

The Pediatric Clinical Manual

The International Center for AIDS Programs

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Introduction

The International Center for AIDS Care and Treatment Programs at Columbia University's Mailman School of Public Health (ICAP) supports programs designed to promote wellness and to improve health care for HIV-infected individuals and families around the world. By providing a continuum of services, from patient education to HIV-specific treatment, programs such as the MTCT-Plus Initiative and the Multicountry Columbia Antiretroviral Program (MCAP) support the provision of high quality family-focused care for HIV-infected adults and children.

Unfortunately, as access to ART increases, treatment of pediatric HIV/AIDS has not always been prioritized. Despite the challenges, high-quality care for HIV-infected children can be effectively provided in resource-limited settings. We strongly support access to care and treatment for children, which should be part of every HIV/AIDS treatment program.

Children enrolled in ICAP programs have access to regular clinical and laboratory assessments, diagnostic testing, nutritional support, prophylaxis and management of opportunistic infections, and antiretroviral treatment (ART). Multidisciplinary teams empower families through psychosocial assistance, patient education, peer outreach programs, and counseling, adapted by sites to meet the needs of specific cultural environments. The programs also support community outreach and education, and work to build linkages to local organizations and resources.

ICAP sites are located in a wide range of settings, from urban to rural, across many countries and cultures. As programs are adapted to national and local guidelines, program specifics may vary accordingly. All sites, however, receive the support required to enable them to provide the basic set of clinical services outlined in this manual. Standardized clinical protocols facilitate procurement of drugs and supplies, development of education and training interventions, and collection of outcomes and quality assurance data. The shared protocols also enable sites to deliver uniformly excellent care.

The ICAP Pediatric Clinical Manual provides an overview of essential pediatric services, implementation recommendations, clinical guidelines, and treatment algorithms. It is complemented by *The Columbia Clinical Manual*, which includes similar guidelines for adults. These are intended to enhance rather than to replace the judgment and expertise of health care workers, and to add to the clinical support tools developed by others.

We anticipate that HIV care and management protocols will evolve over time. Both *The ICAP Pediatric Clinical Manual* and *The Columbia Clinical Manual* are updated regularly, available in print and electronic versions, and are formatted to accommodate frequent changes. Suggestions, comments, and corrections are encouraged.

Family Care Coordination

What is family care coordination?

Family care coordination (FCC) is an approach to the care of patients with complex needs, for whom integrated medical and supportive services are critically important. Evaluation, communication, and advocacy are hallmarks of FCC, which also encourages providers to consider the needs of all family members, appreciating that children's needs are linked to those of their family and community.

Why is family care coordination important?

Experience caring for people with HIV/AIDS has shown that coordination of medical and supportive services and communication among providers optimizes patient health and well being. Different members of the care team have different "pieces of the puzzle." Regular and organized communication among providers can put the pieces together to identify barriers to wellness and to formulate a patient- and family-centered plan of action. This, in turn, promotes better care, supports adherence, and empowers patients. When multiple family members participate in a care program, their ability to support one another is enhanced.

- *Family care coordination describes communication between caretakers of an individual patient.* For example, a counselor may know that a child's mother has returned to work and that the child is now being watched by an aunt during the day. A clinician may know that the child's illness has progressed. Only by sharing this information can they realize that the child has been missing doses of medication while staying with her aunt. And only by discussing this with the family can they develop a strategy to help.
- *Family care coordination describes communication between caretakers of different family members.* For example, a pediatrician may know that a child is failing to thrive, while another clinician may know that the mother has newly-diagnosed tuberculosis; a community outreach worker may know that the mother is too ill to work in the garden and the family is short of food. When the providers meet to discuss the family, they can put all the information together to develop a support plan for both mother and child.

Who should be involved in family care coordination?

There are many successful care models, but all involve the multidisciplinary cooperation of providers of clinical and supportive services. A team approach is recommended; one in which staff providing medical, counseling, outreach

and social services meet periodically – often weekly – to discuss specific patients (see below).

Multidisciplinary teamwork may be new in some settings, particularly those in which a traditional hierarchical model separates cadres and discourages equal partnerships between physicians and other providers of care. It is important to recognize that the contributions of all members of the team are equally valuable and that non-medical staff (counselors, peer educators, community outreach workers, etc.) have access to critically important information that nurses and doctors do not. We note that multidisciplinary care for patients with HIV/AIDS has been successfully introduced and enthusiastically adopted in widely varied settings throughout the world.

How should family care coordination be provided?

At its heart, FCC is patient-oriented and family-focused. When done well, it is comprehensive, collaborative, and efficient. FCC includes:

- Initial assessment of a patient's needs with careful attention to the family setting, social supports, and potential barriers to care
- Development of a care plan for the patient and family
- Regular communication among the providers of care of different family members (with the patients' permission)
- Coordination of the services required to implement the plan
- Patient monitoring to assess the effectiveness of the plan
- Periodic re-evaluation and revision of the plan as necessary

How should team meetings be conducted?

Weekly multidisciplinary team meetings are an ideal way to communicate, exchange information, and develop and monitor a care plan. Although it may initially be difficult to set aside time for such meetings, they clearly save time in the long run by optimizing communication and efficiency. It is important for clinicians (physicians, nurses, and medical officers) and non-clinicians (outreach workers, counselors, pharmacists, and health educators) to attend these meetings. These groups are most effective when a team leader, often a nurse, counselor, or social worker, plans the weekly patient list and agenda, distributes it to the team in advance, and chairs the meeting.

A common strategy is to discuss a subset of the patients each week (one-fourth, for example) as well as any patients with urgent or emergent issues. Each patient on the list is discussed, a brief update provided, and key issues highlighted. Input is solicited from the team, and the team leader confirms and records action items for the week. Notes are taken and become part of the patient record. Often a specific team member is assigned to follow up on the plan, ensuring that the interventions discussed take place. This structure allows ongoing monitoring and evaluation of care plans, permits team members to share information efficiently, and strengthens multidisciplinary collaboration and camaraderie.

Diagnosing HIV Infection in Infants and Children

While the diagnosis of HIV in adults is relatively straightforward, establishing the HIV infection status of an infant or young child is more complex. Specialized tests, not available in all resource-limited settings, are required to determine whether or not a baby has been infected with HIV. Additional diagnostic challenges arise when children of HIV-infected mothers are breast fed. This chapter reviews pediatric HIV diagnosis in resource-limited settings and outlines the diagnostic approach recommended by ICAP.

Diagnostic Challenges:

- **Transmission of HIV from mother to child**

Pediatric HIV infection can occur during pregnancy, during labor and delivery, and throughout the duration of breast feeding. This fact is essential to remember when developing diagnostic algorithms, particularly as it may take several months for a child infected via breast milk to develop detectable levels of HIV antibody. As a rule, it is prudent to wait at least three months after cessation of breast feeding before using antibody tests to determine whether a baby has HIV.

- **Maternal HIV antibodies**

The HIV antibody is passively transmitted across the placenta during pregnancy, and all babies born to HIV-infected women will test HIV antibody positive at birth. However, the HIV virus itself is not always transmitted and only some babies become infected. The likelihood that a baby will get the virus is dependent upon a number of factors, including the health of the mother, the use of pMTCT prophylaxis, the mode of delivery, and other issues discussed in more detail in *The Columbia Clinical Manual's* chapter on pregnancy and HIV.

At a minimum, maternal antibody is present in the baby's blood for the first six months of life. Sometime after six months, levels of maternal HIV antibody fade, and most babies who are not infected test negative for the HIV antibody by 12 months of life. Occasionally, it takes HIV-uninfected children as long as 18 months to lose maternal antibody. In contrast, babies who are infected with HIV produce their own HIV antibody, and their antibody tests remain positive for life. Any child 18 months or older with a positive HIV antibody test is infected with HIV.

HIV antibody testing can be used to exclude HIV infection as long as the child ceased breast feeding at least three months prior to the test. A child who has

not breast fed for the past three months and whose HIV antibody test is negative is not infected with HIV.

While it would, therefore, be theoretically possible to defer pediatric diagnosis until 18 months of age and use the standard HIV antibody test, this approach is clinically unwise. HIV disease may progress very rapidly in infants – mortality at two years approaches 50 percent if HIV is not treated. Early identification and treatment of pediatric HIV disease can have a dramatic impact on outcome, and should be a priority whenever possible.

In summary:

- ✓ A positive HIV antibody test in a child of 18 months or older means the child *is* infected with HIV.
- ✓ A positive HIV antibody test in a child of less than 18 months does not help to distinguish the HIV-infected child from the HIV-uninfected child.
- ✓ A negative HIV antibody test three or more months after the cessation of breast feeding (or in a child who has never breast-fed) means that the child is *not* infected with HIV.
- ✓ A negative HIV antibody test in a child who is still breast feeding, or who recently stopped breast feeding is insufficient to exclude HIV infection. The test must be repeated at least three months after breast feeding ceases.

● **Virologic testing**

In contrast to HIV antibody tests, specialized virologic tests can differentiate the infected baby from the uninfected baby during the first months of life. HIV DNA polymerase chain reaction (PCR) and HIV RNA PCR are two different tests that detect HIV in blood; either test can be used to diagnose HIV infection in infants. Of note, these tests are relatively expensive and technically more demanding than antibody testing; they are not available in all resource-limited settings. Other virologic diagnostic tests are under development (for example, immune complex dissociated p24), but are not yet commercially available.

While virologic tests offer a clear diagnostic advantage, it is important to time their use correctly. Twenty to forty percent of perinatally-infected babies (those infected during pregnancy, or labor and delivery) will test HIV positive by HIV DNA or RNA PCR *at birth*, and the majority will test positive by *14 days* of life. However, as many as ten percent of HIV-infected children, may not have detectable HIV DNA or RNA until *six weeks* after birth.

The sensitivity and specificity of virologic tests is generally excellent. False positive tests can occur, particularly in laboratories inexperienced with the use of PCR, and all positive tests should be confirmed on a repeat specimen. Low levels of HIV RNA (<10,000 copies/ml), are particularly likely to be false positives, as infants usually have very high levels. False negative tests can

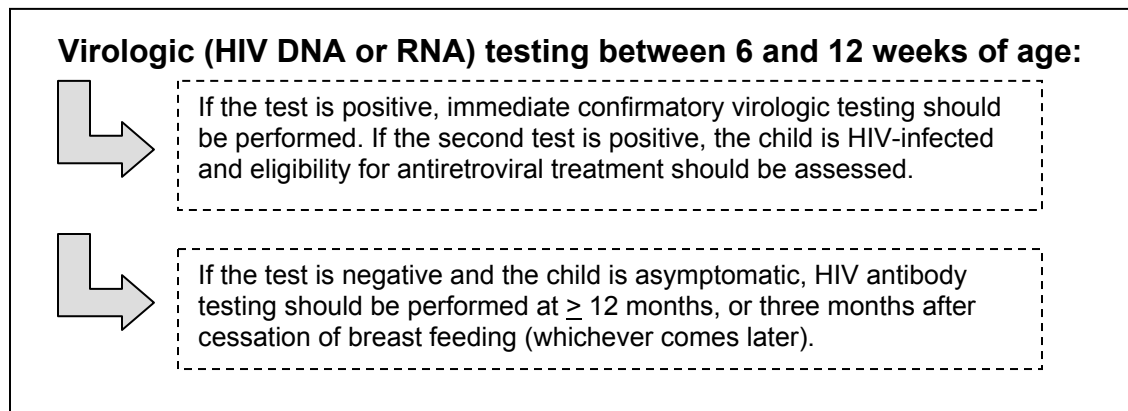
also occur. Although studies have shown that, in some laboratories, a single negative virologic test done after the first month of life has sufficient negative predictive value to exclude HIV infection in a non-breast feeding infant, laboratory capabilities around the world vary widely. In most settings, two virologic tests after one month of age are required to confirm that a child is not HIV-infected.

Recommended Diagnostic Algorithms

Taking these considerations into account, we recommend the following diagnostic algorithm, developed for settings where access to virologic testing is limited and breast feeding is common. In this context, the most appropriate use of virologic testing is to provide early identification of HIV-infected children. Thus, **our goal is to permit early identification of the HIV-infected child i.e. to find HIV-infected babies who need care and treatment rather than to confirm the absence of HIV infection in HIV-exposed, uninfected babies.** These protocols have been designed for breast-feeding infants; they can be adapted to settings where children receive exclusive replacement feeding (see Figure 2).

The first step in ICAP diagnostic protocols is a virologic test (HIV DNA or RNA PCR) at six to twelve weeks of life. If this test is positive, it should immediately be repeated on a second specimen. Two positive virologic tests indicate that the child is infected with HIV; guidelines for the care of HIV-infected children can be found in Chapters 6.3 and 6.4.

Figure 1: Early virologic testing



While a positive test (if confirmed) indicates that the infant is HIV-infected, a single negative virologic test does not provide definitive evidence of a child's HIV status, as noted above. It does, however, indicate that the infant is not at high risk of HIV progression and infants whose early virologic test is negative and who remain asymptomatic can simply receive HIV antibody testing once breast feeding has ceased (≥ 3 months later) and they are ≥ 12 months of

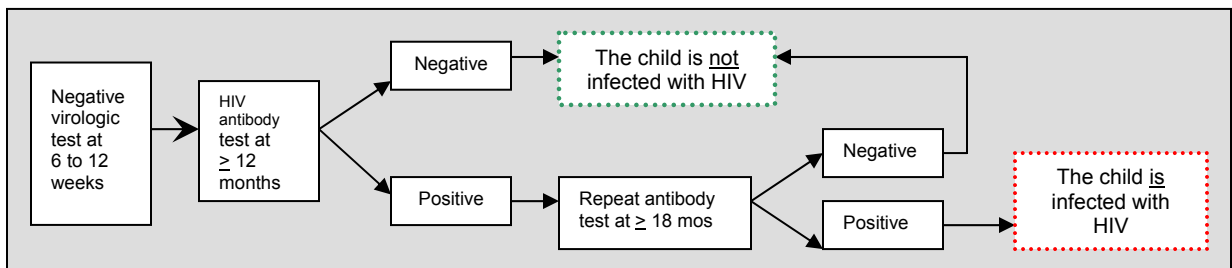
age. In contrast, a child with symptoms of HIV whose initial virologic test is negative will require further diagnostic testing.

Asymptomatic infants:

The decision regarding when to perform an antibody test on an asymptomatic child whose initial early virologic test was negative is directly related to whether and for how long the child breast feeds (see Appendix A). As the majority of children lose maternal antibody by 12 months of age, an antibody test can generally be done at this point – unless the child has breast fed within the previous three months. A negative test in a 12-month old child who has not breast fed in at least three months indicates that the child is *not* infected with HIV. A positive antibody test in this setting, however, may simply mean that maternal antibodies persist. In this case, the antibody test should be repeated at 18 months, at which point a positive test is the result of indigenous antibody production and indicates that the child is HIV-infected.

In an asymptomatic breast-feeding child, HIV antibody testing can generally be deferred until three months after breast feeding has stopped. While a negative test indicates that the baby is not infected, the interpretation of a positive test will, again, depend on the child’s age. A positive test in a child younger than 18 months should be repeated at 18 months of age.

Figure 2: Asymptomatic children, initial negative virologic test, not breast feeding



Symptomatic infants:

If a child whose early virologic test is negative has symptoms or illnesses consistent with HIV infection, it is unwise to wait months before definitively establishing his or her HIV status. Although symptoms of HIV/AIDS overlap with those of other common childhood diseases and efforts should be made to exclude other diagnoses, repeat virologic testing with HIV DNA or RNA is recommended if HIV infection is suspected. As noted, any positive test should immediately be repeated on a second specimen. If the repeat test is negative and an explanation for the child’s symptoms cannot be found, consultation with an expert in pediatric HIV disease is recommended where available.

In summary:

- ✓ Infants with negative initial virologic test results who cease breast feeding by 9 months of age should have an HIV antibody test at ≥ 12 months.

- ✓ Infants with negative initial virologic test results who continue to breast feed beyond 9 months of age should have an HIV antibody test ≥ 3 months after breast feeding ceases.
- ✓ Infants with a negative initial virologic test result who are symptomatic or have illnesses consistent with HIV infection should have a repeat virologic test.
- ✓ Positive virologic tests should be repeated immediately to confirm infection.

Common Clinical Scenarios:

- Example 1: Negative early virologic test in an asymptomatic infant
 In a healthy asymptomatic baby, a single negative early diagnostic test is a reassuring result. It indicates that the child does not have detectable virus in his/her blood, and that s/he is unlikely to have been infected with HIV during pregnancy and delivery. The child remains at risk for acquiring HIV through breast feeding. If s/he remains healthy, cotrimoxazole prophylaxis should be prescribed, the pediatric follow-up schedule described in Chapter 6.2 should be followed, and HIV antibody testing should be performed once breast feeding ceases (≥ 3 months later) and s/he is ≥ 12 months of age.
 - ✓ If the child ceases breast feeding by 9 months (or if the child is not breast fed), antibody testing should be performed at 12 months of age, as outlined in Figure 2 and Appendix A.
 - ✓ If the child continues to breast feed, antibody testing should be performed three months after breast feeding ceases. If, at this time, the antibody test is negative, the child is not infected with HIV. If the test is positive and the child is 18 months of age or greater, the child is infected with HIV. If the test is positive, and the child is < 18 months of age, the test should be repeated at 18 months, as outlined in Appendix A.
- Example 2: Negative early virologic test in a symptomatic infant
 If a child whose virologic test was negative at 6-12 weeks subsequently develops symptoms consistent with HIV infection, efforts should be made to exclude other diagnoses, and repeat virologic testing with HIV DNA or RNA should be performed if HIV infection is suspected. (All positive tests should be confirmed on a second specimen). As above, if the repeat test is negative and an explanation for the child's symptoms cannot be found, consultation with an expert in pediatric HIV disease is recommended where available.
- Example 3: Positive early virologic test with a positive confirmatory test
 In this instance, the infant has had an initial virologic test between 6 and 12 weeks of life. The test has been repeated on a second specimen, and the second virologic test is also positive. This infant should be considered to be HIV infected, whether or not the baby has symptoms of HIV. Care of the HIV-infected child is described in Chapters 6.3, and 6.4.

- Example 4: Discordant tests
On rare occasions, a child will have an initial positive virologic test which, when repeated, is negative. The simplest explanation is that an error has occurred in the handling or labeling of the specimen, the laboratory test itself, or the reporting of results. The first step, therefore, should be a review of the specimen label and laboratory report form, if available. If no obvious laboratory error can be found, three types of data can assist providers to determine the child's HIV status: the child's clinical condition, repeat virologic testing, and CD4 enumeration. Consultation with an expert in pediatric HIV disease is recommended in such circumstances.

Frequently Asked Questions:

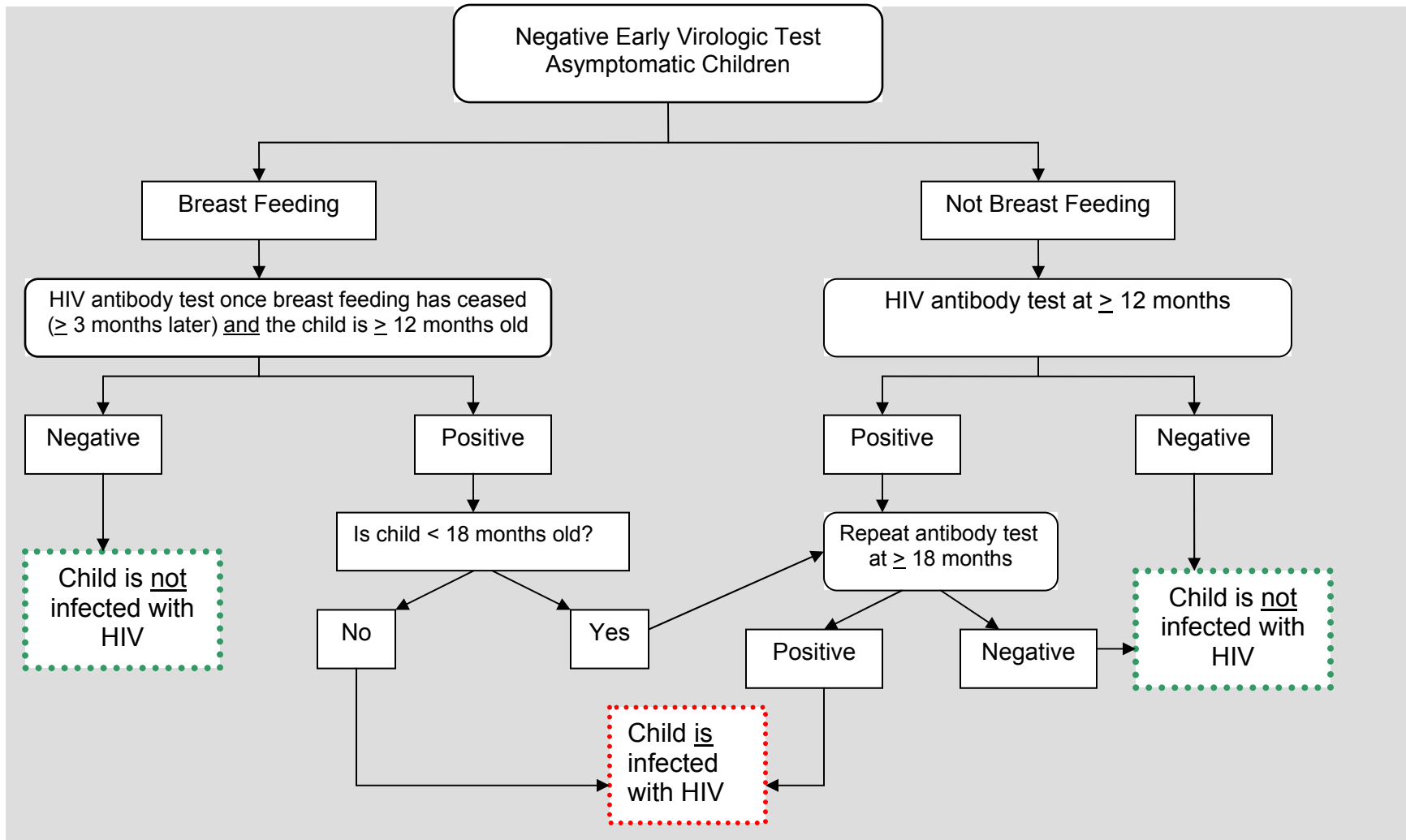
- *Is it always necessary to have two positive tests in order to be confident that a baby has HIV infection?*
ICAP recommends repeat testing to confirm all positive virologic tests. However, in a child with AIDS, advanced clinical findings, and/or evidence of immune suppression (low CD4 number or percent), a single positive test is adequate to support clinical decision making and the assessment of eligibility for antiretroviral treatment. While sending a confirmatory test in this circumstance may still be prudent, treatment should not be delayed.
- *When are you sure a child is HIV infected?*
 - ✓ In a child 18 months of age or older, a positive HIV antibody test indicates that the child is HIV infected.
 - ✓ In a child younger than 18 months, any of the following criteria indicate that they are HIV infected:
 - 2 positive virologic tests or
 - 1 positive virologic test and
 - evidence of immune deficiency (low CD4 count or percent)¹ and/or
 - symptoms and/or illnesses consistent with HIV infection
- *When are you sure a child is not HIV infected?*
 - ✓ In an asymptomatic child of any age who has not breast fed for three months (or who never breast fed), one negative HIV antibody test indicates that s/he is HIV-negative.
- *In settings where virologic testing is unavailable, how should the diagnosis of HIV in infants and young children be approached?*
 - ✓ A definitive diagnosis of HIV infection in an infant or young child cannot be made without virologic testing. All babies born to HIV-infected women should be followed closely and monitored for clinical evidence of HIV infection. In settings where virologic testing is unavailable, CD4 testing should be done at 6-12 weeks of age in lieu of virologic testing. A

¹ e.g. CD4 percent < 20%

combination of clinical symptoms/diagnoses and CD4% can be used to support the diagnosis of HIV infection. Low CD4% and severe symptoms, particularly poor growth, are highly suggestive of HIV disease. Any child less than 18 months of age who meets criteria for WHO stage II or III HIV disease and has a CD4 < 20% should be considered HIV infected and eligible for antiretroviral therapy. For children not meeting these criteria, close clinical follow-up is necessary. CD4 testing can be repeated in the event of new or progressive symptoms.

- *In settings where neither virologic nor CD4 testing are available, how should the diagnosis of HIV in infants and young children be approached?*
 - ✓ In settings where CD4 testing is not available, total lymphocyte count (TLC) can be used in conjunction with clinical symptoms to support the diagnosis of HIV infection in an infant or young child. Any child < 18 months of age who meets criteria for WHO stage II or III and has a TLC < 3500 should be considered HIV infected and eligible for antiretroviral therapy.

Appendix A: Diagnostic Algorithms for Asymptomatic Children Whose Early (6-12 week) Virologic Test is Negative



Appendix B: Talking to Parents about Pediatric Diagnosis

Parents and caretakers of HIV-exposed infants are understandably anxious about the health of their children. Most are worried that their child has or will have HIV infection. Given the complexity of the subject, it can be very difficult to explain the issues around infant diagnosis to parents and caretakers. However, a number of steps can be taken to help them better understand the situation.

