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). • 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, have sustained virologic suppression and CD4 count values that are well above the threshold for opportunistic infection risk, and have stable clinical status (AII). Viral load measurement every 3 to 4 months is generally recommended to monitor ART adherence (AIII). • 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). See Drug-Resistance Testing in the Adult and Adolescent Antiretroviral Guidelines. • 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). • 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). • 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*). See Co-Receptor Tropism Assays in the Adult and Adolescent Antiretroviral Guidelines. • 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.
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*

Laboratory monitoring of children with HIV poses unique and challenging issues. In particular, the normal ranges of CD4 T lymphocyte (CD4) cell counts and plasma HIV RNA concentrations (viral loads) can vary significantly by age. The CD4 counts and viral load values that predict the risk of disease progression also change as a child ages. This section will address immunologic, virologic, general laboratory, and clinical monitoring of children with HIV, with information that is relevant to both those who have recently received an HIV diagnosis and those who are receiving antiretroviral therapy (ART).

Clinical and Laboratory Monitoring of Children with HIV

Initial Evaluation of Children Who Recently Received an HIV Diagnosis, or Are Entering or Transferring to a New Care Setting

Children who have recently received an HIV diagnosis should have their CD4 counts and plasma viral loads measured. Children with HIV should have a complete, age-appropriate medical history and physical examination (see Table 6 below). Their growth and development should be evaluated for signs of HIV-associated abnormalities. Testing also should be performed to assess for HIV-associated conditions, including the following:

- Anemia, leukopenia, thrombocytopenia
- Hypoalbuminemia
- Nephropathy (urinalysis)
- Renal insufficiency (creatinine)
- Hyperglycemia
- Hepatic transaminitis

Baseline screening tests for coinfections and opportunistic infections (OIs), including tests for the following, should be performed:

- Tuberculosis, with tuberculin skin test if aged <2 years, or an interferon gamma release assay if aged ≥2 years
- Hepatitis B virus (HBV), with HBV surface antibody, HBV surface antigen, and HBV core antibody tests
- Hepatitis C virus (HCV), with HCV nucleic acid (HCV RNA) testing if aged <18 months or HCV antibody if aged ≥18 months
- Cytomegalovirus (CMV), with CMV antibody tests if aged >12 months

Monitoring for OIs should follow the guidelines that are appropriate for the child's exposure history and clinical setting (see the Pediatric Opportunistic Infection Guidelines). Children with HIV who are relocating from outside the United States may benefit from additional evaluations—such as gastrointestinal parasites, lead level, and thyroid function. See Centers for Disease Control and Prevention International Adoption.[1]

Laboratory confirmation of HIV infection should be obtained when available documentation is incomplete (see Diagnosis of HIV Infection in Infants and Children). Genotypic resistance testing should be performed, even if ART is not initiated immediately. In addition, a full antiretroviral (ARV) drug history should be obtained; this history should include any exposure to

ARV drugs for the prevention of perinatal HIV transmission (see Drug-Resistance Testing in the Adult and Adolescent Antiretroviral Guidelines). HLA-B*5701 testing should be conducted on initial laboratory screening to allow for possible abacavir (ABC) initiation, and an alternative ARV drug should be used if the HLA-B*5701 test result is positive[2] (see the Abacavir section in Appendix A. Pediatric Antiretroviral Drug Information).

Before initiating therapy or making changes to a patient's ARV regimen, a clinician and multidisciplinary team members (where available) should assess potential barriers to adherence and discuss the importance of adherence with the patient and/or their caregiver (see Adherence to Antiretroviral Therapy in Children and Adolescents with HIV).

If a child does not initiate ART after receiving an HIV diagnosis, the child's CD4 count and plasma viral load should be monitored at least every 3 to 4 months.

Evaluation at Initiation of Antiretroviral Therapy

At the time of ART initiation, a physical examination should be performed, including assessment of weight and height, sexual maturity rating, and baseline labs for CD4 count, and plasma viral load should be obtained to monitor ART response (see Table 6 below). To set the baseline for monitoring ART toxicity (see Management of Medication Toxicity or Intolerance), a complete blood count, urinalysis, and serum chemistry panel (including levels of electrolytes, creatinine, glucose, and hepatic transaminases) should be performed (see Table 6 below). The levels of serum lipids (cholesterol and triglycerides) also should be measured. For information about the adverse effects (AEs) associated with a specific ARV drug, see Appendix A. Pediatric Antiretroviral Drug Information for complete information on each drug. Tables 17a–17k in Management of Medication Toxicity or Intolerance provide information about specific toxicities associated with ARV drugs (e.g., osteopenia and osteoporosis, lipodystrophies and weight gain, nephrotoxic effects) and include guidance for prevention, monitoring, and management.

