Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Diagnosis of HIV Infection in Infants and Children (Last updated March 1, 2016; last reviewed March 1, 2016)

Panel's Recommendations

- Virologic assays that directly detect HIV must be used to diagnose HIV infection in children younger than 18 months with perinatal HIV exposure; HIV antibody tests should not be used **(AII)**.
- HIV RNA and HIV DNA nucleic acid tests are recommended as preferred virologic assays **(AII)**.
- Virologic diagnostic testing at birth should be considered for HIV-exposed infants at high risk of perinatal HIV transmission **(AIII)**.
- Virologic diagnostic testing is recommended for all infants with perinatal HIV exposure at the following ages:
  - 14 to 21 days **(AII)**
  - 1 to 2 months **(AII)** (preferably, 2 to 4 weeks after cessation of antiretroviral prophylaxis **[BIII]**)
  - 4 to 6 months **(AII)**.
- A positive virologic test should be confirmed as soon as possible by a repeat virologic test on a second specimen **(AII)**.
- Definitive exclusion of HIV infection in non-breastfed infants is based on 2 or more negative virologic tests, with 1 obtained at age ≥1 month and 1 at age ≥4 months, or 2 negative HIV antibody tests from separate specimens obtained at age ≥6 months **(AII)**.
- Some experts confirm the absence of HIV infection at 12 to 18 months of age in children with prior negative virologic tests by performing an antibody test to document loss of maternal HIV antibodies **(BIII)**.
- Children aged 18 to 24 months with perinatal HIV exposure may have residual maternal HIV antibodies; definitive exclusion or confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on a nucleic acid test (see Diagnostic Testing in Children with Perinatal HIV Exposure in Special Situations) **(AII)**.
- Diagnostic testing in children with non-perinatal exposure or children with perinatal exposure aged >24 months relies primarily on the use of HIV antibody (or antigen/antibody) tests; when acute HIV infection is suspected, additional testing with an HIV nucleic acid test may be necessary to diagnose HIV infection **(AII)**.

Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = One or more randomized trials in children† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion*

† Studies that include children or children/adolescents, but not studies limited to post-pubertal adolescents

Virologic Assays to Diagnose HIV Infection in Infants Younger than 18 Months with Perinatal HIV-1 Exposure

HIV infection can be definitively diagnosed through use of virologic assays in most non-breastfed HIV-exposed infants by age 1 to 2 months and in virtually all infected infants by age 4 months. HIV antibody tests, including newer tests, do not establish the presence of HIV infection in infants because of transplacental transfer of maternal antibodies to HIV; therefore, a virologic test should be used.[1,2] Positive virologic tests (i.e., nucleic acid tests [NAT]—a class of tests that includes HIV RNA and DNA polymerase chain reaction [PCR] assays, and related RNA qualitative or quantitative assays) indicate likely HIV infection. The first test result should be confirmed as soon as possible by a repeat virologic test on a second specimen because false-positive results can occur with both RNA and DNA assays.[3]

HIV culture is not used for routine HIV diagnostic testing.[4] Antigen/antibody combination immunoassays (fourth- and fifth-generation tests) which detect HIV-1/2 antibodies as well as HIV-1 p24 antigen are also not recommended for infant diagnosis in the United States because the sensitivity and specificity of the assay in

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the first months of life are less than that of HIV virologic tests.[5-7]

Infants who are found to have positive HIV antibody tests but whose mothers' HIV status is unknown (see Identification of Perinatal HIV Exposure) should be assumed to be HIV-exposed and undergo the HIV diagnostic testing described here[8] (see Infant Antiretroviral Prophylaxis in the Perinatal Guidelines for recommendations on infant antiretroviral [ARV] prophylaxis and management).

HIV RNA Assays

HIV quantitative RNA assays detect extracellular viral RNA in the plasma. Their specificity (for results ≥5,000 copies/mL) has been shown to be 100% at birth and at 1, 3, and 6 months of age and is comparable to HIV DNA PCR.[9] HIV RNA levels <5,000 copies/mL may not be reproducible and should be repeated before they are interpreted as documenting HIV infection in an infant. Testing at birth will detect infants who were infected *in utero* and not those who become infected from exposure during or immediately prior to delivery (i.e., in the intrapartum period). Studies have shown that HIV RNA assays identify 25% to 58% of infected infants from birth through the first week of life, 89% at age 1 month, and 90% to 100% by age 2 to 3 months (similar to results of HIV DNA PCR for early diagnosis of HIV).[3,8-10]

