

Online Learning Module: HIV and Cervical Cancer

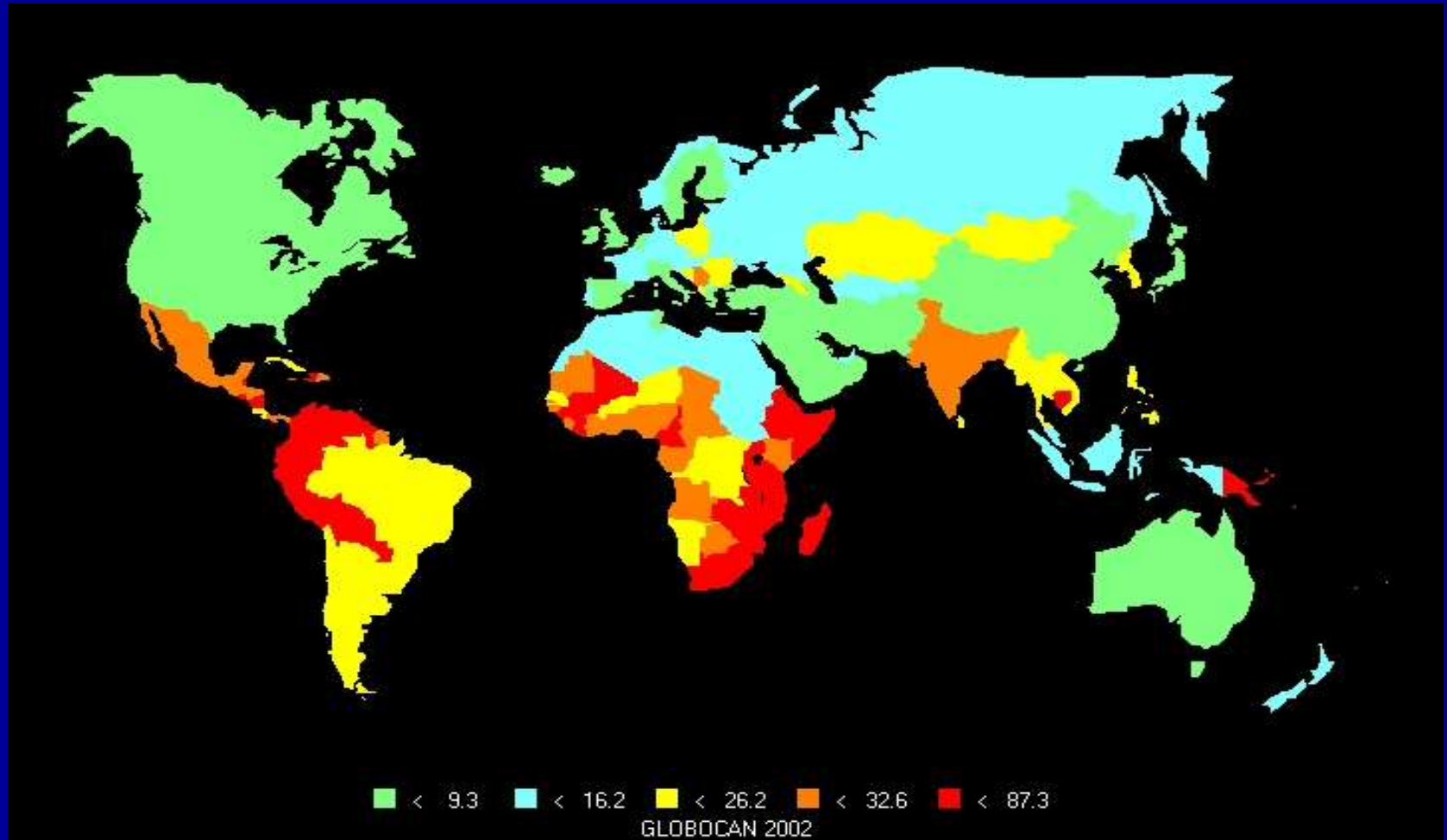
Course Objectives

- 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

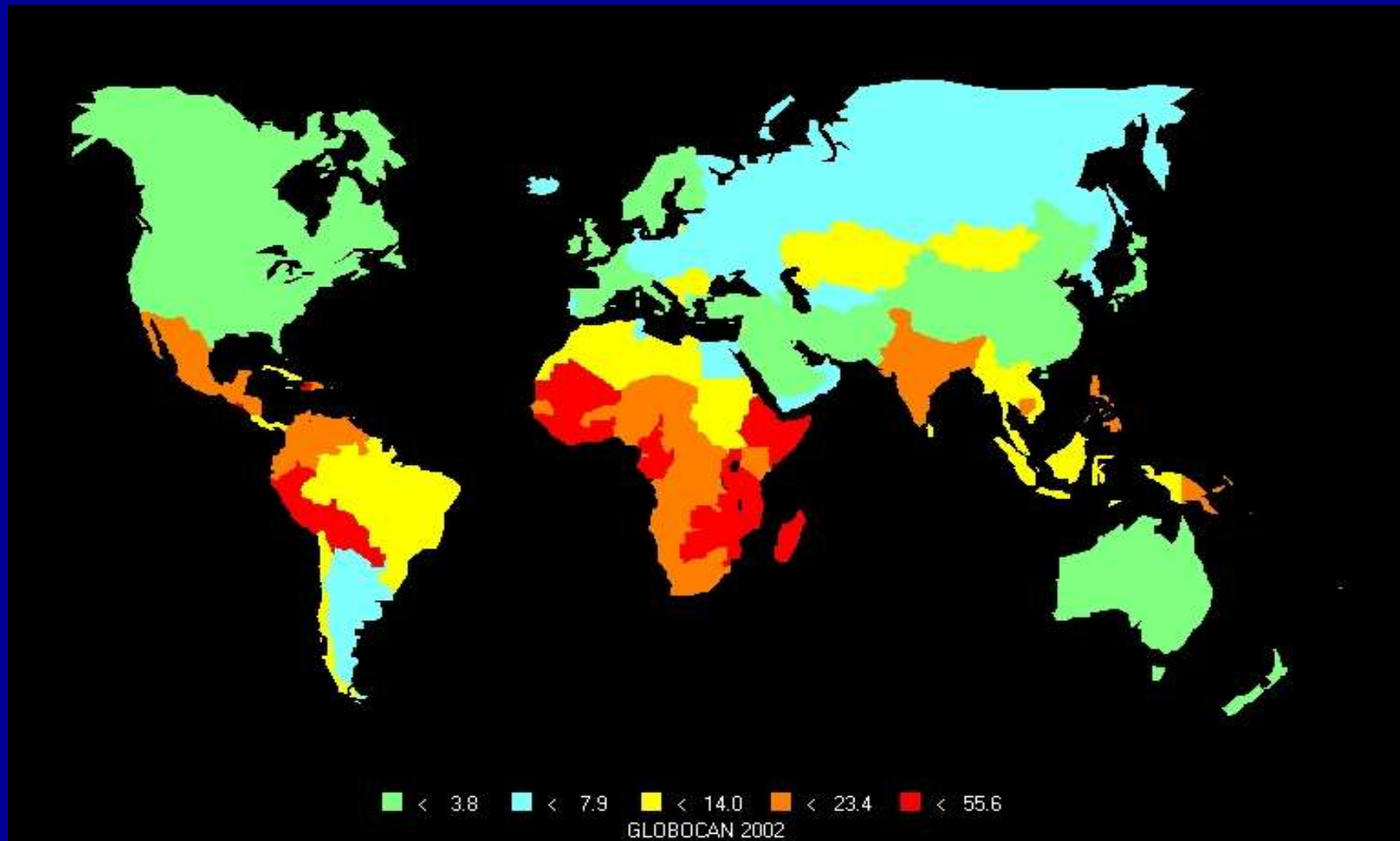
- Worldwide – 2nd most common female cancer
- ~500,000 new cases & ~275,000 deaths per yr
- >80% new cases/deaths in developing nations
- Sub-Saharan Africa – Most common ♀ cancer
- 20% of deaths occur in sub-Saharan Africa
- Zambia: 2nd highest incidence in Africa, 6th highest incidence in the world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

