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AIDS EDUCATION AND TRAINING CENTER

19th Annual HIV CONFERENCE
May 14-15, 2010 • Orlando, FL

**The Wellness and Health of
HIV Infected Women**
May 14, 2010 from 1:45pm to 3:15pm

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Disclosure of Financial Relationships

This speaker has the following significant financial relationships with commercial entities to disclose:

- **Research support from:**
 - **Pfizer, Tibotec, BMS, Salix (Avent), Bavaria-Nordic, Avexa**
- **Advisory board: Tibotec**

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.



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**Only one thing defines
an impossible
dream: the fear of
failure**

**Paulo Coelho
The Alchemist**



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The Wellness and Health of HIV-infected Women:

- **Special issues related to HIV care and treatment will be discussed.**
- **The management of women in pre-planning for pregnancy, management during pregnancy, labor, and postpartum will be reviewed.**
- **Issues of aging in women will be presented from a preventive health format.**



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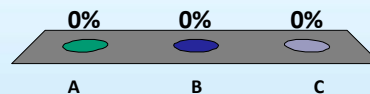
Pregnancy Considerations

- Pre-conception Care is important for those women living with HIV who have postponed a pregnancy and want to achieve it now
- Therapy options might be different if you acknowledge a potential future pregnancy
- For new patients in care, the suspicion and detection of early pregnancy is crucial



Are you or someone offering pre-conception care at your clinic?

- A. yes**
- B. No**
- C. Don't know**



Preconception Care



- The main goal of preconception care is to provide health promotion, screening, and interventions for women of reproductive age to reduce risk factors that might affect future pregnancies
- It is part of a larger health-care model that results in healthier women, infants and families

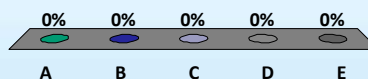


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Which topics should be discussed as part of preconception counseling?

- Contraceptive use
- Type of HAART and viral control
- Folic acid supplementations and vaccines
- HIV status of partner (donor)
- all of the above



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Preconception Counseling/care for women living with HIV

PHS Perinatal Guidelines April, 2009 <http://aidsinfo.nih.gov>

- Contraception counseling to avoid unintended pregnancy is an essential part of care
- Select effective and appropriate contraceptive methods
- Counsel on safe sexual practices, eliminating alcohol, illicit drug use, and smoking
- Educate about risk factors for perinatal HIV transmission and strategies for reducing them
- Encourage testing and counseling of partners
- Choice of ARV needs to consider **effectiveness and potential for teratogenicity**
- Attainment of maximally suppressed viral load **prior to conception**
- Counsel on reproductive options that prevent HIV exposure to uninfected partner



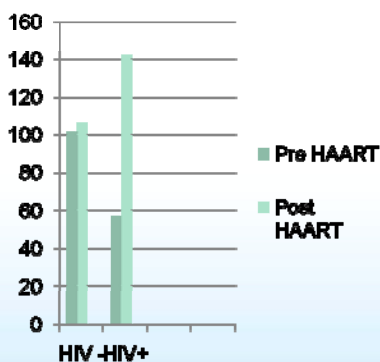
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Live birth patterns among HIV infected women before and after the availability of HAART

A. Sharma, Minkoff et al Am J Obstet Gynecol 2007;196:541

Live birth rate per 1000 person/yr



N= 2,488 HIV+ vs. 974 HIV-

- Among HIV+, the HAART era live birth rate was 150% higher than in the pre-HAART era ($P=.001$) vs. a 5% increase among HIV- women
- The rate of increase in live birth rate was higher for women 35 years old (vs. younger than 25 years, $P=.02$), and with more than a high school education (vs. less than high school, $P=.05$)



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Key issues when treating pregnant women

- Drugs that **“cross the placenta”** and reach fetal circulation (such as NRTI’s and NNRTI’s)
- Drugs that **do not** (or very limited) **“cross the placenta”** (PI’s)
- Know the **PK profile** of the drugs
- Avoid drug interruptions in pregnancy
- Labor and Delivery treatment (if labor is prolonged)
- Neonatal ART and infant formula

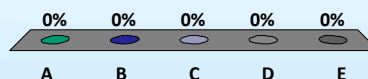


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Regarding Trans-placental transfer of HIV drugs, which is correct?

