CLINICIAN CONSULTATION CENTER
National rapid response for HIV management and bloodborne pathogen exposures.

CCC Testing Recommendations for HIV-exposed infants Updated 7.15.16

USERS NOTE: Please note this document does not provide guidance on overall decision-making regarding what medication(s) to use for HIV-exposed infants, nor does it provide guidance on dosing of these medications. <u>This document is meant to facilitate HIV testing and laboratory monitoring for HIV-exposed infants, AFTER conversation with a CCC consultant in reference to a particular case</u>. Please do NOT keep this document for reference for other patients, as the information may be out of date. 24/7 expert telephone consultation is available via the National Perinatal HIV Hotline: 888-448-8765 (nccc.ucsf.edu).

The testing recommendations in this document are from DHHS Pediatric HIV Guidelines (https://aidsinfo.nih.gov/guidelines/html/2/pediatric-arv-guidelines/0) and DHHS Perinatal HIV Guidelines (https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0#), unless otherwise noted; refer to these Guidelines for the most current information.

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General tips:

- Do NOT use umbilical cord blood for HIV DNA or RNA testing, given concern for contamination with maternal blood.
- Do NOT send HIV antibody tests (including 4th generation HIV Ag/Ab tests) on neonates of mothers known to have HIV. A positive antibody test in the first 18 months of life would likely represent maternal antibody, and not necessarily the HIV status of the infant; these misleading results can lead to confusion in the infant's medical records.
- HIV RNA vs DNA PCR: HIV RNA PCR identifies plasma virus which may be suppressed by 3-drug ARV therapy. HIV DNA PCR identifies cell-associated virus which is not as easily suppressed by ARVs. Therefore, cellular DNA should be positive even if plasma RNA is negative. However, early ARV treatment can still dampen the reservoir (cell-associated), so false negatives may still occur with DNA testing but to lesser extent.

Labs at birth:

- HIV-1 DNA and/or RNA PCR (see above): Order birth DNA or RNA PCR for all "higher-risk" HIV-exposed infants. Per the Perinatal HIV guidelines, birth PCR is optional on "low-risk" infants, but clinicians may consider testing all infants to evaluate for *in utero* transmission.
- While the Perinatal HIV guidelines recommend ordering either RNA or DNA PCR at birth, the CCC recommends both if possible (particularly in the setting of treatment-based dosing), to know the infant's baseline viral load, in the case of potential infant infection. **In order to confirm infant HIV infection, tests must be positive from two separate specimens.**
- CBC with differential: order for all HIV-exposed infants per Perinatal HIV guidelines.
- ALT, AST: Order for infants on treatment-based dosing of nevirapine (see CCC Dosing Recs document for details on dosing). This expert opinion recommendation is based on concern for potential liver toxicity from investigational NVP dosing: therefore, baseline LFTs may be helpful.

Labs at ~2 weeks of life:

- HIV-1 DNA or RNA PCR: Order for all HIV-exposed infants. Per Perinatal HIV guidelines, DNA or RNA is acceptable. However, particularly in the setting of treatment-based dosing, there is theoretical concern for false negative RNA, so the CCC recommends DNA PCR if available.
- CBC: Order for HIV-exposed infants who receive combination zidovudine/lamivudine-containing ARV regimens due to concern for anemia.
- ALT, AST: Order for infants on treatment-based dosing. This expert opinion recommendation is based on concern for potential liver toxicity from investigational NVP dosing as indicated above.

Labs at 4-8 weeks of life:

- HIV-1 DNA or RNA PCR: **Test all HIV-exposed infants at ~4 weeks of life.** DNA or RNA is acceptable. However, particularly in the setting of treatment-based dosing, there is theoretical concern for false negative RNA, so the CCC recommends DNA PCR at 4 weeks of life.
- The DHHS Pediatric HIV guidelines recommend deferring the 1-2 month PCR until 2-4 weeks after finishing combination prophylaxis due to concerns for false negatives. For some infants, this would mean deferring this test until 8+ weeks. However, a test at 4 weeks remains valuable because, if negative, along with a negative 2-

