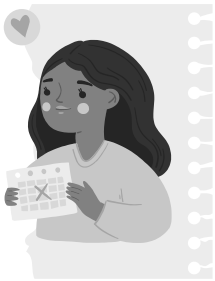
HIV, Baby, and Me: Preventing Perinatal Transmission of HIV



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Conflict of Interest Disclosure Statement

Dr. Hoang has no financial relationships with ineligible companies

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Learning Objectives

Define	Perinatal transmission of HIV and its risk factors
Review	Different therapies of ARV during antepartum, intrapartum and postpartum
Recognize	Difference between infant prophylaxis/treatment
Review	Breastfeeding risks and recommendations in HIV+ patients

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ABOUT PERINATAL HIV

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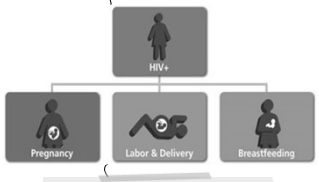
Perinatal Transmission[1]

HIV can be passed from a person with HIV to their child during pregnancy, childbirth, or breastfeeding

Other terms:
Maternal-child transmission, Mother-to-Child Transmission, Vertical Transmission



U=U
Undetectable=Untransmittable
With an undetectable HIV viral load with ART compliance – HIV cannot be transmitted

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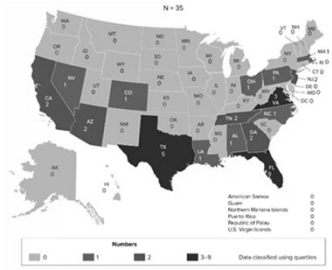
PREVALENCE

Diagnosis of Perinatally Acquired HIV Infection among Children Born During 2018—United States[3]



1.2 million

Globally, 1.2 million pregnant women with HIV in 2022. Estimated 82% received ARV[2]

12,355 (1%)

Were diagnosed with perinatal HIV in 2019[2]

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Key Information

Risk Factors

- Viral load of mother
- Use of ART during pregnancy and childbirth
- Mode of delivery
- Breastfeeding

Prevention Strategies[1]

- Routine HIV testing
- Available ART to pregnant women living with HIV
- Elective C-section when appropriate
- Counseling on breastfeeding/formula options

The Joint United Nations Programme on HIV/AIDS (UNAIDS) have set a goal to eliminate new HIV infections among children by 2030[4]

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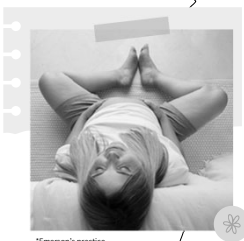

*Emerson's practice

CDC recommends all pregnant patients be tested for HIV in the first trimester[5]

Opt In:
- Pregnant patients are given pre-HIV counseling and must agree to receiving HIV testing

Opt Out*:
- Pregnant patients are told that HIV is part of the standard prenatal tests and they may decline

Re-test Third Trimester
- High risk patients
  - Incarcerated
  - High prevalence of HIV in care setting

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Antepartum Management

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Effects of Antiretroviral Therapy on Risk of HIV Transmission[6]

Without ART	With ART
25%*	<1 %

*40% if breastfeeding

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Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention[7]

Published: November 3, 2016

Authors: Mary G. Fowler., MPH., Min Qin, Ph.D., Susan A. Discus Ph.D., et.al

Background	ART **vs** Zidovudine + nevirapine data lacking
Method	RCT in 14 sites in seven countries (India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe)
Intervention	Zidovudine + (single dose) nevirapine Zidovudine + lamivudine + lopinavir-ritonavir Tenofovir + emtricitabine + lopinavir-ritonavir
Results	The rate of transmission was significantly lower with ART than with zidovudine alone (0.5% in the combined ART groups vs. 1.8%)
Conclusion	Antenatal ART resulted in significantly lower rates of early HIV transmission compared to zidovudine alone

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Table 2. Infant HIV Infection through Week 1 (Periods 1 and 2 Combined) in All Mother–Infant Sets and According to Subgroup.*

