

Updates to Testing and Prophylaxis for Infants With HIV Exposure

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Objectives

- Discuss current recommendations for ARV management of infants with perinatal HIV exposure
- Discuss current recommendations for diagnostic testing for infants with perinatal HIV exposure
- Highlight the changes in the US Pediatric guidelines and provide rationale

Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Department of Health and Human Services. 2023. Available at <https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv>.



Disclaimer

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Definitions

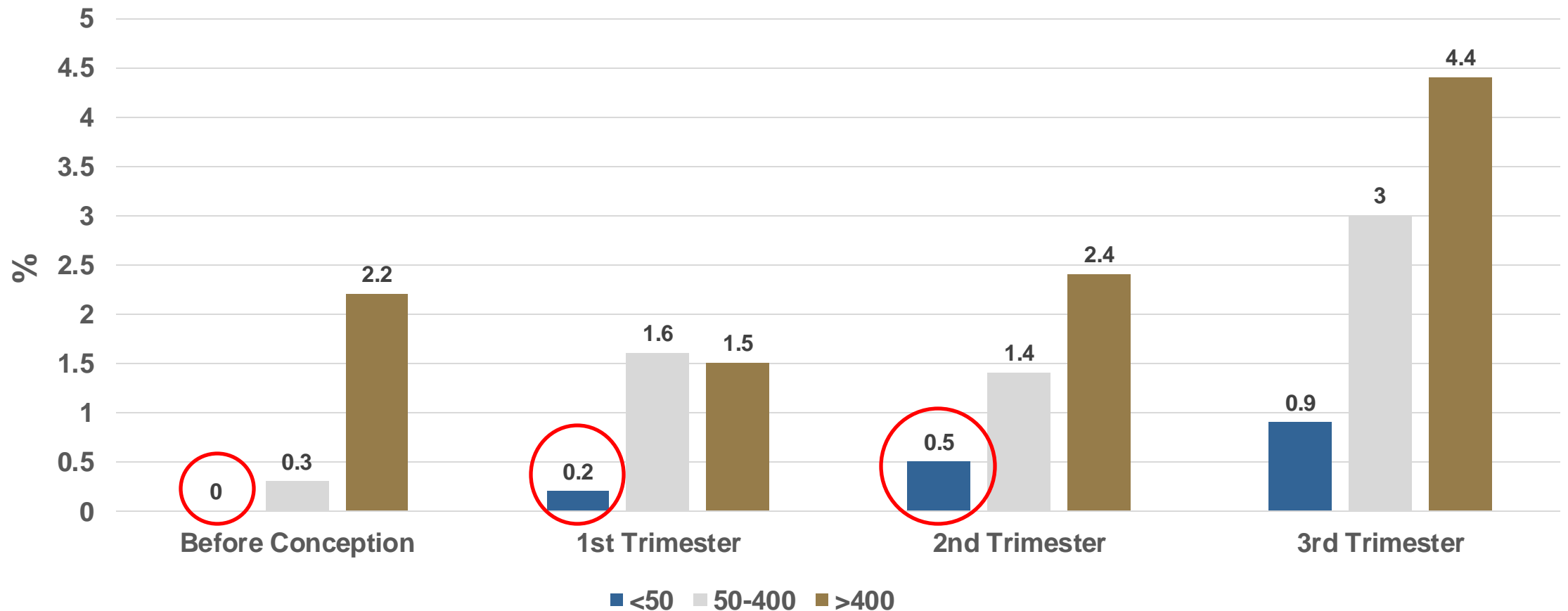
- ARV prophylaxis: The administration of ARV drugs to a newborn without documented HIV infection to reduce the risk of HIV acquisition
- Presumptive HIV therapy: The administration of a three-drug ARV regimen to newborns at highest risk of HIV acquisition
 - Presumptive HIV therapy also provides ARV prophylaxis
- HIV therapy: The administration of a three-drug ARV regimen to newborns with documented HIV infection

Infants at low risk of perinatal HIV transmission

- Born to a person who:
 - Is currently receiving and had received at least 10 consecutive weeks of ART during pregnancy **and**
 - Has sustained antenatal viral suppression (**at least two consecutive tests obtained at least 4 weeks apart with HIV RNA level <50 c/ml**) for the duration of pregnancy **and**
 - Has HIV RNA < 50 c/ml at or after 36 weeks and within 4 weeks of delivery **and**
 - Did not have acute HIV infection during pregnancy **and**
 - Adherence concerns have not been identified **and**
 - Delivered a gestational age of ≥ 37 weeks
- Neonatal ARV management:
 - **2 weeks of ZDV**

Timing of ART and viral load at delivery – perinatal transmission rates

French Perinatal Cohort – 8075 mothers on ART, not breastfeeding, 2000-2011



Further rationale for 2 weeks ZDV prophylaxis

- 312 infants at low risk for transmission
- 127 received 2 weeks ZDV
- 184 received > 2 weeks
- No transmissions in the 2 week group
- Grade 1 or higher anemia
 - 31 vs 52% at 1 month
 - 12 vs 30% at 3 months
- Swiss guidelines have recommended no infant PEP for infants at low risk for transmission since 2016
- Report available on 87 infants managed without neonatal ARV PEP between 2016-2018
- No HIV transmissions reported

