CLINICAL GUIDELINES PROGRAM
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

Guidance: Questions, Answers, and Best Practices for Medical Management of Perinatal HIV Exposure in New York State

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Developed by the NYSDOH AIDS Institute's Perinatal HIV Prevention Program, Office of Sexual Health & Epidemiology, and Office of the Medical Director

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Purpose of This Guidance

The questions and answers below are presented as guidance for clinicians in New York State who provide medical care for newborns and infants with perinatal HIV exposure. With 2 exceptions, the New York State Department of Health AIDS Institute (NYSDOH AI) supports the U.S. Department of Health and Human Services (DHHS) recommendations for Diagnosis of HIV Infection in Infants and Children [DHHS 2023]. However, the NYSDOH AI strongly advises clinicians to 1) perform at-birth testing of all exposed infants, regardless of the assessed risk of HIV acquisition (DHHS recommends birth testing for high-risk exposures only); and 2) recognize fewer than 3 prenatal care visits as a criterion for high-risk exposure (DHHS considers 0 prenatal care visits high risk).

The goals of this guidance are to:

- Increase New York State clinicians' awareness of the rationale for, benefits of, and best practices for at-birth HIV testing of all infants with perinatal exposure, while reinforcing DHHS recommendations in general
- Reinforce the procedure for confirmatory testing following a positive HIV test result
- Highlight the New York State criteria for high-risk perinatal HIV exposure
- Clarify the post-birth serial HIV testing schedule based on exposure risk and method of infant feeding
- Encourage New York State clinicians to use the free-of-charge pediatric HIV testing services at the Wadsworth Center and to seek consultation with an experienced HIV clinician through the Clinical Education Initiative (CEI) Line: 1-866-637-2342, option 2 (available 24/7)

Rationale: Perinatal HIV transmission continues. In New York State there were 20 perinatal HIV transmissions detected between 2010 and 2020; these infants were among the 4,599 born to 4,501 unique individuals diagnosed with HIV before or at the time of delivery. Approximately 70% (n=3,219) of the infants perinatally exposed to HIV received their first nucleic acid test (NAT) within 0 to 2 days after birth, 9% within 3 to 4 days after birth, and 14% more than 4 days after birth. HIV transmission was detected from specimens collected within 0 to 2 days after birth in 10 of 20 (53%) infants in whom HIV transmission was detected [NYSDOH 2022].

Antiretroviral therapy (ART) initiated as close to the time of birth as possible reduces the risk of HIV acquisition in perinatally exposed infants; the benefit of ART for newborns decreases when initiation is delayed [Fiscus, et al. 1999; Wade, et al. 1998]. Therefore, experts recommend initiating ART as promptly as possible after delivery and preferably within 6 hours of birth; see DHHS > Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection.

HIV Testing at Birth

Q: When should clinicians perform the first HIV NAT in an infant perinatally exposed to HIV?

A: The DHHS recommends HIV testing at birth in infants with high-risk exposures and testing at 14 to 21 days after birth in infants with low-risk exposures. Risk refers to the risk that an infant will acquire HIV and is based on maternal factors explained below (see Box 1, below).

The NYSDOH AI strongly advocates for at-birth HIV testing for all infants perinatally exposed to HIV, regardless of the exposure risk.

Q: Why does the NYSDOH AI advocate testing at birth if an infant's risk of HIV acquisition is low?

A: Birth testing provides an opportunity for timely HIV diagnosis in exposed infants.

Among the benefits of at-birth HIV testing is the immediate activation of New York State surveillance activities that ensure an infant's linkage to care and address obstacles to follow-up, such as 1) infant/family relocation within and outside of New York State; 2) infant name change(s); 3) infant involvement with foster care and/or adoption services; and 4) factors, whether anticipated or unexpected, that impede a family's ability to access care.

The NYSDOH AI asserts that facilitating timely HIV diagnosis and linkage to care are crucial for infants perinatally exposed to HIV and for their families or guardians.

Q: Is there an optimal time for collecting an infant's specimen for HIV testing at birth?

A: Ideally, the specimen should be collected within 6 hours, before antiretroviral (ARV) prophylaxis is initiated; if it is impossible to obtain a specimen before ARV prophylaxis is initiated, the newborn's specimen may be obtained for up to 48 hours after delivery.

The ideal sequence is to collect a specimen for HIV testing as soon as possible after birth, then initiate ARV prophylaxis. Early neonatal initiation of ARV prophylaxis is associated with a decline in HIV-1-infected cells and low or undetectable levels of HIV-1 RNA and DNA, which may delay HIV diagnosis.

The NYSDOH AI endorses the DHHS recommendation that ARV prophylaxis for exposed infants should be initiated as soon as possible after delivery, ideally within 6 hours of birth. Initiation of ARV prophylaxis should not be delayed by specimen collection and HIV testing.

