



First program in the four part web series
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Women and HIV

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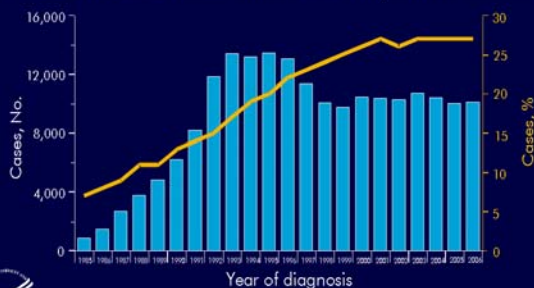




Epidemiology, Unplanned Pregnancy Rates & Risk Factors



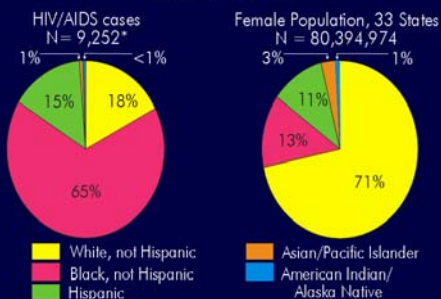
Estimated Number and Proportion* of AIDS Cases among Female Adults and Adolescents 1985–2006—United States and Dependent Areas



Note. Data have been adjusted for reporting delays.
*Proportion of all cases that were diagnosed among females.



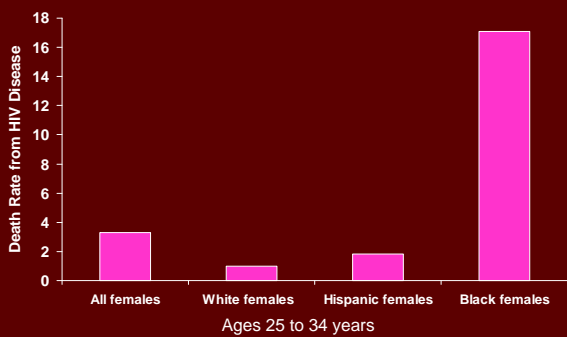
Proportion of HIV/AIDS Cases and Population among Female Adults and Adolescents, by Race/Ethnicity 2006—33 States



Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status at diagnosis. Data from 33 states with confidential name-based HIV infection reporting since or near 2003. Data have been adjusted for reporting delays.
*Includes 41 female adults and adolescents of unknown race or multiple races.



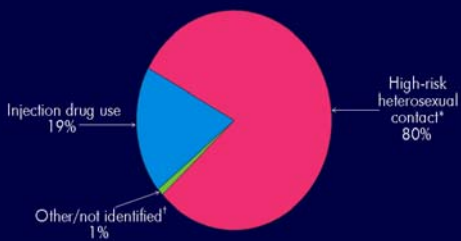
HIV Disease: Leading Cause of Death for Black Women (25-34)



National Center for Health Statistics: 2005.

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Proportion of HIV/AIDS Cases among Female Adults and Adolescents, by Transmission Category 2006—33 States

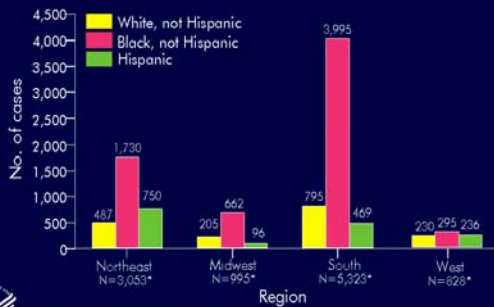


Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status or diagnosis. Data from 33 states with confidential name-based HIV infection reporting areas at least 2003. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.

*Heterosexual contact with a person known to have, or to be at high risk for, HIV infection. †Includes blood transfusion, perinatal exposure, and risk factor not reported or not identified.

CDC

Reported AIDS Cases among Female Adults and Adolescents, by Region and Race/Ethnicity, 2006 50 States and DC



* Region totals include females of unknown race or multiple races.

