

# HIV Infection and Women's Health Issues Throughout the Lifespan

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# Objectives

- Discuss considerations for HIV+ adolescent women
- Discuss issues relevant to HIV+ women of childbearing age
  - Contraception
  - Preconception care
  - Pregnancy
- Review general gynecologic care for HIV+ women
- Discuss special concerns in the HIV+ postmenopausal woman

# Case # 1:

- 36 yo P2012 HIV+ diagnosed 1990, current substance abuse
  - Long hx of nonadherence
  - Hx HSIL dating to 1998
    - S/P LEEP 5/99: diffuse HSIL, +margins
    - Pap 12/00 HSIL/CIS
  - Jan 2002: CD4 182; HIV-RNA 13,000; Hx PCP-on SMX-TMP only
    - Pap HSIL, Bx/ECC HSIL
    - Scheduled for cervical conization (CKC)-did not show

# Case # 1: continued

- Oct 2004: presentation to JH HIV WHP, recently resumed care and on ART (CD4186, HIV-RNA 271)
  - Pap HSIL, Bx LSIL, ECC HSIL, cannot R/O invasion
  - CKC 12/04: HSIL, + endocx margin, ECC no endocx tissue
- June 2005: doing well on ART, ND-VL since 12/04, CD4 390
  - Expresses interest in getting pregnant: preconception counseling given
  - Unprotected sex-counseled on condom use
  - Pap/ECC: HSIL, atyp keratinized squamous cells
- Aug 2005: scheduled for CKC
  - Preop visit: + UCG

# Case #1 (cont)

- October 2005: LEEP-HSIL, possible microinvasion
- March 2006: C-section at term; baby with Down syndrome
- June 2006: modified radical hysterectomy with no residual tumor
- Today: mother and baby doing well

# Adolescent Women and HIV

- Epidemiology: 85% of HIV due to high-risk sex; account for 43% of AIDS cases in 13-19 yr olds
- Developmental issues:
  - Puberty: earlier onset in girls; Tanner staging for ART dosing
  - Sexual activity: vulnerable to coercion and violence; adolescent females with highest age-specific rates of STDs; male partners often older; may have more limited ability to negotiate condom use
  - Denial/feelings of invulnerability: impact on condom use, adherence, contraception
  - Peer pressure/peer acceptance: disclosure
- Perinatally-infected women and pregnancy
  - Psychosocial problems
  - Frequent history of multiple ARV exposure
- Transition to adult care

# HIV and Fertility

- HIV appears to have an adverse effect on fertility in both symptomatic and asymptomatic women (16-55% decrease)
  - worsened prognosis with increased duration of infection
  - decreased pregnancy rate
  - increased pregnancy loss
- Desgrees 1999;Zaba 1998;Lee 2000;Glynn 2000;Gray 1998

# WHO Medical Eligibility Criteria for Contraceptive Use

- Category 1
  - Use method in any clinical circumstances
- Category 2
  - With clinical judgment, generally use method
  - With limited clinical judgment, use method
- Category 3
  - With clinical judgment, use of method not generally recommended unless more appropriate methods not available or acceptable
  - With limited clinical judgment, do not use method
- Category 4
  - Do not use method

# WHO: Contraceptive Categories

	COC/ P/R	CIC	POP	Depo- Prov	LNG- impl	CU- IUD	LNG- IUD
Hi risk	1	1	1	1	1	2	2
HIV	1	1	1	1	1	2	2
AIDS	1	1	1	1	1	3/2	3/2
ART	2	2	2	2	2	2	2
Rif	3	2	3	2	3	1	1

# Dual Protection

- Dual protection: Protection against pregnancy, HIV and other STDs
- Achieved by:
  - Avoidance of penetrative sex
  - Condom use alone
  - Dual method: Condom use in combination with other contraceptives



# Why consider other BC in addition to condoms?

- Condoms alone have higher failure rate in prevention of pregnancy with typical use than most other methods of BC (Contraceptive Technology 19<sup>th</sup> ed, 2007)
  - Typical failure rate in first yr of use: male condom (14%); female condom (21%)
  - COC (8%); DMPA (0.3%); Transdermal patch (0.8%); Vaginal ring (0.6%); IUD-Mirena-5 yr (0.3%)
  - Diaphragm (+spermicides) (12%)
  - Spermicides (26%)
  - Sterilization: female (0.4); male (0.15%)
- Seroconcordant couples
  - May be less likely to use condoms consistently but more likely to desire prevention of pregnancy
- Noncontraceptive benefits of hormonal methods

