Handbook on Pædiatric AIDS in Africa

by the African Network for the Care of Children Affected by AIDS

Editors

Denis Tindyebwa
Janet Kayita
Philippa Musoke
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ANECCA is an informal network of health workers and social scientists committed to finding ways to improve care for HIV-exposed and -infected children in Africa. Members of the network identified the fact that while there are widespread knowledge gaps in the care of HIV-infected children in Africa, there are nonetheless scattered experiences across the continent that need to be shared. They thus volunteered their time to put together this book. It was a long and sometimes stressful process. Because some issues concerning paediatric AIDS had no clear-cut international or national guidelines, network members had to reach consensus, sometimes through intense discussions. I thank them for the mature and professional manner in which they held these discussions to reach the consensus reflected in this handbook.

As much as possible, and where they do exist, we have tried to remain within the available international guidelines from WHO or UNICEF, and these are acknowledged.

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The handbook will be available at the Regional Centre for Quality of Health Care Web site: www.rcqhc.org

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Acronyms and Abbreviations

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ANC	Antenatal Care
ART	Antiretroviral Therapy
ARV	Antiretroviral Drugs
AZT	Zidovudine
BCC	Behaviour Change Communication
CBC	Complete Blood Count
CDC	United States Centers for Disease Control and Prevention
CFR	Case Fatality Rate
CSF	Cerebrospinal Fluid
CMV	Cytomegalovirus
CNS	Central Nervous System
CRC	United Nations Convention on the Rights of Children
CT	Computerized Tomography
CTZ	Cotrimoxazole
d4T	Stavudine
ddI	Didanosine
DNA	Deoxyribonucleic Acid
DOT	Directly Observed Therapy
EBV	Epstein Barr Virus
EEG	Electroencephalograph
EFV	Efavirenz
ELISA	Enzyme-Linked Immunosorbent Assay
EPI	Expanded Programmes on Immunisation
FHI	Family Health International
gp	Glycoprotein
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HRSA	Health Resources and Services Administration
HSV	Herpes Simplex Virus
IDU	Injecting Drug User

IMCI	Integrated Management of Childhood Illnesses
I/O	Input and Output
IU	International Units
IPT	Intermittent Preventative Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
KS	Kaposi's Sarcoma
LBM	Lean Body Mass
LBW	Low Birth Weight
LIP	Lymphoid Interstitial Pneumonitis
LPV/RTV	Lopinavir/Ritonavir
LRTI	Lower Respiratory Tract Infection
MCH	Maternal and Child Health
MRI	Magnetic Resonance Imaging
MTB	Mycobacterium Tuberculosis
MTCT	Mother-to-Child Transmission
mths	Months
MUAC	Mid-Upper-Arm Circumference
NASBA	Nucleic Acid Sequence-Based Amplification
NCHS	National Center for Health Statistics
NFV	Nelfinavir
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitors
NRTI	Nucleoside Reverse Transcriptase Inhibitors
NSI	Non-Syncitium Inducing
NVP	Nevirapine
OI	Opportunistic Infection
OVC	Orphans and Vulnerable Children
PACTG	Pediatric AIDS Clinical Trials Group
PCP	Pneumocystis Pneumonia
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PGL	Persistent Generalized Lymphadenopathy
PI	Protease Inhibitor
PLHA	People Living with HIV/AIDS
PML	Progressive Multifocal Leukoencephalopathy
PMTCT	Prevention of Mother-to-Child Transmission

RNA . . . . . Ribonucleic Acid
RSV . . . . . Respiratory Syncytial Virus
RT . . . . . Reverse Transcriptase
RTV . . . . . Ritonavir
RV . . . . . Rotavirus
SFT . . . . . Skin-Fold Thickness
SMX . . . . . Sulfamethoxazole
SSA . . . . . Sub-Saharan Africa
STI . . . . . Sexually Transmitted Infection
TB . . . . . Tuberculosis
TLC . . . . . Total Lymphocyte Count
TMP . . . . . Trimethoprim
UNAIDS . . . . . United Nations Joint Programme on HIV/AIDS
UNFPA . . . . . United Nations Population Fund
UNICEF . . . . . United Nations Children's Fund
URI . . . . . Upper Respiratory Infection
USAID . . . . . United States Agency for International Development
VCT . . . . . Voluntary Counselling and Testing
VZIG . . . . . Varicella-Zoster Immune Globulin
WBC . . . . . White Blood Count
WHO . . . . . World Health Organization
wk . . . . . Week
wks . . . . . Weeks
ZDV . . . . . Zidovudine

Chapter 1
Introduction

Introduction

HIV/AIDS is a major cause of infant and childhood mortality and morbidity in Africa. In children under five years of age, HIV/AIDS now accounts for 7.7% of mortality worldwide. AIDS already accounts for a rise of more than 19% in infant mortality and a 36% rise in under-five mortality. Together with factors such as declining immunisation, HIV/AIDS is threatening recent gains in infant and child survival and health.

Yet, for the most part, HIV infection in children is preventable. In industrialised countries in North America and Europe, paediatric HIV infection has largely been controlled. In these settings, HIV testing as part of routine antenatal care, combinations of antiretroviral (ARV) drug regimens, elective caesarean section, and complete avoidance of breast-feeding have translated into mother-to-child transmission (MTCT) rates of less than 2%.

In Africa, on the other hand, high rates of maternal HIV infection, high birth rates, lack of access to currently available and feasible interventions, and the widespread practice of prolonged breast-feeding translate into a high burden of paediatric HIV disease. The transmission risk for a child born to an HIV-infected mother in an African setting without interventions for prevention of mother-to-child transmission (PMTCT) is about 30–40%. The other 60–70% of children, although not HIV-infected, still have a 2- to 5-fold risk of mortality as a direct consequence of the mother's HIV disease, when compared to children born to uninfected mothers.