Global cervical cancer incidence



Age Standardized Incidence Rates (ASR) (All ages)

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

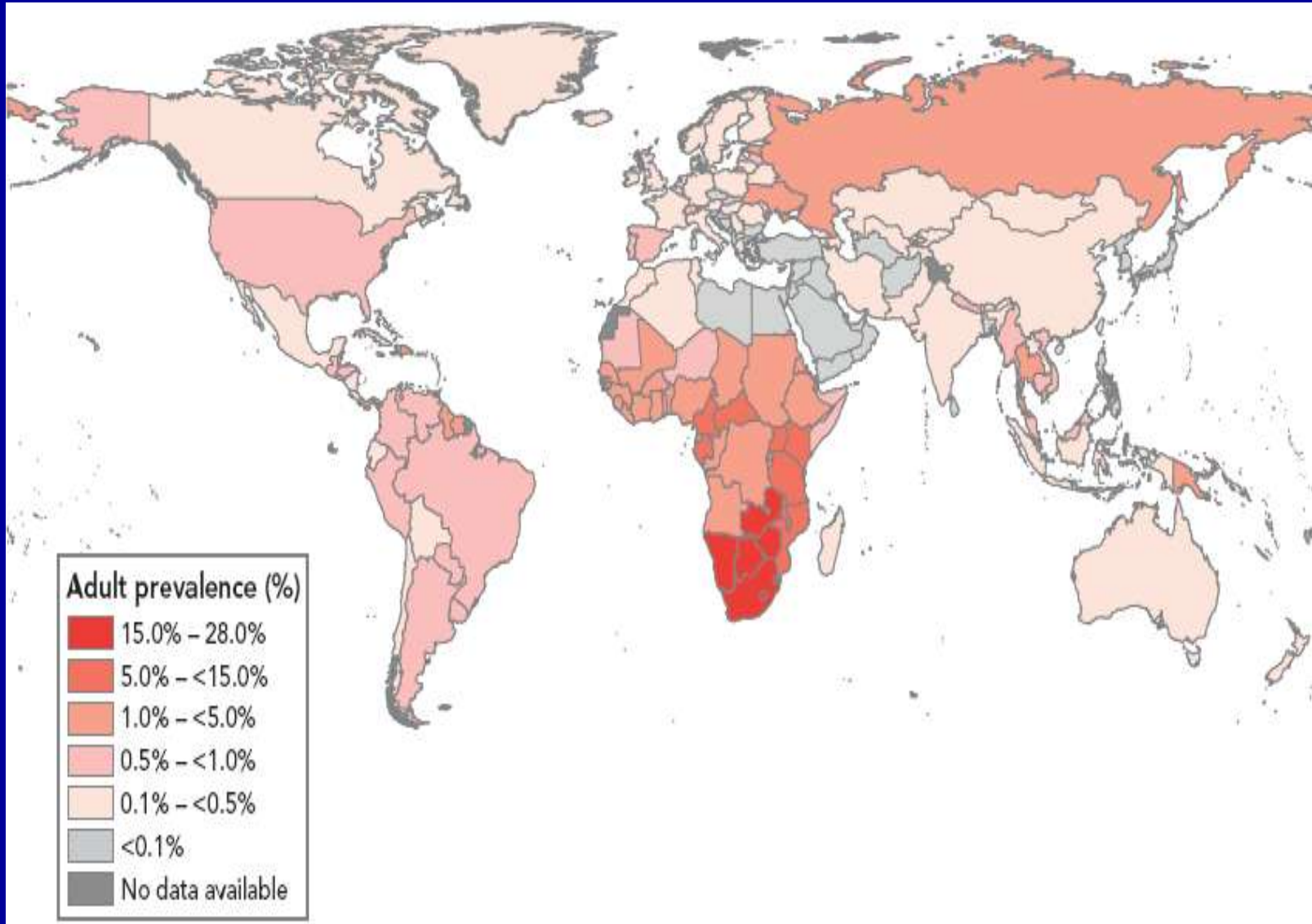
