Human Papillomavirus (HPV) in HIV-infected Latinas

Amneris E. Luque, M.D.
Professor of Medicine/Infectious Diseases
UT Southwestern/PHHS
Disclosures

- I have no disclosures for this presentation
Objectives

- Describe the epidemiology of HPV Infection in HIV-infected women.
- Outline the impact of HIV on HPV infection.
- Discuss the current cervical cancer screening guidelines.
- Outline strategies to prevent cervical cancer.
Human Papillomavirus (HPV)

- More than 150 types identified
- 40 types can infect the cervix
- 12 carcinogenic HPV types
  - HPV 16 (50-55%) & 18 (10-15%) account for majority of invasive cervical cancer cases worldwide

Bosch FX et al Vaccine 2008
Schiffman M et al; JNCI 2011
HPV Infections in the US

- There are more than 14 million new HPV infections annually.

- It is estimated that 50% of sexually active men and women will get HPV at some point in their lives.

- Almost 50% of new infections occur in women ages 15-24.
HPV Infection and Cancer

- There are more than 150 strains of HPV, more than 40 strains can cause cancer.

- In particular, HPV is related to almost 100% of cervical cancer cases, with two strains (16 and 18) related to approximately 70% of cervical cancer cases.

- Cervical cancer in HIV-infected women: 26/100,000 (compared to 6/100,000 HIV-uninfected women)
HPV Infection and Cancer

- Persistent infection with oncogenic HPV types can lead to cervical dysplasia and precancerous lesions.

- Cervical cancer is the third most common cancer in women worldwide. Virtually all cervical cancers are attributable to HPV.

- Cervical cancer mortality is an avoidable cause of death and marker of health disparities.
Based on this model, a woman with a normal Pap smear and no oncogenic HPV should have low risk of cervical precancer/cancer for several years—Regardless of HIV Status.
HPV-Associated Cancers

Annual number of cases worldwide

- Cervix
- Anus
- Vagina/Vulva
- Penis
- Mouth
- Throat
Number of new HPV–associated cancers overall, and by sex, in the US, 2009

Total (N = 34,788)
- Oropharynx: 32.7% (n = 11,388)
- Anus: 9.3% (n = 3,242)
- Cervix: 15.6% (n = 5,434)
- Vagina: 2.9% (n = 1,001)
- Vulva: 2.1% (n = 734)
- Penis: 37.3% (n = 19,344)

Men (N = 13,446)
- Oropharynx: 14.4% (n = 1,934)
- Anus: 7.4% (n = 1,001)
- Cervix: 53.4% (n = 7,051)
- Vagina: 3.4% (n = 734)
- Vulva: 16.4% (n = 3,500)
- Penis: 37.3% (n = 19,344)

Women (N = 21,342)
- Oropharynx: 15.2% (n = 3,242)
- Anus: 11.6% (n = 2,478)
- Cervix: 78.2% (n = 16,388)
- Vagina: 3.4% (n = 734)
- Vulva: 53.4% (n = 11,388)
- Penis: 37.3% (n = 19,344)

National Program of Cancer Registries and Surveillance, Epidemiology, and End Results areas reported by the North American Association of Central Cancer Registries.
Age-adjusted Incidence Rates for HPV-associated Cervical Cancer by Race Ethnicity

HPV in Latinas

- Latinas in the US have higher rates of cervical cancer than women in other racial/ethnic groups (incidence 50% and death 70% higher than non-Hispanic whites).

- Among Latinas there is low knowledge about cervical cancer, HPV and HPV vaccines.

- Inconsistent beliefs about susceptibility to HPV infection and cervical cancer.

- Concerns about vaccination/Cost of the vaccine/Availability of insurance coverage.
HIV in Hispanics/Latinos

- Hispanics/Latinos are disproportionately affected by HIV.
- 7 in 10 new HIV diagnoses among Hispanics/Latinos occur in gay and bisexual men.
- Less than half of Hispanics/Latinos with HIV are receiving ARV medications to treat their infection.

HIV in Hispanics/Latinos

- In 2013, Hispanics/Latinos accounted for 23% (10,888) of the estimated 48,145 new diagnoses of HIV in the USA.
  - 85% men (9,266)
    - 81% (7,527) in MSM
  - 15% in women (1,610)
    - 86% (1,389) were attributed to heterosexual contact
Effect of HIV on HPV

- HIV-infected women have a greater persistence of HPV infection.

- Association of persistent HPV comparing HIV-infected and HIV-uninfected women
  - Any HPV type: 2 to 6
  - HPV types: 16 & 18: 6

Sun, XW et al : NEJM 1997
Human immunodeficiency virus type 1 (HIV-1)—infected women grouped according to HIV-1 RNA plasma level (> or <10,000 copies/mL) and percentages of each group with positive tests for high-risk human papillomavirus DNA types.


