Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Developed by the HHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure

Updated: January 31, 2024
Reviewed: January 31, 2024

Panel's Recommendations
• HIV testing is recommended for all sexually active people and should be a routine component of pre-pregnancy care **(AII).** • All pregnant people should receive opt-out HIV testing as early as possible during each pregnancy (see Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations and 2018 Quick Reference Guide: Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens from the Centers for Disease Control and Prevention [CDC]) **(AII).** • Partners of all pregnant people should be referred for HIV testing when their status is unknown **(AIII).** • Repeat HIV testing in the third trimester is recommended for pregnant people with negative initial HIV tests who are at increased risk of acquiring HIV, including those receiving care in facilities that have an HIV incidence of ≥1 case per 1,000 pregnant people per year, those who reside in jurisdictions (states or counties) with elevated HIV incidence among females aged 15 to 45 years (>17 per 100,000 females aged 15–45 years), or those who reside in states or territories that require third-trimester testing **(AII).** Annual state and county-level HIV diagnosis rates are available at CDC's National Center for HIV, Viral Hepatitis, Sexually Transmitted Diseases, and Tuberculosis Prevention AtlasPlus webpage. • Repeat HIV testing is recommended for pregnant people with a sexually transmitted infection, with signs and symptoms of acute HIV infection, or with ongoing exposure to HIV **(AIII).** Initiation of pre-exposure prophylaxis (PrEP) is recommended if HIV testing is negative **(AIII).** See Pre-Exposure Prophylaxis (PrEP) to Prevent HIV During Periconception, Antepartum, and Postpartum Periods for more information. • Expedited[a] HIV testing should be performed during labor or after delivery for people with undocumented HIV status and for those who tested negative early in pregnancy but are at increased risk of HIV infection and were not retested in the third trimester **(AII).** HIV antigen/antibody testing should be available 24 hours a day, and results should be available within 1 hour. If results of expedited[a] HIV testing are positive, intrapartum intravenous zidovudine prophylaxis should be initiated immediately **(AI)**; see Intrapartum Care for People with HIV. • When acute HIV infection is suspected during pregnancy or the intrapartum period or while breastfeeding, a plasma HIV RNA assay should be performed in conjunction with an antigen/antibody immunoassay **(AIII).** • When a person has a positive HIV test result during labor and delivery or postpartum, an HIV-1/HIV-2 antibody differentiation assay and an HIV RNA assay should be performed on the birthing parent **(AI).** In these situations, an HIV nucleic acid test (NAT) should be performed on the infant, with immediate initiation of presumptive HIV therapy appropriate for an infant at high risk of perinatal HIV transmission **(AI);** see Diagnosis of HIV Infection in Infants and Children for additional information. • If HIV test results of the birthing parent are unavailable at birth, the newborn should be tested using an expedited[a] antibody test to identify perinatal HIV exposure **(AI).** If positive, an HIV NAT should be performed on the infant, and the birthing parent should be offered standard HIV diagnostic testing as soon as possible **(AI).** ○ In this situation, presumptive HIV therapy appropriate for infants who are at high risk of perinatal HIV transmission should be initiated immediately **(AI).** See Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection for guidance. ○ For people with an initial positive HIV test during labor or delivery or immediately postpartum who were planning to breastfeed, the Panel recommends against breastfeeding. Breast milk should be expressed and stored appropriately until all supplemental HIV tests are reviewed and are negative **(AI).**

- For postpartum people at increased risk of HIV acquisition, HIV testing and PrEP should be offered. If the parent is breastfeeding, consult an HIV specialist regarding frequency of HIV testing for the breastfeeding parent and/or infant **(AIII).**
- HIV test results of the birthing parent should be documented in the newborn's medical record and communicated to the newborn's primary care provider **(AIII).**
- To identify perinatal HIV exposure and possible HIV infection, HIV testing is recommended for infants and children in foster care and adoptees for whom the HIV status of the birthing parent is unknown **(AIII)** (see Diagnosis of HIV Infection in Infants and Children).

