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 that a three-part zidovudine regimen reduced perinatal HIV transmission by 67.5% compared with placebo.[5] In the United States, the widespread implementation of highly effective measures to prevent perinatal HIV transmission has dramatically reduced the number of children born with HIV from a peak of more than 1,700 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 providing care for infants and children with HIV should be aware of the unique characteristics of these populations, integrate age-specific primary care measures into 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 lesson will focus on the diagnosis and management of HIV in infants and children through 12 years of age. The topic of antiretroviral prophylaxis for infants born to mothers with HIV is addressed in the Preventing Perinatal HIV Transmission lesson in the Prevention of HIV Module.

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 these children (Figure 2).[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, comprising 56% (629 of 1,124) of children younger than 13 years of age living with diagnosed HIV at year-end 2022.[10]

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.[12] Note that, due to concerns for contamination with maternal blood, umbilical cord blood sample should not be used for an HIV diagnostic evaluation at birth. The following summarizes the tests to be utilized in the diagnosis of HIV in infants.[12] Detailed information related to the HIV testing schedule for infants exposed to mothers with HIV is addressed in the lesson on Preventing Perinatal HIV Transmission in the Prevention of HIV module

- **Virologic Assays**: The diagnosis of HIV among infants and children younger than 18 months 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.[12] 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.[12]
- **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 compared with virologic tests, such as HIV nucleic acid testing.[12,13] 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.

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.[12,14]

Exclusion of HIV Diagnosis

The diagnosis of HIV can be excluded in a non-breastfed infant with:[12,14]

- 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

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 follow the CDC/APHL HIV Laboratory Testing Guidelines.[11] The initial screening test is 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.

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.[15] Stages 1, 2, and 3 are determined based on the CD4 count, stratified by age (Table 1).[15] 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.[15] 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.[15,16]

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 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 unexplained diagnosis of an opportunistic illness.[15]

Baseline Evaluation and Monitoring

Baseline Evaluation

Children diagnosed with HIV should have a complete medical history, physical examination, and laboratory evaluation upon entering care.[17] This history should include a detailed medical and social history (including immunizations, nutrition, physical and social/emotional environments) and an evaluation for HIV-specific physical problems (e.g., growth delay, motor or neurocognitive problems). Youth with perinatal HIV acquisition may be particularly vulnerable to cognitive problems, especially in the executive function domain.[18,19,20] Baseline laboratory evaluation for all children diagnosed with HIV at entry into care should include the following:[17]

- **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 of 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 and assess adherence. These visits can be conducted in-person or via telehealth communication platforms at the provider's discretion and based on the comfort level of the child and guardian.[17]

- **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.[17]
- **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 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.[17] The 2- to 4-week visit should

include a quantitative HIV RNA test and other laboratory studies depending on the antiretroviral regimen.[17]

- **Long-Term Monitoring of Children on Antiretroviral Therapy**: Long-term monitoring of children maintained on antiretroviral therapy should occur every 3 to 4 months and includes the following: HIV RNA level, absolute CD4 cell count, chemistries, complete blood count with differential, assessment of medication toxicity, adherence assessment, and antiretroviral medication dosage adjustment for growth and weight if needed.[17] Urinalysis, lipid panel, and random plasma glucose should be obtained every 6 to 12 months.[17] 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.[17] In contrast, HIV RNA monitoring should continue to be performed every 3-4 months to assess adherence to the antiretroviral regimen.[17]
- **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.[17] 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.[21,22]
- **Children with Suspected Virologic, Immunologic, and/or Clinical Deterioration**: Evaluation of children with suspected virologic, immunologic, and/or clinical deterioration should include expert consultation and, in the setting of virologic failure, undergo adherence assessment and HIV drug resistance testing.[17]

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 without 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.[23] In addition, HIV RNA values are 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.[17]

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.[24,25,26,27] 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.[27] Studies in children have demonstrated benefits from earlier initiation of antiretroviral therapy at higher CD4 counts, including improved immune response, reduced proviral reservoirs, and more rapid growth reconstitution.[27,28,29,30,31] 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.[32,33] Several studies have shown that initiating antiretroviral therapy is associated with decreased systemic inflammation, lower risk of cardiomyopathy, and improved neurocognitive outcomes.[34,35,36]