Clinical and Laboratory Monitoring After Initiating or Changing an Antiretroviral Regimen

Children who start ART or who change to a new regimen should be monitored to assess the effectiveness, tolerability, and AEs of the regimen and to evaluate medication adherence. Clinicians and multidisciplinary teams should schedule frequent clinical in-person and/or telemedicine visits to monitor patients closely during the first few months after initiating a new ARV regimen. The first few weeks of ART can be particularly difficult for children and their caregivers; they must adjust their schedules to allow consistent and routine administration of medication doses. Children also may experience the AEs of medications, and both children and their caregivers need assistance to determine whether the effects are temporary and tolerable or more serious or long term, requiring a clinical visit. It is critical that providers communicate with caregivers and children in a supportive, nonjudgmental manner and use plain language. This approach promotes interactive reporting and ensures that providers can have a productive dialogue with both children and their caregivers, particularly in situations where medication adherence is reported to be inconsistent.

Telemedicine visits and telehealth communication platforms are particularly relevant to the care of adolescent patients based on their technology access and habits.[3,4] Additional check-ins via telephone and/or telehealth (emails, text messaging, app-based communications) may support adherence and early identification of medication side effects. The continuity of patient and caregiver interactions is an opportunity for clinicians and the multidisciplinary team to provide support and discuss adherence with patients and their caregivers.

A systematic review of randomized controlled trials from the last 10 years that used a telemedicine approach as a study intervention or assessed telemedicine as a subspecialty of pediatric care found that telemedicine services for the general public and pediatric care are comparable to or better than in-person services.[5] Use of telemedicine as remote, technology-based access to clinical services in HIV care is growing and has been shown to achieve similar outcomes as those associated with in-person care.[6] People with HIV on ART achieve similar clinical responses to therapy, adherence to treatment, quality-of-life scores, and psychological and emotional status, whether treated through telemedicine or in person.[7-9]

When selecting the format for clinical follow-up, it is important to recognize differences and similarities between in-person and telemedicine visits (see Table 4 below). The benefits of telemedicine visits include patient and caregiver convenience, lack of travel, flexibility, and ability to visualize ART handling/swallowing and conduct directly observed therapy in the home setting. Telemedicine visits, however, require technological access and capacity and limit the provider's ability to conduct physical examinations and obtain laboratory testing on site,[6-8] as well as to perform periodic measurements of body weight, which are important for dose modification in rapidly growing infants, and to monitor for excessive weight gain as a possible AE of some ARVs. Cooperative children can be weighed and have their height measured at home if a scale and measuring tape are available, with simple instructions for continuity, or directly observed during a synchronous visit or obtained from a recent pediatric or other specialty in-office visit.[10] Additionally, providers need to arrange and coordinate access to the laboratory testing and be familiar with state and local requirements for carrying out, documenting, and billing telemedicine visits. Although both in-person and telemedicine visits involve considerations for stigma, privacy, and confidentiality, these considerations differ between health care and home/community-based settings. For example, the caregiver who has not disclosed the HIV and ART status of the child at home might prefer in-person visits at the clinic or specific hours and/or alternative locations for a telemedicine visit.

Table 4. Characteristics and Requirements for In-Person Clinic Visits vs. Telemedicine Visits

	In-Person Visits	Telemedicine Visits
Patient/caregiver convenience		✓
Flexibility (time and locations) of appointments		✓
Confidentiality concerns	✓	✓
Directly observed therapy in home settings		✓
Physical assessment (e.g., skin rashes)	✓	✓
Physical exam, including weight and height	✓	✓[a]
Adherence support and counseling	✓	✓
Mental health assessment and counseling	✓	✓
Multidisciplinary support (assessment and coordination of nutritional and social services)	✓	✓
Laboratory testing on site	✓	
Travel to clinic	✓	

Table 4. Characteristics and Requirements for In-Person Clinic Visits vs. Telemedicine Visits

Technology requirements (internet access, equipment, skills)		✓
Legal and administrative guidelines for visit documentation and billing	✓	✓

[a] Cooperative children can be weighed and have their height measured at home if a scale and measuring tape are available, with simple instructions for continuity, or directly observed during a synchronous visit or obtained from a recent pediatric or other specialty in-office visit.