Subgroup	ZDV Alone	ZDV-Based ART	TDF-Based ART	Difference, ZDV-Based ART and TDF-Based ART vs. ZDV Alone	P Value for Interaction
	no. of mother–infant sets/total no. (%)			percentage points (repeated CI)	
All mother–infant sets	25/1386 (1.8)	7/1385 (0.5)	2/325 (0.6)	−1.3 (−2.1 to −0.4)	
Maternal gestational age at trial entry†					0.68
<34 wk	16/1229 (1.3)	6/1230 (0.5)	1/274 (0.4)	−0.8 (−1.6 to −0.1)	
≥34 wk	9/157 (5.7)	1/154 (0.6)	1/51 (2.0)	−4.8 (−8.9 to −0.6)	
Maternal CD4 count at trial entry					0.70
350–499 cells/mm³	16/577 (2.8)	4/592 (0.7)	1/136 (0.7)	−2.1 (−3.7 to −0.5)	
≥500 cells/mm³	9/809 (1.1)	3/793 (0.4)	1/189 (0.5)	−0.7 (−1.6 to 0.2)	
Maternal viral load at trial entry					0.22
<1000 copies/ml	0/299	1/253 (0.4)	0/57	0.3 (−0.4 to 1.0)	
≥1000 copies/ml	25/1083 (2.3)	6/1129 (0.5)	2/268 (0.7)	−1.7 (−2.8 to −0.7)	
Missing data	4	3	0		

* The analysis of infant HIV infection according to maternal gestational age at trial entry was a prespecified analysis; the other two subgroup analyses were post hoc analyses. CI denotes confidence interval, and HIV human immunodeficiency virus.
† Data on maternal gestational age at trial entry were missing for one woman in the group assigned to ZDV-based ART.

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Pregnant Patients Receiving ART Prior to Pregnancy[8]

01 Patients already on ART should continue their regimen throughout pregnancy and up to delivery
- Some therapies may require discontinuation due to lower drug exposure in pregnancy (cobicistat)
  - If continued, take with food to optimize absorption
- NOT recommended due to toxicity: stavudine, didanosine

02 Discontinuing or altering therapy could cause an increase in viral load, leading to disease progression, a decline in immune status, and an increased risk of perinatal HIV transmission[8]

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ART for Antiretroviral Naive Pregnant Patients[9]

Backbone NRTI

- Tenofovir alafenamide (TAF) + lamivudine or emtricitabine
  - Once daily dosing
  - TAF + emtricitabine is associated with fewer adverse birth outcomes and less risk of weight gain in pregnancy
- Tenofovir disoproxil fumarate (TDF) + lamivudine or emtricitabine
  - Once daily dosing
  - TDF + lamivudine or emtricitabine have similar efficacy and toxicity
- Abacavir + lamivudine
  - Once daily dosing
  - Requires HLA-B*5701 testing

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ART for Antiretroviral Naive Pregnant Patients[9]

Third Drug

- Integrase Inhibitors
  - Dolutegravir
    - Once daily dosing
    - Preferred in ARV-naive pregnant women who present to care later in pregnancy
    - Conderns for excess weight gain
- Protease Inhibitors
  - Darunavir + ritonavir
    - Preferred in patients with previous exposure to cabotegravir PrEP due to concerns for resistance to integrase inhibitors

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Assessment Question #1

SATA: Which antiretroviral therapy may be inappropriate in pregnant patients and require switching therapies?

A. Stavudine
B. Lamivudine
C. Emtricitabine
D. Didanosine

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Intrapartum Management

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Intrapartum Management[10]

Patient's HIV Status

- **HIV Status Unknown**
  - Obtain HIV Testing if:
    - Unknown HIV status
    - Increased risk of HIV who have not re-tested in the third trimester
  - Positive: Start IV Zidovudine
- **HIV Positive**
  - Continue home ARV while in hospital
    - <50 copies/mL and no concerns for adherence → IV Zidovudine not required
    - >1,000 copies/mL and concerns for adherence → Start IV Zidovudine
- **HIV Negative**
  - Standard of Care

Zidovudine Resistance

IV ZDV has proven record to reduce risk of perinatal HIV transmission regardless of resistance

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Zidovudine[10]

01 **Class:** Nucleoside reverse transcriptase inhibitor

02 **Dosing**
Load: 2 mg/kg for 1 hour, continuous infusion: 1 mg/kg/hour until delivery
- If scheduled c-section: IV zidovudine should be given at least 3 hours prior
- If unscheduled c-section: Give IV load
- Administer: 1 bag and adjust titration