1. Begin talking about infant diagnosis as early as possible, preferably during the antenatal period or the first pediatric appointment.
2. Let parents know that it can take many months, often as long as 18 months, to be sure that the child doesn't have HIV infection.
3. Prepare them for early diagnostic testing by letting them know that the child will have a blood test during the first months of life (6-12 weeks) that will help to see if the virus is in the baby's blood.
 - If the early diagnostic test is negative, parents can be reassured that the virus can't be found so far. It may still be there, but this is a good sign. As long as s/he stays healthy, the baby will be tested again when s/he is older (>12 months).
 - If the early diagnostic test is positive, parents will need to be told that the child is likely to have HIV infection. The test will be repeated to make sure it is correct and other tests will be done to evaluate the baby's health status. It can be reassuring for parents to learn that care and treatment will be available to the child now and in the future.
4. Speaking openly with parents at each visit can be very helpful. Eliciting and addressing their questions and concerns can mitigate their anxiety. Telling them about the baby's progress and highlighting positive findings (good growth, normal examination) can also be reassuring.
5. Prepare parents of infants with initial negative virologic testing for HIV antibody testing at >12 months. Since babies determined to be uninfected are discharged from ICAP programs, parents should also begin to consider alternate options for pediatric follow-up.

Care of the HIV-Exposed Infant

When a woman with HIV becomes pregnant, her infant is at risk of infection *in utero*, during labor and delivery, and throughout the duration of breast feeding. Although the majority of children born to women with HIV disease are not infected with HIV themselves, discriminating HIV-infected from HIV-uninfected babies is challenging. As described in Chapter 2, it may take a year or more to definitively establish whether or not a child has been infected with HIV. When following ICAP diagnostic algorithms, a small group of babies will be found to have HIV in the first three months of life via early virologic testing. HIV infection may be excluded early in a few children who are not breast feeding. But the majority of infants will fall into a third category – one in which HIV infection has neither been definitively established nor completely excluded.

Because pediatric HIV disease can progress very rapidly, both HIV-infected babies and those whose HIV status has yet to be determined require special care and attention during the first years of life. This chapter will focus on the care of the HIV-exposed infant, including the recommended schedule and types of assessments and guidelines for prophylaxis against *Pneumocystis* pneumonia (PCP). Recommendations for the treatment of children known to be HIV-infected can be found in Chapters 4 and 5.

Care of the HIV-exposed infant centers around three basic goals:

- **Identifying the HIV-infected child:** Comprehensive assessments, frequent monitoring, and special diagnostic testing will help distinguish which HIV-exposed infants are HIV-infected (see Chapter 2).
- **Preventing opportunistic infections:** All HIV-exposed infants should receive prophylactic cotrimoxazole to prevent *Pneumocystis* pneumonia (PCP). Tuberculin skin testing and isoniazid preventive therapy can reduce the risk of tuberculosis; these are discussed in Chapter 4.
- **Maximizing family health and well being:** Enhanced health care services for infants born to women in ICAP programs can lead to improved health outcomes for both HIV-infected and HIV-exposed, uninfected children.

Identifying the HIV-infected child

In resource-limited settings, it is difficult to distinguish the infected from the uninfected child during the first year of life. As described in Chapter 2, HIV antibody is passively transmitted from an infected mother to her child. Since all HIV-exposed infants test HIV antibody positive, special virologic testing is necessary to discern HIV infection status. In addition, babies who breast feed

remain at risk throughout the period of lactation, further complicating the goal of learning which HIV-exposed children have been infected with HIV.

Since the laboratory diagnosis of HIV infection in infants is complex, close clinical monitoring and assessment are essential. HIV-infected infants, particularly those who are infected during pregnancy, labor or delivery, have a very high rate of disease progression; without treatment, half will die by their second birthday. Poor growth and/or abnormal physical findings such as lymphadenopathy or organomegaly may be the first signs of HIV disease. Delayed acquisition of developmental milestones and abnormal neurologic findings also suggest HIV infection. Clinical vigilance and frequent monitoring will help identify the infected infant as early in life as possible.

Clinical Assessment of the HIV-exposed Infant

HIV-exposed infants should be seen frequently during the first six months of life. Because HIV disease progression can be very rapid during this time, a baby who appears well at two months may have many abnormal findings when examined a month later. Monthly visits during this period are prudent (see Figure 1). Each visit should include a *history, physical examination*, the provision of *PCP prophylaxis*, and an *assessment and plan*.

Taking the History

A comprehensive birth history should be obtained during the first evaluation of the HIV-exposed infant. Many factors influence the risk of mother to child transmission, including pMTCT regimen, maternal health status, and mode of delivery. Information about the mother's health, medical history, and use of pMTCT prophylaxis may help identify infants at higher risk for infection.

Table 1: The Birth History

✓ Birth weight	✓ Maternal ART use
✓ Mode of delivery	✓ Infant ART use
✓ Maternal health (WHO stage, CD4 count)	✓ Neonatal complications

The parent or caregiver is often keenly sensitive to the child's health status and can provide vital information. A history should be obtained at all follow-up visits. Several key questions should be asked *each time* the child is seen:

- Has the child been ill?
- How is the child eating?
- What new milestones has the child gained?
- Are there any new parental concerns?
- Has anyone in the household been diagnosed with or developed symptoms of tuberculosis?

Ongoing assessment of nutrition and growth is essential, and is discussed at greater length in Chapter 7. Mothers should be asked about frequency, duration, and adequacy of supply for infants who are breast fed. Details of preparation and volume of feeds should be reviewed when formula is used.

Developmental assessment should be performed at regular intervals. Delayed acquisition of normal developmental milestones or loss of previously acquired skills can be the first sign of HIV encephalopathy. Simple questions should assess four critical developmental domains: cognitive, motor, language, and social. Much of the assessment will be done through observation during the physical examination. However, asking questions like “Does the baby smile at you?” or “Is she rolling over now?” will provide important information and will actively engage the parent or caregiver. Parents relish the opportunity to talk about their child’s new accomplishments. Use of the developmental checklist in Table 2 (or a similar list of age-appropriate milestones) may be helpful.

Table 2: The Developmental Checklist

1 month: raises head, crawling movement, alerts to sound
2 months: head midline, lifts chest off table, smiles socially
4 months: rolls front to back, laughs
6 months: sits unsupported, babbles
9 months: pulls to stand, says “mama”
12 months: walks alone, knows two words

Parents and caregivers are usually keenly alert to the health of their child and often are the first to identify changing or failing health. Asking simple and direct questions of the caretaker may offer insight into the health status of the child. Parents of HIV-exposed infants may also have great anxiety about their child’s health. Addressing these concerns is a fundamental aspect of each visit.

Examining the HIV-exposed Infant

When HIV-exposed but uninfected infants are compared to HIV-infected infants, differences in weight and height are detectable within the first months of life. Careful monitoring of growth is an essential part of each medical encounter since weight gain can be a sensitive indicator of changes in health status. Weight, height, and head circumference should be measured at each visit and plotted on growth curves. Chapter 7 describes the importance and use of growth charts and the evaluation of children with poor growth.

The physical examination should include the usual components of pediatric care with special attention to stigmata of HIV infection. In addition to poor growth, oral candida, rashes, and lymphadenopathy are common findings for infants with HIV infection.

Prevention of *Pneumocystis pneumonia*

PCP is a severe and rapidly progressive pneumonia with a fatality rate of 40 to 90 percent. HIV infected infants are at very high risk for this infection. It

generally occurs between three to six months of life, often as the first sign of HIV infection and before the child is definitively determined to be HIV-infected. In resource-rich settings, prophylaxis of all HIV-exposed infants with trimethoprim/sulfamethoxazole (TMP/SMX) has led to a dramatic reduction in PCP in infants. ICAP programs provide TMP/SMX for all infants beginning at four weeks of age. Therapy should be continued through the first year of life for all infants. For ease of administration, once daily therapy of TMP/SMX at a dose of 4mg/kg is recommended.

Table 3: Dosing recommendations for PCP prophylaxis

TMP/SMX 4 mg/kg daily		
Infant's weight in kilograms	Amount of 8mg/ml suspension	Tablet 80mg TMP/400mg SMZ
3.0 – 4.9 kg	2 ml daily	
5.0 – 6.9 kg	3 ml daily	
7.0 – 9.9 kg	4 ml daily	½ single-strength tab
10.0 – 11.9 kg	5 ml daily	½ single-strength tab
12.0 – 14.9 kg	7 ml daily	1 single-strength tab

TMP/SMX is generally well tolerated in infants. Rash and fever are rare but reported side effects. Bone marrow suppression can be seen as well, most commonly in HIV-infected children receiving multiple medications. Dapsone can be dispensed to children (>1 month of age) intolerant to TMP/SMX. The appropriate dose is 2mg/kg/day with a maximum of 100mg/day.

In settings where replacement feeding (formula) is widely available and where women can safely choose not to breast feed, local guidelines may suggest discontinuing PCP prophylaxis in asymptomatic infants with negative early virologic diagnostic testing results. In these circumstances it is recommended that PCP prophylaxis stop at four or more months of age with continued monitoring until the child's infection status is conclusively determined through HIV antibody testing after one year of age.

Assessment and Plan

Each visit should conclude with an assessment of the child's health, including his/her likely HIV infection status. Reviewing the following points will be helpful:

- What is the child's HIV status?
 - known to be HIV-infected;
 - known to be HIV-uninfected; or
 - unknown HIV status
- Are there clinical and/or laboratory findings suggestive of HIV infection?
- Does the child have any new problems?
- Does the child require any laboratory studies?
- Has the child received the proper vaccinations? Are any new ones due?
- When should the child return for the next visit?

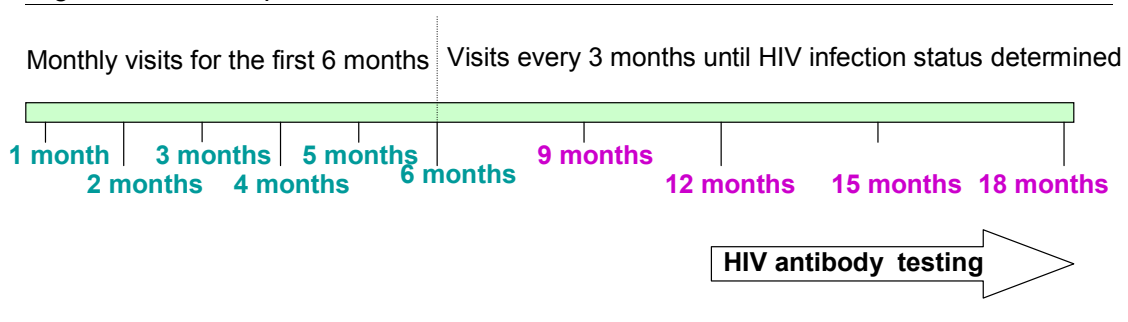
Early diagnostic testing for HIV infection is recommended between 6 and 12 weeks of age as described in Chapter 2. Laboratory results and findings from

the history and physical examination should enable the clinician to make a reasonable determination of the child's infection status. New exam findings may require additional testing for HIV or other medical problems.

ICAP programs support the coordination of HIV-specific and routine pediatric care. This model enhances follow-up by decreasing the burden of visits to other pediatric providers, and by increasing maternal familiarity with the program during pediatric visits. Immunizations, for example, can be administered at the initial and follow-up visits, according to national guidelines.

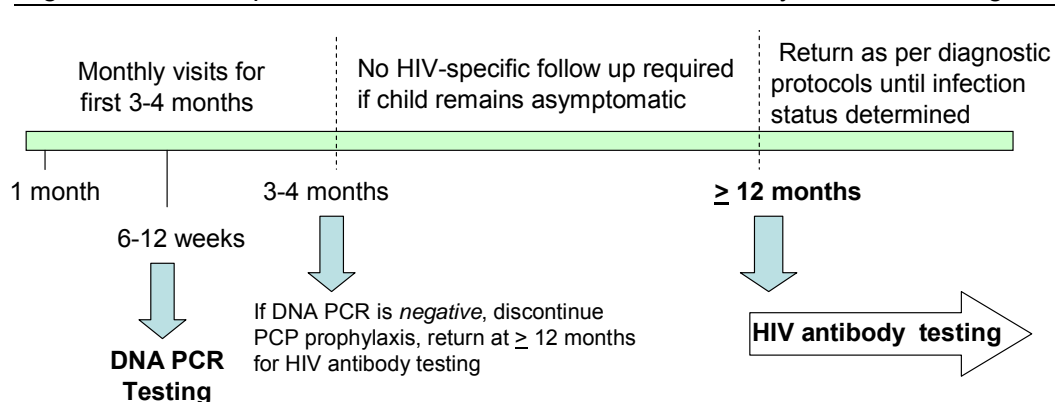
HIV-exposed infants should be seen frequently during the first six months of life while the risk of HIV disease progression is greatest. Visits every three months thereafter are recommended until the child is definitively determined not to have HIV infection (see Figure 1).

Figure 1: Follow-up schedule for breast-fed infants



Infants who receive exclusive replacement feeding (formula) starting at the time of birth are not at risk for acquiring HIV infection beyond the perinatal period. If alternatives for routine pediatric care are available for these children, follow-up can be abbreviated for clinically well children with negative early virologic testing. It is recommended that children return for care after a year of age to document HIV infection status with antibody testing (see Figure 2).

Figure 2: Follow-up schedule for infants who are exclusively formula feeding



Maximizing family health and well being

While the birth of a baby is a joyful event, knowing that the child is at risk for HIV infection brings fear and anxiety. Families will benefit from the open and honest exchange of information about the child's health status. The use of simple language to explain the difference between exposure to HIV and HIV infection can help parents and caregivers grapple with complex scientific concepts. Repeating information at each visit can be helpful to ensure comprehension. Families may also greatly benefit from psychosocial support during this period of uncertainty.

Care of an infant always requires an understanding of the family and social context. Exchange of information with members of the multidisciplinary team can provide important information about the care of the child. For example:

- ✓ The clinician has prescribed daily TMP/SMX, and believes that the child is receiving the medicine daily. A counselor, however, may learn that for several days each week, the baby stays with his aunt, who does not know his HIV status. On these days, he is not given TMP/SMX.
- ✓ The clinician taking care of a baby may note a period of poor growth, and fear that it is due to HIV. The clinician taking care of the adults in the family, however, may know that the baby's father has lost his job, and that the family has limited resources for food.

Thus, ongoing communication between multidisciplinary team members and between adult and pediatric providers can inform the care of each member of the family.

Ongoing care and treatment for HIV-exposed and HIV-infected babies will likely result in decreased morbidity and mortality for this high risk group. Similarly, engaging their parents in care and providing treatment as needed will decrease the burden of disease, prevent orphanage, and keep families healthy, reversing the devastating effects of the HIV epidemic during the last several decades.

Care of the HIV-Infected Child

The goals of care for the HIV-infected child are to promote health and prevent disease progression. This is best accomplished by integrating HIV services and primary health care, addressing the ordinary threats to the health and well being of infants and children while at the same time attending to the special circumstances of HIV infection. A multidisciplinary, family-focused model of care has been shown to be effective for engaging children and their families in the long term care and management of HIV disease.

Several chapters in this manual are devoted to the care of the HIV-infected child. This chapter will review the general approach to and management of the HIV infected child. Chapter 5 describes pediatric antiretroviral treatment and Chapter 6 focuses on the particular issues around adherence to antiretroviral treatment. Pediatric nutrition and the evaluation and management of poor growth are addressed in Chapter 7. The challenging subject of disclosure of HIV status to children is reviewed in Chapter 8.

Background

HIV disease progression in infants and young children is rapid compared to adults. Although disease manifestations vary considerably from child to child, most babies develop HIV-related symptoms by 12 months of age, and half of children infected during pregnancy or labor/delivery will die by their second birthday. The most common symptoms of HIV/AIDS during infancy include poor growth, recurrent infections (particularly pneumonia), and severe diarrhea. *Pneumocystis pneumonia* (PCP) and HIV-related encephalopathy are common diagnoses in early childhood. Children who survive the first years of life often have evidence of poor growth and suffer from recurrent infections. Lymphoid interstitial pneumonitis (LIP), a chronic pneumonia that can cause respiratory insufficiency, is not uncommon in older children. Tuberculosis is frequently seen in HIV-infected children and is associated with significant morbidity and mortality.

Because care of HIV-infected children is complex and it is critically important to prevent disease progression, ICAP has developed guidelines for pediatric care and treatment. These algorithms represent a minimum 'backbone' of care on which to build the specialized systems required to address the needs of infants and children with HIV. As always, guidelines are not meant to replace the judgment and expertise of individual clinicians.

HIV care for children includes intensive clinical and immunologic monitoring, provision of prophylaxis against PCP, nutritional assessment and management, assessment and management of disease manifestations and, when necessary, antiretroviral treatment. In addition, attention to the psychosocial and emotional needs of children as they age and develop is critical to the success of any pediatric program. Every pediatric evaluation should include a history, physical examination, appropriate laboratory testing, HIV staging, assessment for eligibility for PCP prophylaxis and antiretroviral treatment, and an assessment and plan. Each component of the evaluation is discussed below.

History – Learning the Story

Initial History

Most children enrolled in ICAP programs will be infants whose infection status is identified through early diagnostic testing (see Chapter 2). However, older children with established HIV infection will also be enrolled in care. While clinicians will be familiar with the medical history of those they have followed from birth, a comprehensive initial history will facilitate the development of a clinical profile for older children entering the program.

The initial evaluation of the older child should include a review of the birth history including the use of antiretroviral drugs for perinatal prophylaxis, if any. Similarly, once a baby is determined to be infected, the birth history should be reviewed.

Birth History	
✓	Birth weight
✓	Mode of delivery
✓	Maternal health status (CD4, WHO stage)
✓	Maternal ART
✓	Infant ART
✓	Neonatal complications

The initial history should also include a review of past medical history including HIV-related hospitalizations, illnesses, and medications. Previous and/or current antiretroviral treatment, exposure to TB vaccines (e.g. BCG), tuberculosis treatment and prophylaxis for opportunistic infections should be recorded. Developmental history is also crucial to include, as HIV infection

frequently affects the central nervous system and can cause neurologic manifestations, developmental delays, and cognitive as well as motor disabilities.

Interim History

A history should be obtained at each follow-up visit. This will help the clinician to determine if there have been changes in the child's health status or changes in the home setting that may affect the child's health. Asking the parent or caretaker open ended questions like "how is the baby doing?" or "is s/he having any new medical problems?" can be helpful to target the evaluation. In addition, the symptom checklist should be reviewed at each visit (see Figure 1). The interim history should also assess the child's diet with attention to adequacy of caloric intake as well as the availability of adequate food resources within the household. If the child is receiving medications, information about the dosage,

frequency and adherence should be recorded. Providers should also ask about the health of family and household members, and should enquire whether anyone in the household has been diagnosed with or developed symptoms of tuberculosis since the child’s last visit.

Figure 1: Symptom Checklist

Sign or Symptom	Yes	Sign or Symptom	Yes
Cough	<input type="radio"/>	Pain – muscles	<input type="radio"/>
Depression	<input type="radio"/>	Pain – legs/feet	<input type="radio"/>
Diarrhea	<input type="radio"/>	Pain – other	<input type="radio"/>
Difficulty breathing, shortness of breath	<input type="radio"/>	Poor appetite	<input type="radio"/>
Fatigue	<input type="radio"/>	Rash	<input type="radio"/>
Fever	<input type="radio"/>	Thrush	<input type="radio"/>
Headache	<input type="radio"/>	Visual problems (new)	<input type="radio"/>
Memory problems	<input type="radio"/>	Weakness	<input type="radio"/>
Nausea and/or vomiting	<input type="radio"/>	Weight loss, failure to thrive	<input type="radio"/>
Night sweats	<input type="radio"/>	Other 1 (specify):	<input type="radio"/>
Numbness or tingling in legs and/or feet	<input type="radio"/>	Other 2 (specify):	<input type="radio"/>
Pain - abdominal	<input type="radio"/>	Other 3 (specify):	<input type="radio"/>

The history should always include an assessment of the child’s development. Normal expectations of childhood include the acquisition of new developmental milestones as the child ages. Delayed acquisition of milestones or loss of previously acquired skills can be the first sign of HIV encephalopathy. Simple questions should assess four critical developmental domains: cognitive, motor, language, and social. Much of the assessment will be done through observation during the physical examination. However, asking questions like “Is the child walking?” or “Does s/he have any words?” will provide important information – as well as actively engage the parent or caregiver. Parents enjoy the opportunity to talk about their child’s new accomplishments. Use of the developmental checklist in Table 1, or a similar list of age-appropriate milestones can be helpful.

Table 1: Developmental Checklist

<i>1 month</i>	Raises head, makes crawling movements, alerts to sound
<i>2 months</i>	Holds head at midline, lifts chest off table, smiles socially
<i>4 months</i>	Rolls front to back, laughs
<i>6 months</i>	Sits unsupported, babbles
<i>9 months</i>	Pulls to stand, says “mama”
<i>12 months</i>	Walks alone, uses two words together
<i>18 months</i>	Can remove garment of clothing, scribble, use 6 words, run
<i>24 months</i>	Can wash hands, jump up, combine words
<i>36 months</i>	Can put on shirt, speech is understandable, can balance on one foot
<i>48 months</i>	Can dress alone, draw a person, use complex speech (adjectives, prepositions), hop

For children in school, it is essential to discuss and monitor the child’s academic progress. Frequent absences secondary to illness may interfere with academic success. Early signs of neurological involvement may also manifest as learning problems or difficulties with attention to and retention of information.

Examining the Child

Each visit should include an assessment of growth. Weight, length, and head circumference for children less than 2 years of age should be measured at each visit and plotted on age-appropriate growth curves. The height and weight of older children should be recorded and charted regularly. Growth is a very sensitive indicator of disease severity: weight loss or inadequate weight gain can be the first indication of HIV disease progression and are criteria for initiation of antiretroviral treatment. Chapter 7 is devoted to pediatric growth and nutrition.

The initial physical examination should be comprehensive, including a full evaluation of all organ systems. Subsequent exams can be guided by findings on the symptom checklist, but should also focus on the identification of HIV-related stigmata, particularly oral thrush, lymphadenopathy, organomegaly, and dermatitis.

Laboratory Evaluation, Immunologic Staging, and Laboratory Monitoring

Once the diagnosis of HIV infection has been confirmed, a complete blood count and CD4 lymphocyte subsets (count and percent) should be obtained. CD4 cell count and percentage will provide an assessment of the child's level of immune suppression. In healthy children, the normal CD4 count is age dependent. It is generally very high in infants (3000 – 4000 cells/ μ l) and decreases with age, until approximately six years of life when it approaches adult values. A similar trend occurs for CD4 cell percentage. Therefore, when CD4 cell count/percentage is measured, the degree of immune suppression should be evaluated in the context of the child's age.

CD4 cell *percentage* is generally considered to be a more reliable and stable value than CD4 cell *number*. It is less subject to variation in measurement or changes associated with rapid elevation of white blood cell count during acute illnesses. CD4 cell number and percentage have been shown to be predictive of disease progression in children greater than one year of life. ICAP programs use CD4 cell percentage to determine eligibility for antiretroviral treatment as described below.

Immunologic staging of HIV disease should be performed using the Center for Disease Control and Prevention (CDC) classification system.² Taking into account current age and CD4 number/percentage, children's immune systems can be classified as normal (1), moderately (2), or severely (3) suppressed. This system provides a simple way to track changes in CD4 and to account for these changes relative to age-adjusted normal values. For example, a six year old with a CD4 cell count of 580 cells/ μ l would be considered to have normal immune function while a baby with the same value would be classified as severely

² CDC. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43 (no. RR-12):1-10.

immune compromised. Like adults, children over six years of age with a CD4 cell count less than 200 cells/ μ l are classified as severely suppressed.

Table 2: Age-adjusted Immune Categories

Age	< 12 months	1-5 years	6-12 years
Immune category			
1 No evidence of suppression	$\geq 1,500$ cells/ μ l ≥ 25 %	$\geq 1,000$ cells/ μ l ≥ 25 %	≥ 500 cells/ μ l ≥ 25 %
2 Moderate suppression	750-1,499 cells/ μ l 15-24 %	500-999 cells/ μ l 15-24 %	200-499 cells/ μ l 15-24 %
3 Severe suppression	< 750 cells/ μ l < 15 %	< 500 cells/ μ l < 15 %	< 200cells/ μ l < 15 %

Children with HIV infection are frequently anemic and may benefit from vitamin and mineral supplementation. ICAP programs provide multivitamins for all children in care. Total white blood cell count may also be low in children with HIV. In adults, total lymphocyte count (TLC) has been shown to be correlated with CD4 cell count and can be used in its stead when CD4 cannot be measured. Less data are available in children.

The complete blood count and CD4 cell number and percent should be measured at regular intervals for all HIV infected children according to the following schedule. Because of the rapidity of disease progression in young infants, CD4 cell number and percent are monitored more frequently during the first months of life:

- ✓ At the time of diagnosis
- ✓ Every two months during the first six months of life
- ✓ Every three months from 6-18 months of age
- ✓ Every six months for children > 18 months of age

These intervals represent the minimum immunologic monitoring that should be performed. New symptoms or other changes in a child's clinical condition may motivate additional CD4 lymphocyte subset testing.

