HIV in Infants and Children

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Module 6: Key Populations
Lesson 1: HIV in Infants and Children

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Background

The first reports of HIV in children in the United States emerged in December 1982, when the Centers for Disease Control (CDC) described four children under the age of 2 years who had unexplained immunodeficiency and opportunistic infections.[1] Several subsequent published reports described young children with AIDS.[2,3,4] In 1994, the Pediatric AIDS Clinical Trials Group (PACTG) 076 trial reported a three-part zidovudine regimen reduced perinatal HIV transmission by 67.5% when compared with placebo.[5] In the United States, due to the widespread implementation of highly effective measures to prevent perinatal HIV transmission, the number of children born with HIV has dramatically declined from a peak of more than 1,700 babies born with HIV per year in the early 1990s to fewer than 70 per year in recent years (Figure 1).[6,7,8,9,10]

Unique Aspects of Pediatric HIV

Clinicians who provide care for infants and children with HIV should be aware of the unique characteristics of these populations, integrate age-specific primary care measures with HIV management, and be sensitive to the social and developmental aspects involved in the care of young people with HIV. Although most principles and concepts related to the diagnosis and management of HIV are similar in adults and children, the following summarizes some key aspects of pediatric HIV care:

- Diagnosing HIV in a newborn is confounded by the transfer of maternal anti-HIV antibodies to the baby.
- Interpretation of CD4 cell count values in children requires adjustment based on age-specific criteria.
- Urgent initiation of antiretroviral therapy is indicated for infants and young children with HIV as they are at risk for rapid disease progression and death.
- Antiretroviral medications have age-specific approvals with different dosing requirements.
- Children present special challenges in terms of adherence to antiretroviral therapy.

This Core Concept will focus on the diagnosis and management of HIV in infants and children through age 12 years of age. The topics of Preventing Perinatal HIV Transmission and HIV in Adolescents and Young Adults are addressed in separate Topic Reviews.

Epidemiology of HIV in Children Younger than Age 13

Almost all children younger than 13 years of age with HIV in the United States have acquired HIV via perinatal transmission.[10,11] The following summarizes key epidemiologic features of children younger than 13 years of age in the United States (Figure 3).[10]

- At year-end 2022, in the United States, 1,124 children younger than age 13 were living with diagnosed HIV, which was approximately 0.1% of all persons living with diagnosed HIV.[10]
- In recent years, the number of children younger than age 13 living with diagnosed HIV in the United States has declined steadily.[10]
- Black children are disproportionately affected—at year-end 2022 among children younger than 13 years of age living with diagnosed HIV, 56% (629 of 1,124) were Black children.[10]

Staging of Pediatric HIV Disease

Staging

In the 2014 case definition, which provides real-time assessment, stage 0 indicates early HIV, inferred from a negative or indeterminate HIV test result within 6 months prior to a confirmed positive result.[12] Stages 1, 2, and 3 are determined based on the CD4 count, stratified by age (Table 1).[12] The presence of an AIDS-defining (stage 3) opportunistic infection confers a stage 3 diagnosis regardless of the CD4 cell count or percentage. The absolute CD4 count takes precedence over the CD4 percentage, even in children, and the percentage is only considered if the corresponding CD4 count is unknown.[12] In children with laboratory-confirmed HIV, stage 3 (AIDS) is defined based on laboratory criteria (CD4 cell count) or clinical conditions. The list of AIDS-defining clinical conditions is extensive.[12,13]

Clinical Criteria for HIV Diagnosis

According to the 2014 case definition, clinical criteria for a confirmed case of HIV are met when there is a note in a medical record by a physician or other qualified medical provider stating that the patient has HIV, followed by either laboratory criteria meeting the case definition, presumptive evidence of HIV infection (e.g., receipt of HIV antiretroviral therapy or prophylaxis for an opportunistic infection), an otherwise unexplained low CD4 count, or an otherwise unexplained diagnosis of an opportunistic illness.[12]

Diagnosis of HIV in Infants and Children

Recommended Diagnostic Tests

The greatest diagnostic challenges in young children occur with infants born to mothers with HIV. The diagnosis of HIV should be made as soon as possible in an infant exposed to HIV.[14] Note that, due to concerns for contamination with maternal blood, blood samples from the umbilical cord should not be used for diagnostic evaluation for HIV at birth. The following summarizes the tests to be utilized in the diagnosis of HIV in infants.[14]

- **Virologic Assays**: The diagnosis of HIV among infants and children younger than 18 months who are born to mothers with HIV is best made with the use of virologic assays (HIV nucleic acid testing [NAT]) that directly detect HIV RNA or HIV DNA.[14] The HIV RNA assays detect extracellular HIV RNA in plasma and the HIV DNA assays detect intracellular HIV DNA in peripheral blood mononuclear cells. Since false-positive tests can occur with both HIV DNA and RNA assays, a repeat HIV NAT should be done to verify the initial positive test.[14]
- **HIV Antigen-Antibody / p24 Antigen / HIV Antibody Tests**: The use of HIV-1/2 antigen-antibody immunoassays (or the HIV p24 antigen test alone) is not recommended for infants in the setting of perinatal HIV exposure because of the lower sensitivity of the p24 antigen test in the first months of life when compared with virologic tests, such as HIV nucleic acid testing.[14,15] In addition, HIV antibody testing in newborns is problematic due to maternal anti-HIV antibodies that persist in the infant's blood for 15–18 months. Serologic HIV-1/2 antigen-antibody immunoassay testing can be used for HIV diagnosis in infants and children with non-perinatal HIV exposure or for perinatally-exposed children older than 24 months of age.

Determining HIV Risk Status of Infants Born to Mothers with HIV

For infants born to mothers with HIV, the recommended HIV diagnostic evaluation varies based on the estimated perinatal HIV transmission risk. The Pediatric ART Guidelines identify two levels of HIV acquisition risk for infants: low risk and high risk.[14]

- ***Low Risk***: Infants born to mothers who—
    - Received antiretroviral therapy during pregnancy,
    - Had sustained suppression of HIV RNA levels (usually defined as less than 50 copies/mL), *and*
    - Were adherent to their antiretroviral regimen
- ***High Risk*:** Infants born to mothers who—
    - Did not receive prenatal care,
    - Received no antepartum antiretroviral therapy or only intrapartum antiretroviral therapy,
    - Initiated antiretroviral therapy 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 antiretroviral therapy but did not achieve sustained viral suppression.

