AETC AIDS Education & Training Center Program Southeast

Perinatal Care and Prevention

Jennifer Janelle, MD
Assistant Professor of Medicine
University of Florida at Gainesville

Objectives

- Develop patient centered, team based, treatment and delivery plans to prevent perinatal HIV Transmission
- Describe antiretroviral treatment for people living with HIV infection who are pregnant
- Provide Perinatal HIV Transmission prophylaxis to exposed infants based on current DHHS guidelines

Case

- BP is a 23 year old woman diagnosed with HIV at age 16 following a rape. Multiple complications.
- Nonadherence to antiretrovirals and outpatient appointments for last 2 years
- Spontaneous abortion after sepsis in 2016
- Entered into perinatal care at 18 weeks gestation in June of 2017
- Not seen at HIV clinic during pregnancy
- Delivered HIV positive baby in 9/2017

Perinatal Prevention of HIV: Overview

- Plan pregnancies
  - Optimize maternal health
  - Plan conception
  - Test for HIV
- Prenatal care for women with HIV infection
  - Support systems
  - Antiretroviral therapy (ART)
- Intrapartum decisions
  - C section
  - IV zidovudine (AZT)
- Post-exposure prophylaxis for infant
- Avoidance of breastfeeding

Conversations

Infant post-exposure prophylaxis and followup testing

Infant feeding

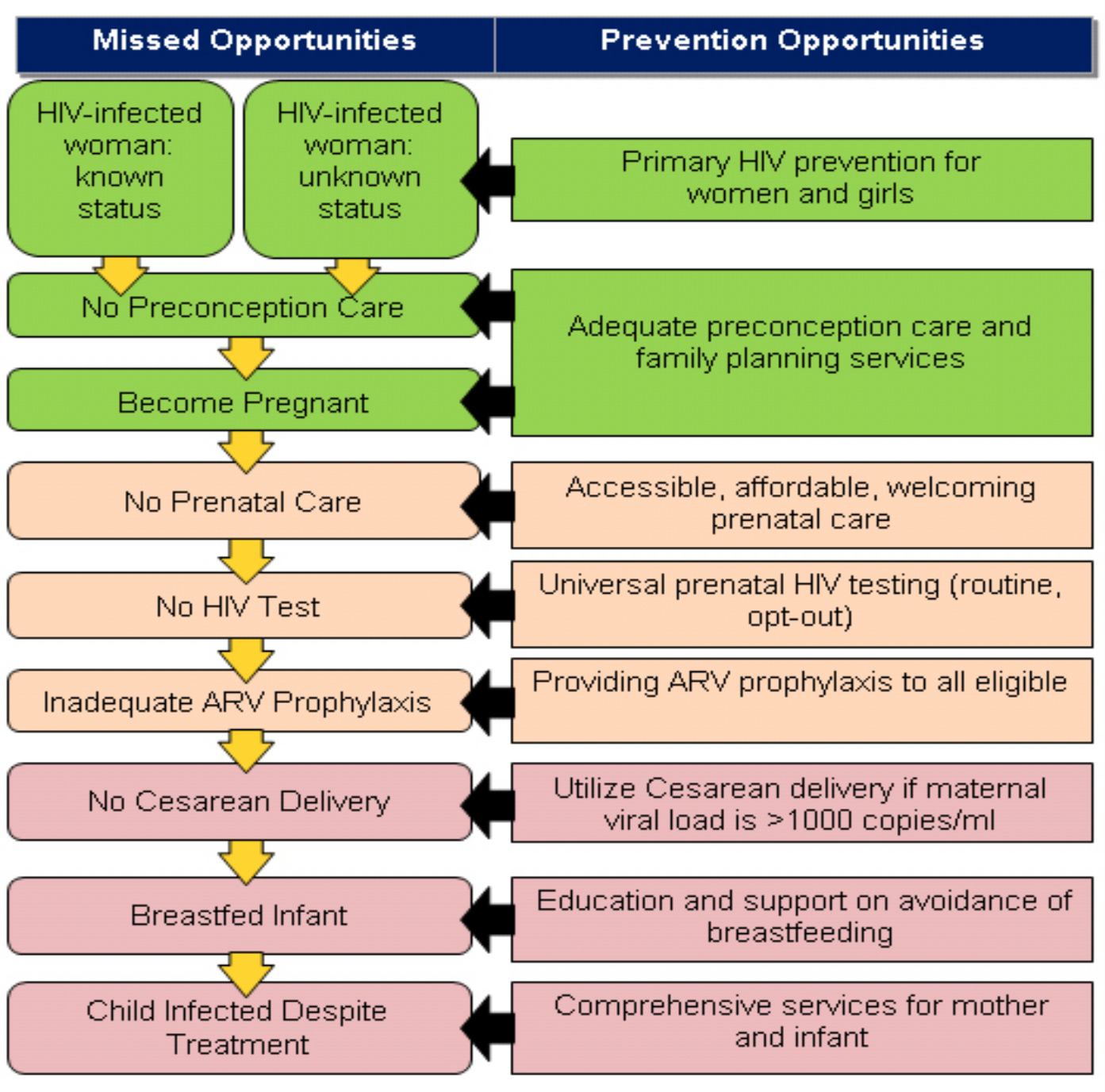
Mode of delivery

Postpartum contraception

Neonatal circumcision

Maternal lifelong ART
Goal VL < 20 copies/mL

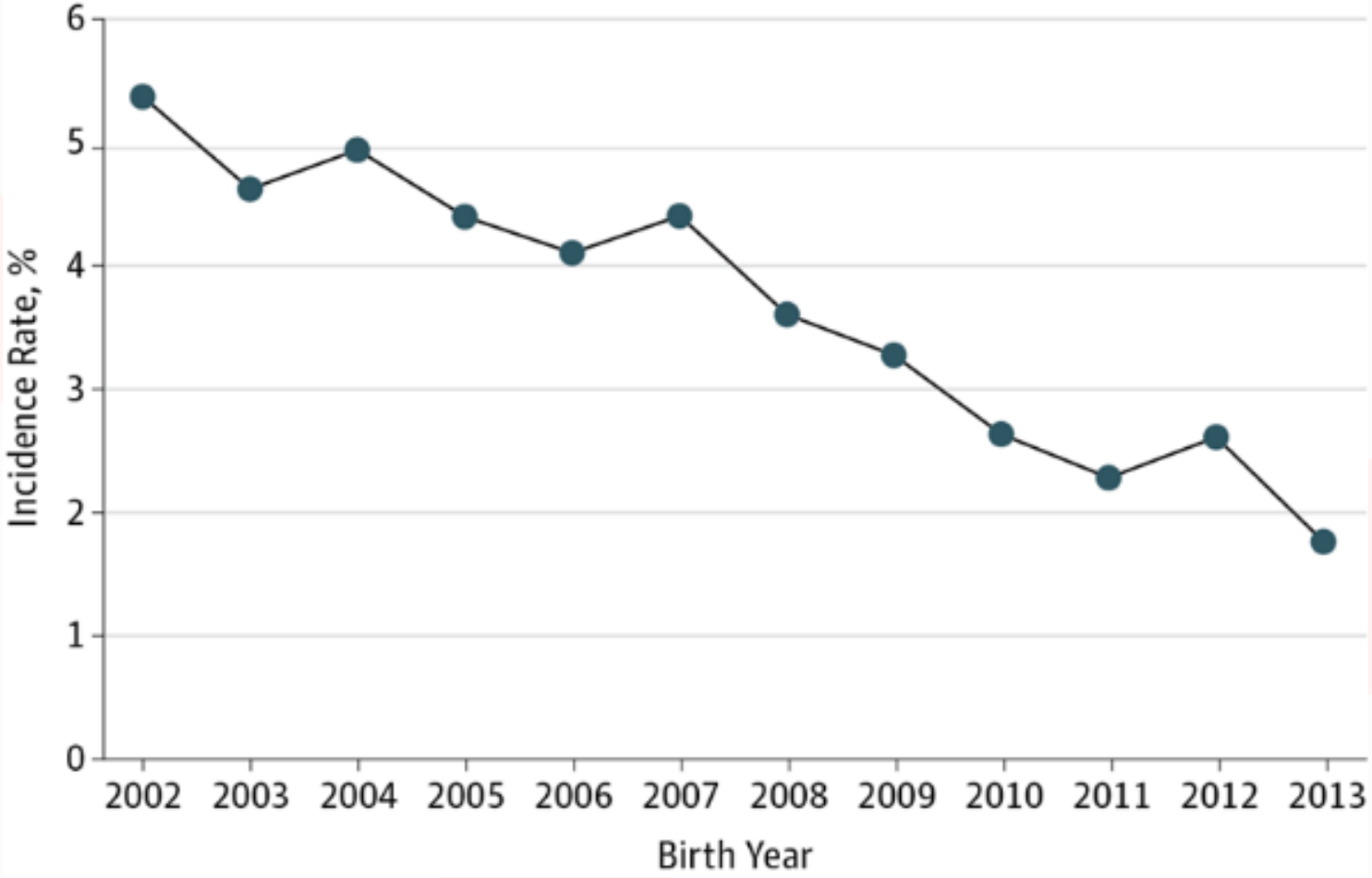
Contraception after delivery



Framework for elimination of perinatal HIV transmission

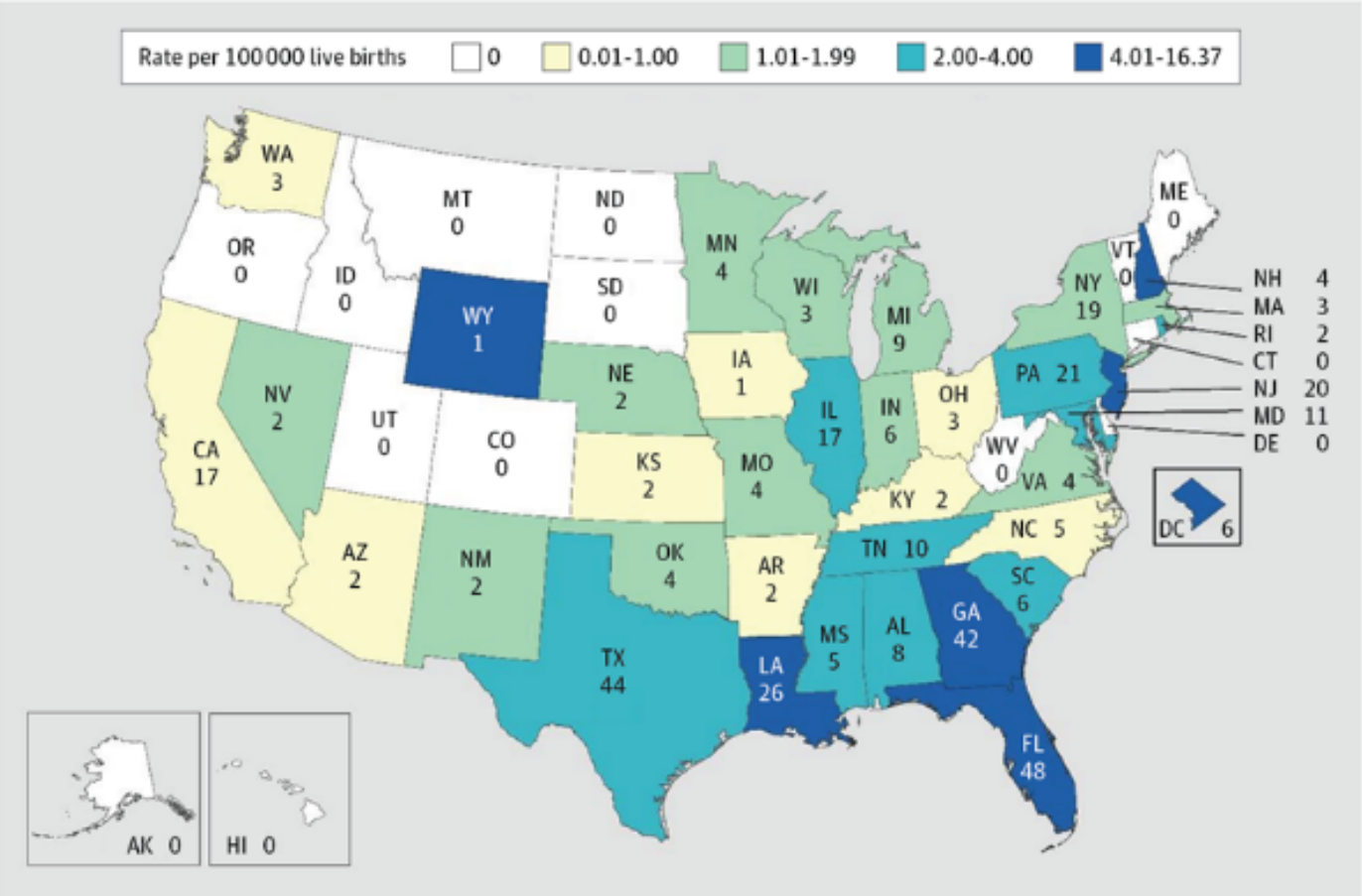
Framework graphic from
http://www.cdc.gov/hiv/group/gender/pregnantwomen/emct.html