HIV/AIDS

- 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

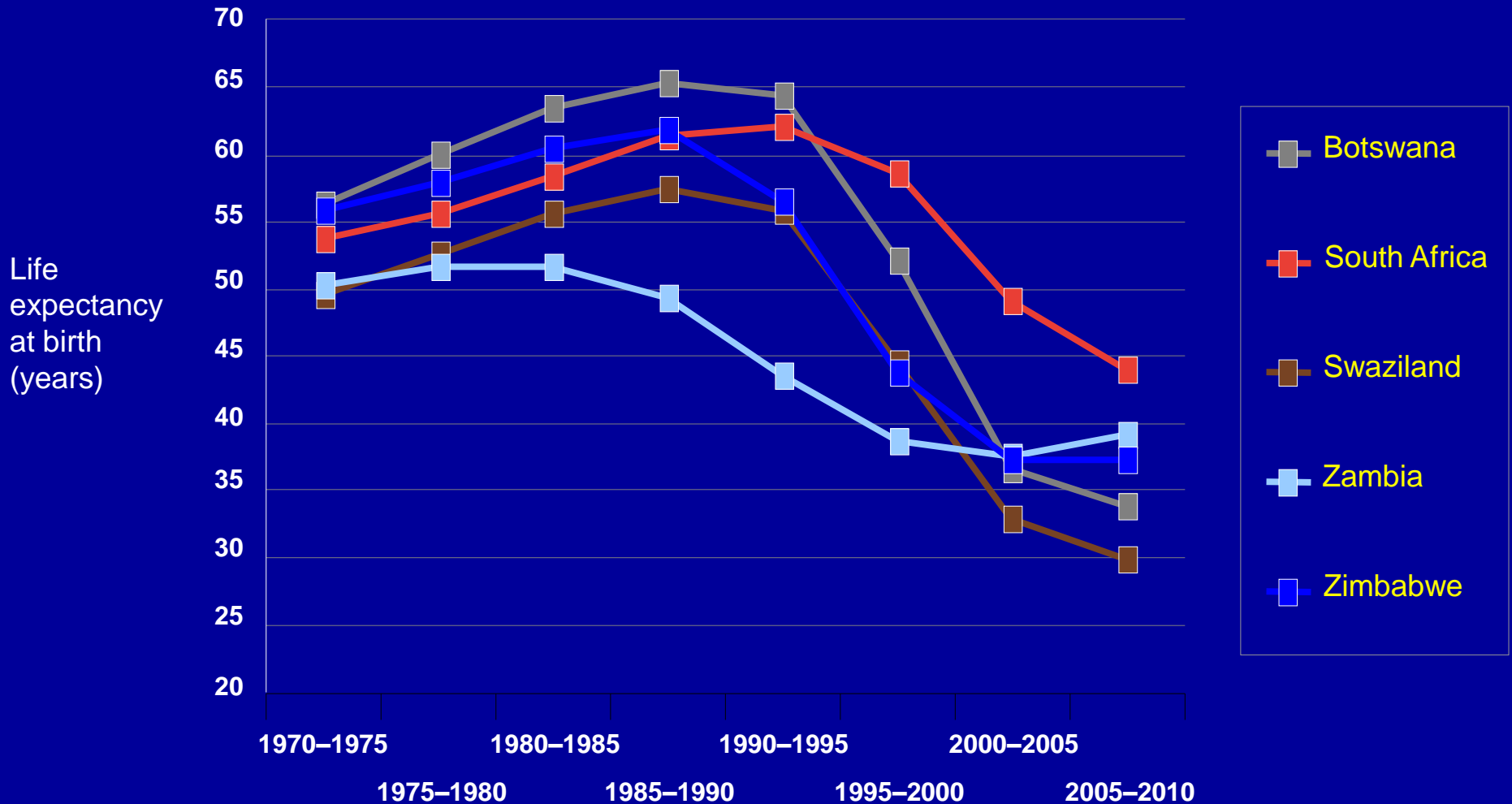
Global prevalence of HIV Infection (2007)