CDC



Women of Child Bearing Potential: Management Considerations



Risk of Unplanned Pregnancies in HIV+ Women

49% of pregnancies are unplanned

By age

- 82% women 15-19
- 60% women 20-24
- 43% women 25-29
- 33% women 30-34
- 29% women 35-39
- 38% women over 40

Risk increases for HIV+

- Adolescents
- Minorities
- Lower income
- Less education
- Unmarried status

Risk from menarche to menopause

Perspectives on Sexual and Reproductive Health, 2006, 38(2):90-96

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Preconception Counseling & Care

For *all* reproductive age women including those not intending pregnancy¹

Promotes health before conception

Improves pregnancy-related outcomes²

For new HIV patients, detection early pregnancy essential

Avoid teratogenic drug treatments

Begin preventive strategies i.e. folic acid supplements³

1. Henshaw Fam Plann Perspect 1998
 2. MMWR Morbid and Mortality Wkly Report 2006
 3. Zorilla. IAS Topics in HIV Medicine, Vol 15, Issue 1, Feb/Mar 2007





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





When to Discuss Pregnancy

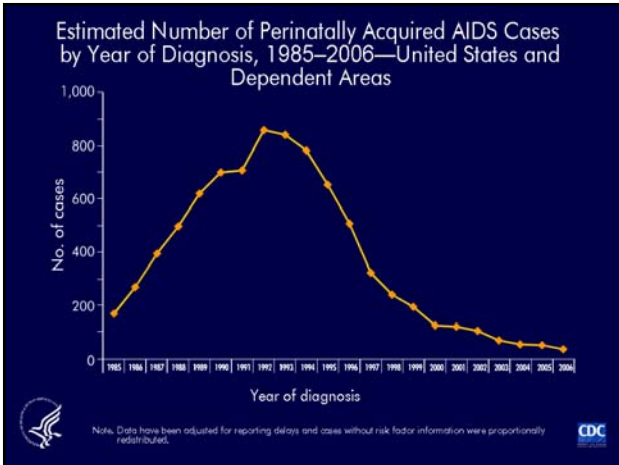
- At intervals during routine care, especially:
 - interest in conceiving
 - nonuse/inadequate use of contraception
 - change in relationship
 - medications with potential reproductive toxicity
 - new developments in pregnancy and HIV
 - at risk for unintended pregnancy
 - enrollment in clinical trials





Perinatal Care





NY/NJ AETC ON-DEMAND Prenatal HIV Transmission

- **Accounts for nearly all pediatric AIDS cases:** Approximately 91% of all AIDS cases reported among U.S. children between 1985 and 2004.
- **Can be prevented:** 2% risk with appropriate treatment compared with approximately 25% when no interventions are given.

MMWR 1999;48 (19):401-404

NY/NJ AETC ON-DEMAND

NY/NJ AETC ON-DEMAND Early Diagnosis

- HIV screening should be routine in the medical care of women prior to pregnancy
- It is part of preconception care
- Becoming pregnant w/o knowing HIV status = important missed prevention opportunity

NY/NJ AETC ON-DEMAND



Universal Opt Out Screening

- All pregnant women should be screened
- Before screening, explain opt out process
 - HIV screening recommended for all pregnant patients
 - HIV testing is part of routine panel of prenatal tests unless declined (opt-out screening)
- Testing must be voluntary & free from coercion.
- No woman should be tested without her knowledge.