Estimated Incidence Rates of Perinatal HIV in U.S. 2002-2013



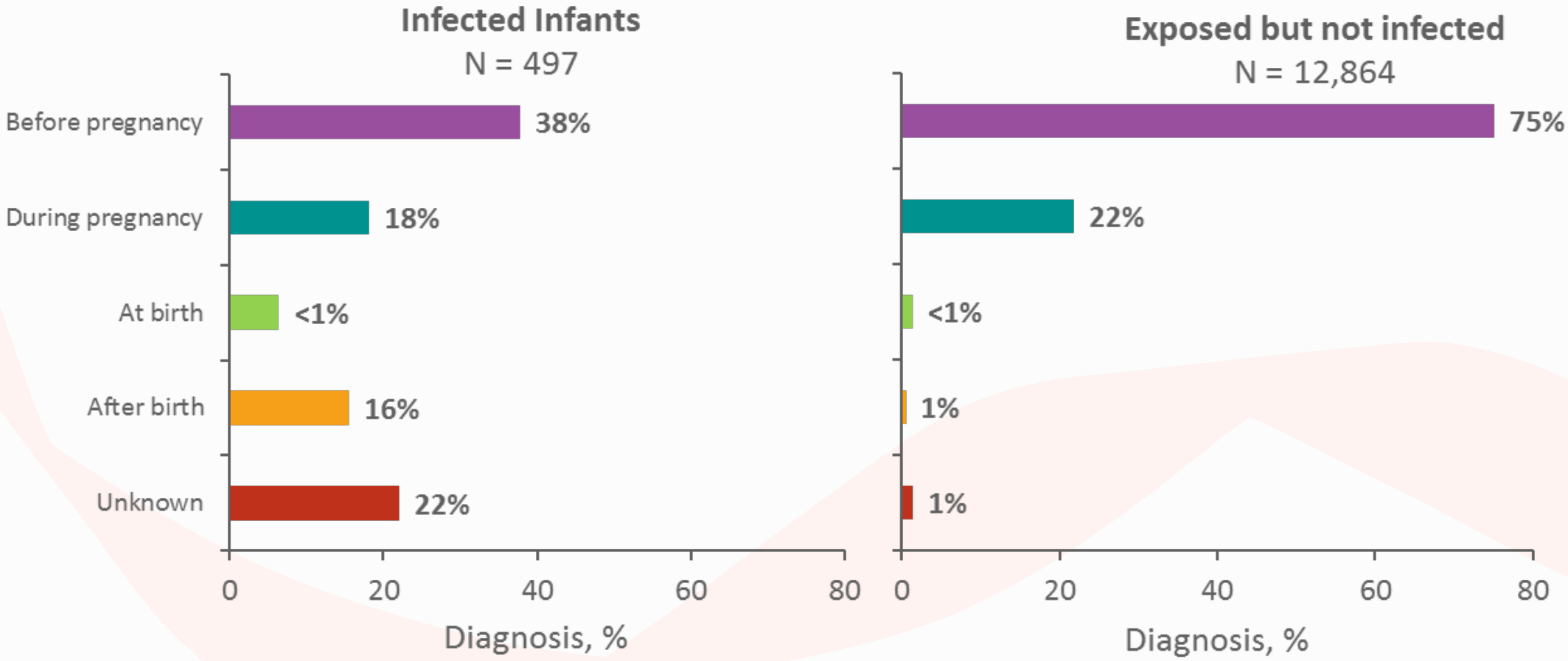
Taylor AW et al. Estimated Perinatal HIV Infection Among Infants born in the United States, 2002-2013. JAMA Peds 3/20/17.

Estimated Numbers and Rates of Perinatally Acquired HIV in Children, U.S. 2010-13



Taylor AW et al. Estimated Perinatal HIV Infection Among Infants born in the United States, 2002-2013. JAMA Peds 3/20/17.

Time of Maternal HIV Testing among Children with Diagnosed Perinatally Acquired HIV Infection and Children Exposed to HIV, Birth Years 2009–2013—United States and Puerto Rico



Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis.

Perinatal HIV Infection in the U. S. 2002 - 2013

- Estimated Annual number of perinatally infected infants in the U.S. was 216 (95% CI, 206-230) in 2002 and was 69 (95% CI, 60-83) in 2013.
- ARV prophylaxis or treatment (all 3 arms) was provided to 22.4% of dyads in 2002-05 (28.4% any Rx) to 31.8% of dyads in 2010-13 (40.3% any Rx)

Taylor AW et al. Estimated Perinatal HIV Infection Among Infants born in the United States, 2002-2013. JAMA Peds 3/20/17.

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

DHHS Guidelines Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B**: Moderate recommendation for the statement **C**: Optional recommendation for the statement	**I**: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints **II**: One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes **III**: Expert opinion

Vocabulary for HIV in Pregnancy

- Concordant couples: both members of couple either have or do not have HIV infection
- Discordant couples: one member of the parenting pair has HIV infection and the other is HIV uninfected

Preconception Counseling

- Safer sex practices (AI)
- Elimination of alcohol, tobacco and other drugs of abuse (AII)
- All HIV infected women should be on ART with fully suppressed HIV viral load before conception (AII)
- Vitamins containing at least 400 mcg folic acid to prevent neural tube defects

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Pre-Conception Considerations

- For concordant and discordant couples
  - Partners should be screened and treated for genital tract infections before attempting conception (AIII)
  - Infected partners should attain maximal virologic suppression before trying to conceive (AIII)

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

HPTN 052

ART for Prevention of HIV Transmission in Serodiscordant Couples

Stable, healthy, sexually active HIV-discordant couples with CD4 350-500 cells/mm^3
n = 1763 couples

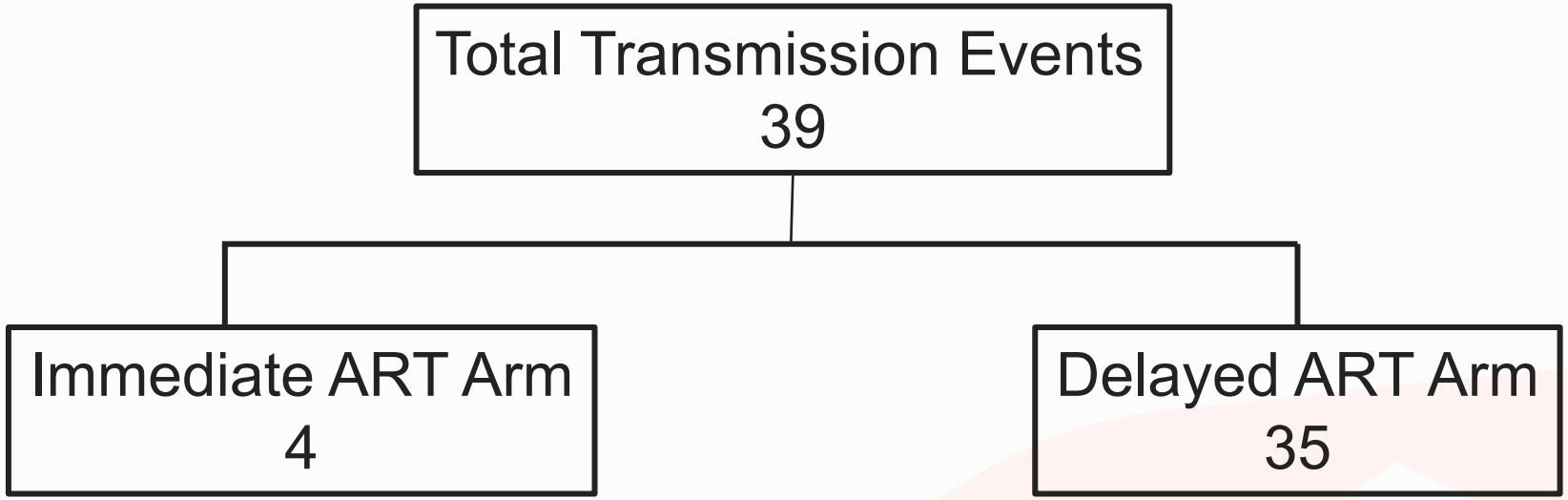
Early ART Arm
Initiate ART immediately
n = 886 couples

Delayed ART Arm
Initiate ART at CD4 ≤ 250 cells/mm^3
Or AIDS Defining Illness
n = 877 couples

Cohen MS, et.al. N Engl J Med 2011;365:493-505.