Clinical Staging

Two staging systems, developed by WHO and CDC, are currently used to categorize the clinical manifestations of pediatric HIV infection (Appendix A and B). Each has advantages and disadvantages. The WHO system classifies children into three stages (I, II, and III) representing progressively more severe disease and worsening prognosis. The WHO system is easy to use and is dependent upon clinical findings and diagnoses rather than laboratory testing; it is well suited for settings with limited diagnostic capabilities. In its simplicity, however, the system does not always account for the wide variety of disease

manifestations seen in pediatric HIV infection thus making it difficult to classify some children. The clinical classification system developed by the CDC to be used in conjunction with the immune categories described above, also aims to classify children by severity of disease manifestations and includes a broad list of diagnoses. In contrast to the WHO system, diagnostic criteria are very precise but often dependent upon laboratory diagnoses. Furthermore, these criteria were developed by experts from the US and Europe and some manifestations commonly seen in less resourced settings are not included.

Each ICAP program should choose one classification system, (WHO or CDC), and then consistently use it for every child at every pediatric visit. This will enhance familiarity with the system, and clinicians will develop facility with classifying and describing children by standardized disease stage or category.

Note that these clinical staging systems categorize individuals by their most advanced clinical indicator. Because staging is based on past *history* of illness as well as current illness, an individual's stage can advance, but not improve. (The child's condition, of course, can improve, even if his/her stage remains the same). Thus, a child with an AIDS-defining opportunistic infection will always be WHO category III and CDC category C, even if s/he makes a complete recovery. A baby with failure to thrive meets criteria for WHO category II – and will be classified as such (WHO II) even after a successful intervention results in weight gain. Thus, when evaluating an older child for the first time, history of prior illness is a critically important staging consideration.

Prophylaxis of Opportunistic Infections

PCP Pneumonia

As noted in Chapter 3, *Pneumocystis* pneumonia (PCP) can occur during the first months of life and is often fatal in young infants. Not infrequently, PCP occurs before the infection status of the HIV-exposed infant is determined. Because PCP is so dangerous and prophylaxis so effective, guidelines suggest that *all* HIV-exposed infants, not just those known to be HIV-infected, receive cotrimoxazole prophylaxis. In resource-rich settings, this strategy has led to a dramatic reduction in the incidence of PCP.

ICAP programs provide cotrimoxazole for all infants starting at four weeks of age. Therapy should be continued through the first year of life for all infants, and the following guidelines should be followed:

- All children known to be HIV-infected should receive cotrimoxazole until at least 12 months of age.
- Continuation of PCP prophylaxis beyond one year of life is based upon the child's age and immunologic status. HIV-infected children and those whose HIV status has not yet been determined should be given cotrimoxazole if they meet the following criteria:

- ✓ All children < 12 months
- ✓ Ages 1–5 years: CD4 < 15% or CD4+ < 500
- ✓ Ages 6–11 years: CD4 < 15% or CD4+ < 200
- ✓ All children previously diagnosed with PCP. If ARV treatment produces immune reconstitution, discontinuation of prophylaxis can be considered if normal immune function is sustained.

In circumstances where CD4+ monitoring cannot be done, all children who meet criteria for WHO stage II or III, or CDC category B or C should receive PCP prophylaxis.

As indicated in Chapter 3, cotrimoxazole (trimethoprim-sulfamethoxazole, TMP/SMZ), 4mg/kg, should be administered once daily. While alternate regimens and dosing schedules have been widely used, this regimen is recommended for ICAP program participants.

Table 3: Dosing recommendations for PCP prophylaxis

TMP/SMX 4 mg/kg daily		
Infant's weight in kilograms	Amount of 8mg/ml suspension	Tablet (single-strength) 80mg TMP/400mg SMZ
3.0 – 4.9 kg	2 ml daily	
5.0 – 6.9 kg	3 ml daily	
7.0 – 9.9 kg	4 ml daily	½ tab
10.0 – 11.9 kg	5 ml daily	½ tab
12.0 – 14.9 kg	7 ml daily	1 single-strength tab
15 – 16.9 kg	8 ml daily	1 single-strength tab
17 – 19.9 kg	9 ml daily	1 single-strength tab
20 – 24.9 kg	11 ml daily	1 single-strength tab
25 – 29.9 kg	14 ml daily	2 single-strength tabs*
30 – 34.9 kg	17 ml daily	2 single-strength tabs*
≥ 35 kg	20 ml daily	2 single-strength tabs*

*One double strength tab (160mgTMP/800SMZ) can be substituted for 2 single strength tabs.

The most common side effects of co-trimoxazole are rash and bone marrow suppression. Co-trimoxazole can also contribute to hepatic dysfunction particularly when administered with other hepatotoxic drugs. It is generally well tolerated in children, though those with advanced HIV disease are often most likely to develop toxicities. Dapsone can be dispensed to children (>1 month of age) who are intolerant to cotrimoxazole. The appropriate dose is 2mg/kg/day with a maximum dose of 100mg/day.

Tuberculosis

Tuberculosis is the most common opportunistic infection in HIV-infected individuals as well as the leading cause of death. One third of HIV/AIDS-related deaths worldwide are attributed to TB, and children with HIV are particularly vulnerable. The risk of disease progression appears to be greater compared to adults, and children are more likely to suffer severe complications including

meningitis and miliary TB. Prompt diagnosis and correct treatment of HIV-associated TB disease are critically important, and reviewed in *The Columbia Clinical Manual*. In addition, the use of preventive therapy to treat *latent* tuberculosis infection can prevent tuberculosis disease in children as well as adults.

The diagnosis of both latent TB infection and active TB disease in HIV-infected children is challenging. Tuberculin skin testing (TST) is an effective way to identify children with latent tuberculosis infection. Two issues have been raised with respect to the use of TST in this context:

- Most children at ICAP program sites are vaccinated with BCG, which can lead to positive TST testing in children who do not have tuberculosis. Nonetheless, several studies have shown that TST is useful for the diagnosis of latent TB in children who have received BCG and that a positive TST is strongly associated with TB exposure. In Ghana, infants and young children < 5 years old were five times as likely to test TST positive if they lived in a household with an adult with active TB compared with children in households without a sick adult. And, despite the fact that all of the children in the study had received BCG, the number of children who tested TST positive from households without an adult with TB was very low.
- The TST result can be affected by the immune suppression due to HIV infection. Thus, TST results can be negative in children with HIV infection even in the presence of active tuberculosis, as the immune response necessary to result in a positive TST can be impaired secondary to the immune dysfunction caused by HIV infection.

ICAP programs support the use of routine tuberculin skin testing in HIV-infected children for the purposes of identifying and treating children with latent TB infection. The use of isoniazid (INH) for treatment of latent TB significantly decreases the rate of active tuberculosis in TST-positive adults with HIV infection. Although there are few studies in infants and children, the success of this strategy in adults and the serious threat of TB disease in HIV-infected children support its extension to a pediatric population.

ICAP recommends annual tuberculin skin testing (TST) using PPD (5 units) in HIV-infected children to identify those eligible for isoniazid (INH) treatment (“prophylaxis”) of latent tuberculosis infection, LBTI.

- TST should be placed annually starting at 12 months of age (or at the time of diagnosis for older children) for all HIV-infected children. TST should not be placed in those who previously tested TST positive, received INH prophylaxis or were previously treated for TB.

If TST positive (\geq 5mm):

- Exclude active TB as per local and national guidelines and then
- Provide INH (10–15mg/kg, maximum 300mg) daily for nine months (with pyridoxine as per local guidelines).
- INH should also be given to all children under the age of three years who are in contact with an adult diagnosed with active tuberculosis disease.

- INH prophylaxis should also be considered for *any* child with known contact with an active case of TB disease.
- INH should *not* be given to children who have previously received INH prophylaxis, were previously treated for TB, have contraindications to INH or who are suspected to have active tuberculosis.

Vaccination

Comprehensive care for infants and children includes immunization. HIV-infected children may have limited responses to immunizations, especially if there is significant immune compromise. However, most vaccines are routinely given to children with HIV and few complications have been reported. Children enrolled in ICAP programs should be immunized according to local/country guidelines. Immunizations can be provided during follow-up visits for children of all ages. In some settings, vaccines may be provided in other venues, for instance at local child health stations. Vaccine type and date of administration should then be documented in program records. Documentation of immunizations should be sought for older children enrolling in the program, and missing or undocumented vaccines should be administered and recorded.

Assessing Eligibility for Antiretroviral Treatment

Antiretroviral treatment (ART) is a crucial component of care for the HIV-infected child, and is discussed at length in Chapter 5. The decision to begin antiretroviral treatment is complex and requires consideration of both biomedical and psychosocial factors. HIV-infected children should be assessed at each visit to see if they meet treatment eligibility criteria. Eligibility criteria take into consideration the child's age, clinical status and level of immune suppression:

Infants (1–12 months):

- Failure-to-thrive (no weight gain or weight loss or z score < -2) OR
- Advanced symptomatic disease (WHO stage II, CDC category B) OR
- AIDS-defining illness (WHO III, CDC C) OR
- Any child with CD4% <20

Children (> 1 year):

- Failure-to-thrive (no weight gain or weight loss or z score < -2) OR
- Advanced symptomatic disease (WHO stage II, CDC category B) OR
- AIDS-defining illness (WHO III, CDC C) OR
- Any child with CD4% <15 (CDC category 3) *see below

In an asymptomatic child ≥ 6 years of age, the clinician may consider waiting until the CD4 reaches 10%, or until there is evidence of rapid immune deterioration. In the absence of data, some argue that the difficulties of maintaining adherence in an asymptomatic child and the potential toxicities of antiretroviral use outweigh the benefits of earlier treatment. If treatment is postponed in this setting, we recommend more frequent monitoring of CD4 counts/% (every three to four months).

ICAP recommends that children meeting any of the above criteria be prepared for initiation of ART. These recommendations are not intended to supplant the clinical judgment of the child's providers, but to present a framework within which to weigh the risks and benefits of treatment.

Concluding the Evaluation: Assessment and Follow-up Plan

Each visit should conclude with an assessment of the child's health status. It may be helpful to review a number of key questions as a way to synthesize information obtained during the evaluation:

- Does the child have any new findings on history or physical examination?
- Are there any acute problems that require immediate evaluation or treatment?
- Is there evidence of HIV disease progression?
- Does the child meet criteria for a more advanced WHO stage/ CDC category?
- Are there any new laboratory studies from the last visit to review?
- Is the child due for CD4+ testing today?
- Is the child eligible for PCP prophylaxis?
- Is the child eligible for isoniazid for treatment of latent TB infection?
- Is the child eligible for ARV treatment?
- Does the child or family need any referrals?
- When is the next visit?

The follow-up schedule will be determined by the child's age, clinical stage and immune status. Infants and young babies should be seen frequently when the risk of disease progression is greatest.

Table 4: Follow-up Schedule for HIV-infected Infants and Children

Age	Visit Interval
0-6 months	Monthly
6-24 months	Every 3 months
> 24 months	
Symptomatic	Every 3 months
Asymptomatic	Every 6 months
Receiving ART	Weekly for 8 weeks, then monthly

ICAP program participants should also have access to care between regularly scheduled visits. Parents and caregivers must have a way to contact a member of the team if the child falls ill between visits. This will allow them to seek advice and arrange to bring the child in for evaluation, if needed. Enabling families to obtain both routine and urgent care within the same program will enhance the overall management of the child's disease.

Care of the HIV-infected child includes attention to the psychological and social needs of the child and his/her family. Children may benefit from a variety of services including individual and group counseling, peer support, and socialization activities. Developmental and educational assessments as well as educational remediation may also be warranted for some children. While all of

these services may not be available within the context of ICAP programs, the multidisciplinary team should be sensitive to these potential needs and be aware of resources within the community where appropriate services can be obtained.

Talking with Parents and Caregivers

Few families are accustomed to or prepared for the rigor and commitment of caring for a child with HIV infection. The development of a trusting relationship between the HIV/AIDS care team and the child's parents or caretakers is critical to the engagement of families in long-term care. Speaking openly and honestly about the child's health, using simple language and terms, and including the parents/caretakers in the decision making process are all ways to enhance the relationship between the care team and the family. The topic of pediatric disclosure – telling a child that s/he is HIV-positive – is discussed at length in Chapter 8.

Parents are experts about their children and their insights and concerns can provide valuable information about the health of the child. They are also likely to carry many anxieties and fears. Taking time to address their questions and worries at each visit will build trust and respect. The care of the child is a partnership between the clinician, the parents, and the child, particularly as s/he ages. Recognition of this relationship and respectful support of the crucial role of the child and his/her caregivers will support successful engagement in care and treatment.

Care and Treatment of Adolescents

Adolescents will enroll in most, if not all, ICAP programs. It is appropriate for pregnant and postpartum teens to receive care with other adults according to adult guidelines. For other teens, their age and developmental status may better determine the site of care. When performing clinical staging and determining eligibility for ART, adult guidelines should be used for children over the age of 13 (see *The Columbia Clinical Manual*). Dosing of medications, however, is best determined by physical maturity rather than age. For young teens, dosing of medications should follow pediatric guidelines until Tanner V staging³ has been reached, at which time adult dosing guidelines can be used.

Independent of setting, the care of teens often requires special expertise and a careful consideration of the complex needs of young people as they enter adulthood. An understanding of developmental needs, emerging sexuality, the role of the individual within the household, the presence of supportive relationships, and the special considerations of maintaining adherence will facilitate successful engagement of adolescents in a strong therapeutic relationship.

³ Tanner V staging: adult distribution of pubic hair, adult size penis/testes or mature breast (nipple elevated, areola contour continuous with breast).

Appendix A: CDC Staging for Infants and Children

CDC categories based on age-specific CD4+ counts and % of total lymphocytes

Age	<12 mos	1-5 yrs	6-12 yrs
Immunologic category	uL (%)	uL (%)	uL (%)
1: No evidence of suppression	≥ 1,500 (≥ 25%)	≥1,000 (≥ 25%)	≥ 500 (≥ 25%)
2: Evidence of moderate suppression	750-1,499 (15-24%)	500-999 (15-24%)	200-499 (15-24%)
3: Severe suppression	< 750 (<15%)	< 500 (<15%)	< 200 (<15%)

CDC clinical categories

CATEGORY N: NOT SYMPTOMATIC

Children who have no signs or symptoms considered to be the result of HIV infection or who have only one of the conditions listed in Category A.

CATEGORY A: MILDLY SYMPTOMATIC

Children with two or more of the conditions listed below but none of the conditions listed in Categories B and C.

- Lymphadenopathy (≥ 0.5 cm at more than two sites; bilateral = one site)
- Hepatomegaly
- Splenomegaly
- Dermatitis
- Parotitis
- Recurrent or persistent upper respiratory infection, sinusitis, or otitis media

CATEGORY B: MODERATELY SYMPTOMATIC

Children who have symptomatic conditions other than those listed for Category A or C that are attributed to HIV infection. Examples of conditions in clinical Category B include but are not limited to:

- Anemia (<8 gm/dL), neutropenia (<1,000/mm³), or thrombocytopenia (<100,000/mm³) persisting ≥ 30 days
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Candidiasis, oropharyngeal (thrush), persisting (>2 months) in children >6 months of age
- Cardiomyopathy
- Cytomegalovirus infection, with onset before 1 month of age
- Diarrhea, recurrent or chronic
- Hepatitis
- Herpes simplex virus (HSV) stomatitis, recurrent (more than two episodes within 1 year)
- HSV bronchitis, pneumonitis, or esophagitis with onset before 1 month of age
- Herpes zoster (shingles) involving at least two distinct episodes or more than one dermatome
- Leiomyosarcoma
- Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
- Nephropathy
- Nocardiosis
- Persistent fever (lasting >1 month)
- Toxoplasmosis, onset before 1 month of age
- Varicella, disseminated (complicated chickenpox)

CATEGORY C: SEVERELY SYMPTOMATIC

Conditions included in clinical Category C for children infected with human immunodeficiency virus (HIV)

- Serious bacterial infections, multiple or recurrent (i.e., any combination of at least two culture-confirmed infections within a 2-year period), of the following types: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and indwelling catheter-related infections)
- Candidiasis, esophageal or pulmonary (bronchi, trachea, lungs)
- Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis or isosporiasis with diarrhea persisting >1 month
- Cytomegalovirus disease with onset of symptoms at age >1 month (at a site other than liver, spleen, or lymph nodes)
- Encephalopathy (at least one of the following progressive findings present for at least 2 months in the absence of a concurrent illness other than HIV infection that could explain the findings): a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychological tests; b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerized tomography or magnetic resonance imaging (serial imaging is required for children <2 years of age); c) acquired symmetric motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbance
- Herpes simplex virus infection causing a mucocutaneous ulcer that persists for >1 month; or bronchitis, pneumonitis, or esophagitis for any duration affecting a child >1 month of age
- Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
- Kaposi's sarcoma
- Lymphoma, primary, in brain
- Lymphoma, small, noncleaved cell (Burkitt's), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
- Mycobacterium tuberculosis, disseminated or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)
- Pneumocystis carinii pneumonia
- Progressive multifocal leukoencephalopathy
- Salmonella (nontyphoid) septicemia, recurrent
- Toxoplasmosis of the brain with onset at >1 month of age
- Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings: a) persistent weight loss >10% of baseline OR b) downward crossing of at least two of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child \geq 1 year of age OR c) <5th percentile on weight-for-height chart on two consecutive measurements, \geq 30 days apart PLUS a) chronic diarrhea (i.e., at least two loose stools per day for >30 days) OR b) documented fever (for \geq 30 days, intermittent or constant)

Appendix B: WHO Staging for Infants and Children*

WHO Clinical Stage I	WHO Clinical Stage II	WHO Clinical Stage III
<ul style="list-style-type: none"> • Asymptomatic • Generalized lymphadenopathy 	<ul style="list-style-type: none"> • Unexplained chronic diarrhea • Severe persistent or recurrent candidiasis outside the neonatal period • Weight loss or failure to thrive • Persistent fever • Recurrent severe bacterial infections 	<ul style="list-style-type: none"> • AIDS-defining opportunistic infection • Severe failure to thrive • Progressive encephalopathy • Malignancy • Recurrent septicaemia or meningitis

* use locally modified staging where appropriate

Antiretroviral Treatment for Infants and Children

The use of highly active antiretroviral treatment (ART) has dramatically reduced HIV-associated mortality and morbidity among children and adolescents in resource-rich settings. In settings where ART is available, pediatric HIV has been transformed from a debilitating and rapidly fatal infection of early childhood to a manageable chronic disease, and many children with perinatal HIV infection are aging into adolescence and early adulthood.

Although ART for children has immense benefits, enhancing health and prolonging life, the medications are not always easy to use. In addition to the potential for toxicity and viral resistance recognized in adults, there are special issues to consider when prescribing ART to pediatric patients. These include the complexity of pediatric dosing and formulation, the critical role of the caregiver-child relationship, and the need to pay special attention to the developmental stage of the child in care.

Unfortunately, as access to ART increases, treatment of pediatric HIV/AIDS has not always been prioritized. Despite the challenges, high-quality care for HIV-infected children can be effectively provided in resource-limited settings, as evidenced by the success of the MTCT-Plus program. We strongly support access to care and treatment for children, which should be part of every HIV/AIDS treatment program.

This chapter will review ICAP guidelines and algorithms regarding ART use in children. While provision of ART where appropriate is critically important, it is, of course, not the sole element of pediatric HIV care. Chapter 2 addresses the diagnosis of pediatric HIV, Chapter 3 reviews care of the HIV-exposed infant, and Chapter 4 details guidelines for care of the HIV-infected child. The issue of pediatric adherence is discussed in Chapter 6; disclosure of HIV status to children in Chapter 8; and nutrition of infants and children in Chapter 7.

Topics covered in this chapter include:

- Key issues in the use of pediatric ART
- When and how to initiate ART in infants and children
- How to monitor children receiving ART (clinical and laboratory monitoring)
- When and how to switch ARVs due to toxicity
- When and how to switch ARVs due to therapeutic failure.

Key Issues in the Use of Pediatric ART

Patient readiness: Readiness for ART is especially complex when successful treatment requires the collaboration of both children and their caregivers. Not only must a child agree to take (or cooperate with taking) the medications, an adult must administer or supervise administration twice daily. In some cases, this requires little preparation. In others, a significant amount of patient support is needed before ART can be prescribed. Issues to consider include:

- Children are not always supervised by their parents or primary caregivers. Some attend school or work, or spend time with other family members or baby sitters. These normal circumstances of child rearing present particular challenges for ART, which must be administered on a set schedule each day without missed doses. Unless the family is prepared to disclose the child's HIV status to others, medication administration in these circumstances cannot be assured. The health care team should explore these issues sensitively and thoroughly before prescribing treatment, and work with the caregiver to find feasible solutions when these challenging situations exist.
- Involvement of children in their own care is critical to successful treatment. Children's needs and comprehension evolve with age and developmental stage. A mother may be surprised that her previously adherent baby, now two years of age, hides when he sees her preparing his medications. Similarly, a seven year-old who used to remind his mother of the time to take medication may refuse treatment several years later when adolescent behaviors emerge. Assisting families to recognize and address the evolving developmental needs of their children will enhance long-term treatment success.

Minimizing viral resistance: Providers can play an important role in delaying the occurrence of HIV resistance by assisting patients to optimize adherence (Chapter 6) and maintaining good prescribing practices. These include:

- ✓ Never prescribing ARVs in the absence of adherence preparation and support.
- ✓ Working with families to minimize barriers to medication adherence.
- ✓ Paying meticulous attention to other medications and treatments and their potential to interact with ARV therapies.
- ✓ Never prescribing monotherapy or dual therapy for treatment of chronic HIV infection (as opposed to preventing mother to child transmission or for post-exposure prophylaxis).
- ✓ Never adding a single drug to a failing regimen.
- ✓ Following protocols with care when switching or stopping ARVs.

Drug-drug interactions: ARV agents, particularly protease inhibitors, have multiple interactions with other medications and should not be prescribed without a careful review of each patient's regimen, including herbal and traditional agents. HIV-TB coinfection requires special attention, as noted below.

Drug-food interactions: While the first-line agents used by ICAP do not have dietary restrictions, some second-line medications require specific timing of

medicine and food. This can be extremely complex in the case of infants or young children who require frequent feeds.

Drug Formulations: Not all ARVs are available in pediatric formulations. The first-line treatments chosen for ICAP programs are child-friendly, with palatable, well tolerated, and easily administered agents. Many other ARVs, however, are not available in formulations suitable for young children. Some taste bad or are poorly tolerated, making adherence extremely difficult. Health care teams should work closely with children to insure that prescribed formulations are sufficiently palatable. Chapter 6 (Appendix A) reviews ways in which providers can assist families to administer ART to children.

ART Dosing: Unlike adults, for whom standard doses are usually prescribed, dosing requirements for children vary with age and size (weight and/or body surface area). Children must be measured at each visit, and the dose of treatment recalculated as the child grows. Puberty is another time of changing metabolic requirements, as dosing moves from pediatric to adult guidelines. MTCT-Plus, in collaboration with the Global AIDS Program and Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention and the Baylor International Pediatric Initiative, has developed a pediatric antiretroviral dosing guide to facilitate treatment (Appendix B).

Special considerations in children with tuberculosis who require ART: At most ICAP sites, the local TB program will treat active tuberculosis as per local and national protocols. There are significant interactions between rifampin and several antiretroviral agents. Communication between providers of anti-TB therapy and providers of HIV care is critical, both to avoid drug-drug interactions that may threaten successful therapy, and to heighten awareness of the potential for immune reconstitution syndromes.

When to Initiate Antiretroviral Treatment

ART should never be initiated without preparation of the child and family for the complex task of long-term therapy. Similarly, ART should never be prescribed without assuring a secure drug supply, as unplanned interruptions of treatment can lead to therapeutic failure.

The decision about when to start treatment in an infant is particularly challenging. One school of thought is that all HIV-infected infants should begin ART whether or not they have clinical symptoms or evidence of immune suppression. Advocates of this approach note that disease progression may occur very quickly during infancy, and that neither CD4 nor HIV viral load is a good predictor of which children are likely to get sick. Only by treating all infants can one assure that these “rapid progressors” will be protected. Critics of this approach point to concerns regarding efficacy, toxicity, and long term adherence. Proper dosing for many ARVs has not been established for infants. Several studies have shown that while infants on ART do well clinically, many do not have full viral suppression and are at risk of developing resistance. And the long term side

effects of ART that is initiated during the first months of life and continued throughout childhood have not been studied.

In light of these issues, ICAP recommends treatment for HIV-infected infants with evidence of symptomatic disease and /or immune compromise as per current WHO guidelines. These recommendations will be re-evaluated as more information becomes available.

Indications for Initiation of ART in Children	
Children < 12 months	<ul style="list-style-type: none">• Failure-to-thrive (no weight gain or weight loss or z score < -2)• Advanced symptomatic disease (WHO Stage II, CDC Category B*)• AIDS-defining illness (WHO III, CDC C)• Any child with CD4 percentage < 20%
Children 1-12 years of age	<ul style="list-style-type: none">• Failure-to-thrive (no weight gain or weight loss or z score < -2)• Advanced symptomatic disease (WHO Stage II, CDC Category B*)• AIDS-defining illness (WHO III, CDC C)• Any child with CD4 percentage <15%*
Children ≥ 13 years (as per adult guidelines**)	<ul style="list-style-type: none">• WHO stage 4 disease (clinical AIDS) irrespective of CD4 cell count• WHO stage 3 HIV disease and CD4 ≤ 350• CD4 ≤ 200 irrespective of WHO stage

*Some category B diagnoses may not warrant ART unless there is also evidence of immune suppression. In particular, mild bone marrow abnormalities or a single episode of pneumonia may not require ART initiation. Similarly, WHO guidelines suggest considering CD4 percentage when deciding to start therapy for a WHO II indication. Clinical judgment should balance the potential benefit of treatment with the long term toxicities and adherence challenges.