Within 2 Weeks of Initiating Antiretroviral Therapy

Within 2 weeks of initiating ART, children should be evaluated either in person, through telemedicine, or by telephone. During this evaluation, clinicians should identify clinical AEs and provide support for adherence. Many clinicians plan additional contacts (in person, through telemedicine, by telephone, or via email/texts/apps) with children and caregivers to support adherence during the first few weeks of therapy.

Two to 4 Weeks After Initiating Antiretroviral Therapy

Most experts recommend performing laboratory testing at 2 to 4 weeks (but no later than 8 weeks) after initiating ART to assess virologic response and laboratory toxicities, although this recommendation is based on limited data. The laboratory chemistry tests that a patient requires will depend on the ARV regimen that the patient is receiving (see Table 6 below). Plasma viral load monitoring is important as a marker of response to ART because a decline in viral load suggests that the patient is adherent to the regimen, that the appropriate doses are being administered, and that the virus is susceptible to the drugs in the regimen. Some experts favor measuring viral load at 2 weeks to ensure that viral load is declining. A significant decrease in viral load should be observed 4 to 8 weeks after initiation of ART.

Clinical and Laboratory Monitoring for Children Who Are Stable on Long-Term Antiretroviral Therapy

After the initial phase of ART initiation (1–3 months), clinicians should assess a patient's adherence to the regimen and the regimen's effectiveness (as measured by CD4 count and plasma viral load) every 3 to 4 months. Additionally, clinicians should review a patient's history of drug toxicities and evaluate each patient for any new AEs using physical examinations and the relevant laboratory tests. Generally, if laboratory evidence of toxicity is identified, testing should be performed more frequently until the toxicity resolves, but specific management is guided by the degree of toxicity and ARV regimen. Tables 17a–17k in Management of Medication Toxicity or Intolerance provide information about specific toxicities associated with ARV drugs.

Table 6 below provides one proposed general monitoring schedule, which should be adjusted based on the specific ARV regimen that a child is receiving.

A patient's baseline CD4 count affects how rapidly CD4 count improves after ART initiation; children with very low CD4 counts may take longer than 1 year to achieve their highest values after viral load suppression.[11] Studies that have critically evaluated the frequency of laboratory monitoring in both adults and children, particularly CD4 count and plasma viral load, support less frequent monitoring in stable patients who have been consistently virologically suppressed for ≥1 year.[12-18]

The Adult and Adolescent Antiretroviral Guidelines—Laboratory Testing currently supports performing plasma viral load testing every 6 months for individuals who have both—

- Consistent virologic suppression ≥2 years *and*
- CD4 counts that are consistently >300 cells/mm^3.

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV finds value in continuing to perform viral load testing every 3 to 4 months to provide enhanced monitoring of adherence or disease progression among children and adolescents. Some experts monitor CD4 count less frequently (e.g., every 6–12 months) in children and adolescents who are adherent to therapy, who have CD4 count values well above the threshold for OI risk, and who have had sustained virologic suppression and stable clinical status for more than 2 years.[19] Furthermore, some experts monitor viral load more often (with each injection) in adolescents receiving injectable cabotegravir and rilpivirine.[20]

Testing at the Time of Switching Antiretroviral Regimens

When a patient switches regimens to simplify ART, clinicians should obtain the appropriate laboratory test results at baseline for the toxicity profile of the new regimen. Follow-up should include a measurement of plasma viral load at 4 weeks (and not >8 weeks) after the switch to ensure that the new regimen is effective. If the regimen is switched because the regimen is failing (see Recognizing and Managing Antiretroviral Treatment Failure), resistance testing should be performed while a patient is still receiving the failing regimen. This optimizes the chance of identifying resistance mutations, because resistant strains may revert to wild type within a few weeks of stopping ARV drugs (see Drug-Resistance Testing in the Adult and Adolescent Antiretroviral Guidelines). Clinicians should consider performing phenotypic resistance testing, including co-receptor tropism testing, in addition to genotypic viral resistance testing in children who have experienced prolonged or repeated periods of viral nonsuppression on multiple ARV regimens.[21]

Immunologic Monitoring in Children: General Considerations

When interpreting CD4 counts and percentages in children, clinicians must consider age as a factor. CD4 count and percentage values in healthy infants without HIV are considerably higher than values observed in adults without HIV; these infant values slowly decline to adult values by age 5 years (see Table 5 below).[22]

Table 5. CD4 Cell Counts and Percentages in Healthy Children: Distribution by Age