[a] The term "expedited" is used to designate HIV testing performed in situations when a very short turnaround time is optimal. Expedited testing is dependent on the available HIV tests in each facility and may include antigen/antibody immunoassays or antibody-only assays; see Approved HIV Tests in the text below.

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 and adolescents, but not studies limited to postpubertal adolescents

Infant Feeding for Individuals with HIV in the United States

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Panel's Recommendations
• People with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding. Counseling about infant feeding should begin prior to conception or as early as possible in pregnancy; information about and plans for infant feeding should be reviewed throughout pregnancy and again after delivery **(AIII).** During counseling, people should be informed that— o Replacement feeding with properly prepared formula or pasteurized donor human milk from a milk bank eliminates the risk of postnatal HIV transmission to the infant **(AI).** o Achieving and maintaining viral suppression through antiretroviral therapy (ART) during pregnancy and postpartum decreases breastfeeding transmission risk to less than 1%, but not zero **(AI).**
• Replacement feeding with formula or banked pasteurized donor human milk is recommended to eliminate the risk of HIV transmission through breastfeeding when people with HIV are not on ART and/or do not have a suppressed viral load during pregnancy (at a minimum throughout the third trimester), as well as at delivery **(AI).**
• Individuals with HIV who are on ART with a sustained undetectable viral load and who choose to breastfeed should be supported in this decision **(AIII).**
• Individuals with HIV who choose to formula feed should be supported in this decision. Providers should ask about potential barriers to formula feeding and explore ways to address them **(AIII).**
• Engaging Child Protective Services or similar agencies is not an appropriate response to the infant feeding choices of an individual with HIV **(AIII).**
• Clinicians are encouraged to consult the national Perinatal HIV/AIDS hotline (1-888-448-8765) with questions about infant feeding by individuals with HIV **(AIII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Optional* ***Rating of Evidence**: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Diagnosis of HIV Infection in Infants and Children

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Panel's Recommendations
Virologic assays (HIV RNA or HIV DNA nucleic acid tests [NATs]) that directly detect HIV must be used to diagnose HIV in infants and children aged <18 months with perinatal and postnatal HIV exposure; HIV antibody and HIV antigen/antibody tests should not be used **(AII)**.
Plasma HIV RNA or cell-associated HIV DNA NATs are generally equally recommended **(AII)**. However, the results of plasma HIV RNA NAT or plasma HIV RNA/DNA NAT can be affected by maternal antiretroviral therapy (ART), or by antiretroviral (ARV) drugs administered to the infant as prophylaxis or presumptive HIV therapy.
An assay that detects HIV non-B subtype viruses or Group O infections (e.g., an HIV RNA NAT or a dual-target total DNA/RNA test) is recommended for use in infants and children who were born to mothers with known or suspected non-B subtype virus or Group O infections **(AII)**.
Virologic diagnostic testing (see Table 3 below) is recommended for all infants with perinatal HIV exposure at the following ages: 14 to 21 days **(AII)** 1 to 2 months **(AII)** 4 to 6 months **(AII)**
For infants who are at high risk of perinatal HIV infection, additional virologic diagnostic testing is recommended at birth **(AII)** and at 2 to 6 weeks after ARV drugs are discontinued **(BII)**.
For infants with perinatal HIV exposure who are being breastfed, virologic diagnostic testing is recommended at birth, 14 to 21 days, 1 to 2 months, and 4 to 6 months of age **(AII)**. An additional virologic test should be performed between the 1-to-2-month and 4-to-6-month time points if the gap between tests is greater than 3 months. See Infant Feeding for Individuals With HIV in the United States. Virologic diagnostic testing should be performed every 3 months during breastfeeding **(BII)**; After cessation of breastfeeding, irrespective of when breastfeeding ends, virologic diagnostic testing should be performed at 4 to 6 weeks, 3 months, and 6 months after cessation **(BII)**.
A positive virologic test should be confirmed as soon as possible by a repeat virologic test **(AII)**.
Definitive exclusion of HIV infection in non-breastfed infants is based on two or more negative virologic tests, with one negative test obtained at age ≥1 month (and at least 2 -6 weeks after discontinuation of multi-drug ARV prophylaxis/presumptive HIV therapy) and one at age ≥4 months, or two negative HIV antibody tests from separate specimens that were obtained at age ≥6 months **(AII)**.
Additional HIV testing (e.g., HIV RNA or HIV DNA NAT, HIV antibody, HIV antigen/antibody) is not needed routinely for non-breastfed infants who meet the criteria for definitive exclusion of HIV and who have had no known or suspected HIV exposure after birth.
Infants with potential HIV exposure after birth (e.g., from maternal HIV diagnosis during breastfeeding, premasticated feeding, sexual abuse, contaminated blood products, percutaneous exposure) who are aged <18