While HIV DNA PCR remains positive in most individuals receiving ARV treatment, HIV RNA assays could potentially be affected by maternal antenatal treatment or infant combination ARV prophylaxis.[11] In one study, the sensitivity of HIV RNA assays was not associated with the type of maternal or infant ARV prophylaxis, but HIV RNA levels at 1 month were significantly lower in infants receiving multidrug prophylaxis (n = 9) compared to levels among infected infants receiving single-drug zidovudine prophylaxis (n = 47) (median HIV RNA 2.5 log copies/mL vs. 5.4 log copies/mL, respectively). In contrast, the median HIV RNA levels were high (median HIV RNA 5.6 log copies/mL) by age 3 months in both groups after stopping prophylaxis.[9] Further studies are necessary to evaluate the sensitivity and predictive value of HIV RNA assays during and after receipt of infant ARV prophylaxis.

An HIV RNA assay can be used as the supplemental test for infants who have an initial positive HIV DNA PCR test. In addition to providing virologic confirmation of infection status, the expense of repeat HIV DNA PCR testing is spared and an HIV RNA measurement is available to assess baseline viral load. HIV RNA assays may be more sensitive than HIV DNA PCR for detecting HIV non-subtype B (see Virologic Assays to Diagnose Group M Non-Subtype B and Group O HIV-1 Infections).

The HIV qualitative RNA assay (APTIMA HIV-1 RNA Qualitative Assay) is an alternative diagnostic test that can be used for infant testing. It is the only qualitative RNA test that is Food and Drug Administration (FDA)-approved.[12-16]

HIV DNA Polymerase Chain Reaction

HIV DNA PCR is a sensitive technique used to detect specific HIV viral DNA in peripheral blood mononuclear cells. The specificity of the HIV DNA PCR is 99.8% at birth and 100% at ages 1, 3, and 6 months. Studies have shown that HIV DNA PCR assays identify 20% to 55% of infected infants from birth through the first week of life (with the same caveat as for RNA testing that testing at birth will detect infants infected *in utero* and not those infected during the intrapartum period) but increases to more than 90% by 2 to 4 weeks of age and to 100% at ages 3 months and 6 months.[8-10,15]

Two studies provide data on diagnostic testing at different time points in HIV-infected infants including those who had negative testing at birth (i.e., infants considered to be infected during the intrapartum period). A randomized, international study of 1,684 infants evaluated the efficacy of 3 different regimens of postpartum prophylaxis containing 6 weeks of zidovudine either alone or with 2 or 3 other ARVs; none of their mothers had received prenatal ARV drugs. Infant testing was performed at birth, 10 to 14 days, 4 to 6 weeks, and 3 and 6 months (no testing was performed between 6 weeks and 3 months). Ninety-three (66.4%) of 140 infected infants were identified at birth. Overall, by 4 to 6 weeks of age, 89% of 140 infected infants were identified. Of the 47 infected infants who had negative DNA PCR tests at birth, 68% were identified during the period of

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neonatal ARV prophylaxis at 4 to 6 weeks; by 3 months, all 47 infants were identified.[17] Another randomized trial comparing short and long maternal and infant zidovudine prophylaxis regimens in Thailand tested infants at 0 to 5 days, 6 weeks, 4 months, and 6 months. Although there was variability in the infant testing dates, this was independent of the treatment duration. Of the 45 confirmed infected infants who had negative testing in the first 5 days of life, diagnostic testing was positive at an earlier time point (median 10.5 days) when the mother received less than 7.5 weeks of zidovudine prior to delivery and the infant received only 3 days of prophylaxis compared with infected infants whose mother received longer zidovudine (>7.5 weeks) and/or who received longer infant prophylaxis (at least 4 weeks), where the median time to detection was 24.8 to 42.5 days.[18]

Although the AMPLICOR® HIV-1 DNA test has been widely used for diagnosis of infants born to HIV-1-infected mothers since it was introduced in 1992, it is no longer commercially available in the United States. The sensitivity and specificity of non-commercial HIV-1 DNA tests (using individual laboratory reagents) may differ from the sensitivity and specificity of the FDA-approved commercial test.