# Why consider other BC in addition to condoms?

- Risk of birth defects with conception on EFV-containing regimens (Fundaro et al. AIDS 2002, USPHS Perinatal Guidelines 2006)
  - FDA pregnancy category D
  - Teratogenic in primates
  - Retrospective case reports of CNS defects in infants of women who received efavirenz at conception and during the first trimester
  - Efavirenz should be avoided during the first trimester, and in women at risk of becoming pregnant
  - Pregnancy should be avoided in women receiving efavirenz
- Other potential teratogens: alcohol, statins, ACE inhibitors, warfarin, lithium, carbamazepine, MTX, megestrol, phenytoin, TCN, valproic acid, vitamin A

# Disadvantages of Dual Method Use

- Potentially less likely to use condoms consistently
  - General population: more effective primary method for pregnancy prevention, less likely consistent use of male condoms (Fam Plann Perspect 1997;29:67; J Adol Hlth 1998;23:205)
- Possible negative impact on adherence to ART with use of OCPs
- Adverse effects with hormonal methods

# Contraceptive Methods and HIV

## ➤ Spermicides

- Possible increase in mucosal irritation and genital ulcers, especially with frequent use
- Recent UNAIDS clinical trial in Africa and Thailand found significantly higher HIV seroconversion rates in nonoxynol-9 users
- WHO category 4



# Emergency Contraception

- Should be considered when there is an episode of unprotected intercourse or broken condom
- Combined OCPs with EE and norgestrol or levonorgestrol reduces pregnancy by at least 74%
- Take within 72 hours
- No STI/HIV protection

# Special ART Issues in Women

- Drug-drug interactions: hormonal contraception
- When to start issues: women with lower HIV-RNA, higher CD4 soon after seroconversion
- Toxicity issues:
  - NVP and rash-associated hepatotoxicity with CD4>250: 10x increase
  - Lactic acidosis
- ART in pregnancy
  - Fetal risks-Efavirenz
  - Pharmacokinetics
  - Need for treatment irregardless of CD4/viral load

# Oral Contraceptives and Antiretrovirals

(<http://www.aidsinfo.nih.gov>)

## ➤ Protease inhibitors

- RTV, NFV, LPV— 40-50% decrease EE levels,
- APV (and probably fAPV)-decrease in EE and norethindrone levels; 20% dec in APV levels: do not co-administer
- ATV-EE inc 48%, norethindrone inc 110%
- TPV-EE dec 50%
- DRV-potential for dec EE from RTV

## ➤ NNRTIs

- NVP— 20% decrease EE levels, use altern/additional method
- EFV— 37% increase EE levels, clinical significance unknown; use alternative / additional method

# Pregnancy After Diagnosis of HIV

- 18% to 40% of US women become pregnant after HIV diagnosis (Stephenson 1996, Bedimo 1998)
- 12% of all HIV+ women and 26% of women <30 yr -HCSUS study (Shuster 2000)
- WIHS cohort: 7% reported conception annually (1994-2002) (Massad 2004)
  - 77% pregnancies occurred with use of contraception

# When to Discuss Pregnancy

- Initial evaluation: assess childbearing plans/desires
- Early in course of care
  - desire for future pregnancy or uncertain
  - nonuse/inadequate use of contraception
- At intervals during routine care, especially:
  - interest in conceiving
  - nonuse/inadequate use of contraception
  - change in relationship
  - medications with potential reproductive toxicity
  - new developments in pregnancy and HIV
  - at risk for unintended pregnancy
  - enrollment in clinical trials

# Goals of Discussion

- Prevention of unintended pregnancy
- Protection of maternal and fetal health during pregnancy
- Prevention of MTCT



# Preconceptional Counseling and Care for HIV-Infected Women

## ➤ Care

- Contraception to reduce unintended pregnancy.
- Initiate/modify ARV therapy before conception, if indicated:
  - Avoid drugs with possible reproductive toxicity
  - Attain stable, maximally suppressed viral load
  - Evaluate/treat ARV side effects that could effect maternal-fetal outcome or adherence
- Address other medical/psychosocial issues