When to Start Antiretroviral Therapy

The Pediatric ARV Guidelines recommend rapid initiation of combination antiretroviral treatment for all children diagnosed with HIV, regardless of age, CD4 count, or HIV RNA level.[37] 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 before starting antiretroviral therapy—in order to reduce the risk of immune reconstitution inflammatory syndrome (IRIS).[37] In addition, consulting a pediatric HIV specialist is recommended to determine the optimal timing for initiating antiretroviral therapy.[37] For infants younger than 12 months of age who are diagnosed with HIV, urgent initiation of antiretroviral therapy is critical because they are at great risk of accelerated HIV disease progression, clinical illness, and death.[37] For older asymptomatic children diagnosed with HIV, data on 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 ARV Guidelines are based on the child's age, including gestational age and weight.[38] 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.[38]

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.[38] 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).[38]

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.[38] Note that no tenofovir medications are used for children younger than 2 years of age. (Table 3).[38]

Age: 2 Years to 12 Years

The following table summarizes the preferred and alternative regimens recommended for initial therapy in children 2 years through 12 years of age.[38] Note that none of the preferred dual-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.[38,39,40,41] 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).[38]

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 ARV Guidelines maintain an excellent compendium of pediatric antiretroviral drug information, including an overview of the FDA approval status of antiretroviral medications in children, specific formulations, drug interactions, toxicities, and dosing recommendations for children of different ages.[42] The following factors should be considered when selecting an optimal HIV treatment regimen for children:[38]

- 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 tolerability
- 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 reduce the likelihood of virologic suppression, increase the risk of developing drug resistance mutations and virologic failure, limit future treatment options, and can lead to disease progression and secondary transmission. Children with HIV may struggle with adherence due to complex dosing regimens, age-appropriate behaviors, dependence on an adult caregiver to reliably provide therapy, and social issues within the family unit, such as substance use or homelessness.[43] To improve adherence, the Pediatric ARV Guidelines recommend antiretroviral regimens with reduced pill burden and once-daily dosing whenever feasible. Strategies to optimize adherence are organized into three categories: (1) initial intervention strategies, (2) medication strategies, and (3) follow-up intervention strategies.[44] To promote adherence, the Pediatric ARV Guidelines recommend regular viral load monitoring and at least one other measure of medication adherence (Table 5).[44]

Management of Antiretroviral Toxicity

Children on lifelong antiretroviral therapy need to be monitored for acute and chronic adverse effects, which can involve multiple organ systems.[45,46,47] This is particularly important as new antiretroviral treatment options become available that lack a long track record of pediatric use. The Pediatric ARV Guidelines have compiled reference tables of potential adverse effects associated with different antiretroviral agents, with detailed summaries of adverse effects.[47] 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.[40]

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.[48,49,50]

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.[49,50] 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.[50,51]

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.[50]

- **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.[50]
- **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%).[50]
- **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.[50]
- **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%).[50]
- **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%.[50]

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 in children with HIV. The Pediatric OI Guidelines provide detailed information regarding prevention and treatment of the major opportunistic infections that occur in children.[52] 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.[53,54,55] For additional information on the prevention and treatment of opportunistic infections in children, see the detailed discussion in the Pediatric OI Guidelines.[56]

Pneumocystis Pneumonia Prophylaxis in Children

Prophylaxis against *Pneumocystis jirovecii* pneumonia is an extremely beneficial intervention for infants with HIV, especially for those 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.[54] In resource-limited settings, autopsy studies have shown *Pneumocystis* pneumonia accounts for up to 44% of HIV-associated deaths in children with HIV.[57]

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:[54]

- **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

- At year-end 2022, an estimated 1,124 children younger than 13 years of age were living 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 test) 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.
- An HIV diagnosis 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 that 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 younger 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 and *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.