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

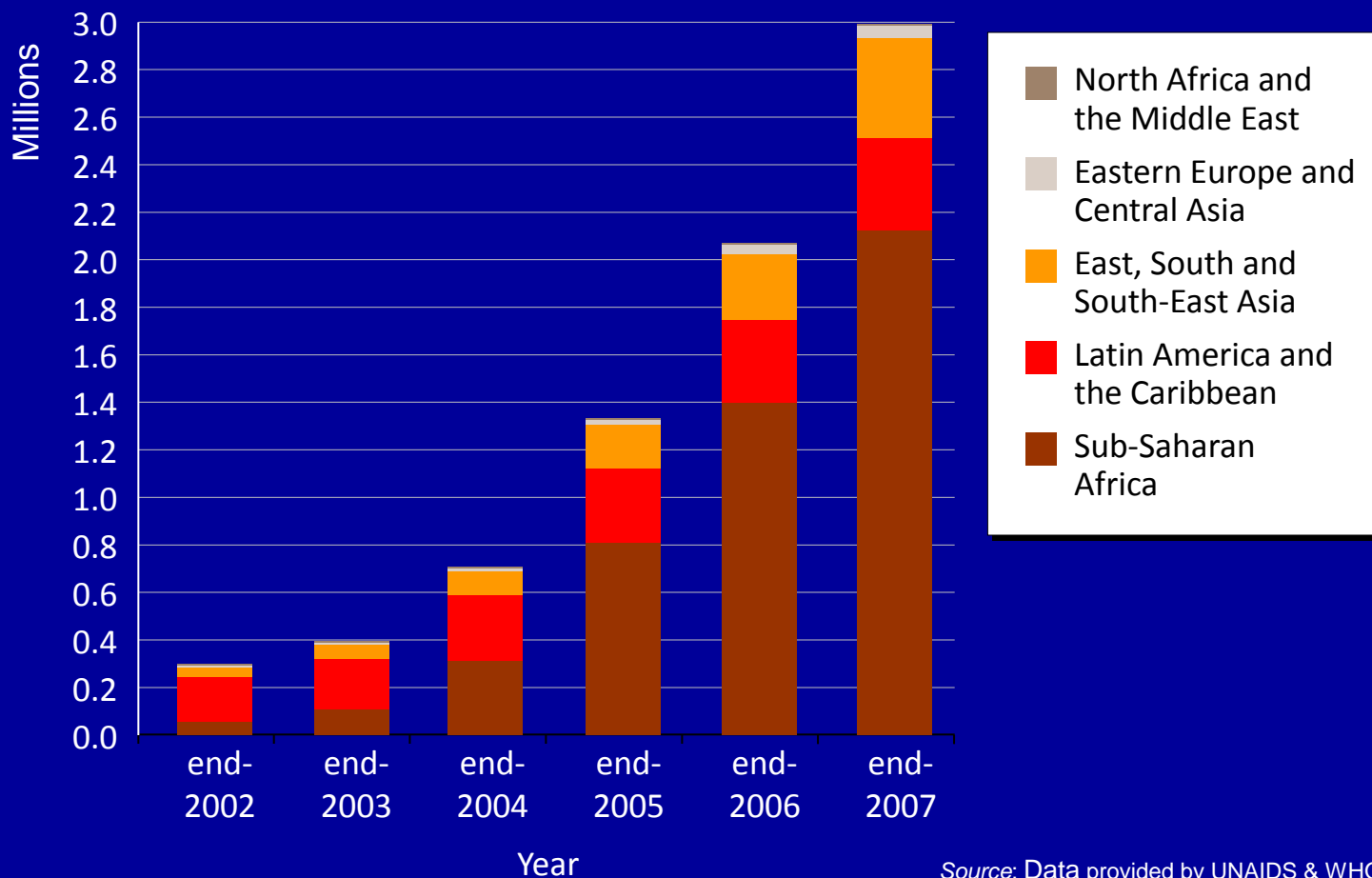
Impact of AIDS on life expectancy in five African countries, 1970–2010



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

Chaturvedi et al 2005, Watts et al 2005, Silverberg et al 2002, Jamieson et al 2002, Ellerbrock et al 2000, Moscicki et al 2000, Ahdieh et al 2000, Cu-Uvin et al 1999, Massad et al 1999, Palefsky et al 1999, Sun et al 1997, Queiroz et al 2004, Garzetti et al 1995, Petter et al 2000, Uberti-Foppa et al 1998, Miotti et al 1996, Temmerman et al 1999, Seck et al 1994, Hawes et al 2003, Chen et al 2005, Rugpao et al 1998, 10 other ref.

