest case of a woman diagnosed in the United States was in 1981; though there are documented cases of HIV as early as 1959 in this country. In the beginning, HIV was primarily diagnosed only in males who were gay or bisexual, intravenous drug users, or those who received blood products prior to routine screening for HIV. While women make up a smaller percentage of total HIV cases and overall new infections in females is on the decline –women are still not being regularly screened and tested for HIV. Without improving our HIV testing services, we cannot hope to identify those women living with HIV who need our care nor can we identify those women at-risk for HIV who could benefit from behavioral and biomedical interventions such as Pre-Exposure Prophylaxis (PrEP), to remain HIV negative. We have all the tools we need to end this epidemic, but what we need now is greater competency in finding and testing undiagnosed persons. Through a more competent system of care and empowering women to effectively navigate our healthcare system, we can continue to bend the curve and end this epidemic. This article will explore the current epidemiology of the domestic women's epidemic, the primary routes of transmission, and practical steps providers can take to improve care continuum outcomes for women.

Epidemiology

Currently the Centers for Disease Control and Prevention (CDC) estimates there are over 1.2 million persons living with HIV in the United States including, 156,300 persons who are living with HIV infection but are not yet diagnosed.[1] The CDC regularly reports HIV incidence and prevalence rates in the United States, including data sets on annual incidence in adult and adolescent females stratified by race and ethnicity. Reviews of the data show that women and Black women in particular, experience disparities in disease burden.

Diagnoses of HIV Infection among Adult and Adolescent Females, by Race/Ethnicity, 2013 – United States[2]

Race/Ethnicity	Number of Cases	Rate per 100,000
Black/African American	5,867	34.8
Hispanic/Latino	1,419	7.0
White	1,579	1.8
American Indian/Alaska Native	49	5.1
Native Hawaiian/ other Pacific Islander	15	7.3
Asian	159	2.2
Multiple Races	190	9.3
Total	**9,278**	**6.9**

Comparison of Racial/Ethnic Female Subpopulations in the United States by Percent of Female Population and Percent of 2013 HIV Female Incidence[3]

Race/Ethnicity	Percent Total Population	Percent HIV Diagnoses
Black/African American	13%	63%
Hispanic/Latino	15%	15%
White	65%	17%
American Indian/Alaska Native	1%	1%
Native Hawaiian/	<1%	<1%
Asian	5%	2%
Multiple Races	2%	2%

As you can see in the data from the CDC, Black/African American women are the only racial category to report a higher percentage of infection versus percent of the total female population. Compared to other female racial and ethnic groups, Black women bear a significant burden of disease when it comes to HIV infection.

Transmission

Domestically, many women who are diagnosed with HIV often report condom-less vaginal and anal intercourse making sexual transmission the dominant mode for all women diagnosed with HIV in the United States.

Many of these women living with HIV infection reside in the Northeast and the South, followed by the Midwest and West. The death rates have been highest among Black/ African American females followed by Hispanic females.

Primary Transmission Route for Females in the United States by Select Race/Ethnicity[4]

Race/Ethnicity	Sexual Transmission	Sharing Injection Equipment	Other
Black/African American	90%	9%	1%
Hispanic/Latino	86%	13%	1%
White	74%	24%	1%

Many of my female patients have disclosed to me that they believed they were in a monogamous relationship while others report sharing needles or engaging in commercial sex work to support their addiction. Some believed that they may have acquired HIV through oral sex and although this is less likely to occur, cases have been documented here in this country. For both men and women living with HIV, the risk of HIV being transmitted is highest during acute HIV infection 2-7 weeks following acquisition or in untreated infection with severe immunosuppression.

Discussion

As healthcare professionals we should be asking ourselves many questions. Why do some women bear a disproportionate burden of disease than others? What barriers do these women face to counseling and testing services; how can we reduce those barriers? What kinds of care can we offer that will support these women in combatting stigma and discrimination? Ultimately, how do we engage and empower all women to fight HIV? I will try to provide some solutions to some of these questions that have plagued me over the years. If nothing else I hope to generate a discussion and dialogue in the communities who care for women.

The CDC estimates that there are 50,000 new HIV infections annually. Therefore the current recommendation is to offer HIV testing to all persons (ages 13-64 years old) in any healthcare setting. We know that early testing not only improves health outcomes for those diagnosed with HIV, but it also decreases the likelihood of further transmission. With guidelines and evidence to support early testing then why are women still not being tested?

It's simple…we're not testing them.

We aren't offering testing to our female patients unless they are pregnant, an injection drug user, or if they have had a sexually transmitted infection. Data show that only 60 % of all domestic healthcare providers have offered HIV testing. Physicians and other healthcare providers need to look around their medical neighborhood and know what care environments provide what services; particularly identifying those who can provide services to the un- and underinsured in our communities. Many female patients can't afford commercially available home testing kits so we need to ensure access and linkage to free testing programs. We need to ensure that providers realize that written consent is no longer necessary, and that verbal consent is satisfactory in most states. We need to determine whether we are comfortable counseling our patients related to HIV risk and if not, provide referrals to those who do. If you are seeking to conduct a risk assessment to determine if a woman is high risk for HIV disease, there are many tools that can support your efforts. For example, our partners at the Office of National AIDS Policy make the following question recommendations to identify HIV infection risk:

- Have you had sex with someone who is HIV-positive or a person whose HIV status you didn't know since your last HIV test?
- Have you injected drugs (including steroids, hormones, or silicone) and shared equipment (or "works," such as needles or syringes) with others?
- Have you exchanged sex for food, shelter, drugs, or money?
- Have you been diagnosed with, or sought treatment for a sexually transmitted disease, like syphilis?
- Have you been diagnosed with or sought treatment for hepatitis or tuberculosis (TB)?
- Have you had sex with anyone who has any of the risk factors listed above or whose history you don't know?[4]

These questions can help you start a conversation and dialogue with your patients about their risk profile. By adhering to guidelines and improving access to healthcare systems, we can seek to better implement HIV testing interventions.

