Guidelines for Paediatric HIV/AIDS Care and Treatment in Ethiopia

Federal HIV/AIDS Prevention and Control Office

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FMOH

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Foreword

HIV/AIDS has created an enormous challenge to mankind since its recognition; close to 65 million people are infected and about 40 million people are living with HIV, out of which about 2.1 million are children under 15 years of age. Of these children, 90% live in sub-Saharan Africa and about 64,813 live in Ethiopia.

Mother-to-child transmission is the primary mode of HIV acquisition in children accounting for about 90% of cases; therefore, the most efficient and cost-effective way to tackle paediatric HIV globally is to reduce mother-to-child transmission (MTCT). Despite ongoing efforts to prevent transmissions, there are nearly 1200 new infections each day, indicating a critical need to provide antiretroviral treatment for HIV-infected children.

Cognizant of this, the Government of Ethiopia launched fee-based antiretroviral treatment in 2003 and free ART in 2005. To date, about 97,000 adults and 4,800 children are accessing ART services.

ART has radically changed the natural course of HIV infection in countries where it has been successfully implemented and HIV-infected infants and children now survive to adolescence and adulthood.

In resource-limited countries, despite many challenges to programme implementation, committed efforts have made remarkable progress in making ART accessible to HIV-infected children.

Significant challenges to the scale-up of paediatric care and treatment include: limited screening of HIV-infected children, lack of affordable simple diagnostic tests, lack of trained human resources, insufficient advocacy and lack of understanding that ART is efficacious in children. Limited experience with simplified standardized treatment guidelines and lack of affordable paediatric ARV formulations further compound the situation.

ART for children was addressed within the guidelines for adults published in 2005, but emphasis was given only to ART and the comprehensive management of an HIV-exposed or infected child was not addressed.

In order to support and facilitate management and scale-up of ART in infants and children, these comprehensive guidelines have been developed. This stand-alone treatment guide serves as a framework for provision of comprehensive care for HIV-exposed and infected children. Emphasis is given to infant diagnosis, adherence, disclosure, management of co-infection and opportunistic infections.

Its use alongside other contemporary guidelines will be instrumental in the national effort to curb the spread of infection and ultimately improve the quality of life for HIV-exposed and infected children.

Dr. Betru Tekle
Director General FHAPCO

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List of Abbreviations

AB	Antibody	FBC	Full blood count
ABC	Abacavir	FDC	Fixed-Dose Combination
AFASS	Acceptable, feasible, affordable, safe, sustainable	FHAPCO	Federal HIV/AIDS Prevention and Control Office
AIDS	Acquired Immunodeficiency Syndrome	FMOH	Federal Ministry of Health
ALT	Alanine aminotransferase	FTT	Failure to thrive
ANC	Absolute neutrophil count	GI	Gastrointestinal
ART	Antiretroviral therapy	HA	Headache
ARV	Antiretroviral	HAART	Highly Active Antiretroviral Therapy
AST	Aspartate aminotransferase	Hb	Hemoglobin
AZT	Zidovudine	HC	Head circumference
CD4	T-lymphocyte CD4+	HCT	HIV Counseling and Testing
CMV	Cytomegalovirus	HDL	High-density Lipoprotein
CNS	Central nervous system	HIV	Human immunodeficiency virus
CPK	Creatinine Phosphate Kinase	Ht	Height
CPT	Corimoxazole Prophylactic Therapy	IMAI	Integrated Management of Adult Illnesses
CSF	Cerebrospinal fluid	IMCI	Integrated Management of Childhood Illnesses
CTX	Cotrimoxazole	INH	Isoniazid
d4T	Stavudine	IPT	Isoniazid Prophylactic Therapy
ddI	Didanosine	IRS/IRIS	Immune reconstitution syndrome
DBS	Dried Blood Spot	KOH	Potassium Hydroxide
DNA	Deoxyribonucleic acid	LDH	Lactate Dehydrogenase
DOT	Directly observed therapy	LDS	Lipodystrophy
EBF	Exclusive Breast Feeding	LGE	Linear gingival erythema
EFV	Efavirenz	LIP	Lymphocytic interstitial pneumonia

LTBI	Latent Tuberculosis Infection	RNA	Ribonucleic acid
M&E	Monitoring & Evaluation	RT	Randomized trial
Mo	Month	RTI	Reverse Transcriptase Inhibitor
MRI	Magnetic Resonance Imaging	RTV-PI	Ritonvair-boosted PI
MTCT	Mother-to-child transmission	SJS	Steven Johnson Syndrome
NFV	Nelfinavir	SQV	Saquinavir
NNRTI	Non-nucleoside reverse transcriptase inhibitor	TB	Tuberculosis
NRTI	Nucleoside reverse transcriptase inhibitor	TDF	Tenofovir
NUP	Necrotizing Ulcerative Periodontitis	TEN	Toxic epidermal necrolysis
NVP	Nevirapine	TLC	Total lymphocyte count
OHL	Oral hairy leucoplakia	Toxo	Toxoplasmosis
OI	Opportunistic infection	TST	Tuberculin skin test
PACTG	Paediatric AIDS Clinical Trial Group	ULN	Upper Limited of Normal
PCP	*Pneumocystis carinii* pneumonia	URTI	Upper respiratory tract infection
PCR	Polymerase chain reaction	VCT	Voluntary Counselling and Testing
PGL	Persistent generalized lymphadenopathy	WBC	White blood cell count
PI	Protease inhibitor	WHO	World Health Organization
PMTCT	Prevention of mother-to-child transmission of HIV	Wt	Weight
/r	Low-Dose Ritonavir	Yr	Year
RHB	Regional Health Bureau		

Introduction

These guidelines address the care and treatment of HIV-exposed and infected infants and children. The recommendations are based on current knowledge regarding the use of antiretroviral drugs in children, both published and unpublished data, regarding treatment of HIV infection in infants, children and adults.

The guidelines focus on:

- Early identification of HIV infection in HIV-exposed infants through routine prenatal HIV testing of all pregnant women in Ethiopia
- Early diagnosis in older children through routine screening of sick children and active case finding
- Provision of HIV/AIDS care to infected children, including ART to eligible children, regular laboratory and clinical assessments, prophylaxis and management of opportunistic infections
- Effective management of the complex and diverse needs of HIV-infected children and their families using a multidisciplinary team approach
- Monitoring growth and development, short and long-term toxicities and nutrition support for children and their families
- Special considerations associated with adherence to antiretroviral care and treatment for infants, children and adolescents

The objectives of the guidelines are to:

- Facilitate standardised provision of integrated comprehensive care and treatment to HIV-infected and exposed infants and children
- Ensure evidence-based, safe and rational use of antiretroviral drugs
- Serve as a resource to health care providers and people living with HIV/AIDS

The target users are physicians, nurses and other healthcare providers, HIV/AIDS program managers, health planners in both private and public sectors and other health professionals.

1.Overview of Paediatric HIV/AIDS Care and Treatment

Ethiopia has an estimated population of 77 million people, of whom 44% are under 15 years of age.[1] Adult prevalence of HIV is an estimated 10.5% in urban areas and 1.9% in rural areas. The exact prevalence of HIV in children is not known; however, there are currently 134,586 children under 14 years living with HIV/AIDS in Ethiopia.[2] While it can be expected that more than half of these (67,000) require ART, only 4863, fewer than 7%, were receiving ART as of March 2008.[3] Without treatment, 75% of HIV-infected children will die before their fifth birthday.[4]

More than 90% of children acquire HIV from their mothers; currently less than 10% of HIV-infected pregnant women in sub-Saharan Africa receive any form of prevention of mother-to-child transmission (PMTCT).[5] In Ethiopia the number is expected to be much lower. There were 30,338 new infections in children under 15 years in 2005 in Ethiopia.[2] The need to treat an ever-increasing number of children highlights the importance of preventing paediatric HIV infection.

The most effective way to tackle paediatric HIV is to reduce mother-to-child transmission. The major paths of transmission occur during delivery or during breastfeeding. Offering HIV testing to all pregnant women as standard practice is the first step toward preventing HIV infection in the unborn child. Provision of highly active antiretroviral therapy (HAART) to eligible mothers and ARVs for PMTCT can significantly decrease vertical transmission the virus. Knowledge of a mother's HIV positive status provides an entry point for appropriate care of the mother, HIV-exposed infant and other family members including children. Follow-up of HIV-exposed infants provides the opportunity to provide life-saving cotrimoxazole prophylactic therapy and early HIV diagnostic testing, also enabling infected children to be enrolled in care and started on HAART early.

In resource rich settings HAART has changed the face of paediatric HIV. HIV-infected children now survive to adolescence and adulthood; the challenges of care have evolved into those of chronic as well as acute care. The experience in paediatric HIV/AIDS care and treatment in Ethiopia is limited.[6] Major obstacles to scaling up paediatric care include: lack of human resources and scarcity of paediatric providers, no systematic effort to identify and follow HIV-exposed infants, limited availability of virologic testing, lack of provider-initiated HIV testing, missed opportunities for testing children, insufficient advocacy and understanding that ART is efficacious in children, and limited experience with program implementation to provide paediatric HIV/AIDS care and treatment. Consequently too few children have been started on ART in Ethiopia. In order to support and facilitate the care and treatment of children, the Federal Ministry of Health has made paediatric HIV care and treatment a priority. These guidelines support the FMOH commitment to achieve universal access to HIV/AIDS care and treatment for all HIV-infected children living in Ethiopia using a family-centred approach.

[1] FMOH, Fifth Report, AIDS in Ethiopia. June 2004.
[2] FMOH, Sixth Report, AIDS in Ethiopia. June 2006.
[3] FMOH/HAPCO, March 2008.
[4] Newell ML, Coovadia H, Cortina-Borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet* 2004.368:1236-43.
[5] UNAIDS/WHO. AIDS Epidemic update.2005 Geneva http://w3whosea.org/linkfiles/facts_and Figures_PDFepi-update2005.pdf
[6] Paediatric HIV/AIDS Care and Treatment in Ethiopia: Results of a Situational Analysis. FMOH, ICAP. February 2006.

1.1 Comprehensive Paediatric HIV/AIDS Care and Treatment

The FMOH approach to paediatric HIV/AIDS care and treatment is to maximize resources while ensuring provision of equitable care. The table below outlines the approach to care and treatment for Ethiopian HIV-exposed and infected children. To provide comprehensive HIV/AIDS care and treatment, family care coordination is important. Experience caring for HIV-infected persons has shown that coordination of medical and supportive services and communication amongst providers optimizes health and wellbeing. This approach has at its heart the patient and family with a multidisciplinary team of clinical and supportive staff providing efficient comprehensive care. Its goal is to reduce barriers within the health care system, improve the health of HIV-affected families, reduce the risk of perinatal transmission, support adherence to treatment and understand the role of families in HIV prevention. The multidisciplinary team may include counsellors, peer educators, community health workers, nutritionists, pharmacists, medical officers, nurses, and physicians. This team should meet periodically to exchange information, develop and monitor patient care plans. This group is most efficient when a team leader, usually a counsellor or nurse, plans the weekly patient list and agenda and distributes it to the team in advance of the meeting. A specific team member should be assigned to follow-up on the plan and ensure that interventions discussed are implemented.

Table 1-1 Components of paediatric HIV care and treatment

Family-Centred Care

- Improve linkages between paediatric, ANC, PMTCT, TB and adult care and treatment programs
- Dedicated paediatric care and treatment team at each site providing adult HIV/AIDS services

Prevention of Paediatric Infection

- Primary prevention of HIV infection in women
- Provision of ARVs to pregnant women to prevent MTCT
- Provision of HAART to pregnant women meeting eligibility criteria
- Provision of ARV prophylaxis for infants
- Identify and follow HIV-exposed infants

Care of HIV-exposed infants

- Linking ANC, PMTCT, maternity to paediatric care and treatment to facilitate identification of the HIV-exposed infant
- Growth monitoring and developmental assessment
- Counselling on infant feeding, maternal nutrition and support
- Early infant HIV diagnosis using age appropriate test (DNA PCR or rapid antibody test)
- Cotrimoxazole prophylactic therapy
- TB risk assessment
- Routine preventive paediatric services including immunizations
- Facilitated enrolment of HIV-infected children into care and treatment

Care and treatment of HIV-infected children

- Promote and support active case detection
- Growth monitoring and developmental assessment
- Nutrition counselling and support
- Clinical and immunological staging
- Laboratory tests
- Cotrimoxazole prophylactic therapy
- TB risk assessment
- Treatment of OIs, HIV-associated TB infection and other common childhood illnesses
- Routine preventive paediatric services including immunizations
- Provision of ART for eligible infants and children
- Management of drug toxicities, treatment failure and provision of second-line regimen
- Psychosocial support, adherence and disclosure
- Management and appropriate referral for complicated patients

2. Diagnosing HIV Infection in Infants and Children

More than 90% of HIV infection in children is acquired from the mother during pregnancy, labour and delivery, and after childbirth through breastfeeding. Early diagnosis of HIV infection in infants and children is important since the disease progresses rapidly in children with 50% mortality by age two. Passively transferred maternal HIV antibodies make interpretation of positive antibody tests difficult in children less than 18 months of age. In order to diagnose HIV infection definitively in children less than 18 months, assays that detect the virus or its components (i.e. virologic tests) are required. DNA PCR is the preferred method of choice for HIV diagnosis in infants and children under 18 months. Use of Dried Blood Spots (DBS) for DNA PCR has been shown to be a robust reliable means of increasing access to infant HIV diagnosis since it is easier to obtain, store and transport for centralized testing. In children 18 months and older, rapid antibody tests reliably diagnose HIV infection.

2.1. Goals of Early Diagnosis of HIV in Infants and Children

- To identify HIV-infected infants early in order to provide them with life-saving ART, not to exclude infection
- To facilitate early access to care and treatment which reduces morbidity and mortality

2.2 Opportunities and Entry Points for HIV Testing in Children

Healthcare providers often miss opportunities for identifying children who need testing:

- PMTCT Programs and EPI for HIV-exposed infants
- Paediatric inpatient units
- Malnutrition units
- TB clinics
- Paediatric outpatient units
- Children of adults attending HIV prevention, care and treatment centres
- Siblings of children enrolled in HIV care
- Orphanages

Experience in Ethiopia has shown that HIV prevalence in urban hospitalized children is high, about 10% of hospitalized children.[7] Therefore it is recommended to offer HIV testing routinely to *all* children admitted to paediatric inpatient units.

2.3 Counselling and Support

A child with suspected HIV infection generally implies a family member with suspected HIV. Counselling should take into consideration the parents and issues of consent, competence to consent, disclosure and confidentiality needs. Testing for HIV in children should be initiated by a healthcare worker, after pre test information has been provided to the parent(s) or legal guardian. The best strategy to increase uptake is opt-out, where the test is routinely recommended as a standard part of medical care, and the patient or caregiver is informed of his/her right to refuse. It is the responsibility of the provider to ensure the test is actually performed, and results made available in a timely manner to the caregiver. Avoid referring children to VCT since each additional step is a potential barrier to testing. If HIV infection is diagnosed in a young child or infant usually the mother herself is also infected, and the father and other siblings may be also. It is the provider's responsibility to ensure family members also receive appropriate counselling and testing. Refer to Ethiopian National Guidelines on HCT for additional information.

[7] Personal Communication, CU: ICAP Supported sites at Jimma and Adama

2.4 Diagnosing HIV Infection in Infants and Children <18 Months of Age

In infants under 18 months, special tests are needed because of the persisting presence of maternal antibodies. The main options are DNA PCR or RNA PCR or p24 antigen tests. Each test has advantages and disadvantages that determine which is most appropriate, depending on resources. However, DNA or RNA PCR is considered best for infant diagnosis; in most settings, the DNA PCR (a qualitative test) is the preferred method for infant diagnosis. All infants born to HIV-infected women should have DNA PCR at six weeks of age or at the first opportunity thereafter. If the test is positive, the infant is presumed to be HIV-infected and should be referred for care and treatment. In all such cases a confirmatory antibody test should be done at 18 months of age. For infants < 12 months of age, with an initial positive DNA PCR, a confirmatory test should be performed if feasible. However, this should not delay referral for initiation of ART. A negative DNA PCR in a breastfeeding infant does not rule out HIV infection.

In infants 9 months and older at the time of breastfeeding cessation, a rapid antibody test can be done. A positive test in a symptomatic infant should be confirmed with DNA PCR. If the infant is asymptomatic, repeat antibody testing should be done at 18 months of age. Any infant with a negative initial DNA PCR who falls sick or develops signs and symptoms suggestive of HIV should have a repeat DNA PCR test. For details refer to national algorithm on infant HIV diagnosis (Figure 2.1).

For children under 18 months of unknown HIV-exposure status, perform a rapid antibody test first. If the rapid test is positive, perform a confirmatory DNA PCR. If the rapid test is negative and the infant is breastfeeding evaluate maternal HIV status. If the mother is HIV-infected and the infant is breastfeeding, the infant remains at risk of infection and requires evaluation as described above for the HIV exposed infant. Refer to Figure 2-1 for details.

While HIV antibody testing cannot be used to diagnose infection in children less than 18 months, it can confirm HIV exposure, enabling these infants to be enrolled into care and started on life-saving cotrimoxazole prophylaxis. Rapid antibody tests can also be used to confirm a negative diagnosis in infants who have ceased breastfeeding.

In situations where virologic testing is unavailable, a presumptive diagnosis of severe HIV can be made in order to provide life-saving ART for infants under18 months (Figure 2-2 and Table 7-1). Every effort must be made to confirm the diagnosis as soon as possible with DNA PCR for infants less than 18 months or rapid antibody test if the infant is above 18 months of age. Criteria for presumptive diagnosis of HIV infection should be applied by a provider with experience in paediatric HIV.

2.5 Use of Dried Blood Spots (DBS) for DNA PCR

Dried blood spots have been used in newborn screening programs to determine maternal HIV seroprevalence, measure viral load, proviral DNA and HIV subtype; they are an easy way to obtain blood without phlebotomy, which is difficult in children. Recent availability of dried blood spots for DNA PCR in Ethiopia has made infant diagnosis a reality. DBS does not require venipuncture and blood is obtained by a heel-prick in infants or a finger-stick in older children. This is less traumatic than venipuncture and uses only a small volume of blood; it carries less biohazard risk than liquid samples and can be stored at room temperature, making it easier to transport to central sites for testing. The use of DBS for PCR is recommended when available at a facility. DBS for DNA PCR has been validated in several resource-limited settings including Botswana, Rwanda and South Africa. Clinic staff who perform routine immunizations or blood collection (nurses, midwives, or doctors) can readily be trained to collect blood for early infant diagnosis. Appropriate universal blood and fluid precautions should be followed. Annex A contains detailed information on collection, storage and transportation of DBS samples.

2.6 Diagnosing HIV Infection in Children >18 Months of Age

In children 18 months and older, HIV antibody tests, (either rapid HIV tests or HIV ELISA or a combination), can be reliably used to diagnose HIV infection definitively in the same manner as in adults. Any child >18 months with a negative antibody test does not have HIV infection. The exception is a child still breastfeeding; in this case, the HIV antibody test should be repeated 6-12 weeks after complete cessation of breastfeeding.

Figure 2.1 HIV testing in HIV-exposed infants <12 months of age where virologic tests are available

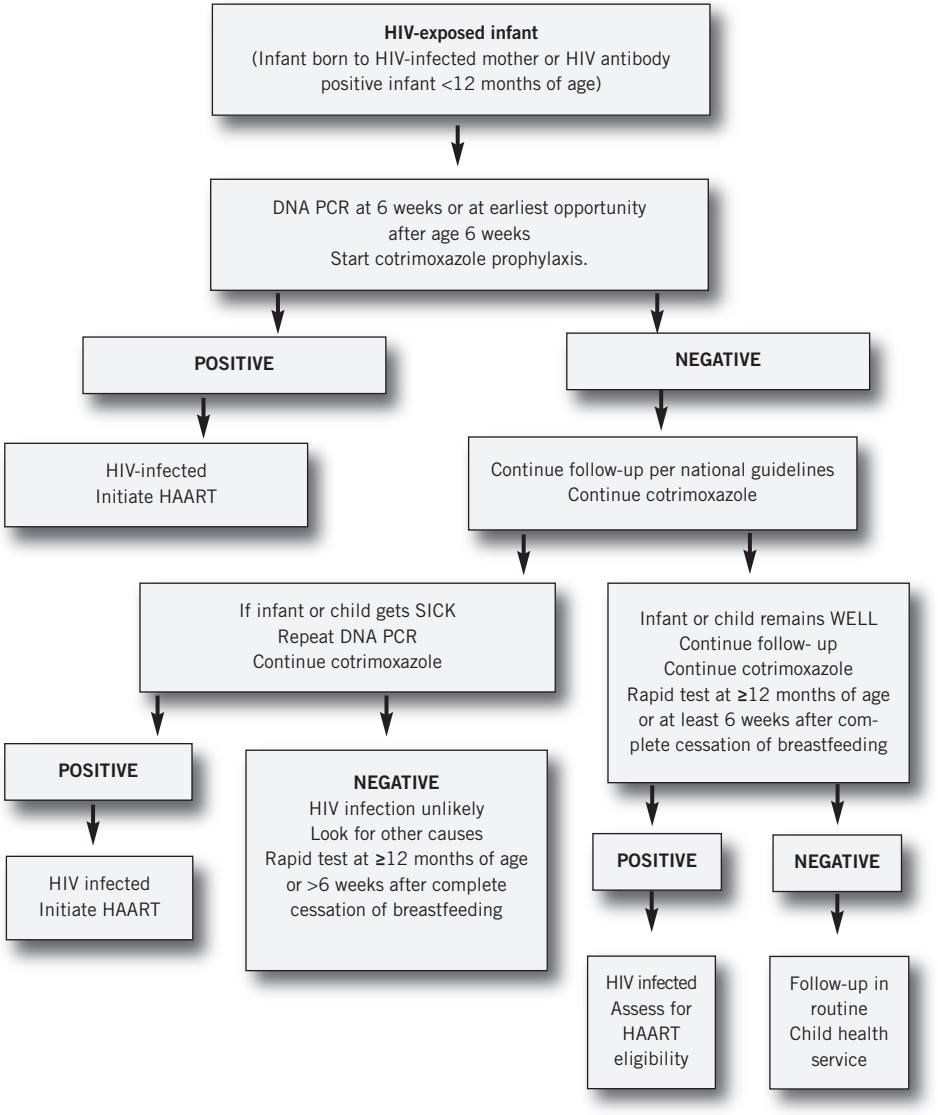
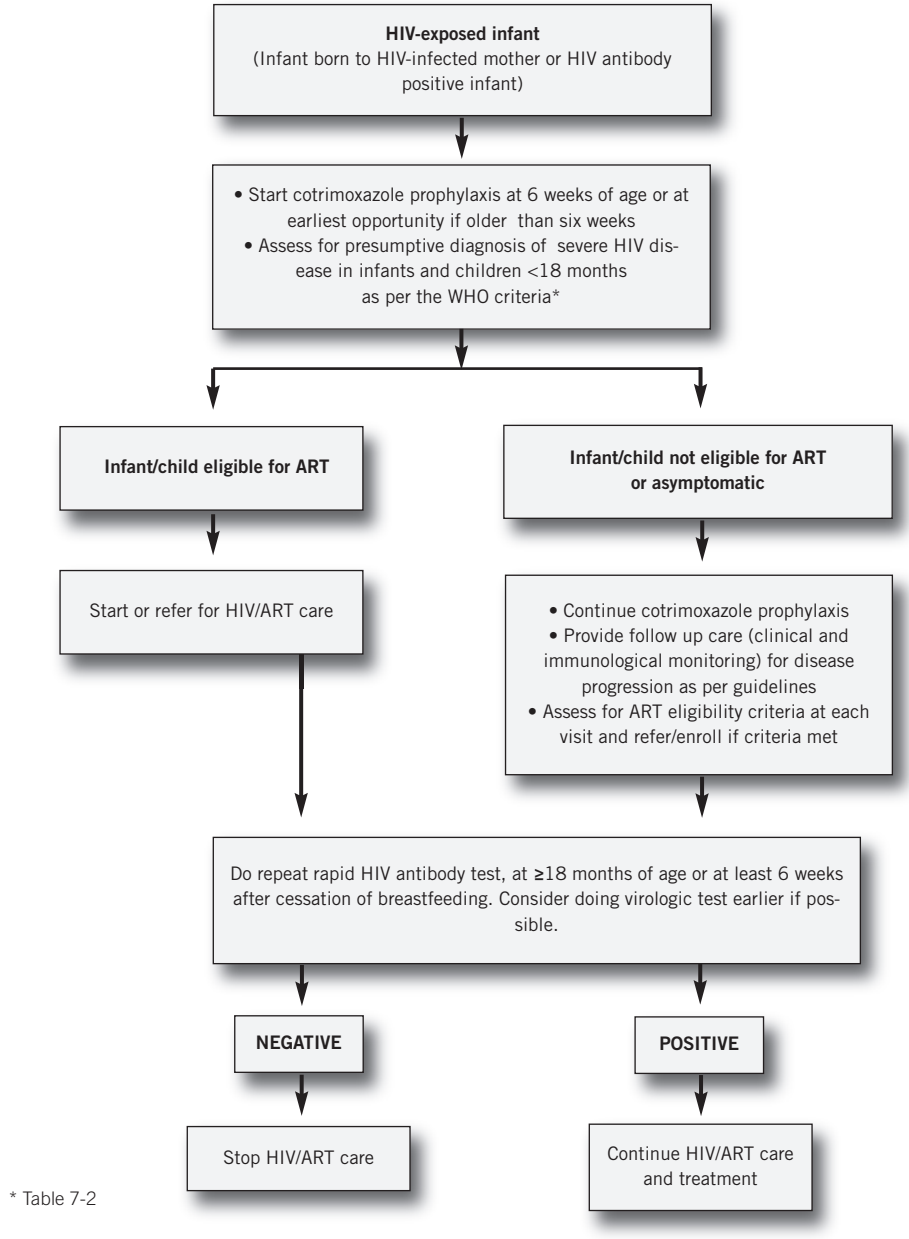


Figure 2.2 Diagnostic algorithm for infants <18 months of age where virologic tests are unavailable



* Table 7-2

3. Care of the HIV-Exposed Infant

HIV-exposed infants need regular follow-up since they are at risk of morbidity and mortality regardless of infection status.[10] Linking PMTCT to infant follow-up is an important step in ensuring HIV-exposed infants are enrolled into care. Where PMTCT programs are non-existent, maternal and child health, immunization and under-5 clinics are excellent venues to identify HIV-exposed infants. Rapid antibody tests performed on mother or infant can confirm HIV exposure, enabling these infants to be enrolled into care. Basic care for HIV-exposed infants can be provided in under-5 clinics, paediatric outpatient clinics and health centres.