Other Issues

Virologic Assays to Diagnose Group M Non-Subtype B and Group O HIV-1 Infections

Although HIV-1 Group M subtype B is the predominant viral subtype found in the United States, multiple subtypes and recombinant forms are found in the United States with a widespread geographic distribution.[19] In an evaluation of perinatally infected infants diagnosed in New York State in 2001 and 2002, 16.7% of infants were infected with a non-subtype B strain of HIV, compared with 4.4% of infants born in 1998 and 1999.[20] In an analysis of 1,277 unique sequences collected in Rhode Island from 2004 to 2011, 8.3% were non-B subtypes (including recombinant forms). Twenty-two percent of non-B subtypes formed transmission clusters, including individuals with perinatally acquired infection.[21] In an analysis of 3,895 HIV-1 sequences collected between July 2011 and June 2012 in the United States, 5.3% were determined to be non-B subtypes (including recombinant forms). Among individual states, the percentage of non-B subtypes ranged from 0% (in 12 states) to 28.6% in South Dakota, with 7 states having greater than 10%.[22] Evolving immigration patterns may be contributing to local and regional increases in HIV-1 subtype diversity. Non-subtype B viruses predominate in other parts of the world, such as subtype C in regions of Africa and India and subtype CRF01 in much of Southeast Asia. Group O HIV strains are seen in West-Central Africa. Non-subtype B and Group O strains may also be seen in countries with links to these geographical regions.[23-26] Geographical distribution of HIV groups is available at http://www.hiv.lanl.gov/components/sequence/HIV/geo/geo.comp.

HIV DNA PCR tests have decreased sensitivity for detection of non-subtype B HIV, and false-negative HIV DNA PCR test results have been reported in infants infected with non-subtype B HIV.[27-29]

Currently available real-time HIV RNA PCR assays and the qualitative diagnostic RNA assay have improved sensitivity for detection of non-subtype B HIV infection and the more uncommon Group O strains, compared to older RNA assays that did not detect or properly quantify all non-B subtypes and Group O HIV[30-35] (see HIV RNA Monitoring in Children: General Considerations in Clinical and Laboratory Monitoring).

Thus, a real-time PCR assay or qualitative RNA assay should be used for infant testing when evaluating an infant born to a mother whose HIV infection is linked to an area endemic for non-subtype B HIV or Group O strains, such as Africa or Southeast Asia. Another indication is when the initial testing is negative using a HIV DNA PCR test and non-subtype B or Group O perinatal exposure is suspected. Two negative HIV antibody tests obtained at age ≥6 months provide further evidence to definitively rule out HIV infection. Clinicians should consult with an expert in pediatric HIV infection; state or local public health departments or the Centers for Disease Control and Prevention (CDC) may be able to assist in obtaining referrals for diagnostic testing.

Virologic Assays to Diagnose HIV-2 Infections

HIV-2 infection is endemic in Angola; Mozambique; West African countries including Cape Verde, Ivory Coast, Gambia, Guinea-Bissau, Mali, Mauritania, Nigeria, Sierra Leone, Benin, Burkina Faso, Ghana,

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Guinea, Liberia, Niger, Nigeria, Sao Tome, Senegal, and Togo; and parts of India.[36,37] It also occurs in countries such as France and Portugal, which have large numbers of immigrants from these regions;[38,39] HIV-1 and HIV-2 coinfections may also occur but are rare outside areas where HIV-2 is endemic. HIV-2 is rare in the United States. Although accurate diagnosis of HIV-2 can be problematic, it is clinically important because HIV-2 strains are naturally resistant to several ARV drugs developed to suppress HIV-1.[40,41]

Infant testing with HIV-2-specific DNA PCR tests should be performed at time points similar to those used for HIV-1 testing when evaluating an infant born to a mother with a known or suspected HIV-2 infection. A mother should be suspected of being HIV-2 infected if her infection is linked to an area endemic for HIV-2 infection or if her HIV testing results are suggestive of HIV-2 infection (i.e., HIV-1 antibody-positive on an initial immunoassay test, repeatedly indeterminate results on HIV-1 Western blot, and HIV-1 RNA viral loads at or below the limit of detection).[42,43] HIV-2 DNA PCR testing can be arranged by the HIV surveillance program of the state or local health department through their public health laboratory or the CDC since this assay is not commercially available.[44-46] Clinicians should consult with an expert in pediatric HIV infection when caring for infants with suspected or known exposure to HIV-2.[36,47]

Timing of Diagnostic Testing in Infants with Perinatal HIV Exposure

Virologic diagnostic testing should be considered at birth for HIV-exposed infants at high risk of perinatal HIV transmission. Virologic diagnostic testing should be performed for all HIV-exposed infants at age 14 to 21 days, at age 1 to 2 months (preferably 2 to 4 weeks after cessation of ARV prophylaxis), and at age 4 to 6 months.