But access and guidelines do not guarantee outcomes, especially in a disease such as HIV. In my practice, I see a variety of women from various socioeconomic backgrounds, working women, non-working women, professionals as well as non-professionals. Many of the women that I see are mothers, and many are married or in long-term relationships. Society and healthcare providers in particular, need to realize that HIV can affect anyone and recognize that our clinical practice continues to drive stigma and the epidemic. Among my patients, about 50% of HIV-infected women have partners who are infected, another 30-35% has no idea who infected them, and the other 15% aren't comfortable discussing how they became infected. As one of my patients told me, "It's just too painful to discuss, I just want to focus on getting better?" I've

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found that many women carry this heavy burden by themselves because of shame and frustration and for fear of being judged by their friends, their families, their communities, and unfortunately their healthcare providers. Many blame themselves for not asking the right questions or for not insisting on use of a condom. Some didn't at that time understand the importance of a sexual history, while others felt that they asked the important questions and they were lied to or their partners told them that they tested negative.

For the women who are and have dealt with substance abuse, many shared with me their dark past of how they began using drugs and what got them there. I've witnessed patients with active substance abuse who were once HIV negative and within a year or two become positive and there are needle exchange programs available in my area! Something is prohibiting these women from accessing these services – perhaps they are unaware or uncomfortable. But as a result, I try to keep the HIV-uninfected women who engage in substance abuse close to my practice by offering them treatment programs with the assistance of social workers in my hospital, case managers, and free testing at my office.

By providing better access and attending to the needs of our female patients we can only get so far. In addition to improved testing services, we as physicians and other healthcare providers should be asking questions to determine what our female patients know about HIV. Helping to educate women about the risk behaviors associated with HIV as well as the need for HIV testing can support women in making better decisions related to risk as well as asking for HIV testing instead of waiting for the healthcare provider to offer it. Information about HIV testing and how to ask your provider about your HIV risk and need for testing could be disseminated in public places through our outreach workers. Engaging women and their social networks through community gatekeepers can facilitate the delivery of health information. Coaching women to ask questions of their providers such as, "Have you ever tested me for HIV?" and "If not, why?" can all support community transformation around HIV testing. We can change to better support empowerment at the patient level and improve services at the provider level.

So what else can we do as a medical community to help empower women to stop the spread of HIV? First I want to commend those of you who are already doing it, but we collectively have to make improvements on our 60% testing rate by reaching 100% in our medical communities.

1. Advocate for screening and testing for every female patient in your care setting.
2. Reach out to 5 practices or clinics in your communities and educate those providers on the need to test all women at least once, regardless of the socioeconomic background.
3. Ensure women understand how HIV works in their bodies – including the potentially more rapid disease progression when compared to men.
4. Empower women to feel comfortable in asking questions of their partners and the use of prevention tools such as condoms and PrEP.
5. Establish environments where HIV-uninfected women can gather and build the relationships that will keep them uninfected.

Closing

By focusing on the person and not the disease, we can better partner with women. And by addressing women holistically, we can support their journey to wellness. All of this is necessary if we as a medical community want to empower women with the knowledge and tools to stop the spread of new infections in their communities. We can decrease the rates of new infections by collectively fighting to empower women. So let's pick up the pieces and collaborate with our communities so that rates of new infections will go down by 10% per year by 2020. It is our public health duty and responsibility. As we approach World AIDS Day, don't just test on that day, test every day. Speak about HIV with patients that you have the privilege of engaging with each and every day!

References

1 Source: CDC Surveillance Data Accessed from: http://www.cdc.gov/hiv/statistics/basics/ataglance.html on October 2015

2 "HIV Surveillance in Women." Centers for Disease Control and Prevention. Accessed from http://www.cdc.gov/hiv/pdf/q-z/cdc-hiv-surveillance-in-women-2013.pdf on October 20, 2015

3 "HIV Surveillance in Women." Centers for Disease Control and Prevention. Accessed from http://www.cdc.gov/hiv/pdf/q-z/cdc-hiv-surveillance-in-women-2013.pdf on October 20, 2015

4 "HIV Surveillance in Women." Centers for Disease Control and Prevention. Accessed from http://www.cdc.gov/hiv/pdf/q-z/cdc-hiv-surveillance-in-women-2013.pdf on October 20, 2015

5 Margoles, Shari. "Less Than Half of America is Getting Tested for HIV. Here's Why." The Huffington Post. Accessed from http://www.huffingtonpost.com/2014/06/16/hiv-testing-day-_n_5439171.html on October 20, 2015

6 Source: Office of National AIDS Policy accessed from https://www.aids.gov/hiv-aids-basics/prevention/reduce-your-risk/who-is-at-risk-for-hiv/ on October 20, 2015

New Jersey HIVLinks Winter 2015
HIV, STD, and TB news and information for health professionals

The Status of HIV among

Men Who Have Sex with Men

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Introduction

The National HIV Behavior Surveillance System (NHBS) was initiated in 2003 by the Centers for Disease Control and Prevention (CDC) to monitor HIV associated behaviors by conducting surveys in populations at high risk of HIV infection. The system is designed to aid state and local health departments in areas of high HIV prevalence. Information presented in this report can identify prevention needs, allocate resources, and develop programs to address at-risk communities. The NHBS monitors selected risk behaviors, HIV testing experiences, use of prevention services and HIV prevalence among men who have sex with men (MSM), injection drug users (IDUs) and heterosexual adults at increased risk. The following is a summary of the NHBS findings in the MSM community in the Newark-Union, NJ-PA Metropolitan Division of The New York-Northern New Jersey-Long Island Metropolitan Area.