- All drugs should cross the placenta and have equal levels in the fetus as in the mother
- No drug should reach the fetal compartment for protection of teratogenic effects
- Some drugs should reach the fetal compartment to provide pre-exposure prophylaxis
- The fetus will have the same adverse effects as the mother due to transplacental passage
- The fetus will always be protected even with minimal adherence



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ARV during pregnancy

- In contrast with the guidelines for the management of adults, antiretroviral (ARV) therapy should be initiated and continued for the duration of the pregnancy, **regardless of viral load and CD4** cell count in order to reduce MTCT .
- In developed countries, the use of HAART, ARV prophylaxis for the mother and fetus and then the infant, elective Cesarean delivery, and infant formula rather than breastfeeding, have reduced the incidence of MTCT from between 15% to 25% **to less than 2%**



Transplacental transfer

- The most common mechanism for drug transfer is **passive diffusion**. The factors defining Fick's law of diffusion (membrane thickness, surface area, and the concentration gradient) determine the placental drug transfer.
- In general, compounds with **molecular weight** of less than 500 Da exhibit complete transfer across the human placenta and **nonionized** compounds cross the placenta more readily than do ionized compounds, as do drugs with greater **lipophilicity** (ability of a compound to dissolve in lipids and nonpolar solvents). Zorrilla, C and Tamayo, V. Pharmacologic and Nonpharmacologic Options for the Management of HIV Infection During Pregnancy, HIV/AIDS - Research and Palliative Care. Published Date December 2009 , Volume 2009:1



<http://aidsinfo.nih.gov>

NRTIs

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Rationale for Use in Pregnancy
Zidovudine (ZDV)	PK not altered; no change in dose.	No teratogenicity, short-term safety for mother and infant.	Preferred NRTI based on efficacy and extensive experience.
Lamivudine (3TC)	PK not altered; no change in dose.	No teratogenicity, short-term safety for mother and infant.	3TC plus ZDV is the recommended dual NRTI backbone for pregnant women.
Didanosine (ddl)	PK not altered; no change in dose.	Lactic acidosis, sometimes fatal, in pregnant women receiving ddl and d4T.	Alternate NRTI for dual nucleoside backbone of combination regimens.
Stavudine (d4T)	PK not altered; no change in dose.	No teratogenicity. Lactic acidosis, sometimes fatal, in pregnant women receiving ddl and d4T.	Alternate NRTI for dual nucleoside backbone of combination regimens..



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NRTIs

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
Emtricitabine	No PK studies.	No studies in human pregnancy.	Alternate NRTI for dual nucleoside backbone
Abacavir	PK not altered; no change in dose.	Hypersensitivity reactions occur in ~5%–8% ; smaller percentage are fatal and associated with rechallenge.	Alternate NRTI for dual nucleoside backbone
Tenofovir	AUC lower in 3rd trimester than PP but trough levels similar.	Decreased fetal growth and reduction in fetal bone porosity within 2 months of starting maternal therapy (monkeys). Bone demineralization with chronic use in children	Should be used as a component of a maternal combination only after careful consideration of alternatives.



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NNRTIs

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
Nevirapine	PK not altered; no change in dose.	No evidence of human teratogenicity	Increased risk of symptomatic, often rash-associated, and potentially fatal liver toxicity among women with CD4 counts >250/mm ³ . Women on nevirapine regimens and are tolerating them well may continue therapy, regardless of CD4 counts
Efavirenz†	No studies in human pregnancy.	FDA Pregnancy Class D; significant malformations (anencephaly, anophthalmia, cleft palate) were observed in 3 (15%) of 20 infants born to cynomolgus monkeys receiving efavirenz during the first trimester at a dose comparable to systemic human therapeutic exposure; 3 case reports of NTD in humans after first trimester	Use of efavirenz should be avoided in the first trimester, and women of childbearing potential must be counseled regarding risks and avoidance of pregnancy. Use after the second trimester of pregnancy can be considered if other alternatives are not available and if adequate contraception can be assured postpartum.
Delavirdine	No studies in human pregnancy.	Rodent studies indicate potential for carcinogenicity and teratogenicity	Given lack of data and concerns regarding teratogenicity in animals, not recommended for use in human pregnancy.
Etravirine	No studies in pregnancy (TMC114HIV3015)	Animal studies (rats and rabbits) show no fetal harm (category B)	Unknown