months require additional testing using HIV RNA/DNA NAT assays to establish their HIV status. Infants aged ≥18 months who have these potential exposures require HIV antigen/antibody testing.

Age-appropriate HIV testing also is recommended for infants and children with signs and/or symptoms of HIV, even in the absence of documented or suspected HIV exposure.

For children aged >24 months and for children aged 18 to ≤ 24 months with non-perinatal HIV exposure only, HIV antibody (or HIV antigen/antibody) tests are recommended for diagnostic testing **(AII).**

When acute HIV infection is suspected, additional testing with an HIV NAT may be necessary to diagnose HIV infection **(AII).**

Note: The National Clinician Consultation Center- Perinatal HIV/AIDS provides consultations on issues related to the management of perinatal HIV infection, including diagnostic testing (1-888-448-8765; 24 hours a day, 7 days a week).

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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

Clinical and Laboratory Monitoring of Pediatric HIV Infection

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Panel's Recommendations
• Absolute CD4 T lymphocyte (CD4) cell count and plasma HIV RNA (viral load) should be measured at the time of HIV diagnosis, and, if a child is not started on antiretroviral therapy (ART) after diagnosis, this monitoring should be repeated at least every 3 to 4 months thereafter (AIII). • Absolute CD4 count is recommended for monitoring immune status in children with HIV of all ages, with CD4 percentage as an alternative for children aged <5 years (AII). • Antiretroviral (ARV) drug-resistance testing is recommended at the time of HIV diagnosis, before initiation of therapy in all ART-naive patients, and before switching regimens in patients with treatment failure (AII). Genotypic resistance testing is preferred for this purpose (AIII). • After initiation of ART or after a change in ARV regimen, children should be evaluated for clinical adverse effects and should receive support for treatment adherence within 1 week to 2 weeks; laboratory testing for toxicity and viral load response is recommended at 2 to 4 weeks after treatment initiation or change in ARV regimen and every 3 to 4 months thereafter (see Table 6 below) (AIII). • Children on ART should be monitored for therapy adherence, effectiveness, and toxicities routinely (every 3–4 months) (see Table 6 below) (AII*). See the sections on Adherence to Antiretroviral Therapy in Children and Adolescents With HIV and Management of Medication Toxicity or Intolerance. • Additional CD4 count and plasma viral load monitoring should be performed to evaluate children with suspected clinical, immunologic, or virologic deterioration or to confirm an abnormal value (AIII). CD4 count can be monitored less frequently (every 6–12 months) in children and adolescents who are adherent to therapy, who have sustained virologic suppression and CD4 count values that are well above the threshold for opportunistic infection risk, and who have stable clinical status (AII). Viral load measurement every 3 to 4 months is generally recommended to monitor ART adherence (AIII). • Phenotypic resistance testing should be considered (usually in addition to genotypic resistance testing) for patients with known or suspected complex drug resistance mutation patterns, which generally arise after a patient has experienced virologic failure on multiple ARV regimens (CIII). • Review the history of all previously used ARVs and available resistance test results when making decisions about the choice of new ARVs because mutations may not be detected once the prior drugs have been discontinued (AII). • Viral co-receptor tropism assays are recommended whenever a CCR5 antagonist is being considered for treatment (AI*). The use of tropism assays also should be considered for patients who demonstrate virologic failure while receiving therapy that contains a CCR5 antagonist (AI*).
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When to Initiate Therapy in Antiretroviral-Naive Children