Background

As of December 31, 2013, there were 12,894 known HIV infections attributable to MSM behavior in New Jersey (NJ). In 2011, 626 new HIV diagnoses in the state of NJ were attributed to MSM exposure. During 2011, NJ ranked 44th in the percentage (52%) of HIV diagnoses attributable to MSM compared with 62% of diagnoses for the nation as a whole. The state of NJ has a population of over 8.4 million people, which is equivalent to 3%

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of the nation's population. Although NJ is the ninth most populated state, it is the fifth smallest state geographically.

As a whole, the incidence of HIV is decreasing in NJ, but the percentage of cases attributed to MSM exposure has increased. A steady decrease has been noted in all new diagnoses from 2002-2011. Among Black non-Hispanics, there has been a 45% decline, and among white non-Hispanics, a 44% decline. However, the least amount of decrease was noted among the Hispanic population, only a 26% decline. From the years 1990-2011, the Hispanic population has increased in NJ from 10% to 18%. The increase in exposure among Hispanic MSM could be attributed to the fact that the Hispanic population has grown in the two decades.

In addition to race and ethnicity, age is a correlated factor in the rising rate of HIV diagnoses attributable to MSM exposure. From 2002-2011, the number of diagnoses among MSM males ages 13-24 doubled. The number of diagnoses among Hispanic MSM rose 32%, white MSM decreased 28% and the percent of black MSM remained consistent since 2002. Among the 13-24 age group, minorities accounted for 92% of all diagnoses among young MSM in 2011. The number of diagnoses among Hispanic MSM 13-24 years old tripled between 2002 and 2011. Seventy-two percent of new infections among all MSM are among minorities compared to diagnoses among whites in which 26% of new infections were among MSM. In 2009, the number of Hispanic MSM overtook the number of diagnosis among white MSM. Among all adult/adolescent males, the largest percentage of diagnoses in 2011 occurred in males ages 25-34. Overall, MSM diagnoses are occurring at a younger age compared with all male HIV/AIDS diagnoses.

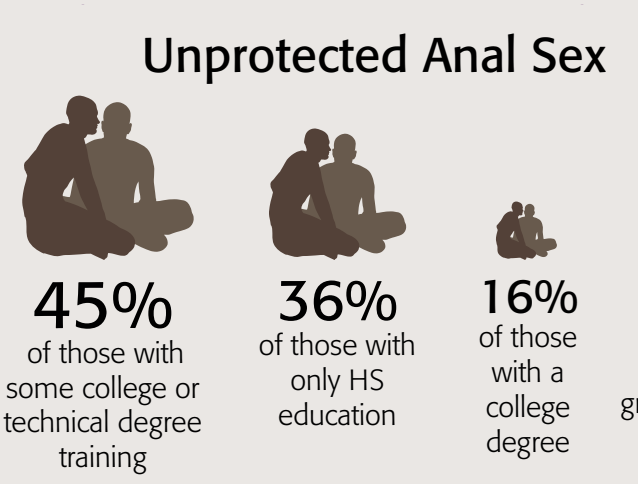
NHBS Study Findings

Time location sampling was used for the 2011 NHBS. Time location sampling is used to reach populations such as MSM who are small in number and reside in disperse geographical locations but can be found at identifiable locations. Males eligible to participate in the study had to be 18 or older and current residents of the Newark-Union, NJ-PA Metropolitan Division of the New York-Northern New Jersey-Long Island Metropolitan Area. An electronic standardized questionnaire was used to collect data. Questions assessed revolved around behavioral risks for HIV infection, HIV testing (all survey respondents were offered HIV testing) and use of HIV prevention services. The data analyzed were collected from a total of 270 participants, 208 of whom consented to HIV testing. The study was conducted between September 2011 and December 2011. Recruitment locations occurred at venues frequented by MSM such as informal gatherings (fashion shows, restaurants, etc.), bars and dance clubs.

Seventy three percent of survey respondents identified as homosexual or gay, while 27% identified as bisexual or heterosexual/straight. The average age of participants was 30 years old and the range was 18-69 years with 47% under 25. About 26% were Hispanic/Latino and about 58% were Non-Hispanic black. Over half of the survey respondents that were Hispanic identified as Puerto Rican. Ninety percent of survey participants were U.S. born. An estimated 28% were unemployed and living below the poverty threshold during the study. The poverty rate was highest among men ages 18-24 at 44%. About 38% of survey respondents had no health insurance and of those with health coverage, most were privately insured.

Ninety three percent of survey participants admitted revealing to someone that they were attracted to men. They admitted to being "out" to their gay, lesbian, or bisexual friends. Slightly fewer were out to non-gay, lesbian or bisexual friends and family. Twenty six percent reported that they were not out to their health care provider. Participants reported the presence of discrimination due to their sexual orientation in the form of verbal name calling or insults, receipt of poorer services in restaurants, stores

Ninety three percent of survey participants admitted revealing to someone that they were attracted to men. They admitted to being "out" to their gay, lesbian, or bisexual friends. Slightly fewer were out to non-gay, lesbian or bisexual friends and family. **Twenty six percent reported that they were not out to their health care provider.**