Confirmation of HIV infection should be based on 2 positive virologic tests from separate blood samples in children younger than 18 months. Children with perinatal HIV exposure aged 18 to 24 months may have residual maternal HIV antibodies; definitive confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on a NAT (see Diagnostic Testing in Children with Perinatal HIV Exposure in Special Situations). Diagnosis in children aged >24 months relies primarily on HIV antibody and antigen/antibody tests (see Diagnostic Testing in Children with Non-Perinatal HIV Exposure or Children with Perinatal Exposure Aged >24 Months).[1]

HIV infection can be **presumptively** excluded in non-breastfed infants with two or more negative virologic tests (one at age ≥14 days and one at age ≥4 weeks) or one negative virologic test (i.e., negative NAT [RNA or DNA]) test at age ≥8 weeks, or one negative HIV antibody test at age ≥6 months.[1,8] *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis is recommended for infants with indeterminate HIV infection status starting at age 4 to 6 weeks until they are determined to be HIV-uninfected or **presumptively** uninfected.[48] Thus, initiation of PCP prophylaxis can be avoided or discontinued if HIV infection is presumptively excluded.

Definitive exclusion of HIV infection in a non-breastfed infant is based on 2 or more negative virologic tests (i.e., negative NATs [RNA or DNA]), one at age ≥1 month and one at age ≥4 months, or 2 negative HIV antibody tests from separate specimens obtained at age ≥6 months.

For both **presumptive** and **definitive** exclusion of HIV infection, a child must have no other laboratory (i.e., no positive virologic test results or low CD4 T lymphocyte (CD4) cell count/percent) or clinical evidence of HIV infection and not be breastfeeding. Many experts confirm the absence of HIV infection in infants with negative virologic tests by performing an antibody test at age 12 to 18 months to document seroreversion to HIV antibody-negative status.

Virologic Testing at Birth (Optional)

Virologic testing at birth should be considered for newborns at high risk of perinatal HIV transmission, such as infants born to HIV-infected mothers who did not receive prenatal care or prenatal ARVs, were diagnosed with acute HIV infection during pregnancy, or who had HIV viral loads >1,000 copies/mL close to the time of delivery.[49-53] In one study, 66.4% of infected infants whose mothers had not received prenatal ARVs were identified at birth.[17] Prompt diagnosis is critical to allow for discontinuing ARV prophylaxis and instituting early ARV therapy (see When to Initiate Therapy). Blood samples from the umbilical cord should not be used

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for diagnostic evaluations because of the potential for contamination with maternal blood. Working definitions have been proposed to differentiate acquisition of HIV infection *in utero* from the intrapartum period. Infants who have a positive virologic test at or before age 48 hours are considered to have early (i.e., intrauterine) infection, whereas infants who have a negative virologic test during the first week of life and subsequent positive tests are considered to have late (i.e., intrapartum) infection.[15,49,50]

Virologic Testing at Age 14 to 21 Days

The diagnostic sensitivity of virologic testing increases rapidly by age 2 weeks,[8] and early identification of infection would permit discontinuation of neonatal ARV prophylaxis and initiation of ARV therapy (see Infants Younger than Age 12 Months and Table 5 in When to Initiate Therapy).

Virologic Testing at Age 1 to 2 Months

Virologic diagnostic testing should be considered 2 to 4 weeks after cessation of ARV prophylaxis. In such situations, the test would be obtained at 6 weeks (in the case of 4 weeks of neonatal ARV prophylaxis) or at 2 months (in the case of 6 weeks of prophylaxis) (see Infant Antiretroviral Prophylaxis in the Perinatal Guidelines).[54,55] Although the use of antepartum, intrapartum, and neonatal zidovudine single-drug prophylaxis did not delay detection of HIV by culture in infants in Pediatric AIDS Clinical Trials Group protocol 076 or affect the sensitivity and predictive values of many virologic assays,[8] this may not always apply to current prenatal and neonatal ARV regimens if the test is obtained while the infant is receiving neonatal ARV prophylaxis.[9]

Testing performed at this age is intended to maximize the detection of HIV-infected infants.[9,56] Two studies found that although the sensitivity during prophylaxis was not associated with the type of maternal or neonatal ARV prophylaxis, the sensitivity of diagnostic HIV testing during the period of infant ARV prophylaxis was lower compared to the sensitivity during the subsequent testing interval at 3 months of age. Overall, in both studies, 89% of infected infants were identified by 4 to 6 weeks of age. Of those infants who had negative testing in the first 7 days of life, repeat testing at 4 weeks to 6 weeks of age during the period of neonatal ARV prophylaxis identified 76% of infected infants in one study,[9] and 68% of infected infants in the second study.[17] In both studies, infants with negative testing in the first 7 days of life were diagnosed when the next diagnostic test was performed at 3 months of age.