Infants at high risk of perinatal HIV transmission

- Born to a person who:
 - Did not receive antepartum ARVs **or**
 - Received only intrapartum ARVs **or**
 - Received antepartum ARVs but did not have sustained viral suppression for the 4 weeks prior to delivery **or**
 - Experienced acute/primary HIV infection during pregnancy
- Neonatal ARV management:
 - Presumptive HIV therapy with either ZDV/3TC/NVP or ZDV/3TC/RAL
 - 2-6 weeks duration for all three drugs
 - **If the 3 drug regimen is discontinued prior to 6 weeks, ZDV should be continued to complete a total of 6 weeks of prophylaxis**

Other scenarios

- Born to a person who does not meet either scenario of low or high risk of perinatal transmission
 - Infant born at <37 weeks but is otherwise at low risk for transmission
 - Does not meet definition for low risk but is born to a person with an HIV RNA of <50 c/ml at or after 36 weeks gestation
 - Infant should receive 4-6 weeks ZDV
- Presumed neonatal HIV exposure
 - Positive maternal HIV serology at delivery/post-partum
 - Initiate presumptive HIV therapy for the infant
 - Discontinue if supplemental testing does not confirm maternal HIV infection

How long to continue 3-drug preemptive ART in an infant at high risk for HIV transmission?

- Three drugs (ZDV/3TC + either RAL or NVP) may be continued for 2-6 weeks
- Data to consider when making this decision
 - Maternal viral load at the time of delivery
 - Infant NAT results
 - Other risk factors for transmission
- Consultation with an expert in Pediatric HIV is recommended
- NCCC – 888 448 8765- [Perinatal HIV/AIDS | National Clinician Consultation Center \(ucsf.edu\)](https://www.ucsf.edu/perinatal-hiv-aids)

Infant ARV prophylaxis while breastfeeding

- No definitive recommendation was provided in the guidelines
 - 2 weeks ZDV
 - 4-6 weeks ZDV (or NVP)
 - NVP (or other ARV) throughout the duration of breastfeeding
- Area for shared decision making with the breast feeding parent

HIV transmission maternal ART during breastfeeding

- IMPAACT PROMISE study → 2400 women with HIV
 - Randomized to maternal ART vs infant NVP during breastfeeding
 - Transmission rate was 0.6% at 12 months in both arms
 - At 18 months 0.7% in the maternal ART and 0.9% in the infant NVP arm were infected
 - 2 infants in the maternal ART arm acquired HIV even though the maternal viral load was <40 copies/ml at the time the infant's samples tested positive, although earlier samples had detectable VLs
- Retrospective analysis from sites in US and Canada – 72 infants
 - No transmissions in the 68 with data
 - Infant prophylaxis ranged from 6 weeks ZDV or NVP to three drug ART throughout breastfeeding

HIV transmission maternal ART during breastfeeding

- Breastfeeding, Antiretrovirals and Nutrition (BAN) study
 - 221 mothers with ≥ 1 paired plasma/BM VL
 - <1% had detectable HIV RNA in BM when paired plasma RNA was <40 c/ml
 - Detectable breastmilk RNA associated with BM transmission (HR 3.8, 95%CI 1.2-12.1) compared to undetectable (<56 c/ml) breastmilk RNA
 - No BM transmissions in women with all plasma VLs <100 c/ml

Considerations for decision making- against additional infant ARV prophylaxis

- Multiple studies have shown low risk for HIV transmission via breastfeeding when mothers were receiving ART
- No transmissions documented from women who meet the criteria for low risk proposed by the guidelines (but no studies with this exact situation)
- No clear additional benefit to the addition of infant ARVs over maternal ART
- Potential toxicity of prolonged infant ARVs
- Challenges administering medications to infants

Considerations for decision making- for additional infant ARV prophylaxis

- Risk is increased with increased maternal plasma viral load during breastfeeding
- Maternal adherence to ART and VL suppression decrease after delivery
- Infant ARV prophylaxis during breastfeeding would provide additional protection for the infants if there is breakthrough viremia during breastfeeding
- Cell-associated HIV DNA associated with BM transmission
 - Association is higher in the early post-partum period
 - Maternal ART has less effect on cell-associated HIV DNA load in BM

Update on Infant Diagnosis

- Virologic diagnostic testing is recommended for all infants with perinatal HIV exposure at the following ages:
 - 14 to 21 days
 - 1 to 2 months
 - 4 to 6 months
- For infants who are at high risk of perinatal HIV infection, additional virologic diagnostic testing is recommended at birth and at 2 to 6 weeks after ARV drugs are discontinued
- The additional virologic testing for infants at high risk of perinatal HIV infection is recommended because of the increased risk of infection and concern that ARV prophylaxis, particularly combination ARV prophylaxis or presumptive HIV therapy, may reduce the sensitivity of diagnostic testing