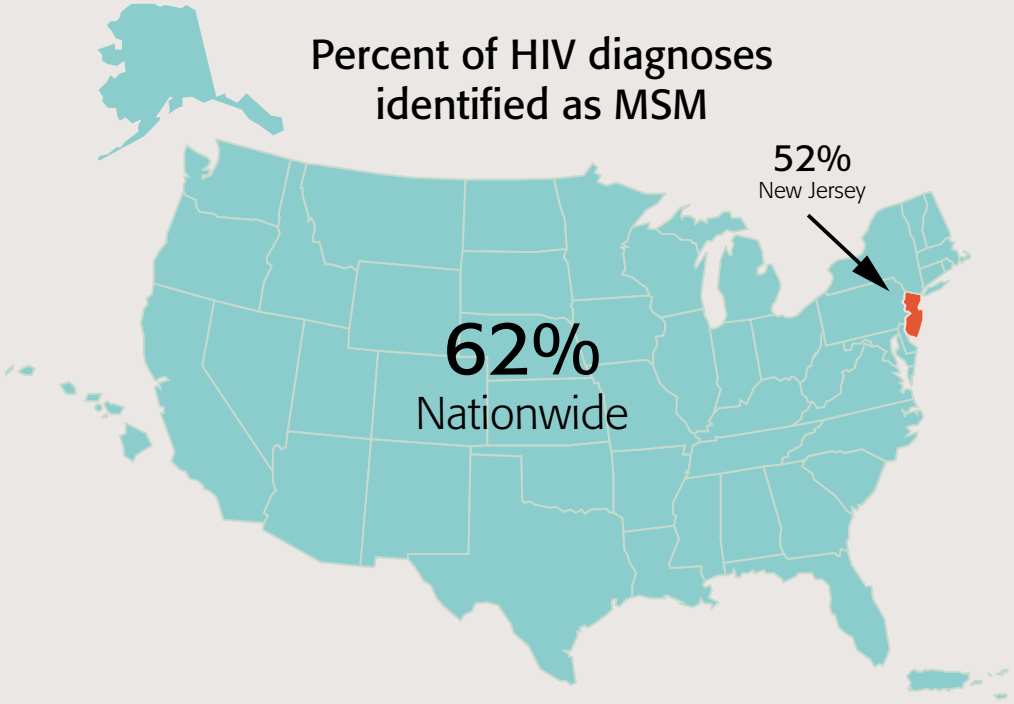
or other business agencies, and lower quality healthcare. Discrimination of any kind was reported by 46% of survey respondents. Verbal discrimination was reported by 36%, receiving poorer services was reported by 20%, lower quality healthcare was reported by 2% and discrimination in the form of physical attack and or injury was reported by 11%.

Behavioral risk findings include reporting of unprotected anal sex and lack of condom use. Unprotected anal sex within the last 12 months was reported by 51% of participants. Reporting of unprotected anal sex was higher with main partners then with casual partners at 35% and 24%, respectively. Respondents who had both a main partner and a casual partner(s) were more likely to use a condom with their casual partner(s) than with their main partner(s). Unprotected anal sex was found to be more common among Hispanic/Latinos (58%) and African Americans (54%) compared to all other race/ethnicity groups (23%). By age group, the lowest prevalence of unprotected anal sex was reported among 20-24 year olds; the percentage of unprotected sex increased in older age groups.

Reporting of unprotected anal sex was highest among those with some college experience or a technical degree (45%). The least educated and the college educated are more likely to use condoms: just 3% of persons with less than a high school education and 16% of persons with a college degree engaged in unprotected anal sex in the prior year. Persons with a high school diploma were intermediate in their risk behavior, 36% of high school only graduates engaged in unprotected sex.

In terms of most recent sexual encounter, 23% of survey respondents reported that in their most recent encounter a condom was not used. Twenty six percent of these encounters involved alcohol or drugs. Of the 23% that did not use a condom during their last sexual encounter, 22% reported this behavior with main partners and 15% reported this behavior with their casual partners. However, 65% reported recently receiving free condoms and 82% admitted to using condoms during intercourse if they received the condoms for free. While the topic of (IDU) drug use (IDU) was investigated, it was found to be uncommon in this population. About 4% reported ever using injection drugs and less than 1% reported current use. For the purpose of this particular study, IDU was found to be minimal.

Use of counseling and testing services was assessed among the survey respondents 39% reported to having engaged in counseling within the past year. Fifty percent of those who received counseling were African American, 28% were Hispanic and 18% were of other race/ethnicity. Ninety-two percent of survey respondents who had seen a provider had done so within the last six months. Eighty four percent of self-reported HIV-infected men were current on their HIV care. For the purpose of this study, current was defined by behaviors such as following their prescribed regimen, consistently keeping their appointments,



Due to the lack of awareness of PrEP and PEP as preventative measures, more education and awareness needs to be done in the community about their effectiveness in HIV prevention.

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etc. Two thirds of self-reported HIV-infected men were taking Antiretroviral (ARV) medication. Knowledge of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) as preventative measures was uncommon. Of the survey respondents, 20% were aware of the use of ARVs for prevention of HIV infection. Less than 5% had used ARVs for PEP and none had used it for PrEP.

An interesting trend was observed with respect to HIV testing by age group. Ninety-four percent of eligible venue attendees reported ever having an HIV test. Out of the 270 men included in the analysis, 208 consented to taking an anonymous HIV test. Among the age group 18-24, 21% were HIV-infected compared to 27% in the 25 and above age group. HIV prevalence was found to be the highest among those 40 and older. Among eligible study participants who did not report prior knowledge of being HIV-infected, 76% reported having been tested in the past 12 months. Reported testing rates were observed to be highest among those 18-24 and to decline with age.

Conclusion

There is an inconsistency in terms of condom usage between main versus casual partners. A preventative measure could include encouraging consistency in condom use with all sexual partners as the chance of transmission needs to be addressed in all scenarios. Reporting of unprotected anal sex and seeking HIV counseling was found to decrease with age. Increasing cultural competencies to ensure all populations are reached would be a good measure to enhance prevention behavior. Due to the lack of awareness of PrEP and PEP as preventative measures, more education and awareness needs to be done in the community about their effectiveness in HIV prevention. A future analysis of testing and behavioral differences between HIV-infected versus HIV-uninfected survey respondents can be conducted for a more comprehensive look at the issue. Of particular interest to investigate will be the relationship between the higher use of condoms and the higher rate of HIV testing coupled with an increasing rate of HIV infection among young MSM, aged 18-24 years old.