HPTN 052

ART for Prevention of HIV Transmission in Serodiscordant Couples

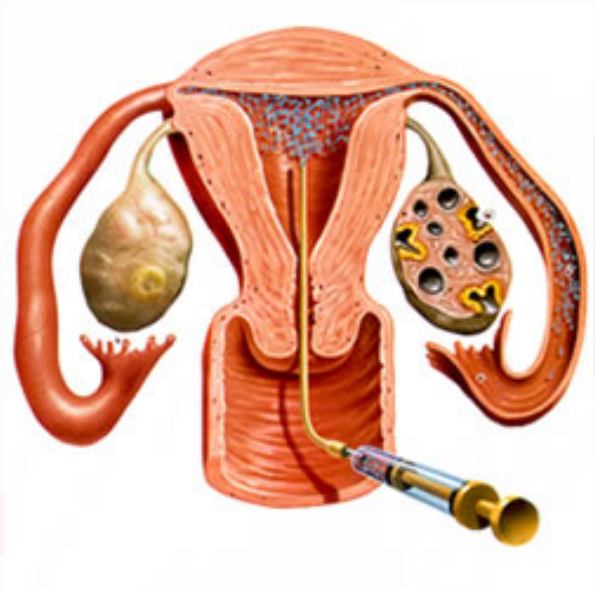


96% reduction with early ART
P = .0001

Cohen MS, et.al. N Engl J Med 2011;365:493-505.

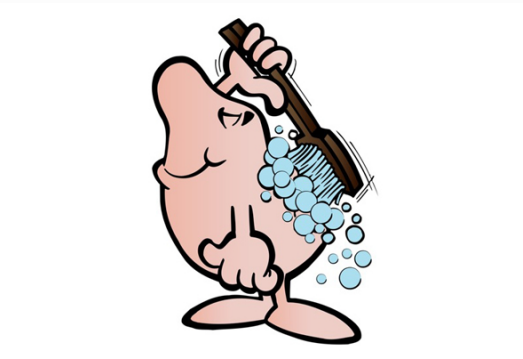
Discordant Couples: HIV Infected Women

- Assisted insemination at home or in a provider's office with a partner's semen during the peri-ovulatory period **(AIII)**



DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Discordant Couples: HIV-Infected Man

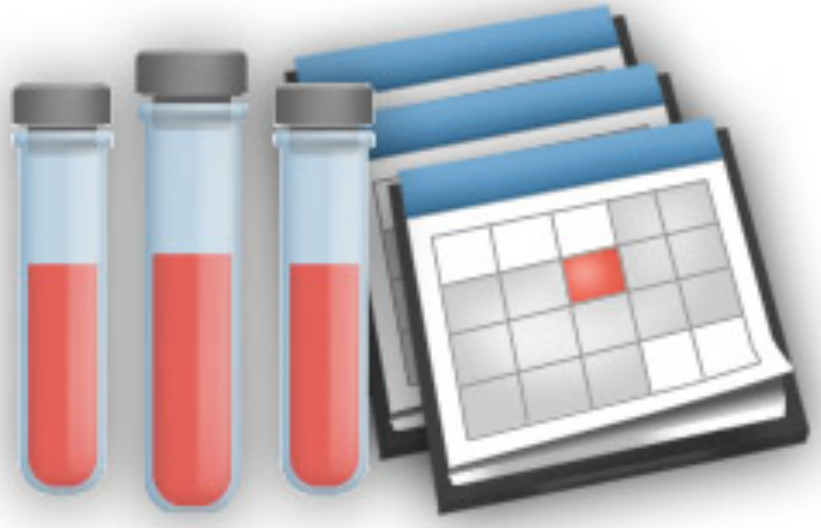


- Donor sperm from an HIV-uninfected man with artificial insemination is the safest option **(AIII)**
- Semen preparation techniques ("sperm washing") coupled with either intrauterine insemination or *in vitro* fertilization should be considered **(BII)**
- Semen analysis is recommended for HIV-infected men before conception **(AIII)**

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Pre-exposure Prophylaxis

PrEP IS AN HIV PREVENTION METHOD IN WHICH PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK OF BECOMING INFECTED



ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. AN HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.

http://aids.gov/hiv-aids-basics/prevention/reduce-your-risk/pre-exposure-prophylaxis/

Poll

Which of the following statements about HIV PrEP is false?

1. Pregnancy and breastfeeding are contraindications to PrEP
2. Truvada® daily is the only current FDA approved HIV PrEP regimen
3. Adherence to PrEP is critical to success
4. To date, there has been no increase in congenital abnormalities among children exposed to PrEP

Correct Answer

Which of the following statements about HIV PrEP is false?

1. Pregnancy and breastfeeding are contraindications to PrEP
2. Truvada® daily is the only current FDA approved HIV PrEP regimen
3. Adherence to PrEP is critical to success
4. To date, there has been no increase in congenital abnormalities among children exposed to PrEP

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Care for the HIV-infected pregnant woman

Antiretroviral Therapy in Pregnancy

- Start as soon as possible, even prior to results of genotype
- French Perinatal Cohort
  - 8075 HIV-infected mother-infant pairs
  - 2000 to 2011
  - Mothers received ART, delivered live-born children with determined HIV status, and did not breastfeed

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.
Mandelbrot L, et al. Clin Infect Dis, 2015 Dec 1;61(11):1715-25.