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Panel's Recommendations
• Antiretroviral therapy (ART) should be initiated in all infants and children with HIV infection (AI for children aged <3 months, AI* for older children). o Rapid ART initiation (defined as initiating ART immediately or within days of HIV diagnosis), accompanied by a discussion of the importance of adherence and provision of subsequent adherence support, is recommended for all children with HIV. • If a child with HIV has not initiated ART, health care providers should closely monitor the virologic, immunologic, and clinical status at least every 3 to 4 months (AIII).
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 postpubertal adolescents*

What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children

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Panel's Recommendations
• The selection of an initial antiretroviral (ARV) regimen should be individualized based on several factors, including the characteristics of the proposed regimen, the patient's characteristics, drug efficacy, potential adverse effects, patient and family preferences, and the results of viral resistance testing (AIII). • For treatment-naive children, the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV (the Panel) recommends initiating antiretroviral therapy with three drugs: a dual-nucleoside/nucleotide reverse transcriptase inhibitor backbone plus an integrase strand transfer inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a boosted protease inhibitor (AI*). • Table 8 below provides a list of Panel-recommended ARV regimens that are designated as *Preferred* or *Alternative*; recommendations vary by a patient's age, weight, and sexual maturity rating.
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 postpubertal adolescents*

Antiretroviral Management of Newborns With Perinatal HIV Exposure or HIV Infection

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Panel's Recommendations

- All newborns who were exposed perinatally to HIV should receive postpartum antiretroviral (ARV) drugs to reduce the risk of perinatal transmission of HIV (AI).
- Newborn ARV regimens administered at doses that are appropriate for the infant's gestational age should be initiated as close to the time of birth as possible, preferably within 6 hours of delivery (AII).
- A newborn's ARV regimen should be determined based on maternal and infant factors that influence the risk of perinatal transmission of HIV (AII). The uses of ARV regimens in newborns include the following:
  - ARV Prophylaxis: The administration of one or more ARV drugs to a newborn without documented HIV infection to reduce the risk of perinatal acquisition of HIV.
  - Presumptive HIV Therapy: The administration of a three-drug ARV regimen to newborns who are at highest risk of perinatal acquisition of HIV. Presumptive HIV therapy is intended to be preliminary treatment for a newborn who is later documented to have HIV, but it also serves as prophylaxis against HIV acquisition.
  - HIV Therapy: The administration of a three-drug ARV regimen at treatment doses (called antiretroviral therapy [ART]) to newborns with documented HIV infection (see Diagnosis of HIV Infection in Infants and Children).
- For newborns at low-risk of perinatal HIV acquisition, a 2-week zidovudine (ZDV) ARV regimen is recommended for ARV prophylaxis if the newborn is ≥37 weeks gestation and is born to a person with HIV who—
  - Is currently receiving and has received at least 10 consecutive weeks of ART during pregnancy (BII); *and*
  - Has achieved and maintained *or* maintained viral suppression (defined as at least two consecutive tests with HIV RNA <50 copies/mL obtained at least 4 weeks apart) for the remainder of the pregnancy (AII); *and*
  - Has a viral load <50 copies/mL at or after 36 weeks (AII); *and*
  - Did not have acute HIV infection during pregnancy (BII); *and*
  - Has reported good ART adherence, and adherence concerns have not been identified (BII).
- Infants born to individuals who do not meet the criteria above but who have a viral load <50 copies/mL at or after 36 weeks gestation should receive ZDV for 4 to 6 weeks (BII).
- Newborns at high risk of perinatal acquisition of HIV should receive presumptive HIV therapy with 3-drug regimens administered from birth for 2 to 6 weeks (see Tables 10 and 11); if the duration of the 3-drug regimen is shorter than 6 weeks, ZDV should be continued alone, to complete total of 6 weeks of prophylaxis. Newborns at high risk of HIV acquisition include those born to people with HIV who—
  - Have not received antepartum ARV drugs (AI), *or*
  - Have received only intrapartum ARV drugs (AI), *or*
  - Have received antepartum ARV drugs but who did not achieve viral suppression (defined as at least two consecutive tests with HIV RNA level <50 copies/mL obtained at least 4 weeks apart) within 4 weeks of delivery (AIII), *or*
  - Have primary or acute HIV infection during pregnancy (AI).
- All premature infants <37 weeks gestation who are not at high risk of perinatal acquisition of HIV should receive ZDV for 4 to 6 weeks (BII).