MMWR Sept. 2006 55(rr14) 1-17 revised guidelines for HIV/AIDS testing Adults Adolescents and pregnant women



Universal Opt Out Screening

- Provide information about (in person or in writing)
 - HIV infection
 - interventions that can reduce HIV MTCT transmission
 - meanings of positive & negative test results
- Give opportunity to ask questions & to decline
- Use standard prenatal consent documentation/process
- Nothing additional required for HIV prenatal testing
- Document if decline





Addressing Reasons for Declining Testing

- Discuss patient's reasons
- Resolve any logistical reasons
- Explain importance of retesting
- Might accept if their concerns are discussed
- Might continue to decline
- Patient decisions should be respected & documented



MMWR Sept. 2006 55(rr14) 1-17 revised guidelines for HIV/AIDS testing Adults Adolescents and pregnant women



Pregnant Woman with an HIV-Infected Male Partner

- Test for HIV (unless declined)
 - 2nd test 3rd trimester, before 36 wks (if poss)
- If presents in labor: rapid HIV test
- If seroconversion suspected, do HIV RNA & antibody test; repeat HIV test in 4-6 weeks
 - HIV+ interventions to ↓ perinatal transmission
 - HIV- counsel about HIV risk reduction



U.S. Public Health Service Perinatal Guidelines November 2007



HIV+ Women Planning a Pregnancy

Preconception care must focus on

- maternal infection status
- viral load
- immune status
- therapeutic regimen
- education re perinatal transmission risks & prevention
- expectations for the child's future
- effective contraception until the optimal maternal health status for pregnancy is achieved





Barrier to Care





What Is the Barrier to Care?

- Many HIV-infected women cite discrimination & discomfort as reasons for avoiding prenatal care
- Providing accessible, welcoming prenatal care services for all women is an important strategy for prevention of perinatal HIV infection and for providing opportunities to protect women's health.

Division HIV/AIDS Prevention
National Center for HIV/AIDS Viral Hepatitis & TB Prevention
October 10 2007





Linkage to HIV Care

- For woman & exposed infant
- Req medical & support services





Updated Perinatal Guidelines





Care Guidelines for HIV+ Pregnant Women

- Provide standard clinical evaluation:
HIV disease stage
- Evaluate degree of immunodeficiency:
CD4+ count, CD4%
- Assess risk of disease progression:
HIV-RNA plasma levels

U.S. Public Health Service Perinatal Guidelines Nov 2007





Care Guidelines for HIV+ Pregnant Women

- Document ARV use history
- Discuss +/- of therapy during pregnancy
- Develop strategy for long term evaluation & management of mother and infant

U.S. Public Health Service Perinatal Guidelines Nov 2007





Revised Guidelines November 2007

- Before starting ARVs: resistance testing
- Resistance testing also w. virologic failure
- Counsel re the importance of adherence

U.S. Public Health Service Perinatal Guidelines Nov 2007





Revised Guidelines Nevirapine

- Addition of single dose nevirapine to a potent regimen is not recommended
 - Leads to drug resistance in the mother
- If prevention only nevirapine based regimen
 - continue nucleoside analogs for 3-7 days after stopping nevirapine

U.S. Public Health Service Perinatal Guidelines Nov 2007





Revised Guidelines November 2007

- Even w AZT resistance, give IV AZT during labor & delivery
- Optimal prophylactic regimen for newborns whose mothers have ARV resistance should be chosen before delivery with a pediatric specialist

U.S. Public Health Service Perinatal Guidelines Nov 2007





Special ARV Use Considerations

- Pregnancy may alter ARV absorption, distribution, & metabolism
 - ARV dosing and toxicity risk may be affected
 - Some PIs may require altered dosing
- Limited data
- Report all cases of ARV drug exposure to Antiretroviral Pregnancy Registry

U.S. Public Health Service Perinatal Guidelines Nov 2007





Perinatal HIV Transmission

- Without ARV: 16%–25% rate in North America & Europe
- 1994: 21% rate (before ZDV recommendation)
- 1995: 11% rate (practice change)
- Today: risk of perinatal transmission can be <2% with
 - effective antiretroviral therapy
 - elective cesarean section as appropriate
 - formula feeding