**In an asymptomatic child ≥ 6 years of age, the clinician may consider waiting until the CD4 reaches 10%, or until there is evidence of rapid immune deterioration. In the absence of data, some argue that the difficulties of maintaining adherence in an asymptomatic child and the potential toxicities of antiretroviral use outweigh the benefits of earlier treatment. If treatment is postponed in this setting, we recommend more frequent monitoring of CD4 counts/% (every three to four months).

**ICAP recommends that adolescents ≥ 13 years of age follow adult guidelines for treatment *eligibility*. Decisions about whether to initiate the pediatric or adult ART regimen and dosing should be based on physical maturity (e.g. Tanner staging) rather than age, as discussed below.

Initial ARV Regimens for Children

The ARV regimens selected by ICAP are all highly active. They balance efficacy, toxicity, palatability, logical sequencing of treatments to maintain future options, and cost-effectiveness. We suggest the use of a single first-line regimen for all children within a program, following the public health approach endorsed by WHO. We have prioritized the use of zidovudine, lamivudine, and a non-nucleoside reverse transcriptase inhibitor (NNRTI), a highly active regimen that is potent, palatable and has a well established, tolerable side effects profile. Nevirapine is the NNRTI of choice for children < 3 years and < 10 kg, while either efavirenz or nevirapine are recommended for children ≥ 3years and ≥ 10kg. In special circumstances, alternate regimens may be selected.

Recommended Initial Regimens

Children \leq 3 years

Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP)

Stavudine (D4T) + Lamivudine (3TC) + Nevirapine (NVP)

Children \geq 3yrs \geq 10kg

Zidovudine (AZT) + Lamivudine (3TC) + NVP or Efavirenz (EFV)

Stavudine (D4T) + Lamivudine (3TC) + NVP or Efavirenz (EFV)

When selecting an initial pediatric ARV regimen, there are several special issues to consider:

- The use of stavudine (D4T) is complicated by the absence of an ideal formulation for small children. While liquid stavudine is available, it requires refrigeration and an intact cold chain, often unavailable in ICAP program settings. Another option is to open capsules of D4T and to dissolve the powder in a small volume of water. This requires parents to learn how to prepare and measure doses, which can be both cumbersome and time consuming. Once children reach 7kg, the full 15-mg capsule can be used, as noted in the pediatric dosing guidelines (Appendix B).
- Proper dosing for EFV has not been determined for children $<$ 10 kg and $<$ 3 years. Therefore, NVP liquid should be used for young children. EFV can be given once daily and is available in small capsules of 50 mg. Many small children have learned to swallow these capsules. Otherwise, they can be opened and the granules can be combined with something sweet (like jam or jelly) to mask the bitter taste.
- While it is often appropriate for adolescents to receive care in pediatric programs, teens 13 years and older should be staged according to the adult WHO classification system. Similarly, the decision to initiate treatment should follow adult guidelines as noted above. The decision to start efavirenz (EFV) in a young girl entering her child-bearing years requires careful consideration. The use of EFV has been associated with birth defects and is contraindicated during the first trimester of pregnancy. Young teens who are sexually active may not be able to ensure regular use of contraception, and it is prudent to avoid EFV in such circumstances.
- The use of nevirapine-based ART in infants who have previously received nevirapine to prevent mother-to-child transmission raises concerns about resistance. Many infants and young children identified as HIV-infected have received single-dose nevirapine (SD-NVP) during the first days of life for perinatal prevention. Several studies have shown that both women and children who receive SD-NVP are at risk for the development of NNRTI resistance mutations. These mutations, often detectable during the first

months of life generally fade over the first year of life. There is concern that these mutations will adversely impact the efficacy of NNRTI-based therapeutic treatment,⁴ although there are currently no available data specifically addressing this question in children. While ICAP currently recommends NNRTI-based first line therapy, relevant data will be reviewed as they become available and recommendations will be modified if indicated.

Because of concerns regarding potential NNRTI resistance in infants with previous exposure to SD-NVP, some programs have chosen to avoid NNRTI-based first-line therapy in this setting. When local or national guidelines suggest avoidance of NNRTI treatment, use of protease inhibitor-based regimens is reasonable, and the following alternatives are recommended:

**Recommended Initial Regimens
When NNRTI-Based Therapy is Contraindicated**

Zidovudine (AZT) or Stavudine (D4T) + Lamivudine (3TC) +
Lopinavir/ritonavir (LPV/r)

Or, if cold chain requirements cannot be met:

Zidovudine (AZT) or Stavudine (D4T) + Lamivudine (3TC) + Nelfinavir (NLF)

When choosing a PI-based first-line therapy, several issues must be considered:

- LPV/r requires a secure cold chain until the medication is dispensed to the patient, at which point it can be maintained at 25 degrees centigrade for up to 30 days. While families do not need to have refrigeration they must understand the importance of maintaining the medication in a cool spot in the household away from direct sunlight and large temperature fluctuations. If such storage is not available, nelfinavir (NLF) is preferable.
- As noted, nelfinavir can be considered for first-line treatment in settings where temperature control is not feasible. However, there is no liquid formulation for NLF, and its administration to small children is inconvenient. The powder formulation is poorly tolerated; tabs must be crushed and suspended in a small volume of liquid for administration.
- Another concern when choosing PI-based first-line therapy is the choice of second-line treatment. Few data are available to inform the choice of second-line treatment for children who have failed PI treatment. The effectiveness of NNRTI-based treatment in this context is currently unknown, particularly if there is significant resistance to the NRTI backbone at the time of failure.

⁴ N Eng J Med 2004;351:229-240.

How to Initiate ART in Children

Before prescribing ART, the following questions should be asked and answered:

- **Does the patient have a medical indication for antiretroviral therapy?**
These are outlined above.
- **Is there a medical contraindication to the planned first-line regimen?**
The next step is to exclude medical contraindications to the specific first-line regimen (Table 1) via medical history, symptom checklist, physical examination and laboratory testing. Minimal laboratory investigation includes assessment of renal function, liver function and a complete blood count.

Table 1: Medical contraindications to initiation of first-line ARV regimen

Contraindication	Definition	Comments	Recommendation
Severe anemia	Hb \leq 6.9 g/dL	Contraindication to use of AZT	Use alternate first-line regimen: D4T + 3TC + NVP (or EFV)
Severe neutropenia	ANC \leq 250 mm ³	ZDV use requires close monitoring	First-line regimen may be started, but ANC measurement should be repeated within two weeks of initiation. If repeat labs show ANC has fallen, make a single-drug substitution to alternate first-line regimen: D4T + 3TC + NVP (or EFV)
Severe renal insufficiency	Creatinine > 3 times normal	Contraindication to ARV use	Patient not currently eligible for ARVs. Conduct diagnostic evaluation as per local guidelines and reassess for ARV eligibility if renal function improves. Expert consultation recommended if available.
Severe hepatic insufficiency	LFTs > 5 times normal	Contraindication to NVP use	EFV can be initiated in children >3yr and > 10kg. For smaller children PI treatment is suggested.
History of prior ARV intolerance	If intolerant of AZT, use D4T + 3TC + NVP (or EFV) If intolerant of D4T, use ZDV + 3TC + NVP (or EFV) Other substitutions may require expert advice.		
History of prior ARV use (other than pMTCT)	Use of any ARV for more than four weeks	Potential for ARV resistance	Expert management required. Consult local expert or Secretariat for case-by-case advice.
Current use of rifampin-containing anti-TB regimen	Use of rifampin	Drug-drug interactions with NVP	If CD4 count is high, consider deferring ART until TB therapy is complete. If not, use ritonavir-containing regimen for < 3yr and EFV-containing regimen \geq 3yr.

- **Is there a non-medical contraindication to antiretroviral use?**
One purpose of multidisciplinary, psychosocial, and adherence assessments is to exclude “non-medical” contraindications to ARV use, and to confirm that child and their families are prepared to take the medications consistently and correctly. While many patients will be ready to begin treatment, identifying modifiable barriers to adherence will enable providers to intervene for others prior to ARV initiation.

○ **Has adherence been formally addressed?**

A comprehensive and detailed approach to adherence is provided in chapter 2.4. The four-part approach should focus on education, preparation, ongoing assessment and support. In preparation for beginning therapy, four key questions should be addressed:

- 1) **Who** will administer the medications?
- 2) **What** medications will be given?
- 3) **When** will medications be given?
- 4) **How** will medications be given?

Working with families to address these questions and to address barriers to treatment will enhance the likelihood of successful ART.

○ **What is the appropriate dose of ARVs for this child at this time?**

Dosing for children is calculated based on weight or surface area. As children grow, their medication doses must be adjusted accordingly. This is particularly important in the case of a child with failure-to-thrive who responds to ARV treatment with a robust increase in weight. In such cases, dosing is likely to increase frequently and often dramatically. ARV doses should be recalculated at each visit based on the child's current weight and height. This is a complex process, and may be challenging for families, who need to be counseled about dosing changes and assured that they are based on growth rather than an indication that the treatment is not working.

Infants and young children often metabolize medications very rapidly. For some medications, the daily dose is greater for children than for adults. It is generally recommended that children continue to receive pediatric dosing throughout the course of pubertal development. While clinicians should follow adult guidelines to determine treatment eligibility for teens ≥ 13 years, pediatric dosing guidelines should be followed until full physical maturity is reached (Tanner V), at which point standard adult dosing should be used.

Nevirapine is always initiated at half the full daily dose for 14 days to minimize the risk of toxicity. The dose is escalated after two weeks of treatment to the recommended twice daily dose.

In collaboration with the Global AIDS Program & Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, and the Baylor International Pediatric Initiative, ICAP has developed a convenient dosing guide for pediatric antiretroviral therapy (Table 2 and Appendix B). Conversion of body surface area into equivalent weight categories has been pre-calculated and dosing guidelines for liquids and pills have been established for children of different weights.

Table 2: Dosing of First-Line ARVs

Weight (kg)	Lamivudine (Epiriv®, 3TC)		Zidovudine (Retrovir®, ZDV, AZT)		Stavudine (Zerit®, D4T)	Nevirapine (Viramune®, NVP)						Efavirenz (Sustiva®, Stocrin®, EFV)
	4 mg/kg twice daily		240 mg/m ² twice daily		1 mg/kg twice daily	Induction dose		Maintenance dose				Dose as shown once daily
						4 mg/kg once daily x 14 days		< 8 yrs 7 mg/kg twice daily		≥ 8 yrs 4 mg/kg twice daily		
	Liquid 10 mg/ml	Tab 150 mg	Liquid 10mg/ml	Capsule 100 mg, Tablet 300 mg	Capsules 15, 20, 30 mg	Liquid 10 mg/ml	Tab 200 mg	Liquid 10 mg/ml	Tab 200 mg	Liq 10 mg/ml	Tab 200 mg	Caps 50, 100, 200 mg
5-6.9	2 ml		7 ml			2 ml		4 ml				
7-9.9	3 ml		9 ml	1 cap	15 mg	3 ml		6 ml				
10-11.9	4 ml		12 ml	1 cap	15 mg or (20 mg ¹)	4 ml		8 ml	½ tab			200 mg
12-14.9	5 ml		14 ml	1 cap	15 mg or (20 mg ¹)	5 ml		9 ml	½ tab			200 mg
15-16.9	6 ml	½ tab	15 ml	2 caps	15 mg or (20 mg ¹)	6 ml		10 ml	½ tab			200 mg + 50 mg
17-19.9	7 ml	½ tab	17 ml	2 caps	20 mg	7 ml		13 ml	1 tab AM + ½ tab PM			200 mg + 50 mg
20-24.9	9 ml	½ tab	20 ml	2 caps	20 mg	9 ml	½ tab	16 ml	1 tab AM + ½ tab PM	9 ml	½ tab	200 mg + 100 mg
25-29.9	11ml	1 tab	24 ml	3 caps or 1 300-mg tab	30 mg	11 ml	½ tab	20 ml	1 tab	11 ml	½ tab	200 mg + 100 mg + 50 mg
30-32.9	13 ml	1 tab	27 ml	3 caps or 1 300-mg tab	30 mg	13 ml	1 tab			13 ml	1 tab AM + ½ tab PM	200 mg + 100 mg + 50 mg
33-34.9	13 ml	1 tab	27 ml	3 caps or 1 300-mg tab	30 mg	13 ml	1 tab			13 ml	1 tab AM + ½ tab PM	200 mg + 200 mg
35-40	15 ml	1 tab	30 ml	3 caps or 1 300-mg tab	30 mg	15 ml	1 tab			15 ml	1 tab AM + ½ tab PM	200 mg + 200mg

How to Monitor Pediatric Antiretroviral Therapy

Careful monitoring is an essential component of effective ARV use, permitting early detection of adverse effects, ongoing reinforcement of adherence, and periodic assessment of treatment efficacy. The type and frequency of monitoring will be somewhat dependent on local resources. The following are clinical and laboratory monitoring recommendations for children receiving ART in ICAP programs; these represent *minimal* monitoring requirements and should be modified for individual patients at their clinicians' discretion.

Clinical monitoring for children receiving ART:

As patients initiate ART, weekly evaluations are recommended for the first 8 weeks. These "initiation" visits should focus on adherence assessment and support, and on assessing adverse events and ARV toxicity via the structured

symptom checklist. Generally only one week of treatment is dispensed at each visit to underscore the need for strict adherence. If symptoms indicate a problem, a targeted physical examination is indicated. At the one month visit, a complete physical examination should be conducted including measurement of growth; ART doses should be recalculated if the child's weight has changed.

Weekly Visits for the first 8 weeks of ART

Week 0:

- Initiate ART. Dispense 1 week's worth of medication.
- Ensure that patient/family know what to do in the event of new symptoms or problems

Week 1:

- Symptom checklist (and targeted physical examination if needed).
- Adherence assessment and support
- Dispense 1 week's worth of ART

Week 2:

- Symptom checklist (and targeted physical examination if needed).
- Adherence assessment and support
- Dispense 1 week's worth of ART. If using NVP, escalate dose as indicated.

Week 3:

- Symptom checklist (and targeted physical examination if needed).
- Adherence assessment and support
- Dispense 1 week's worth of ART

Week 4:

- Symptom checklist
- Comprehensive physical examination – recalculate ART dosing based on new height/weight
- Adherence assessment and support
- Dispense 1 week's worth of ART

Weeks 5-7:

- Symptom checklist (and targeted physical examination if needed).
- Adherence assessment and support
- Dispense 1 week's worth of ART

Week 8:

- Symptom checklist
- Comprehensive physical examination – recalculate ART dosing based on new height/weight
- Adherence assessment and support
- Dispense ART – if patient is doing well and adherence is excellent, consider dispensing 1 month's worth of ART.

These weekly visits need not always involve a clinician. Other members of the multidisciplinary team can participate in the adherence assessments and support. For example, a counselor could review the symptom checklist and conduct an adherence assessment, referring the patient to a clinician only if a new symptom or problem is identified. In some settings, home visits may also be a useful tool to provide adherence support during the first weeks of therapy.

While ART is generally well-tolerated, it is important to be vigilant about potential adverse effects. Common early symptoms of toxicity depend on the regimen used, and may include rash, nausea, diarrhea, headache, fatigue, irritability, or diminished appetite. Several of these symptoms—headache and fatigue, for example—often resolve over time. Others can be treated symptomatically (diarrhea, nausea). In infants these symptoms may be subtle and difficult to

distinguish from signs of acute illness. Some findings may require changes in drug dosing or drug regimen. Some children may develop symptoms early after initiation of ART (e.g. cough, fever, lymphadenopathy) that indicate an underlying infectious process that has become evident due to a vigorous immunologic reconstitution. A number of cases of such immune reconstitution syndromes have been seen in children, primarily older children and teens. Appropriate management of these symptoms and conditions should be instituted as per usual site procedures.

After the 8-week initiation period, children who are doing well may be seen monthly. Adherence should be reviewed with the parent/caregiver as well as the older child at every visit. The visits should also include:

Monthly Visits for Children Receiving ART

- ✓ interval medical history
- ✓ symptom checklist
- ✓ targeted physical examination
- ✓ growth monitoring and nutritional assessment
- ✓ developmental assessment
- ✓ psychosocial assessment
- ✓ referral for supportive services if indicated
- ✓ ARV prescription (with recalculated doses as needed)
- ✓ Cotrimoxazole prescription

Laboratory monitoring for children receiving ARV therapy:

As noted above, baseline laboratory studies should always be obtained prior to starting ART. These include assessment of renal function (serum creatinine and blood urea nitrogen level) and liver function (serum alanine and/or aspartate aminotransferase level), a complete blood count, and CD4 enumeration. These results will determine whether the child is eligible for ART, whether there are medical contraindications to the usual first-line regimen, and whether close laboratory monitoring is required.

ICAP supports a model of clinical monitoring for children receiving ART. With the exception of children who begin therapy with baseline laboratory abnormalities (elevated liver function, anemia, neutropenia), laboratory monitoring for ART toxicity is not routinely recommended. Abnormal findings on history or physical examination should, however, prompt appropriate laboratory investigation at the discretion of the treating clinician. If laboratory studies are obtained, the clinician will need to distinguish between toxicities caused by the medications, intercurrent illnesses and advancing HIV disease. Further evaluation should be dictated by

local guidelines for care and treatment. However, if the abnormalities listed in Table 4 are identified, it may be necessary to stop or change ARV treatment, as discussed in the following section on toxicity. Furthermore, if a child begins therapy with baseline laboratory abnormalities (particularly elevated liver function tests) it may be prudent to monitor laboratory values until abnormalities resolve or are determined to be stable.

CD4 count and percent should be obtained every six months for children on treatment to monitor the efficacy of ARV therapy. Inadequate immune response should prompt investigation of adherence and meet criteria for therapeutic failure. This is discussed in more detail below.

When to Change ARVs

The first ARV regimen should be both potent and durable. If adherence is adequate, clinical and immunologic benefits should be long lasting. Changing ARV medication should be done with caution; resistance and cross-resistance are important considerations, and ARV sequencing can have significant impact. Premature changes risk exhausting future options. Nonetheless, some children will need to change therapy due to toxicity or to therapeutic failure. In the case of **toxicity**, a single drug substitution may be indicated. In the case of **therapeutic failure**, the entire regimen should be changed.

Changing ARVs due to toxicity

ARV-associated adverse events may be detected by symptoms or laboratory investigation. Some symptoms are mild and/or transient, while others require supportive therapy (such as antiemetics or antimotility agents) or more frequent clinical monitoring. Severe side effects may require interruption of ART. When serious toxicity appears to be caused by a specific ARV, a single-drug substitution can be made. In some cases, however, the entire regimen will need to be changed. Tables 3 and 4 detail criteria for changing ARVs due to toxicity; Table 5 indicates which drugs to substitute. Appendix A reviews commonly-used ARV drugs and their most common adverse effects.

Medication changes based on laboratory values should be carefully considered, guided by the clinician's experience and judgment, and viewed in the clinical context of the patient's care. No changes should be made on the basis of a single test, although if the laboratory abnormalities are severe (grade 4) the medications should be stopped pending laboratory confirmation. Intercurrent illness may create transiently abnormal laboratory values as may concomitant medications. Repeat testing should be completed and evaluated for trends over time. If a treatment change is indicated, new drugs should not be started until toxicities have resolved to \leq grade 2. Appendix A provides guidelines for the management of rash or hepatotoxicity secondary to NVP.

Table 3: Clinical indications to change ARVs due to toxicity

Symptom	
Nausea	Severe discomfort or minimal intake for ≥ 3 days
Vomiting	Severe vomiting of all foods/fluids in 24 hours or orthostatic hypotension or IV therapy required
Diarrhea	Bloody diarrhea or orthostatic hypotension or IV therapy required
Fever	Unexplained fever of ≥ 39.6 C (103 F) > 1-2 weeks
Headache	Severe or requires narcotic therapy
Rash	Moist desquamation, ulceration, or mucous membrane involvement, suspected Stevens-Johnson (TEN), erythema multiforme, exfoliative dermatitis, or necrosis requiring surgery
Allergic reaction	Angioedema or anaphylaxis
Peripheral neuropathy	Severe discomfort, objective weakness, loss of 2–3 previously present reflexes or absence of 2–3 previously present sensory dermatomes
Fatigue	Normal activity reduced ≥ 50 %

Table 4: Laboratory indications to change ARVs due to toxicity

Parameter	Grade 3 toxicity
Hematology	
Hemoglobin	≤ 7.0 g/dL
Absolute neutrophil count	≤ 250 mm ³
Chemistries	
Bilirubin	≥ 3.0 – 7.5 x upper limits of normal
Creatinine	≥ 1.2 – 1.5 (<2 yr), 1.7 – 2.0 (>2yr)
Liver function tests	
AST (SGOT)	≥ 10 upper limits of normal or rapidly increasing
ALT (SGPT)	≥ 10 upper limits of normal or rapidly increasing
Pancreatic enzymes	
Amylase, lipase	≥ 2 – 3 x upper limits of normal

Table 5: Single-drug substitutions for early toxicity

Primary regimen:	Single-drug substitution for toxicity
AZT + 3TC + NVP	
	<i>If AZT toxicity: D4T + 3TC + NVP</i>
	<i>If NVP toxicity: AZT + 3TC + NLF</i>
	<i>* If > 3yr & 10kg and toxicity is not grade 4 rash: ZDV + 3TC + EFV</i>
Primary regimen:	Single-drug substitutions for toxicity
D4T + 3TC + NVP	
	<i>If D4T toxicity: AZT + 3TC + NVP</i>
	<i>If NVP toxicity: D4T + 3TC + NLF</i>
	<i>* If > 3yr & 10kg and toxicity is not grade 4 rash: AZT + 3TC + EFV</i>
Primary regimen:	Single-drug substitutions for toxicity
AZT + 3TC + EFV*	
	<i>If ZDV toxicity: D4T + 3TC + EFV</i>
	<i>If EFV-associated neuropsychiatric symptoms: AZT + 3TC + NVP</i>
	<i>If EFV-associated rash or hepatotoxicity: AZT + 3TC + protease inhibitor</i>
Primary regimen:	Single-drug substitutions for toxicity
D4T + 3TC + EFV*	
	<i>If D4T toxicity: AZT + 3TC + EFV</i>
	<i>If EFV-associated neuropsychiatric symptoms: D4T + 3TC + NVP</i>
	<i>If EFV-associated rash or hepatotoxicity: D4T + 3TC + protease inhibitor</i>
Primary regimen:	Single-drug substitutions for toxicity
AZT + 3TC + NLF	
	<i>If ZDV toxicity: D4T + 3TC + NLF</i>
	<i>If NLF toxicity: AZT + 3TC + EFV*/NVP</i>
Primary regimen:	Single-drug substitutions for toxicity
D4T + 3TC + NLF	
	<i>If D4T toxicity: AZT + 3TC + NLF</i>
	<i>If NLF toxicity: AZT + 3TC + EFV*/NVP</i>
Primary regimen:	Single-drug substitutions for toxicity
AZT + 3TC + LPV/r	
	<i>If AZT toxicity: D4T + 3TC + LPV/r</i>
	<i>If LPV/r toxicity: AZT + 3TC + NLF</i>
Primary regimen:	Single-drug substitutions for toxicity
D4T + 3TC + LPV/r	
	<i>If D4T toxicity: AZT + 3TC + LPV/r</i>
	<i>If LPV/r toxicity: D4T + 3TC + NLF</i>

*EFV can only be prescribed for children ≥ 10 kg and ≥ 3 yr

Changing ART due to therapeutic failure

Successful ARV therapy leads to clinical and immunologic improvements with associated suppression of HIV replication. It is reasonable to expect a symptomatic patient to show significant clinical improvement within three months of initiating treatment. Within six months, CD4 counts can be expected to rise, although the magnitude of the rise in CD4 cell count is dependent on the baseline value. In general, however, one can expect a significant increase in CD4 number/percent for children with adequate viral suppression.

The most common reason for treatment failure is inadequate adherence. **Before any regimen is changed, adherence should be carefully assessed.** If adherence cannot be assured, the decision to change therapy may need to be postponed until the child and family are ready to address the barriers to treatment. However, if poor adherence is related to drug formulation or palatability, a regimen change may result in improved adherence. Efforts should be made to insure that the child will be able to tolerate the new regimen before it is dispensed. Recall that pediatric adherence is discussed in Chapter 2.4, which includes an approach to assessing and reinforcing the pediatric treatment.