03 **Adverse Effects:** Nausea, vomiting, diarrhea, insomnia,myalgias

04 **Monitoring:** Viral load, CBC, LFT, renal function

05 **DDI**
Methadone: increased plasma concentration of methadone
Fluconazole: increased plasma concentrations of zidovudine

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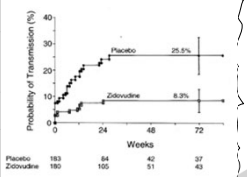
Authors: Edward M. Connor, Rhoda S. Sperling, Richard Gelber, et.al — Published: November 3, 1994

Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment[11]

Method	RCT, double blind, placebo controlled trial in 59 centers Total: 477 patients
Exclusion	Patients who received any antiretroviral treatment during pregnancy
Intervention	Zidovudine vs placebo
Results	Zidovudine administration Reduced transmission by two-thirds



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Intrapartum ART DDI's[10]

Epidural Use
Ritonavir inhibits CYP3A4 which can decrease the elimination of fentanyl by 67%
Pharmacokinetic studies have suggested that epidural anesthesia can be used safely

Post-Hemorrhagic Medications
Methergine should NOT be co-administered with potent CYP3A4 enzyme inhibitors (protease inhibitors or cobicistat)
Effects: Exaggerated vasoconstrictive responses (acute ischemia or the lower extremities)
Consider Alternatives: misoprostol or oxytocin

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Assessment Question #2

Which patient would **NOT** require IV Zidovudine?

A. Patient has a HIV viral load of >1,000 copies/mL
B. Patient receiving ART, however not adherent to their medication regimen
C. Patient who was negative for HIV during first trimester but had a positive expedited HIV test result during labor and delivery
D. Patient who has a viral load of <50 copies/mL within 4 weeks of delivery, on ART, and adherent to regimen

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Postpartum Management

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Recommendations[6]

01 ART
Should be continued postpartum

02 Adherence
Monitor for postpartum depression

Poor adherence can lead to virologic failure, drug resistance and decrease long-term effectiveness of ART

03 Contraceptives
Women with HIV can use all forms of contraceptives

04 Formula
Properly prepared formula or pasteurized donor human milk from a milk bank

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Breastfeeding[6]

Fully suppressive ART during pregnancy can decrease HIV transmission to less than 1%, but not zero
If mother is **NOT** virally suppressed, breastfeeding is strongly advised against

ART during Breastfeeding

- Tenofovir concentrations are undetectable in breastfed infants
- Emtricitabine (19%) and lamivudine (36%) can be detected in breastfed infants
- Dolutegravir has limited data, but 3% can be found in maternal plasma
- There are some recommendations to have infant prophylaxis of zidovudine for 2 weeks while starting to breastfeed

Adverse Events Among Infants

- Comparison from maternal ART and infant HIV prophylaxis shows no significant difference in adverse events
  - Side effects include: rash, hepatitis, IRIS
- An infant who acquires HIV while breastfeeding is at risk for developing ARV drug resistance

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Assessment Question #4

Which medication is not detected in breastfed infants?

A. Lamivudine
B. Emtricitabine
C. Tenofovir
D. Dolutegravir

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06 Neonatal Management

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Term	Definitions[12]
ARV Prophylaxis	The administration of one or more ARV drug to a newborn without documented HIV infection to reduce the risk of perinatal acquisition of HIV
Presumptive HIV Therapy	The administration of a three-drug ARV regimen to newborns who are at highest risk of perinatal acquisition of HIV
HIV Therapy	The administration of three-drug ARV regimen at treatment doses to newborns with documented HIV infection

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Authors: Ary Violari, F.C.Paed., Mark F. Cotton, M.Med., Ph.D., et.al Published: November 20, 2008

Early Antiretroviral Therapy and Mortality among HIV-Infected Infants[13]

Method	Phase 3, RCT, open-label trial conducted in South Africa
Inclusion	Infants 6-12 week of age with positive HIV infection
Intervention	Early antiretroviral therapy vs deferred with zidovudine
Results	Reduced early infant mortality by 76% and HIV progression by 75%