U.S. Public Health Service Perinatal Guidelines Nov 2007





Monitoring during Pregnancy

- CD4 cell count
 - initial visit
 - every 3 months afterwards
- Plasma HIV RNA levels
 - Initial visit
 - 2-6 weeks after starting/changing ARV therapy
 - Monthly until RNA levels undetectable
 - Every 2 months during pregnancy
 - At 34-36 weeks for decision on mode of delivery

U.S. Public Health Service Perinatal Guidelines Nov 2007





Monitoring during Pregnancy

- Perform resistance testing for women with suboptimal VL suppression or rebound
- Monitor for ARV drug complications
- Ultrasound recommendations:
 - 1st trimester – gestational age & timing for cesarean delivery (if needed)
 - 2nd trimester – fetal anatomy for women on combination ARVs (especially efavirenz) during 1st trimester

U.S. Public Health Service Perinatal Guidelines Nov 2007





Perinatal Care

The number of cases of perinatally acquired infection in 2004 decreased by approximately 95% from the peak reported incidence in 1992, largely because of antiretroviral drug therapy during pregnancy.



Zorrilla, IAS Topics in HIV Medicine, Vol 15, Issue 1, Feb/Mar 2007



Maternal HIV RNA Viral Load

Correlation between maternal VL & transmission risk, even in pregnant women treated with ARV agents

- Risk of transmission with undetectable VL is extremely low
- Transmission has occurred at all VL levels
- ZDV ↓ transmission regardless of VL level
- ZDV prophylaxis should be given even to women with very low or undetectable VL levels



U.S. Public Health Service Perinatal Guidelines Nov 2007



Pregnancy

- Pregnancy does not accelerate HIV disease
- Disease stage can impact pregnancy outcome
- Perinatal transmission rates depend on multiple factors
- The use of ARVs → decrease transmission rates





Pediatric AIDS Cases

1992 to 2005: parentally acquired AIDS cases declined 93% in the USA from 855 to 57 cases

Division HIV/AIDS Prevention
National Center for HIV/AIDS
Viral Hepatitis & TB Prevention
October 10 2007



Time of Maternal HIV Testing among Children with Perinatally Acquired AIDS, HIV Exposure or HIV Infection Reported in 2006—United States and Dependent Areas

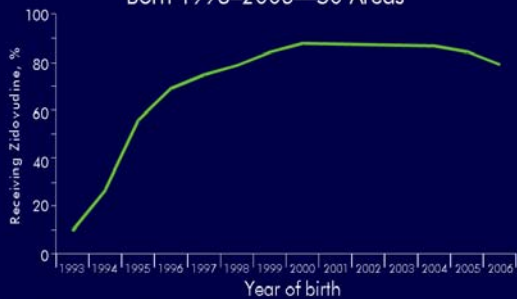
Time of maternal HIV test	Perinatally Acquired AIDS N=74		HIV Exposure* N=1,883		HIV Infection [†] N=447	
	No.	%	No.	%	No.	%
Before or at birth	28	38	1,746	93	168	38
After birth	28	38	65	3	137	31
Unknown	18	24	72	4	142	32



*From 33 areas that report perinatal exposure.
[†]From 50 areas with confidential name-based HIV infection reporting.



Zidovudine Use for HIV-infected Pregnant Women or for Perinatally Exposed* or Infected Children Born 1993–2006—50 Areas



Note: Includes prenatal, intrapartum, or neonatal receipt of Zidovudine to reduce perinatal HIV transmission.
As of 2006, 50 areas conducted confidential name-based HIV surveillance.
* Perinatal exposure data from 32 areas that report perinatal exposure.