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PIs

Antiretroviral Drug	Pharmacokinetics in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
Lopinavir/ritonavir	PK of LPV/RTV capsules (3 capsules twice daily) during 3 rd trimester were significantly lower than during PP period; an increased dose of 4 capsules of LPV/RTV twice daily starting in the 3 rd trimester resulted in adequate LPV exposure; by 2 weeks postpartum, standard dosing was again appropriate. PK studies of the new LPV/RTV tablet formulation are underway.	No evidence of human teratogenicity. Well-tolerated, short-term safety demonstrated in Phase I/II studies.	PK studies of the new tablet formulation are underway. Some experts would administer standard dosing (2 tablets twice daily) and monitor virologic response and LPV drug levels. Others would increase the dose during the 3 rd trimester (from 2 to 3 tablets twice daily), returning to standard dosing postpartum. Once daily LPV/RTV dosing is not recommended during pregnancy
Indinavir (combined with low dose ritonavir boosting)	Two studies including 18 women receiving IDV800 mg three times daily showed markedly lower levels compared to PP.	Theoretical concern: increased indirect bilirubin. Unboosted IDV not recommended	Alternate PI to consider if unable to use LPV/RTV, but would need to give IDV as RTV-boosted regimen. Optimal dosing of IDV/RTV is unknown
Nelfinavir	Adequate levels with NFV 1,250 mg, bid although levels are variable in late pregnancy. In a study of pregnant women in their 2 nd and 3 rd trimester dosed at 1,250mg bid, women in the 3 rd trimester had lower concentration of NFV than in their 2 nd trimester. In a study of the new 625 mg tablet at 1,250 mg bid, lower AUC and peak levels were observed during the 3 rd trimester of pregnancy than PP	No evidence of human teratogenicity. Well tolerated, short-term safety	Given PK data and extensive experience with use in pregnancy, NFV is an alternative PI for pregnant women receiving HAART only for perinatal prophylaxis. NFV-based regimens had a lower rate of viral response compared to LPV/RTV or EFV-based regimens, but similar viral response to atazanavir or NVP



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PIs

Antiretroviral Drug	PK in Pregnancy	Concerns in Pregnancy	Rationale for Recommended Use in Pregnancy
Darunavir	No PK studies in pregnancy PK study in progress	No experience in human pregnancy. (TMC114HIV3015)	Data are insufficient to recommend use during pregnancy.
Fosamprenavir	No PK studies in pregnancy.	Limited experience in human pregnancy.	Data are insufficient to recommend use during pregnancy
Tipranavir	No PK studies in pregnancy.	No experience in human pregnancy.	Data are insufficient to recommend use during pregnancy.



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Entry Inhibitors

Antiretroviral Drug	PK in Pregnancy	Concerns in Pregnancy	Rationale for Use in Pregnancy
Enfuvirtide	No PK studies in human pregnancy.	Minimal data in human pregnancy.	Insufficient data to recommend use during pregnancy.
Maraviroc	No PK studies in human pregnancy.	No experience in human pregnancy	Insufficient data to recommend use during pregnancy
Raltegravir	No PK studies in human pregnancy.	No experience in human pregnancy	Insufficient data to recommend use during pregnancy



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Summary and gaps: PIs in pregnancy

- Nelfinavir: adequate levels
- SQV-SGC/r: adequate levels(not available); tablets/r seem to be OK
- Atazanavir: new data: Atazanavir/ritonavir 300/100mg QD is an option for protease inhibitor use in HIV-infected pregnant women. *Safety, Efficacy and Dose Considerations for Once Daily Ritonavir-Boosted Atazanavir in HIV-Infected Pregnant Women (submitted)*
- Lopinavir/r: need to increase dosing in the 3rd trimester
- Darunavir: **PK study in pregnant women in progress**
- Fosamprenavir: no data
- Tipranavir: no data

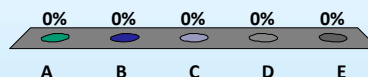


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Select the incorrect statement about the essential elements of management during pregnancy and labor:

- HAART should be provided during pregnancy and labor
- HAART should be provided only during pregnancy
- Cesarean sections depend on several factors such as: viral load, patient preferences, timing of labor, rupture of membranes)
- All pregnant women should have the best therapy with the least side effects and adherence should be monitored
- Some drugs have serious complications during pregnancy and can increase maternal mortality