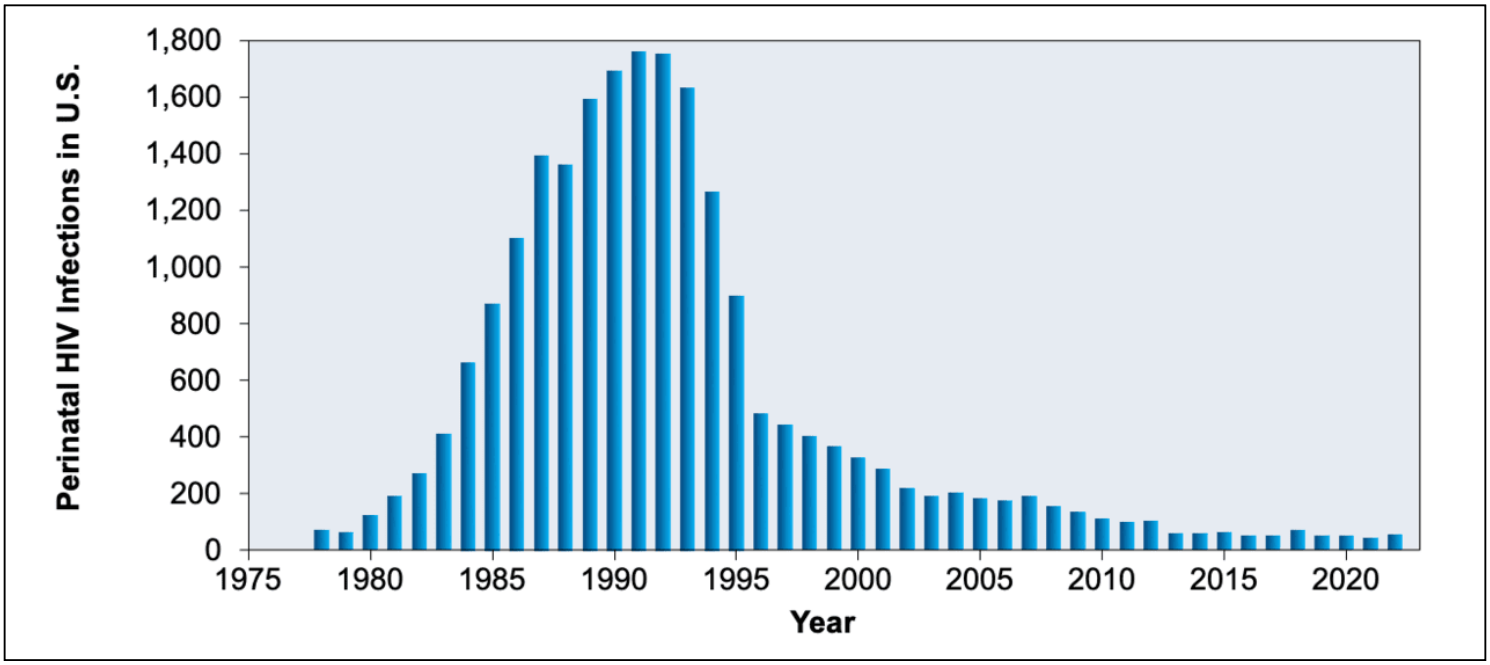


Figure 2 (Image Series) - HIV Epidemiology for Children in United States (Image Series) - Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2A: Persons Living with Diagnosed HIV. by Age, Year End 2022

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.