- Infants of people who have primary or acute HIV infection while breastfeeding should be managed like infants at high risk of perinatal transmission with presumptive HIV therapy (see Table 12) (AII).
- The use of ARV drugs other than ZDV, lamivudine, and nevirapine cannot be recommended for any indication in premature newborns (<37 weeks gestational age) because of the lack of dosing and safety data (BII).
- If an individual presents with unknown HIV status and has a positive expedited HIV test during labor or shortly after delivery, the infant should begin presumptive HIV therapy (AII). If supplemental maternal testing is negative, the infant's ARV regimen should be discontinued (AII).
- For newborns with HIV infection, ART should be initiated (AI) (see What to Start in the Pediatric Antiretroviral Guidelines).
- People with HIV should receive patient-centered, evidence-based counseling to support shared decision-making about infant feeding. See Infant Feeding for Individuals With HIV in the United States.
- Providers with questions about ARV management of perinatal HIV exposure should consult an expert in pediatric HIV infection or the National Perinatal HIV hotline (1-888-448-8765), which provides free clinical consultation on all aspects of perinatal HIV, including newborn care (AIII).

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

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Special Considerations for Antiretroviral Therapy Use in Adolescents With HIV

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Panel's Recommendations
• All adolescents with HIV should receive maximally suppressive antiretroviral (ARV) therapy; this is urgent for those who are sexually active, considering pregnancy, or pregnant (AII). • ARV regimen selection should include consideration of the adolescent's individual needs and preferences (AIII). See What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children and Management of Children Receiving Antiretroviral Therapy for more information. • All adolescents with HIV should be screened for mental health disorders and substance use disorders (AII). • Reproductive and sexual health issues—including pregnancy intentions, contraceptive methods, safer sex techniques to prevent transmission of HIV and other sexually transmitted infections (STIs), regular STI screening, pre-exposure prophylaxis for partners, pregnancy planning, and preconception care—should be discussed regularly (AII). • Adolescents with HIV can use all available hormonal contraceptive methods (e.g., pill, patch, ring, injection, implant); however, providers should consider potential drug–drug interactions between hormonal contraceptives and ARV medications that could affect contraceptive efficacy (AII*). See Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives in the Perinatal Guidelines. • Pediatric and adolescent care providers should prepare adolescents for the transition into adult care settings (AIII).
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 postpubertal adolescents.*

Adherence to Antiretroviral Therapy in Children and Adolescents With HIV

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Panel's Recommendations
• Strategies to maximize adherence should be discussed before and/or at initiation of antiretroviral therapy (ART) and before changing regimens (AIII). • Adherence to therapy must be assessed and promoted at each visit, and strategies to maintain and/or improve adherence must be continually explored (AIII). • In addition to viral load monitoring, at least one other method of measuring adherence to ART should be used (AIII). • Once-daily antiretroviral regimens and regimens with a low pill burden should be prescribed whenever feasible (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 postpubertal adolescents*