# HIV Serodiscordant Couples

- HIV+ woman
  - Artificial insemination
- HIV+ man
  - Antiretroviral treatment
  - Semen analysis (hypogonadism frequent occurrence in HIV-infected men with dec. serum testosterone; abnormal semen analyses)
  - Screen for genital tract infections
  - Timed intercourse (ovulation predictors)
  - Peri-exposure prophylaxis
  - ART
    - Semen washing
    - IVF/ICSI

# Effect of Pregnancy on HIV

- CD4 count decreases in all pregnancies due to dilutional effect; CD4% remains stable in HIV-positive women
- HIV-RNA levels (viral load) remain stable during pregnancy in absence of treatment
- No significant differences in HIV progression or survival between pregnant and nonpregnant women with HIV infection

# Frequency of Gynecologic Problems in HIV+ Women

- 46.9% of 262 HIV-infected women had at least one incident gyn condition with serial assessment (Minkoff.AJOG 1999)
- In an inpatient AIDS service 83% of women had coexisting gynecologic disease, although only 9% were admitted with a primary gyn problem (Frankel.Clin Infect Dis,1997)
- Gyn problems may be:
  - Directly related to HIV or HIV-related immunosuppression
  - Indirectly related to HIV (common risk factors)
  - Unrelated to HIV

# Gynecologic Problems Commonly Seen in Setting of HIV

- Menstrual disorders
- Genital ulcer disease
- Abnormal vaginal discharge
- Pelvic inflammatory disease
- HPV, cervical dysplasia and neoplasia

# Routine Gyn Care for the HIV+ Woman

- At each clinical visit review sexual activity, contraception and condom use, and interval menstrual hx
- Screening for depression/domestic violence
- Screening for STDs: syphilis/GC/CT at baseline and periodically based on risk behaviors, signs and symptoms
- Pap smears yearly if remain normal; evaluate with colposcopy with ASC or greater
  - Role of adjuvant HPV testing unclear
  - Role of anal paps

