NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Issues in Perinatal HIV

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Talking points…

• First…the numbers
• Important studies impacting perinatal HIV
• How the July 2012 guidelines for Perinatal care of the HIV positive woman has changed
Adults and children estimated to be living with HIV | 2011

Total: 34.2 million [31.8 million – 35.9 million]
Over 7000 new HIV infections a day in 2011

- About 97% are in low and middle income countries
- About 900 are in children under 15 years of age
- About 6000 are in adults aged 15 years and older, of whom:
  - almost 47% are among women
  - about 41% are among young people (15-24)
Women as Share of People Living with HIV by Region, 2009

- **Global**: 52%
- **Sub-Saharan Africa**: 60%
- **Caribbean**: 55%
- **Middle East/ North Africa**: 48%
- **Eastern Europe/ Central Asia**: 49%
- **Oceania**: 46%
- **South/ South-East Asia**: 35%
- **Central/ South America**: 35%
- **East Asia**: 29%
- **Western/ Central Europe**: 29%
- **North America**: 26%

**NOTE**: Among adults, aged 15 and older.

2009: 23% of new infections (11,200) were in women.
Adult and Adolescent Females Living with an AIDS Diagnosis, by Transmission Category, 1985–2009—United States and 6 U.S. Dependent Areas

- Injection drug use
- Heterosexual contact
- Other

No. of persons (in thousands)

Year


Note: All displayed data have been statistically adjusted to account for reporting delays and missing risk-factor information, but not for incomplete reporting.

- 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.
3 Landmark Studies
Results of ACTG 076

66% reduction in risk for transmission ($P = <0.001$)

Efficacy observed in all subgroups

Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
1,763 HIV Serodiscordant Couples (97% heterosexual)

- **n = 872**
- **n = 853**
- **n = 37**
- **n = 1**

**HIV Prevention Trials Network (HPTN) Study 052**

**Study Features**

- N = 1,763 HIV serodiscordant couples
- Phase 3, Randomized Trial
- Age Requirement: > 18 years
- Enrollment: April 2005-May 2010
- Location: 13 sites (international)
- Enrollment CD4 count: 350-550 cells/mm³
- HIV uninfected: (-) HIV test < 14 days of entering study
- Randomized to Immediate or Deferred ARV Treatment
- All antiretroviral naïve
- Antiretroviral therapy consisted of 3-drug regimens
- Genetic analysis of all HIV transmissions for linkage

### Immediate Therapy

- n = 886

### Deferred Therapy

- CD4< 250 or AIDS-Related Event
- n = 877

All received safe sex counseling, free condoms
All received STI treatment and regular HIV testing

HIV Prevention Trials Network (HPTN) Study 052

### HPTN 052 Transmission Endpoints

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Overall Number Infections</th>
<th>Linked Number Infections*</th>
<th>Follow-up (PY)</th>
<th>Incidence/100PY [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>4</td>
<td>1</td>
<td>1,585</td>
<td>Linked: 0.1 [0.0 – 0.4]  Overall: 0.3 [0.1 – 0.6]</td>
</tr>
<tr>
<td>Delayed</td>
<td>35</td>
<td>27</td>
<td>1,585</td>
<td>Linked: 1.7 [1.1 – 2.5]  Overall: 2.2 [1.6 – 3.1]</td>
</tr>
</tbody>
</table>

* 18/28 (64%) transmissions from HIV+ participants with CD4 >350 cells/mm³
* 23/28 (82%) transmissions occurred in sub-Saharan Africa couples
* 18/28 (64%) transmissions were from female to male partners

Cohen M et al.  NEJM 2011;365:493-505
HIV Prevention Trials Network (HPTN) Study 052

Deferred Therapy (n = 877)

Early Therapy (n = 886)

Linked Transmissions

96% Reduction

P ≤ 0.001

Initiating Antiretroviral Therapy in Treatment Naïve Patients

Change in CD4 Threshold in HHS Guidelines
PrEP
Preventing Sexual Transmission of HIV: ARV PrEP
Male-to-Male

HIV (+)

HIV (-)

Tenofovir-Emtricitabine (Truvada)
Oral Tenofovir-Emtricitabine as PREP

- **Tenofovir**
- **Emtricitabine**

Cell Types:
- Dendritic Cell
- CD4 Cell
- Macrophage
Oral Tenofovir-Emtricitabine as PREP
Oral Tenofovir-Emtricitabine as PREP