	Age						
	0–3 Months	3–6 Months	6–12 Months	1–2 Years	2–6 Years	6–12 Years	12–18 Years
CD4 cell count[a,b]	2,600 (1,600–4,000)	2,850 (1,800–4,000)	2,670 (1,400–4,300)	2,160 (1,300–3,400)	1,380 (700–2,200)	980 (650–1,500)	840 (530–1,300)
CD4 percentage[a,c]	52 (35–64)	46 (35–56)	46 (31–56)	41 (32–51)	38 (28–47)	37 (31–47)	41 (31–52)

[a] Values presented as median (10th to 90th percentile)

[b] n = 699

[c] n = 709

Source: Shearer WT, Rosenblatt HM, Gelman RS, et al. Lymphocyte subsets in healthy children from birth through 18 years of age: the Pediatric AIDS Clinical Trials Group P1009 study. *J Allergy Clin Immunol.* 2003;112(5):973-980.

The current pediatric HIV disease classification is based on absolute CD4 count, which is the preferred assay for monitoring and estimating the risk for disease progression and OIs[23] (see Table A. HIV Infection Stage Based on Age-Specific CD4 Count or Percentage in Appendix C: CDC Pediatric HIV CD4 Cell Count/Percentage and HIV-Related Diseases Categorization). However, some clinicians find it useful to monitor CD4 percentages because they remain relatively consistent, whereas absolute CD4 counts vary with age and changes in total leukocyte counts. CD4 counts and percentages are best measured when patients are clinically stable, as several factors, including mild intercurrent illness and exercise, can transiently decrease levels.[24] Low CD4 values should be confirmed by a repeat test at least 1 week after the first test to inform clinical decisions.

CD4 count and percentage decline as HIV infection progresses; patients with lower CD4 counts or percentage values have a poorer prognosis than patients with higher values (see Tables A, Table B, and Table C in Appendix D: Supplemental Information). Children with higher baseline CD4 percentages, younger ages (<4 years), or early ART initiation[25] can potentially recover normal CD4 counts, whereas children with severe baseline immune suppression may not achieve normal CD4 levels with ART.[26-28] Although CD4 cells decline as a result of HIV infection, CD8 T lymphocyte (CD8) cells expand soon after infection. In adults with HIV, low CD4/CD8 ratios are a prognostic indicator for serious non-AIDS events.[29] In children with perinatal HIV, the CD4/CD8 ratio inversely correlates with immune activation, senescence, and exhaustion.[29] Some clinicians find CD4/CD8 ratios useful for gauging overall immune dysfunction. Guidelines recommend that all people with HIV receive ART, regardless of their CD4 count and clinical stage. However, CD4 counts are used to determine HIV stage, potential for immunologic recovery, and when to initiate or stop OI prophylaxis (see When to Initiate Antiretroviral Treatment in Children with HIV Infection).

HIV RNA Monitoring in Children: General Considerations

Quantitative HIV RNA assays measure the plasma concentration of HIV RNA as copies/mL. Without therapy, plasma viral load initially rises to peak level during the period of primary infection in adults and adolescents and then declines by as much as 2 to 3 $\log_{10}$ copies to reach a stable lower level (the virologic set point) approximately 6 to 12 months after acute infection.[30,31] In adults with HIV, the virologic set point correlates with the subsequent risk of disease progression or death in the absence of therapy.[32]

The pattern of change in plasma viral load in untreated infants with perinatal HIV differs from that in adults and adolescents with HIV. In the absence of treatment, plasma viral load peaks by age 2 months and remains high until 12 months, and then slowly declines until age 4 to 5 years.[33-34,35] This pattern probably reflects the lower efficiency of a developing immune system in containing viral replication and, possibly, the rapid expansion of HIV-susceptible cells that occurs with somatic growth.[36]

Despite the established association between high plasma viral load and disease progression, a specific HIV RNA concentration has only moderate predictive value for disease progression and death in an individual child.[37] In both children and adults with HIV, CD4 count or percentage and plasma viral load are independent predictors of disease progression and mortality risk, and using the two markers together more accurately defines prognosis.[37-40]

Methodological Considerations When Interpreting and Comparing HIV RNA Assays

Based on accumulated experience with currently available assays, the current definition of virologic suppression is a plasma viral load that is below the quantification limit of the assay used (generally

<20 copies/mL to 75 copies/mL) (see Table 7 below). This definition of suppression has been much more thoroughly investigated in adults with HIV than in children with HIV (see the Adult and Adolescent Antiretroviral Guidelines). Temporary viral load elevations ("blips") are often detected in adults on ART[41] and generally defined as up to 200 copies/mL, but they may be as high as 500 copies/mL in children on ART[42]; these temporary elevations do not represent virologic failure as long as the values have returned to below the level of detection when testing is repeated. For definitions and management of virologic treatment failure, see Recognizing and Managing Antiretroviral Treatment Failure. These definitions of virologic suppression and virologic failure are recommended for clinical use. Research protocols or surveillance programs may use different definitions.