HIV Testing Schedule of Infants Born to Mothers with HIV

The following summarizes Pediatric ART Guidelines for HIV testing of infants based on whether the infant is considered to be low-risk or high-risk for acquiring HIV, including HIV testing for infants who are

breastfeeding (Figure 2).[14]

- **Recommended Testing Schedule for Infants at Low Risk**: Infants considered at low risk of perinatal transmission should have HIV virologic testing (HIV NAT) done at 3 time points after birth: 14 to 21 days, 1 to 2 months, and 4 to 6 months.[14]
- **Recommended Testing Schedule for Infants at High Risk**: In general, HIV virologic testing (HIV NAT) Infants at high risk of perinatal HIV transmission should have HIV virologic testing (HIV NAT) done just after birth prior to initiating antiretroviral therapy and at the following additional ages after birth: 14 to 21 days, 1 to 2 months, 2 to 3 months, and 4 to 6 months. Virologic testing (HIV NAT) is also indicated 2 to 6 weeks after cessation of antiretroviral prophylaxis, which usually corresponds with the recommended testing at 2–3 months after birth.[14,16] The rationale for the extra testing 2 to 6 weeks after cessation of antiretroviral prophylaxis is that combination antiretroviral prophylaxis in infants exposed to HIV may diminish the sensitivity of diagnostic virologic assays normally performed at age 1 to 2 months.[14,16]
- **Testing for Infants and Mothers Druing Breastfeeding**: For mothers with HIV who are breastfeeding, virologic testing of the infant should be done at birth, 14 to 21 days, 1 to 2 months, and 4 to 6 months of age.[14] In the event that a gap of longer than 3 months occurs between the testing at 1 to 2 months and 4 to 6 months, then one additional virologic test should be performed.[14] If breastfeeding continues beyond 6 months of age, virologic testing of the infant should be done at least every 3 months during breastfeeding.
    - In addition, the breastfeeding mother should have HIV RNA testing every 1 to 2 months during breastfeeding.[17] At any point, if there is a detectable maternal HIV RNA level, expert consultation should be obtained, and prompt testing of the infant with an HIV NAT should be performed.[17]
    - If a person with a detectable HIV viral load continues to breastfeed, some experts recommend infant testing monthly for early detection of HIV in the setting of ongoing exposure.[17] Following cessation of breastfeeding, regardless of the child's age, virologic tests should be performed 4 to 6 weeks, 3 months, and 6 months post-cessation.[14,17]

Confirmatory Testing

Any infant with a positive virologic assay should have a confirmatory test performed as soon as possible after the initial positive test result. In children 24 months of age or older, the diagnosis of HIV can also be confirmed with an HIV-1/2 antigen-antibody immunoassay testing.[14,16]

Exclusion of HIV Diagnosis

The diagnosis of HIV can be excluded in a non-breastfed infant with:[14,16]

- Two negative virologic tests: one test at age 1 month or older (and at least 2 to 6 weeks after discontinuation of multi-drug antiretroviral prophylaxis) and a negative test at age 4 months or older, *or*
- Two negative HIV antibody tests from separate specimens obtained at age 6 months or later

HIV Testing of Children Born to Mothers with Unknown HIV Status

Newborn infants or children whose maternal HIV status is not known, such as those in foster care or adoptees, should be promptly tested for HIV using age-appropriate diagnostic testing.[18]

Children Older than 24 Months or with Non-Perinatal HIV Exposure

For children with non-perinatal exposure to HIV or children with perinatal HIV exposure who are older than 24 months of age, the diagnostic testing approach should be the same as used to diagnose HIV in adolescents and young adults. This approach should utilize the approach outlined in the CDC/APHL HIV Laboratory Testing

Guidelines.[11] The initial screening test consists of an HIV-1/2 antigen-antibody combination Immunoassay; positive screening tests should be followed by testing with an HIV-1/2 antibody differentiation immunoassay.[11] A positive screening test followed by a negative differentiation test warrants further testing with an HIV RNA assay.[11] For more details on HIV diagnostic testing in adolescents and adults, see Lesson HIV Diagnostic Testing in Module 1.

Clinical and Laboratory Monitoring

Baseline Evaluation

At entry to care, children with HIV should have a complete medical history, physical examination, and laboratory evaluation.[19] This history should include a detailed social history component (including immunizations, nutrition, physical and social/emotional environment) and evaluation for HIV-specific physical problems (e.g., growth delay, motor or cognitive neurological problems). Youth with perinatal acquisition of HIV appear to be particularly vulnerable to cognitive problems, especially in the executive function domain.[20,21,22] Baseline laboratory evaluation for all children diagnosed with HIV at entry into care should include the following:[19]

- **HIV-Specific Laboratory Studies**
  - HIV RNA level
  - CD4 cell count
  - HIV drug-resistance testing (genotype assay)
  - HLA-B*5701 test (if abacavir is being considered as part of the initial antiretroviral therapy regimen)
- **Screening for HIV-Associated Condition**s
  - Complete blood count
  - Serum creatinine
  - Serum glucose
  - Hepatic aminotransferase levels
  - Serum albumin
  - Urinalysis
- **Screening for Coinfections and Opportunistic Infections**
  - Hepatitis B virus (HBV), with HBV surface antigen, HBV surface antibody, and HBV core antibody
  - Hepatitis C virus (HCV), (using HCV RNA for children younger than 18 months of age and HCV antibody for children 18 months of age and older)
  - Cytomegalovirus antibody (for children older than 12 months of age)
  - Screening for tuberculosis infection (using a tuberculin skin test for children younger than 2 years of age and interferon-gamma release assay (IGRA) for children 2 years of age and older
- **Screening Children with HIV who Relocate to the United States from Other Countries**
  - Consider obtaining thyroid function tests, lead levels, and screening for gastrointestinal parasites.

Routine Monitoring

In general, all children living with HIV should undergo regular evaluation for growth and development, as well as for clinical signs and symptoms. At each visit, the medical provider should address the efficacy, safety and tolerability of the antiretroviral regimen as well as assess adherence. These visits can be in-person or using telehealth communication platforms at the provider's discretion and based on the comfort level of the child and guardian.[19]

- **Children Not Taking Antiretroviral Therapy**: For children who are not receiving antiretroviral therapy, absolute CD4 cell count and HIV RNA should be monitored every 3 to 4 months, regardless of whether they have HIV-related symptoms.[19]
- **Monitoring of Children after Initiating or Changing Antiretroviral Therapy**: After initiating or changing antiretroviral therapy, children should have an evaluation after 1 to 2 weeks and again after 2 to 4 weeks. Both of these evaluations should include a medical history, physical examination, and evaluation for medication adherence, mental health assessment and care coordination of multidisciplinary services, such as nutrition counseling and case management.[19] The 2- to 4-week

visit should include testing for an HIV RNA level and laboratory testing that varies depending on the antiretroviral regimen.[19]