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week test, it will enable providers to "presumptively" rule out infection and thus avoid initiating *Pneumocystis* prophylaxis at 6 weeks of life. Conversely, if the test is positive, it allows for prompt diagnosis of an infected infant. **For infants on combination prophylaxis, the CCC recommends nucleic acid tests at BOTH ~ 4 AND ~8 weeks of life.**

- At 8 weeks of life, since the infant should no longer be on medications, DNA or RNA is appropriate. The CCC recommends RNA for this test because it is cheaper and faster.
- CBC: order at 4 weeks for HIV-exposed infants who receive combination zidovudine/lamivudine-containing ARV prophylaxis regimens (per the Perinatal Guidelines) due to concern for anemia or in symptomatic infants receiving ZDV alone. Consider in all HIV-exposed infants receiving ZDV alone.
- ALT, AST: **Consider a single test between 4 and 8 weeks** of life for infants who received treatment-based (investigational) dosing of NVP for more than 2 weeks. This expert opinion recommendation is based on concern for potential liver toxicity from investigational NVP dosing as indicated above.

Labs at 4-6 months of life:

- HIV-1 DNA or RNA PCR: order for all HIV-exposed infants to definitively rule-out HIV infection. Per Perinatal HIV guidelines, DNA or RNA is acceptable. The CCC recommends RNA for this test because it is cheaper and faster.

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Perinatal HIV Hotline: HIV-exposed infant follow-up testing (not breastfed)

	Within 48 hours	2 weeks	4 weeks	6 weeks	8 weeks	3 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos
HIV testing NOTE: see text for details regarding timing and options for indicated testing	HIV DNA or RNA PCR *(optional if low-risk infant, but consider testing all infants to rule out* in utero *infection)*	HIV DNA or RNA PCR	HIV DNA or RNA PCR		HIV DNA or RNA PCR in high-risk infants		HIV DNA or RNA PCR	HIV **definitively** ruled out with: a) two or more negative virologic tests, one obtained at age ≥1 month and one at ≥4 months; or b) two negative HIV antibody tests from separate specimens obtained at age ≥6 months. Many clinicians confirm HIV negative status with an HIV antibody at 12-18 months. HIV **ruled in** with two positive virologic tests from separate blood samples at any age.[3]				
CBC monitoring	✓ for all HIV-exposed infants	✓ for infants receiving ZDV AND 3TC	✓ for infants receiving ZDV AND 3TC or in any infant who is symptomatic (consider for infants receiving ZDV alone)			***Follow up abnormalities as clinically indicated.***						
AST and ALT monitoring[4]	✓ for infants receiving treatment-dosed NVP	✓ for infants on treatment-dosed NVP	Consider for infants who are still receiving treatment-dosed NVP, or if symptomatic									
***Pneumocystis* prophylaxis: TMP/SMZ**	If the standard testing algorithm is followed TMP/SMZ can be avoided. TMP/SMZ can be stopped (or not started) if HIV has been **presumptively** ruled out with: a) two negative virologic tests, one at ≥14 days of age and one at ≥1 month of age; or b) one negative virologic test result obtained at ≥2 months of age; or c) one negative HIV Ab test result obtained at ≥6 months of age. *(Note: most infants in US do NOT start this if standard testing schedules are followed)*			Start TMP/SMX 75/375 mg/m^2 BSA/dose PO 2x/day T IW[2]	Adjust TMP/SMZ	Adjust TMP/SMZ						
Immunizations	All HIV-exposed infants should be given standard vaccinations. The only vaccines contraindicated for an HIV-infected child would be live vaccines such as MMR or MMRV in the context of severe immunosuppression.											

Additional considerations/references:

(1) Perinatal HIV Guidelines: https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0

(2) TMP/SMX comes in several formulations. See Pediatric OI Guidelines for weight-based dosing, dosing options: https://aidsinfo.nih.gov/guidelines/html/5/pediatric-oi-prevention-and-treatment-guidelines/0. **Figure 1 is recommended immunization schedule.**

(3) Pediatric ARV Guidelines: https://aidsinfo.nih.gov/guidelines/html/2/pediatric-treatment-guidelines/0

(4) Some experts recommend additional monitoring for infants exposed *in utero* to combination ARVs (i.e. maternal ARV regimen)

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