Q: If a positive HIV NAT result is obtained at birth or at any time after, what is the procedure for confirming an HIV diagnosis in an exposed infant?

A: The procedure for confirmatory testing if an infant's HIV nucleic acid test (NAT) result is positive at any age is to obtain a new specimen as quickly as possible and perform an HIV NAT using the new specimen. If a second positive HIV NAT result is obtained, no additional testing is required and a definitive diagnosis of HIV infection may be made.

Risk of Infant HIV Acquisition

Q: If HIV testing is performed in all exposed infants at birth in New York State, is it still important to assess an infant's risk of HIV acquisition as high or low?

A: Yes. The number of serial HIV tests performed after the first test at birth is determined based on the infant's risk of HIV acquisition. Infants at high risk are recommended to receive additional tests at critical timepoints.

Q: How are "low risk" and "high risk" defined with regard to an exposed infant's risk of HIV acquisition?

A: The risk of an infant's perinatal exposure to HIV is based on maternal factors and refers to the risk that the infant will acquire HIV as a result of the exposure.

Per the DHHS, infants are at low risk of HIV acquisition if born to mothers who received and were adherent to ART during pregnancy and who sustained an HIV RNA level (viral load) <50 copies/mL. The NYSDOH AI agrees with this definition.

Per the DHHS, infants are at high risk of HIV acquisition if born to mothers who meet any of the following criteria:

- No antepartum ARVs or only intrapartum ARVs
- ART initiated late in pregnancy (e.g., after week 20)
- Acute HIV diagnosis during pregnancy or labor
- HIV viral load ≥50 copies/mL close to the time of delivery (includes those who did not achieve viral suppression while taking ART)
- Fewer than 3 prenatal care visits per NYSDOH AI (0 prenatal care visits per DHHS)

Box 1: DHHS and NYSDOH AI Criteria for Low and High Risk of HIV Acquisition From Perinatal Exposure

Low Risk	High Risk
Per DHHS and NYSDOH AI: Infants at low risk of acquiring HIV from perinatal exposure are those born to mothers who: • Received ART during pregnancy, *and* • Had sustained viral suppression (usually defined as HIV RNA <50 copies/mL), *and* • Were adherent to their ART regimen	**Per DHHS and NYSDOH AI:** Infants at high risk of acquiring HIV from perinatal exposure are those born to mothers who: • Received no antepartum ARVs or only intrapartum ARVs *or* • Initiated ART late in pregnancy (during the late second or third trimester) *or* • Were diagnosed with acute HIV during pregnancy or while in labor *or* • Had a detectable viral load (HIV RNA >50 copies/mL) close to the time of delivery, including those who received ART but did not achieve sustained viral suppression *or* **Per DHHS:** Did not receive prenatal care **Per NYSDOH AI:** Had <3 prenatal care visits

Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral medication; DHHS, U.S. Department of Health and Human Services.

Recommendations for ARV Initiation in HIV-Exposed Infants

Q: Does the NYSDOH AI have a guideline on ARV initiation in infants perinatally exposed to HIV?

A: The NYSDOH AI endorses the DHHS recommendations in Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection for all clinicians managing the care of infants diagnosed with or perinatally exposed to HIV.

Q: Is expert consultation required for infant ARV initiation?

A: Expert consultation is not required but is encouraged. When consultation would be helpful, New York State clinicians can consult with an HIV expert regarding maternal or fetal HIV exposure by calling the CEI Line: 1-866-637-2342, option 2 (available 24/7).

Expert Consultation

Q: Under what circumstances should a clinician consult with an expert in managing the medical care of an HIV-exposed infant?

A: Consultation with an experienced HIV care provider is especially helpful when there are maternal factors that may increase the risk of transmission. Such factors include but are not limited to:

- Primary or acute HIV during pregnancy
- Inconsistent adherence to ART
- HIV viral load ≥50 copies/mL
- Nonadherence to prenatal visits
- Undocumented HIV viral load within 4 weeks before delivery or undocumented HIV status at time of delivery
- Preliminary positive HIV test result during labor or shortly after delivery

- Intrapartum HIV prophylaxis not administered when indicated
- Diagnosis of acute or primary HIV infection in the breast/chest-feeding parent
- Expert consultation is also advised when considering:
- Administration of ARVs in addition to or instead of zidovudine for infant HIV prophylaxis
- Early discontinuation of infant HIV prophylaxis
- Indications for opportunistic infection prophylaxis in an infant diagnosed with HIV

CEI Line: New York State clinicians can consult an HIV expert 24/7 regarding maternal or fetal HIV exposure by calling the CEI Line: 1-866-637-2342, option 2.

National Perinatal Hotline: Clinicians outside of New York State can call the National Perinatal HIV Hotline 24/7: 1-888-448-8765.