- **Long-Term Monitoring of Children on Antiretroviral Therapy**: The long-term monitoring of children maintained on antiretroviral therapy should typically occur every 3 to 4 months and include the following: HIV RNA level, absolute CD4 cell count, chemistries, complete blood count with differential, medication toxicity, and adherence assessment, and antiretroviral medication dosage adjustment for growth and weight if needed.[19] Urinalysis, lipid panel, and random plasma glucose should be obtained every 6 to 12 months.[19] Monitoring of CD4 cell count and laboratory studies to detect antiretroviral medication toxicity can be done less frequently (every 6 to 12 months) in children who have been clinically stable for at least 2 years and (1) are adherent on a stable antiretroviral therapy regimen, (2) have sustained virologic suppression, with HIV RNA levels less than 50 copies/mL, and (3) have a CD4 count above the threshold for opportunistic infection risk.[19] In contrast, HIV RNA monitoring should continue to be performed every 3-4 months in order to assess adherence to the antiretroviral regimen.[19]
- **Type of Immunologic Monitoring**: The use of absolute CD4 cell count is preferred for monitoring the immunologic status of children. For children younger than 5 years of age, monitoring CD4 percentage is an acceptable alternative.[19] The risk of disease progression associated with a specific CD4 count or percentage varies with the age of the patient, with younger children (less than 1 year of age) experiencing a higher risk of progression and death.[23,24]
- **Children with Suspected Virologic, Immunologic, and/or Clinical Deterioration**: Evaluation of children with suspected virologic, immunologic, and/or clinical deterioration should ideally include expert consultation and, in the setting of virologic failure, undergo adherence assessment and HIV drug resistance testing.[19]

Interpreting Immunologic and Virologic Parameters in Children

When interpreting immunologic laboratory parameters in children with HIV, age is a crucial determinant because of widely variable age-appropriate norms for absolute CD4 count and CD4 percentage. Young children typically have CD4 counts that are much higher than those seen in adults. For example, among children younger than 12 months of age who do not have any immunologic deficiency, most will have a CD4 count of at least 1,500 cells/mm^3. The normal CD4 count declines during the first few years of life. Conceptually, it is very important to understand that children with HIV, especially very young children, can develop HIV-related opportunistic infections at significantly higher CD4 cell counts than adults who develop HIV-related opportunistic infections.[25] In addition, HIV RNA values are also typically higher in very young children who acquire HIV perinatally than in adolescents and adults. Although high HIV RNA levels correlate with more rapid disease progression in adults, the predictive value for HIV RNA concentration in a specific child is only moderate; the range of HIV RNA values overlaps in young children who experience rapid disease progression and those who do not.[19]

Antiretroviral Treatment for Children with HIV

Principles of Antiretroviral Therapy in Children

Antiretroviral therapy has been shown to significantly reduce morbidity, mortality, and hospitalizations among children with HIV in the United States.[26,27,28,29] A large clinical trial that randomized infants 6 to 12 weeks of age with HIV to receive early antiretroviral therapy versus deferred therapy (based on CD4-related criteria) found a 75% reduction in mortality when using the more aggressive policy of early treatment of infants.[29] Studies in children have demonstrated benefits from earlier initiation of antiretroviral therapy at higher CD4 counts, including improved immune response, reduction in proviral reservoirs, and more rapid growth reconstitution.[29,30,31,32,33] Similar to adults, ongoing viral replication in children is believed to cause a persistent inflammatory state that increases the risk of developing non-AIDS complications, such as renal disease, cancer, liver disease, and cardiovascular disease.[34,35] Several studies have shown that initiating antiretroviral therapy is associated with decreased systemic inflammation, lower risk of cardiomyopathy, and improved neurocognitive outcomes.[36,37,38]

When to Start Antiretroviral Therapy

The Pediatric ART Guidelines recommend rapid initiation of combination antiretroviral treatment for all children diagnosed with HIV, regardless of age, CD4 count, or HIV RNA level.[39] Exceptions include a diagnosis of cryptococcal meningitis, tuberculosis meningitis, or disseminated *Mycobacterium avium* complex; with any of these diagnoses, initiation of treatment for the opportunistic infection should occur first before starting antiretroviral therapy—in order to reduce the risk of immune reconstitution inflammatory syndrome (IRIS).[39] Consulting a pediatric HIV specialist is recommended in such clinical scenarios to determine the exact timing of starting the antiretroviral therapy.[39] For infants younger than 12 months of age who are diagnosed with HIV, urgent initiation of antiretroviral therapy is critical since they have the greatest risk of accelerated HIV disease progression, clinical illness, and death.[39] For older asymptomatic children who are diagnosed with HIV, the data regarding the risks and benefits of immediate antiretroviral therapy are more limited.

Antiretroviral Regimens for Initial Therapy

The antiretroviral therapy regimens recommended for initial therapy in the Pediatric ART Guidelines are based on the child's age, including gestational age and weight.[40] In general, antiretroviral therapy should be initiated with a 3-drug regimen consisting of a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone plus an integrase strand transfer inhibitor (INSTI) anchor drug, when possible.[40]

Age: Birth to 30 Days

The following table summarizes the preferred and alternative regimens recommended for initial therapy in infants from birth up to age 30 days.[40] Although abacavir is presently not FDA-approved for use in infants younger than 3 months of age, it can be considered for use in newborns if zidovudine is not available or the infant has zidovudine-associated toxicity (Table 2).[40]

Age: 30 Days to 2 Years

The following table summarizes the preferred and alternative regimens recommended for initial therapy in children older than age 30 days and younger than age 2 years.[40] Note that no tenofovir medications are used for children younger than 2 years of age. (Table 3).[40]

Age: 2 Years to 12 Years

The following table summarizes the preferred and alternative regimens recommended for initial therapy in

children 2 years of age and older up to 12 years of age.[40] Note that none of the preferred 2-NRTI backbones in children up to 12 years of age include tenofovir DF due to concerns about bone toxicity and disruption of vitamin D metabolism, especially since children with perinatally-acquired HIV already have reduced bone mineral density.[40,41,42,43] Since tenofovir alafenamide is associated with less bone and renal toxicity than tenofovir DF, tenofovir alafenamide is now included in preferred regimens for children 2-12 years of age (Table 4).[40]

Factors to Consider when Choosing Antiretroviral Regimen

For many of the approved antiretroviral agents, the FDA has stipulated specific age or weight restrictions based on limited available data in pediatric populations. The Pediatric ART Guidelines maintain an excellent compendium of pediatric antiretroviral drug information that includes an overview of the FDA approval status of the antiretroviral medications in children, specific formulations, drug interactions, toxicities, and dosing recommendations in different aged children.[44] The following factors should be considered when selecting an optimal HIV treatment regimen for children:[40]

- Age and weight
- Potential for acquired antiretroviral drug resistance
- Frequency of dosing
- Available formulations of drugs
- Medication preparation and administration requirements
- Potential drug interactions
- Palatability and tolerance
- Medication toxicities
- Contraindications
- Co-morbidities potentially impacting antiretroviral choices
- Ability of the patient to swallow medications
- Medication availability, cost, and coverage by insurance

Adherence with Antiretroviral Therapy

Difficulties with antiretroviral therapy adherence reduces the likelihood of virologic suppression, increases the risk of developing drug resistance mutations and virologic failure, limits future treatment options, and can lead to both disease progression and secondary transmission. Children with HIV may struggle with adherence due to complex dosing regimens, age-appropriate behaviors, dependency on an adult caregiver to reliably provide therapy, and social issues within the family unit, such as substance use or homelessness.[45] To improve adherence, the Pediatric ART Guidelines recommend using antiretroviral regimens with reduced pill burden and once-daily dosing frequency whenever feasible. Strategies to optimize adherence are organized into three categories: (1) initial intervention strategies, (2) medication strategies, and (3) follow-up intervention strategies.[46] To promote adherence, the Pediatric ART Guidelines recommend regular viral load monitoring and at least one other measure of medication adherence (Table 5).[46]