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Management during pregnancy, labor and post partum

- Antepartum: HAART, PCP prophylaxis, other vaccines, specialized prenatal care
- Intrapartum: continue HAART, IV ZDV, Avoid manipulations, shorten rupture of membranes
- Post-partum: avoid breastfeeding, linkage to care for continuation of HAART if needed



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Update: Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the US April 29, 09

- Etravirine (Intelence™), the new NNRTI, was added. No PK studies in human pregnancy and insufficient safety data to recommend its use in pregnancy.
- Atazanvir is recommended as an alternative agent in combination with low dose ritonavir. **New data on PK studies will allow 300/100 dose (CZ edit)**
- Tenofovir has been placed under “Use in Special Circumstances” because of limited data on use in pregnancy but unique indication for hepatitis B co-infected women or women with antiretroviral resistance. Renal function should be monitored



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**Update: Recommendations for Use of Antiretroviral
Drugs in Pregnant HIV-Infected Women for Maternal Health *and*
Interventions to Reduce Perinatal HIV Transmission in the US**

April 29, 09

- Both tenofovir and lamuvidine have activity against hepatitis B and if discontinued after pregnancy can result in a flare of hepatitis
- PK data on boosted indinavir and saquinavir tablets demonstrate adequate levels during pregnancy
- Emtricitabine levels are slightly lower in the third trimester but no dose adjustment is recommended
- There is no or limited data on the use of many of the new antiretroviral agents in pregnancy. This includes darunavir, tipranavir, maraviroc, enfuvrtide and raltegravir.



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Prevention strategies during breastfeeding

- **Extended maternal anti-retrovirals (ARV)**
 - Triple-ARV (ZDV+3TC+LPV/r to 6.5 months post-delivery or breastfeeding cessation if earlier
 - Maternal ZDV+3TC and LPV/r twice daily (MHAART)
- **Extended infant ARV**
 - NVP only or NVP+ZDV to age 14 wks
 - infant NVP daily (INVP)



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Prevention strategies during breastfeeding

- **Triple-antiretroviral (ARV) prophylaxis during pregnancy and breastfeeding compared to short-ARV prophylaxis to prevent mother-to-child transmission of HIV-1 (MTCT): the Kesho Bora randomized controlled clinical trial in five sites in Burkina Faso, Kenya** [L. de Vincenzi](#), Kesho Bora Study Group IAS 2009; LBPEC01
- Reduction in HIV infections by 12 months was 40% (p=0.052). There was no increase in adverse events with triple-ARV
- **Infant extended antiretroviral (ARV) prophylaxis is effective in preventing postnatal mother-to-child HIV transmission (MTCT) at all maternal CD4 counts** IAS 2009 TUPEC053
[L.M. Mofenson](#)¹, [T.E. Taha](#)², [Q. Li](#)², [J. Kumwenda](#)³, [G. Kafulafula](#)⁴, [M.G. Fowler](#)⁴, [D.R. Hoover](#)⁵, [M. Thigpen](#)⁶, [N.I. Kumwenda](#)³, and the PEPI Malawi Study Group
- **Both maternal HAART and daily infant nevirapine (NVP) are effective in reducing HIV-1 transmission during breastfeeding in a randomized trial in Malawi: 28 week results of the Breastfeeding, Antiretroviral and Nutrition (BAN) Study** IAS 2009 WELBC103
[C. Chasela](#)¹, [M. Hudgens](#)², [D. Jamieson](#)³, [D. Kayira](#)¹, [M. Hosseinipour](#)¹, [Y. Ahmed](#)³, [G. Tegha](#)¹, [R. Knight](#)⁴, [A.P. Kourtis](#)³, [D. Kamwendo](#)¹, [I. Hoffman](#)⁵, [S. Ellington](#)³, [Z. Kacheche](#)¹, [J. Wiener](#)³, [F. Martinson](#)¹, [P. Kazembe](#)⁶, [I. Mofolo](#)¹, [D. Long](#)², [A. Soko](#)¹, [S.B. Smith](#)², [C. van der Horst](#)⁷



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Infant extended antiretroviral (ARV) prophylaxis is effective in preventing postnatal mother-to-child HIV transmission (MTCT) at all maternal CD4 counts