Serial HIV Testing Schedule After the At-Birth Test

Q: Is there a set schedule for additional (serial) HIV testing in exposed infants after they are tested at birth?

A: Yes. Box 2, below, specifies the serial HIV testing schedule recommended by the DHHS for infants perinatally exposed to HIV and for infants with ongoing exposure to HIV through breast milk from a parent with HIV.

Box 2: New York State Age Intervals for HIV Nucleic Acid Testing in Infants With Perinatal and Ongoing HIV Exposure

Ages for HIV NAT with low-risk exposure [a]:	**Ages for HIV NAT with high-risk exposure [e]:**	**HIV NAT schedule for ongoing exposure through breast milk:**
• Birth [b,c] • 14 to 21 days • 1 to 2 months [d] • 4 to 6 months	• Birth [b,c] • 14 to 21 days • 1 to 2 months [d] • 2 to 3 months • 4 to 6 months	• Follow HIV NAT schedule for high-risk exposure AND perform the following additional testing: – HIV NAT every 3 months for the duration of exposure – HIV NAT at 4 to 6 weeks, 3 months, and 6 months after the last exposure to breast milk

Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral medication; NAT, nucleic acid test; PCP, *Pneumocystis jiroveci* pneumonia (previously *P. carinii* pneumonia).

Notes:

a. Infants with low-risk HIV exposure are those born to mothers who received and were adherent to ART during pregnancy and had sustained viral suppression (usually defined as HIV RNA <50 copies/mL).
b. Obtain the specimen for HIV testing before antiretroviral medications are initiated whenever possible and without delaying ARV initiation.
c. At-birth HIV testing of all exposed infants activates critical NYSDOH surveillance activities that ensure linkage to care after hospital discharge, regardless of an infant's relocation within or outside of New York State, name change, entry into the foster care or adoption system, and any other factors that may impede a family's access to care.
d. Clinicians should initiate PCP prophylaxis at 6 weeks of age for all HIV-exposed infants unless HIV diagnostic testing definitively or presumptively excludes HIV infection; if HIV diagnostic testing results are negative by 5 weeks of age, PCP prophylaxis is not necessary.
e. Infants with high-risk exposure are those born to mothers who had <3 prenatal care visits, or acute HIV diagnosed during pregnancy or labor, or late ART initiation (e.g., after week 20 of pregnancy), or no antepartum ARVs or intrapartum ARVs only, or an HIV viral load ≥50 copies/mL close to the time of delivery.

Q: Can ARV use affect the results of an infant's HIV test?

A: Results of plasma HIV RNA nucleic acid tests (NATs) or plasma HIV RNA/DNA NATs can be affected by ARVs administered to newborns as prophylaxis or presumptive HIV therapy [DHHS 2023; Patel, et al. 2020; Mazanderani, et al. 2018; Veldsman, et al. 2018; Uprety, et al. 2015]. In New York State, a case of perinatal HIV transmission was identified through HIV NAT at 4 months of age following 3 prior negative NAT results (at birth, 2 weeks of age, and 4 weeks of age). The newborn was at high risk of perinatal HIV infection and received a 3-drug ARV regimen for presumptive HIV therapy, which was discontinued at 6 weeks of age. The infant was not exposed to HIV through breast milk, and there was no other postnatal HIV exposure risk. For

this reason, the NYSDOH AI strongly advises adhering to the DHHS-recommended additional diagnostic HIV NAT, to be performed at 2 to 3 months of age after the time most 6-week multiagent ARV preventive regimens have been completed.

Q: Is additional HIV testing required for infants with ongoing exposure through breast milk from a parent who has HIV?

A: Yes. The DHHS recommends and the NYSDOH AI agrees that with ongoing exposure through breast milk from a parent with HIV, infants should be tested for HIV every 3 months for the duration of exposure. HIV testing is also recommended at 3 times after the last exposure to breast milk: 4 to 6 weeks, 3 months, and 6 months.

Coordination between the pediatric care provider and the maternal HIV care provider is critical. Maternal viral load monitoring is recommended every 1 to 2 months during breastfeeding. Additional infant virologic testing, including an immediate NAT, is indicated if maternal viral load becomes detectable during breastfeeding. For additional testing recommendations for infants exposed to breast milk in the setting of detectable maternal viral load, refer to DHHS > Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States.

Congenital Syphilis, cCMV, and PCP Prophylaxis

Q: Is congenital syphilis a concern for infants with perinatal HIV exposure?

A: Yes. Concomitant sexually transmitted infections (STIs), including syphilis, are common in individuals with HIV. Comprehensive STI screening to identify disease is critical because coinfection increases the risk of adverse perinatal and neonatal outcomes, including likely higher rates of in utero transmission. Infants born to individuals with HIV and concurrent STIs require prompt evaluation to exclude the possibility of transmission of additional infectious agents [Adachi(a), et al. 2018].