Management of Antiretroviral Toxicity

Children taking lifelong antiretroviral therapy need to be monitored for both acute and chronic adverse effects, which can potentially involve different organ systems.[47,48,49] This is particularly important as new antiretroviral treatment options become available that do not have a long track record of pediatric use. The Pediatric ART Guidelines have compiled reference tables of potential adverse effects associated with different antiretroviral agents, and these guidelines provide detailed summaries for different types of adverse effects.[49] The implications of long-term exposure (from infancy or childhood) to antiretroviral medications remain an area of active study, and it is unclear whether life expectancy will be altered in individuals who survive into adulthood with perinatally-acquired HIV.[42]

Immunizations for Children with HIV

Immunization Guideline Resources

The Advisory Committee for Immunization Practices (ACIP) publishes annual guidelines for the use of vaccines for all children and adolescents, including specific recommendations for vaccines based on medical conditions.[50,51,52]

Immunization Recommendations for Children with HIV

All inactivated vaccines are safe to administer to children with HIV, irrespective of their immune status. Accordingly, all infants and children with HIV should receive inactivated vaccines per standard recommended pediatric schedules. Children with HIV may also need to receive additional vaccinations if the vaccines were not administered in infancy.[51,52] For routine immunization recommendations for children with HIV, see the most recent guidance from the Advisory Committee on Immunization Practices and the American Academy of Pediatrics.[52,53]

Use of Live Vaccines in Children with HIV

The ACIP defines high-level immunosuppression for children aged 18 years or younger as a CD4 percentage less than 15 or an absolute CD4 count less than 200 cells/mm^3.[52]

- **Live Influenza Virus Vaccine**: The live attenuated influenza vaccine is not recommended for children and adolescents with HIV, regardless of CD4 cell count or percentage.[52]
- **Live Measles Mumps-Rubella (MMR) Vaccine**: This vaccine is recommended for children or adolescents with HIV, unless they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or CD4 percentage less than 15%).[52]
- **Live Rotavirus Vaccine**: Although rotavirus is a live vaccine, it is recommended (with precaution) for all children with HIV, according to the usual dosing schedule.[52]
- **Live Varicella Vaccine**: This vaccine is recommended for children or adolescents with HIV, unless they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or a CD4 percentage less than 15%).[52]
- **Dengue Vaccine**: Dengue vaccine should not be administered to children or adolescents with HIV if they have high-level immunosuppression (CD4 cell count less than 200 cells/mm^3 or a CD4 percentage less than 15%); dengue vaccine can be administered with precaution to children with HIV if they have a CD4 count of at least 200 cells/mm^3 and they have a CD4 percentage of at least 15%.[52]

Opportunistic Infection Prophylaxis in Children with HIV

It is beyond the scope of this review to address the prevention and treatment of all opportunistic infections that occur in children with HIV. The Pediatric OI Guidelines provide detailed information regarding prevention and treatment of the major opportunistic infections that occur in children.[54] The following discussion will focus on the prevention of three important opportunistic infections that can occur in children: *Pneumocystis* pneumonia, *Toxoplasma* encephalitis, and disseminated *Mycobacterium avium* complex.[55,56,57] For additional information on the prevention of opportunistic infections in children and for information related to the treatment of opportunistic infections in children, see the detailed discussion in the Pediatric OI Guidelines.[58]

Pneumocystis Pneumonia Prophylaxis in Children

Prophylaxis against *Pneumocystis jirovecii* pneumonia is an extremely beneficial intervention among infants with HIV, especially for those infants not yet on antiretroviral therapy. The incidence of *Pneumocystis* pneumonia in children with HIV is highest during the first year of life, with cases peaking at 3 to 6 months of age.[56] In resource-limited settings, *Pneumocystis* pneumonia has been shown in autopsy studies to cause up to 44% of HIV-associated deaths in children with HIV.[59]

Initiating *Pneumocystis* Pneumonia Prophylaxis in Children

The Pediatric OI Guidelines recommend administering *Pneumocystis* pneumonia prophylaxis in children with HIV who meet the following age-specific requirements:[56]

- **Age 1 month to 12 months (including when HIV cannot be presumptively excluded by 4–6 weeks of age)**: All should receive *Pneumocystis* pneumonia prophylaxis, regardless of CD4 cell count or CD4 percentage, beginning at age 4–6 weeks. Reassess at 1 year of age with updated CD4 cell count and CD4 percentage.
- **Age 1 year to ≤6 years**: CD4 count

Summary Points

- In the United States, at year-end 2022, there was an estimated 1,124 children younger than 13 years of age with HIV in the United States; this number represents approximately 0.1 percent of all persons living with HIV in the United States.
- A virologic assay (HIV nucleic acid testing, or NAT) that directly detects HIV RNA or HIV DNA is required to diagnose HIV among perinatally-exposed infants younger than 18 months of age.
- For infants born to mothers with HIV with a low risk of transmission, the recommended HIV diagnostic evaluation includes HIV nucleic acid testing at 3 time points after birth: 14 to 21 days, 1 to 2 months, and 4 to 6 months. For higher-risk infants, testing is also recommended at birth and 2 to 6 weeks after cessation of antiretroviral prophylaxis.
- The diagnosis of HIV can be excluded in a non-breastfed infant with (1) two negative virologic tests (at 1 month or later, and at 4 to 6 months or later) or (2) two or more negative antibody tests performed at 6 months of age or older.
- Monitoring for CD4 cell count and HIV RNA should be based on the child's immune status, whether they are taking antiretroviral therapy, and whether they have suppressed HIV RNA levels.
- For women breastfeeding, most experts recommend maternal HIV RNA monitoring should be done every 1 to 2 months during breastfeeding. A detectable maternal HIV RNA level should prompt expert consultation.
- Preferred and alternative pediatric antiretroviral therapy regimens are based on a child's age and special circumstances, and many antiretroviral agents have age restrictions based on limited data in pediatric populations.
- *Pneumocystis* pneumonia prophylaxis should be given to all children with HIV (or HIV indeterminate) who are less than 12 months of age, regardless of CD4 cell count or CD4 percentage. *Pneumocystis* pneumonia prophylaxis in older children, as well as prophylaxis against *Toxoplasma* encephalitis *Mycobacterium avium* complex (MAC) disease in children of all ages, is based on the degree of immunosuppression.

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Figures

Figure 1 Annual Number of Perinatally-Acquired HIV Infections, United States, 1978–2022

During the years 1978-1993, the estimates were generated through a back calculation method.

Source: Centers for Disease Control and Prevention.