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Postnatal HIV MTCT at Age 14 Weeks by Study Arm and Baseline Maternal CD4 Count

Study Arm	CD4 ≤200		CD4 200-350		CD4 >350	
	%MTCT (95% CI)	RR (95% CI)	%MTCT (95% CI)	RR (95% CI)	%MTCT (95% CI)	RR (95% CI)
Control	17.6% (12.2-25.2)	1.0	9.0% (5.9-13.8)	1.0	5.5% (3.8-7.9)	1.0
Ext NVP	5.8% (3-10.8)	0.33 (0.16-0.68)	3.4% (1.7-6.7)	0.37 (0.17-0.84)	1.4% (0.7-3.0)	0.25 (0.12-0.59)
Ext NVP+ZDV	6.1% (3.3-12.4)	0.36 (0.17-0.78)	3.2% (1.3-6.3)	0.32 (0.13-0.78)	2.3% (1.3-4.1)	0.42 (0.22-0.83)



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Depression and HIV disease progression

- Depression may be a contributory factor for HIV progression in women. In a prospective longitudinal cohort study of 765 HIV seropositive women in the United States, those with chronic depressive symptoms were twice as likely to die as those with mild or no depressive symptoms, after controlling for clinical features and treatment
- Ickovics, JR, Hamburger, ME, Vlahov, D, et al. Mortality, CD4 Cell Count Decline, and Depressive Symptoms Among HIV-Seropositive Women: Longitudinal Analysis From the HIV Epidemiology Research Study. JAMA 2001; 285:1466.

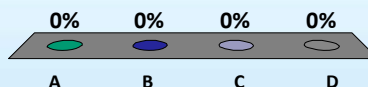


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What do you recommend to your patients about the AH1N1?

- They should not get vaccinated due to adverse effects
- All persons living with HIV should be vaccinated against AH1N1 according to CDC guidelines
- Only vaccinate pregnant women
- Your patients can opt for vaccination although you do not recommend it



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CDC Recommendations

- January 19, 2010 3:00 PM ET
- People living with HIV infection, especially if they have AIDS or have low CD4 cell counts (sometimes called T-cell counts), can develop severe complications from influenza.
- This group is recommended to get vaccinated against 2009 H1N1 with the inactivated form of the vaccine (flu shot). They should also be vaccinated against seasonal flu with the seasonal flu shot.
- People with HIV infection who develop flu-like symptoms should consult their health care provider right away to determine if they need treatment.
- Along with everyone else, people with HIV infection should take everyday precautions to protect themselves from the flu this season.
- http://www.cdc.gov/h1n1flu/People_with_HIVAIDS.htm



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Is there treatment against the 2009 H1N1 flu for people with HIV/AIDS?

- **Yes. The 2009 H1N1 flu virus is sensitive to two antiviral drugs: oseltamivir and zanamivir.**
- **HIV-infected adults and adolescents with suspected flu infection (including 2009 H1N1 flu) should contact their health care provider to determine if antiviral treatment is needed.**
- **Treatment is most effective if started within 48 hours of symptom onset.**



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Cervical Cytology screening

- One multicenter, prospective cohort study evaluated the accuracy of Pap smears versus colposcopy and biopsy in 284 women, 189 of whom were HIV-infected .
- Overall, the correlation of cytologic findings with colposcopic and/or histologic findings was high. 19 HIV-infected patients with a normal Pap smear had abnormal histology; however, 95 percent of those with discordant results had an abnormal Pap smear within one year of follow-up, supporting the accuracy of cytologic examinations in HIV-infected women. *Anderson, JR, Paramsothy, P, Heilig, C, et al. Accuracy of Papanicolaou test among HIV-infected women. Clin Infect Dis 2006; 42:562.*
- However, even mildly abnormal cytology is a potential sign of cervical neoplasia and an indication for colposcopy
- *Wright, TC, Moscarelli, RD, Dole, P, et al. Significance of mild cytological atypia in women infected with human immunodeficiency virus. Obstet Gynecol 1996; 87:515*