3.1 Goals of Care for the HIV-Exposed Infant

- To minimize risk of vertical transmission of HIV
- To recognize HIV infection early using age-appropriate testing
- To prevent opportunistic infections
- To enroll HIV-infected children into ART care early

3.2 Comprehensive Care for the HIV-Exposed Infant

HIV-exposed infants must have regular visits for health assessment and promotion. Infants should be seen monthly for the first six months then every three months. Infants with poor growth, failure to thrive, or recurrent illnesses should have more frequent close follow-up.

[10] Kuhn L, Kasonde P, Sinkala M, et al. Does severity of HIV Disease in HIV-infected Mothers affect Morbidity and Mortality among their uninfected infants? CID 2005;41:1654-1661.

3.2.1. Birth

Mothers should be given appointment for the first postnatal visit at delivery. Mothers who do not deliver at a health facility should be given appointments at first contact with the healthcare system. Refer to Ethiopian National PMTCT Guidelines for details.

HIV status of the mother should be clearly indicated on the infant's immunization card in a non-stigmatizing way. (Use identification method used for the PMTCT enrolled pregnant women on infant's immunization card)

- **Mother should be counselled on infant prophylaxis** (see Ethiopian National Guidelines on PMTCT)
- **Immunizations**- per National Expanded Program on Immunization
- Counselling on infant feeding, maternal nutrition and support (Section 11)

3.2.2 Initial Visit at 4-6 weeks

Every effort should be made to engage the HIV-exposed infant into care by six weeks of age. Review the following at the first postnatal visit:

- **History** – including use of PMTCT, parental concerns, intercurrent illness.
- **Nutrition and growth assessment** – plot weight, height and head circumference on the growth chart (Annex G).
- **Developmental assessment** using reference provided (Annex H)
- **TB risk assessment** (Section 5.3)
- Targeted **physical exam** looking for symptoms and signs suggestive of HIV infection.
- **Determination of HIV status** -all exposed infants should have the initial DNA PCR test done at six weeks (Section 2). Caregivers should be counselled on the rationale for infant diagnosis; explain the possible test results, and need for additional testing to determine infection status definitely.
- **Cotrimoxazole preventive therapy** should be provided to all HIV-exposed infants starting at six weeks, and continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding (Section 5.2).
- **Immunizations** according to the National Expanded Program on Immunization (Table 3.1).
- **Counselling on infant feeding, maternal nutrition and support** as necessary (Section 11).

3.2.3 Second Follow-Up Visit for HIV-Exposed Infants at Two Months

Infants should be assessed to ensure they are tolerating cotrimoxazole. Results of the initial DNA PCR test should be made available to caregiver. Review the following at the second visit:

- **History** – including parental/caregivers concerns, intercurrent illness.
- **Nutrition and growth assessment** – plot weight, height and head circumference on the growth chart (Annex G).
- **Developmental assessment** using reference provided (Annex H)
- **TB risk assessment** (Section 5.3)
- Targeted **physical exam** looking for symptoms and signs suggestive of HIV infection.
- **Determination of HIV status** – Review initial test results with caregiver. Any infant with a positive DNA PCR should be referred for staging, care, and treatment. Asymptomatic infants who have a negative DNA PCR test should have confirmatory testing with antibody at >9 months. Symptomatic infants with negative DNA PCR should have repeat virological testing done immediately. If infant diagnostic testing was not done at six weeks, counsel parent and test infant (Section 2).
- **Cotrimoxazole preventive therapy** should be continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding (Section 5.2).
- **Immunize** according to the National Expanded Program on Immunization. (Table 3.1).
- **Counselling on infant feeding, maternal nutrition and support** as necessary (Section 11).
- **Adherence** to care and cotrimoxazole preventive therapy should be reinforced at each visit (Section 8).

3.2.4 Follow-Up Visit Schedule for HIV-Exposed Infants (3 to 18 Months)

HIV-exposed infants who are asymptomatic should be seen monthly until six months of age then every three months until 18 months of age. HIV-exposed infants, who are symptomatic, have poor growth, failure to thrive or recurrent illnesses should have more frequent follow-up. HIV-exposed infants should be discharged from care only after final determination of HIV status. This means the majority of infants will have to be followed until 18 months of age. HIV-infected children should be referred to a HIV care and treatment centre. Children determined to be uninfected can be discharged and followed-up in the under-5 clinics or EPI.

Review the following at each visit:

- **History** – including parental concerns, intercurrent illness
- **Nutrition and growth assessment** – plot weight, height and head circumference on the growth chart at every visit (Annex G)
- **Developmental assessment** using reference provided (Annex H)
- **TB risk assessment** (Section 5.3)
- Targeted **physical exam** looking for symptoms and signs suggestive of HIV infection
- **Determination of HIV status** – any symptomatic child should have repeated diagnostic testing during this period. Infants presenting for the first time at >9 months of age should have a screening HIV antibody test done first. Any positive test should be confirmed with DNA PCR. Any infant with a positive DNA PCR should be referred for staging, care, and treatment. Breastfeeding infants should have repeat testing at least 6 weeks after complete cessation of breastfeeding. If the infant is >9 months at that time, a screening rapid antibody test can be performed. Testing must always be accompanied with counselling of caregivers, explaining the possible test results, and the need for additional testing to determine infection status definitely (Section 2)
- **Cotrimoxazole preventive therapy** should be continued until HIV infection has been excluded and infant is no longer at risk from breastfeeding (Section 5.2)
- **Immunizations** according to the National Expanded Program on Immunization. (Table 3.1)
- **Counselling on infant feeding, maternal nutrition and support** as necessary (Section 11)
- **Adherence** to care and cotrimoxazole preventive therapy should be reinforced at each visit (Section 8)

Table 3-1 National EPI Schedule
Immunization schedule for infants and children recommended by the WHO Expanded Program on Immunization

	Age					
Vaccine	**Birth**	**6 weeks**	**10 weeks**	**14 weeks**	**6 months**	**9 months**
BCG	**X**!					
Oral Polio	**X**	**X**	**X**	**X**		
DPT		**X**	**X**	**X**		
Measles						**X**

!Individuals with symptomatic HIV should not receive live attenuated BCG vaccine

NB. Where Hepatitis B and Haemophilus Influenza B vaccines are available, immunization can be provided as per WHO guidelines.

Table 3-2 Follow-up visit schedule for HIV-exposed infants

Age in weeks/ months	Birth	6 weeks	10 weeks	14 weeks	6 months	9 months	12 months	15 months	18 months
History	X	X	X	X	X	X	X	X	X
Nutrition and growth assessment	X	X	X	X	X	X	X	X	X
Developmental assessment	X	X	X	X	X	X	X	X	X
Physical exam	X	X	X	X	X	X	X	X	X
Determination of HIV status		DNA PCR	Repeat DNA PCR if infant is sick OR perform rapid antibody test at least 6 weeks after cessation of breastfeeding						Rapid antibody test
Cotrimoxazole preventive therapy		X	← Continue until HIV is excluded and infant is no longer at risk from breastfeeding →						
TB risk assessment	← At each visit →								
Immunizations	X	X	X	X		X			
Nutrition counseling and support	X	X	X	X	X	X	X	X	X
Adherence counselling	X	X	X	X	X	X	X	X	X

NB: This is the minimum; children should be seen more frequently if clinically indicated.

4. Care of the HIV-Infected Child

Management of the HIV-infected child is best achieved through integrated HIV services and primary health care. A multidisciplinary, family-centred approach to care is effective in engaging children and their families into long-term care.

4.1 Goals of Care for the HIV-Infected Child

- To promote health and well-being
- To prevent disease progression
- To prevent opportunistic infections

4.2 Comprehensive Care for the HIV-Infected Child

Comprehensive care and support for the HIV-infected child should be provided in a care and treatment centre, preferably where the parent/caregiver receives treatment. Close regular follow-up is essential since these children are at risk of morbidity and mortality; mortality estimates in Africa show that without treatment 35.2% of HIV-infected children will die in their first year and 52.5% by age two.[11] This underscores the importance of timely antiretroviral treatment care and support.

[11] Newell ML, Coovadia H, Cortina-borja M, et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa; a pooled analysis. *Lancet* 2004; 364:1236-1243.

4.2.1 Initial Intake Visit

Clinical assessment of the HIV-infected child should focus on the following:

- **History**, with particular emphasis on previous AIDS defining conditions, history of ARV exposure (PMTCT or previous antiretroviral therapy), family members who are aware of the diagnosis, parental concerns, intercurrent illness.
- **Nutrition and growth assessment** – plot weight, height and head circumference on the growth chart (Annex G).
- **Developmental assessment** using reference provided (Annex H).
- Detailed **physical exam** looking for symptoms and signs suggestive of severe HIV infection.
- **Clinical staging** using WHO clinical staging (Annex B).
- **Immunological staging** using WHO immunological classification (Annex C).
- **TB risk assessment** – ask about history of TB contact, TST for TB screening, and chest radiograph if clinically indicated (Section 5.3).
- **Cotrimoxazole preventive therapy** – check eligibility based on clinical stage and or CD4 if available (Section 5.2).
- **Immunizations** according to the National Expanded Program on Immunization.
- **Nutrition counselling** on provision of adequate nutrition, offer support as necessary (Section 11).
- **ART eligibility** should be reviewed based on clinical stage and immunological criteria (Section 7).
- **Adherence** to care and cotrimoxazole preventive therapy should be reinforced at each visit (Section 8).
- **Disclosure** of HIV status to a child should be discussed with the caregiver. Disclosure should be introduced early on in a neutral way, and should be tailored to the developmental maturity of the child. It is particularly important that adolescents be informed of their status so they can become active participants in their own care (Section 12).
- **M & E** complete all paediatric intake forms.

4.2.2 Follow-Up Visits for HIV-Infected Children

HIV-infected children (both pre-ART and on ART) need close clinical and laboratory monitoring. Follow-up schedule for HIV-infected children on ART is discussed in detail in Section 7. At each visit review the following:

- **History**, with particular emphasis on family members who are aware of the diagnosis, parental concerns, and intercurrent illness
- **Nutrition and growth assessment** – plot weight, height and head circumference on the growth chart (Annex G)
- **Developmental assessment** using reference provided (Annex H)
- Targeted **physical exam** looking for symptoms and signs suggestive of HIV disease progression or development of OI
- **Clinical staging** using WHO clinical staging (Annex B) should be done every visit.
- **Immunological staging** using WHO immunological classification (Annex C)
- **TB risk assessment** – ask about history of household contact with TB, TST annually, and chest radiograph (CXR) if clinically indicated (Section 5.3)
- **Cotrimoxazole preventive therapy** – check eligibility for cotrimoxazole prophylaxis based on clinical stage and/or CD4 if available (Section 5.2)
- **Immunizations** according to the National Expanded Program on Immunization
- **Nutrition counselling** on provision of adequate nutrition and offer support as necessary (Section 11)
- **ART eligibility –** the need for ART should be reviewed based on clinical stage and immunologic criteria (Section 7)
- **Adherence** to care and medications should be addressed at each visit (Section 8)
- **Disclosure** of HIV status to a child should be discussed with the parents or guardians. Disclosure should be introduced early on in a neutral way, and should be tailored to the developmental maturity of the child. It is particularly important that adolescents be informed of their status so they can become active participants in their own care (Section 12)

Table 4-1 Follow-up schedule for HIV-infected children	
Age	**Visit Interval***
0-12 months	Monthly
12-24 months on ART	Monthly
>24 months pre-ART	Every 2-3 months if asymptomatic, monthly if symptomatic
>24 months on ART**	See Section 7

*This is the minimum; children should be seen more frequently if clinically indicated.
**Children >24 months should be seen monthly for the first 6 months after initiation of ART then every 2-3 months if stable

5. Opportunistic Infection Prophylaxis in Children

5.1 Goals of OI Prophylaxis

- To reduce morbidity and mortality from PCP and other bacterial infections
- To reduce morbidity and mortality from TB

5.2 Recommendations on the Use of Cotrimoxazole Prophylaxis in Children (refer to Ethiopian guidelines on CPT)

In high-income countries, cotrimoxazole prophylactic therapy amongst children both HIV-exposed and infected has been standard care. Recent data from a large randomized clinical trial in Zambia provides further evidence that daily cotrimoxazole prophylactic therapy is effective in reducing morbidity, mortality, and hospitalizations in HIV-infected children regardless of CD4 value.[12]

5.2.2 Initiating Cotrimoxazole Prophylaxis in HIV-Infected Infants and Children

Prophylaxis is recommended for the following:

- All HIV-infected children <12 months regardless of CD4 value
- All HIV-infected children 1-4 years with:
  - o Clinical stage 2, 3, or 4 disease
  - o CD4 <25%
- All HIV-infected children >5 years with:
  - o Clinical stage 3 or 4 disease
  - o CD4 <350
- All HIV-infected children with prior PCP pneumonia
- Children <18 months of age with presumptive clinical diagnosis of severe HIV disease

[12] Chintu C, Bhat GJ, Walker AS, et al. Cotrimoxazole as prophylaxis against opportunistic infections in HIV-infected Zambian children (CHAP): a double blind randomized placebo controlled trial. *Lancet*. 2004; 362:1865-1867.

5.2.3 Discontinuing Cotrimoxazole Prophylaxis in HIV-Infected Children

Since most children with HIV-infection are at increased risk of bacterial infections, it is recommended that children with confirmed HIV infection in resource-limited settings continue to receive cotrimoxazole prophylaxis irrespective of immune response to antiretroviral therapy.

However, some experts suggest that discontinuation may be safe in children >5 years of age if all the criteria listed below are met:

- CD4 remains above the threshold adopted for starting CPT (CD4 >200cells/mm^3 for children >5 years) on at least two occasions, three months apart
- Has been on ART at least for 6–12 months with no WHO stage 2, 3 and 4 events
- Evidence of good adherence
- Access to secure drug supply

Cotrimoxazole should be recommenced if the CD4 drops to below 200 cells/mm^3.

5.2.4 Cotrimoxazole Dosage for Infants and Children

Cotrimoxazole should be administered according to body weight: 4mg of TMP/kg once a day. Age based dosing is also acceptable as demonstrated in the CHAP trial. Table 5.1 gives the dosage based on age. Children (>1 month) who are intolerant to CTX can be given Dapsone 2mg/kg/day, with a maximum dose of 100mg/day.

5.2.5 Contraindications to CTX

CTX should not be given to children with:

- Sulpha allergy
- Severe renal insufficiency (Creatinine >3 times normal)
- Severe liver insufficiency (LFTs >5 times normal)

5.2.6 Monitoring

Children on cotrimoxazole should be clinically assessed for evidence of toxicity (nausea, vomiting, and skin rash). Skin rash is the most common adverse event; however this is rare in children. Laboratory monitoring should be symptom-directed. Monitoring adherence to cotrimoxazole is important in preparing children for future ART.

Table 5-1 Dose of CTX for prevention of PCP in infants and children				
Age	**Suspension Per 5ml (200/40mg)**	**Paediatric Tablet (100/20mg)**	**Single Strength Adult Tablet (400/80mg)**	**Double Strength Adult Tablet (800/160mg)**
< 6mo	2.5 ml	1 tablet	1/4 tablet	–
6 mo-5yrs	5 ml	2 tablets	1/2 tablet	–
6-14 yrs	10 ml	4 tablets	1 tablet	1/2 tablet
> 14 yrs	–	–	2 tablets	1 tablet

5.3 TB Risk Assessment

HIV increases susceptibility to Mycobacterium tuberculosis and risk of progression from TB infection to active disease in children and reactivation of latent TB in older children. All HIV-infected and exposed children should be screened for active TB. Children who have a positive TST in whom active TB has been excluded should be offered Isoniazid prophylactic therapy since this has been proven to decrease progression to active TB and reactivation of latent disease in adults and children.

5.3.1 TB Screening

All HIV-exposed and infected children should be screened for TB using a combination of targeted history, TST if available and laboratory tests.

- **Targeted History**
  - o chronic cough for >3 weeks
  - o fever >38^{0}C for >2 weeks
  - o documented weight loss/failure to thrive
  - o household contact with active TB

If yes to any of these questions exclude active TB using combination of TST, CXR, and gastric aspirate if CXR is abnormal. Refer to Ethiopian National TB Guidelines for further details.

- **Tuberculin Skin Testing**
  - o annually for all HIV-infected children beginning at 1 year of age
  - o screen children with positive symptoms
  - o household contacts of active TB case

5.3.2 Recommendations for the Use of INH Prophylaxis in Children

INH preventive therapy has shown early and significant survival benefits and reduction in TB incidence in HIV-infected children. Isoniazid preventive therapy is recommended for HIV-infected children in high prevalence areas with LTBI. Figure 5-1 shows the proposed algorithm for Isoniazid Prophylactic Therapy.

5.3.3 Initiating INH Prophylaxis in Children

HIV-infected children should have annual TST starting at 12 months of age or at time of HIV diagnosis if available. Active TB should be excluded before initiation of INH prophylaxis. 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 TB.

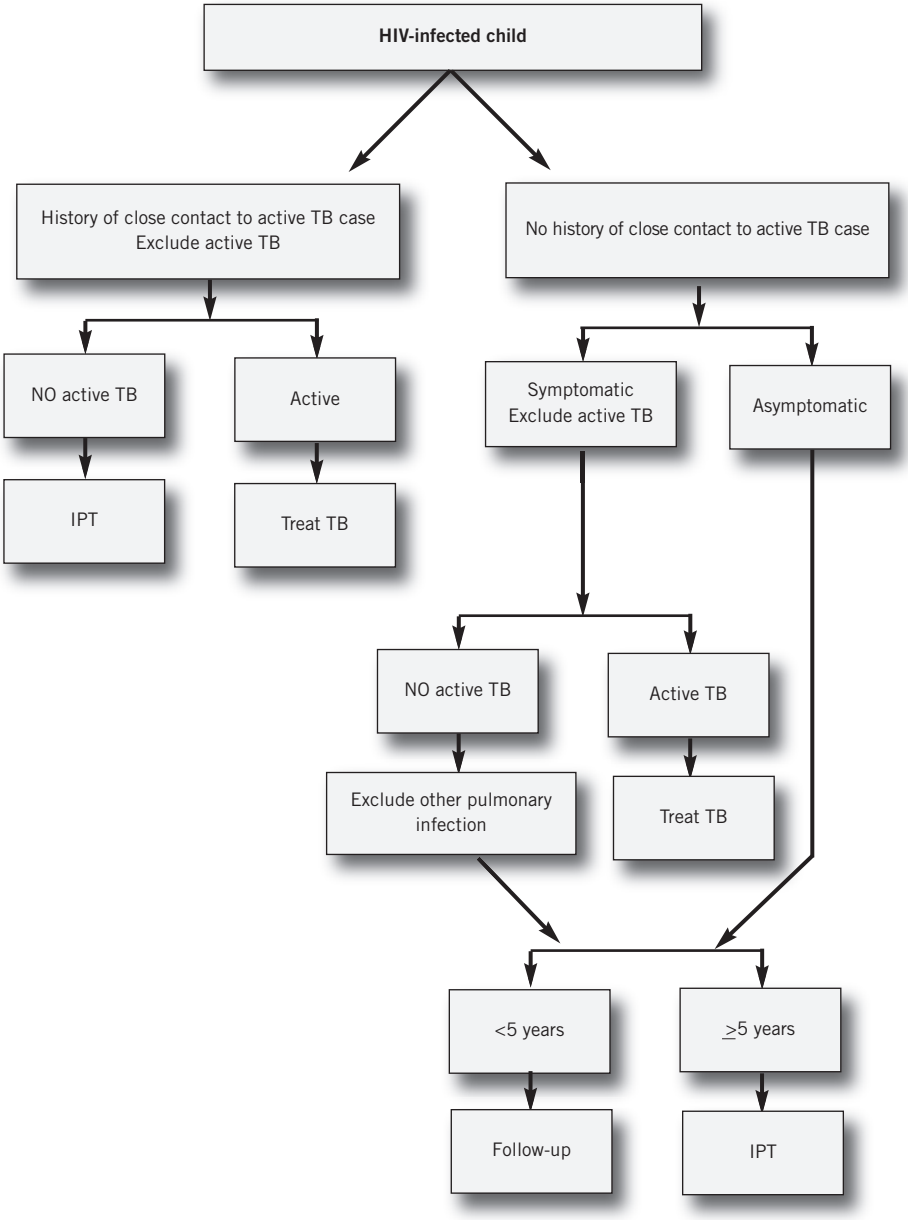
Prophylactic INH therapy should be given after ruling out active disease to the following:

- HIV-infected children with positive TST >5mm
- All HIV-infected children who are household contacts of an active TB case

5.3.4 INH Dosage for Infants and Children

INH 5 mg/kg (maximum 300mg) daily for 6-9 months. Pyridoxine should be given to children with severe malnutrition, breastfeeding infants, pregnant adolescent females, and children with AIDS.