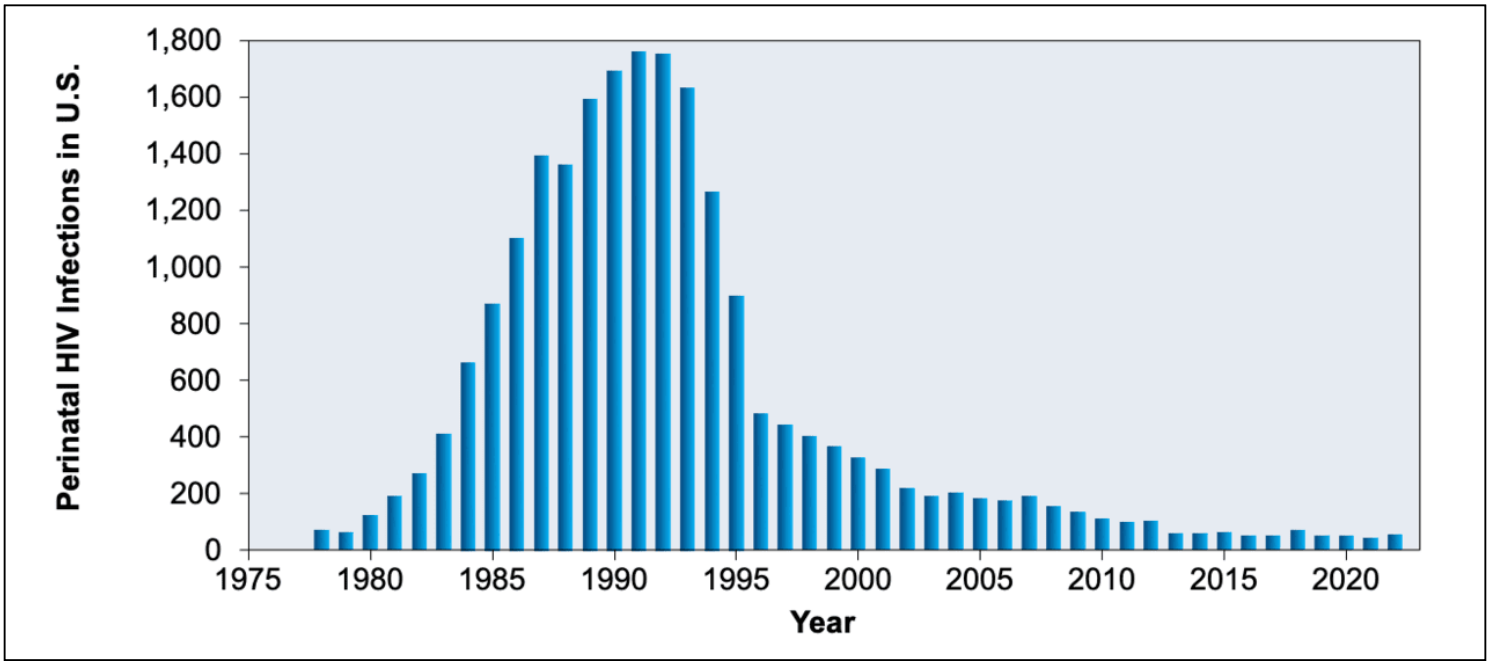

Figure 2 Recommended Virologic Testing Schedules for Infants Exposed to HIV

*High risk = mother with HIV RNA ≥50 copies/mL in the 4 weeks prior to delivery, early (acute or recent) HIV during pregnancy, or HIV diagnosed in labor or postpartum
†Low risk = mother with Ssustained viral suppression (<50 copies/mL) from 20 weeks of gestation through delivery
^A birth test generally should be performed but is not necessary for infants at low risk of HIV acquisition unless there are concerns that the newborn could be lost to follow-up without further testing.
Abbreviation: NAT = nucleic acid test (e.g., HIV RNA or HIV DNA PCR)

Source: Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Diagnosis of HIV infection in infants and children. December 19, 2024.

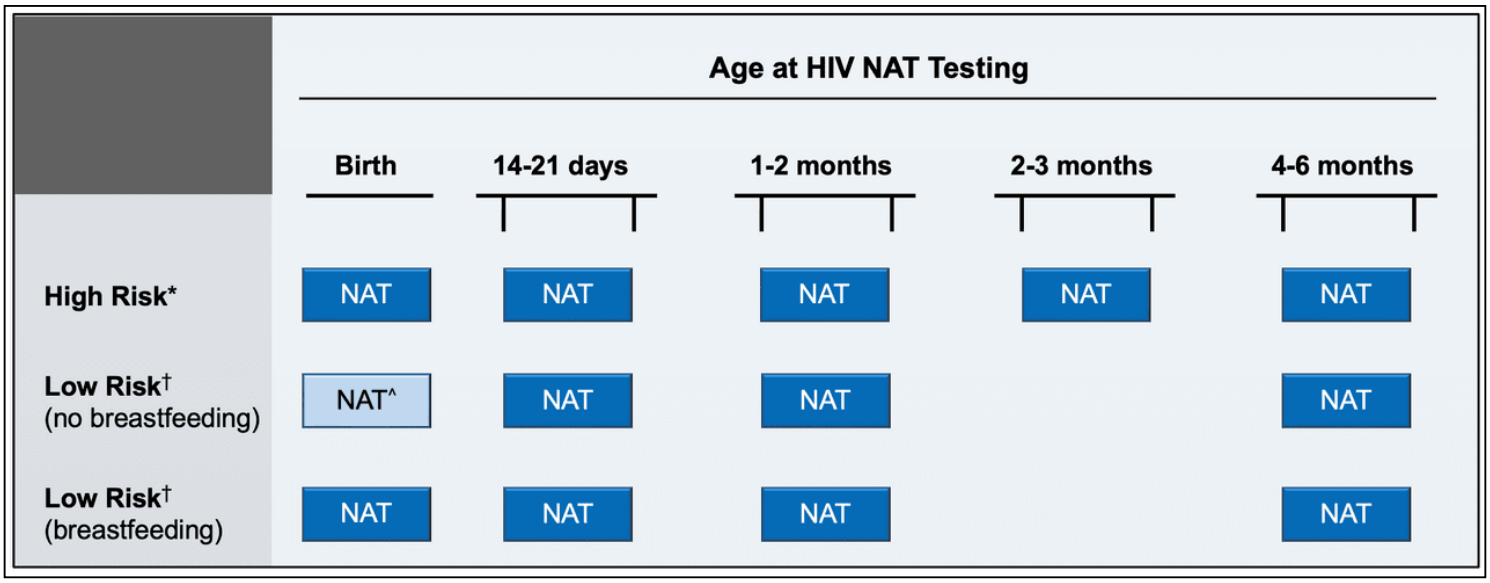

Figure 3 (Image Series) - HIV Epidemiology for Children in United States (Image Series) - Figure 3 (Image Series) - HIV Epidemiology for Children in United States
Image 3A: Persons Living with Diagnosed HIV. by Age, Year End 2022

Source: Centers for Disease Control and Prevention. Diagnoses, deaths, and prevalence of HIV in the United States and 6 territories and freely associated states, 2022. HIV Surveillance Report, 2022; vol. 35:1-177. Published May 2024.