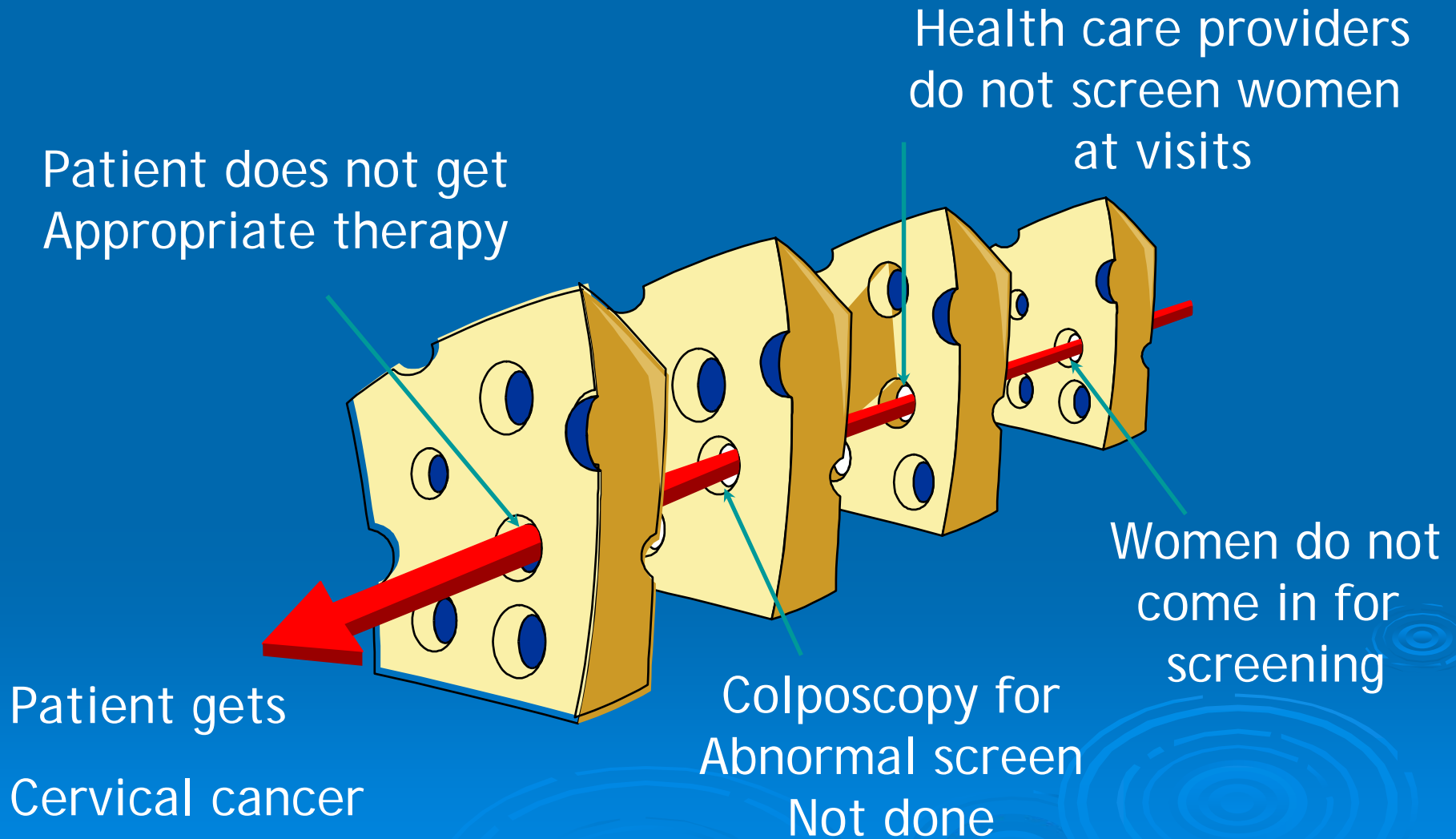
# Interrelationship of HIV and HPV

- HIV-infected women have:
  - higher prevalence and incidence of HPV
  - longer persistence of HPV
  - higher HPV viral loads
  - higher likelihood of multiple HPV subtypes
  - greater prevalence of oncogenic subtypes
- Abnormal cervical cytology more common among HIV+ women; frequency and severity of abnormal pap smears/dysplasia increase with declining CD4 counts and higher HIV-RNA levels
- Invasive cervical cancer is AIDS-defining illness-tends to occur at younger ages/higher CD4 than other ADI

# Screening for Cervical Cancer in HIV-infected Women

- HCSUS: 81% women had a Pap test in last 12 months; women with a gynecologist and PCP at same site were twice as likely to have a Pap (Stein 2001)
- Johns Hopkins AIDS service: only 48% of women had Pap within one yr of enrollment in clinic; 87% cumulative probability within 6 yr (40% Paps abnormal)

# System Failures leading to Cervical Cancer Diagnosis



# Incidence of SIL Associated with HPV Status-WIHS (JAMA 2005;293:1471)

HIV+, CD4<200	HPV- (2 yr)	HPV- (3 yr)	HPV+ (nononc) (2 yr)	HPV+ (onc) (2 yr)
	9%	29%	31%	45%
HIV+, CD4 200-500	9%	14%	24%	28%
HIV+, CD4>500	4%	6%	6%	27%
HIV-	3%	5%	8%	0%

# ARV Therapy and Cervical Dysplasia/HPV

- Data mixed re: effect of ARV on HPV prevalence/persistence, regression/progression of dysplasia (Duerr 2000, Heard 2002, Minkoff 2001, DelMistro 2004)
- Recommendations for evaluation and follow-up are unchanged in women on HAART

# HIV and Menopause

- Increasing number of HIV+ women living past menopause, undergo surgical menopause, or become infected at later ages
- HIV may be associated with premature menopause
- Little information on ART toxicity or PK alterations with aging; no info on drug interactions with HRT
- Continued need for safer sex counseling
- Depression more common in older women
- HRT-generally used only for symptom control (hot flashes, vaginal dryness) at low doses and short-term
- Increased risk for osteopenia/osteoporosis: consider periodic DXA screening

# Summary

- Considerations in the care of HIV+ women change over the lifespan
  - Contraception and preconception planning should be offered to all HIV+ women of childbearing age
  - Certain ART toxicities and drug interactions are important to consider in women
  - Gynecologic problems are common in the setting of HIV and regular gyn care is a critical part of primary HIV care
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