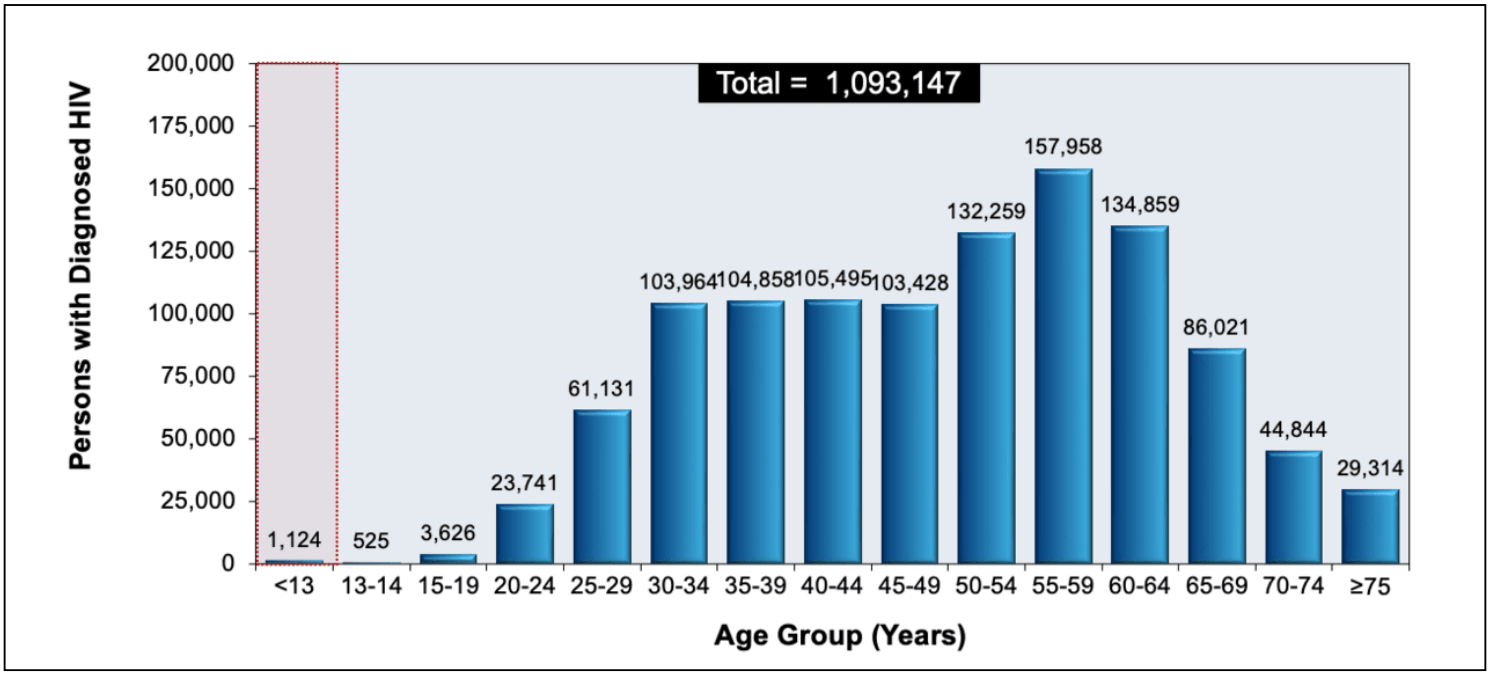


Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2B: Children