Acknowledgements

Data obtained from the New Jersey Department of Health HIV Registry and the New Jersey National HIV Behavioral Surveillance Study. ❖

The painting featured on the cover and shown at left is "Couple at the Window; Paar am Fenster". Karl Hofer (1878-1955). Oil on canvas. Signed and dated 1954. 97 x 67.5cm.

Karl Hofer was a German expressionist painter whose work was labeled degenerate by the Nazis in 1943. Much of his early work was destroyed in a bombing attack. After the war, he regained recognition as one of Germany's most prominent painters.

https://www.van-ham.com/en/van-ham-art-estate/karl-hofer.html

Implementing Trauma-Informed CARE

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Abstract

Exposure to trauma and adverse childhood experiences are related to a higher risk for HIV and poor health outcomes. Trauma-informed care is an approach that can be used in the practice of caring for individuals living with HIV. Delivered in an environment that safeguards clients and staff, trauma-informed care appreciates the impact of trauma, responds in a manner that prevents further trauma, and requires educated, culturally sensitive health care providers and practice settings. Organizations and their leadership must lead the efforts to incorporate the principles of trauma-informed care throughout their clinics. This article presents an overview of trauma and trauma-informed care and its relationship to the population at risk for and living with HIV.

Background

Trauma has been experienced by most Americans through community violence, domestic violence, medical trauma, natural disasters, neglect, abuse, war, terrorism or sudden death.[1,2] Exposure to traumatic events or adverse childhood experiences (ACEs) can have lasting effects on physical and emotional health. The Centers for Disease Control and Prevention[3] and Kaiser Permanente investigated the relationship between adult health and ACEs, reporting a correlation between traumatic experiences as a child and risk for the leading causes of morbidity and mortality in United States adults. Understanding the science of the developing brain has further clarified this issue.[2]

Trauma impacts the brain negatively and excessive trauma has biological consequences on the brain. Information enters the brain through the thalamus region, which asks, "Is this a threat?" The prefrontal cortex, the thinking area of the brain, considers the experience and sends a signal to the amygdala, which provides an emotional response. Repeated trauma changes the connections that the brain makes. When confronted with a threat, the traumatized brain receives the information in the thalamus, and then bypasses the prefrontal cortex and goes directly to the amygdala. The prefrontal cortex is lost in the process. A prefrontal cortex that is not fully developed affects an individual's attention and executive functions: planning, strategy, organization, setting goals and attention to detail.[2]

Telomeres are repetitive DNA elements, and their length declines normally with cell division and ageing. In 2011, Kiecolt-Glaser et al.[4] found that childhood maltreatment and adversity were linked to shorter telomere length. Additionally, for adults and children, accelerated telomere shortening is linked to cardiovascular disease, obesity, and diabetes.[5,6] Drury et al.[7] completed their research on telomeres, which adds evidence to the impact of trauma during early childhood on their length. They measured telomere length taken from children's blood, and saliva. The children had a known history of physical maltreatment, and some were living in institutional settings or poverty. Drury et al.[7] found that children exposed to violence in the home, and family disruptions had significantly shorter telomeres.[7]

The Impact of Trauma across the Lifespan

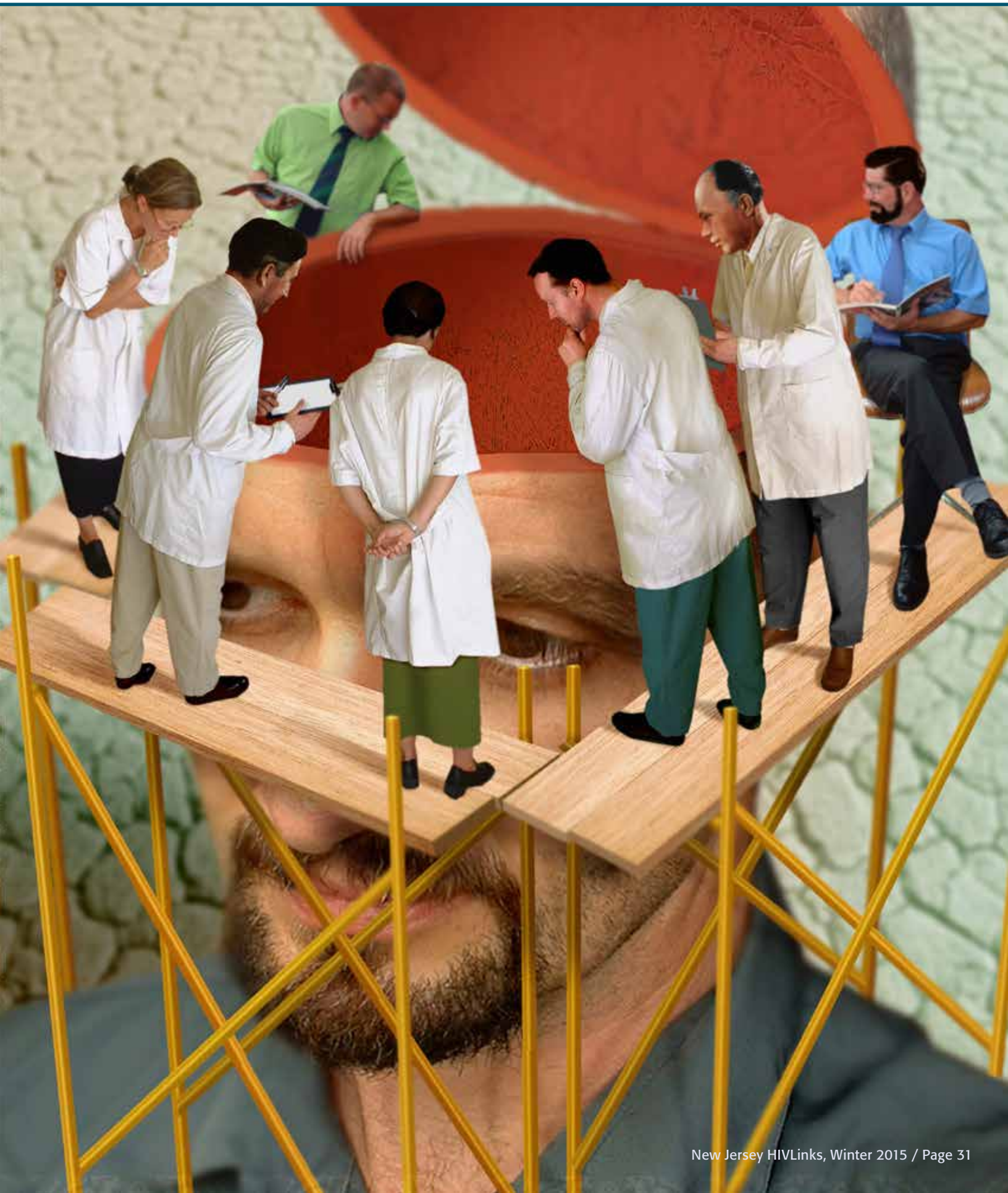
Trauma can change a person's self-concept, the way a person learns, remembers, and interacts with the world. These alterations can result in the adoption of risky behaviors such as smoking, drinking to excess, aggressive behavior or drug use. Across the lifespan the consequences are manifested in disease, disability or marginal societal participation, and untimely or premature death is the worst outcome.[3,2,8]