Several different methods can be used for quantitating HIV RNA, each of which has a different level of sensitivity (see Table 7 below). Because different assays use different methods to measure HIV RNA, and because the tests have different levels of sensitivity, clinicians should consistently use a single HIV RNA assay method to monitor an individual patient when possible.[43-45] Moreover, because of biologic variability, only differences >0.7 $\log_{10}$ copies/mL (a fivefold difference) in infants aged <2 years and differences >0.5 $\log_{10}$ copies/mL (a threefold difference) in children aged ≥2 years should be considered as clinically significant plasma viral load changes.

The predominant HIV-1 subtype in the United States is subtype B, and early assays were designed to detect this subtype. Current kit configurations for all companies have been designed to detect and quantitate essentially all viral subtypes (see Diagnosis of HIV Infection in Infants and Children). This ability is important in many regions of the world where non-B subtypes are predominant, as well as in the United States for immigrant and adopted children who are born outside the United States or to non–U.S.-born parents.[43,46-50]

Genetic Testing for Management of HIV

Modern disease intervention strategies often employ genetic testing to evaluate the genes of humans and pathogens. This approach to treatment is an important component in the rise of precision medicine. Clinicians who manage HIV have routinely probed HIV genetic sequences for mutations that are associated with HIV drug resistance. Some ARV drugs are metabolized differently based on specific human genotypes. For example, studies have shown that certain genotypes can affect efavirenz exposure in young children.[51-54] In addition, some human genetic polymorphisms are associated with drug toxicity or AEs (e.g., using HLA-B*5701 testing to predict ABC hypersensitivity)[55]; for more information, see the Abacavir section in Appendix A. Pediatric Antiretroviral Drug Information. Future clinical practice will likely feature broader applications of multiple forms of genetic testing to guide management of health and disease.

Table 6. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy[a]

Laboratory Testing	Entry Into Care[a,b]	ART Initiation[c]	Weeks 1–2 on Therapy	Weeks 2–4 on Therapy	Every 3–4 Months[d]	Every 6–12 Months[d]	Virologic Failure (Prior to Switching ARV Regimens)
Medical History and Physical Examination[e,f]	✓	✓	✓	✓	✓		✓
Adherence Evaluation[f]		✓	✓	✓	✓		✓
CD4 Count[d]	✓	✓			✓	✓	✓
Plasma Viral Load[g]	✓	✓		✓	✓		✓
Resistance Testing	✓						✓
CBC with Differential[d]	✓	✓		✓	✓	✓	✓
Chemistries[d,h]	✓	✓		✓	✓	✓	✓
Lipid Panel[i]	✓	✓				✓	
Random Plasma Glucose[j]		✓				✓	
Urinalysis	✓	✓				✓	
HBV Screening[k]	✓						✓
Pregnancy Test for Youth and Young Adults of Childbearing Potential[l]	✓	✓					✓
HLA-B*5701[m]	✓						
HCV Screening[n]	✓						
TB Screening[o]	✓					✓	
CMV Ab[p]	✓					✓	

[a] See the texts on immunologic, virologic, general laboratory, and clinical monitoring of children with HIV for details on recommended laboratory tests to perform.

[b] If a child does not initiate ART after receiving an HIV diagnosis, the child's CD4 count and plasma viral load should be monitored at least every 3 to 4 months.

[c] If ART is initiated within 30 to 90 days of a pre-therapy laboratory result, repeat testing may not be necessary.

Table 6. Sample Schedule for Clinical and Laboratory Monitoring of Children Before and After Initiation of Antiretroviral Therapy

[d] CD4 count, CBC, and chemistries can be monitored less frequently (every 6–12 months) in children and youth who are adherent to therapy, who have CD4 count values that are well above the threshold for opportunistic infection risk, and who have had sustained virologic suppression and stable clinical status for more than 2 to 3 years. Viral load testing every 3 to 4 months is generally recommended to monitor ARV adherence.

[e] Pay special attention to changes in weight that might occur after altering an ARV regimen. Weight gain or weight loss may occur when using some ARV drugs (see Table 17h. Lipodystrophies and Weight Gain).