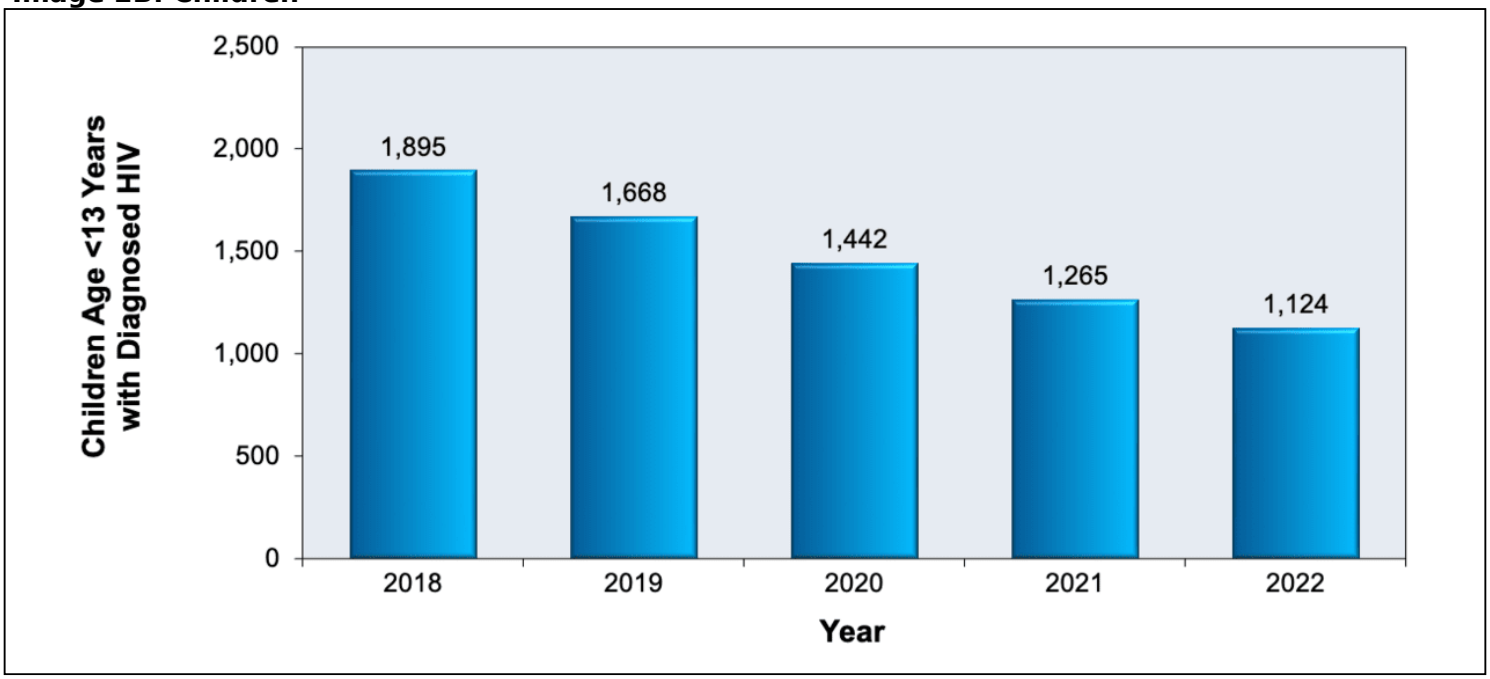


Figure 2 (Image Series) - HIV Epidemiology for Children in United States
Image 2C: Children