Therapeutic failure of ARV treatment

- No improvement or worsening of clinical status after 3 months of therapy
 - Inadequate growth or weight loss
 - New or recurrent AIDS-defining illness*
 - Loss of developmental milestones or new onset encephalopathy
- Inadequate immune response
 - Failure to improve (~ 50 cells/mm³ or 3 percent) at 6 months of ART
 - Return of CD4 percent to or below baseline value**
 - Fall of >30% in CD4 percent from peak values**

*Exclude immune reconstitution syndrome

** CD4 number can be used in addition to % for children > 6yrs.

Secondary ARV Regimens:

The following sequencing suggestions have been developed for settings where providers and patients lack ready access to viral load or viral resistance testing. In this context, ART sequencing is based on resistance patterns associated with specific agents, replacing a failing first-line regimen with a second that has minimal potential for cross resistance. The choice of secondary regimens also balances potency, toxicity, formulation, and cost. As new data become available, it is likely that recommendations for second-line regimens will change

Recommended second-line regimens for NNRTI-based first-line regimens

zidovudine (ZDV) or stavudine (D4T)	→	abacavir (ABC)
+		+
lamivudine (3TC)	→	didanosine (DDI)
+		+
nevirapine (NVP) or efavirenz (EFV)	→	lopinavir/ritonavir (LPV/r) <i>or, if no cold chain available,</i> nelfinavir (NLF)

Recommended second-line regimens for PI-based first-line regimens

zidovudine (ZDV) or stavudine (D4T)	→	abacavir (ABC)
+		+
lamivudine (3TC)	→	didanosine (DDI)
+		+
lopinavir/r (LPV/r) or Nelfinavir (NLF)	→	nevirapine (NVP) < 3 years or efavirenz (EFV) ≥ 3 years

Issues around the use of LPV/r, NLF and the NNRTI agents have already been described, and information about ART toxicity can be found in Appendix A. Important considerations include the fact that LPV/r has a bitter taste and is often better tolerated when administered with food. In contrast, DDI must be given on an empty stomach either 30 minutes before a meal or two hours after having eaten. This restriction complicates medication administration as each daily dose must be given in two parts – DDI alone on an empty stomach, and then ABC and LPV/r at a different time, most often with food. Caretakers must be carefully instructed about the food requirements of these medications. Information about ART toxicities can be found in Appendix A.

Summary

Antiretroviral treatment is never an emergency. Adequate preparation of the child and family is crucial to successful long-term success. Careful selection of first- and second-line regimens, monitoring of side effects, ongoing assessment and support of adherence, and attention to the social and psychological needs of the child and his/her family are all critical components of the complex task of treating children with HIV infection.

Appendix A: Information about Selected Antiretroviral Agents

Zidovudine (ZDV) is generally well-tolerated, although headache, nausea, and fatigue can occur in some children. These symptoms are often transient, and ZDV should not be discontinued unless they are severe (see Tables 3 and 4). Bone marrow suppression can also occur; anemia usually occurs within four to six weeks and neutropenia can be seen within the first six months. Anemia should, thus, be considered in patients who develop, pallor fatigue, shortness of breath or weakness while on zidovudine. Macrocytosis is almost universal and is not an indication to switch agents or to conduct further diagnostic evaluation. Less common toxicities include cardiomyopathy, peripheral myopathy and lactic acidosis.

Lamivudine (3TC) is an extremely well-tolerated agent with minimal toxicity. As with all nucleoside analogs, 3TC has been associated with lactic acidosis and hepatic steatosis, although the syndrome is more common with stavudine (D4T).

Stavudine (D4T) is generally well-tolerated in children. It has been associated with peripheral neuropathy and lactic acidosis, particularly when used in combination with didanosine (DDI) though reports are less common in children compared with adults. Peripheral neuropathy can often be treated symptomatically, but in severe cases treatment will need to be discontinued. While the majority of patients taking D4T have no toxicity at all, providers should be aware of the possibility of lactic acidosis because of its potential severity. Symptomatic lactic acidosis is rare (less than 0.1 percent), but up to five percent of asymptomatic patients on NNRTIs may have elevated lactic acid levels. Symptoms include fatigue, abdominal pain, nausea/vomiting, and weight loss and laboratory investigation reveals elevated serum lactate with or without metabolic acidosis. An elevated anion gap, creatinine phosphokinase (CPK), transaminases, and lactate dehydrogenase may also be seen. The most important response is to stop the offending antiretroviral agent; lactic acidemia often resolves over a period of three to six months. Restarting ARVs will often require expert consultation, as the safety of reintroducing NRTIs in this setting has not been firmly established.

Nevirapine (NVP) The most common toxicity in adults and children receiving nevirapine is rash, which may develop in up to 20 percent of those taking the drug. Skin manifestations are generally mild to moderate, but two to five percent may need to discontinue therapy because of this side effect. Skin rash can include systemic reactions and can progress to a Stevens Johnson Syndrome. Skin manifestations generally occur within the first 2–6 weeks of treatment. Rash can be minimized by introducing drug at a reduced dose for 14 days and then increasing to full dose, and this “dose escalation” is the standard of care in ICAP programs. If rash occurs, the dose should not be escalated until resolution and the child should be evaluated for systemic symptoms. Liver function should be

evaluated for rash \geq Grade 2. In general, nevirapine treatment should be continued for grade 1 and 2 toxicities, but discontinued for grade 3 or greater

Nevirapine treatment can also result in hepatotoxicity. Less commonly described in children than adults, liver dysfunction can range from mild elevation of transaminase to frank hepatotoxicity including fulminant and cholestatic hepatitis, hepatic necrosis and hepatic failure. Liver dysfunction generally recovers when medication is discontinued, but fatal cases have been described. It generally occurs during the first weeks of therapy, but may occur at any time throughout the course of treatment. Liver function will be monitored at the discretion of the treating clinician. If liver dysfunction is detected, an evaluation of the etiology should be undertaken. Nevirapine should be permanently discontinued if Grade 3 or greater toxicities develop or for any child with symptoms of clinical hepatitis (fatigue, anorexia, nausea, bilirubinuria, jaundice, liver tenderness or hepatomegaly).

Grading the Severity of a Rash:

Grade 1 (Mild):

- Erythema with or without pruritis

Grade 2 (Moderate):

- Diffuse maculopapular rash *or*
- Dry desquamation *or*
- Urticaria *or*
- Typical target lesions without blistering, ulceration, or vesicles
- *And* absence of systemic symptoms (fever, muscle pain, joint pain, elevated transaminases). NB, liver function tests should be ordered in all patients whose clinical symptoms are consistent with Grade 2 rash.

Grade 3 (Severe):

- Vesiculation *or*
- Moist desquamation *or*
- Ulceration *or*
- Diffuse rash and serum sickness-like reaction (fever, lymphadenopathy, muscle and or joint pain) *or*
- Diffuse rash and systemic symptoms (fever, blistering, elevated transaminases)

Grade 4 (Potentially life-threatening):

- Mucous membrane involvement *or*
- Suspected Stevens-Johnson syndrome (TEN) *or*
- Erythema multiforme *or*
- Exfoliative dermatitis

Efavirenz (EFV): Efavirenz is generally well tolerated in children. It is associated with side effects of the central nervous system: children experience vivid dreams, disrupted sleep, agitation, hallucinations, feelings of dissociation, depression and other mood changes. Many of these effects will resolve with time and can often be alleviated by taking the medication before bedtime. Some patients cannot tolerate these side effects and require a change of treatment. The most common side effect of EFV for children is rash, which is generally a mild to moderate maculopapular pruritic rash that does not require discontinuation of treatment. Liver dysfunction is not generally associated with EFV use in children.

Nelfinavir (NLF): Nelfinavir is generally well tolerated in children, but can cause loose stools, diarrhea, abdominal bloating and discomfort. Most of these side effects can be managed symptomatically. Protease inhibitors have also been associated with long term metabolic complications including lipodystrophy, elevated lipids (cholesterol and triglycerides) and new onset diabetes mellitus.

Lopinavir/ritonavir (LPV/r): Lopinavir/r has been associated with abdominal discomfort, nausea and headache. It is generally well tolerated in children. Like most drugs of the same class (PI) LPV/r use can lead to hyperglycemia, lipid elevations and lipodystrophy.

Didanosine (DDI) is generally well-tolerated. The most severe adverse effect is pancreatitis, though it occurs rarely in children. Nausea and diarrhea are more common events. DDI should be discontinued if pancreatitis is suspected. Peripheral neuropathy has also been reported and, as with all with all nucleoside analogs, didanosine has been associated with lactic acidosis and hepatic steatosis, though generally in association with other NRTI agents, particularly D4T.

Abacavir: The most serious adverse effect associated with abacavir is an acute hypersensitivity reaction. Up to five percent of children starting abacavir will develop signs and symptoms consistent with this syndrome. Symptoms include flu-like symptoms, fever, cough, chills, malaise, rash, vomiting, diarrhea, respiratory distress, headache and bone/joint pain. If a hypersensitivity reaction is suspected, abacavir should be discontinued immediately. The syndrome is generally reversible while continuation of treatment can lead to death. Reintroduction of abacavir therapy at a later point can also be fatal. Families should be counseled about these potential side effects and instructed to contact the health care team of any if such symptoms occur.

Appendix B: Pediatric Dosing in Resource-constrained Settings: Antiretroviral and Cotrimoxazole Dosing Chart, page 1

Weight	Abacavir (Ziagen®)		Stavudine (Zerit®, d4T)	Lamivudine (Epivir®, 3TC)		Zidovudine (Retrovir®, ZDV, AZT)		Didanosine (Videx®, DDI)	Nevirapine (Viramune®, NVP)						Efavirenz (Stocrin®, Sustiva®, EFV)	
	8 mg/KG twice daily		1 mg/KG twice daily	4 mg/KG twice daily		240 mg/m ² twice daily		120 mg/m ² twice daily	Induction dose: 4 mg/KG once daily for first 14 days, then give maintenance dose→	Maintenance dose						Dose as shown once daily
KG	Liquid 20 mg/ml	Tablet 300 mg	Caps 15, 20, 30 mg	Liquid 10 mg/ml	Tablets 150 mg	Liquid 10 mg/ml	Caps 100 mg	Chewable tablets 25, 50, 100 mg		Liquid 10 mg/ml	Tablet 200 mg	Liquid 10 mg/ml	Tablet 200 mg	Liquid 10 mg/ml	Tablet 200 mg	
5 – 6.9	2 ml			2 ml		7 ml			2 ml		4 ml					
7 – 9.9	3 ml		15 mg	3 ml		9 ml	1 cap	25mg + 25mg	3 ml		6 ml					
10 – 11.9	4 ml		15 mg or (20 mg ¹)	4 ml		12 ml	1 cap	25mg + 25mg	4 ml		8 ml	½ tab			200 mg	
12 – 14.9	5 ml		15 mg or (20 mg ¹)	5 ml		14 ml	1 cap	50mg + 25mg	5 ml		9 ml	½ tab			200 mg	
15 - 16.9	6 ml		15 mg or (20 mg ¹)	6 ml	½ tab	15 ml	2 caps	50mg + 25mg	6 ml		10 ml	½ tab			200 mg + 50 mg	
17 – 19.9	7 ml	½ tab	20 mg	7 ml	½ tab	17 ml	2 caps	50mg + 50mg	7 ml		13 ml	1 tab AM + ½ tab PM ⁴			200 mg + 50 mg	
20 – 24.9	9 ml	½ tab	20 mg	9 ml	½ tab	20 ml	2 caps	50mg + 50mg	9 ml	½ tab	16 ml	1 tab AM + ½ tab PM ⁴	9 ml	½ tab	200 mg + 100 mg	
25 – 29.9	25 – 27.9 KG	11 ml	30 mg	11 ml	1 tab ²	24 ml	3 caps or 300 mg tab	100mg + 25mg	11 ml	½ tab	20 ml	1 tab	11 ml	½ tab	200 mg + 100 mg + 50 mg	
	28 – 29.9 KG	12 ml														1 tab
30 – 34.9	13 ml		30 mg	13 ml	1 tab	27 ml	3 caps or 300 mg tab	100mg + 25mg	13 ml	1 tab ³			13 ml	1 tab AM + ½ tab PM ⁴	30 – 32.9 KG	200 mg + 100 mg + 50 mg
															33 – 34.9 KG	200 mg + 200 mg
35 – 40	15 ml		30 mg	15 ml	1 tab	30 ml	3 caps or 300 mg tab	100mg + 25mg	15 ml	1 tab ³			15 ml	1 tab AM + ½ tab PM ⁴	200 mg + 200 mg	

Appendix B: Pediatric Dosing in Resource-constrained Settings: Antiretroviral and Cotrimoxazole Dosing Chart, page 2

Weight	Lopinavir/ritonavir (Kaletra®)		Nelfinavir (Viracept®)	Indinavir (Crixivan®)	Trimethoprim/sulfamethoxazole TMP/SMZ (Septrin®, Bactrim®, various)		
	< 15 KG = 12 mg lop/KG ≥ 15 KG = 10 mg lop/KG twice daily (lop = lopinavir; r = ritonavir)		60 mg/KG twice daily	500 mg/m ² every 8 hours	~4 mg/KG once daily (For prophylaxis against opportunistic illnesses. Doses for treatment of bacterial and protozoal infections are higher than listed here)		
KG	Liquid 80 mg lopinavir/ml ⁵	Capsule 133.3/33.3 mg lopinavir/r	Tablet 250 mg	Capsule 200 mg	8 mg/ml	Liquid	Single-strength (SS) Tablet 80mg TMP/400mg SMZ
5 – 6.9			2 tabs ⁷	1 cap		3 ml	
7 – 9.9	1.5 ml		2 tabs ⁷	1 cap		4 ml	½ SS tab
10 – 11.9	2 ml		2 tabs	1 cap		5 ml	½ SS tab
12 – 14.9	2 ml		3 tabs	1 cap		7 ml	1 SS tab
15 - 16.9	2.5 ml	1 cap	3 tabs	2 caps		8 ml	1 SS tab
17 – 19.9	2.5 ml	2 caps ⁶	4 tabs	2 caps		9 ml	1 SS tab
20 – 24.9	3 ml	2 caps	5 tabs	2 caps		11 ml	1 SS tab
25 – 29.9	3.5 ml	2 caps	5 tabs	2 caps		14 ml	2 SS tabs
30 – 34.9	4 ml	3 caps	5 tabs	3 caps		17 ml	2 SS tabs
35 – 40	5 ml	3 caps	5 tabs	3 caps		20 ml	2 SS tabs

Appendix B continued:

Abacavir – Tablets may be swallowed whole or crushed and dispersed in water or onto a small amount of food and immediately ingested.

Stavudine – Capsules may be opened and dispersed in water or onto a small amount of food and immediately ingested. Stavudine capsules are not recommended for use in children < 7 KG since dose size from smallest capsule would be too large. Stavudine oral solution is stable at room temperature for 24 hours or under refrigeration for 30 days.¹In settings where households do not have access to refrigeration, the oral solution should not be used. In the event that 15 mg capsules are not available, consider giving the 20 mg capsule to children in the 10-16.9 KG range. Though these may result in doses higher than the recommended 1mg/kg dose, higher doses than this have been used in clinical trials and were generally well tolerated. However, for children < 10 KG a capsule size larger than 15 mg is not advised.

Lamivudine – Tablets are not scored, but can be divided into two equal halves with a pill splitter in the pharmacy. Tablets may be crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution should be used in children < 15 KG since accurate dosing with tablets is not practical in smaller children. Oral solution is stable at room temperature.² The dose changes from ½ to 1 tablet as a child enters this weight range, however, lamivudine has few adverse effects and this dose should be generally well tolerated.

Zidovudine – Capsules may be opened and dispersed in water or onto a small amount of food and immediately ingested. Tablets may be crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution should be used in children < 7 KG since accurate dosing with capsules is not practical in smaller children. Oral solution is stable at room temperature. Weight based doses were determined by using body surface area values calculated from typical heights for weight.

Didanosine – Must use 2 tablets with each dose to provide adequate antacid to buffer stomach acid to allow absorption. The tablets may be dispersed in water before administering. Alternatively, the tablets may be chewed and swallowed. Must be administered on an empty stomach at least 30 min-

utes before or 2 hours after eating. Oral suspension requires addition of antacid and water and is stable at room temperature for only 24 hours or under refrigeration for 30 days. In settings where households do not have access to refrigeration, the oral suspension should not be used. If taken with indinavir, the drugs must be separated by one hour. Weight based doses were determined by using body surface area values calculated from typical heights for weight.

Nevirapine – Tablet is scored and may be divided into equal parts. Tablet may be crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature. Nevirapine induction dose is 4 mg/KG once daily for 14 days and if no rash develops is followed by a maintenance dose of for children < 8 yrs old of 7mg/KG twice daily or for children ≥ 8 yrs old of 4 mg/KG twice daily.³ Consider using liquid for the induction dose in children in this weight range to give a more precise dose.⁴ If using tablets for children in this weight range, this chart suggests 1 tablet in the AM and ½ tablet in the PM to yield a dose that approximates that of the liquid -- the half-life of nevirapine is long enough that the fluctuation in drug levels from this staggered dose is considered clinically acceptable.

Efavirenz – Capsules may be opened and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature. Dose for oral solution is greater than that for capsules or tablets. The dose and pharmacokinetics of the oral solution is not as well established as with the capsules and tablet. Thus, although the liquid may be available in some areas, it is advisable to use the capsule or tablet forms when possible.

Lopinavir/ritonavir – Dose is calculated based on lopinavir component. Capsules may NOT be opened or crushed and must be swallowed whole, but may be used for children who can swallow capsules. Capsules or oral solution should be taken with food. Capsules and oral solution must be refrigerated until dispensed. After removing from refrigeration capsules and oral solution are only stable for 60 days at room temperature (up to 25° C). Where temperatures are expected to exceed 25°C, the feasibility of dispensing smaller amounts and giving more frequent refills

should be considered (for instance, no more than monthly supplies dispensed at one time). Lopinavir/ritonavir is not recommended for children < 6 months old.⁵The amount of solution has been rounded up to nearest ½ ml from manufacturer's recommendation for easier measurement.⁶ In the 17 – 19.9 KG range, two capsules twice daily would result in a dose that is ~40-60% higher than recommended, however, using only one capsule twice daily would result in a dose that is ~20-30% lower than recommended. Consider using liquid for children in this weight range.

Nelfinavir – Tablets may be crushed and dispersed in water or onto a small amount of food and immediately ingested. Must be taken with food to improve absorption. Oral powder for administration requires complicated administration technique that may not be practical in resource-poor settings.⁷ Doses for children < 2 years of age are not well established. The dose listed for children < 10 KG is within a range of up to 75 mg/kg/dose twice daily that has been used for small children by some clinicians.

Indinavir – Inconvenience of administration, toxicity, and tolerability are limitations to use. Every 8 hr dosing makes adherence difficult, but little information is available on twice daily dosing when co-administered with ritonavir. Attempts should be made to have children swallow the capsules whole as powder from opened capsules has a very bitter taste. Take on an empty stomach (1 hr before or 2 hrs after a meal). If taking along with DDI, separate drugs by 1 hr. Patients must drink lots of water to prevent development of kidney problems.

Trimethoprim/sulfamethoxazole – Recommendations for prophylaxis against opportunistic infections for HIV-infected children are to give 5 mg/kg given twice daily for 3 consecutive days/week. Considering the dosage strength of the TMP/SMZ suspension and in efforts to support medication adherence, dosing children once daily every day of the week may be a simpler alternative. The dose of 4 mg/kg is an easy conversion from the child's weight to the milliliters of suspension because the 8 mg/ml dosage strength of the TMP/SMZ suspension allows the dose to be calculated as ½ ml of suspension per KG. Doses are higher for treatment of bacterial and protozoal infections and other sources should be consulted.

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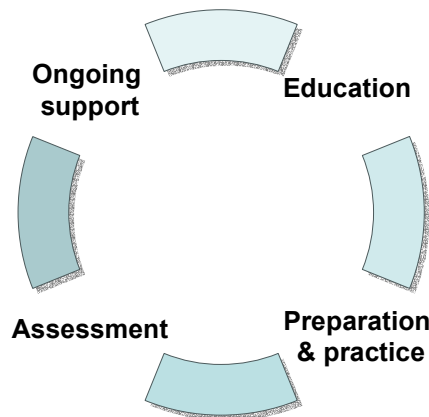
The MTCT-Plus Initiative & Multicountry Columbia AIDS Program Mailman School of Public Health Columbia University New York, New York, USA

Baylor International Pediatric AIDS Initiative Baylor College of Medicine, Houston, Texas, USA

Adherence in Children

Adherence can be particularly difficult for children and their caretakers. It requires both the commitment of a responsible adult and the involvement of an ill child. The child's developmental stage will influence the extent to which s/he can or will cooperate with medication administration, as will the parent-child relationship. Pediatric formulations are not always suited for administration to infants and young children; they may taste bad or be difficult to swallow. Pediatric antiretroviral regimens are frequently complex, requiring caretakers to measure liquid formulations, crush pills, open capsules, or dissolve tablets in water; doses may increase as the child gains weight. Furthermore, children are often tended by more than one caretaker, complicating both administration and assessment of adherence, and provoking disclosure issues.

These factors should not discourage programs from including children – after all, the lifesaving benefits of pediatric antiretroviral treatment dramatically outweigh the challenges. But they do mean that special attention to and expertise in pediatric adherence is an essential component of care. We recommend a four-part approach to pediatric adherence, focusing on education, preparation, ongoing assessment, and support. This chapter will focus on adherence to treatment; adherence to care is also of utmost importance.



Education

Pediatric care is a partnership between clinicians, caregivers and children. This collaboration is particularly important in HIV/AIDS care, and is critical to the success of pediatric antiretroviral treatment. Clinicians cannot simply write a prescription and recommend that an infant take his medication twice daily! An

informed and committed adult, supported by an experienced multidisciplinary care team, is a mandatory part of the equation.

The baseline assessment will guide the team's thinking about who to educate. Ideally, all caretakers will learn how to support the child's medication-taking, but this may not be an option if disclosure of HIV status has not taken place. The child's developmental stage will dictate what he or she can learn about adherence; many children, particularly older children, can participate in their own care.

Education is an ongoing process, and each family will have different needs and questions. At a minimum, caretakers should know what adherence is, learn why it is important and what the consequences of nonadherence can be, as well as understand the importance of communication with the care team.

- *Defining adherence:* Antiretroviral treatment is likely to be different than any other medications the child (or family) has taken. It is important to explore expectations, and to explain exactly what is required for treatment success. Caretakers should know that the goal is to take *every dose, every day, for life*. Medications must be taken on schedule, in the right combination, and at the correct dose. Coordinating treatment with meals, school, and other activities is a challenge, and caretakers should be aware of how difficult it can be.
- *Explaining the importance of adherence:* Using simple terms, visual aids, and relevant analogies, program staff should clearly explain *why* such high levels of adherence are required. Caretakers should understand that missing doses of medications can lead to treatment failure, and that taking medications irregularly or intermittently may confer all of the risks and none of the benefits of antiretroviral treatment.
- *Emphasizing the need for communication:* Patients and caretakers often want to please those providing treatment, and may feel uncomfortable admitting that they do not understand instructions, that they have questions or mixed feelings about antiretroviral treatment, or that children have not been taking their medications properly. These things, however, are exactly what program staff need to know in order to support and improve adherence. It is hard to overstate the importance of developing trust, partnership, and honest communication with children and their caretakers.

Preparation

Antiretroviral treatment is almost never an emergency. Taking the time to prepare patients and families can make the difference between treatment success and treatment failure, and should be a routine part of prescribing antiretroviral therapy. The caretakers should be able to confidently answer the questions

below before medication is prescribed. The team should help caretakers practice medication administration, anticipate problems and solutions, and understand what to do in case of difficulty. Peer support can be invaluable; parents may learn as many practical tips from other parents as they do from the care team.

- **Who will administer the medications?** While the primary caretaker is likely to be the person working with the multidisciplinary team, other adults may also be involved with the child's care. It would be a mistake to work only with the child's mother, for example, if she leaves the child with an aunt while she goes to work. Teaching a child's father about the medications would be insufficient if he is away from the home on weekends. Planning ahead for schedule changes, emergencies, and illness is an important part of a successful routine.

Ideally, everyone who cares for the child would know how to administer the treatments. In some households, however, this is complicated by the issue of disclosure. It would be difficult to explain ART administration to a grandmother who did not know that her grandchild (and therefore her daughter-in-law) is HIV-positive. A woman who has not disclosed her status to her husband is likely to have great difficulty giving medications to their new baby. Stigma and secrecy complicate adherence for children, as they do for adults, and ART preparation will need to be personalized to the circumstances of each household.

- **What medications will be given?** While children and caregivers do not necessarily need to know the formal or technical names of each medication, they must be able to confidently identify each one, and know how it is to be stored, measured, and administered. Pediatric formulations can make this particularly difficult – for example, many of the ARV syrups are the same color. Clearly labeling, marking, or color-coding the medications can be enormously helpful, and a close partnership with the dispensing pharmacist is important.
- **When will medications be given?** Antiretroviral medications should be given at the *same time* every day. While the first-line regimens used by ICAP programs do not have stringent dietary requirements, some ARVs do need to be taken on an empty stomach, others with food. Caretakers should know when to give medications – a watch is not required, but some practical system of timekeeping (e.g. sunrise, sunset) will be important.
- **How will medications be given?** The details of ART administration are particularly complex for children, and this aspect of preparation should be reviewed in detail and practiced carefully. Caretakers must know how to measure the doses – do tablets need to be cut or crushed? Should syrups be measured with a specific measure or with a syringe? Should medicines be taken with or without food? Does the taste of a particular ARV need to be

masked? Can the medicines be taken at the same time? What should be done if a child spits out or vomits the medication?

