Online Learning Module: HIV and Cervical Cancer
Course Objectives

• Describe the effect of HIV infection on HPV infection and HPV-related cervical neoplasia
• Describe the mechanism for the effect of HIV on HPV infection and HPV-related cervical neoplasia
• Discuss management issues of HIV-infected women with HPV infection or HPV-related cervical neoplasia
Invasive Cervical Cancer

- Worldwide – 2nd most common female cancer
- ~500,000 new cases & ~275,000 deaths per yr
- >80% new cases/deaths in developing nations
- Sub-Saharan Africa – Most common ♀ cancer
- 20% of deaths occur in sub-Saharan Africa
- Zambia: 2nd highest incidence in Africa, 6th highest incidence in the world (61.1/100,000)
Global cervical cancer mortality

Age Standardized Mortality Rates (ASR) (All ages)
Human Papillomavirus (HPV)

- The causative agent of cervical cancer
- Double stranded DNA virus
- >130 genotypes
- >30 genotypes infect the lower genital tract
- Grouped into low and high risk depending on malignant potential
- Virus integrates into host cell genome
HIV/AIDS

• Single greatest reversal in human development in modern history
• 25 million deaths from HIV-related causes over 27 years
• Reduced life expectancy by 20 years, slowed economic growth, deepened household poverty
• 2007: 33 million PLWA; 2.7 million new infections; 2 million people died of HIV-related causes
• Number of new infections 2.5x’s higher than increase in number of people on ARVs
HIV/AIDS in women

• ~17.5 million women living with HIV/AIDS
  – 60% reside in Africa
• >85% live in developing nations
• 95% of deaths occur in developing countries

Global prevalence of HIV Infection (2007)
HIV/AIDS in Africa

- Sub-Saharan Africa most heavily affected by HIV: 67% of all PLWA and 75% of all AIDS deaths in 2007
- Orphaned 12 million children in sub-Saharan Africa

Access to HAART

• More women now have access to highly active anti-retroviral therapy (HAART)
Number of people receiving antiretroviral drugs in low- and middle-income countries, 2002–2007

Source: Data provided by UNAIDS & WHO, 2008.
Risk factors for HIV Infection

- Early age of onset of sex
- Number of lifetime sexual partners
- Number of partners with multiple sex partners
- Presence of STIs
- Smoking
- Immune suppression

Protective factors: circumcision, condom use
Risk factors for HPV infection

• Early age at sexual debut
• Number of lifetime sexual partners
• Number of pregnancies
• Smoking
• Immune suppression
Effect of HIV on HPV infection

HIV-infected women have a greater prevalence of HPV infection

Range of HPV prevalence ratios: HIV+/HIV-

- N. America: 1.7 - 2.7
- S. America: 1.5 - 3.2
- Asia: 2.2 - 2.4
- Europe: 1.1 - 9.3
- Africa: 1.0 - 3.6

Effect of HIV on HPV infection

HIV-infected women have a greater persistence of HPV infection

Range of ratio of persistent HPV infection:
HIV+/HIV
- Any HPV type: 2.6 - 6
- HPV types 16 & 18: 6.5

HIV/AIDS and cervical intraepithelial neoplasia (CIN)

- Higher prevalence rates of LSIL and HSIL
- More rapid progression rates
- Lower rates of spontaneous regression
- Higher persistence/recurrence rates following treatment

Effect of HIV on HPV Infection

HIV-infected women have

- Greater diversity of HPV types
- Greater prevalence of multiple HPV types
- Greater preponderance of types other than HPV-16 and HPV-18
- Increased HPV viral load across spectrum of cytology
- Possible reactivation of obscure HPV types

HIV/AIDS and invasive cervical cancer

• AIDS-defining malignancy
• Onset ~10 years younger
• Higher progression rates
• Stage is more advanced
• Higher recurrence rates
• Overall poor prognosis
Impact of ART on HPV infection and cervical neoplasia

• High-risk HPV ➔ persistent, irrespective of CD4+ T-cell counts
• Debatable impact of ART on CIN progression/regression
• Insufficient data on ART impact on invasive cervical cancer
• Prolongs life expectancy
Mechanism for increased risk of HPV-infection and cervical neoplasia in HIV-infected women

- HIV-related immune suppression
- HIV-induced inflammatory responses
- Direct cancer growth (in-vitro)
- Other sexual behavior and STI cofactors

Management Issues

• High rate of recurrence/persistence of CIN-2,3 after treatment in HIV+ women
• Recurrence rate correlates with the level of immunosuppression
• However, treatment appears effective in preventing progression of CIN 2,3 to invasive cervical cancer

Tate 2001; Holcomb 1999; Wright 1994; Maiman1998; Pfaendler 2008; Hawes 2003
HPV-specific mechanisms that could facilitate HIV acquisition?

- Recruitment of CD4 cells
- Stimulation of cytokines that increase HIV transcription/replication
- Angiogenesis
- Loss of hemidesmosomes
**Ectocervix with HIV infection**

A) Abundant CD4+ T cells present in both epithelium and stroma.

**Ectocervix with no HIV infection**
Angiogenesis

• Colposcopic views of cervix

Normal

Cervical condylomata

Angiogenesis

- Colposcopic views of cervix

LGSIL

HGSIL

IHC analysis of blood vessels in cervical tissue

Normal

Invasive cancer

Detachment of epithelium from basement membrane

1. HIV-infected women are more likely to be infected with HPV.
   
   (a) True
   (b) False

2. HIV-infected woman with cervical cancer is said to have an AIDS-defining malignancy:
   
   (a) If her CD4 count is <200
   (b) If her CD4 count is <200 and her viral load is >50
   (c) Irrespective of her CD4 count and viral load
   (d) If her viral load is > 50
Evaluation Score

• Congratulations!
• You passed this evaluation with a score of __________

• Please click on the CERTIFICATE button below to print your certificate. Be sure to print & sign your name before submitting the certificate to your supervisor.
“Every woman has the right to live a life free from cervical cancer”