French Perinatal Cohort

- Overall rate of perinatal transmission 0.7%
- 2651 children born to women on ART prior to conception, ART throughout pregnancy, HIV viral load < 50 copies/mL at delivery
  - No HIV transmission
- Regardless of viral load at birth, risk of transmission varied based on when ART was started
  - ART prior to conception 0.2%
  - ART started in first trimester 0.4%
  - ART started in second trimester 0.9%
  - ART started in third trimester 2.2%

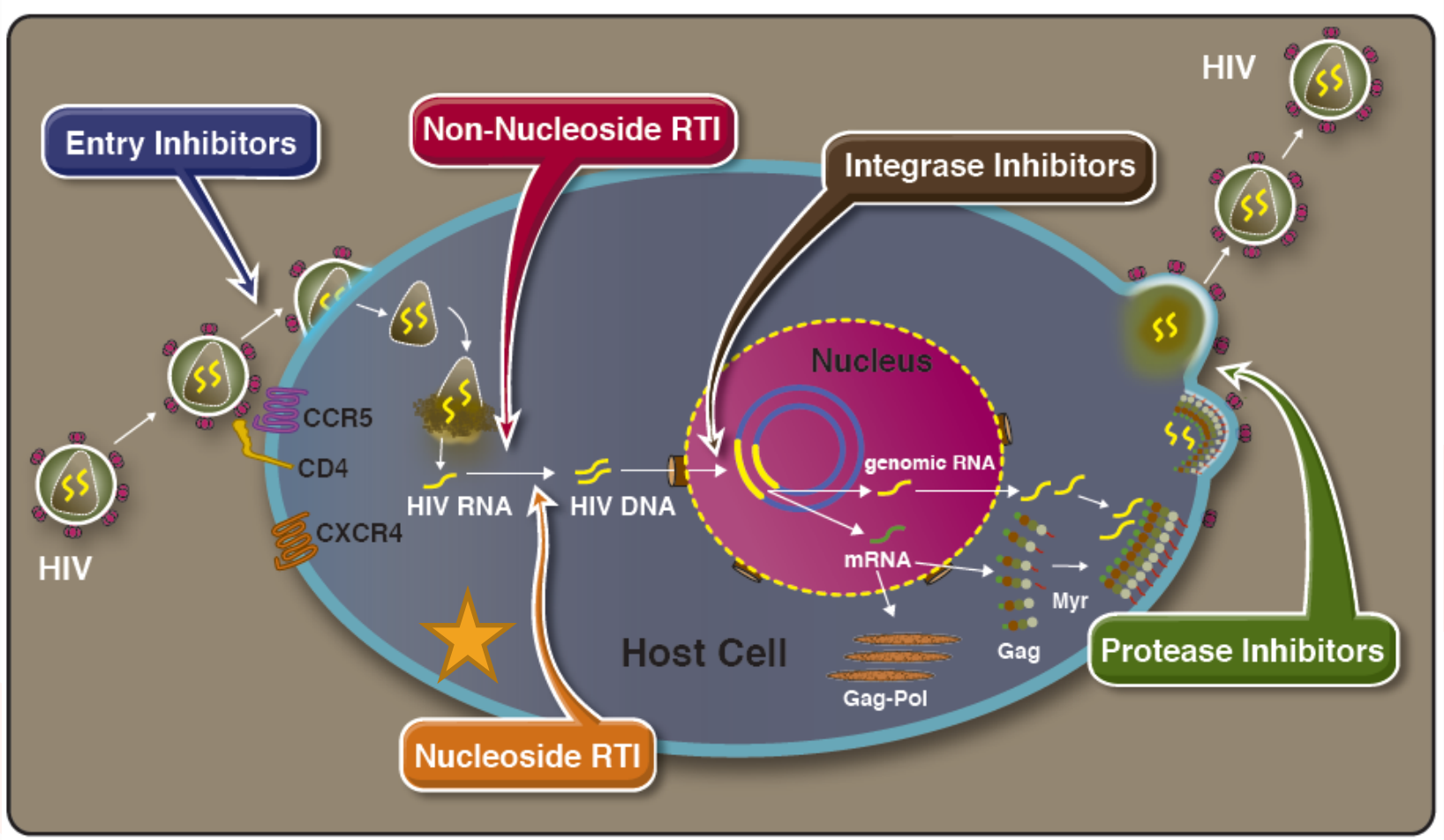
P < .001

Mandelbrot L, et al. Clin Infect Dis. 2015 Dec 1;61(11):1715-25.

Medications in Pregnancy

- Many physical changes occur in pregnancy that affect drug pharmacokinetics
  - Decrease in serum proteins
  - Increased plasma volume
  - Increase in kidney filtration
  - Delayed stomach emptying
- What does this mean for the pregnant woman?
  - Some HIV medications need to be dosed twice daily
  - May have to take more pills to get good blood levels

HIV Life Cycle



http://depts.washington.edu/nwaetc/Pill_Chart.pdf

Preferred Regimens in Pregnancy

2 NRTIs + PI/r OR INSTI

NRTI = Nucleoside Reverse Transcriptase Inhibitor
PI/r = Ritonavir boosted protease inhibitor
INSTI = Integrase Strand Transfer Inhibitor

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Preferred 2-NRTI Backbone

- Abacavir/lamivudine (Epzicom®)
  - HLA-B*5701
  - HIV viral load > 100,000 – don't combine with ATV/r or EFV
- Tenofovir (TDF)/emtricitabine (Truvada®)
  - Hepatitis B
  - Potential renal toxicity
- Tenofovir (TDF)+ lamivudine
  - Hepatitis B
  - Potential renal toxicity

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Preferred Protease Inhibitors

- Atazanavir/r (Reyataz® + Norvir ®))
  - Once daily in pregnancy – many would increase atazanavir dose to 400 mg daily in 2nd and 3rd trimesters
  - Maternal hyperbilirubinemia
  - Interactions with acid reducing agents
  - Requires food for absorption
- Darunavir/r (Prezista® + Norvir ®)
  - Dose in pregnancy is darunavir 600 mg + ritonavir 100 mg twice daily
  - Requires food for absorption

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Preferred Integrase Inhibitor

- Raltegravir (Isentress®)
  - Must be dose twice daily
  - Rapid viral load reduction
  - Few drug interactions
  - Low genetic barrier to resistance

Alternative Regimens in Pregnancy

2 NRTIs **+** **NNRTI** **OR** **PI/r**

NRTI = Nucleoside Reverse Transcriptase Inhibitor
NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor
PI/r = Ritonavir boosted protease inhibitor

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Alternative 2-NRTI Backbone

- Zidovudine/Lamivudine (Combivir®)
  - Twice daily administration
  - Increased risk for hematologic toxicities

Alternative Protease Inhibitors

- Lopinavir/r (Kaletra®)
  - Nausea
  - Twice daily administration required/High pill burden
    - 2 tablets BID with increase to 3 tablets BID in 2nd & 3rd trimester

Alternative Regimen: NNRTI

- Efavirenz (Sustiva®)
  - Birth defects in primates; human risk less clear
  - Neuropsychiatric side effects
  - Once daily, single tablet combination available (Atripla®)
- Rilpivirine (Edurant®)
  - Available as fixed drug single tablet regimen with tenofovir df/emtricitabine (Complera®)
  - Contraindicated with proton pump inhibitors
  - Requires food (490 cal) for absorption
  - Not recommended if pre-treatment HIV viral load > 100,000 copies/mL or CD4 cell count < 200 cells/mm^3