[f] Virtual visits may be appropriate at some time points, particularly for adherence assessments and for visits for established patients, see Table 4 above.

[g] Some experts monitor viral load more often (with each injection) in adolescents initiating injectable CAB and RPV. Viral load monitoring should be performed 4 to 8 weeks after a switch to long-acting CAB and RPV. HIV RNA also should be checked in patients with unplanned missed visits and delayed dosing of long-acting CAB and RPV. When viremia develops during long-acting therapy, resistance testing, including integrase resistance testing, should be performed. Follow-up dosing in patients with missed doses should not be delayed while waiting for viral load and resistance test results. However, regimen changes should be prompted if resistance to CAB and/or RPV is discovered (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression in the Adult and Adolescent Antiretroviral Guidelines).

[h] Chemistries refer to a comprehensive metabolic panel. Some experts perform a comprehensive panel at entry and routinely test Cr, ALT, AST, with additional tests tailored to the history of the individual patient.

[i] If lipid levels have been abnormal in the past, more frequent monitoring may be needed. For patients treated with TDF, more frequent urinalysis should be considered.

[j] Random plasma glucose is collected in a gray-top blood collection tube or other designated tube. Some experts would consider monitoring HgbA1C, rather than routine blood glucose, in children at risk for prediabetes/diabetes.

[k] Baseline HBV screening is recommended with HBsAb, HBsAg, and HBcAb. HBV screening is also recommended for individuals who have previously demonstrated no immunity to HBV and who are initiating a regimen that contains ARV drugs with activity against HBV, specifically 3TC, FTC, TAF, or TDF.

[l] See the Prepregnancy Counseling and Care for Persons of Childbearing Age with HIV in the Perinatal Guidelines.

[m] Conduct HLA-B*5701 on entry or prior to initiating ABC if not done previously. Choose an alternative ARV drug if the patient is HLA-B*5701 positive (see the Abacavir section in Appendix A: Pediatric Antiretroviral Drug Information).

[n] Baseline hepatitis C screening is recommended with HCV nucleic acid (HCV RNA) testing if aged <18 months or Hepatitis C antibody if aged ≥18 months. If HCV testing is positive, refer to the Infectious Diseases Society of America HCV in Children guidelines for management.

[o] TB screening is recommended at baseline and annually with tuberculin skin test if aged <2 years or interferon gamma release assay if aged ≥2 years (see *Mycobacterium tuberculosis* in the Pediatric Opportunistic Infection Guidelines).

[p] CMV antibody testing is recommended at age 1 year (or at baseline evaluation if aged >1 year at initial visit) and then annually for CMV-seronegative infants and children with HIV who are immunosuppressed (i.e., CD4 count <100 cells/mm^3 or CD4 percentage <10%) (see Cytomegalovirus in the Pediatric Opportunistic Infection Guidelines).

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; CAB = cabotegravir; CBC = complete blood count; CD4 = CD4 T lymphocyte; CMV = cytomegalovirus; Cr = creatinine; FTC = emtricitabine; HBV = hepatitis B virus; HBsAb = HBV surface antibody; HBsAg = HBV surface antigen; HBcAb = HBV core antibody; HCV = hepatitis C virus; HgbA1C = glycosylated hemoglobin; RPV = rilpivirine; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate

Table 7. Primary Food and Drug Administration–Approved Assays for Monitoring Viral Load

Assay	Abbott Real Time	NucliSens EasyQ v2.0	COBAS AmpliPrep/ TaqMan v2.0	Versant v1.0	Aptima HIV-1 Quant Assay
Method	Real-time RT-PCR	Real-time NASBA	Real-time RT-PCR	Real-time RT-PCR	Real-time TMA
Dynamic Range	40–10^7 copies/mL	25–10^7 copies/mL	20–10^7 copies/mL	37–11×10^7 copies/mL	30–10^7 copies/mL
Specimen Volume[a]	0.2–1 mL	0.1–1 mL	1 mL	0.5 mL	≥0.4 mL
Manufacturer	Abbott Laboratories	bioMérieux	Roche	Siemens	Hologic, Inc.

[a] Laboratories often request large blood volumes for standard viral load testing. Consider contacting the local laboratory to determine minimum blood volume required to run the assay. Smaller volumes for children can be accommodated.

Key: NASBA = nucleic acid sequence–based amplification; RT-PCR = reverse transcription-polymerase chain reaction; TMA = transcription-mediated amplification

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