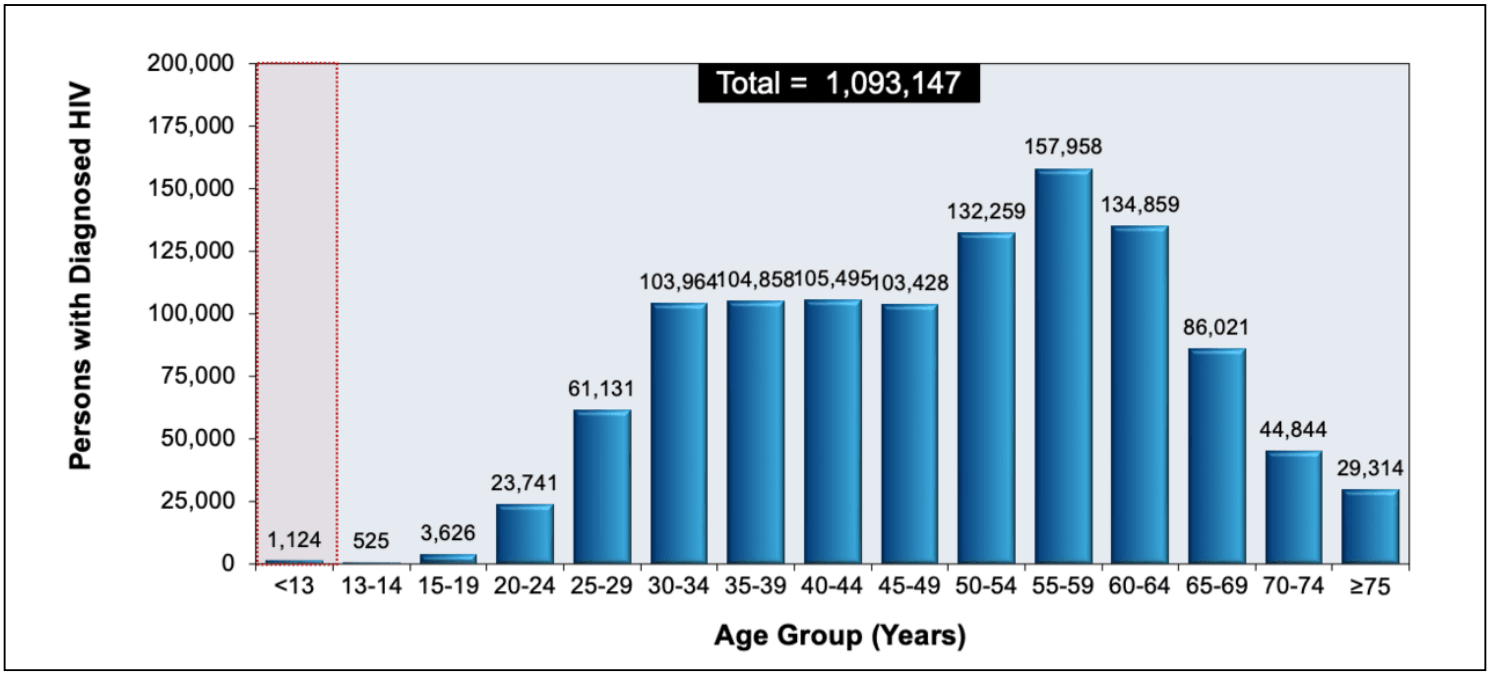

Figure 3 (Image Series) - HIV Epidemiology for Children in United States
Image 3B: Children

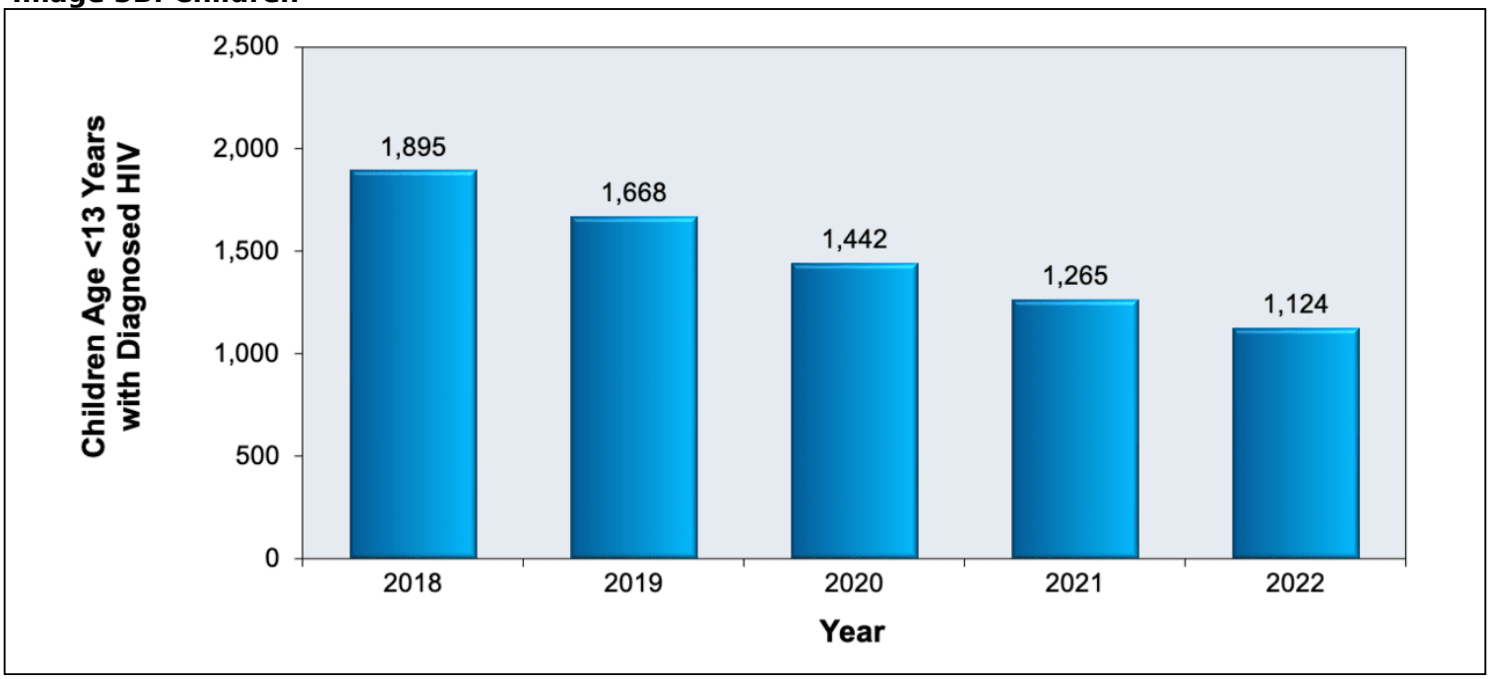

Figure 3 (Image Series) - HIV Epidemiology for Children in United States
Image 3C: Children