Table 2. **Mortality Rates.**

Variable	Early Antiretroviral Therapy (N = 252)	Deferred Antiretroviral Therapy (N = 125)	Total (N = 377)	Hazard Ratio (95% CI)*	P Value
Deaths — no. (%)	10 (4)	20 (16)	30 (8)	0.24 (0.11–0.51)	<0.001
Person-years of follow-up — no.	205	94	299		
Overall death rate per 100 person-years — % (95% CI)	4.9 (2.3–9.0)	21.2 (13.0–32.7)	10.0 (6.8–14.3)		
Rate of death during follow-up — % (95% CI)					
0–13 wk	9.8 (3.6–21.4)	40.6 (21.0–71.0)			
>13–26 wk	3.7 (0.4–13.2)	19.7 (6.4–45.9)			
>26–52 wk	3.1 (0.4–11.2)	6.8 (0.8–24.7)			

* Hazard ratios for death are for the comparison of the early-therapy groups with the deferred-treatment group.

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Low Risk of Perinatal HIV Transmission[12]

Age	Description	ARV Management
≥37 weeks	- Mother received atleast 10 weeks of ART during pregnancy **and** maintained viral suppression OR - Has HIV RNA <50 copies/mL after 36 weeks and within 4 weeks of delivery **and** no acute HIV infection with good adherence	Zidovudine for 2 weeks
≥37 weeks	- Do not meet above criteria or for high risk but have a HIV RNA <50 copies/mL	Zidovudine for 4-6 weeks
<37 weeks (premature)	- Regardless of risk	

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Other Risk of Perinatal HIV Transmission[12]

Risk	Description	ARV Management
High Risk	- Mother did not receive antepartum ARV - Mothers who only received intrapartum ARV - Did not meet viral suppression - Acute or primary HIV infection	Presumptive HIV therapy with zidovudine, lamivudine and nevirapine (or raltegravir) from birth to 6 weeks
Presumed newborn HIV exposure	- Mothers with unconfirmed HIV status who have at least one positive HIV test	As above. ARV should be d/c if mother is confirmed to not have HIV
Newborn with HIV	- Positive newborn HIV test	Therapeutic doses of ARV above

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ARV Dosing in Infants[12]

Drug	Age	Dosing
Zidovudine May be given IV = 75% of oral dose with same interval Available: tablet, syrup, IV	Birth to age 4 weeks	4 mg/kg PO twice daily
	>4 weeks	12 mg/kg PO twice daily
Lamivudine Available: tablet, oral suspension	Birth to age 4 weeks	2 mg/kg PO twice daily
	>4 weeks	4 mg/kg PO twice daily
Nevirapine Available: tablet, oral suspension	Birth to age 4 weeks	6 mg/kg PO twice daily
	>4 weeks	200 mg/m² PO twice daily *only dose increase with confirmed HIV
Raltegravir Available: tablet, oral suspension	Birth to age 1 week	1.5 mg/kg PO once daily
	1 week - 4 weeks	3 mg/kg PO twice daily
Duration of therapy is recommended depending on infant HIV NAT results, maternal viral load, and risk factors for HIV transmission		

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Management of Medication Toxicity or Intolerance in Infants[14]

Adverse events can range from mild (GI intolerance, fatigue) to severe and life threatening illnesses (hepatotoxicity, insulin resistance, neurotoxicity, nephrotoxicity)
- Acute: occur soon after drug is administered
- Subacute : within 1-2 days
- Late: prolonged drug administration

Management includes
- Symptomatic treatment of mild-to-moderate
- Stopping all components of drug regimen if severe
- Switching therapies
  - Ex: changing to abacavir if infant has ZDV-related anemia
- Consider dose reduction (not recommended)

Resource from clinicalinfo.hiv.gov to manage by adverse event

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Assessment Question #3

What is the preferred regimen for presumed HIV in infants?

A. Zidovudine
B. Efavirenz, abacavir, and raltegravir
C. Zidovudine, lamivudine, and nevirapine

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CONCLUSIONS

Major progression towards preventing perinatal HIV transmission
- Access to healthcare is limited in some countries
- Stigma, discrimination, and social barriers can hinder efforts to prevent transmission
- Comprehensive HIV care and prevention services are critical to reduce rates and improve health outcomes to mothers and infants

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THANKS!

Do you have any questions?
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