© 1999 by the Infectious Diseases Society of America
Percentage of human immunodeficiency virus type 1 (HIV-1)—infected women with abnormal Pap smears according to HIV-1 RNA plasma levels (> or < 10,000 copies/mL).

$P = .01$

Cervical Cancer Risk Increases with Immunosuppression in HIV-infected Women

Abraham AG J AIDS 2013;62:405-413
Human papillomavirus (HPV) genotype occurrences in 480 cervicovaginal lavage specimens from 202 HIV-infected women attending the University of Rochester’s AIDS Center, 1996–2003.


© 2006 by the Infectious Diseases Society of America
Abnormal Pap Rates in HIV-infected Women

Cumulative risk of any abnormal cytology after >10y was 77% among HIV+s and 50% among HIV-s

Cumulative risk of HSIL was 4% in HIV-infected women and 1% in HIV uninfected women

Massad LS 2008 Am Obs Gyn
Effect of HIV on HPV

- HIV-infected women have:
  - Greater diversity of HPV types
  - Greater prevalence of multiple HPV types
  - Greater preponderance of oncogenic types other than HPV 16 and 18
  - Higher prevalence rates of LSIL and HSIL
  - More rapid progression rates
  - Lower rates of spontaneous regression
  - Higher persistence/recurrence rates following treatment
Effect of HAART use on HPV

- HAART Initiation in adherent HIV-infected women
  - Reduced prevalence of oncogenic HPV by 40%
  - Reduced incidence of oncogenic HPV by 50%
  - Increased clearance of HR-HPVSIL by 235%

- Benefits are less among non-adherent women

- HAART use may reduce cervical cancer risk

Minkoff H. JID 2010;201:680-690
Proportion of SIL by Year for Premenopausal and Menopausal HIV-infected Women

Effect of HAART and Menopause on the Risk of Progression of Cervical Dysplasia in HIV-infected Women

- Women receiving HAART had a 52% reduced risk in the progression to SILs compared to women receiving any other antiretroviral regimen or no regimen (CI: 0.33–0.70, P = 0.0001).
- A greater increase of CD4+ cell counts was associated with a greater reduction on the risk of progression to SILs.
- Menopausal women had a 70% higher risk of progression to SILs than premenopausal women (CI: 1.11–2.62, P < 0.0001), adjusting for HIV medications, CD4+ count, duration of HIV infection, moderation effect of menopause by age, prior IV drug use, and smoking.

Effect of HAART and Menopause on the Risk of Progression of Cervical Dysplasia in HIV-infected Women

- HAART reduces the risk of progression to SILs in HIV-infected women.

- Menopause is a risk factor to the progression to SILs. HIV-infected women who reach menopause early have higher risk of progression to SILs.

HPV-Associated Cervical and Anal Diseases in HIV-Infected Women

- HIV-infected women
  - High risk of cervical (RR = 5.4; 95% CI: 3.9-7.2) and anal cancer (RR = 6.8; 95% CI: 2.7-14)

- Potential for increase in disease burden
  - Living longer on ARVT
  - Potentially longer duration of HPV persistence
  - Increasingly entering the age groups in which cervical cancer rates reach their peak
Cervical Cancer Screening Guidelines in Sexually Active HIV-infected Women

- Pap test twice the first year after HIV diagnosis or entry to care
  - If both Pap tests are normal, then annual screening with Pap
  - If abnormal, follow-up will depend on the abnormality
- **Refer to colposcopy if:**
  - ASCUS (Atypical squamous cell of undetermined significance)
  - ASC-H (Atypical squamous cells-cannot exclude high grade)
  - AGC (Atypical glandular cells)
  - LSIL (Low-grade squamous epithelial lesion)
  - HSIL (High-grade squamous epithelial lesion)
## Cervical Cancer Screening Guidelines

<table>
<thead>
<tr>
<th></th>
<th>USPSTF/ACS/ASCCP Women without HIV</th>
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<tr>
<td><strong>Age at initiation</strong></td>
<td>21, regardless of risk factors</td>
<td>Onset of sexual activity</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age: 21-29</td>
<td>Pap every 3 years</td>
<td>Annually</td>
</tr>
<tr>
<td>Age: ≥30</td>
<td>Pap q/3 years OR Pap + HPV “co-testing” q/5 years</td>
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<tr>
<td><strong>Discontinuation</strong></td>
<td>Age 65</td>
<td>Never</td>
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<tr>
<td>S/P Hysterectomy</td>
<td>D/C if for benign reasons AND no history of CIN 2+ for 20 years; otherwise screen for 20 years after</td>
<td>Same (?)</td>
</tr>
<tr>
<td>HPV Vaccinated</td>
<td>No change</td>
<td>No change</td>
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Impact of Serial negative Paps in HIV-infected Women

- Among 942 HIV-infected women with negative Pap, high grade CIN developed in:
  - 1% within 15 months, 4% within 39 months