Useful strategies include practicing medication preparation and administration in the clinic, conducting “taste tests” with the child to see if s/he finds the medication palatable, training children to swallow pills by starting with very small candies, developing behavioral reward systems, and involving children in planning as behaviorally appropriate. As above, peer educators can be invaluable, as other parents and children may offer practical and emotional support. Written and pictorial information, videotapes, and tools such as pill boxes, blister packs and premarked syringes or measuring cups can also assist caretakers with the difficult task of supporting pediatric adherence.

The risk of nonadherence can be reduced by preparing caretakers for common problems such as refusing or spitting out medications, reminding them of children’s need for ritual, consistency, and supervision, and preparing them to deal with common side effects. Offering hypothetical scenarios – what would you do if the child vomits? Refuses one medication? Leaves home for the day without the medication? – and practicing role plays with both adults and older children can also be quite helpful.

Assessment

Adherence assessment is an integral part of an adherence support program. Although clinicians – particularly doctors – often feel that they know which of their patients do and do not take their medications, research has shown that they are often wrong. For many patients, formal and systematic assessment by a multidisciplinary team is the best way to identify problems with medication-taking.

There is no perfect way to measure adherence in the clinical setting, although the importance of good communication between family and provider, and the utility of multidisciplinary teams cannot be overstated. A mother may feel most comfortable telling the counselor that her child runs away when she tries to administer the medications. A home visitor may notice that the ARVs are not stored correctly, or that the measuring spoon is being used for something other than syrup. The team that treats families with respect and with a nonjudgmental approach is more likely to identify nonadherence than one that relies solely on pill counts.

At a minimum, families should be asked about adherence at every visit and pharmacy records should be reviewed on a regular basis. Asking patients to report on missed doses during the last week prior to the visit can be a useful way to assess adherence. Asking specific, open ended questions about concerns with administration or tolerance of medication is often a good way to learn of adherence problems. Pill counts, home visits, and parallel histories from different

family members can also be helpful, although these will not be appropriate in all settings. As children age, they should be included in the discussion of adherence. Many children learn to participate in their own care, and take on increasing responsibilities as they age. Older children should be asked about missed doses and about problems taking the medications.

Pediatric adherence is very likely to change over time as children themselves change and grow. An infant who took medications without difficulty may refuse them as a toddler during the “terrible twos.” An adherent 10-year old may become a nonadherent adolescent – or vice versa. Pediatricians caution us to “beware of adherence fatigue,” noting that children may tire of taking medications; adults may tire of administering or supervising them; and even providers may tire of providing ongoing assessment and support.

Ongoing Support

Adherence support should not be reserved for only those with problems taking medications, but should be offered to all patients throughout the course of treatment. Lifelong adherence to complex regimens is a difficult task and it is far better to prevent problems by identifying and supporting effective strategies, than to remedy them once they have occurred.

Psychosocial support for adherence can take the form of counseling to explore disclosure issues, peer groups to provide emotional support, or adherence partners who make a commitment to help with the child’s ART. Practical support includes adherence aids (pillboxes, blister packs, calendars, labeled syringes etc.), the preparatory steps above, and a creative and personalized approach to problem-solving.

By anticipating that adherence may falter over time, providers can develop a systematic approach to prevention and correction. If problems are identified, the cycle starts again, with education, preparation, assessment, and support.

Appendix A:

Practical Tips for Medication Administration to Infants and Children

Preparation of daily medications:

Reviewing medication preparation with the child's caretaker is an essential part of pediatric care. Establish which adult will prepare and supervise the medicines, and ask if other members of the family will also be involved. If so, they should also receive the appropriate skills training. Each time a dose is adjusted or medication is changed, these instructions should be repeated.

1. Display pills or liquids by preparing doses for patient and caretaker.
 - For pills, fill a pill box with one week's worth of daily doses.
 - For liquids, draw up one day's worth of doses in syringes.
2. Have the caretaker repeat the exercise by filling the pill box with one week's worth of medication and/or drawing up one day's worth of doses in syringes.
3. Many liquid preparations and medication bottles look alike. Consider labeling each with a piece of colorful tape. For liquid medicines, use the same color tape on the bottles and syringes.
4. Stress the importance of allotting adequate time and providing a quiet environment when preparing daily meds, especially during the first few weeks of treatment.
5. Explain the advantages of a medication routine; taking the medicines at the same time each day is easier when a pattern is established.

Measurement of daily doses:

Pediatric dosing must be precise to insure adequate therapeutic levels. When possible, caregivers should use syringes to measure and administer liquid medications. Caretakers should be discouraged from using household spoons as they may vary in size which can lead to inaccurate dosing.

1. Use brightly colored tape to mark the correct volume of syringes.
2. Use a different syringe for each medication. Consider labeling each type of syringe and its appropriate bottle with the same color tape.
3. Syringes can be reused until the markings or tape begins to wear off or the plunger becomes difficult to manipulate. Syringes should be gently washed with warm soapy water, rinsed well, and allowed to air dry.
4. As above, have the caretaker practice drawing up medications while at the clinic. Discuss common problems and solutions with measuring liquids – what if the medicine is too sticky? What if it spills?

Medication storage:

It is best to avoid high temperatures for all medications. Medications should not be stored in direct sunlight or in other spots likely to become very hot. Most drugs should be kept in a cool place. In particular, lopinavir/ritonavir (Kaletra™) needs to be stored in a cool place. If refrigeration is available, caregivers should be informed to keep this medication in the refrigerator. If not, ask where in the home cool items are stored – is there a cool pot, extra water jug, or cooler? If not, it may be prudent for the program to obtain a cooler or cool box for the family, particularly if ice is easily obtained.

Lopinavir/ritonavir (Kaletra™) liquid must be stored in a glass container, as the liquid may corrode plastic. The pharmacist will dispense this medication in a glass container,

and patients should be advised to draw medications into the syringes only at the time of administration. A filled syringe should not be used to store or transport doses.

It is important to counsel caregivers about safe storage of meds – away from children who are always curious about something new. Medication should never be referred to as candy!

Masking the taste of medications:

Not all medications are unpalatable, but when they do taste bad, it can be extremely difficult to convince children to take them. It is prudent to conduct a “taste test” in clinic with each child to see if any of the medications you have prescribed will be problematic in this regard. If the child finds any of the tastes offensive, assure both child and caretaker that the taste can be partly or wholly masked, and work with them to find the most successful approach.

1. For liquid medications, first draw up the medicine in a syringe to measure the proper volume. Combine with 5-10 cc of tasty liquid such as juice, milk, or local pediatric beverage. (Do not combine with large volumes). Mix vigorously. Be sure that the caregiver is aware the child must drink the full amount.
2. Alternatively, dip the syringe tip into something sweet to mask the initial taste or give small amounts of beverage pre- and post- medication administration.
3. For pills, crush with a mortar and pestle until fine. For capsules, open the capsule into a small bowl. Add 1-2 teaspoons of food (jelly, jam, crushed banana, cereal) and combine vigorously. Feed child *all* of the food to insure that all medication is consumed.
4. Review which medications in tablet form can be broken in half and swallowed for older children. Hard tablets may be dipped and coated with sauce or any other viscous food product to help the older children swallow pills.
5. Immediately after administering medications, offer child a sweet-tasting food to mask the taste of the medication. Administration of sweet or tangy substance prior to giving medication may also be helpful.
6. Remember to give lots of praise after each dose!

Avoiding or Minimizing Nausea

It is important to ask if medications cause nausea, since this will be a powerful barrier to adherence. If the medications do make children nauseated, the following interventions may be helpful.

1. Offer the child a small meal of bland food (cereal, crackers, bread). Shortly thereafter, administer medication.
2. Administer tablets and capsules with only enough water or beverage needed to swallow. Children have a tendency to drink much more water than necessary which often leads to vomiting due to the large volume of liquid.
3. Reassure the caregiver that the nausea is usually temporary until the child’s body gets “used to” the medicine. Stress importance of giving meds in a calm, unhurried manner, especially during the first few weeks.

Special Circumstances

The resistant child: In cases where children are reluctant to take medications or are refusing some doses, a reward system can be helpful. It may be useful, particularly for school age children, to make a visible calendar. Each time the child takes their

medication successfully, the caregiver can make a mark on the calendar (a “happy” face). When the child accumulates a particular number of successful days he/she is rewarded with a small token. The program may want to purchase small toys or gifts to use as rewards for successful adherence. Based on the age and the developmental stage of the child, he/she can be asked to participate in the preparation / administration of the medication to promote child’s participation as well as sense of accomplishment.

Preparation of stavudine: The liquid formulation of stavudine requires refrigeration, which may not be an option for some program and/or families. Since the lowest-dose stavudine capsule has 15mg, it may be necessary to open the capsule and measure the powder for children who need lower doses.

1. Open a 15-mg capsule and add the powder to 15cc of liquid, preferably water.
2. The solution will now contain 1mg of stavudine in every 1 cc of liquid.
3. Using a pre-marked syringe, the caregiver should now draw up the correct dose and give it to the child.
4. The remainder of the liquid should be discarded.

Stavudine capsules may also be opened if mixing the powder with food or drinks assists the child to take the medication.

Nutritional Assessment and Support for Infants and Children

What is pediatric nutritional assessment?

Children with HIV, like adults, are at risk of malnutrition. In contrast to adults, this may present as growth failure rather than overt weight loss. Nutritional assessment, the systematic evaluation of current nutritional status and diet, is an important component of care.

Why is pediatric nutritional assessment important?

Malnutrition in HIV-infected children is common, and its effects can be profound. Routine and systematic evaluation can identify problems early, allowing the multidisciplinary team to determine why the child is malnourished and to develop an effective intervention. Poor growth may be the first indication that an HIV-exposed child is infected, prompting further evaluation of the child's infection status. For a child with known HIV infection, growth failure can warrant the initiation of antiretroviral therapy or a change of therapy for those already on treatment.

How often should pediatric nutritional assessment be conducted?

Routine nutritional assessment should be performed at every clinical visit. A more extensive evaluation may be required for children with growth failure or other evidence of malnutrition, as described below.

Who should perform pediatric nutritional assessment?

All clinicians working with children should be able to conduct a pediatric nutritional assessment. At sites where more specialized expertise is available, children with growth abnormalities or dietary problems may be referred to a clinical nutritionist or dietician.

How should pediatric nutrition be assessed?

Routine nutritional assessment should be performed at every clinical visit. Its components can be thought of as screening questions and include:

- Asking parents and caretakers about the child's diet and availability of food in the household.
- Asking about symptoms that may prevent food intake and absorption.
- Measuring the infant (head circumference, length, weight) or child (height, weight) and plotting his/her growth on standardized and locally appropriate growth charts.

Obtaining a diet history:

At each visit, the parent or caretaker should be asked about the child's diet. The initial interview need not focus on details, particularly if no nutritional problems have been

identified. But each family should be asked how many times the child eats each day, if the child is getting enough to eat, and if a variety of foods are available. If the child is nursing, questions about adequacy of milk supply, frequency of feeds, and any perceived problems with feeding should be asked at each visit. It is also important to ask, in a sensitive way, whether financial constraints or illness in the family have limited the child's access to food. Most parents are concerned about their children's growth and development, and engaging them in this sort of discussion can be easily accomplished, adding to the rapport between the family and the health care team.

Assessing nutrition-related symptoms:

The symptom checklist used by ICAP programs should identify symptoms – such as fatigue, mouth pain, difficulty sucking or swallowing, nausea, vomiting, and diarrhea – that can prevent adequate nutrition. Additional evaluation, described below, will be needed for children with poor growth.

Measuring the child:

It is vitally important to measure the child at each clinical visit. Measurement of weight, length, and head circumference should routinely be performed on children less than 24 months. Older children's height and weight should be recorded at each visit. Because the rate of growth also provides useful information, growth curves should be used – it is not enough to know that the child weighs more than at the previous visit. Sluggish weight gain may be an indication of HIV infection, malnutrition, or both, and can best be appreciated by the routine use of growth curves. Questions which the use of growth curves can answer include: Is this child gaining weight as expected? Has this child's rate of growth changed? Does this child have growth failure? Sample growth curves for boys and girls are included as Appendix A of this chapter. While the growth curves included here are from the United States Centers for Disease Control and Prevention, these may not be appropriate for all settings; each site is encouraged to use whichever graph is most suitable. Many local graphs are only appropriate for infants and young children, however, and it is equally important to plot the growth of older children with HIV infection.

The most commonly used growth curves include weight for height, height for age, and head circumference for age. The graphs include information about normal growth, expressed as “percentiles.” A child in the 90th percentile for weight is as heavy as or heavier than 90% of her peers; only 10% weigh less. A child who is in the 15th percentile for height is shorter than 85% of other children his age. In general, well-nourished children remain at a constant or increasing percentile: a child who has gained weight since his last visit but who has dropped from the 50th to 30th percentile in weight may have a significant nutritional problem and warrants further evaluation.

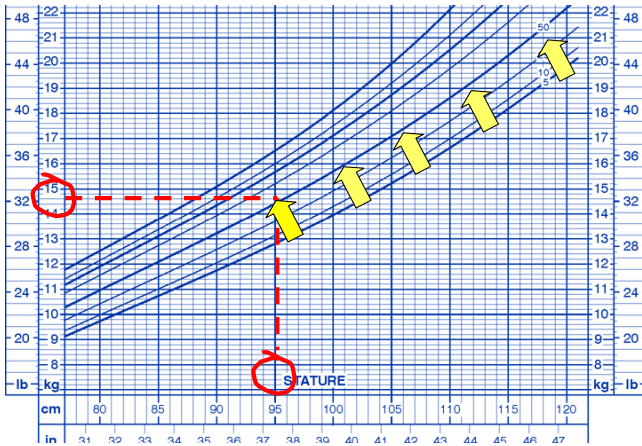


Figure 1: Weight for height

This child is 95 cms tall (X axis) and weighs 14.6 kgs (Y axis). S/he is in the 50th percentile of weight for height.

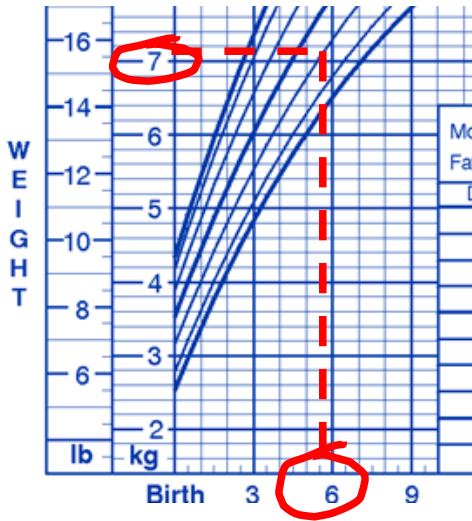


Figure 2: Low weight for age

This child is 6 months old (X axis) and weighs 7 kilograms (Y axis). S/he is in the 25th percentile of weight for age.

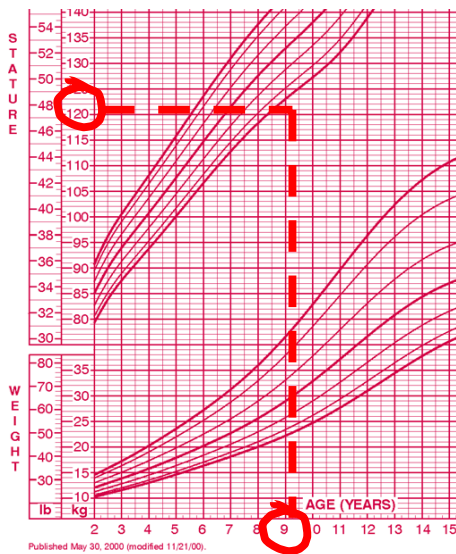


Figure 3: Low height for age

This child is 9 years old (X axis) and 120 cm tall (Y axis). S/he is below the 5th percentile in height for age.

How is growth failure defined?

Significant growth failure for infants and young children is defined as the failure to sustain a normal velocity of weight gain during the first three years of life. This is defined as crossing two major percentile lines on the weight growth curve over at least two months. For children already less than the fifth percentile for age, this is defined as the inability to follow along their own upward curve. Growth failure can also be defined by the loss of greater than or equal to 5 percent of body weight. It is important to be able to distinguish between a short term lack of growth due to intercurrent illness or circumstance, and the sustained lack of growth which defines failure.

“Linear growth failure” is defined by low length or height for age and is particularly important to recognize during the first three years of life. If adequate growth is not attained during this period, it is difficult to “catch up” even if nutritional interventions are subsequently introduced.

How should a child with growth failure be evaluated?

Once growth failure has been identified, prompt evaluation is indicated. The underlying cause may be socioeconomic, biomedical, or a combination of the two. However, as noted above, growth failure may be the first sign that an HIV-exposed infant is infected or that an infected child requires HIV therapy. Therefore, it is crucial to rapidly identify the reason for the inadequate growth.

Assessment should begin with a detailed nutritional history, which will help to differentiate the child with inadequate intake from the one experiencing excessive losses. The nutritional history should be more extensive than the one taken at a routine clinical visit and should include a 24- or 72-hour dietary recall, specifying exactly what the child has eaten in the previous day(s). This will provide insight into how much the child eats and the nutritional value of the foods s/he is given. Questions regarding food availability and security should always be included.

Additional information should include eating behavior – excessive vomiting or spitting after feeds may indicate gastroesophageal reflux, for example. Description of stools will identify those children with diarrhea. Frequent watery stools may indicate gastrointestinal infection. Voluminous, foul-smelling or greasy stools may help to identify the child with malabsorption. Poor appetite and fatigue may be indications of systemic infection such as tuberculosis or HIV.

The next step is a targeted physical examination, which will confirm the extent of malnutrition, and which may also identify the cause. For example, the discovery of painful sores or thrush in the child’s mouth suggests both a diagnosis (impaired intake) and a course of action (treatment of the infection). Neurodevelopmental abnormalities, in contrast, suggest an alternate reason for impaired food intake.

Unless the history and examination reveal clear evidence of specific organ dysfunction, it is not unreasonable to consider HIV and/or TB as the etiology of growth failure. While it is important to exclude correctable causes of poor growth, HIV is frequently the primary cause.

- Early diagnostic results should be reviewed if the child is an HIV-exposed infant and repeat testing should be sent if HIV is suspected (Chapter 6.1).
- If the child is known to be HIV-infected, the child should be evaluated for eligibility for antiretroviral therapy (chapter 6.4).
- If the child is currently receiving antiretroviral therapy, poor growth may indicate that the current regimen is failing. Adherence should be assessed to insure that treatment has not been stopped or interrupted. If nutritional interventions fail to improve weight gain, the child may be eligible for a new treatment regimen.

Tuberculosis should also be considered if a child has growth failure especially if there are other systemic symptoms including fever, fatigue, and cough. Obtaining a contact history, placing a tuberculin skin test and assessing organ specific pathology (chest xray, node biopsy) are useful ways to evaluate the child for TB infection. In light of the difficulties diagnosing TB in children, a trial course of anti-tuberculosis therapy may be necessary.

Laboratory assessment may be helpful, although it is not indicated (or available) in all cases. Clinicians should approach this decision in a logical way, based on information from the history and physical examination. Stool examination, including culture and exam for parasites, may provide the diagnosis for a child with diarrhea. Assessment of hemoglobin may find that anemia is the reason a child lacks the energy needed to feed. Urine testing may detect renal disease, which may hamper growth even in the face of adequate caloric intake. Skin testing for tuberculosis may lead to the diagnosis of active TB, which is associated with growth failure and contributes to a hypermetabolic state, anorexia, pulmonary infection and excessive losses.

How can pediatric nutrition be supported?

All children in ICAP programs receive multivitamins. Additional support includes counseling mothers about breast-feeding (see below), and all patients about food and water hygiene. Sites are strongly encouraged to maintain an inventory of local resources – food pantries, micro-finance programs, and other community-based programs – that may provide support to individuals with HIV/AIDS.

More targeted interventions may be required for children with growth failure or nutritional difficulties. Once the likely cause has been identified, the multidisciplinary team should develop a specific plan of action. This may range from treatment of an acute illness, to provision of family education regarding food choices and preparation, to referral to food programs and community resources. In addition to caloric supplementation, selection of specific foods may ameliorate certain symptoms, such as nausea, sore mouth and throat, or diarrhea (see Table 1).

Table 1: Symptomatic Nutritional Counseling

Symptom or problem	Nutrition advice*
Diarrhea	Encourage the child to drink throughout the day. If no longer breast-feeding, encourage soups, diluted fruit juice, water, or oral rehydration solution. Foods that are soft, mashed, and moist – such as porridge from cereals, rice, bananas, potatoes, and other soft vegetables - may be best tolerated.
Sore mouth or throat	Encourage soft, mashed, or smooth foods such as avocados, squash, pumpkins, papaya, bananas, yoghurt, creamed vegetables, soups and minced foods. Chewing small pieces of mango, kiwi, or green papaya may help to relieve pain. Avoid spicy and salty foods such as chilies and curries, as well as acidic or very sour foods such as oranges, lemons, vinegar, and tomatoes.
Nausea	Encourage dry foods, such as crackers, toast, and cereal. Eating small amounts more frequently is often easier than eating large meals. Avoiding fatty and greasy foods may help. Smelling ginger, lemons, and/or oranges, and drinking herbal or ginger tea may relieve symptoms.

Adapted from “Living Well with HIV/AIDS” (see Appendix B)

*This advice may not be appropriate for all patients. Counseling should, as always, be individualized.

Infant feeding: To breast-feed or not to breast-feed?

The decision to breast-feed or formula feed is based on societal norms, individual and family beliefs, and individual resources. There is no specific ICAP policy concerning infant feeding practices. Recognizing that conditions are different at each site, the programs’ goal is to support each team as they work to develop site-specific guidelines that are consistent with WHO recommendations and which are appropriate to the community in which the site is based. WHO recommendations state:

“When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended; otherwise exclusive breastfeeding is recommended during the first months of life. To minimize HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account local circumstances, the individual woman’s situation and the risks of replacement feeding (including infections other than HIV and malnutrition)”

Background information:

HIV can be transmitted at any point during lactation, and the risk of breast-feeding is cumulative; the longer the HIV-infected mother breast-feeds, the greater the risk of transmission. Breast-feeding by an infected mother increases the risk of HIV transmission to her newborn by 5 to 20 percent. In settings where breast-feeding is common and prolonged, this route of transmission may account for up to half of HIV infections in infants and young children.

Although pMTCT interventions can substantially reduce the risk of transmission during pregnancy, labor, and delivery, the only proven way to prevent HIV transmission via breast-feeding is to avoid the practice. Maternal factors – such as recent HIV infection,

advanced maternal disease, low CD4 count, high HIV RNA viral load, and mastitis – are known to increase the risk of infection, and suggest possible but as-yet unproven interventions such as treatment with ART during lactation, and promotion of breast health/rapid treatment of mastitis when it occurs.

While breast-feeding of all types is associated with a higher rate of HIV transmission than replacement feeding, one study has shown that *exclusive* breast-feeding is associated with a lower transmission risk than *mixed* feeding. It is thought that the introduction of foreign antigens may make it easier for HIV to cross the mucosal surface of the gastrointestinal tract. Mixed feeding with both breast milk and other foods should be avoided since it brings with it both the risk of HIV infection and the risks of diarrhea and other infectious diseases. ICAP program staff may be able to help the mother strategize regarding cessation of exclusive breast-feeding, so that she does not continue intermittent breast-feeding, putting her infant at further risk.

Potential advantages of breast-feeding:

Breast-feeding is the societal norm in many cultures, and advantages include the important bonding that takes place between infant and mother. Breast milk contains maternal antibodies to a wide variety of organisms and may provide protection to the infant from diarrhea, pneumonia, neonatal sepsis and acute otitis media. Successful breast-feeding does not depend on availability of formula or clean water, and has been associated with a decrease in early deaths from infectious diarrhea. In addition there may be child-spacing effects due to the decreased pregnancy rate during the breastfeeding period, due to the lactational amenorrhea that may accompany it.

Potential disadvantages of breast-feeding:

Although breast milk is generally considered nutritionally complete for the first six months of life, it is not clear that this is true in the case of a mother with poor nutritional health herself. It is also unclear that the protection that breast-feeding normally confers against the common childhood infections including infectious diarrhea applies to infants born to HIV-infected women. Advantages to replacement feeding also include the fact that the baby can be fed by other family members. In addition, less energy is required on the part of the baby to feed from a bottle or cup, and some ill infants may be able to increase their overall intake by using this method.