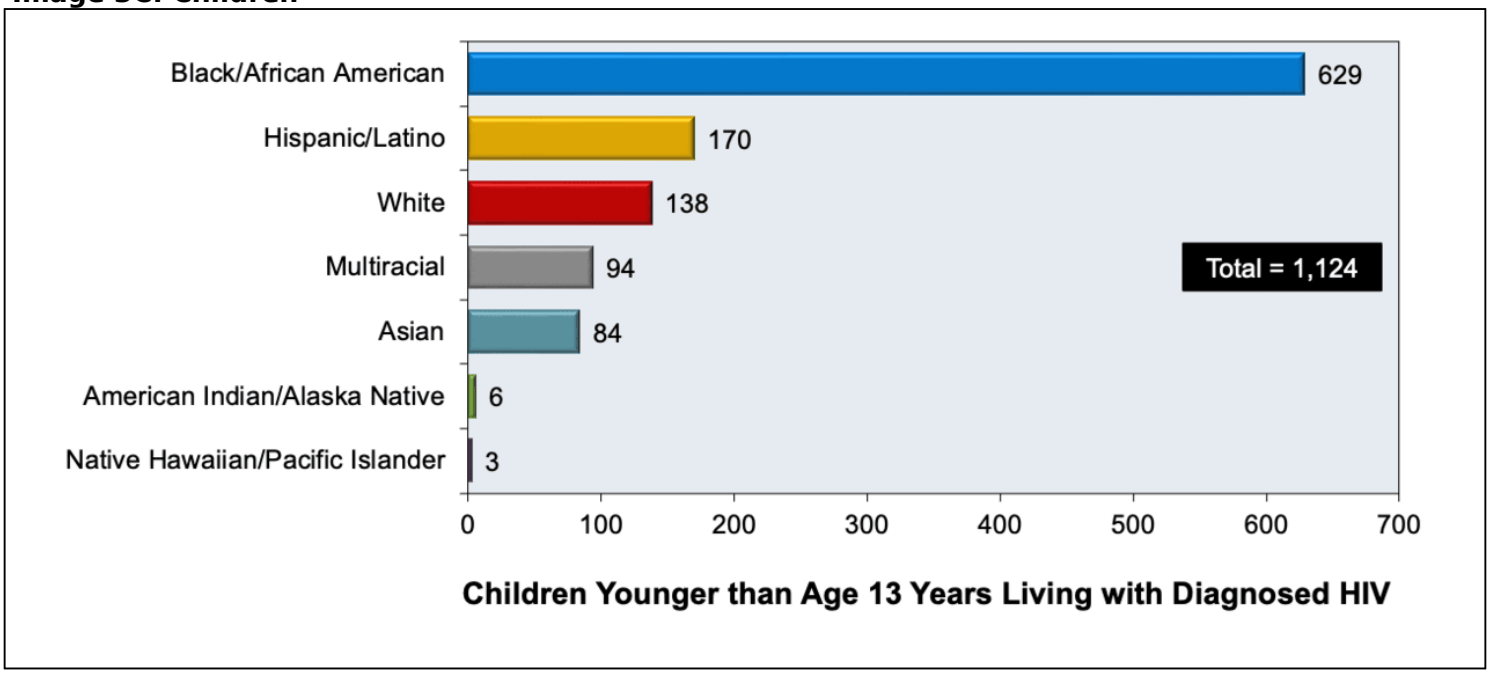

Table 1. HIV Infection Stage in Children

HIV Infection Stage[a] Based on Age-Specific CD4 Cell Count or Percentage	Stage	<1 Ye
		CD4 cells/µL
	1	≥1,500
	2	750-1,499
	3	<750

[a]The stage is based primarily on t
percentage, and the percentage i
illness has been diagnosed, then

Source:

- Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection--United States, 2014. MMWR Recomm Rep. 2014;63:1-10. [PubMed Abstract]

Table 2. Initial Antiretroviral Regimens for Infants Younger than 30 Days of Age

HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants from Birth to <30 Days of Age[a,b]

Age	Regimens
Preferred Initial Regimens	
Term Infants (≥37 weeks of gestation) and aged <30 days *or* Preterm infants with a postmenstrual age of ≥37 weeks at treatment initiation	**NNRTI (Nevirapine) or INSTI (Raltegravir**
	Nevirapine *plus* zidovudine *plus* (lamivudine *o*
	Raltegravir (for infants weighing ≥2 kg to <25 (lamivudine *or* emtricitabine)
Preterm infants ≥32 to <37 weeks gestation	**NNRTI (Nevirapine) plus two NRTIs**
	Nevirapine plus zidovudine *plus* (lamivudine *o*
Preterm infants <32 weeks gestation	Consultation with a pediatric HIV expert or the Hotline (844-275-6222) is recommended.
Alternative Anchor Drug	
Postmenstrual age ≥42 weeks *and* Postnatal age of >14 days	**PI (Lopinavir-ritonavir) plus two NRTIs**
	Lopinavir-ritonavir *plus* zidovudine *plus* (lamiv
Alternative NRTI Backbone	
Infants ≥37 weeks of gestation	Abacavir *plus* (lamivudine *or* emtricitabine) if

[a]Panel recommendations summarized in this table are for children with HIV-1 infection.
[b]Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances a antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c]Fixed dose combinations may be available for some medication combinations.
[d]A negative test for the HLA-B*5701 allele must be obtained prior to use of abacavir. Although abacavir is not appro Administration (FDA) the Panel recommends abacavir as part of an *Alternative* NRTI backbone for full-term infants f

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: antiretroviral treatment regimens recommended for initial therapy in infants and children with HIV. September 30, 2025. [HIV.gov]

Table 3. Initial Antiretroviral Regimens for Infants and Children Aged ≥30 Days to <2 Years

HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Infants and Children Aged ≥30 Days to <2 Years[a,b]

Age	Regimens[c,d,e,f]	Age/Weight Restrictions
Preferred Regimens: INSTI + 2 NRTIs		
Aged ≥30 Days to <2 Years and Weighing ≥3 kg	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	Dolutegravir ≥30 days and ≥3 kg to <25 k
	Dolutegravir *plus* abacavir *plus* (lamivudine or emtricitabine) if HLA-B*5701 negative	Dolutegravir ≥30 days and ≥3 kg to <25 k
Aged ≥3 Months to <2 Years and Weighing ≥6 kg to ≤25 kg	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥3 months and ≥6 kg to <25 kg (in fixed-combination dispersible tablets (*Triumeq* k ≥25 kg if using dolutegravir-abacavir-lamivudine (in fixed-dose combination pe pill) (*Triumeq*)
Alternative Anchor Drugs		
Alternative anchor drugs to replace dolutegravir in an ART regimen with a *Preferred* NRTI backbone for Infants Aged ≥30 days to <2 Years	Lopinavir-ritonavir (boosted PI)	Postmenstrual age ≥42 weeks and postna age >14 days (lopinavir-ritonavir oral solu
	Atazanavir plus ritonavir (boosted PI) in children weighing ≥15 kg	>15 kg to <25 kg (atazanavir is available powder packets; ritonavir is available in 100-mg tablets and 100-mg powder packe
	Nevirapine	<3 years (nevirapine solution)