Infants at high risk	Testing strategy
<ul style="list-style-type: none"> • Did not receive prenatal care; • Received no antepartum ARVs or only intrapartum ARV drugs; • Initiated ART late in pregnancy (during the late second or third trimester); • Received a diagnosis of acute HIV infection during pregnancy or in labor; and/or • Had detectable HIV viral loads (≥ 50 copies/mL) close to the time of delivery, including those who received ART but did not achieve sustained viral suppression 	<p style="text-align: center;"> Birth 14–21 days 1–2 months 2–3 months 4–6 months </p> <p>Any positive NAT should be repeated as soon as possible. Initiation of ART should not be delayed pending result</p>
Infants at low risk	
<ul style="list-style-type: none"> • Received ART during pregnancy; • Had sustained viral suppression (usually defined as < 50 copies/mL); <i>and</i> • Were adherent to their ARV regimens 	<p style="text-align: center;"> 14–21 days 1–2 months 4–6 months </p>

Performance of HIV NAT after birth

Table II. Results of HIV-1 PCR according to age* in the 65 infected infants

	Median age (IQR)	I [†] n	Sensitivity (95% CI), n	Kappa (95% CI) [‡]	Median viral load [§] (IQR)	Frequency of low viral load [¶] % (n ^{**})
Birth: day 1-7	3 (2-4)	55				
Plasma HIV-1 RNA			58.2 (44.1-71.4), 32/55	0.78	3.6 (2.8-4.6)	34 (11/32)
PBMC HIV-1 DNA			54.5 (40.6-68.0), 30/55	(0.61-0.95)	2.8 (2.3-3.2)	23 (3/13)
Day 1-3	2 (1-3)	30				
Plasma HIV-1 RNA			56.7 (37.4-74.5), 17/30	0.86	3.8 (3.1-4.8)	24 (4/17)
PBMC HIV-1 DNA			56.7 (37.4-74.5), 17/30	(0.68-1.00)	2.8 (2.3-3.3)	25 (2/8)
Day 4-7	4 (4-5)	25				
Plasma HIV-1 RNA			60.0 (38.7-78.9), 15/25	0.68	3.1 (2.5-4.2)	47 (7/15)
PBMC HIV-1 DNA			52.0 (31.3-72.2), 13/25	(0.39-0.97)	2.7 (1.7-2.9)	20 (1/5)
1 month: day 15-45 ^{††}						
During any ARV	31 (28-34)	56				
Plasma HIV-1 RNA			89.3 (78.1-96.0), 50/56	0.81	5.1 (3.7-5.8)	20 (10/50)
PBMC HIV-1 DNA			89.3 (78.1-96.0), 50/56	(0.56-1.00)	3.0 (2.6-3.8)	10 (3/30)
In relation to infant ARV						
ZDV	30 (28-34)	47				
Plasma HIV-1 RNA			91.5 (79.6-97.6), 43/47	0.88	5.4 (4.7-5.9)	12 (5/43)
PBMC HIV-1 DNA			89.4 (76.9-96.5), 42/47	(0.64-1.00)	3.3 (2.8-4.0)	8 (2/26)
ARV Combination	32 (30-33)	9				
Plasma HIV-1 RNA			77.8 (40.0-97.2), 7/9	0.61	2.5 (2.2-4.0)	71 (5/7)
PBMC HIV-1 DNA			88.9 (51.8-99.7), 8/9		2.5 (2.2-2.7)	25 (1/4)
3 months: Day 61-121 ^{††}	81 (68-92)	38				
Plasma HIV-1 RNA			100.0 (92.4-100.0), 38/38	1	5.6 (5.1-6.0)	0 (0/38)
PBMC HIV-1 DNA			100.0 (92.4-100.0), 38/38		3.7 (3.3-4.1)	0 (0/32)
6 months: day 122-244 ^{††}	160 (150-196)	12				
PBMC HIV-1 DNA			100.0 (77.9-100.0), 12/12	1	3.9 (3.4-4.3)	0 (0/12)

Presumptive and definitive exclusion of HIV infection

- Presumptive - with two or more negative virologic tests (one at age ≥ 2 weeks and one at age ≥ 4 weeks) or one negative virologic test at age ≥ 8 weeks **at least 2 weeks after discontinuing multi-drug ARV prophylaxis/presumptive therapy**, or one negative HIV antibody test at age ≥ 6 months.
- Definitive - two or more negative virologic tests, **with one negative test obtained at age ≥ 1 month (and at least 2 -6 weeks after discontinuation of multi-drug ARV prophylaxis/presumptive therapy)**

Infant testing while breastfeeding

- Infant HIV testing
 - Should have the same testing as other low risk infants (HIV NAT at 2-3 weeks, 1-2 months and 4-6 months)
 - In addition should have a test at birth and a test at 2-4 months if the gap between 1-2 months and 4-6 months would otherwise be greater than 3 months
 - Every 3 months while breastfeeding
 - 4-6 weeks, 3 months and 6 months after weaning
 - If maternal viral load becomes detectable while breastfeeding the infant should be tested at that time and then follow the same testing schedule as after birth

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