Informed choice:

HIV-infected mothers should receive counseling that includes general information about the risks and benefits of all infant feeding options, as well as guidance in selecting the option most likely to their specific individual and family circumstances. Mothers should understand that exclusive formula feeding remains the most effective method for preventing postpartum HIV transmission via breast milk. However, in areas where this may be unsafe or unavailable, and in circumstances where a woman prefers to breast-feed, exclusive breast-feeding is preferable to mixed feeding. ICAP program staff should be able to discuss this difficult issue with confidence, answer

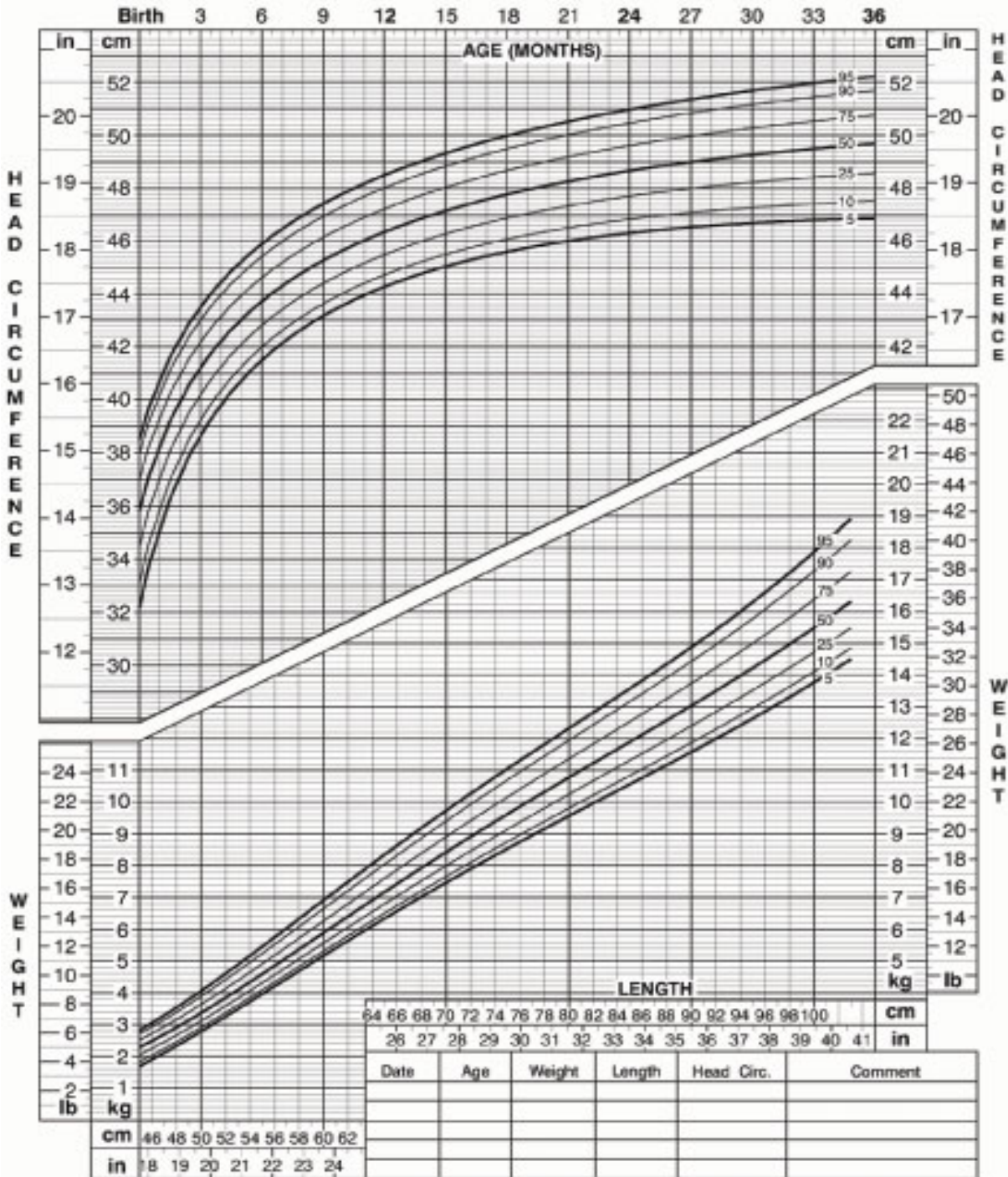
questions, and provide complete and non-judgmental support for each individual mother's decision about what is best for her and her new baby.

Appendix A: Pediatric Growth Curves

Birth to 36 months: Boys Head circumference-for-age and Weight-for-length percentiles

NAME _____

RECORD # _____



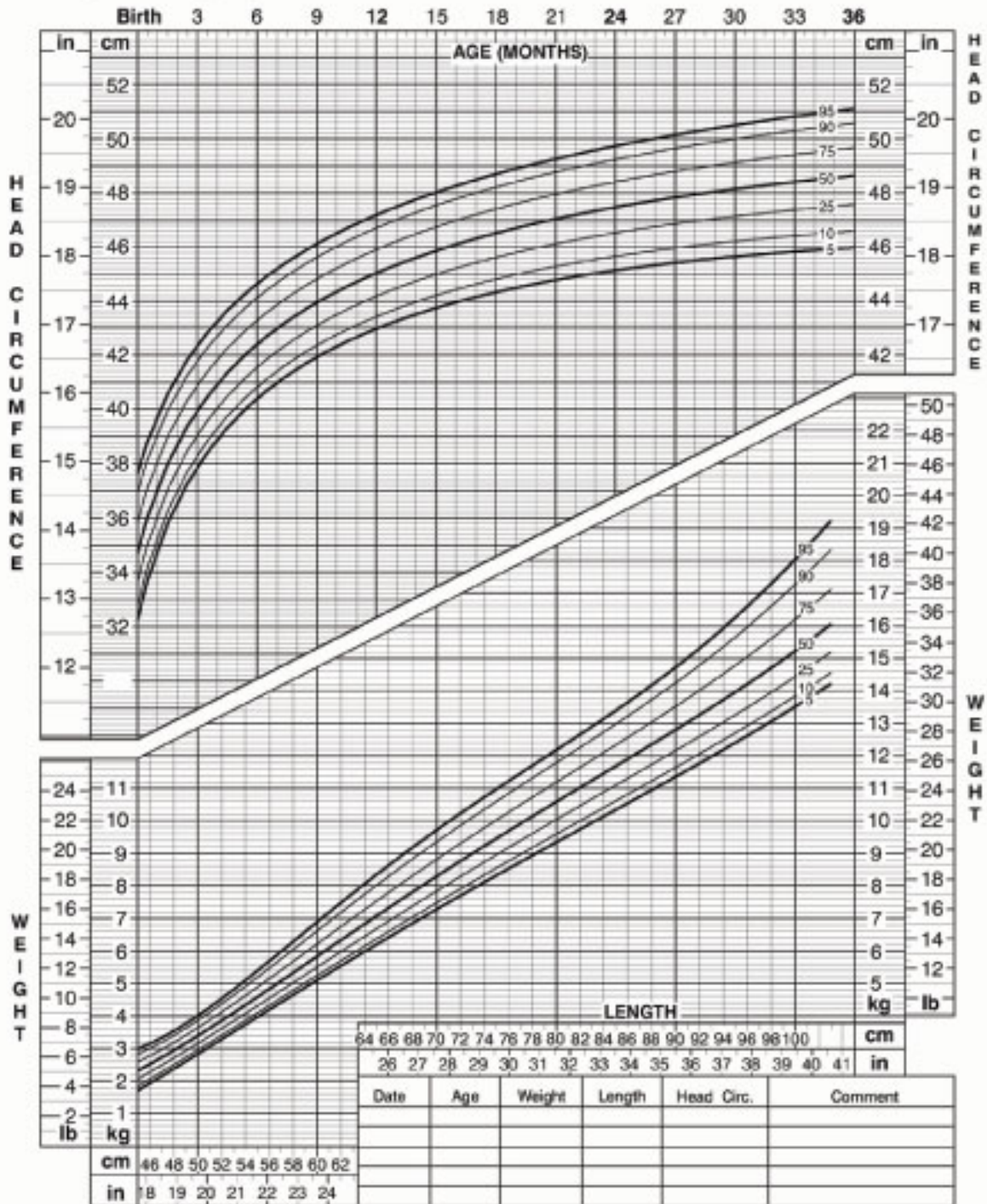
Published May 30, 2000 (modified 10/16/00)
SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.edc.gov/growthcharts>



Birth to 36 months: Girls
Head circumference-for-age and
Weight-for-length percentiles

NAME _____

RECORD # _____



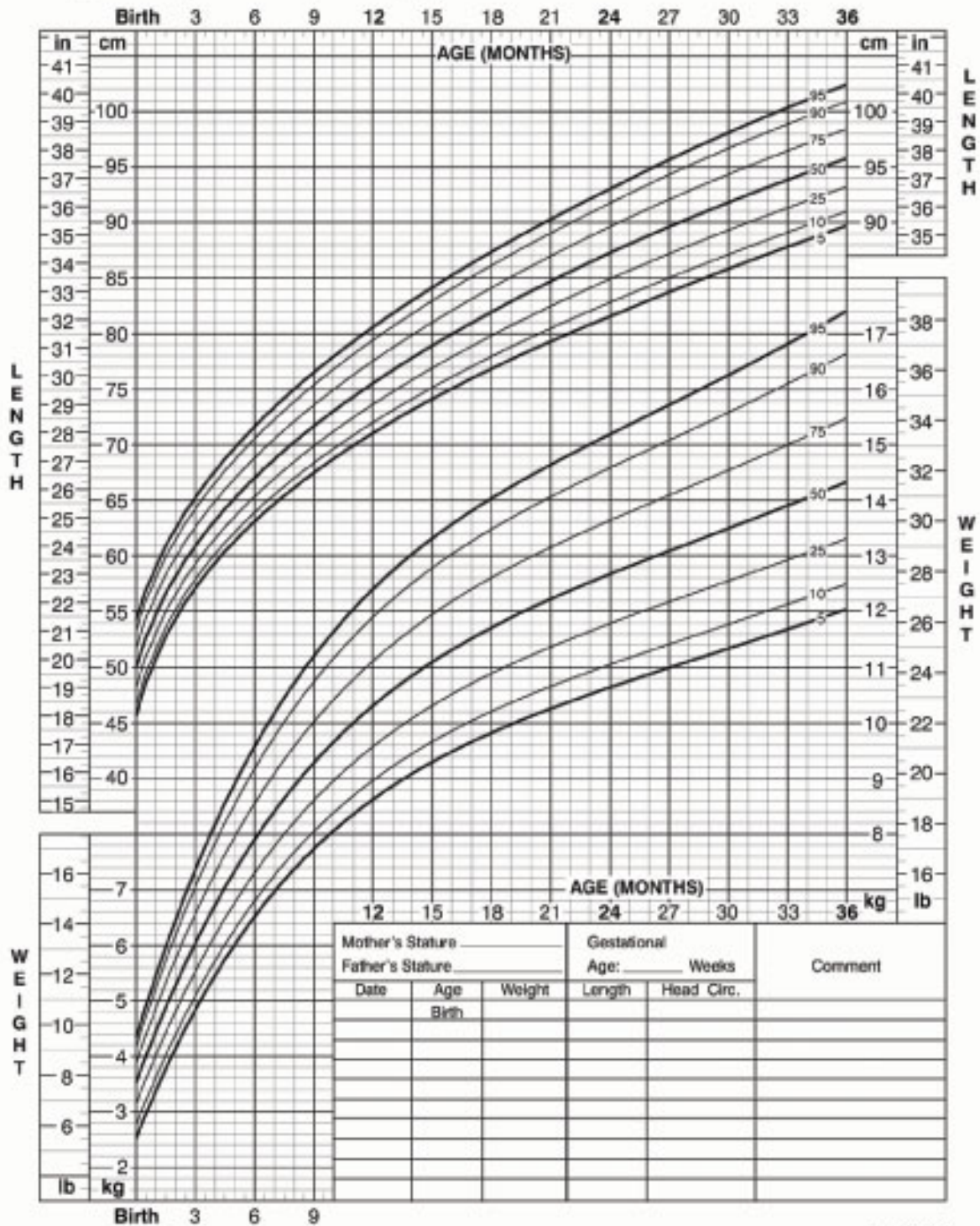
Published May 30, 2000 (modified 10/16/00)
 SOURCE: Developed by the National Center for Health Statistics in collaboration with
 the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>



Birth to 36 months: Boys
Length-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



Published May 30, 2000 (modified 4/20/01).
 SOURCE: Developed by the National Center for Health Statistics in collaboration with
 the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>

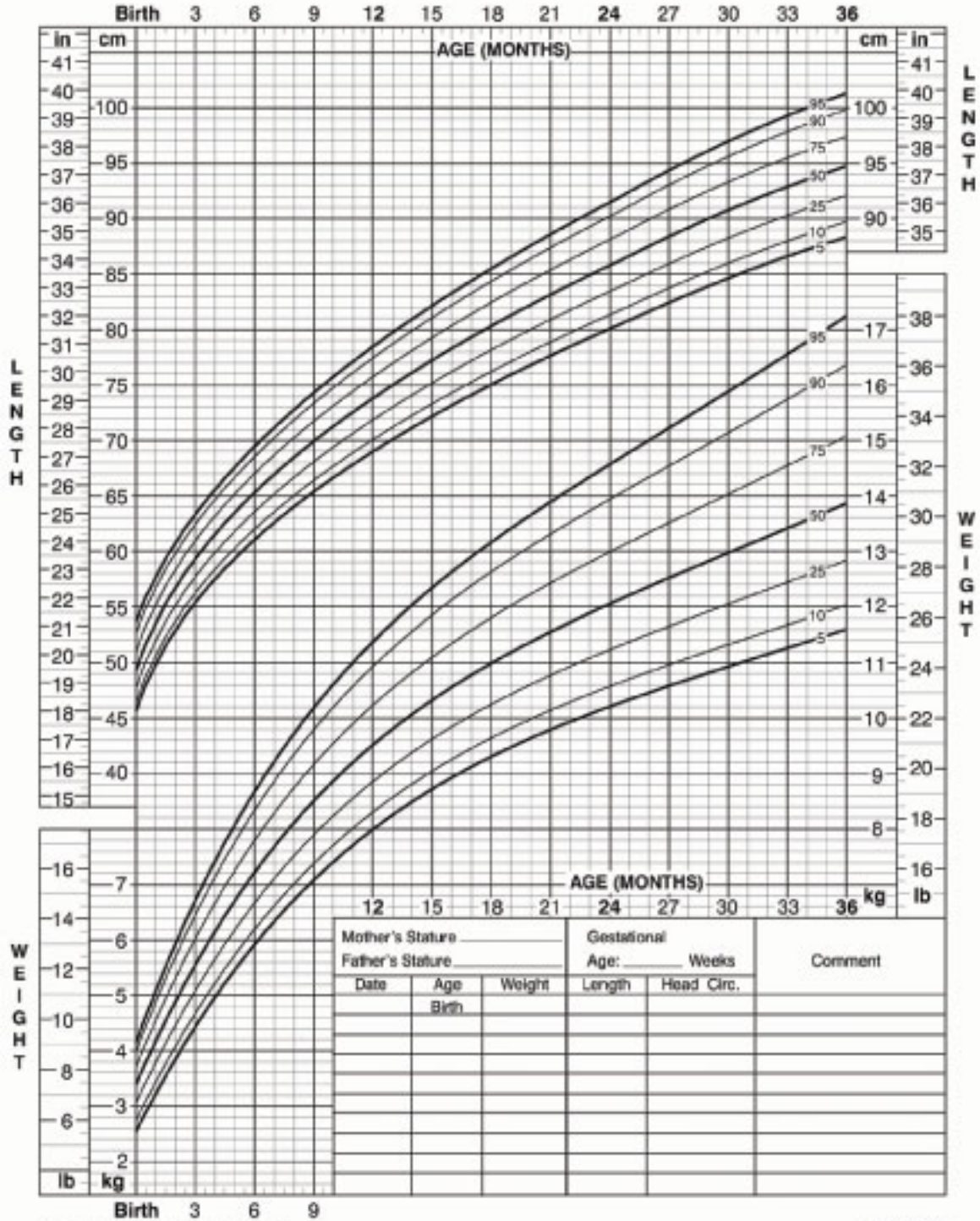


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Birth to 36 months: Girls
Length-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



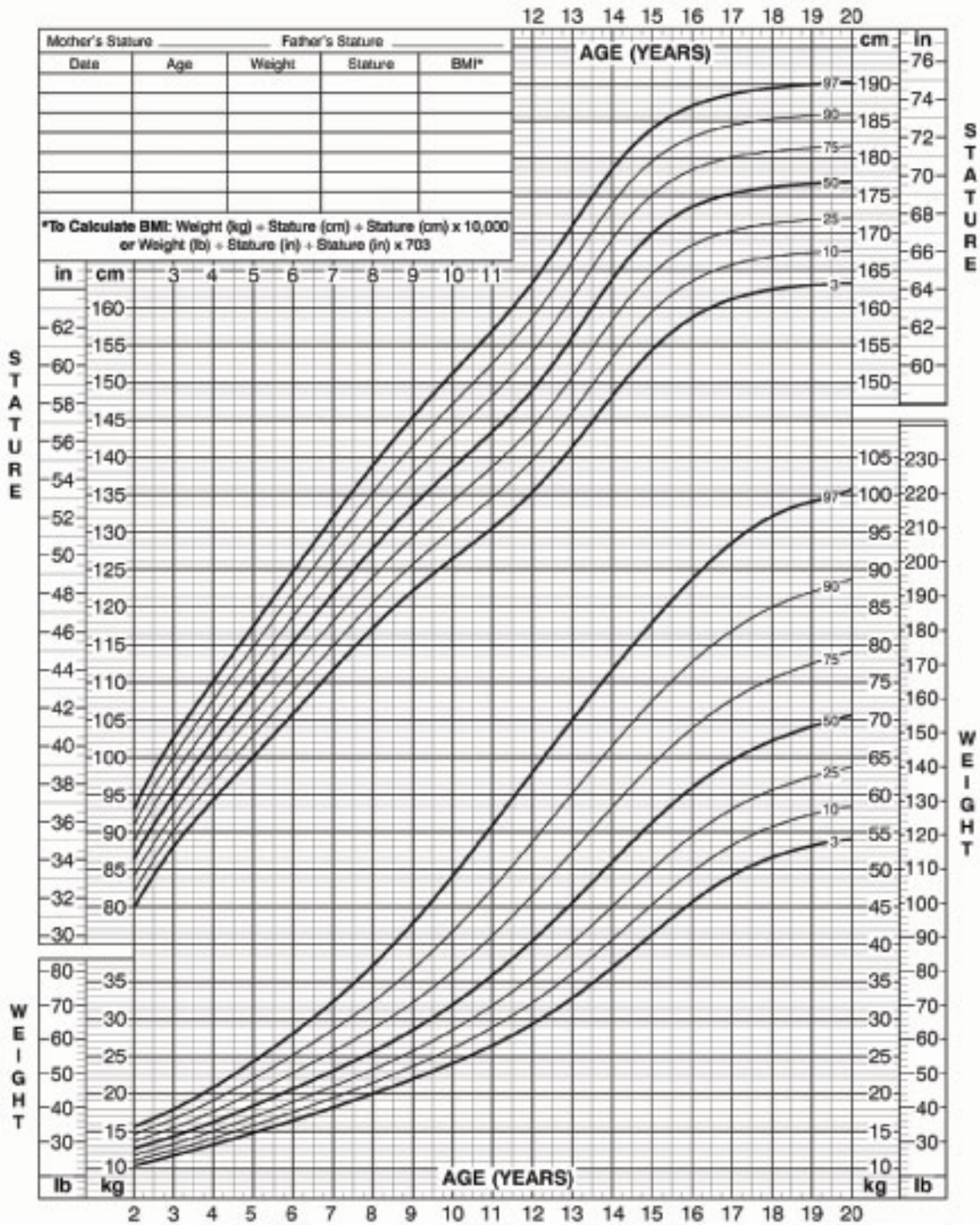
Published May 30, 2000 (modified 4/26/01).
 SOURCE: Developed by the National Center for Health Statistics in collaboration with
 the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>



2 to 20 years: Boys
Stature-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



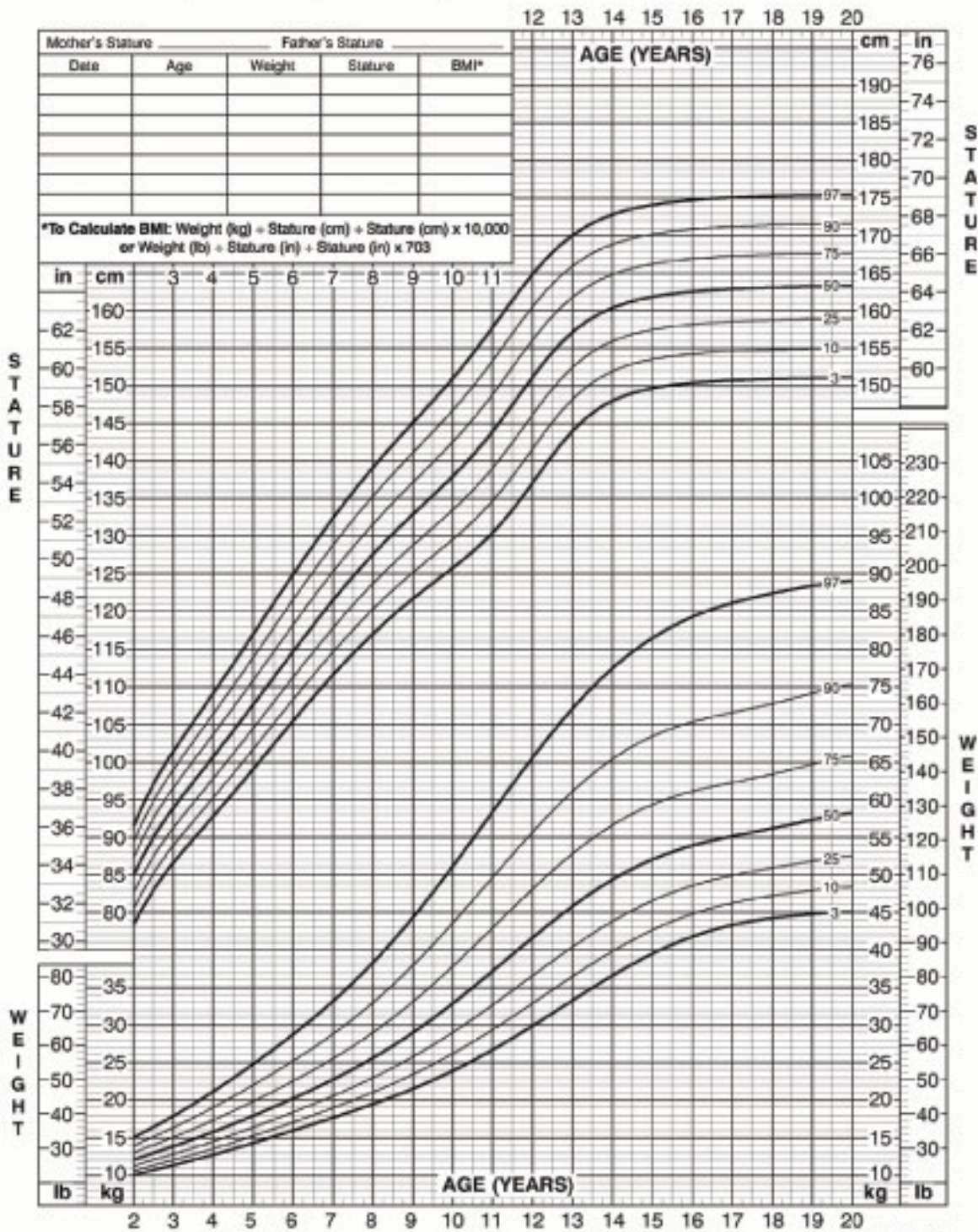
Published May 30, 2000 (modified 11/21/00).
 SOURCE: Developed by the National Center for Health Statistics in collaboration with
 the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>



2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



Published May 30, 2000 (modified 11/21/00).
 SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
<http://www.cdc.gov/growthcharts>

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Appendix B: Additional Resources

Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants: Guidelines on Care, Treatment and Support for Women Living With HIV/AIDS and their Children in Resource-Constrained Settings. WHO 2004.

<http://www.who.int/hiv/pub/mtct/en/arvdrugsguidelines.pdf>

Infant feeding options in the context of HIV

The LINKAGES Project, Academy for Educational Development, April 2004. [PDF, 363K]

http://www.linkagesproject.org/media/publications/Technical%20Reports/IFOptions_04-04.pdf

HIV transmission through breastfeeding: a review of the available evidence.

UNICEF, UNAIDS, UNFPA, WHO, 2004.

http://www.unfpa.org/upload/lib_pub_file/276_filename_HIV_PREV_BF_GUIDE_ENG.pdf

Women, Children, and HIV website (sponsored by the François-Xavier Bagnoud Center at UMDNJ and the Center for Health Information at UCSF)

<http://www.womenchildrenhiv.org/wchiv?page=if-00-00>

Living well with HIV/AIDS: a manual on nutritional care and support for people living with HIV/AIDS. The Food and Agriculture Organization of the United Nations.

<http://www.fao.org/DOCREP/005/Y4168E/Y4168E00.HTM>

Pediatric Disclosure: Talking to Children about HIV

Sharing a diagnosis of HIV may be difficult under the best of circumstances, and discussing HIV/AIDS with children poses additional challenges. Adults invariably struggle with the questions of whether, when, and how to tell children that they have HIV, often agonizing over how to find “the right words” to explain. Twenty years of experience with pediatric disclosure has shown that the support of counselors and clinicians and the shared experience of other parents can be of great help to caretakers. All programs providing HIV/AIDS care should be able to assist families with this difficult subject.

Discussing HIV with children raises complicated issues. While these are largely determined by the unique relationships and personal histories in each household, and by the community and cultural context in which each family lives, common themes do exist. Some caregivers feel very strongly that it is their duty to protect children from learning about the virus and its implications, while others feel that secrecy is harmful. Families may worry about the ability of a child to be discreet and about the impact on their family’s status in the community if the diagnosis is inadvertently shared. Others are reluctant to tell a child that s/he has HIV because of the dual disclosure this requires: that his/her mother is also infected.