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

Selected Ref: Clifford et al 2006, Palefsky et al 1999, Ellerbrock et al 2000, Broker et al 2001, Sahasrabudde et al 2007, Strickler et al 2008, Womack et al 2000, Lefevre et al 2004, Serwadda et al 1999, Jamieson et al 2002, Serwadda et al 1999

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

Ref: Palefsky et al 1999; Jamieson et al 2002; Strickler et al 2005; Clarke & Chetty, 2002; Sun et al 1997; Ahdieh et al 2000; Lillo et al 2001, Dolei et al 1999; Vernon et al 1993; Strickler et al 2008; Broker et al 2001

Management Issues

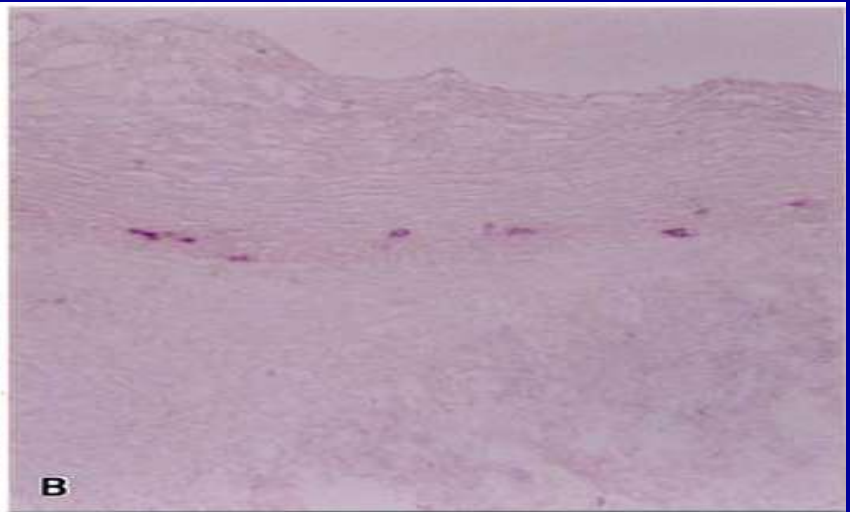
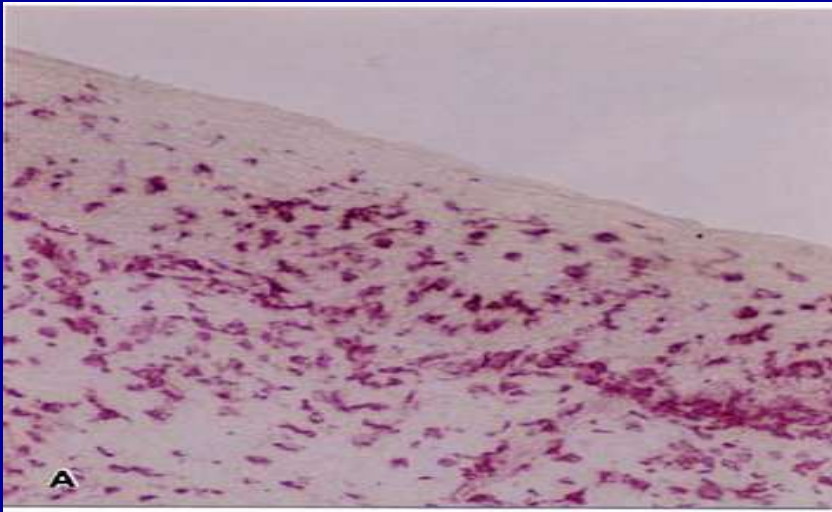
- High rate of recurrence/persistence of CIN-2,3 after treatment in HIV+ women
- Recurrence rate correlates with the level of immunosuppression
- However, treatment appears effective in preventing progression of CIN 2,3 to invasive cervical cancer

HPV-specific mechanisms that could facilitate HIV acquisition?