- Tenofovir
- Emtricitabine

Dendritic Cell

CD4 Cell

Macrophage

HIV
Preexposure Prophylaxis for HIV Prevention in MSM
iPrEx Trial: Results

Preexposure Prophylaxis for HIV Prevention in Men who Have Sex with Men: iPrEx Trial

Detectable Drug Levels in Patients on Tenofovir-Emtricitabine

<table>
<thead>
<tr>
<th></th>
<th>Cases (HIV+) N=34</th>
<th>Active-Arm Matched Control (HIV-) N=43</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Drug Detected N (%)</td>
<td>Drug NOT detected N (%)</td>
</tr>
<tr>
<td>ALL (N, %)</td>
<td>3 (9%)</td>
<td>31 (91%)</td>
</tr>
<tr>
<td>Reporting URAI</td>
<td>0 (0%)</td>
<td>13 (100%)</td>
</tr>
<tr>
<td>Reporting NO URAI</td>
<td>3 (14%)</td>
<td>18 (86%)</td>
</tr>
</tbody>
</table>

Preexposure Prophylaxis for HIV Prevention in Men who Have Sex with Men: iPrEx Trial

Detectable Drug Levels in Patients on Tenofovir-Emtricitabine

A. Intracellular Emtricitabine Levels

- 3/34 Detectable (9%)
- 22/42 Detectable (52%)

B. Intracellular Tenofovir-DF Levels

- 2/34 Detectable (6%)
- 21/42 Detectable (50%)

Heterosexuals: Following the publication of final results from the TDF2 and Partners PrEP trials, in August 2012 CDC published interim guidance to help clinicians safely and effectively provide PrEP for heterosexually-active adults. This guidance included recommendations similar to those for MSM, as well as new recommendations relevant to women who may become pregnant while taking PrEP and to couples in which one partner is HIV-positive and the other is HIV-negative.
Perinatal Guidelines
Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings
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)
Perinatal Guidelines for Serodiscordant Couples

- Screen for other STI
- HIV + partner on HAART with undetectable VL
- Ovulatory cycle recorded
- Optimal timing of intercourse for conception
- Minimize exposure to potentially infective fluids
Perinatal Guidelines for Serodiscordant Couples

- All pregnant women should be screened for HIV at first prenatal
- Consider rescreening at 36 weeks
- All pregnant women with HIV infection should be encouraged to take HAART
Semen analysis is recommended for HIV-infected men. HIV, and possibly ART, may be associated with a higher prevalence of abnormalities.

Sperm preparation techniques + either intrauterine insemination or *in vitro* fertilization should be considered if using donor sperm from an uninfected male is unacceptable.
Reproductive Options for HIV-Concordant and Serodiscordant Couples- Women +

- HIV-infected female with uninfected male partner: The safest option is artificial insemination, including the option of self-insemination, during the periovulatory period.
Efficacy of HIV Prevention Strategies from Randomized Clinical Trials

Abdool Karim, SS et al  Lancet 2011: Jul 17
Reproductive Options for HIV-Concordant and Serodiscordant Couples

- Periconception administration of PrEP for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission.
  - The utility of PrEP of the uninfected partner when the infected partner is receiving HAART has not been studied.
  - Outcome studies are needed to examine adverse events, including risk of congenital abnormalities.
### Old

- **HAART in Pregnancy**
  - Kaletra+ Combivir
    - 3-4 pills BID

- **Intrapartum**
  - IV AZT during delivery for all HIV+ women

### New

- **HAART in Pregnancy**
  - changed Atazanvir/r (preferred) + Truvada (alternative)
    - 3 pills once daily

- **Intrapartum**
  - IF on HAART with a VL of <400 copies/ml – can omit the intrapartum AZT
Perinatal Guidelines July 2012

Old

• Postpartum care of the Infant
  - AZT every 4 hours

• Breastfeeding
  - Not recommended in the US

New

• Postpartum care of the Infant
  - AZT BID

• Breastfeeding
  - Not recommended in the US
  - No premastication of food

AETC National Resource Center, www.aidsetc.org
August 2012
Summary

- HIV/AIDS is remains a horrific pandemic

- The PACTG 076, HPTN 052 and the PrEP studies have dramatically changed how perinatal HIV is dealt with

- The science of HIV continues to evolve. HIV is now a chronic disease and we can assist HIV+ people enjoy normal lifespans and have families.
Thank you!