Mode of Delivery

Counsel re potential +/- of cesarean vs vaginal delivery

- Cesarean ↑ complications risk
 - vaginal delivery in HIV-infected women
 - cesarean in HIV-uninfected women
 - Scheduled C/S less risky than emergent C/S
- Complications do not outweigh benefits of reduced HIV transmission for those at increased risk
- Prophylactic narrow spectrum antibiotic recommended for C/S

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Antiretroviral Use

Use of zidovudine (ZDV) for prevention of mother-child HIV transmission in the U.S. increased substantially between 1993-2003





2nd HIV Test in the 3rd Trimester

Retesting should be considered for all

- preferably before 36 wks
- even in low-prevalence settings
- comparable \$ effectiveness

Specifically recommended when:

- at increased risk of HIV infection
- in certain states and facilities





Scheduled Cesarean Delivery

When maternal VL is not ↓↓ w ART

- Schedule cesarean delivery
- Reduces risk of HIV transmission





Antiretroviral Medications

- Appropriate ART & prophylaxis use can reduce perinatal transmission to <2%
- Antiretroviral medications including zidovudine (ZDV) should be used as appropriate for the woman's health and to reduce HIV-1 transmission risk



Division HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis & TB Prevention, October 10, 2007



Avoidance of Breastfeeding

Approx 1/3 HIV transmission is via breast milk in populations where practice common

- Breastfeeding should be avoided
- Ensure access to a safe & affordable breast milk substitute



Division HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis & TB Prevention, October 10, 2007



Newborn Testing

- Rapid HIV testing of newborns
- Last chance at prophylaxis
- Mothers not screened



Division HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis & TB Prevention, October 10, 2007

ARV Concentration Differences

ARV	Gender	Pregnancy data
NVP	Female AUC ↑ (10)	↓AUC (9)
EFV	Female AUC ↑ (1)	N/A
SQV	Female AUC ↑ (2)	↓AUC (4); ↔ AUC (5)
RTV	↔	↓ AUC (5)
NFV	↔ (3)	↓ AUC (6, 7, 11)
LPV	↔	↓ AUC (13), ↔(14),(15)
IDV	↔	↓ AUC (6, 8)
ATV	↔	↔(12)

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Recommended Perinatal ARVs

	PIs	NNRTIs	NRTIs	Other
Recommended	Lopinavir/r	Nevirapine	Zidovudine* Lamivudine*	
Alternative	Indinavir Ritonavir Saquinavir HGC		Abacavir Didanosine Emtricitabine Stavudine	
Insufficient data	Atazanavir Fosamprenavir Darunavir Tipranavir	Etravirine	Tenofovir DF	Enfuvirtide Maraviroc Raltegravir
Not recommended	Nelfinavir**	Efavirenz Delavirdine	Zalcitabine	

*Zidovudine and lamivudine are included as a fixed-dose combination in Combivir®; zidovudine, lamivudine, and abacavir are included as a fixed-dose combination in Trizivir®.
** Dear Healthcare Professional, Pfizer, May 6, 2008

Available at: <http://aidsinfo.nih.gov/guidelines>. Revision: January 2008

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AZT and Pregnancy

- ACTG 076 in April 1991 50 US sites
- AZT appears to limit the transmission of HIV to fetuses
- Women received 14-34 wks:
 - 100 mg of AZT 5 x day
 - or 200 mg 3 x day
- During pregnancy women
 - received AZT at 2mg/kg by continuous IV over one hour and then 1mg/kg infusion until delivery
- Infants receive 2mg/kg every 6 hours for 6 weeks





Toxicity of AZT

- Can interfere with DNA polymerase
- Increased cancer rate in offspring (obsv'd in mice)
- To date no cases of human cancers have been seen in the with high dose AZT during pregnancy





What Types of ARV Therapy Can Be Used during Pregnancy

- FDA Pregnancy Categories
- AZT & 3TC NNRTI can cross placental barrier
- All other ARVs are classified as category C
- With women not on ART:
 - discuss the +/- of starting before or after 14 wks