Figure 5.1 Isoniazid prophylactic therapy algorithm



6. Treatment of Common Illnesses in HIV-infected children

6.1 Respiratory Conditions in HIV-Infected Children

Pneumonia is one of the most frequently occurring illnesses in HIV-infected children. Bacterial respiratory tract infections occur significantly more frequently in HIV-infected children compared to an age-related control group.

6.1.1 Pneumonia

Epidemiology: Pneumonia is a major cause of morbidity and mortality in HIV-infected children and is one of the most common reasons for hospitalization. In a tertiary hospital in South Africa, 45.1% of children admitted for severe pneumonia were found to be HIV-1 positive. The same bacterial pathogens (S. pneumoniae and H. influenzae type B and S. aureus) are the most frequent pathogens isolated in HIV-infected children, as in non HIV-infected children.

Clinical manifestations: Symptoms and signs of pneumonia are the same as in non HIV-infected children. However, recurrent episodes (two or more per year or more than three in a life time) and bacteraemia are more common. Severe recurrent bacterial pneumonia suggests moderate to severe immune suppression (WHO Stage 3).

Diagnosis: Because of difficulties in obtaining appropriate specimens from children, a presumptive diagnosis is made in a child with fever, pulmonic symptoms and abnormal chest X-ray if available. A chest X-ray is indicated especially if symptoms are recurrent and/or severe or do not respond to standard treatment.

Treatment: Treatment of pneumonia in HIV-infected children should follow the WHO IMCI guidelines for pneumonia. Children who do not respond to standard therapy should be investigated for tuberculosis.

6.1.2 *Pneumocystis jerovecii* (formally *carinii*) Pneumonia (PCP)

This is caused by *Pneumocystis jerovecii*, an organism that has genomic features of fungi and morphologic features and drug susceptibility similar to protozoa.

Epidemiology: Most humans get infected by *P. jerovecii* before the age of four, and in a healthy host these infections are asymptomatic. Pneumonia caused by *P. jerovecii* occurs almost exclusively in severely immune compromised hosts. PCP remains the most common AIDS-indicator disease amongst HIV-infected children. Without prophylaxis 40% of infants and 70% of adults with AIDS will develop *P. jerovecii* pneumonia.

Clinical manifestations: The highest incidence of PCP is between 2-6 months of age and the mean age of death in children with PCP is 3 months. Abrupt onset of fever, tachypnea, dyspnoea, cough progressing to respiratory distress and cyanosis occurs. Rales are not usually detected on physical examination. It is nearly 100% fatal if untreated.

Diagnosis: Chest X-ray: bilateral diffuse alveolar disease with granular pattern. The earliest densities are perihilar and progression proceeds peripherally sparing the apical areas until last. In resource-limited settings diagnosis is clinical. Definitive diagnosis requires demonstration of the organism in the lung. PCP is a WHO Paediatric Stage 4 disease.

Treatment: Trimethoprim/Sulphamethoxazole is the recommended treatment for PCP.

The dose for HIV-infected children is 15-20mg/kg/day of the Trimethoprim component and 75-100mg/kg/day of the Sulphamethoxazole component every 6 hours for 21 days. After resolution of the acute pneumonitis, children with mild to moderate disease who do not have diarrhoea can complete the course with oral treatment at the same dose. Oral predenisolone 2 mg /kg/24 hours for the first 7–10 days followed by a tapering regimen for the next 10–14 days is recommended for severe cases with hypoxia. Life-long suppressive therapy is indicated following treatment for PCP (Section 5).

6.1.3 Lymphoid Interstitial Pneumonitis (LIP)

Epidemiology: LIP is one of the most common chronic lower respiratory conditions occurring in up to 25% of children with HIV/AIDS.

Clinical manifestations: Range from asymptomatic disease with isolated radiographic findings to bullous lung disease with pulmonary insufficiency. Symptomatic children present with insidious onset of tachypnea, cough, and mild to moderate hypoxemia with normal auscultatory findings or minimal rales or wheezing. Progressive disease is accompanied by digital clubbing and symptomatic hypoxemia. Associated physical findings include generalized lymphadenopathy, hepatosplenomegaly and parotid enlargement.

Diagnosis: Usually based on clinical exam findings. Diffuse bilateral reticulonodular infiltrate on X-ray with mediastinal lymphadenopathy. It is important to exclude tuberculosis and other infectious aetiology.

Treatment: Provide symptomatic treatment (hydration, oxygen). Use antibiotics if there is a superimposed bacterial infection. Bronchodilators may be helpful in mild to moderate disease. Corticosteroids are usually reserved for children with significant hypoxemia and symptoms of pulmonary insufficiency. Give 2mg/kg/day for 2-4 weeks then taper to 1mg/kg/day and maintain at the lowest possible dose that controls the symptoms.

6.1.4 Tuberculosis

Epidemiology: One third of the world population is infected by tuberculosis. Risk of disease progression is 50% in infants under one year; 10–20% between 1–2 years and 5% between 2–5 years. Incidence of TB in HIV-infected children is 100 times higher than in uninfected children. Studies have shown that 11-48% of children with TB in resource- limited settings are co-infected with HIV. Extra pulmonary and miliary TB are more common in children <4 years. Children are often infected by an adult with an active case of tuberculosis through inhalation of the bacilli.

Clinical Manifestations: Pulmonary disease is the most common and presents with various types and degrees of respiratory symptoms. Involvement of lymph nodes, CNS, joints and GI leads to symptoms referable to the organs. Clinical presentation of TB is similar in HIV-positive and HIV-negative children but extra pulmonary and disseminated tuberculosis are more common in HIV-infected children with a tendency to recur.

Diagnosis: A history of contact with an adult case of active tuberculosis is very pertinent and should always be sought. Gastric washing from young children and sputum in older children should be sent for AFB smear (and culture if possible). The absence of bacteriologic evidence or failure to obtain a sample should not deter diagnosis of TB in a child not responding to or deteriorating despite adequate treatment for non-tuberculosis infections. X-ray finding are the same as in uninfected children. However interpretation may be more difficult because of other co-morbid illnesses such as LIP. A positive TST is helpful however; a negative test does not exclude TB exposure or infection.

Treatment: Treatment principles are similar in HIV-positive and negative children. Refer to the Ethiopian national guidelines on TB treatment for further details. TB treatment has priority over ART (Section 10). If a child is already on HAART, review drug interactions and assess for development of treatment failure. Use of DOT increases adherence, decreases resistance, treatment failure, and relapse. Directly observed therapy short course (DOTS) is recommended for treatment of tuberculosis in children. Treatment has two phases:

Intensive (Initial) phase: 4 drugs for the first 8 weeks:

INH	5-10 mg/Kg/day
Rifampicin	10mg/Kg/day
Pyrazinamide	25mg/Kg/day
Ethambutol	15mg/Kg/day

Continuation phase: 2 drugs for 4-6 months:

INH	5-10mg/Kg/day for 4 months
Rifampicin	10 mg/Kg/day for 4 months

Co-administration of rifampin and single PIs (except ritonavir) or NNRTIs can accelerate clearance of these drugs resulting in subtherapeutic levels of these drugs. Both anti TB drugs and ARVs have overlapping toxicities especially hepatotoxicity therefore children require close clinical monitoring.

6.2 Oral Lesions

6.2.1 Oral Candidiasis

Epidemiology: The most common oral condition in HIV-infected children is candidiasis, which may be oropharyngeal or oesophageal. Oral candidiasis is strongly predictive of HIV infection if it is recurrent, persistent and occurs outside the neonatal period without prior antibiotic treatment.

Clinical manifestation: Oral candidiasis can occur in several forms. Erythematous (atrophic) candidiasis: characterized by erythematous (raised and reddened) changes of the palate and the back of the tongue. Pseudo membranous candidiasis: characterized by white or yellow plaques on the buccal mucosa, palate, and/or tongue. Angular chelitis is characterized by erythematous fissures in the corners of the mouth. Children present with reluctance to eat, excessive salivation, or crying while feeding. If thrush is associated with dysphasia, odynophagia, and/or retrosternal pain, consider oesophageal candidiasis but this can also occur in the absence of oral thrush.

Diagnosis: Candidiasis is diagnosed by its clinical appearance and by detection of organisms on smears.

Treatment: Most commonly used is nystatin 100,000 units/ml suspension: 1-2 ml into the mouth 4-6 times daily for 7 days; using cotton wool or a piece of cloth to paint the mouth with nystatin may even be better. Other alternatives include Gentian Violet 1% aqueous solution applied 2x daily for 1 week; 2% miconazole gel, applied orally two times/day. Use fluconazole 3 mg/kg daily orally for 7-14 days for recurrent refractory oral candidiasis. In cases of suspected oesophageal candidiasis extend treatment for 21 days.

Use low dose amphotericin B, 0.3mg/kg/dose once per day by IV infusion for 10-14 days (minimum 7 days) if there is lack of response to oral therapy, inability to tolerate oral medications, suspected oesophageal candidiasis or risk of disseminated candidiasis (e.g. child with leucopenia). Relapses and recurrences are common and prophylactic therapy with fluconazole 3-6 mg/kg by mouth daily can be given if available.

6.2.2 Herpes Simplex

Epidemiology: The prevalence of oral herpes simplex virus is reported in 10-35% of adults and children with HIV infection. Herpes simplex causes both primary and secondary or recurrent disease in the oral cavity. Primary herpetic gingivostomatitis commonly occurs in children and young adults and may be followed by frequent recurrences.

Clinical manifestation: Fever, irritability, tender submandibular lymphadenopathy and superficial painful ulcers in the gingiva and oral mucosa characterize primary herpetic gingivostomatitis. This may lead to decreased oral intake and dehydration.

Diagnosis: Appearance of typical ulcers and vesicles around the mouth and nose.

Treatment: HIV-infected children with symptomatic disease should be treated with acyclovir at a dose of 20mg/kg/dose by mouth, administered 3 times per day for 7-14 days. Recurrent episodes of herpes stomatitis (>6 episodes/year) may be prevented with acyclovir 10 mg/kg/dose by mouth 2 times per day.

6.2.3 Periodontal Disease

Epidemiology: Periodontal disease and gingivitis occur frequently in children with HIV infection.

Clinical manifestation: The disease can range from mild redness of the gums to necrotizing ulcerative periodontitis (NUP), severe ulceration and destruction of gum tissue. Necrotizing ulcerative periodontitis can result in extensive soft tissue loss and loss of teeth. Necrotizing stomatitis may develop, and areas of necrotic bone may appear along the gingival margin. Patients with necrotising ulcerative periodontitis and necrotizing stomatitis frequently complain of extreme pain and spontaneous bleeding. Severe periodontal disease and gingivitis can cause pain, leading to decreased oral intake, dehydration and wasting.

Diagnosis: Based on patient history and clinical appearance, it is sometimes difficult to distinguish this type of periodontal disease from non-HIV-related periodontal disease. However, complaints of severe pain, rapid onset, and rapid destruction in an extremely clean mouth are unusual for non-HIV-related periodontal disease.

Treatment: Medicated oral rinses such as chlorhexidine gluconate 1% oral rinse, 15 ml swished in the mouth for 30 seconds then spat out, twice a day. Patients should be cautioned not to swallow the chlorhexidine gluconate rinse and not to eat for 2 hours afterwards. In cases of NUP, metronidazole, amoxicillin-clavulanate (augmentin), or clindamycin should be added to the treatment regimen. Refer patients to a dentist for further management if no response. Periodontal disease is easily prevented with good oral hygiene such as regular brushing and flossing.

6.3 Opportunistic Infections of CNS

6.3.1 *Cryptococcal* Meningitis

Epidemiology: This an AIDS defining fungal CNS infection caused by the organism *Cryptococcus neoformans*. Cryptococcus occurs in 6-13% of adults infected with HIV but is less common in children and usually occurs in those with severe immunodeficiency.

Clinical manifestation: Intermittent fever is the most common clinical manifestation. Headache is present in patients with CNS infection but meningeal signs may be absent and focal neurological signs are seldom seen. However, some patients may present with meningismus, photophobia and seizures. Cutaneous lesions may mimic molluscum contagiosum. CNS *cryptococcus* may be rapidly be complicated by increased ICP and cortical blindness may ensue if untreated. It may also occur as part of IRIS.

Diagnosis: Lumbar puncture: measure opening pressure; CSF India ink and cryptococcus antigen test; fungal culture. Perform ophthalmologic exam and CT scan/MRI if available.

Treatment: High dose fluconazole 12 mg/kg/day in two divided doses (maximum dose 400mg/day) for 10 weeks. If amphotericin B is available start with 0.75-1mg/kg/dose once daily for two weeks, then change to oral fluconazole at dose listed to complete a 10 week course. After therapy secondary prophylaxis should be initiated at a dose of 3-6 mg/kg per day, maximum 200 mg daily. There is no evidence to support cessation of secondary prophylaxis in children.

6.3.2 CNS *Toxoplasmosis*

Toxoplasma encephalitis (TE) is caused by the protozoa *Toxoplasma gondii*.

Epidemiology: Prevalence rates differ by region being higher in warmer climates and at lower attitudes and in populations who eat under-cooked meat. Seropositivity in Ethiopia is estimated to be about 80%.

Clinical manifestation: Toxoplasma encephalitis is the most frequent cause of focal neurological lesions such as hemi paresis, hemiplegia, hemi-sensory loss in HIV-infected persons. Other possible manifestations are headache, fevers, weakness, seizures and altered mental state.

Diagnosis: A presumptive diagnosis is based on clinical symptoms, serologic evidence of infection and a space-occupying lesion on imaging. Presence of Ig M antibody is proof of acute infection as is raising titer of Ig G. Ring enhancing lesions are seen on CT scan.

Treatment: Pyrimethamine loading dose 2mg/kg/day (max 50mg) for 3 days then maintenance 1mg/kg/day (max 25mg) plus sulphadiazine 50mg/kg (max1-1.5gm/dose) every 6 hours plus folinic acid 10-20mg 3 times weekly. Duration of treatment is 6 weeks. Dexamethasone 4mg po or IV every six hours if there is cerebral oedema or CSF protein is very elevated (>1000mg/dl). This should be discontinued as soon as possible.

In Ethiopia: fansidar is used i.e pyrimethamine + sulfadoxine; loading dose of 2 tabs bid for 2 days followed by 1 tab daily plus folinic acid 5–15 mg daily.

Lifelong suppressive therapy is indicated after treatment to prevent recurrence.

6.4 Skin Manifestations in HIV-Infected Children

Skin disorders in HIV-infected children tend to be recurrent, disseminated and respond less consistently to conventional therapy than in HIV-uninfected children. Non-specific generalized papular dermatitis is the commonest dermatological manifestation in children living with HIV/AIDS. Viral, bacterial and fungal skin infections are also common.

6.4.1 Impetigo

This superficial bacterial infection of the skin characterized by honey-coloured crusts is usually caused by Streptococcus pyogenes, Staphylococcus aureus or both.

Epidemiology: Impetigo is common among preschool children and young adults.

Clinical manifestation: The skin lesions begin as an erythematous area progressing to honey coloured crusts. Superficial vesicles and bullae are seen. Systemic findings are not common but may include fever and lymphadenopathy.

Diagnosis: The honey coloured crusts are diagnostic of impetigo. Gram stain is useful in identifying the aetiological organism.

Treatment: Cloxacillin or erythromycin for ten days.

6.4.2 Cutaneous Fungal Skin Infection (Dermatophytosis)

Epidemiology: This infection of skin, hair and nails is caused by three major genera of dermatophytes (*Trichphyton rubrum, Microsporum* and *Epidermophyton).The* term tinea is used to denote fungal infection and is typically modified by the site involved [tinea capitis (scalp), tinea corporis (body)].

Clinical manifestation: Depends on the site affected. Tinea corporis: superficial scaling, round or oval erythematous plaques that expand centrifugally with erythematous age and central clearance. A hypersensitivity reaction can occur resulting in boggy mass kerion. Tinea ungum: lesions appear as white sharply outlined area on nail with rough and friable nail surface. Tinea capitis: non inflammatory scaly plaques with secondary hair loss.

Diagnosis: Clinical and KOH stain.

Treatment: Superficial fungal skin infections are best managed using topical antifungal agents like clotrimazole, miconazole and ketoconazole for an average of six weeks. Continuation of medication one week after clinical clearance is recommended to avoid recurrence. For tinea ungum (nail infection) and tinea capitis gresiofulvin 10-15mg/kg once a day for six weeks is recommended.

6.4.3 Scabies

Epidemiology: Scabies is an infestation by the mite Sarcoptes scabies, characterized by severe itching, and transmitted by close contact with the infested person; pruritis is intense particularly at night. The Norwegian type (disseminated form) is seen in severely immune compromised children.

Clinical manifestations: Intraepidermal burrows and vesicles distributed in web spaces of fingers, wrist, elbows, umbilical area, genitalia and feet are seen. Usually face and neck are unaffected.

Diagnosis: By history and physical findings.

Treatment: Permethrin 5% applied, left on 8-14 hours, then washed off. Other alternatives are 2.5% sulphur ointment 3 times daily for three days or 25% benzyl benzoate applied for 12 hours then washed off. All family members and close contacts should be treated simultaneously.

6.4.4 *Varicella Zoster* Virus (Chickenpox)

Varicella is a highly contagious disease caused by *varicella zoster* virus, typically characterized by a generalized pruritic vesicular rash evolving to pustules and crusts which usually heal without scarring.

Epidemiology: 90% of varicella infection occurs in children under 10.

Varicella virus is spread via air borne droplets between persons as well as by direct contact.

Patients are contagious several days before appearance of the rash and until the last crop of vesicles crusts over.

Clinical manifestations: Usually there is history of exposure in a child who contracted the illness. In immunocompromised persons lesions may be extensive and involve mucosal surfaces. All stages of skin lesions may be noted at the same time: papules, vesicles, pustules and crusts. Secondary bacterial infection can occur or a severe pneumonitis.

Diagnosis: Diagnosis of chickenpox is made by history and characteristic dermatological findings.

Treatment: Acyclovir is the drug of choice for HIV-infected children and should be started as soon as possible. Use acyclovir 20mg/kg per dose orally 4 times a day in patients with minimal decrease in CD4 count. In severe cases or disseminated disease treat with IV acyclovir 10 mg/kg per dose intravenously every eight hours as one hour infusion for seven days. Topical antipruritic agents like calamine lotion can be applied.

6.4.5 Herpes Zoster

Epidemiology: Is caused by reactivation of varicella. Herpes zoster is uncommon in children and usually seen in immunocompromised patients.

Clinical manifestations: Pain and tenderness in the affected dermatome. Pain usually persists through the course of the illness. Systemic manifestations such as fever occur in 5% of patients. Vesicles and bullous lesions seen in the involved dermatome and in some instances multi dermatomes are involved. In ophthalmic zoster there may be an associated conjunctivitis, keratitis, scleritis and iritis.

Treatment: Use oral acyclovir for mild cases. Use intravenous acyclovir in those severely immunocompromised or in those with trigeminal nerve involvement.

6.4.6 Molluscum Contagiosum Virus

Epidemiology: Transmission is by skin to skin contact. There is increased incidence in young children and immunocompromised children.

Clinical manifestations: Typical lesions are discrete round umblicated, pearly white papule nodules of variable size and number. Usually lesions are asymptomatic or mild pruritis may be present. Giant molluscum may indicate advanced immunodeficiency.

Diagnosis: Based on clinical features.

Treatment: Most resolve without any treatment. Large disfiguring lesions can be managed by liquid nitrogen application. For severe and extensive cases curettage can be considered.

6.5 Diarrhoeal Illnesses

Epidemiology: Acute diarrhoea is the most common cause of morbidity and mortality among HIV-infected children. The course of illness tends to be protracted and usually complicated by dehydration and malnutrition. There are similarity in causes of infectious diarrhoea in HIV-infected and non-infected children. The commonest cause is rotavirus followed by bacterial and parasitical causes. Multiple infections are common. Up to 70% of diarrhoeal deaths in HIV- infected children result from persistent diarrhoea. Other causes of diarrhoea in HIV-infected children include:

Malabsorption and intolerance: lactose intolerance, HIV enteropathy.

Medications: particularly protease inhibitors.

Clinical manifestations: Diarrhoea may be acute (<14 days) or persistent (>14 days); it may be watery or bloody with systemic symptoms like fever. Check for signs of dehydration.

Diagnosis: Stool microscopy and culture

Treatment: Management is the same as for HIV-uninfected children. Children with acute gastroenteritis should be managed according to IMCI guidelines. Treat suspected cause of diarrhoea and provide nutritional management and counselling. Use antibiotics when indicated. Micronutrient supplementation: zinc 20mg/day for 10-14 days (10mg/Kg for infants under six months).

7. Antiretroviral Therapy in Children

7.1 Goals for Antiretroviral Therapy in Children

- To restore immune function
- To maintain maximal suppression of viral replication
- To reduce HIV-related morbidity and mortality
- To improve quality of life and prolong survival

7.2 Selecting Children for Antiretroviral Therapy

Children being considered for antiretroviral therapy must meet medical criteria in order to be eligible. Psychosocial factors should be reviewed; however these should not be regarded as exclusion criteria. Every effort should be made to ensure children meeting eligibility criteria are offered ART.

7.2.1 Criteria for Initiation of HAART in Infants and Children

Initiation of HAART in infants < 12 months of age

- All infants under 12 months of age with confirmed HIV infection should be started on HAART irrespective of clinical or immunological stage.
- Where virological testing is not available, infants less than 12 months of age with clinically diagnosed presumptive severe HIV disease should start antiretroviral therapy. Confirmation of HIV infection should be obtained as soon as possible.

Initiation of HAART in infants and children >12 months of age

For children age 12 months or older, clinical and immunological thresholds should be used to identify those who need to start antiretroviral therapy (Table 7.1).

- WHO Paediatric Clinical Stage 4 disease (irrespective of CD4)
- WHO Paediatric Clinical Stage 3 disease (irrespective of CD4). In children >12 months with TB, LIP, OHL or thrombocytopenia, initiation of ART can be delayed if the immune suppression is just mild
- WHO Paediatric Clinical Stage 2 disease and CD4 value at or below threshold
- WHO Paediatric Clinical Stage 1 disease and CD4 value at or below threshold
- HIV antibody positive infants <18 months of age where virologic testing is not available to confirm HIV infection should be considered for ART if they have clinically diagnosed presumed severe HIV disease (Table 7-2)

Table 7.1 Immunologic criteria for starting ART in children				
Age	**Infant <12months**	**12 months through 35 months**	**36 months through 59 months**	**5 years or older**
% CD4	All	<20	<20	<15
Absolute CD4		<750 mm^3	<350 mm^3	As in adults <200 mm^3

Table 7.2 Clinical criteria for presumptive diagnosis of severe HIV disease in infants and children <18 months of age

A presumptive diagnosis of severe HIV disease should be made if:

- The infant is confirmed HIV antibody positive; and
- Diagnosis of any AIDS-indicator condition(s) can be made; or
- The infant is symptomatic with two or more of the following:
  - o Oral thrush[a];
  - o Severe pneumonia[b];
  - o Severe sepsis[c].