Childhood trauma disrupts neurodevelopment, social and emotional development, and cognition; it may damage a child's future abilities, and physical, social, emotional and/or spiritual well-being.[8] Adolescents who have a history of traumatic experiences as children are more likely to be labeled difficult, aggressive, or oppositional, and face disease and disability related to the long term effects of trauma, such as major depression, post-traumatic stress disorder (PTSD), and heart disease.[9] Adults with a history of trauma in childhood are more likely to experience intergenerational abuse, crime, prostitution, and/or violence; they are more likely to be homeless and unemployed as adults—all potential contributors to early morbidity and mortality, and to violent, unhealthy communities.[10]

Victims and survivors of trauma are over-represented in the HIV infected population. Sometimes, the trauma is part of the HIV diagnosis, and the person cannot accept treatment. The diagnosis itself may reawaken reactions to previous trauma.[11] Health care providers and staff members must be sensitized to the distinct needs of people living with HIV (PLWH) and affected by the disease in order to provide culturally appropriate, trauma-sensitive care. Acknowledging the trauma experienced by clients validates their experiences, and helps develop a trusting relationship, which is necessary to engage them in treatment, and impact medi-

continued on page 32

Implementing Trauma-Informed Care



cation adherence. A trauma-informed approach changes the question from "What's wrong with you?" to "What has happened to you?" The National HIV/AIDS Strategy: Updated to 2020[12] calls for advances in support for PLWH to remain engaged in comprehensive care, including support for treatment adherence over the next five years. Trauma-informed care (TIC) is a strategy that can be used to address the trauma of PLWH and improve outcomes.

Trauma-Informed Care

TIC was developed to mitigate the outcomes of a traumatic experience.[13] It is an approach used that appreciates the impact of trauma, identifies the symptoms of trauma in individuals, intervenes with sensitivity to trauma, avoids further traumatization to the individual, and incorporates TIC principles into practice as recommended by the Department of Health and Human Services.[14,15] When providers adopt a TIC approach, they integrate the following trauma-informed principles: safety, trustworthiness, choice, collaboration and empowerment, peer support, resilience, inclusiveness, cultural issues and change.[13,15] Table 1 lists these principles and associated interventions to ensure that care is trauma-informed. Incorporating these values allows providers to identify trauma symptoms in clients, validate with the clients the impact trauma has played in their lives, and offer care that will minimize trauma, and educate clients and caregivers on interventions that support resilience and prevent further trauma.[1]

Victims and survivors of trauma are over-represented in the HIV population. Sometimes, the trauma is part of the HIV diagnosis, and the person cannot accept treatment.

Incorporating TIC within Clinical Practice

Implementation of TIC within an organization requires change throughout the entire service system. First, successful change requires administrative support. Next, educating staff and providers is necessary to develop and maintain a trauma-informed approach to care. Educated providers will screen for trauma, understand the principles of TIC, and respond with strategies that prevent further trauma in PLWH.[16,17,15] Lastly, all policies and procedures should reflect sensitivity to trauma among the individuals and families they serve and the staff they employ, and incorporate the principles of TIC.[18,19,20]

Safety, trustworthiness, choice, collaboration and empowerment, peer support, resilience, inclusiveness, cultural issues and change, the principles of TIC, affect clients and staff alike. Safety is paramount for client interactions, and staff needs a professional, non-threatening environment in which to work.[20] Transparent policies and procedures will contribute to trustworthiness and a respect for all, clients and co-workers alike.[20] A trauma-informed approach will recognize that clients do have a choice in their care and that staff need a degree of autonomy to identify strengths and learning needs.[20] A trauma-informed plan of care will be a collaborative ef-

Table 1

Principles of TIC	Trauma-informed Interventions
Safety	▪ Provide clear directions to location of practice/center ▪ Have security available if necessary ▪ Ensure that all areas (reception, waiting, interview and treatment rooms) and staff are welcoming ▪ Explain goals and mission of practice/center ▪ Be aware of signs that client may be uncomfortable
Trustworthiness	▪ Obtain client's assent/consent to care ▪ Explain role and responsibilities of staff ▪ Clarify responsibilities of client ▪ Inform client of all possible treatment options, with risks and benefits ▪ Outline reasonable expectations

Choice	▪ Offer choices, such as:
	  ▪ Who, when and where care is provided
	  ▪ How will the site follow up with client- phone, in-person, and email?
	  ▪ When to start or stop regimen
	▪ Make client's preference the priority

