WHAT’S NEW IN THE 2015 PERINATAL HIV GUIDELINES?

Today’s Webinar will be starting soon

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Today’s presenters

- Judy Levison MD, MPH
- Carey Eppes MD, MPH

Baylor College of Medicine
Updates from the Perinatal HIV Guidelines

Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

Developed by the HHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission—A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Perinatal Guidelines:

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalHIV.pdf Accessed [insert date] [include page numbers, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDSInfo website (http://aidsinfo.nih.gov).
What’s new?

• Preconception counseling/care for HIV-infected women
• Reproductive options for HIV serodiscordant couples
• General principles regarding use of cART during pregnancy
• Updates on teratogenicity information and pregnancy outcomes related to cART
• Recommendations for use of cART regimens during pregnancy
What’s new?

- Antepartum care

- Special populations:
  - HIV/HCV co-infections
  - HIV-2 during pregnancy
  - New section on perinatally-infected pregnant women

- Intrapartum care

- Postpartum care and breastfeeding
What’s new in the guidelines

• Preconception counseling/care for HIV-infected women
  • Have undetectable viral load (VL) prior to conception
  • Be aware of interactions between hormonal contraceptives and some antiretrovirals (ARVs) — TABLE 3
  • No known risks of increasing transmission of HIV to a partner with hormonal methods
## Interactions of ARVs with Hormonal Contraceptives

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (CIII) (page 1 of 3)

<table>
<thead>
<tr>
<th>ARV Drug</th>
<th>Effect on Contraceptive Drug Levels</th>
<th>Dosing Recommendation/ Clinical Comment for Combined Hormonal Methods and Progestin-Only Pills</th>
<th>Dosing Recommendation/ Clinical Comment for DMPA&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Dosing Recommendation/ Clinical Comment for Etonogestrel Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTIs</td>
<td></td>
<td></td>
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</tbody>
</table>
| EFV      | Oral Ethinyl Estradiol/ Norgestimate:  
• No effect on ethinyl estradiol concentrations  
• ↓ active metabolites of norgestimate (levonorgestrel AUC ↓ 83%; norelgestromin AUC ↓ 64%)  
Implant:  
• ↓ etonogestrel  
Levonorgestrel (Emergency contraception) AUC ↓ 58% | Use alternative or additional contraceptive method. | No additional contraceptive protection is needed. | Use alternative or additional contraceptive method. |

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Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

Downloaded from [http://aidsinfo.nih.gov/guidelines](http://aidsinfo.nih.gov/guidelines) on 10/5/2015
Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives (CIII) (page 2 of 3)

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<tr>
<td>NNRTIs, continued</td>
<td></td>
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<tr>
<td><strong>ETR</strong></td>
<td>Ethinyl estradiol AUC ↑ 22% Norethindrone: • No significant effect</td>
<td>No additional contraceptive protection is needed.</td>
<td>No additional contraceptive protection is needed.</td>
<td>No additional contraceptive protection is needed.</td>
</tr>
<tr>
<td><strong>NVP</strong></td>
<td>Ethinyl estradiol AUC ↓ 20% Norethindrone AUC ↓ 19% DMPA: • No significant change</td>
<td>Can consider an alternative method or a reliable method of barrier contraception in addition to this method.</td>
<td>No additional contraceptive protection is needed.</td>
<td>Can consider an alternative method or a reliable method of barrier contraception in addition to this method.</td>
</tr>
<tr>
<td><strong>RPV</strong></td>
<td>Ethinyl estradiol AUC ↑ 14% Norethindrone: • No significant change</td>
<td>No additional contraceptive protection is needed.</td>
<td>No additional contraceptive protection is needed.</td>
<td>No additional contraceptive protection is needed.</td>
</tr>
<tr>
<td>RTV-Boosted PIs</td>
<td></td>
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</tr>
<tr>
<td><strong>ATV/r</strong></td>
<td>Ethinyl estradiol AUC ↓ 19% Norgestimate &lt;u&gt;AUC ↑ 85%&lt;/u&gt;</td>
<td>Use alternative or additional contraceptive method.</td>
<td>No additional contraceptive protection is needed.</td>
<td>Can consider an alternative method or a reliable method of barrier contraception in addition to this method.</td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>Ethinyl estradiol AUC ↓ 44% Norethindrone AUC ↓ 14%</td>
<td>Use alternative or additional contraceptive method.</td>
<td>No additional contraceptive protection is needed.</td>
<td>Can consider an alternative method or a reliable method of barrier contraception in addition to this method.</td>
</tr>
<tr>
<td><strong>FPV/r</strong></td>
<td>Ethinyl estradiol AUC ↓ 37%</td>
<td>Use alternative or additional</td>
<td>No additional contraceptive protection is needed.</td>
<td>Can consider an alternative method or a reliable method of barrier contraception in addition to this method.</td>
</tr>
</tbody>
</table>
• Options for serodiscordant (one with HIV/one without HIV) couples
  • HIV infected partner on cART with sustained undetectable VL
  • Reproductive technology (ICSI, IUI with washed sperm) vs. periovulatory unprotected sex
  • PrEP for 30 days prior to and 30 days after attempting conception
  • Pregnancy and breastfeeding are not contraindications to PrEP in women with ongoing risk
Pre-exposure prophylaxis (PrEP) for the uninfected partner