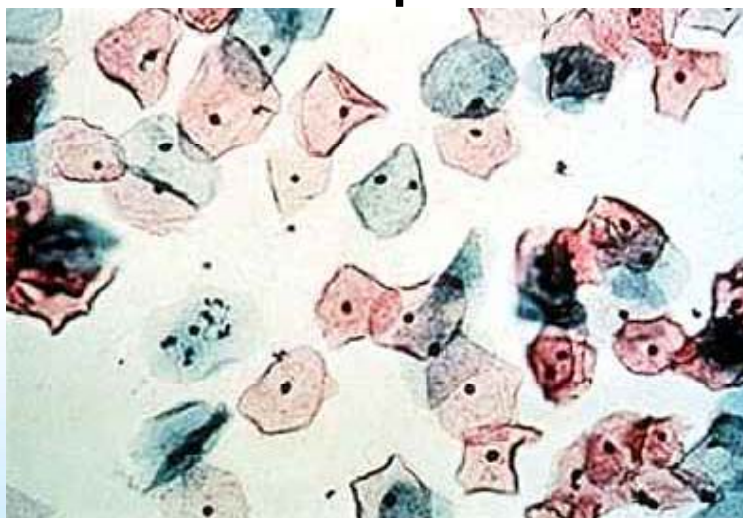


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Normal Pap Smear

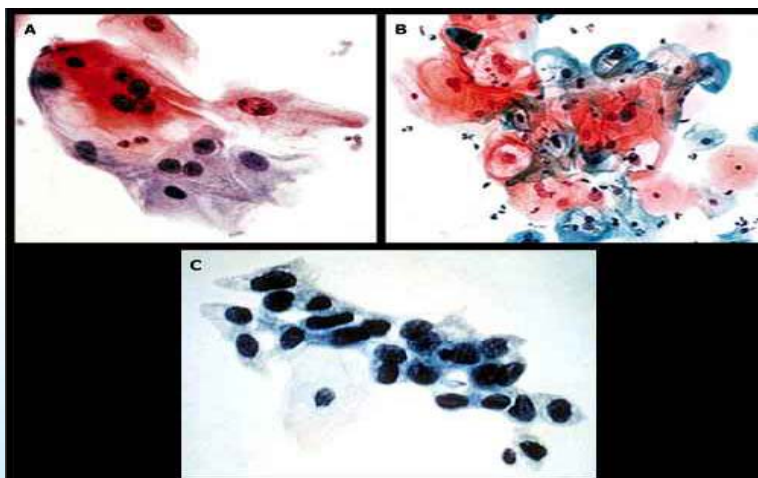


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Abnormal Pap smear



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Cervical Cytology screening

- Although HPV DNA testing is available, there are no formal recommendations that exist for use of this test in HIV-seropositive women
- A study of 101 HIV-infected women with CD4 counts <500/mm³ found that HPV DNA assays did not add to Pap smear in the detection of cervical intraepithelial neoplasia.
- The sensitivity, specificity, and positive predictive values were 85, 42, and 35 percent, respectively, for HPV DNA assays compared to 63, 74, and 47 percent of Pap smear.
- *Kaplan, JE, Benson, C, Holmes, KH, et al. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 2009; 58:1.*
- *Cohn, JA, Gagnon, S, Spence, MR, et al. The role of human papillomavirus DNA assay and repeated cervical cytologic examination in the detection of cervical intraepithelial neoplasia among human immunodeficiency virus-infected women. Am J Obstet Gynecol 2001; 184:322.*



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Cervical Cytology screening

- A cost-effectiveness analysis found that adding HPV DNA screening to two cervical cytology smears during the first year after an HIV diagnosis was found to be more cost-effective than annual screening alone. *Cost effectiveness of human papillomavirus testing to augment cervical cancer screening in women infected with the human immunodeficiency virus. AU Goldie SJ; Freedberg KA; Weinstein MC; Wright TC; Kuntz KM SO Am J Med 2001 Aug;111(2):140-9.*
- *nt cervical cancer screening in women infected with the human immunodeficiency virus. Am J Med 2001; 111:140*



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Cervical Cytology screening

- Cervical cytology screening every six months for women with detectable HPV DNA and annual screening for all others who have not had a previously abnormal Pap smear was the recommended approach based upon this analysis.
- These conflicting data suggest that further evaluation of this test as a routine clinical tool is needed . *Goldie, SJ, Freedberg, KA, Weinstein, MC, et al. Cost effectiveness of human papillomavirus testing to augme*



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Cervical Cytology screening

- Current recommendations published by the Agency for Health Care Policy and Research and the United States Public Health Service are for two biannual screening Pap smears for all women with HIV.
- For those with normal examinations and low risk (no prior abnormal Pap smear, AIDS-defining condition, or HPV infection), annual follow-up suffices ; more frequent examinations are recommended for women at higher risk.
- The potential roles of the HPV vaccine to prevent infection among HIV-infected women are still unknown



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Menstrual abnormalities

- Menstrual abnormalities, including early menopause, have been described in a number of women with HIV infection, but the rates and patterns are not well studied .
- One cohort study found no difference in menstrual patterns between 197 HIV-infected women and 189 HIV-negative controls .