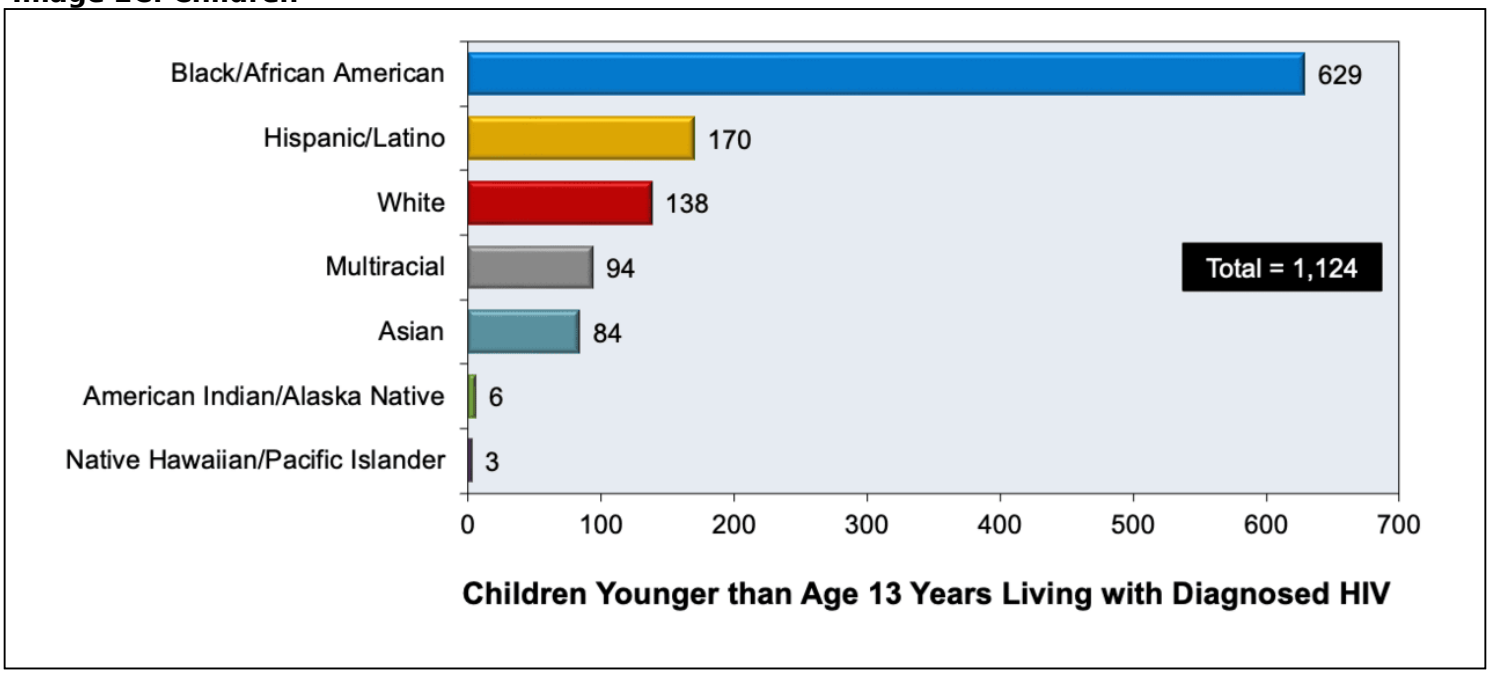


Table 1. HIV Infection Stage in Children Based on Age-Specific CD4 Count and Percentage

Stage	Age When CD4 Test Obtained					
	<1 Year		1 to < 6 Years		≥6 Years	
	CD4 cells/µL	CD4%	CD4 cells/µL	CD4%	CD4 cells/µL	CD4%
1	≥1,500	≥34	≥1,000	≥30	≥500	≥26
2	750-1,499	26-33	500-999	22-29	200-499	14-25
3	<750	<26	<500	<22	<200	<14

Note: The stage is based primarily on the CD4 cell count; the CD4 cell count takes precedence over the CD4 percentage, and the percentage is considered only if the count is missing. If a Stage 3-defining opportunistic illness has been diagnosed, then the stage is 3 regardless of CD4 test results.

Source:

- Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection--United States, 2014. MMWR Recomm Rep. 2014;63(RR-03):1-10. [PubMed Abstract]

Table 2. Recommended Initial ART Regimens for Infants from Birth to <30 Days of Age: Pediatric ARV Guidelines

Preferred Regimens
Term Infants (≥37 weeks gestation) or preterm infants with postmenstrual age (≥37 weeks at the time of treatment initiation) • Dolutegravir (for infants weighing ≥2 kg) *plus* zidovudine *plus* (lamivudine *or* emtricitabine), *or* • Nevirapine (for infants weighing <2 kg) *plus* zidovudine *plus* (lamivudine *or* emtricitabine)
Preterm infants with a postmenstrual age of ≥32 to <37 weeks at the time of treatment initiation • Nevirapine plus zidovudine *plus* (lamivudine *or* emtricitabine)
Preterm infants with a postmenstrual age of<32 weeks gestation at the time of treatment initiation • Consultation with a pediatric HIV expert or the National Perinatal HIV/AIDS Hotline (888-448-8765) is recommended.
Alternative Anchor Drug + Preferred NRTI Backbone
• Raltegravir (for infants weighing ≥2 kg) *plus* zidovudine *plus* (lamivudine *or* emtricitabine), *or* • Nevirapine plus zidovudine *plus* (lamivudine *or* emtricitabine), *or* • Lopinavir-ritonavir *plus* zidovudine *plus* (lamivudine *or* emtricitabine)
Alternative NRTI Backbone
Term infants ≥37 weeks of gestation • Abacavir *plus* (lamivudine *or* emtricitabine) if HLA-B*5701 negative
Abbreviation: ART = antiretroviral therapy; NRTI = nucleoside reverse transcriptase inhibitor

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. June 25, 2026. [HIV.gov]

Table 3. Recommended Initial ART for Infants and Children Aged ≥30 Days to <2 Years: Pediatric ARV Guidelines