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include:

- Recent HIV-related maternal death; or advanced HIV disease in the mother;
- CD4 <20% in infant.

Confirmation of the diagnosis of HIV infection should be sought as soon as possible

IMCI definition:

a. Oral thrush: Creamy white to yellow soft small plaques on red or normally coloured mucosa which cannot easily be scraped off (pseudo membranous), or red patches on tongue, palate or lining of mouth, usually painful or tender.

b. Severe pneumonia: Cough or difficult breathing in a child with chest in-drawing, stridor or any of the IMCI general danger signs: i.e., lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.

c. Severe sepsis: Fever or low body temperature in a young infant with any severe sign such as fast breathing, chest in-drawing, bulging fontanel, lethargy, reduced movement, not feeding or sucking breast milk, convulsions

7.2.2 Psychosocial Considerations (*not exclusion* criteria):

- An identifiable adult who is able to administer/supervise medication
- Demonstrated reliability in the adult caregiver (i.e., has attended three or more scheduled visits to an HIV clinic and the child's immunizations are up-to-date)
- Supportive social environment
- Disclosure to another adult living in the same house is encouraged so that there is someone else who can assist with the child's ART

7.3 Process for Initiating Antiretroviral Therapy

7.3.1 First Screening Visit 2- 4 Weeks Before Starting Antiretroviral Therapy

- Complete **clinical assessment i**ncluding weight, height and head circumference, and plot growth chart (Section 4.2)
- Ensure **medical criteria** have been met, TB has been adequately excluded, and there is **no medical contraindication** to initiation of ART; treat and stabilize any underlying opportunistic infection
- Review **baseline laboratory investigations** (Table 7. 3)
- Assess patient's and caregiver's **readiness for therapy**
- **Disclosure** counselling depending on the developmental maturity of the child (Section 12)
- Explain the **drug schedule** and **possible side effects** of ARVs with emphasis on problems associated with the chosen drug regimen

Before the second visit the multidisciplinary team should meet and assess patient readiness taking all available information into account.

7.3.2 Second Visit

Children who meet treatment readiness criteria should proceed with ART at this visit.

- Complete **clinical assessment** for all children before initiation of ART (Section 4.2 care of the HIV-infected child)
- Assess patient and families **readiness for therapy** (Section 8)
- **Disclosure counselling** depending on the developmental maturity of the child.
- **ARV prescription** (Annex J)
  - o **Calculate dose of medication**, total volume required, and prescribe enough for two weeks
  - o **Provide detailed description of drugs**, explaining exact dosing schedule to caregiver. Instructions should be clearly written on the container; provide leaflet in local language
  - o **Demonstrate use of syringe and cups** to measure medications as appropriate
- Arrange **follow-up in two weeks**

7.4 ARV Follow-Up Treatment Visits

Children should be followed frequently after beginning antiretroviral therapy. A visit two weeks after initiating therapy should assess adherence, side effects, and tolerance of medications.

7.4.1 Follow-Up Visit 1 (Two Weeks After Initiation of ART)

- Review **clinical history** enquiring about skin rash, fatigue etc.
- **Assess nutrition, growth and development** – measure weight and height, update growth chart, and check surface area (Annexes G and H)
- **Clinical exam** – look for evidence of toxicity (pallor, rash and right upper quadrant tenderness)
- **Check adherence** (Section 8)
- **ARV Prescription** (Annex J)
  - o Verify drug dose and schedule, (if patient is on nevirapine, escalate dose)
  - o Dispense **two weeks supply of medication**
- Arrange **follow-up in two weeks**

7.4.2 Follow-Up Visits 2 and 3 (4 and 8 Weeks After Initiation of ART)

- Review **clinical history**
- **Assess nutrition, growth and development** – measure weight, height and head circumference, update growth chart, check surface area (Annexes G and H)
- **Clinical exam** – look for evidence of toxicity (pallor, rash, right upper quadrant tenderness)
- **Laboratory test** – check Hb for patients on AZT at week 4
- **Check adherence** (Section 8)
- **ARV Prescription** (Annex J)
  - o Adjust drug dose appropriately based on weight and body surface area
  - o Dispense **four weeks supply of medication**
- Arrange **follow-up in 1 month**

7.4.3 Subsequent Follow-Up Visits

HIV-infected children should be followed-up monthly to collect medication and assess adherence, and 3-monthly for clinical examination and toxicity assessment. At each visit review:

- **Clinical history**
- **Nutrition and growth assessment** – measure weight, height and head circumference, update growth chart, check surface area (Annex G)
- **Developmental assessment** (Annex H)
- **Physical exam** – looking for evidence of response to therapy or development of disease progression, evidence of toxicity
- **Clinical staging** using WHO clinical staging (Annex B)
- **Immunological staging** every 6 months (Annex C)
- **Laboratory tests** to monitor clinical response and symptom directed
- **Immunization and nutrition counselling** as appropriate for age
- **Check adherence at every visit** (Section 8)
- **Disclosure**
- **ARV Prescription** (Annex J)
  - o Adjust drug dose appropriately based on weight and body surface area.
  - o Dispense **four weeks supply of medication**
- Arrange **follow-up in 1 month to collect medications and every 3 months for clinical evaluation**

7.5 Paediatric First-Line Therapy

Infants and children > 12 months of age

The recommended first-line regimen for children > 12 months of age is 2 NRTIs +1NNRTI (Table 7-3). A fixed dose combination of d4T + 3TC and NVP is the preferred first line drug in children in Ethiopia. FDCs s available in the right strength and combination and should be used for children.

Infants < 12 months of age

For HIV-infected infants with no exposure to maternal or infant non-nucleoside reverse transcriptase inhibitors, or whose exposure to maternal or infant antiretrovirals is unknown, standard nevirapine-containing triple therapy should be started (2 NRTIs + Nevirapine).

For infants < 12 months of age with a history of exposure to single dose nevirapine or non-nucleoside reverse transcriptase inhibitor containing maternal antiretroviral therapy or preventive antiretroviral regimens, a protease inhibitor-based triple antiretroviral therapy should be started (2 NRTIs + Kaletra). Where protease inhibitors are not available, affordable or feasible, nevirapine-based therapy should be used with close monitoring. These recommendations are based on new WHO guidance released in April 2008.[13] There are ongoing studies which are likely to provide information that may result in modification of this recommendation.

Table 7.3 Preferred first-line regimen for children

Children 1-3 years	**Children ≥3 years old**
d4T +3TC + NVP or AZT + 3TC + NVP	d4T + 3TC plus NVP or EFV# or AZT + 3TC plus NVP or EFV#
# EFV should be avoided in post pubertal girls who are either in the first trimester of pregnancy or are sexually active and not using adequate contraception.	
Infants up to 12 months no history of PMTCT or NNRTI exposure	**Infants up to 12 months with history of PMTCT or NNRTI exposure***
d4T +3TC + NVP or AZT + 3TC + NVP	d4T +3TC + Kaletra** or AZT + 3TC + Kaletra**

* For HIV infected infants with a history of exposure to single dose nevirapine or non-nucleoside reverse transcriptase inhibitor containing maternal antiretroviral therapy or preventive antiretroviral regimens, a protease inhibitor-based triple antiretroviral therapy regimen should be started.

**Where protease inhibitors are not available, or feasible, nevirapine-based therapy should be used.

[13] Report of the WHO Technical Reference Group, Pediatric HIV/ART Care Guideline Group Meeting. Geneva, Switzerland. April 2008.

7.6 Paediatric Triple Fixed-Dose Combinations for Antiretroviral Therapy

7.6.1 Overview

Antiretroviral treatment of children living with HIV/AIDS remains a challenge in most resource limited settings. Until recently, the only paediatric formulations available to national programs were syrups and a small number of paediatric-dose capsules and tablets. Syrups have proven difficult for clinicians to dose, pharmacists to dispense, and caregivers to administer. Children often find it difficult to swallow syrups due to their bitter taste. These challenges have made it much harder for caregivers and patients to achieve optimal adherence.

In response, the Ethiopian government is working to increase access to paediatric HIV treatment by providing paediatric triple fixed-dose combination pills. These pills can be administered easily and are more appropriate for paediatric dosing (Tables 7.4 and 7.5).

7.6.2 Advantages of Paediatric FDCs

The advantages of FDCs have been well documented in adults. It is anticipated that paediatric FDCs will offer similar important advantages, and facilitate the scale-up of high-quality treatment for children:

More Accurate Dosing: The simplified approach to accurate dosing made possible by paediatric FDCs will make treatment easier for healthcare providers, who often struggle to correctly dose syrups and single-dose formulations for children. This will also simplify treatment for caregivers who are responsible for administering the drugs every day.

Improved Adherence: Adherence in children can be particularly challenging. In adults, FDCs have been shown to facilitate patient adherence, which in turn results in more durable viral suppression and limits the emergence of drug resistance. It is expected that the use of paediatric FDC tablets, administered twice daily, will result in improved adherence in children.

Simplified Supply Chain: Paediatric FDCs will simplify ARV supply chain management by reducing the number of products required. FDCs are also significantly less expensive to transport and store than syrups.

Cost: In general, tablets are cheaper to manufacture and have a longer shelf-life than syrups. The per patient-year cost of treatment using paediatric FDCs is approximately 60% lower than the cost of treatment using syrups.

7.6.3 The National Paediatric FDC initiative

The government of Ethiopia in collaboration with funding agents and partners has been working to expand access to paediatric HIV/AIDS care and treatment in Ethiopia and as an extension of this it has planned to avail paediatric FDCs, containing stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) as of May 2008.

7.6.4 Dosing Issues

Standard dosing of paediatric ARVs is by body-surface area or weight. However, FDCs containing fixed amounts of individual ARV components are designed to be dosed by weight band.

If all children in one weight band are given the same number of FDC tablets, a child at the lower end of the weight band will receive higher doses relative to a child at the upper end of the weight band. In order to address this issue, in October 2006 the WHO convened an expert panel to establish paediatric ARV dosing.

- Acceptable dose **ranges** were established for all available pediatric ARVs. In general, the lower limit of the range was defined as the currently accepted dose, and the upper limit as 25% above that level. For example, the range for lamivudine (3TC) is 4 to 5 mg/kg. It was noted that younger children may need higher doses of some drugs than older children, because the metabolism of some ARVs is increased in the youngest age group.

- Under-dosing below the lower limit should be avoided wherever possible. Over-dosing up to 10% above the upper limit is generally acceptable, especially if the duration of over-dosing is short. Importantly, the weight bands are close together for children at low weights and more widely spaced as weight increases. Thus, overdosing in a lower weight band is short term and less significant than overdosing in a higher weight band.

7.6.5 Dual FDCs and Lead-In Dosing

Initiation of any nevirapine-based ART regimen in patient who is naïve to non-nucleoside reverse transcriptase inhibitors requires a lead-in period of 2 weeks when the nevirapine is dosed only once a day. This minimizes the risk of NVP related rash. After 2 weeks, provided there is no rash present, the dose may be escalated to the normal twice daily dose.

In order to facilitate lead-in dosing when using FDCs, dual paediatric FDC products, containing only stavudine and lamivudine, is also available. Table 7-7 shows how the dual FDCs may be combined with triple FDCs for lead-in and maintenance dosing. If dual FDCs are not available, syrup and capsules of d4T, together with 3TC syrup and tablets can be used instead of the dual FDC dose. Dual Paediatric FDCs may also be combined with other compounds such as EFV or PI drugs to provide alternate first line, or second line therapy.

7.6.6 Issues Concerning the Use of Stavudine-Based First-Line Regimens for Children

The only paediatric triple FDCs currently available are combinations of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP). This combination of drugs has been used widely in both adults and children. Recent data from adult cohorts suggests that after long-term use, stavudine may be associated with a high degree of toxicity, especially in African patients. In paediatric cohorts evaluated to date, stavudine appears to be well tolerated.

In 2006, the WHO released revised recommendations for adult ART, in which stavudine was relegated to a position as an alternative to zidovudine or tenofovir. The WHO further recommended that the use of stavudine in adult first-line regimens be phased out over time. In contrast, in the WHO's 2006 revised guidelines for paediatric ART, stavudine remains a preferred option for first-line therapy.

7.6.7 Starting FDCs in Patients Who are Already on ART with Single Drug Formulations

Children already on treatment with adult split FDCs or paediatric single drug formulations will benefit by being switched to paediatric FDC tablets. Children who are receiving a regimen of d4T, 3TC and NVP can be switched over to paediatric FDCs easily. A switch to paediatric FDCs may also be considered for children who are on other drug regimens provided there is no evidence of treatment failure. Lead-in dosing is not necessary for patients who have already been on full dose NVP.

7.6.8 Considerations for the Use of Paediatric FDCs in Ethiopia

1. All newly enrolled ART eligible HIV infected children shall be initiated on the new d4T based FDC. In cases of PMTCT failure dual FDCs with PI can be started.

2. All children who have been taking d4T based ART regimen containing NVP shall be shifted to d4T based FDC.

3. All children who have been taking d4T based ART regimen containing EFV can be shifted to d4T based dual FDC and continue with EFV.

4. All infants and children taking AZT based ART regimen will continue with the same regimen

5. Children weighing 25 kg and above can use adult FDC (AZT or d4T based except Atripla)

6. Initiation of NVP based ART regimen requires a lead-in dose in the first two weeks using a Triple FDC in the mornings and a dual FDC (D4T and 3TC) in the evenings followed by the use of Triple FDC twice a day thereafter. Refer table 7.7.

7. In case of TB/HIV co infection use dual FDC plus EFV or PI (double dose of kaletra) or ABC as appropriate.

8. In case of NVP hepatotoxicity use dual FDC plus EFV and in children < 3 years of age use PIs

Table 7.4 Paediatric triple-fixed drug combinations available in Ethiopia					
Manufacturer	Trade Name	WHO abbreviation	Composition		
			Stavudine (d4T) Dose/tablet (mg)	Lamivudine (3TC) Dose/tablet (mg)	Nevirapine (NVP) Dose/tablet (mg)
Cipla	Triomune Baby	FDC 6	6	30	50
	Triomune Junior	FDC 12	12	60	100

Table 7.5 Paediatric dual-fixed drug combinations available in Ethiopia				
Manufacturer	Trade Name	WHO abbreviation	Composition	
			Stavudine (d4T) Dose/tablet (mg)	Lamivudine (3TC) Dose/tablet (mg)
Cipla	Lamivir-S Baby	Dual FDC 6	6	30
	Lamivir-S Junior	Dual FDC 12	12	60
Lamivir-S Baby/Junior is intended for children < 30Kg who are initiating therapy with Triomune Baby/Junior. It should only be used during the 14-day lead in for Nevirapine in combination with Triomune Baby /Junior.				

Table 7.6 Weight-based dosing recommendations for Triple FDC (adapted from WHO)							
Weight range (Kg)	**Formulation**	**Dose (tablets)**			**Formulation**	**Dose (tablets)**	
		AM	**PM**			**AM**	**PM**
3-5.9	Triomune Baby	1	1		Triomune Junior	0.5	0.5
6-9.9	Triomune Baby	1.5	1.5		Triomune Junior	1	0.5
10-13.9	Triomune Baby	2	2		Triomune Junior	1	1
14-19.9	Triomune Junior	1.5	1		Triomune Junior	1.5	1
20-24.9	Triomune Junior	1.5	1.5		Triomune Junior	1.5	1.5
25-34.9	Adult FDC 30/150/200	1	1		Triomune Junior	2	2

Table 7.7 Lead-in and maintenance dosing using triple and dual FDCs

Weight range (Kg)	Lead-in Period Formulation and dosing				Maintenance Formulation and dosing		
	Triple FDC Triomune	AM	Dual FDC Lamivir-S	PM	Triple FDC Triomune	AM	PM
3-5.9	Triomune Baby	1	Lamivir-S Baby	1	Triomune Baby	1	1
6-9.9	Triomune Baby	1.5	Lamivir-S Baby	1.5	Triomune Baby	1.5	1.5
10-13.9	Triomune Baby	2	Lamivir-S Baby	2	Triomune Baby	2	2
14-19.9	Triomune Junior	1.5	Lamivir-S Junior	1	Triomune Junior	1.5	1
20-24.9	Triomune Junior	1.5	Lamivir-S Junior	1.5	Triomune Junior	1.5	1.5
25-34.9	Adult FDC	1	Adult Dual FDC	1	Adult FDC	1	1

7.7 Considerations for Antiretroviral Therapy in Infants Previously Exposed To ARVs

Infants who have received PMTCT prophylaxis (maternal prophylaxis or for her own disease, infant portion of prophylaxis) are at risk of infection from a drug-resistant virus. This is especially true when the mother received nevirapine or 3TC alone. HIV-infected infants < 12 months of age with a history exposure to single dose nevirapine or NNRTI containing materanal antiretroviral therapy or preventive antiretroviral regimens, a protease inhibitor based triple antiretroviral therapy regimen should be started. If PIs are not available, affordable or feasible, a nevirapine –based therapy should be used.

7.8 Clinical and Laboratory Monitoring Of Children on ART

HIV-infected children on ART must be monitored closely for clinical and laboratory evidence of response to therapy, drug tolerance, adverse events, and adherence. Clinical and laboratory monitoring before and during treatment is summarized in Table 7-8. Patients who are not doing well should be seen more frequently at the discretion of the healthcare provider.

Table 7.8 Clinical and laboratory monitoring for HIV-infected children							
Visit Schedule	**Pre-ART visit**	**ART Initiation visit**	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Every 3 months**
	Week -2	**Week 0**	**Week 2**	**Week 4**	**Week 8**	**Week 12**	**>12 weeks**
Growth and developmental assessment	X	X		X	X	X	every visit
Physical exam	X	X	X	X	X	X	every visit
Clinical staging	X	X			X	X	every visit
Cotrimoxazole preventive therapy	Check eligibility and continue						
ART prescription		X	X	X	X	X	X
Discloure	Discuss at each visit based on developmental maturity of the child						
Adherence counseling	X	X	X	X	X	X	every visit
Hb	X			X if on AZT			every 6 months
Platelet count	X						every 6 months
WBC with diff	X						every 6 months
BUN and creatinine	X						every 6 months
AST	X						every 6 months
CD4% and/or count	X						every 6 months
TB screen	X						annually
Pregnancy test	X	If clinically indicated (for sexually active adolescent females)					
Fasting cholesterol and triglyceride		every 6 months if on second-line regimen					

7.9 Treatment Failure

The most common cause of treatment failure is inadequate adherence. Failure of a first-line regimen should be determined by evidence of disease progression using clinical staging, and immunological criteria where available (Tables 7.9 and 7.10). Virologic criteria are not recommended because of the complexity of defining treatment failure in children using viral load and the inaccessibility of routine virologic tests in Ethiopia. Note the following when determining treatment failure in children:

- First check adherence, make sure child has been on therapy at least 24 weeks, and adherence has been assessed and found adequate
- When defining treatment failure because of growth failure, ensure child is not failing to grow because of inadequate nutrition, and that any intercurrent illnesses have been treated and resolved
- Development of pulmonary TB while on first-line therapy may NOT be an indication of treatment failure. Response to TB treatment should be used to evaluate the need for switching therapy
- Always exclude immune reconstitution syndrome (Section 7.12)
- CD4% should NOT be measured during an intercurrent infection – but preferably a month after resolution
- Do NOT use TLC to determine treatment failure

Table 7.9 Clinical definition of treatment failure in children

- Lack of or decline in growth rate in children who show an initial response to treatment (WHO clinical stage 3 or 4; moderate or severe unexplained mal-nutrition; not adequately responding to standard therapy despite adequate nutritional support and without explanation)
- Loss of neurodevelopmental milestones or development of HIV encephalopathy
- Occurrence of new OI or malignancies; recurrence of infections such as oral candidiasis that is refractory to treatment or oesophageal candidiasis

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

Table 7.10 Immunological definition of treatment failure in children
• Development of age-related severe immunodeficiency after initial immune recovery • Development of new age-related severe immunodeficiency, confirmed with at least one subsequent CD4 measurement • Rapid rate of decline to at or below threshold of age-related severe immunodeficiency
Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

7.10 Paediatric Second-Line Therapy

When treatment must be changed because of clinical and/or immunological failure, all the drugs must be changed. Always review adherence and make sure it is adequate. In certain instances directly observed therapy (DOT) may be required. The preferred second-line regimen is a boosted PI combined with two new NRTI agents. For children on standard first-line regimen the preferred second-line regimen is {ddI + ABC + LPV/r}. If there is no cold chain, NFV can be used instead of LPV/r. For infants and children who were started on a PI based first line regimen(because of a history of exposure to PMTCT or NNRTI) who develop treatment failure consult a specialist for construction of a second-line regimen.

7.10.1 Procedure for Introducing Second-Line Therapy

- Do not rush into second-line therapy
- Reassess readiness and adherence support, and address potential adherence barriers before initiating a new regimen
- If it is impossible to improve adherence, attempt DOT with a health care worker or trusted 'other' family member or friend
- Verify child meets clinical and or immunological criteria for treatment failure (Tables 7.9 and 7.10)
- Use both clinical (restaging) and CD4 measurements to assist in deciding if regimen should be changed (Table 7.12)
- It is preferable to have at least two CD4 measurements available
- Ensure second-line therapy does not include any drugs used in first-line therapy (Table 7.11)
- Always consult with an experienced paediatric ART clinician before changing to second-line therapy
- Ensure close frequent follow-up once regimen is changed

Table 7.11 Preferred second-line regimen for children	
First-line regimen	**Preferred second-line regimen**
AZT + 3TC + NVP or EFV	ddI + ABC + LPV/r*
D4T + 3TC + NVP or EFV	ddI + ABC + LPV/r*
* NFV can be substituted for LPV/r if no cold chain is available.	

7.11 Discontinuation/Interruption of ARV Therapy

In paediatric patients short-term therapy interruptions are most often necessitated by acute illnesses that limit oral intake. Discontinuation of ARVs in children is usually a result of:

- Severe life-threatening toxicity such as Stevens Johnson Syndrome or acute fulminant hepatitis (Section 9)
- Acute illnesses or planned surgeries which preclude oral intake
- Repeated and persistently poor adherence with risk of developing drug resistance
- TB co-infection when patient cannot tolerate all medications (Section 10)
- Planned short term interruption of therapy may also be necessary for surgery or short term procedure, but when possible the patient should be allowed to continue regular antiretroviral therapy with minimal fluid intake. When short term therapy interruption is indicated, all the medications should be stopped at the same time. Efavirenz and nevirapine have very long half lives. Except in the case of acute life-threatening toxicity the NRTIs should be continued for at least two weeks after discontinuation of the NNRTIs. If nevirapine has been discontinued more than two weeks and is being reintroduced, it is recommended another two-week escalation be used. There is no data to support long term structured treatment interruptions in children.

7.12 Immune Reconstitution Syndrome

IRS/IRIS is characterized by a clinical deterioration after starting ART, and is a result of the immune system interacting with latent infections. It is important to differentiate IRS from treatment failure since management is very different. Treatment failure results in disease progression with development of opportunistic infection or malignancy after drugs have been given sufficient time to induce a protective degree of immune restoration (at least 24 weeks of ARV therapy). IRIS usually occurs within the first several weeks after initiation of HAART if there is a subclinical infection present at baseline. Several different pathogens can be reactivated causing IRS. In children the most common is *Mycobacterium tuberculosis*; others are *mycobacterium avium complex*, *cryptococcus neoformans*, *varicella zoster* virus and *herpes simplex* virus. Management of IRS includes specific treatment for the infection and symptomatic therapy. In severe cases glucocorticoids are helpful.