- After 3 negative Paps, precancer developed in:
  - 0% after 15 months, 2% after 39 months
  - No cancers

- Consider 3-yr screening intervals if persistently Pap negative

Masad, LS et al Obstet Gynecol 2012;120:791-797
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### Role of HPV Testing

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<th>General Population</th>
<th>HIV-infected Women</th>
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<tr>
<td><strong>USPSTF</strong></td>
<td><strong>CDC/HHS/IDSA</strong></td>
</tr>
<tr>
<td>• Triage ASCUS Result</td>
<td>• “Role of HPV testing for management of HIV-infected women not established”</td>
</tr>
<tr>
<td>• Co-test with Pap ≥30y</td>
<td>• ASCCP</td>
</tr>
<tr>
<td>• Post-menopausal women LSIL</td>
<td>• Triage ASCUS Result</td>
</tr>
<tr>
<td>• Follow-up after Colpo or Treatment procedure (LEEP/CONE) per guidelines</td>
<td>• There is data in HIV-infected women</td>
</tr>
<tr>
<td></td>
<td>• Triage ASCUS Result</td>
</tr>
<tr>
<td></td>
<td>• Co-Test with Pap</td>
</tr>
</tbody>
</table>

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HPV Reflex Testing Potentially Useful in Triage of ASCUS in HIV-infected women

<table>
<thead>
<tr>
<th>Colpo and Histology Results</th>
<th>YES</th>
<th>No</th>
<th>Inadequate</th>
<th>% HPV +</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;CIN 2 (n=116 controls)</td>
<td>35</td>
<td>62</td>
<td>19</td>
<td>36</td>
</tr>
<tr>
<td>CIN 2+ (n=24)</td>
<td>16</td>
<td>1</td>
<td>7</td>
<td>94</td>
</tr>
</tbody>
</table>

**Sensitivity** 94%

**Specificity** 64%

- HPV testing in women with ASCUS followed biannually for 8 years
- High sensitivity and moderate specificity of HPV testing indicate that few CIN 2+ cases would be missed and colposcopy would be avoided in the ~2/3 of women with ASCUS who do not have CIN2+

D’Souza G et al., AIDS 2014;28:1696-1698
# Cervical Cancer Screening Guidelines

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<td><strong>Age at initiation</strong></td>
<td>21, regardless of risk factors</td>
<td>Within 1 year of onset of sexual activity</td>
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<tr>
<td>Age: 21-29</td>
<td>Pap every 3 years</td>
<td>Pap smears at initial HIV dx and if normal repeat in 6-12 months. If 3 consecutive Paps are normal repeat q/3y</td>
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<td>Pap test only or Pap +HPV co-testing acceptable. Initial and 6-12 m Paps, then Pap smears q/3 years if previous 3 consecutive Paps are negative. If Pap normal but HPV + Repeat co-testing in 1 year. If Pap abnormal-&gt; colpo</td>
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Considerations in Pregnant Women

- Pap smear recommended on initial pre-natal visit unless normal within the year.
- Can defer colposcopy for ASCUS and LSIL until 6 weeks post-partum.
- Immediate Colposcopy for HSIL or AGC.
- Treatment of CIN not recommended unless invasive disease expected.
- Invasive cancer affects management, timing, route of delivery.
- HPV vaccination not recommended during pregnancy.
HPV in Latinas

- Knowledge gap among HPV-unvaccinated women.

- Educational interventions for at-risk women needed.
  - Cost-effective campaigns that transcends differences.
  - Education by lay health workers, peers and other trusted community members.
  - Delivery of vaccination in non-traditional delivery sites.
Social, Economic Environment Fostering Disparities

- Classism
- Racism
- Fatalism
- Under-resourced or rural areas

Violence Against Women
Sexual, physical, psychological abuse (coercion/control)

Mechanisms
- ↓ Poverty
- ↓ Education
- ↓ Employment options
- ↓ Insurance
- ↓ Transportation opt.
- ↓ Self agency/control
- ↑ Smoking/drug use
- ↑ Stress
- ↓ Coping/social support
- ↑ PTSD, depression
- ↑ Disabilities
- ↑ Comorbid conditions

Cancer Care
- Delayed screening
  - ↓ Later stage at diagnosis
  - ↓ Suboptimal Treatment (including palliative care)
  - ↓ Quality of life
  - ↓ Survival
Prevention of Cervical Cancer

- You may reduce your risk of cervical cancer if you:
  - Use a condom every time you have sex to reduce your risk of contracting HPV.
  - Delay first intercourse.
  - Have fewer sexual partners.
  - Avoid smoking.
  - Get vaccinated against HPV.
  - Get regular Pap tests screenings.
Three-dose HPV Vaccine Coverage among Girls (13-17) by State in the US, 2010

Thank You