An infant with 2 negative virologic tests—1 at age ≥14 days and 1 at age ≥4 weeks—or one negative test at age ≥8 weeks can be viewed as **presumptively** uninfected and will not need PCP prophylaxis, assuming the child has not had a positive virologic test, CD4 immunosuppression, or clinical evidence of HIV infection.

Virologic Testing at Age 4 to 6 Months

HIV-exposed children who have had negative virologic assays at age 14 to 21 days and at age 1 to 2 months, have no clinical evidence of HIV infection, and are not breastfed should be retested at age 4 to 6 months for **definitive** exclusion of HIV infection.

Antibody Testing at Age 6 Months and Older

Two or more negative HIV antibody tests performed in non-breastfed infants at age ≥6 months can also be used to **definitively** exclude HIV infection in HIV-exposed children with no clinical or virologic laboratory documented evidence of HIV infection.[57]

Antibody Testing at Age 12 to 18 Months to Document Seroreversion

Some experts confirm the absence of HIV infection in infants with negative virologic tests (when there has not been prior confirmation of two negative antibody tests) by repeat serologic testing between 12 and 18 months of age to confirm that maternal HIV antibodies transferred *in utero* have disappeared.[1] In a recent study, the median age at seroreversion was 13.9 months.[58] Although the majority of HIV-uninfected infants will serorevert by age 15 to 18 months, there are reports of late seroreversion after 18 months (see below). Factors that might influence the time to seroreversion include maternal disease stage and assay sensitivity.[58-61]

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Diagnostic Testing in Children with Perinatal HIV Exposure in Special Situations

Late Seroreversion (≤24 Months)

Non-breastfed, perinatally HIV-exposed infants with no other HIV transmission risk and no clinical or virologic laboratory evidence of HIV infection may have residual HIV antibodies up to age 24 months (these infants are called late seroreverters).[58-61] In one study, 14% seroreverted after age 18 months.[58] These children may have positive immunoassay results but indeterminate supplemental antibody tests (using Western blot or IFA). In such cases, repeat antibody testing at a later time would document seroreversion. Due to the possibility of residual HIV antibodies, virologic testing (i.e., with a NAT) will be necessary to definitively exclude or confirm HIV infection in children with perinatal HIV exposure at age 18 to 24 months in situations such as lack of prior testing history or clinical suspicion of HIV infection.

Postnatal HIV Infection in HIV-Exposed Children with Prior Negative Virologic Tests for Whom There Are Additional HIV Transmission Risks

In contrast to late seroreverters, in rare situations postnatal HIV infections have been reported in HIV-exposed infants who had prior negative HIV virologic tests. This occurs in infants who become infected through an additional risk after completion of testing (see Diagnostic Testing in Children with Non-Perinatal HIV Exposure or Children with Perinatal Exposure Aged >24 Months). If an HIV antibody test is positive at age 18 to 24 months, repeated virologic testing will distinguish between residual antibodies in uninfected, late-seroreverting children and true infection.

Suspicion of HIV-2 or Non-Subtype B HIV-1 Infections with False-Negative Virologic Test Results

Children with non-subtype B HIV-1 infection and children with HIV-2 infection may have false-negative virologic tests but persistent positive immunoassay results and indeterminate HIV-1 Western blot results.[27-29] The diagnostic approach in these situations is discussed above in the sections in Virologic Assays to Diagnose Group M Non-Subtype B and Group O HIV-1 Infections and in Virologic Assays to Diagnose HIV-2 Infections.