Table 7.12 Management of treatment failure in children		
Clinical Stage on ART	**Availability of CD4 Measurement**	**Management Options**
New or recurrent T1 and T2 event(s)**	No CD4	• **Do not switch regimen**
	CD4	• Consider switching regimen only if 2 or more values below age-related threshold for severe immunodeficiency are available • Increase clinical and CD4 follow-up if CD4 approaches age-related threshold for severe immunodeficiency
New or recurrent T3 event(s)**	No CD4	• **Consider switching regimen** • If child has pulmonary or lymph node TB or severe recurrent presumed bacterial pneumonia treat condition; the decision to switch regimen should be based on re-evaluation of the child in question.
	CD4	• Switching regimen is recommended if CD4 is at or below age-related threshold for severe immunodeficiency* and particularly if child initially had good immune response to ART
New or recurrent T4 event(s)**	No CD4	• **Recommend switching regimen**
	CD4	• Switching is generally recommended but may not be necessary where CD4 is above age-related threshold for severe immunodeficiency

*Age-related severe immunodeficiency values as defined in Annex B; switching should particularly be considered if values are <15% (12-35 months of age), <10% (36-59 months of age), <100 cells/mm3 (≥5 years of age); use of %CD4 in children under 5 years of age and absolute CD4 count after 5 years of age is preferred; if serial CD4 values are available, the rate of decline should be taken into consideration.

**T1, T2 etc refers to re staging of HIV/AIDS in a patient who is on treatment for 24 or more weeks.

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

8. Adherence in Children

ARV treatment requires collaboration between the child, caregiver and medical provider. Adherence in children is challenging as such efforts to maximize adherence should begin prior to treatment initiation. Continuous assessment and support of adherence is fundamental to successful antiretroviral therapy and to prevent development of drug resistance.

8.1 Goals of Adherence

- To ensure patient takes >95% of prescribed doses
- To prevent development of resistance

8.2 Role of the Heath Care Team in Adherence

Healthcare providers, nurses, pharmacists, counsellors (health professionals, non health professionals or community counsellors) physicians and social workers (case managers) play an important role in ensuring adherence.

- Health providers should develop a trusting relationship with the patient and family
- The provider's role should be supportive, non-judgemental and honest
- Feedback from the counsellor to the rest of the team is important

8.3 Adherence Strategies in Children

Adherence is a complex health behaviour influenced by the regimen prescribed, patient factors, and characteristics of healthcare providers. Adherence support should begin before therapy is initiated and be incorporated into every clinic visit.

8.3.1 Adherence Education

- Define adherence
  - o Never missing a dose
  - o Taking >95% of prescribed doses
  - o Keeping to specific times of administration
  - o Taking it the "right" way
  - o Lifelong treatment, even when feeling well
- Explain importance of adherence
  - o Failure of adherence may be temporary, however the effect on treatment choices may be permanent
  - o Use simple terms, open-ended questions, visual aids, analogies
- Emphasize need for communication
  - o Foster partnership, trust and honesty
  - o Negotiate treatment plan that patient and caregiver can understand
  - o Encourage disclosure to family who can support treatment plan

8.3.2 Preparation and Practice

- Assess family's readiness for therapy (Section 8)
- Discuss medications
  - o Who will administer the medications?
  - o What medications will be given, what do they taste like?
  - o When will the medication be taken?
  - o How frequently will the medications be taken?
  - o How will the medication schedule fit into school routine and caregiver's work schedule?
  - o How will the medication be given?
  - o How will the medications be stored?
- Practice taking medications
  - o Taste testing
  - o Observation of dosing
  - o Training for pill swallowing
  - o Behavioural reward system
  - o Role play

8.3.3 Assessment

There is no perfect way to measure adherence; however it must be assessed at each visit.
Review the following:

- ARV pill count or suspension return
- Pharmacy records must be regular
- Missed or late clinic visits should trigger concerns about adherence
- Monthly visits with counsellor for first three months then every three months
- Arrange regular community visits by patient advocates

8.3.4 Ongoing support

There is no perfect way to measure adherence; however it must be assessed at each visit.
Review the following:

- Psychosocial support in the form of counselling on disclosure
  - o Linkages in the community
  - o Create links with support groups and encourage discussion on adherence
- Provide adherence tools
  - o Pill boxes
  - o Pre-labelled syringes
  - o Calendars
- Anticipate side effects and advise
  - o Beware of adherence fatigue
  - o Hypothetical scenarios (What would you do if the child vomits or spits out medication?)

Table 8-1 Assessing patient and family readiness for therapy

• Identify responsible adult who will ensure medication is administered • Adult should demonstrate reliability • Supportive social environment for adult caregiver and child/adolescent • Disclosure • Review previous records of adherence to chronic medications such as TB meds, CTX prophylaxis	Home visit by counsellor to assess: • Home circumstances • Verify contact details • Support structures including disclosure • Drug storage facilities (e.g. refrigerator)

8.4 Initial Intervention Strategies

- Establish trust and identify mutually acceptable goals for care
- Identify family member, friend or health team member who can help with adherence support
- Educate family about the importance of adherence in therapy outcome
- Identify adherence target; >95% of prescribed doses
- Educate patient and family about the relationship between partial adherence and resistance
- Educate patient about resistance and constraints of later choices of antiretroviral drug (failure of adherence may be temporary, however the effect on treatment choices may be permanent)
- Develop a treatment plan patient and family understand, to which they feel committed
- Establish readiness to take medication by practice sessions

8.5 Follow-Up Adherence Strategies

- Monitor adherence at each visit, and between by home visits
- Provide ongoing support, encouragement and understanding of difficulties of trying to be >95% adherent
- Use adherence support tools: pictures, pill boxes, and calendars
- Provide access to support groups or counselling
- Provide pharmacist-based adherence

8.6 Stepped-Up Adherence for Children with Reduced Adherence

If adherence is found to be suboptimal every effort must be made to improve it.

- Re-educate patient and caregiver about importance of adherence
- Evaluate appropriateness of support structures
- Address medication-related issues
- Use adherence support tools (8.3.3)
- Check family situation with social worker
- Arrange home visits by counsellor and/or social worker
- Check for competing religious and cultural practices
- Consider DOT
- Identify and trace defaulters (use clinic appointment books, community health workers and lay counsellors to help track by phone calls/home visits)

9. Management of Adverse Events in Children

9.1 Grading of Adverse Events in Children

Adverse reactions should be graded according to the PACTG grading (Tables 9.1 and 9.2). Consider grading both laboratory and clinical abnormalities to facilitate management. All ARV drugs-related adverse events should be reported to the Drug Administration and Control Authority using adverse event reporting form.

9.2 Principles of Managing Adverse Events in Children on ART

1. Establish whether the event is due to the ARV or another medication. Alternative explanations for the toxicity must be excluded before concluding the reaction is secondary to the ARV drug. Toxicities that have non-ARV aetiology do not require a change of the ARV drug.

2. Exclude other disease processes (IRS, OI or intercurrent illnesses).

3. Determine the severity of the event (mild, moderate, severe, or life-threatening).

4. Manage the adverse event according to toxicity:

    a. Grade 4 (life-threatening): immediately discontinue all ARVs, manage the medical event, reintroduce ARV using a modified regimen (substitute for the offending drug) when the patient is stabilized (Table 9.4)

    b. Grade 3 (severe): substitute offending drug without stopping ART

    c. Grade 2 (moderate): consider continuation of ART as long as feasible, if patient does not improve, consider single drug substitution

    d. Grade 1 (mild): usually does not require change in therapy

5. If there is need to discontinue ART because of life-threatening toxicity, stop all ARVs at once. The NNRTI has long half-life and some experts recommend continuing dual NRTI drugs for seven days after discontinuation of the NNRTI drug. In situations of life- threatening toxicity all drugs should be discontinued at once.

9.3 Management of Specific Adverse Events Related to Specific ARV Drugs

Serious acute and chronic toxicities due to ARV drugs may require therapy modification. Every effort must be made to manage these toxicities promptly since they have implications for ART adherence (Table 9.3). It is important to take into consideration the rate of change over time, and whenever possible repeat the laboratory test to confirm.

9.4 Single Drug Substitution for Toxicity in Children

In the event of moderate or severe toxicity a single drug can replace the offending drug (Table 9.4). Table 9-5 lists ARV drug combinations to avoid with children.

Table 9-1 Grading of adverse events in children				
Parameter	**Grade 1 Mild**	**Grade 2 Moderate**	**Grade 3 Severe**	**Grade 4 Severe Life-threatening**
Diarrhoea ≥1 year of age <1 year of age	Transient or intermittent episodes of unformed stools OR increase of ≤3 stools over baseline per day. Liquid stools (more unformed than usual) but usual in number.	Persistent episodes of unformed to watery stools or increase of 4-6 stools over baseline per day. Liquid stools with increased number of stools or mild dehydration	Grossly bloody diarrhoea or increase of ≥7 stools per day or IV fluid replacement indicated. Liquid stools with moderate dehydration.	Life-threatening consequences (e.g. hypotensive shock). Liquid stools resulting in severe dehydration with aggressive rehydration indicated or hypotensive shock.
Nausea	Transient (<24 hours) or intermittent nausea with no or minimal interference with oral intake.	Persistent nausea resulting in decreased oral intake for 24-48 hours.	Persistent nausea resulting in minimal oral intake for >48 hours or aggressive rehydration indicated (e.g. IV fluids).	Persistent nausea with no or minimal oral intake resulting in dehydration with aggressive rehydration indicated.
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake.	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension or aggressive rehydration indicated (e.g. IV fluids).	Life-threatening consequences (e.g. hypotensive shock).

Table 9-1 Grading of adverse events in children				
Parameter	**Grade 1 Mild**	**Grade 2 Moderate**	**Grade 3 Severe**	**Grade 4 Severe Life-threatening**
Acute systemic allergic reaction	Localized urticaria (wheals) lasting a few hours.	Localized urticaria with medical intervention indicated or mild angio oedema.	Generalized urticaria or angio oedema with medical intervention indicated or symptomatic mild bronchospasm.	Acute anaphylaxis or life-threatening bronchospasm or laryngeal oedema.
Pancreatitis		Symptomatic and hospitalization not indicated (other than emergency treatment).	Symptomatic and hospitalization not indicated (other than emergency treatment.	Life-threatening consequences (e.g. circulatory failure, haemorrhage, sepsis).
Rash	Localized macular rash.	Diffuse macular, maculopapular, or morbilliform rash or target lesions.	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae or superficial ulcerations of mucous membrane limited to one site.	Extensive or generalized bullous lesions or Stevens-Johnson syndrome or ulceration of mucous membrane involving two or more distinct mucosal sites or Toxic Epidermal Necrolysis.

Table 9-1 Grading of adverse events in children				
Parameter	**Grade 1 Mild**	**Grade 2 Moderate**	**Grade 3 Severe**	**Grade 4 Severe Life-threatening**
Alteration in personality-behaviour or mood	Alteration causing no or minimal interference with usual social and functional activities.	Alteration causing greater than minimal interference with usual social and functional activities.	Alteration causing inability to perform usual social and functional activities and intervention indicated.	Behaviour potentially harmful to self or others or with life-threatening consequences.
Altered Mental Status	Changes causing no or minimal interference with usual social and functional activities.	Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities.	Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social and functional activities.	Onset of delirium, obtundation, or coma.

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

Table 9-2 Grading of selected laboratory toxicities in children				
Parameter	**Grade 1 Mild**	**Grade 2 Moderate**	**Grade 3 Severe**	**Grade 4 Severe Life-threatening**
Haemoglobin (g/dL)	8.5 – 10.0	7.5 – <8.5	6.5 – <7.5	<6.5
ANC (mm^3)	750 – <1,000	500 – 749	250 – 500	<250
Platelets (mm^3)	100,000 – <125,000	50,000– <100,000	25,000 – <50,000	<25,000 or bleeding
ALT (SGPT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
AST (SGOT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	>10.0 x ULN
Bilirubin (>2 weeks of age)	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	>5.0 x ULN
Lipase	1.1 – 1.5 x ULN	1.6 – 3.0 x ULN	3.1 – 5.0 x ULN	>5.0 x ULN
Pancreatic amylase	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	2.1 – 5.0 x ULN	>5.0 x ULN
Cholesterol (fasting, <18 years old) mg/dL	170 – <200	200 – 300	>300	NA
Glucose, serum, Nonfasting (mg/dL)	110 – 126	126 – <251	251 – 500	>500
Glucose, serum, high: Fasting (mg/dL)	110 – 126	126 – <251	251 – 500	>500
Lactate	<2.0 x ULN without acidosis	≥2.0 x ULN without acidosis	Increased lactate with pH <7.3 without life threatening lconsequences or related condition present	Increased lactate with pH <7.3 with life threatening consequences (e.g. neurological findings, coma) or related condition present
Triglycerides: Fasting (mg/dL)	NA	500 – <751	751 – 1,200	>1,200

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

Table 9-3 Management of specific adverse events related to specific ARV drugs		
Clinical manifestations associated with the toxicity	**Laboratory abnormalities**	**Management**
Acute Symptomatic Hepatitis (NNRTI class, particularly NVP, more rarely EFV; NRTIs or PI class)		
• Jaundice • Liver enlargement • Gastrointestinal symptoms • Fatigue, anorexia • May have hypersensitivity component (rash, fever, systemic symptoms); usually occurs within 6-8 weeks • May have accompanying lactic acidosis (see below) if secondary to NRTI drug	• Elevated transaminases • Elevated bilirubin	• Discontinue all ARV until symptoms resolve • If possible, monitor transaminases, bilirubin • If receiving nevirapine, it should NOT be re-administered to the patient in future Once symptoms resolve, either • Restart ART with change to alternative ARV (if on NVP regimen, this is required); *or* • Restart current ART regimen with close observation; if symptoms recur, substitute an alternative ARV
Acute Pancreatitis (NRTI class, particularly d4T, ddI; more rarely 3TC)		
• Severe nausea and vomiting • Severe abdominal pain • May have accompanying lactic acidosis (see next page)	• Elevated pancreatic amylase • Elevated lipase	• Discontinue all ARVs until symptoms resolve • If possible, monitor serum pancreatic amylase, lipase • Once symptoms resolve, restart ART with substitution of an alternative NRTI, preferably one without pancreatic toxicity

Table 9-3 Management of specific adverse events related to specific ARV drugs		
Clinical manifestations associated with the toxicity	**Laboratory abnormalities**	**Management**
Hypersensitivity Reaction (ABC or NVP)		
• Abacavir: Combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC, including fever, fatigue, myalgia, nausea, vomiting, diarrhoea, abdominal pain, pharyngitis, cough, dyspnoea; rash (usually mild) may or may not occur; progressive worsening of symptoms soon after receives ABC dose, usually occurs within 6-8 weeks • Nevirapine: Systemic symptoms of fever, myalgia, arthralgia, hepatitis, with or without rash	• Elevated transaminases • Elevated eosinophil count	• Immediately discontinue all ARVs until symptoms resolve • NVP or ABC should NOT be re-administered to patient in future • Once symptoms resolve, restart ART with substitution of an alternative ARV for ABC or NVP
Lactic Acidosis (NRTI class, particularly d4T)		
• Generalized fatigue and weakness • Gastrointestinal features (nausea, vomiting, diarrhoea, abdominal pain, hepatomegaly, anorexia, poor weight gain and/or sudden unexplained weight loss) • May have hepatitis or pancreatitis (see above) • Respiratory features (tachypnea and dyspnoea) • Neurological symptoms (including motor weakness).	• Increased anion gap • Lactic acidosis • Elevated aminotransferase • Elevated CPK • Elevated LDH	• Discontinue all ARVs until symptoms resolve • Symptoms associated with lactic acidosis may continue or worsen despite discontinuation of ART • Once symptoms resolve, restart ART with substitution of an alternative NRTI with lower mitochondrial toxicity risk (e.g. ABC or AZT)

Table 9-3 Management of specific adverse events related to specific ARV drugs		
Clinical manifestations associated with the toxicity	**Laboratory abnormalities**	**Management**
Severe Rash/Stevens Johnson Syndrome (NNRTI class, particularly NVP, less common EFV)		
• Rash usually occurs during first 6-8 weeks of treatment • Mild to moderate rash: erythematous, maculopapular, confluent, most often on body and arms, with no systemic symptoms • Severe rash: extensive rash with moist desquamation, angio oedema, or serum sickness-like reaction; or a rash with constitutional findings such as fever, oral lesions, blistering, facial oedema, conjunctivitis • Life-threatening Stevens Johnson Syndrome or toxic epidermal necrolysis	• Elevated amino-transferase	• If mild or moderate rash, can continue ART without interruption but with close observation • For severe or life-threatening rash, discontinue all ARVs until symptoms resolve • NVP should NOT be re-administered to patient in the future • Once symptoms resolve, restart ART with substitution of an alternative ARV for NVP (note: most experts would not change to another NNRTI drug if patient had severe or life-threatening Stevens Johnson Syndrome with NVP)
Severe, Life-threatening Anaemia (AZT)		
• Severe pallor, tachycardia • Significant fatigue • Congestive heart failure	• Low haemoglobin	• If refractory to symptomatic treatment (e.g., transfusion), discontinue AZT only and substitute an alternative NRTI
Severe Neutropenia (AZT)		
• Sepsis/infection	• Low neutrophil count	• If refractory to symptomatic treatment (e.g., transfusion), discontinue AZT only and substitute an alternative NRTI

Table 9-3 Management of specific adverse events related to specific ARV drugs		
Clinical manifestations associated with the toxicity	**Laboratory abnormalities**	**Management**
Lipodystrophy/Metabolic Syndrome (d4T; PIs)		
• Fat loss and/or fat accumulation in distregions of the body: • Increased fat around the abdomen, buffalo hump, breast hypertrophy • Fat loss from limbs, buttocks, and face occurs to a variable extent • Insulin resistance, including diabetes mellitus • Potential risk for later coronary artery disease	• Hypertriglyceridemia • Hypercholesterolemia • Low HDL levels • Hyperglycaemia	• Substitution of ABC or AZT for d4T may prevent progression of lipoatrophy • Substitution of an NNRTI for a PI may decrease serum lipid abnormalities
Severe Peripheral Neuropathy (d4T, ddI; more rarely 3TC)		
• Pain, tingling, numbness of hands or feet, refusal to walk • Distal sensory loss • Mild muscle weakness and areflexia can occur	• None	• Stop suspect NRTI only and substitute a different NRTI unassociated with neurotoxicity • Symptoms may take several weeks to resolve
Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006		

Table 9-4 Single drug substitution for toxicity in children		
First-line ARV drug	**Most frequent significant toxicity for the ARV drug***	**Suggested first-line ARV drug substitution**
ABC	Hypersensitivity reaction	AZT
AZT	Severe anaemia or neutropenia	d4T or ABC
	Lactic acidosis	ABC
	Severe gastrointestinal intolerance	d4T or ABC
d4T	Lactic acidosis	ABC
	Peripheral neuoropathy	AZT or ABC
	Pancreatitis	
	Lipoatrophy/metabolic syndrome reaction	
EFV	Persistent and severe central nervous system toxicity	NVP
	Potential teratogenicity	
NVP	Acute symptomatic hepatitis	EFV
	Hypersensitivity reaction	Triple NRTI (disadvantage, may be less potent) PI (disadvantage, premature start of second-line ARV drug)
	Severe or life threatening rash (Stevens-Johnson Syndrome)	

*Definitions for toxicities can be found in Tables 9.1 and 9.2

Source: Antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

Table 9-5 ARV drug combinations to avoid in children	
D4T + AZT	both drugs work through common metabolic pathways
D4T + ddI	both drugs have overlapping toxicities
TDF + ddI	both drugs work through common metabolic pathways
FTC + 3TC	both drugs select for the K65R mutation

10. HIV-Associated TB in Children

Tuberculosis is the most common respiratory opportunistic infection in HIV-infected children in resource-limited settings. When faced with a child with HIV-associated TB disease the priority is to treat TB, and restore immune function by providing ART whilst minimizing toxicity from medications. All children with HIV-associated TB disease should be on prophylactic cotrimoxazole therapy. There are two main scenarios to consider:

- Children presenting with TB disease prior to initiating ART
- Children presenting with TB disease while on ART

10.1 Children Presenting With TB Disease Prior to Initiating ART

Management depends on the clinical stage, degree of immunodeficiency, risk of IRS, and child's tolerance of TB regimen. Table 10.1 details ART regimens for ART naïve children. Management is outlined below.

WHO clinical stage 3

- Mild or no immunodeficiency- initiation of ART may be delayed until after completion of TB therapy; closely monitor response to TB therapy and re-assess for ART after TB therapy; if no improvement, consider starting ART after completion of the intensive phase, which is normally eight weeks
- Advanced or severe immunodeficiency- initiate ART soon after TB treatment (between 2-8 weeks following start of TB treatment)

WHO clinical stage 4

- Regardless of immune category- start ART as soon as possible, preferably two weeks after initiation of TB treatment

Table 10-1 Antiretroviral regimen for ART naive children with HIV-associated TB

	Children <3 years	Children >3 years
Preferred	d4T or AZT + 3TC + ritonavir OR Kaletra	d4T or AZT + 3TC + EFV
Alternative	AZT + 3TC + ABC *or* d4T +3TC +ABC	AZT + 3TC + ABC *or* d4T +3TC +ABC

10.2 Children Presenting With TB Infection While on ART

Management depends on the reason for developing TB, in addition to clinical stage, degree of immunodeficiency, risk of IRS and child's tolerance of TB and antiretroviral regimens.

10.2.1 Children on First-Line Regimen Diagnosed with TB

Continue ART but assess need for change in ART regimen depending on response to TB therapy (Table10.2).

Table 10-2 Treatment options for children on first-line regimen diagnosed with TB

Reason for Developing TB	Management
TB due to primary infection (consider at any time during ART, depending on exposure to TB).	Continue ART: • If on two NRTI + EFV continue • If on two NRTI + NVP and <3 years switch NVP to double dose kaletra or ritonavir. If >3 years switch to EFV
TB as part of immune reconstitution syndrome (consider in first three months of ART).	
TB as a sign of treatment failure of first-line regimen (consider after at least 24 weeks of ART).	• Consider consultation with experts for construction of second-line regimen

Source: Modified from antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

10.2.2 Children on second-line regimen diagnosed with TB

Assess the need for changing or stopping ART regimen; response to TB therapy should be used to evaluate this. Consultation with a specialist is recommended before construction of a salvage regimen (Table10.3)

Table 10-3 Treatment options for children on second-line regimen diagnosed with TB	
Reason for Developing TB	**Management**
TB due to primary infection (consider at any time during ART, depending on exposure to TB)	• If on Kaletra use double dose of Kaletra or consider adding RTV to achieve full therapeutic RTV dose (increase RTV until same dose as LPV in mg) • Consider consultation with experts for construction of salvage regimens
TB as a sign of treatment failure of second-line regimen	• Consider stopping ART until completion of TB therapy • Consider consultation with experts for construction of salvage regimen
Source: Modified from antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006	

11. Nutrition in HIV

Nutrition is an important part of care for both HIV-exposed and infected children. Growth problems in HIV-infected children (growth failure and severe malnutrition not responsive to standard nutrition rehabilitation) may point to disease progression and the need for ART initiation, or treatment failure in a child on ART. In HIV-exposed infants, growth failure may indicate development of HIV infection.