It is not uncommon for family members to disagree about disclosing HIV-related information to children, a topic which is often highly emotionally charged. Similarly, members of the HIV/AIDS care team may disagree as to the best approach for a specific family or child. It is important to acknowledge the complexities of pediatric disclosure, the strong feelings evoked by the topic, and the need to respect the wishes of patients and families.

Pediatric disclosure – e.g. telling a child that s/he is HIV-positive – is an essential part of a child’s health care and is a sign of respect for his/her rights as an individual. Disclosure should, of course, take family and community issues into consideration, should occur when age-appropriate, and should be conveyed with appropriate language and terms. This chapter will briefly introduce ICAP’s recommended approach.

Talking About Disclosure: Early and Often

Because sharing the diagnosis of HIV with children can be complicated and challenging, the subject should be a recurring theme of any family’s treatment plan. Pediatric disclosure is an important subject for the multidisciplinary team to

discuss, and the topic should be introduced and explored with parents and caretakers early in the course of care. Ideally, clinicians and counselors will act as facilitators, helping each family to find its own path, while gently encouraging adults to examine the problem from “all the angles.”

Members of the multidisciplinary team – from clinicians to counselors to peer educators – can be valuable conduits of shared experience and information, helping caregivers to learn from the experiences of others facing similar dilemmas. It can be enormously comforting to know that many other parents have grappled with the same difficult questions. Knowing that others have found successful pathways towards openness and disclosure, and understanding that children have had positive outcomes once HIV was explained to them can be very reassuring. Providers should be generous about offering hope to caregivers as they contemplate talking to their children.

It is much easier to approach the topic if it is routinely and “neutrally” addressed early on, rather than during a health crisis or family change. Providers can help caregivers by giving them private time during each clinic visit in which to discuss their feelings about pediatric disclosure while children are occupied elsewhere, out of listening distance. By creating an accepting and private environment in which to explore the subject, providers can play a crucial role in helping caregivers make fully informed, deliberate, coordinated, and responsible decisions about whether, when, and how to begin the process of sharing a diagnosis of HIV with their children.

While each family will have different needs and questions, it may be helpful to begin the conversation by addressing the four domains listed below. Rather than attempting to answer all questions in one visit, it is more reasonable to pick a few topics each time, gradually constructing a picture of the unique circumstances and context of each family. By gradually reviewing – and expanding upon – each set of questions, families will be more likely to engage in a comprehensive process of considering disclosure. Providers will also have more opportunities to share relevant stories and guidance, and caregivers who decide to disclose will have opportunities to make careful plans and to practice how to begin.

• **The child (or children):**

- ✓ Is the child symptomatic? Taking medication?
- ✓ How old is the child? How verbal? Is s/he functioning as an adult?
- ✓ Is the child living with a sick parent or sick family members?
- ✓ Is the child asking questions about HIV?
- ✓ Does the child appear distressed, anxious, or worried?
- ✓ Is the child sexually active and at risk of contracting or spreading HIV?

• **The parent / adult caregiver(s):**

- ✓ Has the parent/caregiver been tested for HIV?
- ✓ Is the parent/caregiver infected? Symptomatic? Taking medication?

- ✓ If the adult is ill, is s/he in need of help from children in the household?
- ✓ Is the infected adult an important attachment figure for the child?

- **The family / household:**

- ✓ Are any adults in the household HIV-infected? Who is aware?
- ✓ Are any other children in the household HIV-infected? Who is aware?
- ✓ How many family members are taking HIV-related medication?
- ✓ Is the family unit cohesive, or characterized by separations and/or conflicts?

- **The community:**

- ✓ Is testing and treatment generally available in the community?
- ✓ Are there people in the community who are open about their own HIV status? Does the child know anyone in the community who is open about his/her HIV status?
- ✓ How strong is the stigma surrounding HIV in the community? Are there risks to the family (e.g. isolation, discrimination) if inadvertent disclosure occurs?
- ✓ Are there resources within the community for children – e.g. a youth group, and/or trusted adults that they can talk to?

These are just some of the questions that families and providers should consider and document together as they discuss HIV disclosure to a child. It may also be helpful to consider some of the knowledge about pediatric disclosure learned in countries where testing and treatment have been available for decades. While the relevance of these studies may change from setting to setting, there are likely to be some common truths that can help families around the world. For example, researchers found that families most often cited the need to maintain family *trust* as one of the most compelling reasons, along with a child's age, to disclose HIV information. Children living with HIV/AIDS cited the "wish to be trusted with honest answers to their questions" as highly important.⁵ Other research suggested that the lengthy "interval of secrecy" that children with HIV endure before being told of their status may independently contribute to feelings of loneliness and sadness – and that early, open, and hopeful dialogue may enhance adjustment to the news, as it appears to do for children with other life-threatening illnesses.⁶

To Tell or Not to Tell

In our experience, children do better when given developmentally appropriate, truthful statements about HIV and how it affects their own well-being and/or the well-being of a loved one. In most cases, the advantages of disclosure to children old enough to understand far outweigh the disadvantages, especially in settings where testing and treatment is available. Helping children to understand the reasons behind taking medication may play an important role in promoting life-saving adherence to therapies.⁷ As noted, ICAP endorses pediatric disclosure

⁵ DeMatteo et al, 2002.

⁶ Instone, 2000.

⁷ Chesney & Antoni (Eds.), 2002

as a general rule. Nonetheless, the goal of counseling families about pediatric disclosure is to help each to come to its own decision. In some cases, this will mean that families will choose not to disclose HIV-related information to their children.

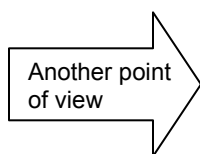
It is essential for providers to consider their own biases and preconceptions regarding pediatric disclosure, and to recall that these have the potential to interfere with effective disclosure counseling. Telling caregivers what to do is not only unhelpful, it may undermine the counseling relationship. Families may decide that the provider will not be able to understand them and their situation. Or, in an effort to please the provider, the family may come to a premature and superficial decision about disclosure, one that is ultimately unsuccessful. Setting biases aside, it is preferable to give family members open and neutral territory to consider their unique situation.

Family members may also have strong biases regarding pediatric disclosure. When the topic is first broached, some parents and caregivers will be resistant to the idea of sharing HIV-related information with children. Some will have reasons why they prefer to keep this information a secret, and it is important for counselors to elicit these reasons through the use of open-ended questions, active listening, and empathy. At the same time, counselors may want to gently explore caregivers' assumptions and biases, asking them to consider different points of view, such as those outlined below. Conversations should always proceed cautiously and gently, in a way that maintains a supportive, trusting, and positive relationship.

Different Points of View

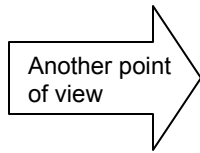
As providers and families discuss the advantages and disadvantages of telling children about HIV, it can be helpful to explore the full range of arguments “for” and “against” disclosure. We illustrate several different points of view in this section; these may serve as examples of themes to explore with parents/caregivers. By discussing these and other “angles” in detail, counselors can assist families to make informed and thoughtful decisions about pediatric disclosure.

Against disclosure: It is not appropriate for children to know about adult matters such as physical illness and death. They should not be made aware of the many hardships in adult life, and they should be excluded as much as possible from painful experiences such as funerals, illness, separations, and difficult emotions.



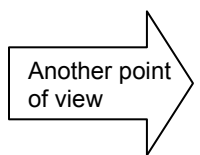
Even young children are keenly aware of when things are “not right” in their environment. They rapidly sense their caregivers' emotions and distress, and are sensitive to changes in the household if someone is sick or absent. Ultimately, they cannot be “walled off” from the difficult realities of life.

Against disclosure: Children deserve to be happy. Childhood is short. Let children live unencumbered by sadness and worry.



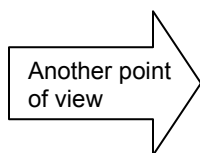
Children are not always happy and carefree. No one is. When children inevitably feel sad or worried or confused, it is especially hard for them if they believe their caregiver does not want to acknowledge how they are feeling. This situation can make a child feel very lonely. A parent or caregiver who expects a child to always feel happy and carefree may inadvertently miss signals that their child needs comfort or reassurance. It may be that sharing HIV-related information with children is a way to offer hope and to *minimize* sadness, worry, and confusion, particularly if a child is experiencing physical symptoms.

Against disclosure: Telling children that they have HIV will rob them of their childhood. Children who know that they have HIV may live “in the shadow of death” without the ability to enjoy their youth, or they may feel deficient or impaired.



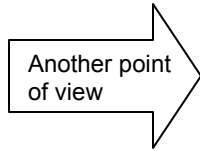
Even a very young child who feels unwell or who is taking medication knows that something is different. They sense that something is out of the ordinary or “not normal.” If no one explains, children will typically come up with an explanation of their own. Often, because children’s knowledge of the world is still so limited and egocentric, they will construct an explanation for themselves that is overly simplistic or grossly misinformed. For example, a young boy who was not told about his diagnosis until age 9 secretly harbored the strong belief that his blood was “poisonous” because he had misbehaved. If caregivers are able to speak to children earlier, they may be able to spare them from suffering with such painful ideas. When children are given factual and realistic information early on, they may experience *fewer* feelings of deficiency and conflict, not more.

Against disclosure: Disclosing HIV-related information to children may lead to questions about intimate details of parents’ lives, e.g. their sexual history. In many instances, parents’ fears are further complicated by guilt and shame. A mother who has transmitted HIV to her child may feel devastated about the situation and may engage in denial – working hard to keep the truth at bay because confronting the reality is so unbearable.



Information about adult behaviors related to HIV transmission need not be revealed in order to share the basic facts about HIV with children. Adults can decide what information is private, and what they will share.

Against disclosure: Secrecy is essential. Caretakers who fear discrimination and stigma may decide not to tell children about HIV in order to keep the “family secret.” Secrecy may become a way of life – medications may be hidden, clinic visits skipped, and discussion of illness forbidden.



The effort to keep HIV secret and to continually hide the truth from a child can be exhausting and ultimately difficult to sustain; it can drain energy and time from more important tasks. Secrecy can also impede a child’s ability to come to terms with his/her illness and may impede older children’s ability to keep themselves safe in sexual relationships. Secrecy may also complicate adherence and make it more difficult for children to stick to medication schedules. While the need for privacy is very important, most children are capable of understanding this.

Assessing Readiness for Disclosure

Parents and caregivers who have decided to discuss HIV with their children will often ask providers if their child is ready for disclosure. While there is no perfect way to determine the answer, adults can easily look for clues that suggest a child is seeking more information. Obviously, if a child is asking questions during clinic visits, this is a positive indicator. Questions such as “Do I really need to take this medicine?” or “What will happen if I do not take it?” may be the child’s tentative way of broaching much deeper concerns. If a parent has not shared HIV-related information with the child, answers should be honest but nonspecific, e.g. “The medicine will keep you strong.” The questions should also be explored to see if there is more below the surface – e.g. “What do you think will happen if you do not take the medicine?” Providers should always actively seek parents’ guidance about how to respond to such questions, taking time to address the issue of disclosure in private (with the child otherwise occupied and out of hearing range) at each visit.

One valuable way to assess a child’s readiness for disclosure is through individual counseling sessions with the child. Another is in the context of group counseling settings, where a number of children in similar circumstances are encouraged to meet together with the guidance of one or more counselors. Clearly, these counseling sessions are only indicated if the parent or caregiver consents to this kind of help. It is essential for the counselor to reassure parents that the information a child presents in counseling sessions will be handled with respect and confidentiality.

Many parents welcome pediatric counseling sessions, regarding them as a way for a “neutral” person to find out what their child knows or may be worrying about. Children often feel more comfortable revealing their concerns and questions to someone they do not know – someone who is unlikely to complicate the process with a reaction of distress, sorrow, or surprise. When children have questions

about HIV or worries about impending changes, they often have an incredible ability to sense that their loved ones will be distressed by these concerns, and may censor themselves to avoid disruptions.

Counseling sessions can be gentle conversations with an older child, supportive open-ended discussions with a group of children, or “play” sessions with a younger child. Encouraging young children to play with family doll figures, or to draw a picture of their families, is an excellent way to assist them to tell the story of their lives and to reveal their inner concerns. Through active listening and open-ended, neutral participation, a counselor may be able to learn a great deal about what a child is worrying about and what s/he already knows or has misconstrued. If, in the course of a counseling session, a child asks direct questions (e.g. “Does my father have AIDS?” “Do I have HIV?”), a counselor should stay neutral and open, redirecting the questions back to the parents who make the choices about what to reveal. A good response might be, “What an important question you are asking – let’s find a way to talk to your mother/father/caregiver about that...” This kind of response respects the risk and legitimacy of the child’s question and allows time to engage the caregiver in an active decision process.

The goal of all good counseling work with children and families is to build trusting ‘therapeutic’ relationships. Through openness, listening, and neutrality, the counselor helps parents and children and to gain trust in the counselor and in themselves. The counselor facilitates the establishment of teamwork among all parties. Ultimately, it is the trust and comfort that a child feels with attentive and concerned adults that will provide the foundation for beginning disclosure.

Ways of Disclosing: How to Begin

In our experience, the best way for a child to learn about their HIV diagnosis is through age-appropriate information shared by a trusted and loving caretaker. The context of disclosure should be a loving one, with caregivers able to make close physical contact with a child during the process. While it may be helpful to have professionals (e.g. counselors and/or clinicians) present during disclosure to children, it is not essential. What matters most is that the child learns HIV-related information from adults who care deeply about the child’s welfare, who are willing to continue the discussion over time, and who will remain involved with the child’s care.

Disclosure with children should never happen casually, inadvertently, or in the heat of anger or conflict. Children may remember the occasion on which disclosure occurred, and an association with family conflict or anger can further complicate the child’s adjustment. Because disclosure is not one discrete event, but a long-term process that lasts throughout childhood, children benefit from ongoing supportive contexts for talking about HIV. For example, making a child aware of all the people in his/her environment who can answer questions about HIV can be very helpful, as can revisiting the topic frequently.

It is very important to tailor discussions about HIV to the child's cognitive level, and to the child's personal and individual issues. Children's maturity and cognitive capacity at different ages may vary widely. Every child and every situation is different. Conversation with a child, no matter what age, should flow naturally from the questions and comments *that the child initiates*. In this way we are more likely to give the child room to express their unique concerns and to respond to their real questions and worries.

Sometimes those concerns will surprise providers. For example, a 6-year-old approached a counselor for a 'serious talk' about her illness. Having secured her parent's permission to enter into a disclosure conversation, the counselor created a quiet space for private conversation. Once assured of privacy, the child looked up, with tears in her eyes, and said, "I missed the first day of school and I really need to know how I am going to catch up." Had the counselor followed her assumptions and initiated a conversation about disclosure, she would have given information that was more than the child was ready to cope with and missed the opportunity to reassure the child about the real issue that was so deeply troubling her.

One of the most important principles in counseling of children is to avoid "telling" or "lecturing." Instead, focus on following the child's lead. There are very few areas in their lives where children are allowed to exert control. During medical visits related to HIV disease this is especially so, as children may have to cooperate with physical exams, difficult blood drawing procedures, and swallowing distasteful medication. When it comes to expression of their own inner experience of illness, children should have total control.

Give the clear message that you want to learn from the child what s/he is thinking and wondering about. The emphasis should be on *asking*, both directly and indirectly, and *listening*. When listening, try to hear both the explicit and *implicit* messages in a child's words. In response to the simple question, "What is it like to take your medicine?" a child's answer may set the tone for disclosure conversation. A 6-year-old's response, "It is yucky!" may suggest the follow-up, "Yes, you are right.....why do you and Mom take the medicine?" If the child is interested in hearing more information, s/he will let you know.

It is hard to generalize, but a young child learning about HIV illness may be content with a straightforward, literal description of a "germ." An older child will require more details and may want to know accurate terms. Older children may want to understand more about transmission, and they may be interested in attaching motive and consequence to events, for example: "Did I get the virus on purpose?" "Will it change the way I look?" "Will I be sick forever?" Discussions with older children may also provide opportunities to discuss HIV prevention.

The following are some examples of language that parents and providers may find helpful as they adjust their comments to a child's questions and

developmental level. But remember, these comments will need to be adapted to the individual child's concerns and capacities, and they should always be woven into a give-and-take conversation in which the child leads the way.

To a 4 or 5-year-old:

"The blood in your body has a germ (or virus) in it that can make you sick---that's why you need to take medicine."

"It is important to take your medicine every day so that your body will stay strong."

"A virus is something that gets inside your body, into your blood, and can make you sick. Like a cold. A cold is a virus. The HIV virus is in your blood (...and in Mommy's/Daddy's)."

To a school-aged child:

"You were born with the HIV virus because it passed from Mommy's blood to yours when you were in her tummy."

"Having HIV does not mean that anything is wrong with who you are. It is a virus in your blood. There are all different kinds of viruses that people can have."

"HIV is the name of the virus in your blood. AIDS is the name of the illness that happens if HIV is not treated. You take medicine to treat the HIV virus so that you will not get sick."

"Having HIV is something private and something that you can decide about telling others. You don't have to tell other people if you don't want to. On the other hand, it is OK to tell other people who may need to know (e.g., teacher, nurse, etc. if parent/caregiver approves). HIV is nothing to be ashamed of."

To an adolescent:

"You have the HIV virus. A virus is something that gets inside your body, into your blood, and can make you sick. It does not necessarily mean that you are going to get very sick. You have the power to control the virus by taking your medication every day."

"Knowing about HIV and having it in your blood, gives you a special responsibility not pass the virus to other people. You can prevent getting the virus again, or giving it to others by ...(explain, based on teen's current risk situation and sexual maturity).

"Having HIV does not mean that you cannot live a full life with loving, sexual relationships. It does mean that you need to plan carefully about your future with others so that you make good decisions about your safety and the welfare of others."

"Lots of teens with HIV around the world have found that having the virus gives them a special kind of strength-- strength to educate others about HIV, to prevent the spread of the virus; and to change people's misinformation and prejudices. You may decide that you want to use your HIV status to make a positive difference in other people's lives."

In all HIV disclosure conversations, no matter what age a child is, it is helpful to let a child/teen know that s/he can always ask more questions, and that adults will do the best they can to supply answers. Let the child know that conversation about the diagnosis is something that can happen again and again, in many different ways — that the subject is always open for discussion. Each disclosure conversation will ideally begin and end with the following three points:

- **Explanation that the child’s questions are normal, important, and welcomed.**
- **Reiteration that HIV infection is not anyone’s “fault.”** It is also important to reassure the child that a virus in his/her blood does not mean that s/he is poison, or evil, or deficient as a human being. It means that s/he needs to be very careful that her/his blood and bodily fluids don’t get into another person’s body. The rule about not letting blood or bodily fluids mix with other people is true for *everybody*....not just people with HIV.
- **Communication of hope and reassurance.** While no one can predict the future, medicines can successfully treat the symptoms of HIV, and that the adults around the child will do their best to take care of the child, no matter what happens.

It is wise to be aware of children’s potential reactions to HIV/AIDS prevention campaigns in the media. These images and messages may inadvertently scare children who are trying to come to terms with the implications of their own diagnosis. Messages about “deaths due to AIDS” will be disturbing to children who are learning about their diagnosis. Try to educate children about the targeted purpose of these messages, and help them to discriminate between their community’s public health agenda for people who don’t know their status, and their own personal situation (e.g., “You take medicine to keep you strong”).

These three general points, repeated and demonstrated frequently, will go a long way towards helping children cope positively with information about HIV/AIDS.

Disclosing the HIV status of other family members:

The decision to inform a child about the HIV status of another family member is just as complex as the decision to inform the child of his/her own HIV status. Again, it is wise to discuss the intention to disclose with all relevant parties before speaking with a child, and to consider the questions a child is asking and the necessity of sharing this knowledge. If a child is asking to know the status of a loved one (e.g., parent, caregiver, or older sibling) it is best to get the permission of the family member, to involve them, and to create dialogues that include everyone. In the case of a younger sibling or absent/deceased parent or caregiver, whenever possible, communications should include the wishes and/or intent of the absent family member. For example, “Your little brother is too young to understand about the virus he has. But you are old enough to know and he needs your help and encouragement to take his medication on time.” Or, “Your

mother is too sick or unable (due to death/absence) to tell you about her HIV status, but she would want you to know so you could keep yourself safe and help others in your family.”

Conversation about the HIV status of other family members is a good opportunity to reiterate and reinforce messages about family trust, privacy, and solidarity. We know that a sense of trust and faith in family members is an important factor in helping people cope positively with HIV/AIDS. Disclosure conversations about family members can be a powerful way to convey love, trust, and reliability to a child. For example, “Yes, Mommy has HIV/AIDS. That means that you and I share a special bond. We can take our medicine together and remind each other not to miss our doses.” Or, “Yes, your father has the same HIV virus that we do. He and I will do everything we can to take care of ourselves and to take care of you.” Or, “We are all in this together...”

These conversations can also be an important opportunity to explicitly talk with children about privacy, respect, and personal boundaries. A parent may feel uncomfortable about revealing the details of their own infection history or personal background. It is acceptable, and often *reassuring* to children, to be reminded of adult boundaries. In response to a young child’s question about how a parent “caught” HIV, it is fine to say, “That is an adult matter that we can talk about when you are older.” Or, to an older child’s similar question, “That is personal between Mom and her doctor. Not something I want to talk about now and not something that you have to worry about.”

Talking about HIV/AIDS with the terminally ill child:

For a child facing end-stage HIV disease, disclosure of diagnosis may take a back seat to the more pressing issue of saying goodbye. Again, as always, the task is to understand what the child is worried about—what the child wants to know. If, during the end-stage of life, the child is preoccupied with the name and nature of his illness, that is something that should be addressed by the family and caregiving team. If, on the other hand, as is often the case in our experience, the child is more concerned with anxieties about death and saying goodbye to loved ones, that is the psychological work that family and providers will want to facilitate and focus on.

Children who are very ill and facing end of life, often have an uncanny sense of what is happening to them. They may be intensely afraid of pain, of being alone, and, they may want to know what will happen to them after death. They may be worried about the welfare of a parent or sibling or pet after they are gone. Adults who are overwhelmed with sadness about a child’s approaching death may find it hard to engage in conversation about the topic and may find themselves avoiding the child and trying to keep things pleasant and light. This is a natural way for adults to defend against the pain of a child’s approaching death, but it is ultimately not helpful to the child. Unfortunately, avoidance of talk about death may actually increase a child’s sense of loneliness and fear at the end of life.

It is important to be available to the dying child and to convey the sense that it is alright for them to have questions and concerns, and that these are discussable. It is often helpful to have several adults available to a child in this way, so that the child has access to more than one "listener." Some children find it easier to approach difficult questions with a neutral adult, rather than with a loved one. That provider can then act as a liaison to family members, helping to communicate to the family what a child wants and needs in the way of conversation, reassurance, and comfort. This will often assist the family to engage in end of life dialogue with a child...giving both the child and the family an important means to saying goodbye and to resolving any unfinished business before a child dies. Full communication between loved ones *before* death can help survivors deal with grief *after* death.

An open-ended approach suggested by Michael Lipson and Stephen Levine, is to ask the dying child, "What does it mean that you are so sick?" This gentle question can provide an invitation for the child who wants to discuss their illness or impending death, and it is easily refused if the child does not want to have this conversation. If children choose to go further and express their worries or questions about impending death, family members and/or providers can make it easier by asking directly, "What do you wonder about? Are you scared?" "How can I help?" Family members will often want to share their belief systems about after life with a child who asks. As always, it is important that providers who are communicating with the child be respectful of a parent or caregiver's wishes about content. Priority should always be given to facilitating communication between loved ones and the child.

Ultimately, the goal is to offer comfort and reassurance to the dying child. Honesty is always the best approach. In response to the child's question, "Am I going to die?" it is better to respect the question with an honest answer (e.g., "You may die...we all die...no one knows when someone will die") than to ignore or belittle the question with a superficial or simplistic answer.

Like family members, providers who work with dying children benefit from support and comfort in the aftermath of a child's death. Caring for sick children and attending to their psychological needs is hard work. The sorrow of watching children suffer ultimately takes a toll on providers' lives. It is critically important to develop systems of support so that providers can share their experiences with each other and find comfort through remembering and memorializing lost patients. Recognizing and dealing with provider emotions related to disclosure and death will help to ensure the strength of the caregiving team.

Conclusion

In summary, disclosure about all things related to HIV/AIDS is a process that requires repeated, continuous, and attentive conversation with children. Once disclosure to a child occurs, dialogue about the topic will need to continue again and again. The dialogue will change and evolve as children progress through

different developmental stages, and as treatments and circumstances change and transform. Revisiting the topic of disclosure frequently with a child, and checking in with them about their worries and concerns, can be a wonderful way to guide and facilitate a young person's development as they learn about who they are and who they have the potential to become. Children who are well informed about all aspects of HIV/AIDS will ultimately contribute to the strength of families and communities who are facing the epidemic. Youth who have experienced open and honest information will, hopefully, mature into adults who are equipped both to manage and prevent HIV/AIDS. By committing to honest and open discussion of the HIV/AIDS diagnosis and its consequences, providers can model powerful messages of compassion, acceptance and strength for the families that they serve.

Acknowledgements:

This chapter was developed by Martha Vibbert, Ph.D. and Rosette Serwanga.

Appendix A: References, Suggested Reading, and Resources

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