Schoenbaum, EE, Hartel, D, Lo, Y, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis* 2005; 41:1517.

Ellerbrock, TV, Wright, TC, Bush, TJ, et al. Characteristics of menstruation in women infected with human immunodeficiency virus. *Obstet Gynecol* 1996; 87:1030



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Menopause

- Normal women have menopause (ovarian failure) at a mean age of 51 years. The resulting lack of estrogen is associated with rapid bone loss due to increased bone resorption, and often consequent osteoporosis.
- Many women also experience menopausal symptoms, including hot flashes, vaginal dryness, and urinary symptoms, all of which are relieved most effectively by estrogen therapy with or without a progestin.
- For women with menopausal symptoms, estrogen is often given short-term (six months to five years), with the goal of eventual tapering and discontinuation.



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Menopause

- As the population with HIV infection ages, the number of women approaching and experiencing menopause is growing.
- The risk-benefit ratio of hormonal replacement for these women remains to be described, as well as potential pharmacologic interactions between protease inhibitors and estrogen replacement.
- The decision about hormonal replacement should be made individually after education and counseling of the woman and determination of risk factors for cardiac disease, osteoporosis, cancer, and other conditions



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Health maintenance

- The care of women with HIV infection must incorporate primary care into their state-of-the-art HIV care.
- As women survive longer with HIV, other co-morbid conditions will increase with age, including cardiac disease, diabetes, and breast cancer.
- Medical care must include routine medical screening (mammograms, breast self-examination, nutritional counseling for osteoporosis, smoking cessation, etc) and a recognition that not all complaints are necessarily HIV-related.



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May 14-15, 2010
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Health maintenance

- The complex psychosocial needs of many women with HIV often requires a multidisciplinary team to address issues such as housing, substance abuse, and mental illness, either on-site or by linkage with other institutions or community-based organizations.
- One group found that case management significantly improved care and use of HIV therapies for individuals with HIV
- **Katz, MH, Cunningham, WE, Fleishman, JA, et al. Effect of case management on unmet needs and utilization of medical care and medications among HIV-infected persons. Ann Intern Med 2001; 135:557**



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Osteopenia

- A meta-analysis, which included 20 cross-sectional studies reporting bone mineral density (BMD) measurements among 884 HIV-infected patients, demonstrated that 67 percent had reduced BMD with 15 percent meeting criteria for osteoporosis .
- Studies performed in ART-naïve patients also indicate a higher prevalence of osteopenia than would be expected in age- and sex-matched sero-negative adults.
- **Brown, TT, Qaqish, RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS 2006; 20:2165.**



Osteopenia

- The clinical significance of osteopenia is unclear, since an elevated fracture risk has not yet been prospectively demonstrated in this population
- On the other hand, a retrospective analysis comparing 8525 patients with HIV and 2,208,792 patients without HIV found an increased fracture prevalence based on ICD-9 coding (2.9 versus 1.9 per 100 persons, $p < 0.0001$)
- **Triant, VA, Brown, TT, Lee, H, Grinspoon, SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. J Clin Endocrinol Metab 2008; 93:3499**



Osteoporosis

- **Certain lifestyle and hormonal factors, which increase the risk of disordered bone metabolism, are prevalent in HIV-infected patients.**
- **These include physical inactivity, decreased intake of calcium and vitamin D, cigarette smoking, alcohol use, depression, opiate use, and low testosterone levels.**
- **These factors place HIV-infected patients at risk for developing osteoporosis.**
- **Arnsten, JH, Freeman, R, Howard, AA, et al. Decreased bone mineral density and increased fracture risk in aging men with or at risk for HIV infection. AIDS 2007; 21:617.**