Diagnostic Testing in Children with Non-Perinatal HIV Exposure or Children with Perinatal Exposure Aged >24 Months

Breastfeeding is a known route of postnatal HIV transmission. Typical scenarios in the United States include women who have not been adequately counseled about infant feeding, women who breastfeed despite being counseled not to do so (e.g., among women from communities in which breastfeeding is the norm, women who fear that not breastfeeding would be a stigma, women who fear that not breastfeeding would raise suspicion about the possibility of HIV infection), and women who learn of their HIV diagnosis only after initiating breastfeeding (e.g., women who were HIV negative during pregnancy but who acquire HIV infection postnatally; breastfeeding during acute HIV infection is associated with an increased risk of perinatal HIV transmission).[62-65] Donor breast milk from an unscreened HIV-infected donor is an additional potential risk factor. Infants who are breastfed by HIV-infected women should undergo immediate HIV diagnostic testing, and counseling to cease breastfeeding should be provided. Follow-up, age-appropriate testing should be performed at 4 to 6 weeks, 3 months, and 6 months after breastfeeding cessation if the initial tests are negative. Diagnostic testing to rule out acquisition of HIV through breast milk will only be accurate after breastfeeding has completely ceased. Factors to consider in the choice of diagnostic tests in breastfed children include the transplacental transfer of maternal antibody resulting in residual antibody in children aged up to 24 months (women who acquired HIV infection before delivery), the potential transfer of maternal antibody from breast milk as well as the possibility of performing the testing during acute HIV infection; thus, a NAT would be the choice for initial test (see Infant Antiretroviral Prophylaxis in the Perinatal Guidelines).[66,67]

Receipt of solid food premasticated or prechewed by an HIV-infected caregiver has been documented to be associated with risk of HIV transmission.[68-73] If this occurs in perinatally HIV-exposed infants 24 months or younger with prior negative virologic tests, it will be necessary for such children to undergo virologic

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diagnostic testing, as they may have residual maternal HIV antibody (see Diagnostic Testing in Children with Perinatal HIV Exposure in Special Situations).

Additional routes of HIV transmission in children include sexual abuse or receipt of contaminated blood products (which could occur in countries in which the administration of contaminated blood products is a possibility). In such cases, maternal HIV status may be negative. If the maternal HIV status is unknown, age-appropriate testing should be performed as described for children with perinatal HIV exposure.

Acquisition of HIV is possible through accidental needlesticks, sexual transmission, or injection drug use in older children. Medical procedures performed in settings with inadequate infection control practices may pose a potential risk; although tattooing or body piercing presents a potential risk of HIV transmission, no cases of HIV transmission from these activities have been documented.[74]

Diagnosis of HIV-1 infection in children with non-perinatal exposure or children with perinatal exposure aged >24 months relies primarily on HIV antibody and antigen/antibody tests.[1] FDA-approved diagnostic tests include:

- Antigen/antibody combination immunoassays detect HIV-1/2 antibodies as well as HIV-1 p24 antigen (fourth and fifth generation tests [the fifth generation test, Bio-Rad BioPlex 2200 HIV, differentiates between HIV-1 and HIV-2 antibodies as well as HIV-1 p24 antigen]): Recommended for initial testing to screen for established infection with HIV-1 or HIV-2 and for acute HIV-1 infection.
- HIV-1/2 immunoassays (third-generation antibody tests): Alternative for initial testing.
- HIV-1/HIV-2 antibody differentiation immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies (Multispot HIV-1/HIV-2 test or Geenius™ HIV 1/2 Supplemental Assay): Recommended for supplemental testing.
- HIV-1 NAT (HIV qualitative RNA assay) may be necessary as an additional test to diagnose acute HIV infection.
- HIV-1 Western blot and HIV-1 indirect IFAs (first-generation tests): Alternative for supplemental testing but will not detect acute HIV infection.

Diagnosis of HIV-2 in children with non-perinatal exposure or children with perinatal exposure aged >24 months relies on the CDC/APHL 2014 Laboratory testing guidelines that recommend using an HIV-1/HIV-2 antibody differentiation immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies (Multispot HIV-1/HIV-2 test or Geenius™ HIV 1/2 Supplemental Assay) for supplemental testing. This is not subject to the same testing ambiguity as when the HIV-1 Western blot is used as a supplemental test; more than 60% of individuals with HIV-2 infection are misclassified as having HIV-1 by the HIV-1 Western blot.[1,75] All HIV-2 cases should be reported to the HIV surveillance program of the state or local health department; additional HIV-2 DNA PCR testing can be arranged by their public health laboratory or the CDC if an HIV-1/HIV-2 antibody differentiation immunoassay is not conclusive; HIV-2 DNA PCR testing may be necessary for definitive diagnosis (this assay is not commercially available).[44-46]

The National Clinical Consultation Center provides consultations on issues related to the management of perinatal HIV infection (1-888-448-8765; 24 hours a day, 7 days a week).

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