Poll

What if a woman with HIV infection becomes pregnant while already on antiretrovirals that are fully suppressing her HIV viral load?

a) Regimen must be changed to a “preferred regimen”
b) An HIV resistance test should be done
c) She can stay on her regimen as long as it is safe and effective in pregnancy and working for her
d) Antiretrovirals should be stopped to prevent injury to the baby

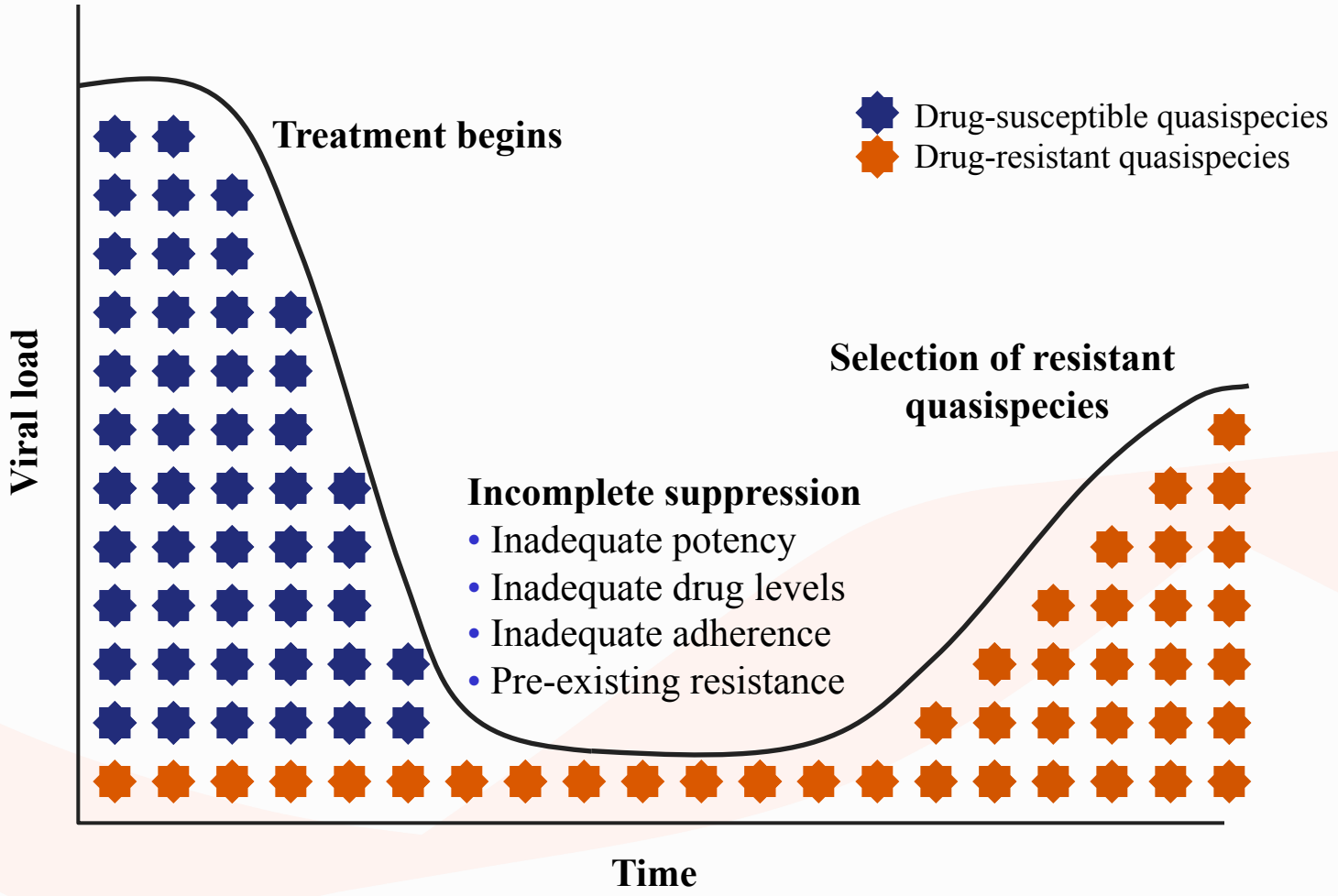
Correct Answer

- What if a woman with HIV infection becomes pregnant while already on antiretrovirals that are fully suppressing her HIV viral load?
  a) Regimen must be changed to a “preferred regimen”
  b) An HIV resistance test should be done
  c) She can stay on her regimen as long as it is safe and effective in pregnancy and working for her
  d) Antiretrovirals should be stopped to prevent injury to the baby

Case

- DH is a 32 year old woman in her 28th week of gestation who has a history of AIDS with multiple antiretroviral resistance mutations due to prior medication nonadherence
- For the last 5 years has been very adherent to her regimen of darunavir 600 mg twice daily + norvir 100 mg twice daily + truvada one tablet daily + raltegravir 400 mg twice daily
- Viral load 600 copies/mL

Selective Pressures of Therapy



Melendez-Rivera, Ivan. Resistance Testing - Where do I Start? 21st Annual HIV Conference. Florida/Caribbean AETC. October 26-27, 2012. Lake Buena Vista, FL.

Case

- Genotype done and patient has developed new resistance to raltegravir
- Raltegravir discontinued and dolutegravir 50 mg twice daily added to regimen
- Viral load 2 weeks later was < 20 copies/mL
- Baby born healthy without HIV infection on subsequent testing
- Mother remains adherent to her regimen with subsequent fully suppressed HIV viral load

Monitoring HIV in Pregnancy

- HIV viral load testing
  - Initial visit (AI)
  - 2-4 weeks after starting or changing ART (BI)
  - Monthly until HIV viral load is below limit of detection of test (BIII)
  - Every 3 months during pregnancy (BIII)
  - 34-36 weeks' gestation to inform delivery decisions (AIII)
- Antiretroviral resistance testing
  - Prior to starting ART if never on treatment (AIII)
  - Prior to changing regimen if HIV RNA above threshold for resistance testing (> 500 to 1,000 copies/mL) (AIII)

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

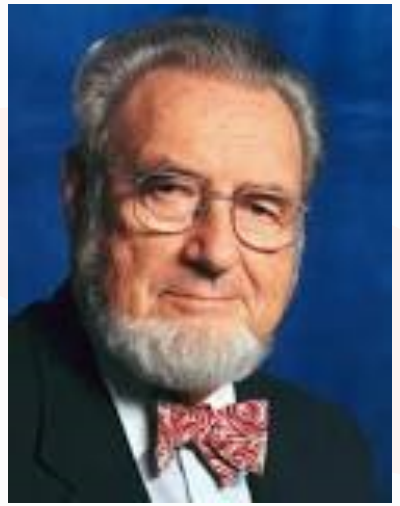
What if virologic suppression is not attained?

1. Test for drug resistance
2. Assess drug adherence, tolerability, dosing, potential problems with absorption, lack of attention to food requirements
3. Consideration of ART modification

- Adherence to ART, labs and appointments (both OB and HIV care) are critical to success in preventing mother to child transmission!