[a]Panel recommendations summarized in this table are for children with HIV-1 infection.
[b]Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c]Fixed dose combinations may be available for some medication combinations.
[d]Before abacavir administration, a negative HLA-B*5701 allele test result should be available.
[e]If dolutegravir dispersible tablets are not available, raltegravir can be administered using either the oral granules for suspension dispersed in water or as the chewable tablets dispersed in juice, formula, or milk.
[f]An NRTI backbone of zidovudine plus

lamivudine twice daily or abacavir plus lamivudine twice daily allows for all medications to be administered at the same time when given in combination with lopinavir-ritonavir or raltegravir. There is considerable experience with zidovudine and lamivudine in this age group. Abacavir is associated with less bone marrow toxicity than zidovudine and may be the preferred NRTI for long-term use.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: antiretroviral treatment regimens recommended for initial therapy in infants and children with HIV. September 30, 2025. [HIV.gov]

Table 4. Initial Antiretroviral Regimens for Children Aged ≥2 Years to <12 Years

HHS Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Initial Antiretroviral Regimens for Children Aged ≥2 Years to <12 Years[a,b]

Regimens[c]	**Age/Weight Restrictions**	
Preferred Antiretroviral Regimens		
Unable to swallow pills	**INSTI (Dolutegravir) plus 2NRTIs**	
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative[d]	≥3 kg to <25 kg (*Triumeq* PD)
	Dolutegravir *plus* zidovudine *plus* (lamivudine or emtricitabine)	≥3 kg (for dolutegravir)
	Dolutegravir *plus* tenofovir alafenamide-emtricitabine	≥3 kg (for dolutegravir) ≥14 kg to <25 kg (for tenofovir alafenami emtricitabine)
Able to swallow pills	**INSTI (Bictegravir or Dolutegravir) plus 2NRTIs**	
	Bictegravir-tenofovir alafenamide-emtricitabine (fixed-dose combination)[e,f]	≥14 kg to <25 kg (use bictegravir 30 mg-alafenamide 15 mg-emtricitabine 120 mg ≥25 kg (use bictegravir 50 mg-tenofovir a mg-emtricitabine 200 mg)
	Dolutegravir-abacavir-lamivudine (in fixed-dose combination) if HLA-B*5701 negative	≥25 kg
	Dolutegravir *plus* tenofovir alafenamide-emtricitabine	≥14 kg (use tablets for both dolutegravir alafenamide-emtricitabine)
Alternative Anchor Drugs with a Preferred NRTI Backbone		
Alternative Anchor Drug (*for use with* Preferred NRTI Backbone)[g]	Atazanavir powder *plus* ritonavir powder (boosted PI)	≥15 kg to ≤25 kg
	Atazanavir powder *plus* ritonavir tablets (boosted PI)	≥15 kg
	Atazanavir plus cobicistat in fixed dose combination tablet (boosted PI)	≥35 kg
	Darunavir *plus* ritonavir (boosted PI)	≥20 kg
	Darunavir *plus* cobicistat in fixed dose combination tablet (boosted PI)	≥40 kg
	Nevirapine	None
	Nevirapine XR	Age ≥6 years
	Efavirenz	Age ≥3 years and ≥10 kg
	Doravirine	≥35 kg

Abbreviations
INSTI = Integrase strand transfer inhibitor; NRTIs = nucleoside reverse transcriptase inhibitors

[a] Panel recommendations

summarized in this table are for children with HIV-1 infection.
[b] Recommendations for antiretroviral drugs or antiretroviral therapy regimens to be used in special circumstances are addressed in the pediatric antiretroviral therapy guidelines (e.g., ARV resistance, HBV coinfection).
[c] Fixed dose combinations may be available for some medication combinations.
[d] Before abacavir administration, a negative HLA-B*5701 allele test result should be available.
[e] There are two different strengths of bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*), with the lower-strength tablet for children weighing ≥14 kg and <25 kg.
[f] The product label for bictegravir-tenofovir alafenamide-emtricitabine (*Biktarvy*) states that for children who are unable to swallow a whole tablet, the bictegravir-tenofovir alafenamide-emtricitabine tablet can be split and each part taken separately, as long as all parts are ingested within approximately 10 minutes.
[g] The tenofovir alafenamide plus emtricitabine is recommended as a *Preferred* NRTI combination for children and adolescents weighing ≥14 kg when used with an INSTI or NNRTI; a fixed dose tablet that contains tenofovir alafenamide plus emtricitabine (*Descovy*) is available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is approved by the FDA for children weighing ≥14 kg when used in the regimen bictegravir-tenofovir alafenamide-emtricitabine, which is also available in two strengths, with dosage determined by a child's weight. Tenofovir alafenamide-emtricitabine is a *Preferred* NRTI combination for children and adolescents weighing ≥35 kg when used with a boosted PI; tenofovir alafenamide-emtricitabine is not approved or recommended for use with a boosted PI in children weighing

<35 kg.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. What to start: antiretroviral treatment regimens recommended for initial therapy in infants and children with HIV. September 30, 2025. [HIV.gov]

Table 5. Evidence-Based Approaches for Monitoring Medication Adherence

Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Evidence-Based Approaches for Monitoring Medication Adherence

Routine Assessment of Medication Adherence in Clinical Care	Description
Monitor viral load.	Viral load monitoring should be done more frequently after initiating or changing medications.
Assess quantitative self-report of missed doses.	Ask patient and/or caregiver about the number of missed doses over defined period (1, 3, or 7 days).
Request a description of the medication regimen.	Ask the patient and/or caregiver about the name, appearance, and number of medications and how often the medications are taken.
Assess barriers to medication administration.	Engage the patient and caregiver in dialogue around facilitators and challenges to adherence.
Monitor pharmacy refills.	Approaches include pharmacy-based or clinic-based assessment of on-time medication refills.
Employ telemedicine to monitor and support medication administration.	Telemedicine visits allow remote and often face-to-face contact and provide new opportunities to support families; to visualize ART preparation, handling, and swallowing; and to conduct DOT in the home setting.
Conduct announced and unannounced pill counts.	Approaches include asking patients to bring medications to clinic, home visits, or referral to community health nursing.
Monitor attendance for injection clinic visits among adolescents on long-acting injectable regimens.	For individuals on long-acting injectable antiretrovirals, adherence is related to receiving scheduled injections on time. Therefore, reducing barriers to adherence should focus on scheduling convenient appointments, minimizing school and work absences, and ensuring transportation to appointments.
Targeted Approaches to Monitor Adherence in Special Circumstances	**Description**
Implement directly observed therapy (DOT) in person and via telemedicine.	Include brief period of hospitalization if indicated.
Measure drug concentration in plasma or dried blood spots.	Measuring drug concentrations can be considered for particular drugs.
Approaches to Monitor Medication Adherence in Research Settings	**Description**
Measure drug concentrations in hair.	Measuring hair drug concentrations can be considered for particular drugs; it provides a good measure of adherence over time.
Use electronic monitoring devices.	Approaches include medication Event Monitoring System [MEMS] caps and Wisepill
Use mobile phone-based technologies.	Approaches include interactive voice response, text messaging, and mobile apps.

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for

the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in children and adolescents with HIV. September 30, 2025. [HIV.gov]