Collaboration	▪ Establish a community advisory board ▪ Listen to client's feedback ▪ Respect client's experience, and incorporate into plan of care
Empowerment	▪ Recognize client strengths, as well as needs, and incorporate them into the plan of care ▪ Offer feedback to client regarding their progress ▪ Validate client experiences ▪ Ensure clients have tools and skills to adhere to their regimen
Peer Support	▪ Encourage client to participate in advisory boards, and to seek support within the family and community ▪ Refer clients to support groups when appropriate
Resilience	▪ Help client identify family and community supports ▪ Consider mentors and support groups ▪ Validate accomplishments with meeting the goals of the plan of care
Inclusiveness	▪ Respect and welcome the client's experience ▪ Commend family, outreach workers, and community advisory boards for their contributions to the client's care ▪ Ensure community participation represents the clients of the practice/center
Cultural Issues	▪ Respect culture and ethnicity ▪ Employ translators as needed ▪ Provide culturally appropriate health education and guidance
Change	▪ Help clients to understand needed lifestyle changes to support health and well-being

fort between providers, clients, families, community and other stakeholders. All contributions will be welcomed and encouraged.[20] This collaboration will lead to empowerment for the client and accountability by staff. Interactions with peers, whether clients or staff, is essential to develop mentors, build strengths, and retain staff.[15] Resilience is developed by seeking connections, support in the family or community, and celebrating accomplishments or adherence rates.[15] Furthermore, a trauma-informed organization fosters a community sense of belonging and acceptance for PLWH by including all stakeholders on advisory boards. Everyone's input is respected; all information is important.[15]

Cultural competence is a foundation of any trauma-informed approach.[15] Knowing the historical background of the culture will assist in developing empathy and the ability to acknowledge the trauma faced by clients and staff. Advocating for translators and providing cultural education will assist with providing appropriate care. Finally, change is an ever-present principle of TIC, and needed for programs to commit to adopting a trauma-informed approach that is responsive to the needs of clients and staff.[15]

Summary

Care of individuals infected and affected by HIV is challenging. The primary goal of incorporating TIC into an organization's culture is to improve the health and well-being outcomes of the clients. A trauma-informed approach to planning care offers clients security, opportunities for optimizing growth, development and healing, and aims to support resilience, prevent additional trauma, and promote stabilization. Additionally, this approach will support the practice and reduce the stress of staff working within the system.[13,8] ❖

continued on page 34

References

1. National Child Traumatic Stress Network. "Defining trauma and child traumatic stress." 2014. Retrieved from http://www.nctsnet.org/content/defining-trauma-and-child-traumatic-stress
2. National Scientific Council on the Developing Child. "Excessive stress disrupts the architecture of developing brain: Working paper #3." 2005, updated 2009. Retrieved from http://www.developingchild.net
3. Centers for Disease Control and Prevention. "Adverse childhood experiences (ACE) study." 2013. Retrieved from http://www.cdc.gov/ace/
4. Kiecolt-Glaser JK, Gouin JP, Weng N, Malarkey WB, Beversdorf DQ, Glaser R. "Childhood adversity heightens the impact of later-life caregiving stress on telomere length and inflammation." *Psychosomatic Medicine*. 2011; 73(1):16–22. http://doi.org/10.1097/PSY.0b013e31820573b6
5. Fitzpatrick A, Kronmal R., Gardner J, Psaty B, Jenny N, Tracey R, Walston J, Kimura M, Aviv A. "Leukocyte telomere length and cardiovascular disease in the cardiovascular health study." *American Journal of Epidemiology*. 2007; 165(1):14-21. doi: 10.1093/aje/kwj346
6. Buxton J, Walters R, Visvikis-Siest S, Meyre D, Froguel P, Blakemore A. "Childhood obesity is associated with shorter leukocyte telomere length." *The Journal of Clinical Endocrinology and Metabolism*. 2011; 96(5):1500-1505. doi: http://dx.doi.org/10.1210/jc.2010-2924
7. Drury SS, Mabile E, Brett ZH, Esteves K, Jones E, Shirtcliff EA, Theall KP. "The association of telomere length with family violence and disruption." *Pediatrics*. 2014; 134(1): e128 DOI: 10.1542/peds.2013-3415
8. Van der Kolk, B.A. Developmental trauma disorder: Towards a rational diagnosis for children with complex trauma histories. *Psychiatric Annals*. 2005;35(5):401-408
9. Briere J, Scott C. *Principles of trauma therapy: A guide to symptoms, evaluation and treatment*. Thousand Oaks: Sage, 2006.
10. Centers for Disease Control and Prevention. "Adverse childhood experiences reported by adults – Five states, 2009." *MMWR*. 2010;59(49):1609-1613.
11. Aaron E, Criniti S, Bonacquisti A, Geller P. "Providing sensitive care for adult HIV-infected women with a history of childhood sexual abuse." *Journal of the Association of Nurses in AIDS Care*. 2013;24:355-367
12. White House Office of National AIDS Policy. "National HIV/AIDS Strategy for the United States: Updated to 2020." 2015. Retrieved from https://www.aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf
13. Harris M, Fallot R. (Eds.). *Using trauma theory to design service systems*. New directions for mental health services. San Francisco: Jossey-Bass, 2001.
14. Department of Health and Human Services. "HHS Strategic Plan (2010-2015)". 2011 Retrieved from http://www.hhs.gov/secretary/about/stratplan_fy2010-15.pdf
15. Substance Abuse and Mental Health Services Administration/National Center for Trauma Informed Care. *"Trauma informed approach."* 2014. Retrieved from http://beta.samhsa.gov/nctic/trauma-interventions
16. Cohen J, Scheid J, Gerson R. "Transforming trajectories for traumatized children." *Journal of the American Academy of Child and Adolescent Psychiatry.* 2014; 53(1):9-13.
17. Conners-Burrow N, Kramer T, Sigel B, Helpenstill K, Sievers C, McKelvey L. *"Trauma-informed care training in a child welfare system: Moving it to the front line."* Children and Youth Services Review. 2013;35(11):1830-1835. Retrieved from http://dx.doi.org/10.1016/j.child/youth.2013.08.013
18. Borckardt J, Madan A, Grubaugh A, Danielson C, Pelic C, Hardesty S, et al. *"Systematic investigation of initiatives to reduce seclusion and restraint in a state psychiatric hospital."* Psychiatric Services. 2011; 62(5):477-483.
19. Chen Y, Fetzer S, Lin C, Huang J, Feng J. "Healthcare professionals' priorities for child abuse educational programming: A Delphi study." *Children and Youth Services Review.* 2013;35(1):168-173.
20. Fallot R, Harris M. "Proceedings from Community Connections: *Creating Cultures of Trauma-Informed Care (CCTIC)*." 2009. Washington, D.C. Retrieved from http://sfbhn.org/misc%20pdf/Fallot%20Tool%20Explanation%20TIC.pdf