Effect of HIV on nutritional status

- HIV infection leads to malnutrition early in life
- In HIV-infected children experiencing weight loss, energy/caloric requirements are increased by 50-100%
- HIV-infected children are likely to have poor oral intake and malabsorption secondary to HIV and/or opportunistic infections

Effect of nutritional status on HIV

- Decrease in CD4 cells, suppression of delayed hypersensitivity and abnormal B-cell response. This leads to reduced body defence and rapid disease progression
- Wasting has been associated with reduced length of survival
- Micronutrient deficiencies lead to increased oxidative stress and further damage to the immune system, viral replication and decrease in CD4

11.1 Goals of Nutritional Assessment

- To decrease transmission of HIV via breastfeeding
- To decrease morbidity and mortality from diarrhoea and other childhood illnesses, opportunistic infections, and HIV disease
- To ensure satisfactory growth and development

11.1.1 Assessment of Growth and Nutritional Status

In view of the close interrelation between HIV infection, nutritional status and growth, nutritional assessment and support should be an integral part of the care of HIV-infected children. Growth monitoring at a minimum should involve measurement of weight, length/height and head circumference and should be done at every visit. The pattern of growth plotted on a standard chart over a period of time is more useful than a single measurement.

- **Weight** – weigh infant or child on every visit and plot on growth charts to see the trend of growth. Use WHO growth chart for children <5 years and CDC growth chart for children ≥5 years
- **Length/Height –** measure recumbent length for infants under two years and standing height for children >2 years. Height should be measured monthly until six months of age then quarterly. Plot on WHO growth chart. Use CDC growth chart for children >5 years
- **Head circumference** – measure head circumference (at widest dimension) for infants monthly until six months of age then quarterly till three years old. Plot on CDC /WHO growth chart

11.2 Growth Failure

This may be an indication of:

- HIV infection in an HIV-exposed infant (development of failure to thrive in a HIV-exposed infant after exclusion of other causes)
- Disease progression and need for ART in an HIV-infected child (child who was clinical stage 2, develops stage 3 signs of severe malnutrition; low weight for age up to two standard deviations, not explained by inadequate nutrition or other infections and not adequately responding to standard management)
- Treatment failure in a child on ART (lack of or decline in growth rate in children who show an initial response to treatment; moderate or severe unexplained malnutrition not adequately responding to standard therapy despite adequate nutritional response)

Children who have growth failure should be referred for nutritional rehabilitation. Establishing linkages to non-governmental and faith-based organisations which provide nutritional support is important.

Clinical indicators of growth failure:

- Weight for age <5% (CDC chart)or <3% (WHO chart)
- Crossing two major percentiles
- Weight for height <5%

If there is evidence of growth failure, evaluate:

- Nutrient intake
- Ongoing losses
- Physical examine for thrush, oral ulcers, skin changes, oedema, GI bleeding and signs of a systemic infection
- Refer infant for nutritional rehabilitation

11.3 Infant Feeding and Maternal HIV Infection

Breastfeeding has unsurpassed advantages over any other infant feeding. In resource-limited countries breastfeeding is a key component of child survival interventions. Infant mortality is higher in settings where infants are not breastfed or breastfed for short periods.[14] Breastfeeding accounts for 30-40% of perinatal transmission in populations where it is practiced up to two years of age. However, replacement feeding, if not instituted properly, is associated with increased risk of morbidity and mortality at a young age in low resource settings.[15] Based on new data, WHO has revised their infant feeding recommendations for HIV-infected mothers to emphasize the benefits of exclusive breastfeeding (EBF) in HIV-exposed and infected infants.[16] Exclusive breastfeeding during the first six months of life is associated with decreased HIV transmission and improved child survival. Because of high infant mortality rates in Ethiopia, EBF for as long as possible, until at least six months, is recommended as the only feasible and safest option for HIV-infected mothers. At six months complementary foods should be introduced to sustain normal growth. Most Ethiopian children will continue to benefit from breastfeeding until 12-18 months of age. Healthcare workers should be trained to provide infant feeding counselling to all mothers in general and to HIV-infected mothers in particular, to support them to breastfeed exclusively. Universal access to antenatal pMTCT services and prioritizing ART for eligible pregnant and lactating women is an important part of decreasing perinatal transmission of HIV.

The primary goals of infant feeding counselling and support are:

- To improve child survival by actively supporting exclusive breastfeeding for the first six months of life
- To decrease HIV transmission via breastfeeding by treating pregnant and lactating HIV-infected women with low CD4 and advanced disease

Factors that increase risk of HIV transmission during breastfeeding:

- Maternal
  - o Advanced HIV/AIDS (low CD4 count and high viral load)
  - o Contracting new HIV infection while breastfeeding
  - o Poor maternal nutritional status (low BMI and anaemia)
  - o Breast problems (cracked nipples, mastitis and breast abscess)
- Infant
  - o Prolonged duration of breastfeeding
  - o Mixed feeding
  - o Lesions in mouth, intestine
  - o Prematurity

[14] WHO Collaborative Study Team on the role of breastfeeding in prevention of infant mortality. Effect of breastfeeding on infant mortality due to infectious diseases in less developed countries; a pooled analysis. *Lancet* 2000;355:451-455.

[15] Thior I, Lockman S, Smeaton LM, et al. Breastfeeding plus infant zidovudine prophylaxis for 6 months vs formula feeding plus zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana. A Randomized Trial: The MASHI Study. *JAMA* 2006; 296:794-805.

[16] Consensus Statement. WHO HIV and Infant Feeding Technical Consultation Report Geneva, October 25-27, 2006.

11.3.1 Infant Feeding During the First Six Months of Life

The most effective way to support exclusive breastfeeding is to provide quality counselling and support to the mother at each health encounter. This should take place at EVERY visit (antenatal, immediate post-partum, within the first week after delivery, during routine postnatal care, and at every follow-up visit). Pregnant HIV-infected women should be counselled on advantages and disadvantages of breastfeeding and supported to breastfeed exclusively for the first six months. Data from South Africa and Zambia suggests that early weaning is associated with increased infant morbidity and mortality and should not be encouraged.[17,18] Lactating mothers should be assessed for ART eligibility and put on treatment if appropriate. They should be provided with nutritional support for themselves.

Preferred Infant Feeding Options in Ethiopia:

The preferred method for infant feeding in HIV-infected women is **exclusive breastfeeding for the first six months of life.** Early cessation of breastfeeding should be avoided since it is associated with increased risk of death from diarrheal illnesses, malnutrition and pneumonia.

- Exclusive breastfeeding for the first six months (breast milk only and medication, *not even water*, should be given)
- Counselling and support on "safer breastfeeding practices" to avoid breast problems associated with increased risk of virus transmission (mastitis, cracked nipples etc.)
- Avoidance of mixed feeding during the first six months since this is associated with increased risk of HIV transmission
- Avoidance of early cessation of breastfeeding since this compromises survival in both HIV-infected and uninfected infants
- Advise about risks of relactation [restarting breastfeeding after weaning] which is associated with increased breast milk viral load
- Prompt treatment of breast problems (cracked nipples, mastitis, breast abscess), and lesions in the infant's mouth
- Check mothers' CD4 status during lactation and start eligible women on HAART

[17] Coovadia HM, Rollins NC, Bland RM, Little K, Coutsoudis A, Bennish ML, Newell ML. Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. *Lancet* 2007; 369: 1107–16.

[18] Sinkala M, Kuhn L, Kankasa C, et al., and Zambia Exclusive Breastfeeding Study Group (ZEBS). No Benefit of Early Cessation of Breastfeeding at 4 Months on HIV-free Survival of Infants Born to HIV-infected Mothers in Zambia: The Zambia Exclusive Breastfeeding Study. CROI 2007 Abstract 74

Alternative Infant Feeding Option:

In the minority of women who choose to use replacement feeding, every effort should be made to ensure that it is done SAFELY.

- Ensure mother can safely provide formula (Table 11.1)
- No breastfeeding should be practiced with replacement feeding [mixed feeding]
- Provide clear information about risks of formula and that this is not the option currently recommended
- Mothers should use commercial infant formula. Home-modified animal milk should only be used as a temporary measure since it does not provide all the micronutrient needs of infants <6 months of age
- Ensure mother has an uninterrupted supply of formula for at least twelve months
- Teach mother how to prepare the replacement feeding and provide intensive counselling on hygienic preparation of formula at each visit
- Avoid bottle feeding, in order to avoid risk of diarrhoea and malnutrition
- Ensure close follow-up to monitor growth and nutritional status monthly to prevent malnutrition and gastroenteritis during the first two years of life.

11.3.2 Feeding of Infants and Children 6-24 Months of Age

At six months of age all infants need complementary food in order to sustain normal growth, and this should be introduced at this time with continued breastfeeding. Breastfeeding should stop only when a nutritionally adequate diet without breast milk can be provided, usually around 12-18 months of age. Infants diagnosed HIV-positive should continue to breastfeed according to recommendations for the general population.

Feeding from 6 to 24 Months

- Ensure appropriate complementary feeding is initiated at six months for all infants whether exclusively breastfed or on exclusive replacement feeding
- Encourage continuation of breastfeeding
- Promote good hygiene, proper food safety and handling
- Continue infant growth monitoring and nutritional advice to mother
- Teach mother to provide suitable complementary foods made from nutrient rich foods, emphasizing use of local energy-dense foods and increased use of fruits and vegetables
- Infants should be weaned only when an adequate diet without breast milk can be provided. This is usually around 12-18 months.

Table 11-1 Questions to ask when mother is using replacement feeding

1. Where do you get your drinking water from?
2. What kind of latrine/toilet do you have?
3. How much money can you afford for formula each month?
4. What will you do if you run out of formula?
5. Do you have money for transportation to buy formula when you run out?
6. Do you have a refrigerator with reliable power?
7. Can you prepare each feed with boiled water and clean utensils?
8. How will you arrange night feeds?
9. Does your family know you are HIV-positive?
10. Is your family supportive of formula feeding and willing to help?
11. How will you cope with the pressure to breastfeed from family, friends and others?
12. Do you have access to a clinic where you can take your infant if s/he develops diarrhoea or falls sick?
13. Do you have money for transportation to bring your child to the clinic for monthly check ups?

Source: Modified from antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

12. Disclosure

Paediatric disclosure is an ongoing process and in the best of circumstances may be difficult. Adults struggle with the question of whether, when or how to tell children that they have HIV, often agonizing over how to find the right words. All families are unique and there are no set rules regarding when and how to disclose to children.

Children react to HIV disclosure in different ways and it is not uncommon for relatives to disagree about disclosing HIV-related information to children. Even amongst the HIV/care team there may be disagreement on the best approach. Disclosure has to be individualized taking into consideration the particular child, parent/s, family, household and community.

12.1 Ways to Begin the Process

HIV disclosure is not a topic that comes naturally for family discussion, especially when children are involved. The best way for a child to learn about his/her HIV status is through age-appropriate information shared by a loving and trusted caretaker. Disclosure to children should never happen casually, inadvertently or in the heat of anger or conflict. A child's maturity and cognitive capacity varies and is not only dependent on age. It is important to tailor the discussion to the child's cognitive level and to the child's personal and individual situation. It is important to assess readiness of the entire family for disclosure and address potential barriers to disclosure (Table 12-1). It is also important to discuss benefits of disclosure which have both short and long term impact on the family.

Disclosure can:

- Help create a sense of closeness in the family
- Help reduce feelings of anxiety and isolation on the part of the parents/ caregiver
- Relieve the burden of living with the secret of being HIV-positive
- Help build social support networks
- Reduce the anxiety children experience when they suspect something is wrong; they will now have information to make better sense of the situation
- May improve adherence in a non-adherent child

Table 12-1 Assessing readiness for disclosure

The child

- Is the child symptomatic? taking medications?
- How old is the child?
- Is the child living with a sick parent or family member?
- 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 or caregiver

- Has the parent or caregiver been tested for HIV?
- Is the parent or caregiver infected? Symptomatic? Taking medication?
- Is the adult 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 or household

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

The community

- Are 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 (isolation, discrimination) if inadvertent disclosure occurs?
- Are there resources within the community for children – a youth group and/or trusted adults they can talk to?

Source: *Columbia Paediatric Clinical Manual* 2005

12.2 Planning for Disclosure

Disclosure is not an event or a one-off conversation. It is a process that takes time and constant communication in an age-appropriate manner. It is important to prepare adequately for disclosure. This involves preparation, education, planning and follow-up (Table 12-2). Once the decision has been to disclose to the child it is important to understand that the topic will have to be visited over and over again. It is important to give a clear message and listen actively; take cues from the child and avoid lecturing; the emphasis should be on asking directly and indirectly and listening. The following examples can serve as a guide:

Pre-schooler 4-6 years old: Younger children if symptomatic generally want to know what will happen to them. They do not need to know their diagnosis but the illness must be discussed with them. Young children may feel responsible for the parent's illness or just pretend nothing is happening. It is important to give reassurance and take cues from younger children.

School aged children 7-13 years: Some may have difficulty coping with disclosure information leading to changes in behaviour (acting out in school, i.e. fights, low grades, truancy, anger, crying fits, or no expression of emotion). Others may have concerns that other children in the school or community will make fun of them. Encourage them to ask questions; do not be disappointed if they do not react in the manner you expected.

Adolescents 14 years and older: Adolescents should know of their HIV status. They must be fully informed in order to appreciate consequences for many aspects of their health, including sexual behaviour and treatment decisions. Be supportive and non judgemental. This is addressed in the adult care and treatment guidelines.

Table 12-2 Getting ready for disclosure

Preparation

- Why disclose now?
- What do you want to communicate to your child?
- What will be the most difficult questions for you to answer when your child knows his/her HIV status?
- How will this information affect the relationship between you?
- Acknowledge difficulty of disclosure and affirm motivation to begin process

Education

- How to explain HIV transmission to a child
- Anticipate questions and responses from child
- Post disclosure expectations

Planning

- When and where?
- Who will be there?
- What will you say?
- Plans after disclosure

Follow-up

- School and family functioning
- Monitor medical treatment adherence
- Disclosure to peers and others
- Support group counselling
- Continue to reinforce the positives

Source: *Columbia Paediatric Clinical Manual* 2005

13. Palliative Care

Children who are terminally ill should be provided with supportive care to:

- Provide emotional support to the dying child and grieving family
- Keep the patient as comfortable as possible and maintain a good quality of life

It is important to

- Relieve stress and pain in the child
- Treat easily manageable conditions
- Limit hospitalizations and reduce length of stay

13.1 Home Care

Palliative care for dying children should be at home if possible. The local primary healthcare service must assist in providing care. It is important to reassure the parents/caregivers, that the child has not been abandoned by the health service. Pain control is an important aspect of palliative care often overlooked in children. Initially it is advisable to use non-opioids such as paracetamol or non-steroidal anti-inflammatory agents. However, if pain control cannot be achieved with these, it is essential children be helped to be pain free, and opioids should be used if unavoidable. Management of the underlying condition is an important part of pain control. Collaboration with NGOs and community groups which provide palliative care services will improve service utilization. Refer to the IMAI Palliative Care Guidelines for first level facility health workers for further details.

13.2 Inpatient Management

Patients should be managed in hospital if they have respiratory distress, need IV/NG fluids or if caregivers are unable to cope at home. Laboratory tests should be kept to a minimum and pain should be controlled. Pain medications should be provided on a regular, not as-needed basis. Assess pain frequently, anticipating complications of analgesic medications (e.g. constipation) and manage accordingly.

14. Annexes

ANNEX A. How to collect, store and transport DBS

How to collect DBS

1. Correctly complete all information requested on the laboratory requisition form.

2. Wash hands and wear powder-free gloves.

3. Confirm identity of infant; write the following information on the DBS filter paper supplied by the Central Laboratory:

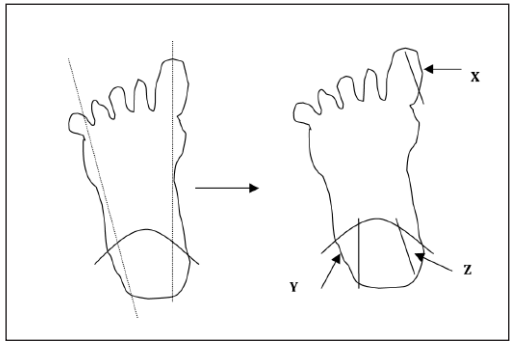
- Infant's name
- Unique identifier
- Date of test
- Hospital name

4. Do not allow water, formulae, powder from gloves, antiseptic solutions to come into contact with filter paper before or after collection of sample since this will affect the result.

5. Draw an imaginary line from midpoint of the big toe to the heel, and one from between the 4th and 5th toe to the heel. **The arrows** indicate safe areas for puncture site namely **X, Y and Z.** Do not puncture the back of the heel, Achilles tendon, or lateral aspect of the big toe.

6. With small infants (<9kg), puncture the heel. Do not puncture the fingers; there is risk of hitting the bone.

7. Larger infants (>9kg), puncture the heel, if callous is visible; you may use the medial aspect of the big toe. Do not stick the fingers or small toes; there is risk of hitting the bone. (*This is also true when doing an HIV rapid test. Do not stick fingers or small toes of small children. Fingers are safe around age two.*)



8. Hold the infant's foot below the level of the heart; this will help blood flow more easily.

9. Warm the area, especially if the infant is cold, with a warm moist cloth for three minutes; this can increase blood flow through the site. The mother can hold baby's foot in her hand, rubbing it gently may help.

10. Clean the area with alcohol, and let it dry for *30 seconds*.

11. Using a lancet or heel incision device puncture the site identified as above. The puncture should be to a depth of less than 2.0mm. *Do not use a needle or scalpel or longer lancet.* The lancets are the correct length to puncture safely without damaging bone.

12. Gently wipe away the first drop of blood with a sterile gauze or clean cotton ball.

13. Allow another large droplet of blood to form at the puncture site.

14. Gently touch the printed side of the filter paper against the large drop and allow it to completely fill the circle on the paper. **The first drop should fill the circle.** Do not press the paper against the heel.

15. Fill in remaining, at least **two or more**, circles in the same manner with successive drops of blood; one circle is not enough to test. If a circle is poorly done, move to the next one. Do not apply blood to both sides of the filter paper. Avoid smearing or touching the spots.

16. If there is not enough blood, you may gently press the area around the puncture site. Do not "milk" the area, or you will get tissue fluid instead of blood, and the lab will not be able to test it.

17. Clean the puncture site and press a cotton swab against it until it stops bleeding. Do not use a bandage.

ANNEX A. How to collect, store and transport DBS

Drying DBS

18. Once the blood spots have been collected, they need to dry.

19. Do not touch or smear the spots.

20. Place the filter paper on a flat surface or a Schleicher and Schuell card board drying rack and allow to AIR DRY overnight (minimum of three hours).

21. Protect them from sunlight, bugs and dust.

22. Do not stack, heat or allow to touch other surfaces during the drying process. INSUFFICIENT DRYING ADVERSELY AFFECTS TEST RESULTS.

NB. Drying is the most important process to assure stability of the HIV viral DNA in the paper. If the DBS is not well dried after staying overnight at room temperature, the silica contained in the desiccant packets packed together with the DBS can remove all the remaining moisture.

Packaging DBS

23. Once DBS are completely dry, stack them between sheets of weighing paper so that DBS cards from different infants are not touching one another.

24. Pack up to 15 DBS cards in a gas-impermeable bag.

25. Add the following items to the bag to preserve the specimens: two desiccant packs per sample (this will remove any residual moisture from cards and humidity indicator card (which will indicate the relative humidity inside the bag).

26. Press as much air out of the bag as possible and seal it shut.

27. The humidity indicator card and the desiccant packs have a colour indicator which changes from blue to pink as humidity increases. All cards and packs should be replaced with fresh material before they change to a pink colour.

NB. Plastic or foil bags used for DBS storage must be gas-impermeable. Bags from grocery stores or other outlets that do not sell scientific supplies are not adequate and should not be used.

ANNEX A. How to collect, store and transport DBS

Storage of DBS

1. For storage before transportation to the laboratory, DBS should be kept in gas impermeable bags with desiccant and humidity indicator cards, and stored at room temperature inside a drawer.

2. Avoid exposing DBS to light. The light and oxygen can react with haemoglobin-producing active oxygen which can damage the viral RNA/DNA material.

Transportation of specimens to the laboratory

3. DBS should be transported to the Central Laboratory on the scheduled day.

4. To prepare DBS for transport, remove bagged samples from the drawer and remove old desiccants. Add fresh desiccants and reseal bag.

5. Use the specimen delivery checklist to verify you have a requisition form for each DBS.

6. Place the bag of DBS, requisition forms, and the specimen delivery checklist into a large cardboard or padded envelope, and seal.

7. Label the envelope with

- Your clinic name
- Infant DBS specimens
- Date you are sending to lab

8. Transport the bag by the fastest means possible to the laboratory. AVOID EXPOSURE TO EXTREMES OF HEAT DURING TRANSPORTATION.

9. If a cooler is available for transport this will protect the samples from short periods of high temperature.

NB. DBS is considered non-infectious and can be sent inside a letter envelope without additional bio safety measures.