• Once daily tenofovir/emtricitabine (Truvada)
• FDA approved since 2012
• Basic requirements:
  • Baseline HIV, renal function, pregnancy test, HepBsAg and HBsAb
  • HIV test and pregnancy test q 3months
  • Renal function q 6 months
  • Immunize against Hep B if not immune
• Pregnancy and breastfeeding are not contraindications to PrEP
General principles regarding ARVs in pregnancy

- “The goal of cART is to maintain a viral load below the limit of detection throughout pregnancy” (supported by studies confirming rate of perinatal transmission is inversely related to duration on cART during pregnancy)
- May start cART before genotype result returns and adjust accordingly after genotype available
- In labor: continue oral cART and give IV AZT if VL>1000
• Teratogenicity
  • Lack of clear association between first-trimester exposure to any ARV drug and increased risk of birth defects
  • The clinical significance of lower bone mineral density in newborns exposed to tenofovir is unknown
Combination antiretroviral therapy (cART)

Literature review divided into pre/post 2005

• Preferred regimens (efficacious, durable, pK data available, no known teratogenicity) — TABLES 6/7
  • NRTIs: ABC/3TC, TDF/FTC; ZDV/3TC (bid)
  • NNRTIs: EFV
  • PIs: ATV/r; DRV/r (bid) in pregnancy
  • INSTIs: RAL (bid)

• Alternative regimens:
  • NNRTIs: RPV if VL<100K and CD4>200
  • PIs: LPV/r (bid)
Combination antiretroviral therapy (cART)

- cART naïve:
  - Initiate cART as soon as HIV is diagnosed/earlier viral suppression is associated with lower risk of transmission.
  - Consider RAL if high VL late in pregnancy (expect 1-log decrease per week)

- Monitoring in pregnancy:
  - Check VL 2-4 weeks after initiating rx, monthly until undetectable, every 3 months, and at 34-36 weeks to inform decision regarding mode of delivery and optimal management of newborn
Antepartum Care

• Resistance testing
  • In ARV naïve women, do not wait for genotype to start cART

• Lack of viral suppression
  • Resistance vs. adherence
  • Consider adding raltegravir
  • Consider directly observed therapy
  • Scheduled Cesarean if VL>1000 at 38 weeks
HIV/HCV co-infections

- All HIV infected pregnant women should be screened during the current pregnancy

- Screening should use the most sensitive immunoassay

- All HIV infected women who are negative for HBV and HAV should be vaccinated
HIV/HCV coinfection

- The management of HIV/HCV coinfection is complex
  - Newer medications exist for HCV treatment
  - These have not been tested in pregnancy
HIV/HCV coinfection

Recommendations for when and in whom to initiate treatment

Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies owing to comorbid conditions.

Rating: Class I, Level A

Immediate treatment is assigned the highest priority for those patients with advanced fibrosis (Metavir stage F3), those with compensated cirrhosis (Metavir stage F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C.

Based on available resources, immediate treatment should be prioritized as necessary so that patients at high risk for...
HIV/HCV coinfection

• Previous regimens: ribavirin and interferon

• Newer regimens:
  • Simepravir (category C)
  • Sofosbuvir (category B)
  • Ledipasvir (category B)
  • Fixed dose combination of ledipasvir/sofosbuvir and paritaprevir/ritonavir/ombitasvir plus twice daily dasabuvir
HIV/HCV coinfection

- HIV/HCV coinfection does **not** necessitate cesarean delivery if not otherwise indicated
  - Liver function tests should be followed carefully
  - Infants born to coinfected women should be assessed for both HIV and HCV
HIV 2 infection

- Should be considered in women who are from (or have partners from) countries where HIV2 is endemic AND who have positive results on an HIV1/HIV2 antibody or HIV1/HIV2 immunoassay.
Number of reported cases of HIV-2 infection, by analytic category* and year of diagnosis --- United States, 1987--2009