LPV PK in HIV+ Pregnant Pts vs Controls

- Multicenter, case control study of HIV+ pregnant subjects (n=101) and non-pregnant subjects (control; aged 29-38), receiving LPV/r 400/100 SGC BID + 2 NRTIs
- Median LPV trough in HIV+ pregnant pts not sig lower in the 3rd trimester (n=74, median LPV Cmin, 3274 ng/mL) vs. 2nd trimester (n=27, median LPV Cmin, 3806ng/mL; p=0.055).
- HIV+ pregnant pts had significantly lower troughs vs control (n=107, median LPV Cmin, 5122 ng/mL; p<0.0001 vs 3rd trimester pts)
- At delivery, 85% HIV+ pts have VL<200 copies/mL
 - 7pts had VL>1000 copies/mL at delivery



Khuong-Josses MA et al. 14th CROI 2007, Los Angeles, poster 743

Adequate LPV Exposure Achieved during 3rd Trimester with Higher LPV/r Dose: PACTG1026s

- PACTG 1026 is an ongoing, prospective, non-blinded study of ARV PK in HIV-infected pregnant women
- Cohort of patients receiving LPV/r 400/100 mg BID in the 2nd trimester, then 533/133 mg BID in the 3rd trimester and 2 weeks post-partum (PP)
- Intensive steady-state 12-hr PK performed during 3rd trimester and at 2 weeks PP
- Maternal and umbilical cord blood obtained at delivery

	Median	Range
Age at delivery (years)	31.2	18.6 - 40.9
Weight at delivery (kg)	80.6	60.4 - 121.8
CD4+ at delivery (cells/uL)	517	190 - 1339
Concomitant ARV's at delivery	17 Combivir, 6 Trazivir, 6 Other	
Ethnicity	11 Hispanic, 8 Black, 6 White, 1 Unknown	

Mirochnik M., et al. 13th CROI, Denver 2005, Poster#710

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PACTG 1026s cont

Median (range)	2nd Trimester 400 mg/100 mg bid n=8	3 rd Trimester 533 mg/133 mg bid n=26	Postpartum 533 mg/133 mg bid n=22
AUC (mcg ² hr/mL)	57.3 (30.2 - 101.9)	87.5 (32 - 153.5)	151.7 (49.1 - 228.4)
C _{predose} (mcg/mL)	2.8 (1.2 - 8.2)	6.4 (BDL - 13.3)	11.0 (0.05 - 20.0)
C _{max} (mcg/mL)	8.0 (3.8 - 12.9)	9.7 (4.4 - 15.2)	15.0 (6.0 - 23.2)
C _{12 hour} (mcg/mL)	2.5 (1.3 - 7.6)	4.6 (0.8 - 9.8)	8.6 (2.4 - 16.5)

Mirochnik M., et al. 13th CROI, Denver 2005, Poster#710

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Stopping ART during Pregnancy

- Avoid interruption of ART, if possible
- If required, stop and reinstate all drugs @ same time except:
 - If on NNRTI: Stop NNRTI first, con't others ~7 days
 - NNRTIs have long half-life; optimal interval between stopping NNRTI and other ARV drugs not known
 - If restarting NVP after interruption of >2 weeks, restart with standard 2-week dose escalation

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Failure of Viral Suppression

- Assess resistance, adherence, dosing, and problems with absorption
- Consider modification of ARV regimen
- Consult an expert
- Scheduled cesarean delivery recommended if HIV RNA >1,000 copies/mL near time of delivery

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Concerns in Pregnancy Nelfinavir

- 9/07: Manufacturer (Pfizer) letter
- Low levels of ethyl methane sulfonate (EMS), a process-related impurity, in nelfinavir
- EMS: teratogenic, mutagenic, & carcinogenic in animals
- No data from humans exists
- No ↑ in birth defects in the ARV Preg Registry

Guideline in use of Antiretroviral therapy in Adolescents and Adults January 2008





Nelfinavir

Not recommended for use in pregnancy until further notice

Note: As of 3/31/08, all nelfinavir (Viracept) manufactured by Pfizer meets the new limits of EMS established by the FDA for all patient populations, including pregnant women and children.