Source: Modified from the *ICAP Infant Diagnosis Manual* 2007

ANNEX B: WHO clinical staging for infants and children <15 years of age
Clinical Stage 1/Asymptomatic
• Asymptomatic • PGL
Clinical Stage 2/Mild
• Unexplained persistent hepatosplenomegaly, papular pruritic eruptions • Extensive wart virus infection, Extensive molluscum contagiosum • Recurrent oral ulcerations • Unexplained persistent parotid enlargement • Linear gingival erythema, Herpes Zoster, fungal nail infection • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhea, sinusitis, tonsillitis)
Clinical Stage 3/Advanced
• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhea (14 days or more) • Unexplained persistent fever (above 37.5^0C, intermittent or constant for longer than one month) • Persistent oral candidiasis (outside neonatal period), oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis /periodontitis • Pulmonary or Lymph node TB, Severe recurrent bacterial pneumonia • Unexplained anemia (<8g/dl), neutropenia (<500/mm^3) or chronic thrombocytopenia (<50,000/mm^3) • Chronic HIV-associated lung disease including bronchiectasis • Symptomatic Lymphoid Interstitial Pneumonitis

ANNEX B continued: WHO clinical staging for infants and children <15 years of age
Clinical Stage 4/Severe
• Unexplained severe wasting or severe malnutrition not adequately responding to standard therapy • *Pneumocystis carinii* pneumonia • Recurrent severe bacterial infections (empyema, pyomyositis, bone or joint infection, meningitis but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous > 1 month, visceral of any duration), Kaposi's sarcoma, extrapulmonary TB • Esophageal candidiasis (or candida of the trachea, bronchi or lungs) • CNS toxoplasmosis (outside the neonatal period), HIV encephalopathy • CMV infection (retinitis or CMV infection affecting another organ, with onset at age over 1 month), extrapulmonary cryptococcosis including meningitis • Disseminated endemic mycosis (e.g. extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis), chronic cryptosporidiosis, chronic isosporiasis • Disseminated non-tuberculous mycobacteria infection, • Cerebral or B-cell Lymphoma Progressive multifocal leukoencephalopathy (PML) • HIV-associated cardiomyopathy or HIV- associated nephropathy

ANNEX C: WHO Classification of HIV-Associated Immunodeficiency in Infants and Children				
Classification of HIV-associated Immunodeficiency	**Age–related CD4 values**			
	<11 months (%)	**12-35 months (%)**	**36-59 months (%)**	**≥5 years (cells/mm^3)**
Not significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-30	20-25	15-20	200-349
Severe	<25	<20	<15	<200 or <15%

ANNEX D: Calculating CD4 percentage

Formula

$$CD4\% = \frac{\text{CD4 absolute X 100}}{\text{TLC}}$$

TLC = WBC x % lymphocytes
12 month old female with CD4 absolute of 1000,
WBC of 12,000 and lymphocytes of 55%
TLC= 12,000 X .55= 6 600

$$CD4\% = \frac{1000 \times 100}{6600} = 15\%$$

ANNEX E: Calculating body surface area

Method 1

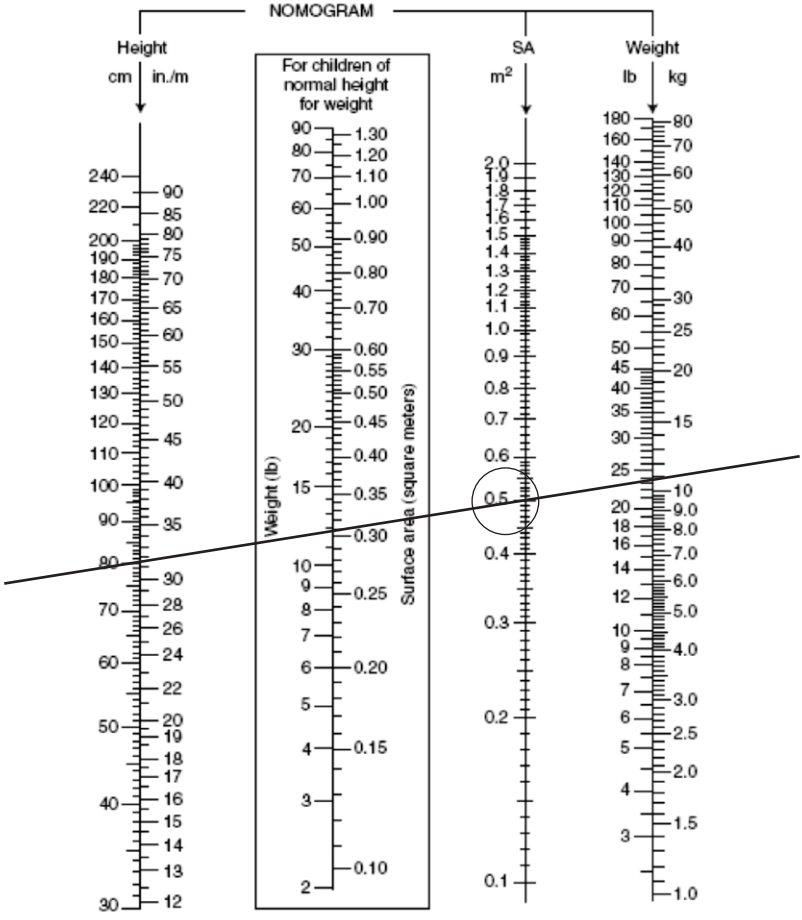
BSA Formula = $\sqrt{\frac{\text{Hgt(cm) x Wgt(kg)}}{3600}}\ m^2$

Example: A 3 year old who weighs 12 kg and is 80 cm tall
Height = 80 cm
Weight = 12 kg
BSA=
80 X 12= 960
960 / 3600 = 0.267
Square root of 0.267 = 0.53m^2

Method 2

The body surface area can be determined using the normogram for infants and children in Annex E-1
Example: A 3 year old who weighs 12 kg and is 80 cm tall
Height = 80 cm
Weight = 12 kg
Draw a straight line from the height in the left column to the weight in the right column. The point at which the line intersects the SA column is the body surface area measured in square meters.
SA= 0.53m^2

ANNEX E-1: Body Surface Area Normogram



Note: Nomogram modified from data of E. Boyd by C.D. West; from Behrman, R.E., Kliegman, R.M., & Jenson, H.B. (eds.). (2000). Nelson textbook of pediatrics (16th ed.). Philadelphia: W.B. Saunders.

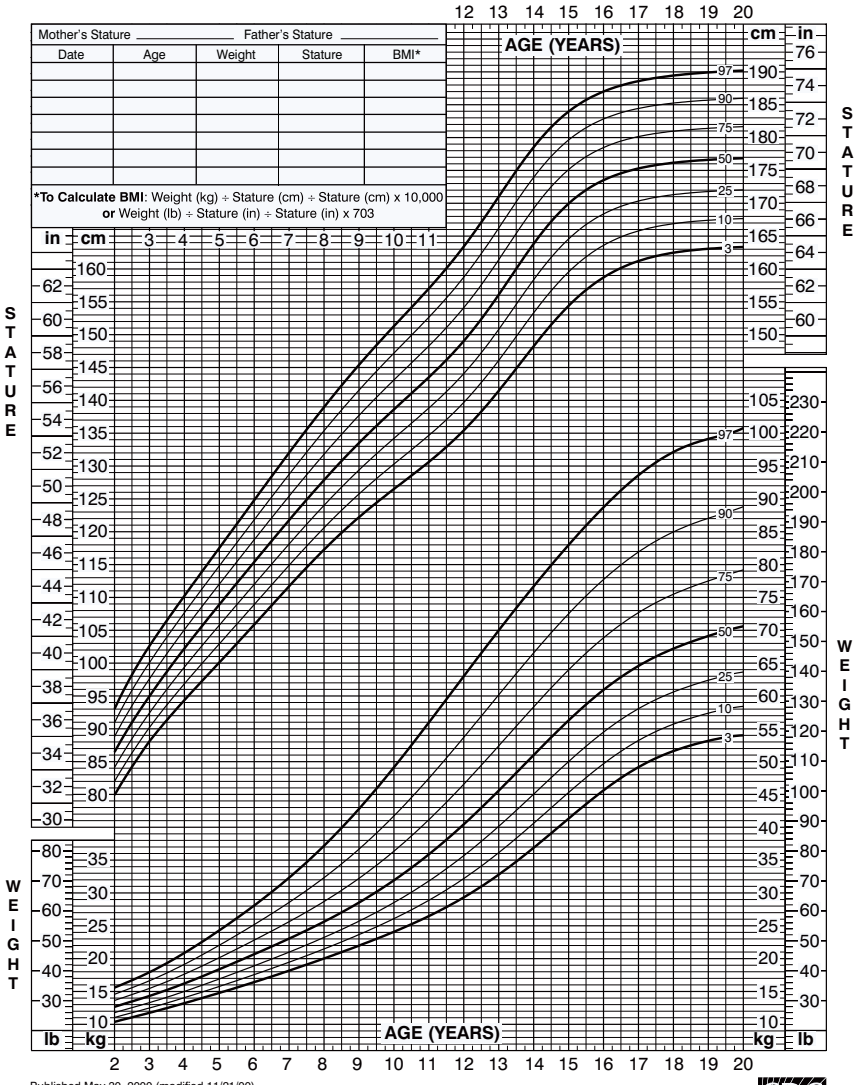
ANNEX F: WHO recommendations for initiating ART in children >12 months according to clinical stage and availability of immunological markers		
Clinical Stage	**Immunologic marker[a]**	**Recommendation**
Stage 4*	**CD4**	**Treat all**
	No CD4	**Treat all**
Stage 3*	**CD4**	**Treat all** CD4 guided in children with TB, LIP, OHL, and thrombocytopenia
	No CD4	**Treat all**
Stage 2	**CD4**	**Treat if CD4 is:**
		< 20% or < 750 cells/mm^3 for child 12-35 months
		< 20% or < 350 cells/mm^3 for child 36-59 months
		< 15% or < 200 cells/mm^3 for child >5 years
	No CD4	**Treat if TLC is:**
		< 3000 cells/mm^3 for child 12-35 months
		< 2500 cells/mm^3 for child 36-59 months
		<2000 cells/mm^3 for child 5-8 years
Stage 1	**CD4**	**Treat if CD4 is:**
		< 20% or < 750 cells/mm^3 for child 12-35 months
		< 20% or < 350 cells/mm^3 for child 36-59 months
		< 15% or < 200 cells/mm^3 for child >5 years
	No CD4	**Do not Treat**

*Stabilize any OI before initiating ART
**Pulmonary TB: Evaluate possibility to defer initiation of ART depending on assessment of clinical status and CD4, and clinical and immunological response to TB therapy (see TB section).

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

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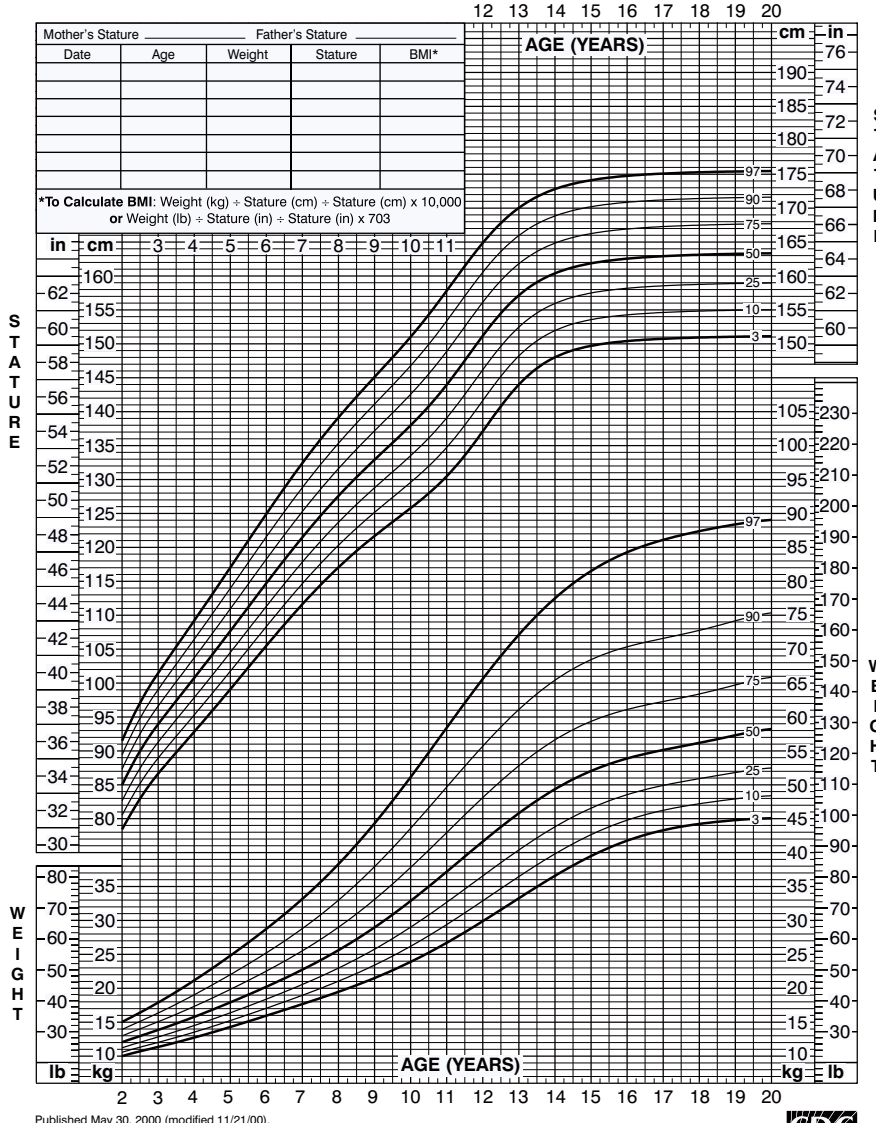
2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



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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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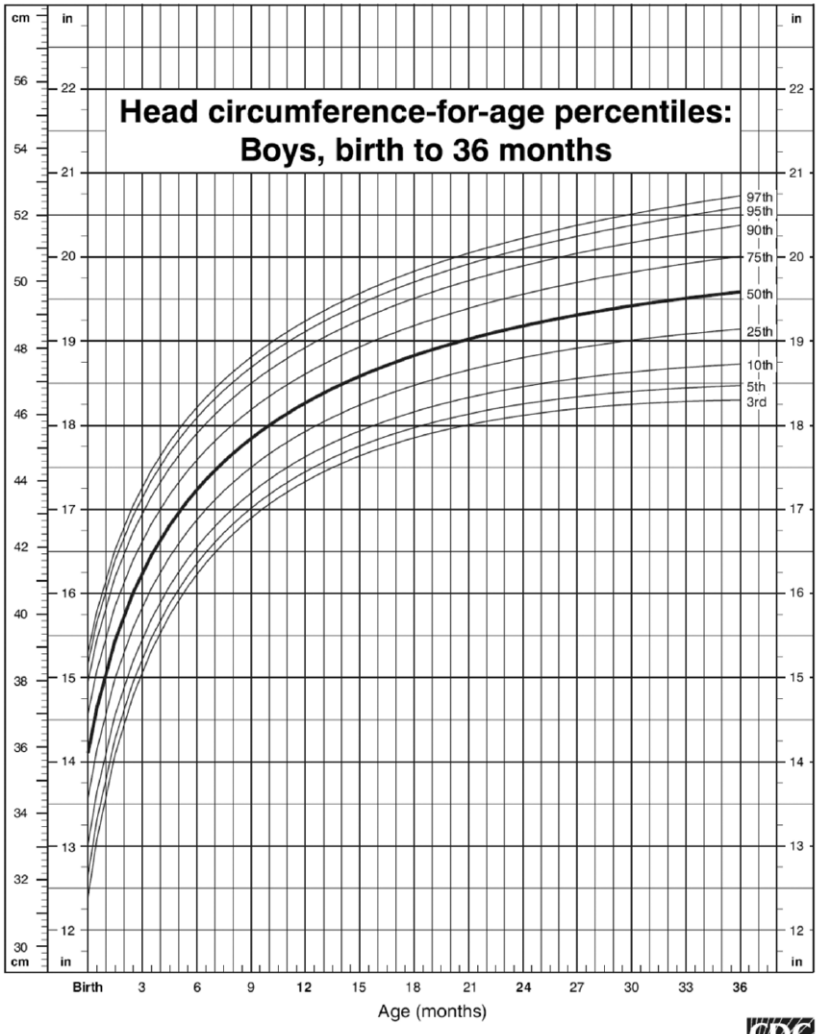
CDC Growth Charts: United States



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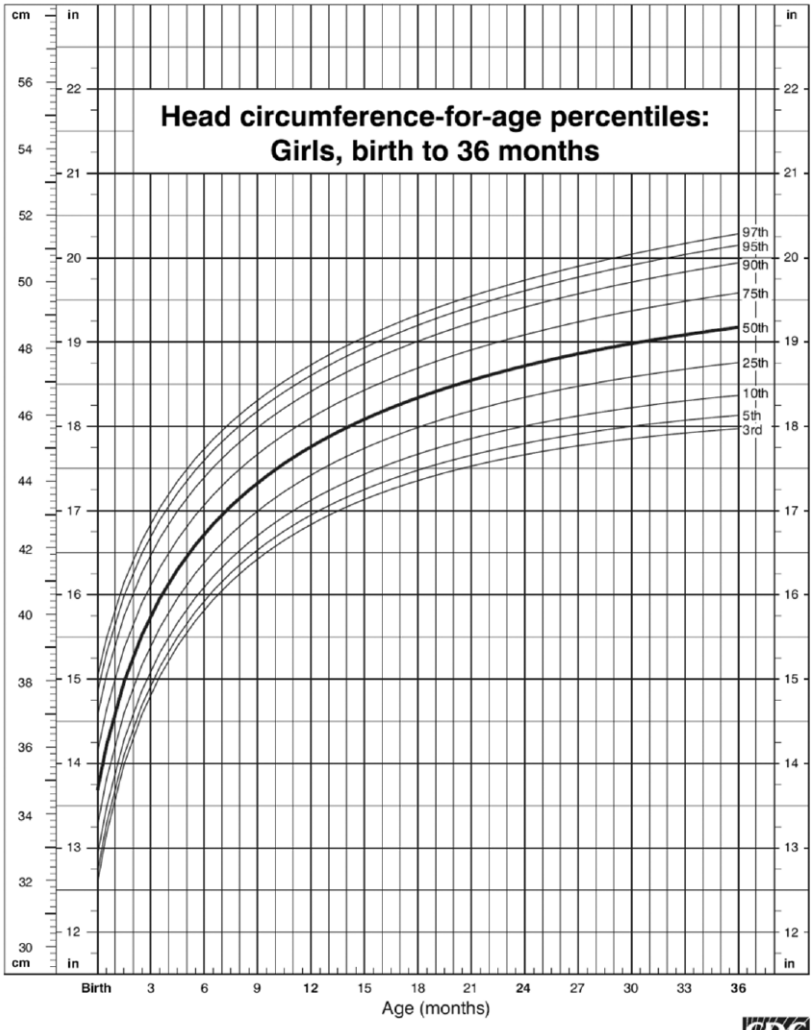
CDC Growth Charts: United States



Published May 30, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

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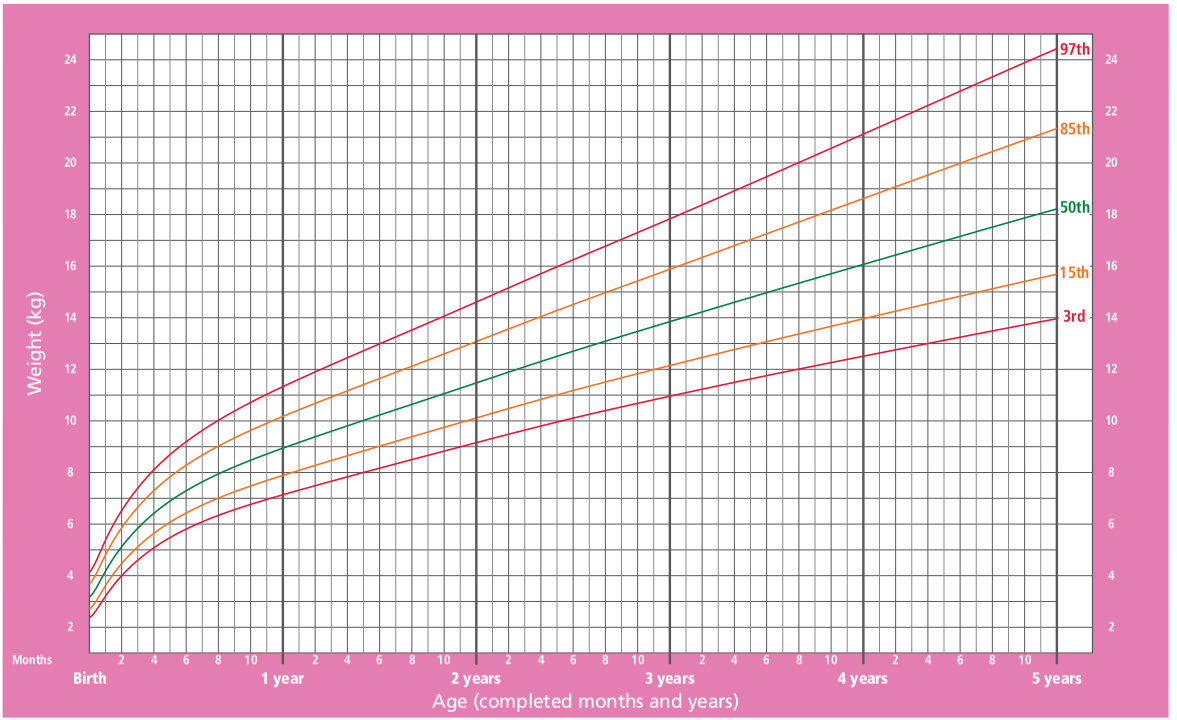
Weight-for-age GIRLS

Birth to 5 years (percentiles)

World Health Organization

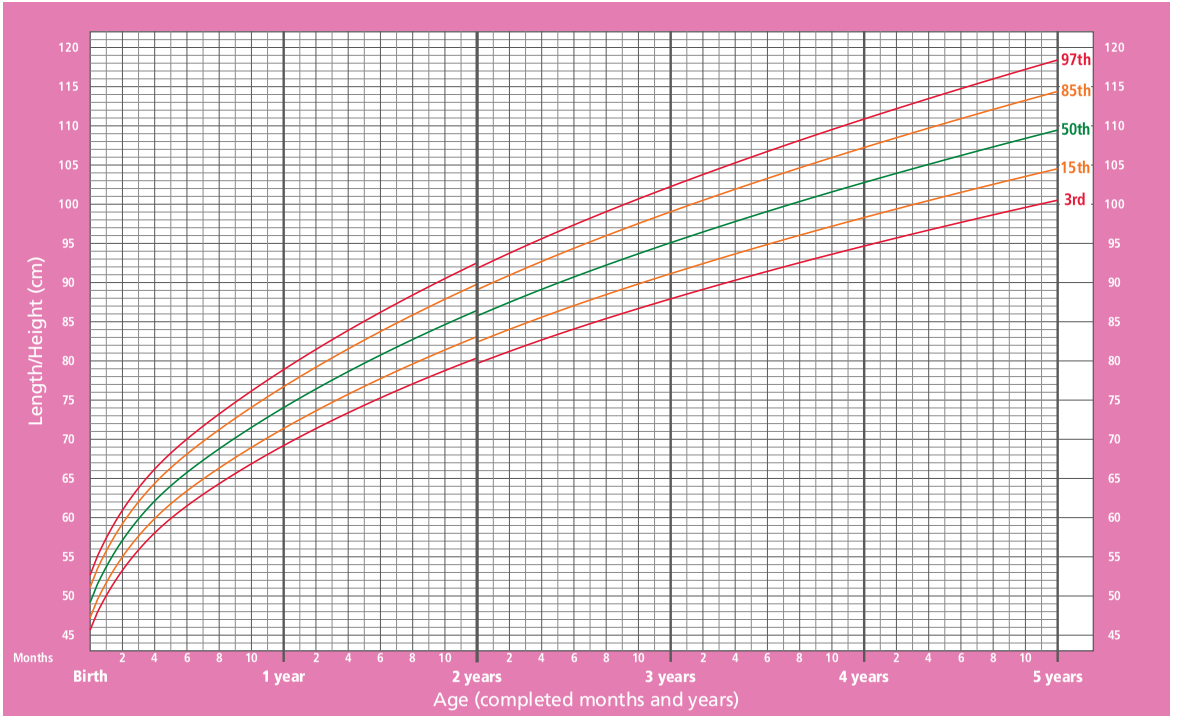


WHO Child Growth Standards

Length/height-for-age GIRLS

Birth to 5 years (percentiles)

