
 **AETC** AIDS Education & Training Center Program
Southeast


Perinatal Care and Prevention

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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 prophylaxis to exposed infants based on current DHHS guidelines



 **AETC** AIDS Education & Training Center Program
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Poll (free text)

What patient care groups are represented in the audience?

 **AETC** AIDS Education & Training Center Program
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HIV Transmission from Mother to Baby

An HIV+ pregnant woman can transmit HIV to her baby **3 WAYS**:

- + During pregnancy
- + During vaginal childbirth
- + Through breastfeeding

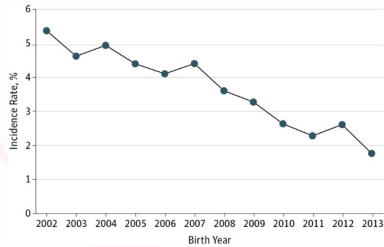


- 25% risk of perinatal transmission in absence of therapy
 - 20% before 36 weeks
 - 50% between 36 weeks and delivery
 - 30% active labor and delivery
- Less than 1% risk if
 - Suppressive antiretroviral therapy (ART) during pregnancy
 - Postnatal infant antiretroviral prophylaxis
 - C-section & AZT if indicated
 - Avoidance of breastfeeding

Connor EM et al. N Engl J Med 1994;331:1173-80.
Kourlis AT et al. JAMA. 2001;285:709-12.



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



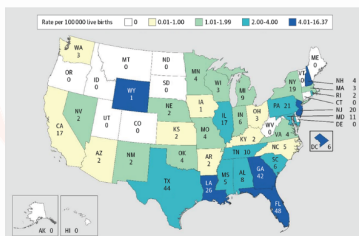
Current rate of perinatal transmission in US and Europe 2% or less

CDC goal: less than 1 per 100,000 live births and < 1% among HIV exposed infants



Taylor AW et al. Estimated Perinatal HIV Infection Among Infants born in the United States, 2002-2013. JAMA Peds 3/2017.

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 3/2017.



Poll

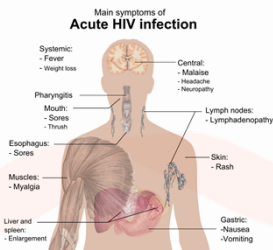
When should pregnant women be screened for HIV?

- A) At entry into care for pregnancy
- B) If they have any signs or symptoms suggestive of acute HIV
- C) In the 3rd trimester if at risk of HIV acquisition
- D) All of the above

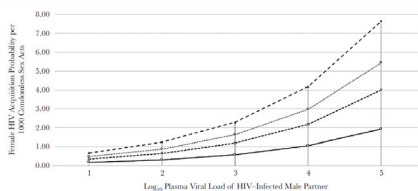


Screening for HIV

- At presentation for pregnancy care
- Repeat in 3rd trimester
- At labor and delivery if HIV status is unknown
- Signs or symptoms of acute HIV if pregnant or breastfeeding
 - Check HIV viral load as well as 4th generation Ag/Ab test



Adjusted HIV Acquisition Probabilities per 1000 Condomless Sex Acts



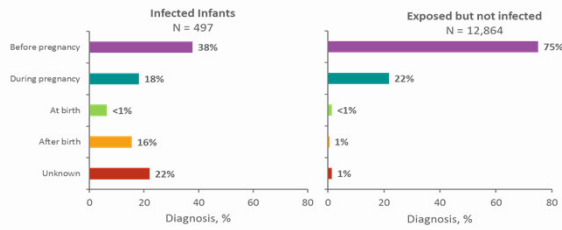
25 yo woman
Not on PrEP
Varying plasma
HIV viral load for
male partner

	1	2	3	4	5
Nonpregnant	0.17	0.31	0.58	1.05	1.93
Early pregnancy	0.36	0.65	1.19	2.19	4.00
Late pregnancy	0.48	0.89	1.62	2.92	5.44
Postpartum	0.68	1.25	2.29	4.18	7.65



Thomson K et al. J Infect Dis. 2018;218:16-25.

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.

CDC. Pediatric HIV Surveillance (through 2016) available at <https://www.cdc.gov/hiv/library/diseases/index.html>. Accessed 2.28.18.