*Dear Healthcare Professional Letter, 5/6/08 available at: http://www.aidsinfo.nih.gov/DrugsNew/DrugDetailNT.aspx?int_id=263





Interactions with Oral Contraceptives



Drugs Affected	Atazanavir (ATV)	Fosamprenavir (FPV)	
	Levels: Ethinyl estradiol AUC \uparrow 48%, norethindrone AUC \uparrow 110% Dose: use lowest effective dose or alternative methods.	An increase in ethinyl estradiol and norethindrone levels occurred with APV, and APV levels \downarrow 30%. Do not coadminister; alternative methods of contraception are recommended.	
Drugs Affected	Darunavir + Ritonavir (DRV/RTV) [†]	Indinavir (IDV)	Lopinavir + Ritonavir (LPV/r)
	Levels: Potential for \downarrow ethinyl estradiol from RTV. Use alternative or additional method with DRV/r.	Levels: Norethindrone \uparrow 39%, Ethinyl estradiol \uparrow 34%. No dose adjustment.	Levels: Ethinyl estradiol \downarrow 42%. Use alternative or additional method.
Drugs Affected	Nelfinavir (NFV)	Ritonavir (RTV)	
	Levels: Norethindrone \downarrow 18%, Ethinyl estradiol \downarrow 47%. Use alternative or additional method.	Levels: Ethinyl estradiol \downarrow 40%. Use alternative or additional method.	
Drugs Affected	Saquinavir* (SQV)	Tipranavir + Ritonavir (TPV/RTV)	Maraviroc (MVC)
	No data.	50%.* Use alternative or additional method. Women on estrogen therapy have increased risk of anovulatory cycle. Used as hormone replacement therapy; monitor clinically for signs of estrogen deficiency.	combination



Interactions with NNRTIs

Delavirdine (DLV)	Efavirenz (EFZ)	Etravirine (ETR)	Nevirapine (NVP)
<ul style="list-style-type: none"> Levels of ethinyl estradiol may ↑ Clinical sig unknown 	<ul style="list-style-type: none"> Levels ethinyl estradiol ↑ 37% No data on other component. Use alt or additional methods 	<ul style="list-style-type: none"> ↑ ethinyl estradiol AUC 22% ↔ Norethindrone Dose: standard 	<ul style="list-style-type: none"> Levels: ethinyl estradiol ↓ ~ 20% Use alt or additional methods

Available at: <http://aidsinfo.nih.gov/guidelines>. Revision: January 29, 2008



Oral Contraceptives Summary

- All NNRTI & PIs impact OCP and HRT EE AUC
- Consider Alt contraceptive methods
- Little info on newer hormonal contraceptives
 - patch, vaginal ring
 - dose adjustment for HAART
- Women with HIV should have the same access to reproductive options as uninfected women





Summary





Summary

- All women should be tested
 - Regardless of childbearing age
- All pregnant women tested in 1st and 3rd trimesters
 - All women should be able to achieve viral suppression by delivery.
- Discordant couples (HIV- woman; HIV+ partner)
 - Counsel on harm and risk reduction for transmission of the virus
- If patients refuse testing, refusal must be documented in patient's chart.





Summary

- All HIV infected women need to be evaluated for family planning.
- Women who have no prenatal care should be started on intrapartum AZT therapy at the rupture of membrane.
- Counsel regarding risk and modes of delivery





Summary

- Adherence, side effects and virologic suppression leads to reduction in maternal child transmission.
- Some ART are not optimal in women of child-bearing age.
- Multidisciplinary approach to women who are HIV+ and pregnant should include infectious diseases, OB/GYN, perinatologist, fetal-maternal medicine, social services and pediatric infectious diseases.





Save the Date!

HIV Across the Lifespan:
Screening & Management
in the Primary Care Setting

Program 2: HIV & Adolescents





Questions?

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