World Health Organization

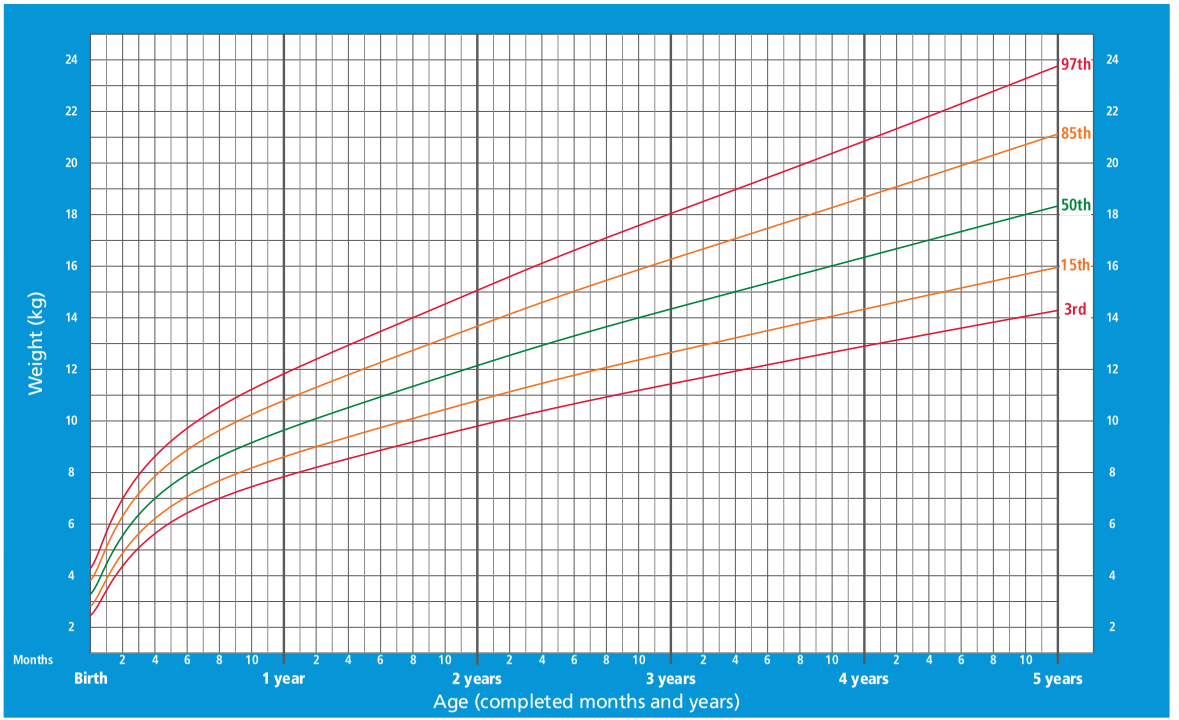


WHO Child Growth Standards

Weight-for-age BOYS

Birth to 5 years (percentiles)

World Health Organization

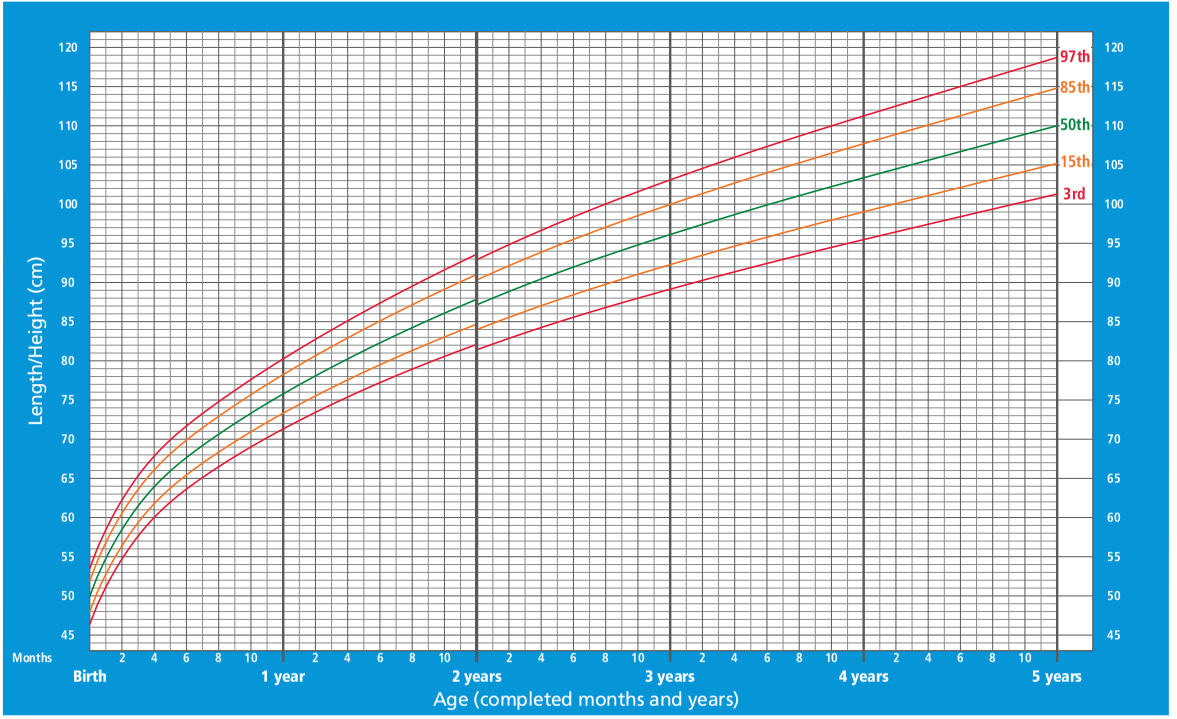


WHO Child Growth Standards

Length/height-for-age BOYS

Birth to 5 years (percentiles)

World Health Organization

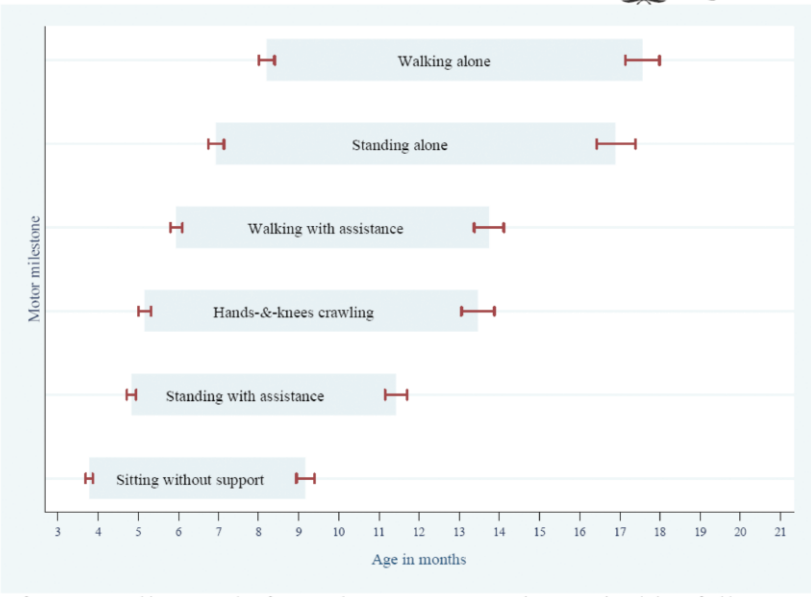


WHO Child Growth Standards

ANNEX H: ICAP Developmental Checklist	
Age	**Milestones**
1 month	Raises head and chest when prone, responds to sound, vocalizes, follows moving object to midline
2 months	Holds head up, lifts chest off table, smiles socially, recognizes primary caregiver, hands together, makes sounds – eh, ugh
3 months	Supports on forearms in prone, holds head up steadily, hands open at rest, recognizes most familiar adults, coos
4 months	Rolls back to front, reaches for objects, laughs, orients to voice, puts objects or toys in mouth
5 months	Rolls over from stomach to back, imitates speech sounds, e.g. makes razzing sounds, reacts differently to strangers
6 months	Sits unsupported, transfers objects from one hand to the other, babbles, reaches for familiar persons
9 months	Pulls to stand, uses finger and thumb to pick up small objects, waves bye-bye, says "mama"
12 months	Walks alone, imitates actions, uses two word together
15 months	Walks backward independently, imitates action, feeds self with spoon
18 months	Runs, kicks a ball, can remove garment of clothing, scribbles, ses 6 words
2 years	Walks up and down stairs, can wash hands, combine words, follows two step command
3 years	Catches a ball and balances on one foot, can put on shirt, speech is understandable
4 years	Can dress alone, draws a person, use complex speech

Windows of achievement for six gross motor milestones

World Health Organization



Reference: WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. Acta Paediatrica Supplement 2006;450:86-95.

ANNEX I: Paediatric ARV drug formulations, side effects and special instructions for Children		
NUCLEOSIDE REVERSE TRANSCRIPTASE		
Drug / Formulation	**Comments**	**Side Effects**
Abacavir (ABC) Oral solution 20mg/ml Tablet: 300mg	Can be given with food. Tablet can be mixed with small amount of water and taken immediately. Instruct patient how to recognize and respond to potentially fatal hypersentivity reaction. Patients should not interrupt therapy without consulting their healthcare provider. DO NOT rechallenge after hypersensitivity reaction.	**Common**: HA, GI upset and rash. **Less common**: lactic acidosis, hepatomegaly with steatosis. **Life-threatening**: potentially fatal hypersensitivity reaction (fatigue, rash, N/V, sore throat, joint and muscle pain, cough, and dyspnea).
Didanosine (ddI) Powder for oral solution: reconstituted 10ml/ml Chewable tablets: 25mg, 50mg, 100mg, 150mg Enteric coated capsules: 200mg, 250mg, 400mg	If tablets are dispersed in water, at least two tablets of appropriate strength should be dissolved to ensure adequate buffer. Keep suspension refrigerated, shake well, stable for 30 days. Enteric formulation may be better tolerated.	**Common:** diarrhoea, abdominal pain, N/V. **Less common:** increased LFTs, lactic acidosis with hepatomegaly and steatosis, peripheral neuropathy, hyperuricemia. **Life threatening:** pancreatitis, which is rare in children.
Lamivudine (3TC) Oral solution 10mg/ml Tablet: 150mg	Can be given with food. Store solution at room temperature and use within one month of opening. Tablet can be mixed with small amount of water and taken immediately. Side effects are rare.	**Common:** HA, nausea, abdominal pain. **Less common:** pancreatitis, neutropenia, increased LFTs.

ANNEX I: Paediatric ARV drug formulations, side effects and special instructions for children		
NUCLEOSIDE REVERSE TRANSCRIPTASE		
Drug / Formulation	**Comments**	**Side Effects**
Stavudine (d4T) Oral solution 1mg/ml Capsules: 15mg 20mg, 30mg, 40mg	Keep liquid refrigerated. Stable for 30 days. Capsules can be opened and mixed with small amount of food or water. **DO NOT USE WITH AZT.**	**Common:** HA and GI intolerance. **Less common:** peripheral neuropathy, lipoatrophy. **Life-threatening:** lactic acidosis with severe hepatomegaly and steatosis.
Zidovudine (AZT or ZDV) Oral solution 10mg/ml Tablet: 300mg Capsule:300mg	Can be given with food. Syrup is light-sensitive, store in a glass jar. Capsule can be opened and contents dispersed or tablet crushed and combined with food or small amount of water. Large volume of syrup not well tolerated in older children. **DO NOT USE WITH d4T**.	**Common:** HA and GI intolerance. **Less common:** peripheral neuropathy, lipoatrophy. **Life-threatening:** lactic acidosis with severe hepatomegaly and steatosis.

ANNEX I: Paediatric ARV drug formulations, side effects and special instructions for children		
NUCLEOSIDE REVERSE TRANSCRIPTASE		
Drug / Formulation	**Comments**	**Side Effects**
Efavirenz (EFV) Syrup: 30mg/ml Capsule:50mg, 100mg, 200mg	Only for children ≥3 yrs. Syrup requires higher dose than capsules. Can be given with food (but avoid high fat foods). Capsule can be opened and added to food: to avoid peppery taste mix with sweet food or jam Best given at night time to avoid CNS effects.	**Common:** skin rash, somnolence, insomnia, abnormal dreams, confusion, hallucinations. **Less common:** increased LFTs.
Nevirapine (NVP) Oral solution 10mg/ml Tablet: 200mg	Store at room temperature. Can be given with food. Tablets can be divided and combined with small amount of water or food and immediately administered. Patients should be warned of rash. Do not escalate dose if rash occurs. For SJS and TEN discontinue drug and do not rechallenge. Multiple drug interactions.	**Common**: skin rash, HA, nausea, diarrhoea. **Less common:** increased LFTs. **Life-threatening:** Steven Johnsons syndrome, TEN, fatal hepatitis.

ANNEX I: Paediatric ARV drug formulations, side effects and special instructions for children		
PROTEASE INHIBITORS		
Drug / Formulation	**Comments**	**Side Effects**
Lopinavir /ritonavir (LPV/r) Oral solution 80mg/ml LPV plus 20mg/ml r capsules:133.3mg LPV plus 33.3mg r Tablet: 200 mg LPV plus 50 mg r	Preferable to store capsules and liquid in a refrigerator. Can be stored at room temp 250C for two months Should be taken with food. Capsules should not be opened or crushed, swallow whole. Liquid has low volume but bitter taste. Tablets require no cold chain; can be used in children on full adult dose.	**Common**: diarrhoea, HA, nausea, vomiting, increase in blood lipids **Less common:** pancreatitis, diabetes, hyperglycaemia, hepatic toxicity, fat redistribution.
Nelfinavir (NFV) Powder for oral suspension (mix with liquid): 200 mg per level teaspoon (50mg per 1.25 ml scoop) Tablet: 250mg	Take with food. Store at room temperature. Crushed tablet preferred even for infants. Drug interactions less than with RTV/PI	**Common**: diarrhoea, nausea, vomiting, HA **Less common**: asthenia, abdominal pain, rash, lipodystrophy.
Ritonavir (RTV) Suspension: 80mg/ml Capsule: 100mg	Take with food to increase absorption and reduce GI side effects. Oral solution must be refrigerated. Can be kept at room temperature (250C) if used within 30 days. Bitter taste, coat mouth with peanut butter or chocolate milk. If given with ddI there should be 2 hours between taking each drug.	**Common**: N/V, diarrhoea, headache, abdominal pain, anorexia **Less Common**: circumoral paraesthesia, increased LFTs, lipodystrophy, elevated cholesterol and triglycerides, hyperglycaemia.
Saquinavir (SQV) Capsule: 200mg Tablet: 500mg	NOT approved for use in children <25kg. Should be used in combination with RTV or LPV/r. Administer two hours before meal to increase absorption. Sun exposure can cause photosensitive reaction.	**Common**: diarrhoea, abdominal pain, HA, nausea; **Less common**: lipodystrophy, hyperglycaemia.

Source: Modified from antiretroviral therapy of HIV infection in infants and children in resource-limited settings. WHO 2006

ANNEX J. Antiretroviral Dosing Guide for Children (modified from WHO Guidelines 2006) NNRTIs						
	ABACAVIR		LAMIVUDINE		STAVUDINE	
Weight in Kg	8mg/kg/dose TWICE daily		4mg/kg/dose TWICE daily		1mg/kg/dose TWICE daily	
	20 mg/ml solution	300 mg tablets	10 mg/ml solution	150mg tablet	1 mg/ml solution	15, 20, 30 mg capsules
5-5.9	2 ml		3 ml		6 ml	
6-6.9	3 ml		3 ml		7 ml	10 mg (as 0.5 x 20 mg)
7-7.9	4 ml		4 ml		8 ml	10 mg (as 0.5 x 20 mg)
8-8.9	4 ml		4 ml		9 ml	10 mg (as 0.5 x 20 mg)
9-9.9	4 ml		4 ml		10 ml	10 mg (as 0.5 x 20 mg)
10-10.9	5 ml		5 ml			15 mg cap
11-11.9	5 ml	0.5 tab	5 ml			15 mg cap
12-13.9	6 ml	0.5 tab	6 ml	0.5 tab		15 mg cap
14-16.9		0.5 tab		0.5 tab		20 mg cap
17-19.9		0.5 tab		0.5 tab		20 mg cap
20-24.9		1 tab in am 0.5 tab in pm		1 tab in am 0.5 tab in pm		20 mg cap
25-29.9		1 tab		1 tab		30 mg cap
30-34.9		1 tab		1 tab		30 mg cap
35-39.9		1 tab		1 tab		30 mg cap

ANNEX J. Antiretroviral Dosing Guide for Children NNRTIs continued						
	ZIDOVUDINE			DIDANOSINE		
Weight in Kg	180-240 mg/m^2/dose TWICE daily			90-120mg/m^2/dose TWICE daily	1 mg/kg/dose TWICE daily	180-240mg/m^2/dose ONCE daily
	10 mg/ml syrup	100 mg capsules	300mg tablets	10 mg/ml suspension	25, 50, 100 mg chewable tablets	125, 200, 250, 400 mg EC capsules
5-5.9	6 ml			4 ml	25 mg + 25 mg tabs	
6-6.9	7 ml			5 ml	25 mg + 25 mg tabs	
7-7.9	8 ml			6 ml	25 mg + 25 mg tabs	
8-8.9	9 ml	1 cap		6 ml	25 mg + 25 mg tabs	
9-9.9	10 ml	1 cap		6 ml	25 mg + 25 mg tabs	
10-10.9	10 ml	1 cap		6 ml	50 mg + 25 mg tabs in am 25 mg + 25 mg tabs in pm	125 mg EC cap
11-11.9	10 ml	1 cap		7 ml	50 mg + 25 mg tabs	125 mg EC cap
12-13.9	11 ml	1 cap		7 ml	50 mg + 25 mg tabs	125 mg EC cap
14-16.9		2 caps in am 1 cap in pm	0.5 tab	8 ml	50 mg + 50 mg tabs in am 50 mg + 25 mg tabs in pm	200 mg EC cap
17-19.9		2 caps in am 1 cap in pm	0.5 tab	9 ml	50 mg + 50 mg tabs	200 mg EC cap
20-24.9		2 caps	0.5 tab		100 mg + 25 mg tabs	250 mg EC cap
25-29.9		2 caps	1 tab in am 0.5 tab in pm		100 mg + 25 mg tabs	250 mg EC cap
30-34.9		3 caps	1 cap		100 mg + 25 mg tabs	250 mg EC cap
35-39.9		3 caps	1 cap		100 mg + 25 mg tabs	250 mg EC cap

ANNEX J. Antiretroviral Dosing Guide for Children NNRTIs continued					
	NEVIRAPINE				EFAVIRENZ
Weight in Kg	Induction Dose 160-200mg/m^2/dose ONCE DAILY		Maintenance Dose 160-200mg/m^2/dose TWICE DAILY		Dose as shown ONCE daily for children 3 YEARS AND OLDER
	10 mg/ml suspension	200 mg tablets	10 mg/ml solution	200 mg tablet	50, 100, 200 mg capsules
5-5.9	6 ml		6 ml		
6-6.9	7 ml		7 ml		
7-7.9	8 ml		8 ml		
8-8.9	9 ml		9 ml		
9-9.9	9 ml	0.5 tab	9 ml	0.5 tab	
10-10.9	10 ml	0.5 tab	10 ml	0.5 tab	200 mg cap
11-11.9	10 ml	0.5 tab	10 ml	0.5 tab	200 mg cap
12-13.9	11 ml	0.5 tab	11 ml	0.5 tab	200 mg cap
14-16.9		0.5 tab		1 tab in am 0.5 tab in pm	200 mg + 50 mg caps
17-19.9		1 tab		1 tab in am 0.5 tab in pm	200 mg + 50 mg caps
20-24.9		1 tab		1 tab in am 0.5 tab in pm	200 mg + 100 mg caps
25-29.9		1 tab		1 tab	200 mg + 100 mg + 50 mg caps
30-34.9		1 tab		1 tab	200 mg cap X 2
35-39.9		1 tab		1 tab	200 mg cap X 2

ANNEX J. Antiretroviral Dosing Guide for Children
Protease Inhibitors

	LOPINAVIR/RITONAVIR			NELFINAVIR		RITONAVIR*	
Weight in Kg	**10-16 mg/kg/dose TWICE daily**			**Target dose <10kg:~75mg/kg/dose >10kg to 19.9kg: 60mg/kg/dose g;max dose of 1250mg TWICE daily**		**Starting dose 250 mg/m^2/ dose TWICE daily**	**Maintenance dose 400 mg/m^2/ dose TWICE daily**
	80mg Lopinavir/ 20mg ritonavir per ml	**133mg Lopinavir/ 33mg ritonavir capsules**	**200mg lopinavir/ 50mg ritonavir tablets**	**250 mg tablets**	**625 mg tablets**	**80mg/ ml solution**	**80mg/ ml solution**
5-5.9	1 ml			2 tabs		1 ml	1.5 ml
6-6.9	1.5 ml			2 tabs		1 ml	2 ml
7-7.9	1.5 ml	1 cap		3 tabs in am 2 tabs in pm		1 ml	2 ml
8-8.9	2 ml	1 cap		3 tabs		1.5 ml	2 ml
9-9.9	2 ml	1 cap		3 tabs		1.5 ml	2.5 ml
10-10.9	2 ml	1 cap		3 tabs		1.5 ml	2.5 ml
11-11.9	2 ml	1 cap		3 tabs		1.5 ml	2.5 ml
12-13.9	2 ml	2 caps in am 1 cap in pm	1 tab	4 tabs		1.5 ml	3 ml
14-16.9	2 ml	2 caps in am 1 cap in pm	1 tab	4 tabs		2 ml	3 ml
17-19.9	2.5 ml	2 caps in am 1 cap in pm	1 tab	5 tabs	2 caps		
20-24.9	3 ml	2 caps	1 tab	5 tabs	2 caps		
25-29.9	3.5 ml	2 caps	2 tabs in am 1 tab in pm	5 tabs	2 caps		
30-34.9	4 ml	3 caps	2 tabs	5 tabs	2 caps		
35-39.9	5 ml	3 caps	2 tabs	5 tabs	2 caps		

* Ritonavir Dosing is based on manufacturers information

ANNEX J. Antiretroviral Dosing Guide for Children Adult Fixed-Dose Combinations				
	STAVUDINE + LAMIVUDINE	**STAVUDINE + LAMIVUDINE+ NEVIRAPINE**	**ZIDOVUDINE + LAMIVUDINE**	**ZIDOVUDINE + LAMIVUDINE + ABACAVIR**
Weight in Kg	**Dose shown TWICE Daily**	**Dose shown TWICE Daily**	**Dose shown TWICE Daily**	**Dose shown TWICE Daily**
	30 mg d4T/ 150 mg 3TC/ tablets	**30 mg d4T/ 150 mg 3TC/ 200 mg NVP tablets**	**300 mg AZT/ 150 mg 3TC tablets**	**300 mg AZT/ 150 mg 3TC/ 300 mg ABC tablets**
10-10.9	0.5 tab	0.5 tab		
11-11.9	0.5 tab	0.5 tab		
12-13.9	0.5 tab	0.5 tab		
14-16.9	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm	0.5 tab	0.5 tab
17-19.9	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm	0.5 tab	0.5 tab
20-24.9	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm
25-29.9	1 tab	1 tab	1 tab in am 0.5 tab in pm	1 tab in am 0.5 tab in pm
30-34.9	1 tab	1 tab	1 tab	1 tab
35-39.9	1 tab	1 tab	1 tab	1 tab

ANNEX J. Antiretroviral Dosing Guide for Children Pediatric Fixed-Dose Combinations							
Weight Range (Kg)	**Lead-in Period Formulation and Dosing**				**Maintenance Formulation and Dosing**		
	Triple FDC Triomune	**am**	**Dual FDC Lamivir-S**	**pm**	**Triple FDC Triomune**	**am**	**pm**
3-5.9	Triomune Baby	1	Lamivir-S Baby	1	Triomune Baby	1	1
6-9.9	Triomune Baby	1.5	Lamivir-S Baby	1.5	Triomune Baby	1.5	1.5
10-13.9	Triomune Baby	2	Lamivir-S Baby	2	Triomune Baby	2	2
14-19.9	Triomune Junior	1.5	Lamivir-S Junior	1	Triomune Junior	1.5	1
20-24.9	Triomune Junior	1.5	Lamivir-S Junior	1.5	Triomune Junior	1.5	1.5
25-34.9	Adult FDC	1	Adult FDC	1	Adult FDC	1	1

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