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- **Calcium and Vitamin D supplementation could protect bone by preventing bone loss and by healing subclinical osteomalacia.**
- **The optimal serum 25OHD concentration to maintain skeletal health is not firmly established, serum values exceeding 19 to 24 ng/mL (47.5 to 60 nmol/L) are supported by observational studies** . Ensrud, KE, Taylor, BC, Paudel, ML, et al. Serum 25-hydroxyvitamin D levels and rate of hip bone loss in older men. J Clin Endocrinol Metab 2009; 94:2773. Cauley, JA, Lacroix, AZ, Wu, L, et al. Serum 25-hydroxyvitamin D concentrations and risk for hip fractures. Ann Intern Med 2008; 149:242.
- **Looker, AC, Mussolino, ME. Serum 25-hydroxyvitamin D and hip fracture risk in older U.S. white adults. J Bone Miner Res 2008; 23:143.**
- **Gerdhem, P, Ringsberg, KA, Obrant, KJ, et al. Association between 25-hydroxyvitamin D levels, physical activity, muscle strength, and fractures in the prospective population-based OPRA study of elderly women. Osteoporos Int 2005; 16:1425**



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May 14-15, 2010
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Therapeutic Interventions

In a cross-sectional study of adults (>50 years) participating in the NHANES III survey, higher 25OHD concentrations were associated with greater BMD measurements throughout the reference range, plateauing in the range of 36 to 40 ng/ml (90 to 100 nmol/L)

Bischoff-Ferrari, HA, Dietrich, T, Orav, EJ, Dawson-Hughes, B. Positive association between 25-hydroxy vitamin D levels and bone mineral density: a population-based study of younger and older adults. Am J Med 2004; 116:634

Another approach would be to maintain serum levels >30 to 40 ng/mL (75 to 100 nmol/L), recognizing that some patients need more than 800 international units daily .

Dawson-Hughes B. Estimates of optimal vitamin D status. Osteoporos Int 2005; 16:713.



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Dosage recommendations

- Based upon the HANES and other studies, we recommend 1200 to 1500 mg of calcium and 800 international units of vitamin D daily in most individuals with osteoporosis with a target serum 25-hydroxyvitamin D (25OHD) concentration >20 ng/mL (50 nmol/L).
- Calcium supplementation in excess of 500 mg/day should be given in divided doses



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May 14-15, 2010
Orlando, FL

Fish oil (Omega 3)

- Fish oil contains two medically relevant long-chain polyunsaturated fatty acids: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), collectively known as omega-3 fatty acids.
- Omega-3 fatty acids are successfully employed to treat hypertriglyceridemia in HIV-negative individuals .
- They are dosed at 4 grams per day either singly or in a divided dose. **Kris-Etherton, PM, Harris, WS, Appel, LJ, et al. Fish consumption, Fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 2002; 106:2747.**



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May 14-15, 2010
Orlando, FL

Fish oil (Omega 3)

- One study randomly assigned 52 HIV-infected patients with hypertriglyceridemia to receive lifestyle modification counseling with or without fish oil supplementation for 16 weeks **Wohl, DA, Tien, HC, Busby, M, et al. Randomized study of the safety and efficacy of fish oil (omega-3 fatty acid) supplementation with dietary and exercise counseling for the treatment of antiretroviral therapy-associated hypertriglyceridemia. Clin Infect Dis 2005; 41:1498.** After four weeks, mean triglyceride levels significantly declined from 461 to 306 mg/dL in the supplementation group and remained low. It was well tolerated when taken daily with food.
- Since fish oil has antiplatelet effects, patients concomitantly using drugs that affect bleeding time should be monitored for adverse effects.



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Other lifestyle changes and recommendations

- Exercise
- Smoking cessation
- Balanced diet
- Stress management
- Regular medical interventions and screenings such as mammography, Pap smear, colonoscopy, etc
- Vaccines
- Screening for violence/abuse, depression



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May 14-15, 2010
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Carry in your memory, for the rest of your life, the good things that came out of your difficulties.

They will serve as a proof of your abilities and will give you the confidence when you are faced by other obstacles.

***Manual of the warrior of light
Paulo Coelho***



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Disclosure of Financial Relationships

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- **Research support from:**
 - **Pfizer, Tibotec, BMS, Salix (Avent), Bavaria-Nordic, Avexa**
- **Advisory board: Tibotec**

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.



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