Labor and Delivery Testing

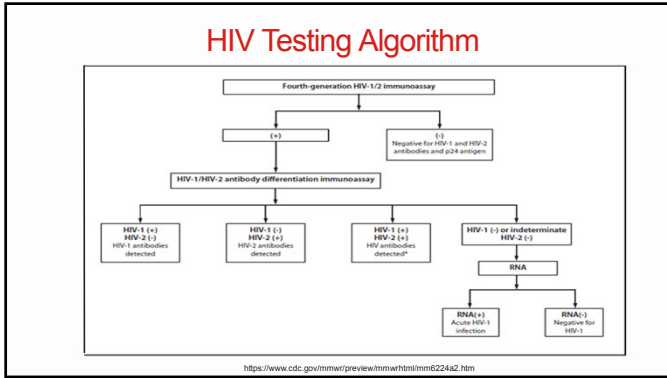
- Expedited or rapid testing
 - Goal is to have results within 1 hour
- Needed if:
 - Prior negative HIV test(s), who are at high risk for new HIV acquisition
 - Ongoing illicit drug use
 - New STD diagnoses during pregnancy
 - Sex partners of individuals with HIV
 - Exchange of sex for money or drugs
 - Teenage mother
 - New or more than one sex partner during the current pregnancy.



Case


- Priscilla is a 32 year old woman who presents in her 4th pregnancy with rupture of membranes at 24 weeks and 3 days gestation
- No prenatal care
- She tested positive for gonorrhea, but negative for chlamydia and syphilis
- Her 4th generation HIV test had an indeterminant result
 - Ag/Ab test positive
 - Ab differentiation was negative
 - HIV viral load pending – run only once a week






Case


- Vaginal delivery 6 days after presented to hospital
- Baby fed formula and mother's breast milk stored until HIV viral load resulted
- Viral load 14 million copies/mL
 - Resulted 12 days after test drawn
- Baby tested HIV positive





Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

www.aidsinfo.nih.gov/guidelines



Preconception Counseling

- Safer sex practices (AI)
- Elimination of alcohol, tobacco and other drugs of abuse (AII)
- All HIV infected women should be on antiretroviral therapy (ART) with fully suppressed HIV viral load before conception (AII)



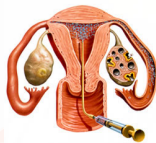
Pre-Conception Considerations

- 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)



Discordant Couples: Woman With HIV Infection

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



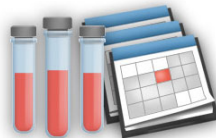
Discordant Couples: Man With HIV Infection



- 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)**



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>

Care for the HIV-infected pregnant woman



Antiretroviral Therapy in Pregnancy

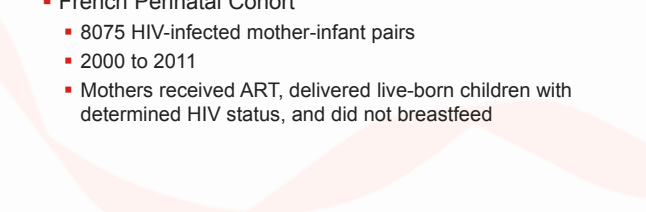
- Start as soon as possible, even prior to results of genotype
 - Modify therapy later if needed





 DHHS Perinatal Guidelines October 26, 2016 available at <http://aidsinfo.nih.gov/content/files/hvguidelines/perinatal/g.pdf>. Accessed 2.1.17.
 Mandelbrot L, et al. *Clin Infect Dis*. 2015 Dec 1;61(11):1715-25.

French Perinatal Cohort

- 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

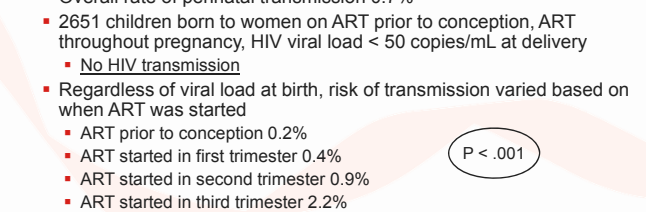




 Mandelbrot L, et al. *Clin Infect Dis*. 2015 Dec 1;61(11):1715-25.

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



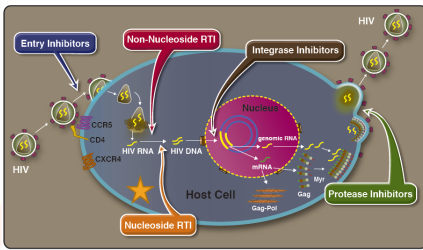

 Mandelbrot L, et al. *Clin Infect Dis*. 2015 Dec 1;61(11):1715-25.

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?
 - May have to take higher doses or take ART more often to get good blood and placental levels



HIV Life Cycle



http://depts.washington.edu/nwaetc/P111_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

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®)**
 - Treats Hepatitis B
 - Potential renal toxicity
- **Tenofovir (TDF)+ lamivudine**
 - Treats Hepatitis B
 - Potential renal toxicity



DHHS Perinatal Guidelines October 26, 2016 available at <http://aidsinfo.nih.gov/contentfiles/guidelines/perinatals.pdf>. Accessed 2.1.17.