Preferred Regimens: INSTI + 2 NRTIs
Aged ≥30 Days to <2 Years: antiretroviral therapy should be initiated with a dolutegravir-based regimen. Transition to a dolutegravir-based regimen should be considered if an infant is initiated on a nevirapine-, raltegravir-, or lopinavir-ritonavir-based regimen in the first month of life. • Dolutegravir *plus* abacavir *plus* (lamivudine or emtricitabine) if HLA-B*5701 negative, *or* • Dolutegravir *plus plus* zidovudine *plus* (lamivudine or emtricitabine)
Aged ≥3 Months Days to <2 Years and Weighing ≥6 kg to ≤25 kg • Dolutegravir *plus* abacavir *plus* lamivudine as fixed-dose combination (*Triumeq PD*) if HLA-B*5701 negative
Alternative Anchor Drug**s**
Alternative Anchor PI • Lopinavir-ritonavir (boosted PI) • Atazanavir plus ritonavir (boosted PI) in children weighing ≥15 kg Alternative Anchor NNRTI • Nevirapine could be considered if there is resistance or intolerance to both PIs and INSTIs. However, nevirapine is generally not recommended as an initial treatment in this age group because the low genetic barrier to resistance during a time of significant viremia may lead to drug resistance to all members of the NNRTI class of drugs.
Nucleoside Reverse Transcriptase Inhibitor Backbones in Alternative Regimens
• Twice-daily dosing: 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.
Abbreviations: ART: antiretroviral therapy; INSTI = integrase strand transfer inhibitors; NRTIs = nucleoside reverse transcriptase inhibitors; NNRTIs = nucleoside reverse transcriptase inhibitors; PI = protease inhibitor	

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. June 25, 2026. [HIV.gov]

Table 4. Recommended Initial ART Regimens for Children Aged ≥2 Years to <12 Years: Pediatric ARV Guidelines

Preferred Antiretroviral Regimens
Not Able to Swallow Pills • Dolutegravir plus abacavir plus lamivudine in the dispersible fixed-dose formulation (*Triumeq* PD) for children weighing 6 kg to <25 kg if HLA-B*5701 negative, *or*   ◦ Dolutegravir film-coated tablets (*Tivicay*) plus abacavir plus lamivudine in the liquid formulations for children weighing >25 kg if HLA-B*5701 negative • Dolutegravir *plus* emtricitabine plus tenofovir alafenamide for children weighing ≥14 kg, *or* • Dolutegravir in dispersible tablets plus zidovudine plus (lamivudine or emtricitabine) in liquid formulations
Able to swallow pills • Bictegravir plus emtricitabine plus tenofovir alafenamide (fixed-dose combination bictegravir-emtricitabine-tenofovir alafenamide (*Biktarvy*) for children weighing ≥14 kg • Dolutegravir plus emtricitabine plus tenofovir alafenamide (Dolutegravir [*Tivicay*] plus the fixed-dose combination emtricitabine-tenofovir alafenamide (FTC/TAF [*Descovy*]) for children weighing ≥14 kg • Dolutegravir plus abacavir plus lamivudine (fixed-dose combination dolutegravir-abacavir-lamivudine [*Triumeq*]) for children weighing ≥25 kg if HLA-B*5701 negative
Alternative Anchor Drugs with a Preferred NRTI Backbone
Boosted PI Anchor Drug • Atazanavir powder *plus* ritonavir powder (or tablet); weighing ≥5 kg to ≤25 kg for atazanavir powder and weighing ≥15 kg for ritonavir powder packet or 100-mg tablet (boosted PI) • Atazanavir plus cobicistat in fixed-dose combination tablet, atazanavir-cobicistat (*Evotaz*); weighing ≥35 kg and able to

swallow pills • Darunavir solution or tablet *plus* ritonavir powder (or tablet); age ≥3 years to <12 years and weighing ≥20 kg • Darunavir plus cobicistat if weighing greater than 15 kg (darunavir-cobicistat 600 mg/90 mg dispersible tablets for children weighing ≥15 kg to <25 kg, darunavir-cobicistat 675 mg/150 mg for children weighing ≥25 kg to <40 kg, and darunavir-cobicistat800 mg/150 mg for those weighing ≥40 kg)	
NNRTI Anchor Drug • Regimen with nevirapine, efavirenz, or doravirine could be considered in the case of resistance or intolerance to both PIs and INSTIs. Efavirenz is not recommended by the Panel for use in children aged <3 years due to highly variable PK in young children, difficulty in determining an appropriate dose without therapeutic drug monitoring, and side effects (i.e., neurologic toxicity). Doravirine is approved for use in children weighing ≥35 kg,	
Abbreviations: ART = antiretroviral therapy; INSTI = integrase strand transfer inhibitor; NRTIs = nucleoside reverse transcriptase inhibitors; PIs = protease inhibitors	

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. June 25, 2026. [HIV.gov]

Table 5. Evidence-Based Approaches for Monitoring Medication Adherence: Pediatric ARV Guidelines

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]