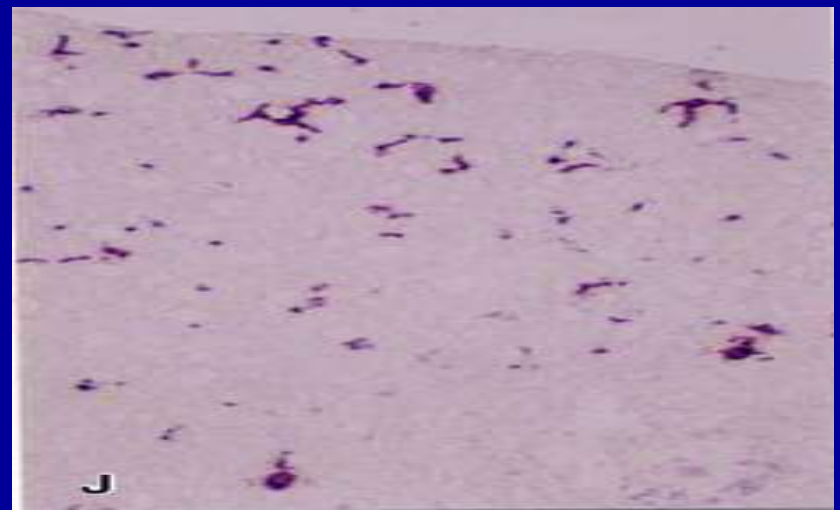
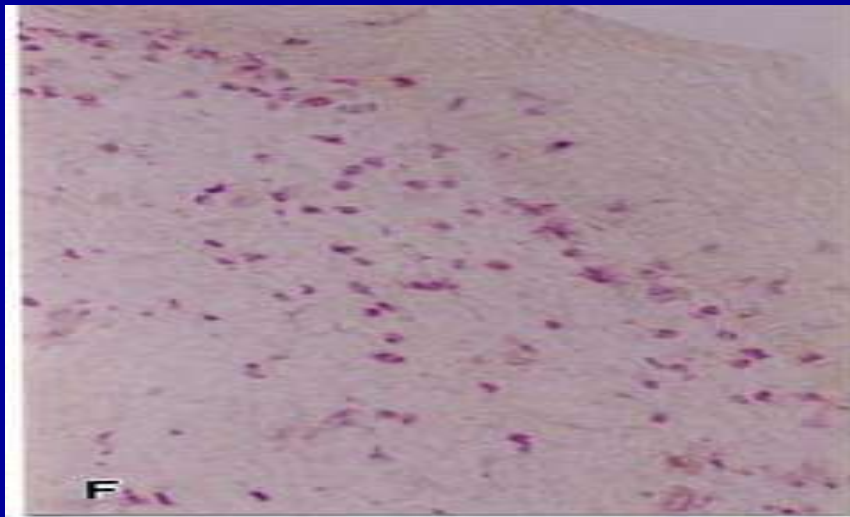
- Recruitment of CD4 cells
- Stimulation of cytokines that increase HIV transcription/replication
- Angiogenesis
- Loss of hemidesmosomes

Ectocervix with HIV infection

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



Ectocervix with no HIV infection

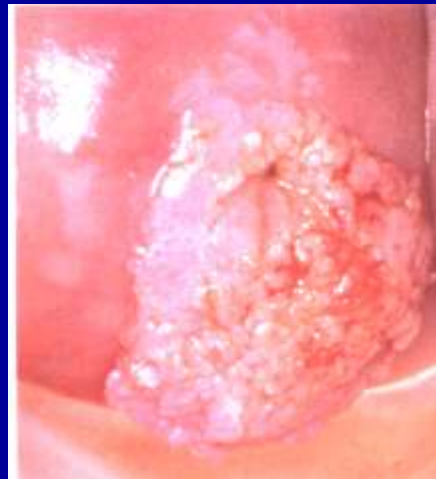


Angiogenesis

- 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



Evaluation – Page 1 of 2

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.

CERTIFICATE

“Every woman has the right to live
a life free from cervical cancer”