Preferred Protease Inhibitors

- **Atazanavir/r (Reyataz® + Norvir®) + preferred 2-NRTI backbone**
 - 300 mg once daily + ritonavir 100 mg daily with food – 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®) + preferred 2-NRTI backbone**
 - Dose in pregnancy is darunavir 600 mg + ritonavir 100 mg twice daily with food



DHHS Perinatal Guidelines October 26, 2016 available at <http://aidsinfo.nih.gov/contentfiles/guidelines/perinatals.pdf>. Accessed 2.1.17.

Preferred Integrase Inhibitor

- **Raltegravir (Isentress®) + preferred 2-NRTI backbone**
 - Must be dose twice daily
 - Rapid viral load reduction
 - Few drug interactions
 - Low genetic barrier to resistance



Alternative Integrase Inhibitor Regimen

- **Dolutegravir (Tivicay®) + preferred two-NRTI backbone**
 - Limited data in pregnancy
 - ~~No safety problems identified to date~~
 - High genetic barrier to resistance
 - Can take with or without food





Breaking News

New study suggests risk of birth defects in babies born to women on HIV medicine dolutegravir

Press release

18/05/2018

New study suggests risk of birth defects in babies born to women on HIV medicine dolutegravir

While EMA review is ongoing, dolutegravir should not be used in women seeking to become pregnant

FDA Drug Safety Communication: FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca, Tivicay, Triumeq)

[05-18-2018]

Dolutegravir Use in Pregnancy

- **DHHS Recommendations**
 - If pregnant and more than 8 weeks from last menstrual cycle, then can initiate or continue a Dolutegravir based regimen
 - It's not clear if this is a integrase inhibitor class effect or just with Dolutegravir
 - Providers are encouraged to report pregnancy exposures to antiretrovirals to the Antiretroviral Pregnancy Registry



Alternative NNRTI Regimens

- **Efavirenz (Sustiva®) + preferred 2-NRTI backbone**
 - Birth defects in primates; human risk less clear
 - Neuropsychiatric side effects
 - Once daily, single tablet combination available (Atripla®)
- **Rilpivirine (Edurant®) + preferred 2-NRTI backbone**
 - Available as fixed drug single tablet regimen with tenofovir df/emtricitabine (Complera®)
 - Contraindicated with proton pump inhibitors, separate from other acid reducing agents
 - Must take with a meal for absorption
 - Not recommended if pre-treatment HIV viral load > 100,000 copies/mL or CD4 cell count < 200 cells/mm³



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



ARVs Not Recommended In Pregnancy

- Stribild® (TDF/FTC/EVG/c) or Genvoya® (TAF/FTC/EVG/c)
 - Concern for viral breakthrough
 - If continue, monitor viral load closely and consider therapeutic drug monitoring
- Tenofovir alafenamide – data lacking in pregnancy
- Stavudine (d4T)
- Didanosine (ddI)
- Treatment dose ritonavir (600 mg BID)

} Toxicity Risks



Monitoring HIV in Pregnancy

- HIV viral load testing
 - Initial visit (A1)
 - 2-4 weeks after starting or changing ART (B1)
 - 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)



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!



Management During Labor

- Guidelines recommend against the following unless clear obstetric indication:
 - Artificial rupture of membranes
 - Invasive fetal scalp monitoring with scalp electrodes
 - Operative delivery with forceps or vacuum extractor
 - Episiotomy



Virologic failure near delivery

- HIV RNA > 1,000 copies/mL or unknown viral load
 - Scheduled cesarean section at 38 weeks (AI)
 - Intravenous zidovudine (AI)
 - Some providers would give IV zidovudine to if last HIV viral load > 50 or any concern for non-adherence



Types of ART for Newborns With Perinatal HIV Exposure

Antiretroviral Prophylaxis	ART for newborns without confirmed HIV AZT + one or two other antiretroviral drugs
Empiric Therapy	Newborn at high risk of HIV acquisition Three drug combination regimen
HIV Therapy	Infants with confirmed HIV Three drug combination regimen Therapy is lifelong

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 ART 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 pre-mastication?

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



Fein SB, et al. Pediatrics. 2008;122(suppl 2):S91-S97.
Gaur AH, et al. Pediatrics. 2009 Aug;124(2):658-66.



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





"Drugs don't work in patients who don't take them."

C. Everett Koop, MD
US Surgeon General, 1985.




Engaging Pregnant Women with HIV

- Involve their support system if patient allows!
 - Father of the baby, or current partner
 - Family
 - Friends
- Encourage linkage to a perinatal coordinator
- Be available and answer questions
- Give hope


10 Action Steps for a Healthy Baby During an HIV Affected 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

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

<http://nccc.ucsf.edu/clinician-consultation/perinatal-hiv-aids/>