Drugs don’t work in patients who don’t take them.

C. Everett Koop



Virologic failure near delivery

- HIV RNA > 1,000 copies/mL
  - Scheduled cesarean section at 38 weeks (AI)
  - Intravenous zidovudine (AI)

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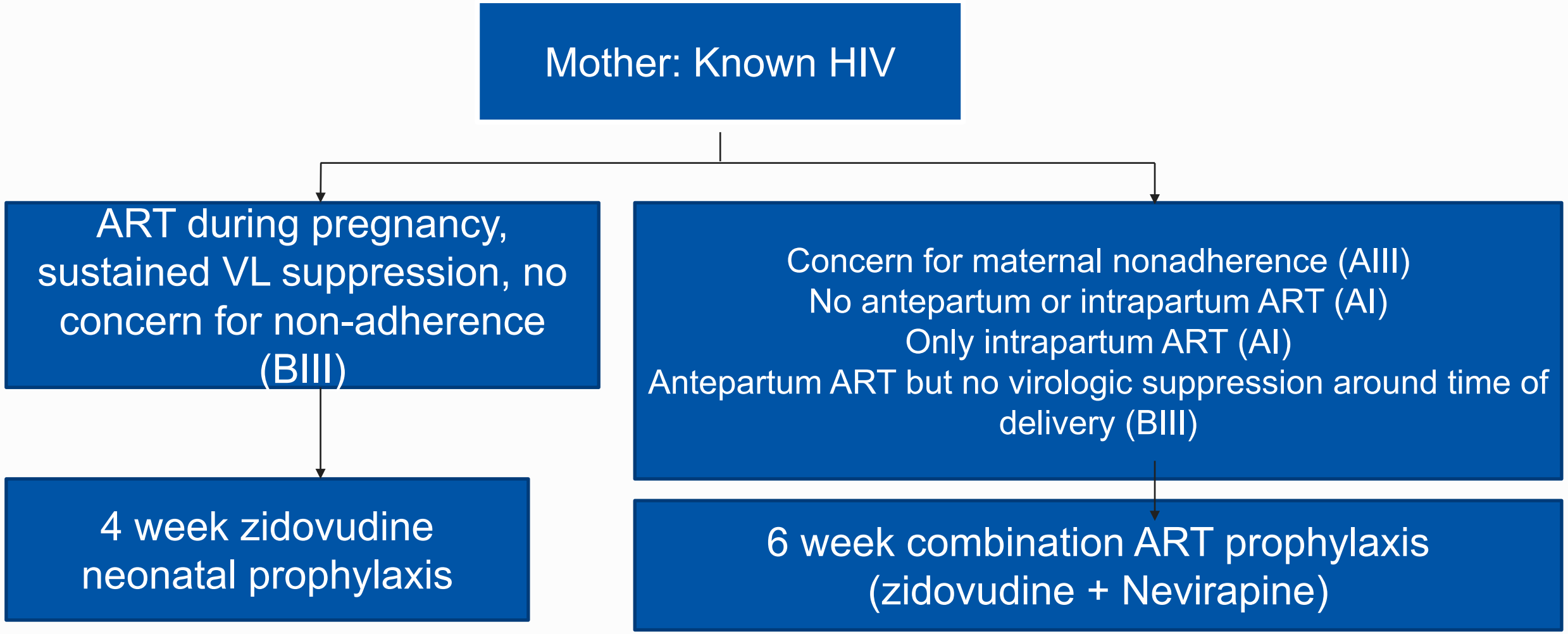
Infant Post-Exposure Prophylaxis



DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Caring for Infant Exposed to HIV

- PCP prophylaxis starting at ages 4 to 6 weeks, after completing prophylactic antiretroviral regimen unless you can exclude HIV infection (AII)
  - Virologic testing is **negative** at 14-21 days and 4 – 8 weeks of age
- Recommended Testing → Virologic tests for HIV infection at 14 to 21 days of life and ages 1 to 2 months and 4 to 6 months (AII)
- HIV Antibody testing at 15-18 months of age – no longer recommended, but some pediatric HIV specialists still do

DHHS Perinatal Guidelines October 26, 2016 available at http:/aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Accessed 2.1.17.

Breastfeeding and HIV Infection

- Risk of HIV transmission occurs throughout the breastfeeding period
- If no infant antiretroviral prophylaxis (or maternal HAART)
  - Highest risk first 4-6 weeks of life (0.7% to 1% per week)
  - Late postnatal infection risk after 4-6 weeks is 0.17% per week

AAP Committee on Pediatric AIDS. Pediatrics 2013;131:391-396.

Factors Increasing Risk of HIV Transmission Through Breastfeeding

- High maternal plasma and human milk viral load
- Low maternal CD4 cell count
- Longer duration of breastfeeding
- Breast abnormalities
- Oral lesions in infant
- Mixed breastfeeding and formula feeding
- Abrupt weaning
- Mother not on HAART and/or infant not on Prophylactic ARVs throughout lactation (+ 6 weeks after ending)

AAP Committee on Pediatric AIDS. Pediatrics 2013;131:391-396.

Why do we recommended avoidance of breastfeeding in the US?

1. 1% to 5% risk of transmission of HIV though exposure to breastmilk containing HIV even if mother on treatment and baby on PEP
2. Transmission possible even if mother's plasma HIV RNA is undetectable
3. Maternal prophylaxis may be less effective if started late in pregnancy or during postpartum period
4. Potential toxicity of ARVs in infant exposed to drugs through breast milk
5. Access to clean water and affordable replacement feeding exists in the US

AAP Committee on Pediatric AIDS. Pediatrics 2013;131:391-396.

What about premastication?

- 2008 US study:14% of mothers of healthy babies premasticated food for their child
- Late HIV transmission has been documented through infant consumption of premasticated food given by their HIV-infected caregivers

Fein SB, et al. Pediatrics. 2008;122(suppl 2):S91-S97.

Gaur AH, et al. Pediatrics. 2009 Aug;124(2):658-66.