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6029a3.htm#fig
4th generation HIV-1/2 immunoassay

HIV-1/HIV-2 antibody differentiation immunoassay

HIV-1 antibodies detected
HIV-2 antibodies detected

Acute HIV-1 infection
Negative for HIV-1
HIV 2 infection and pregnancy

• Women who require treatment for their own health because they have significant clinical disease or CD4 <500 cells/nm\(^3\) should be treated with 2 NRTIs and a boosted protease inhibitor

• Preferred regimens:
  • Lopinavir/ritonavir plus
    • zidovudine/lamivudine
    • or
    • abacavir/lamivudine
    • or
    • tenofovir/emtricitabine
HIV 2 infection

- Optimal treatment regimens for women with CD4>500 and no significant disease are unknown

- **Expert opinion:**
  - A boosted PI based regimen with 2 NRTIs
  - OR
  - Zidovudine prophylaxis alone during pregnancy and intrapartum
Perinatally-infected pregnant women

- A significant number of pregnancies are unintended in this population
- Components of healthcare do not differ — however, unique issues to be aware of include:
  - Adherence is often a problem
  - Overall younger (adolescent)
  - Higher chances of drug resistance due to prolonged exposures
New section on perinatally-infected pregnant women

• *May have increased psychosocial challenges*
  • Depression
  • Loss of parents
  • Presence of long term chronic illness

• *Addressing mental health is critical*
Intrapartum care

• Epidural is safe regardless of cART regimen

Effect of ritonavir-induced cytochrome P450 3A4 inhibition on plasma fentanyl concentrations during patient-controlled epidural labor analgesia: a pharmacokinetic simulation

C.R. Cambic, M.J. Avram, D.K. Gupta, C.A. Wong
Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
Intrapartum Care

• Ritonavir inhibits CYP450 and decreases elimination of fentanyl

• Recent pharmacokinetic simulation study suggest this inhibition is unlikely to produce plasma fentanyl concentrations at levels that would cause respiratory depression
Intrapartum

- IV zidovudine should be given intrapartum to women with a $\text{VL} > 1000 \text{ copies/mL}$

- Scheduled cesarean delivery is recommended at 38 weeks for women who fail to achieve virological suppression ($\text{VL} > 1000 \text{ copies/mL}$)

- Scheduled cesarean delivery performed solely for prevention of HIV transmission in women receiving cART and with HIV RNA $< 1000 \text{ copies/mL}$ is not routinely recommended
Intrapartum

• Insufficient evidence to determine whether cesarean delivery after rupture of membranes or onset of labor reduces risk of transmission.

• Providers may contact the National Perinatal HIV Hotline (1-888-448-8765), which provides free clinical consultation on perinatal HIV care.
Postpartum

• Decisions regarding cART after delivery should be made between the patient and her HIV provider, before delivery
• Contraceptive counseling is a critical step
• The postpartum period creates challenges to antiviral adherence, therefore a plan for postpartum should be made prior to delivery and discharge
  • Supportive services, transportation
  • Linkage to care
  • Appointments should be made prior to discharge
Postpartum

• In discussing the avoidance of breastfeeding as the strong, standard recommendation for HIV-infected women in the United States, the Panel notes that women may face social, familial, and personal pressures to breastfeed despite this recommendation and that it is important to begin addressing possible barriers to formula feeding during the antenatal period.
Infant prophylaxis

• **Standard:** 4-6 weeks of ZDV

• **High Risk:** (no antepartum ARVs +/- intrapartum) then ZDV x 6 weeks PLUS NVP at birth, 48 hours and 96 hours after second dose
Infant anti-retroviral prophylaxis

• Despite the paucity of available data, the use of combination ARV prophylaxis for infants in high risk situations is increasing.

• Canadian investigators have reported outcomes in 136 infants who received treatment-level dose of triple ARV prophylaxis within 72 hours of birth. 12/136 were infected and no major toxicities were identified
Pediatric Treatment Guidelines

• The risks associated with use of a three-drug ARV regimen in neonates as well as the potential benefits, including the possibility of prolonged remission in infected neonates, require further study before a general recommendation can be made.

• The Panel recommends that neonatal care providers, who are considering a 3-drug ARV treatment regimen of term infants younger than 2 weeks or premature infants, contact a pediatric HIV expert for guidance and individual case assessment of the risk/benefit ratio of treatment and for the latest information on neonatal drug doses.

• Providers may contact a local pediatric HIV expert or National Perinatal HIV Hotline (1-888-448-8765), which provides free clinical consultation on perinatal HIV care.
THANK YOU!

Questions?