No data exist to suggest that infants with congenital syphilis born to individuals with HIV and syphilis require evaluation, therapy, or follow-up for syphilis different than what is recommended for all infants with syphilis. The NYSDOH AI recommends that clinicians obtain serologic screening for syphilis for pregnant patients with HIV at the first prenatal visit, during the third trimester (28 to 32 weeks of gestation), and at delivery. See the NYSDOH AI guideline HIV Testing During Pregnancy, at Delivery, and Postpartum and the interim NYSDOH guidance regarding amendments to Public Health Law and prenatal syphilis screening.

Q: What are the recommendations for care in infants with congenital syphilis?

A: Treatment for congenital syphilis in infants is determined based on maternal history of syphilis infection and treatment, and current laboratory and physical examination results. All infants diagnosed with congenital syphilis should be physically and serologically monitored closely in the months following birth.

Clinicians should refer to the current Centers for Disease Control and Prevention Sexually Transmitted Infections Treatment Guidelines for the evaluation and treatment of neonates with congenital syphilis that is confirmed or highly probable, possible, less likely, or unlikely. New York State clinicians may contact the Clinical Education Initiative Sexual Health Center of Excellence to access expert medical consultation on diagnosis, treatment, and management of STD infections at 866-637-2342.

Q: Is cCMV a concern for infants perinatally exposed to HIV?

A: Yes. HIV-exposed infants may be at higher risk for acquiring cCMV during pregnancy. Infants with HIV infection, particularly those who acquired HIV in utero, are at greatest risk for cCMV. Screening for cCMV is an important component of a comprehensive evaluation needed for HIV-exposed infants, particularly those born to individuals not on ART during pregnancy [Adachi(b), et al. 2018].

Screening and early diagnosis of cCMV is the New York State standard of care to promote early intervention, monitoring, and medical care that optimizes hearing and developmental outcomes [American Academy of Pediatrics 2018; Marsico and Kimberlin 2017; Rawlinson, et al. 2017].

For clinical recommendations, see DHHS > Initial Postnatal Management of the Neonate Exposed to HIV. cCMV is the most common intrauterine infection and the leading nongenetic cause of sensorineural hearing loss in children in the United States [Grosse, et al. 2017]. One in every 200 infants is born with cCMV infection, and approximately 20% of these infants will develop long-term health problems such as hearing or vision loss, intellectual disability, seizures, or developmental delay [NYS Senate 2018].

☆ NEW YORK STATE LAW

- Institutions caring for infants 28 days of age or younger must administer a urine polymerase chain reaction test for cCMV, or a diagnostically equivalent test, to any such infant who is identified as or suspected of having a hearing impairment, unless the parent of the infant objects. See New York State Senate Bill S2816 for more information.

Q: Is any prophylaxis against HIV-related opportunistic infections recommended for perinatally exposed infants?

A: Yes. Clinicians should initiate prophylaxis for *Pneumocystis jiroveci* pneumonia (previously *P. carinii* pneumonia; PCP) at 6 weeks of age for all HIV-exposed infants unless HIV diagnostic testing definitively or presumptively excludes HIV infection; if HIV diagnostic testing results are negative by 5 weeks of age, PCP prophylaxis is not necessary. See DHHS > Initial Postnatal Management of the Neonate Exposed to HIV.

Initial Postnatal Management

Q: What are the NYSDOH AI good practices for managing discharge and initial postnatal care of infants perinatally exposed to HIV?

A: NYSDOH AI good practices include:

- Continuing to educate parents or guardians about safe infant feeding options (including avoiding use of premasticated food), medical follow-up, antiretroviral medication (ARV) administration, and available support services
- Scheduling maternal and pediatric appointments prior to discharge
- Informing parents or guardians of the rationale for serial HIV testing, the testing schedule recommended for their infant, how to access HIV testing at the recommended times, and how results will be interpreted and communicated
- Ensuring that parents or guardians are aware of the symptoms of acute HIV infection and how and when to access care if any of those symptoms occur in their infant
- Providing ARV medications (not just prescriptions) to the parent or guardian who accompanies an infant upon hospital discharge. Ideally, any necessary tools, such as an oral syringe, should be provided as well.
- Ensuring that the parents or guardians know how and when to obtain and administer the infant's ARV medications and potential adverse effects

Q: When should clinicians discuss infant feeding with a parent who has HIV?

A: The NYSDOH AI and the DHHS strongly encourage clinicians to engage pregnant patients with HIV in shared decision-making about infant feeding:

- As early as possible in pregnancy and throughout pregnancy
- After delivery
- Before hospital discharge
- At each postnatal visit. Assess the patient's feeding practices, identify barriers, and provide supports for the appropriate implementation of the patient's chosen method, including replacement feeding or formula feeding. See DHHS > Infant Feeding for Individuals With HIV in the United States.

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