HIV and Contraception

- Vasectomy or bilateral tubal ligation safe and effective
- Depot medroxyprogesterone acetate (DMPA) and intrauterine devices (IUDs) are effective in women on ART
- Recommend barrier protection (condoms)
  - Avoid nonoxyl-9 spermicide
- For oral or other hormonal contraception, check for interactions with antiretrovirals – Table 3 in Perinatal Guidelines

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Missed Opportunities for Preventing Perinatal Transmission of HIV: Florida 2007 – 2014

- Retrospective review of de-identified data from Florida's Enhanced HIV/AIDS Reporting System (eHARS)
- 70/4337 (1.6%) known singleton births exposed to maternal HIV infection were perinatally infected
- Among the infected maternal-infant dyads **over 1/3 of mothers used illegal drugs** or **acquired an STD during pregnancy**

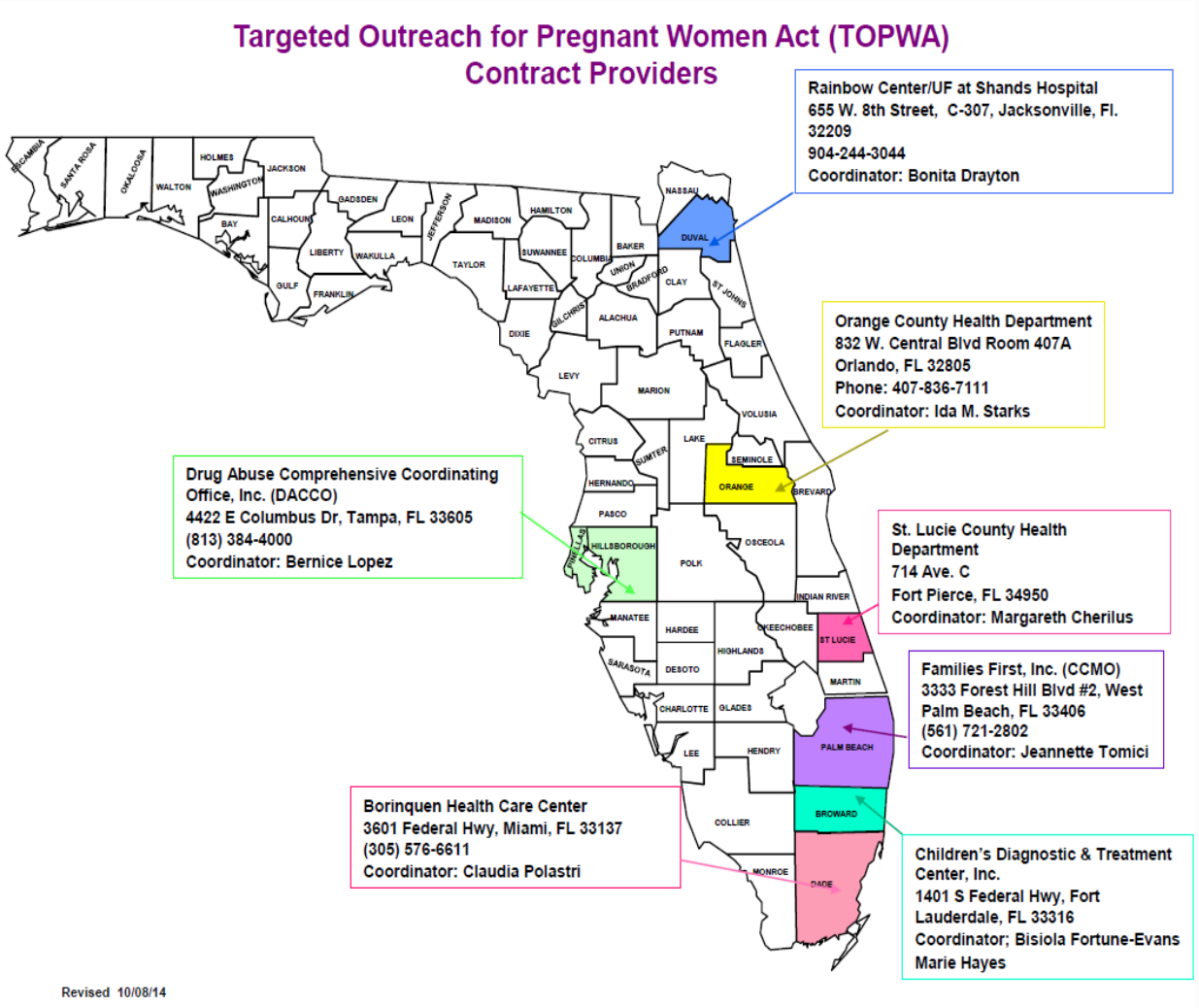
Trepka MJ et al. Southern Med J 2017 Feb;110(2):11-128. PMID: 28158882

Missed Opportunities for Preventing Perinatal Transmission of HIV: Florida 2007 – 2014

- Relative Risk of Perinatal Transmission
  - **Maternal HIV Diagnosis during labor and delivery**
    - RR = 5.66, (95% CI 2.31-13.91) (compared with prenatal diagnosis)
  - **Maternal HIV Diagnosis after birth**
    - RR = 26.50, (95% CI 15.44-45.49)
- Among 29 women whose HIV infection was not known before pregnancy and whose child was perinatally infected
  - 18 were not diagnosed during pregnancy
  - 12 of the 18 had **evidence of Acute HIV Infection**
  - 6 of the 18 had **no prenatal care**

Trepka MJ et al. Southern Med J 2017 Feb;110(2):11-128. PMID: 28158882

Florida System for Perinatal HIV Transmission Prevention



- Ryan White Programs Parts A, B, C, D
  - Patchwork across the state
- Perinatal HIV Prevention Coordinators cover the state
- 115 OB/delivery hospitals
- 35 birthing centers
- FL DOH Surveillance
  - Reporting HIV + deliveries within 30 days of delivery
- Baby Rxpress – ARVs for infants
- Children's Medical Services Pediatric HIV Referral Centers (17)

HIV /AIDS Florida DOH – adapted from http://www.floridahealth.gov/diseases-and-conditions/aids/

10 Action Steps for a Healthy Baby During a HIV + Pregnancy

1. Review **HIV status** (viral loads, CD4 counts, STIs, etc.)
2. Review **health of pregnancy** status (previous pregnancies, deliveries, additional health concerns and healthy steps)
3. Provide Understanding and Support for **Disclosure**
4. Create a **pregnancy plan** with the mother (family)
5. **Problem solve effective therapy and optimal adherence**
6. Initiate/continue an **ARV regimen per guidelines**
7. **Confirm adequate response** to ARVs in 2-4 weeks
8. **Monitor adherence and response** at least every 3 months and at least in each trimester (especially at 34-36 weeks)
9. Create a **delivery plan** based on all the data – review it serially
10. **Implement** the delivery plan and follow-up for mother and infant

Slide courtesy of Robert Lawrence, MD

Action Steps in Florida in Pregnancies without Known HIV

- **Diminish barriers to receiving prenatal care for all women**
- Offer and **recommend HIV testing** for every pregnant woman
- Continue appropriate **screening** for maternal drug use and sexually transmitted infections during pregnancy
- Know the **clinical picture of Acute HIV infection** and ask about clinical illnesses during pregnancy
- Confirm **documented HIV testing results** prior to delivery
- Use **Rapid HIV testing** in Labor & Delivery Units

Slide courtesy of Robert Lawrence, MD

Resources

Perinatal HIV/AIDS

Rapid perinatal HIV consultation from practicing providers

- HIV testing in pregnancy
- Treating HIV-infected pregnant women
- Preventing transmission during labor and delivery and the post-partum period
- HIV-exposed infant care

Call for a Phone Consultation

(888) 448-8765

24 hours,

Seven days a week

CALL