Management of Medication Toxicity or Intolerance

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Panel's Recommendations
• In children with HIV who have severe or life-threatening toxicity (e.g., a hypersensitivity reaction), all antiretroviral (ARV) drugs should be stopped immediately (AIII). Once symptoms of toxicity have resolved, ARV therapy should be resumed with substitution of a different ARV drug or drugs for the offending agent(s) (AII*). • When modifying ARV therapy because of toxicity or intolerance to a specific drug in children with virologic suppression, changing one drug in a multidrug regimen is permissible; if possible, an agent with a different toxicity and adverse effect profile should be chosen (AI*). • The toxicity and the medication presumed responsible should be documented in the medical record of the patient, and the caregiver and patient should be advised of the drug-related toxicity (AIII). • In general, dose reduction is not a recommended option for management of ARV toxicity (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 postpubertal adolescents*

Management of Children Receiving Antiretroviral Therapy

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Modifying Antiretroviral Regimens in Children With Sustained Virologic Suppression on Antiretroviral Therapy

Panel's Recommendations
• Children who have sustained virologic suppression on their current antiretroviral (ARV) regimen should be evaluated regularly for opportunities to change to a new regimen that facilitates adherence, simplifies administration, increases ARV potency or barrier to drug resistance, and decreases the risk of drug-associated toxicity (AII). • Before changing a patient's ARV regimen, clinicians must carefully consider the patient's previous regimens, past episodes of ARV therapy failure, prior drug-resistance test results, drug cost, and insurance coverage, as well as the patient's ability to tolerate the new drug regimen (AIII). Archived drug resistance can limit the antiviral activity of a new drug regimen. • Children should be monitored carefully after a change in treatment. Viral load measurement is recommended 2 to 4 weeks after a change in a child's ARV regimen (BIII).
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 postpubertal adolescents*

Recognizing and Managing Antiretroviral Treatment Failure

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Panel's Recommendations
• The causes of antiretroviral (ARV) treatment failure—which include poor adherence, drug resistance, poor absorption of medications, inadequate dosing, and drug–drug interactions—should be assessed and addressed (AII). • Perform ARV drug-resistance testing when virologic failure occurs, while the patient is still taking the failing regimen (AI*) (see Drug-Resistance Testing in the Adult and Adolescent Antiretroviral Guidelines for more information). • ARV regimens should be chosen based on treatment history and drug-resistance testing, including both past and current resistance test results (AI*). • The new regimen should include at least two, but preferably three, fully active ARV medications; the assessment of anticipated ARV activity should be based on treatment history and past resistance test results (AII*). • The goal of therapy following treatment failure is to achieve and maintain virologic suppression, which is defined as a plasma viral load that is below the limits of detection as measured by highly sensitive assays with lower limits of quantification of 20 copies/mL to 75 copies/mL (AI*). • When complete virologic suppression cannot be achieved, the goals of therapy are to preserve or restore immunologic function (as measured by CD4 T lymphocyte values), prevent clinical disease progression, and prevent the development of additional drug resistance that could further limit future ARV drug options (AII). • Children who require evaluation and management of treatment failure should be managed by or in collaboration with a pediatric HIV specialist (AI*).
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Antiretroviral Treatment Interruption in Children With HIV

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Panel's Recommendations
• Outside the context of clinical trials, structured interruptions of antiretroviral therapy **are not recommended** for children (AII). • Families should receive education and counseling about common causes of temporary unplanned treatment interruptions and ways to prevent them, e.g., automatic refills, mailed prescriptions, planning for the adequate supply of medications when traveling, etc. (see Adherence to Antiretroviral Therapy in Children and Adolescents With HIV). • At times, ARV therapy may need to be interrupted or changed due to drug-related side effects or toxicity. See Management of Medication Toxicity for guidance.
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 postpubertal adolescents*