Ryan White Part D

HIV Case Study Day

AND New Jersey Department of Health (NJDOH)-Division of HIV, STD and TB Services

Perinatal Update

Michelle Thompson, Program Manager
François Xavier Bagnoud Center, School of Nursing, Rutgers The State University of New Jersey

Above: Dr. Warren Y.K. Ng, pictured at right, Joanne Phillips, RN, MS. Photos: Karen A. Forgash

On October 6, 2015, the NJDOH, François Xavier Bagnoud Center, Rutgers School of Nursing, Ryan White Part D Family Centered HIV Care Network and the Rutgers Biomedical and Health Sciences Center for Continuing and Outreach Education hosted the Ryan White Part D HIV Case Study Day and NJDOH Perinatal Update at Rutgers Robert Wood Johnson Clinical Academic Building in New Brunswick, NJ. There were 75 clinicians in attendance.

Dr. Warren Y.K. Ng, Associate Professor of Psychiatry at Columbia University Medical Center gave the keynote address entitled ***Pregnant Women Living with HIV and Mental Health Issues***. Dr. Ng's presentation focused on risk factors, safe pregnancy, effective HIV and mental health care, FDA categories for treatment, psychiatric treatment considerations and the importance of maintaining an ongoing relationship with the mother in postpartum.

Additional presentations and case studies were presented. Joanne Phillips, RN, MS François Xavier Bagnoud Center, Rutgers School of Nursing presented on the ***NJDOH Access to Reproductive Care and HIV Services (ARCH) Nurses In Harm Reduction Programs***. Ms. Phillips gave an overview of the target population, public health goals and the various services provided by the ARCH program. She also identified the locations of the programs and introduced the nurses who staff each site.

Kimberly Connolly, LCSW from Jersey Shore University Medical Center presented ***Preconception Counseling for Women and Men Living with HIV: Cultural and Psychosocial Challenges*** focusing on examining the historical evolution that has led to common attitudes towards sexuality and reproduction and how the current day culture impacts health experiences and behaviors profoundly in the area of reproductive health and family planning. Ms. Connolly outlined alternative approaches that will assist clinicians to provide effective preconception counseling and care to clients.

Gail Burack, PhD, Robert Wood Johnson AIDS Program, Rutgers Robert Wood Johnson Medical School led the group in a discussion of cases on pregnant women with HIV and mental health issues.

Presentation slides can be viewed until March 1, 2016 on the François Xavier Bagnoud Center (FXB) FXB Center website at: http://www.fxbcenter.org/education/CE-16HH15.html.

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HIV, STD, and TB news and information for health professionals

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Northeast/Caribbean AETC Cervical Pap Test Training Program for Clinical Providers http://www.nynjaetc.org/on-demand/cervicalpapprogram.html or (212) 304-5530

Northeast/Caribbean AETC Online training and education for healthcare professionals providing care and services for people living with HIV, the first online learning module is Hepatitis C Medications and Special Considerations for People Living with HIV. https://learn.nynjaetc.org/accounts/login/?next=/

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- NJ HIV/AIDS statistical reports, regulations, forms, and links to HIV care, prevention programs, and training
- New Jersey rapid testing site: www.state.nj.us/health/aids/rapidtesting
- New Jersey AIDS/STD Hotline: (800) 624-2377

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- HIV/AIDS MEDICAL UPDATE SERIES: with funding from NJDHSS
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- National Coordinating Resource Center: www.aidsetc.org
- Northeast/Caribbean AETC: www.nynjaetc.org
- Clinician Consultation Center: http://www.nccc.ucsf.edu/
  Warmline: (800) 933-3413
  Post-Exposure Prophylaxis Hotline/PEPline: (888) 448-4911
  Perinatal HIV Hotline: (888) 448-8765

AIDSinfo: a service of the U.S. Department of Health and Human Services, offers access to the latest, federally approved HIV/AIDS medical practice guidelines, HIV treatment and prevention clinical trials, and other research information. http://www.aidsinfo.nih.gov/

AIDS InfoNet: HIV treatment fact sheets in English and 10 other languages. www.aidsinfonet.org

U.S. National Institutes of Health: a registry and results database of publicly and privately supported clinical studies conducted around the world. http://clinicaltrials.gov

Centers for Disease Control and Prevention (CDC): http://www.cdc.gov/hiv/default.html

Health Resources and Services Administration (HRSA): http://www.hrsa.gov

FDA MedWatch: (800) FDA-1088; Subscribe to **e-bulletin:** www.fda.gov/medwatch/elist.htm

HealthHIV: Advances effective prevention, care and support for people living with, or at risk for, HIV by providing education, capacity building, health services research, and advocacy. http://www.healthhiv.org/index.php

National Quality Center: no-cost, technical assistance for Ryan White funded grantees to improve the quality of HIV care nationwide. www.nationalqualitycenter.org

TARGET Center: technical assistance and training resources for the Ryan White community. www.careacttarget.org

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