Efforts to expand care and treatment for children must go hand in hand with efforts to rapidly improve the uptake of available interventions for reducing MTCT. Currently these reach less than 10% of the population in the countries that are most affected. Access to currently available, effective care and treatment remains a major obstacle.

The fast rate of HIV progression and the high morbidity and mortality among infants and children with perinatally acquired HIV infection means that identifying these children and enrolling them in care

programmes should be considered an emergency. The window of opportunity for effective intervention is much too brief for too many of these children, who often die in infancy and early childhood from preventable and/or treatable common childhood conditions and opportunistic infections (OIs).

While it is true that the diagnosis of HIV/AIDS in children can be technologically complex and clinically unreliable, we must ensure that the absence of a definitive laboratory diagnosis does not become a disincentive to provide (or an excuse to deny) available care to children and their families. We must not only continue to improve access to appropriate diagnostics but must also invest in health workers' skills in suspecting and/or diagnosing HIV in children, in communicating difficult news to parents and guardians, and in positioning families to benefit from the best care available in each setting.

There is a widespread need to train primary healthcare workers in the integrated management of childhood infections (IMCI), including community-based IMCI. This approach empowers households to practice behaviours that are essential in preventing illnesses and seeking appropriate healthcare, as well as in infant and young child feeding and other traditional child survival strategies that are particularly critical for HIV-exposed and -infected children.

Collectively, we have the best opportunity to date of making an impact on the paediatric HIV epidemic. There is international will and commitment (for example, WHO's 3 by 5 initiative, the Global Fund for AIDS, TB and Malaria, and the U.S. government's Presidential Emergency Plan for AIDS Relief) to rapidly expand programmes for identifying HIV-infected adults through voluntary counselling and testing (VCT), preventing mother-to-child transmission of HIV, preventing and treating opportunistic infections (OIs) and other common HIV-related conditions, and providing antiretroviral therapy (ART) to those who need it.

We must exploit these efforts fully to benefit both adults *and children* with HIV infection and disease by implementing child- and fam-

ily-centred care and treatment services. Furthermore, the impact of maternal HIV disease on childhood morbidity and mortality means also addressing parental health, in order to have a meaningful impact on child health and well-being. As national efforts to expand access to HIV prevention, care, and treatment continue, opportunities will increase to identify other at-risk (including HIV-exposed infants) and infected family members.

In most of sub-Saharan Africa there are limited paediatric HIV diagnostic facilities and most HIV-infected children, like adults, are diagnosed very late in the course of illness, or not at all. Children under age 15, who make up nearly 10% of the total HIV-positive population, must also benefit from the best available HIV prevention, care, and treatment in their communities.

Whereas few people dispute children's right to HIV care and treatment, few efforts are made to ensure that children actually benefit from these services. How can we reach children to enroll them in care programmes? Who will pay for their care? Are appropriate drug formulations available? How should we monitor the children on treatment, and what if they are in sibling-headed households? Commitment to care and treatment for children must go beyond tokenism; we must set targets, provide guidance, and plan for paediatric HIV care. Caring for and treating children with HIV will be as complex—or as doable—as our will to make it happen.

While there are many books about HIV/AIDS in Africa, they contain little in the way of practical experiences, insights, or guidelines about the care of children. Most paediatric HIV handbooks are from developed countries and are, therefore, less relevant for practitioners in resource-constrained African settings. We recognise that Africa is not homogeneous—in infrastructure or resources—but our hope is that this handbook will provide users in various countries with a resource that can be adapted to meet their specific needs.

The framework proposed in this handbook follows the United Nations Convention on the Rights of the Child (CRC) and its four principles:

- Right to life, survival, and development
- Right to be treated equally
- Right to participate in activities and decisions that affect them
- All actions should be based on the "best interests" of the child.

This handbook seeks to provide a simple, accessible, and practical handbook for health professionals involved in preventing infection and caring for children infected and affected by HIV. The primary targets are medical students and their lecturers, nurses, clinicians, community health workers, and other service providers in resource-poor settings where there is a significant HIV/AIDS burden.

Research on HIV/AIDS is global and ongoing, and new information becomes available continuously, particularly in the areas of PMTCT and ART; thus, this handbook will be a *living document*, updated as we learn from our experiences. There are many gaps in our knowledge—not only because there is little experience, but also, and perhaps more importantly, because many solid, but small-scale, programmes caring for children are poorly documented.

We hope this handbook will stimulate much-needed dialogue, documentation, dissemination, and learning from these invaluable experiences, however imperfect. In the words of a highly valued colleague and advocate: "We must not allow the excellent to become the enemy of the good." Let's not wait for perfect conditions in terms of infrastructure and resources before we provide the care that HIV-infected children in Africa deserve.

Chapter 2
Epidemiology, Pathogenesis, and Natural History

Summary

- UNAIDS estimated that in 2003 there were 630,000 new paediatric HIV infections, about 90% of which were in sub-Saharan Africa.
- The high HIV infection rate in children in Africa results directly from the high HIV infection rate in women of childbearing age and the efficiency of MTCT.
- Compared to adults, there are age specific differences in the immunologic markers of disease, virologic (HIV ribonucleic acid) pattern, and clinical manifestations of perinatal HIV infection.
- The clinical course of paediatric HIV infection is more rapid than in adults.
- The natural history of children perinatally infected with HIV fits into one of three categories:
  - Category 1: Rapid progressors, who die by age 1 and are thought to have acquired the infection in utero or during the early perinatal period (about 25–30%)
  - Category 2: Children who develop symptoms early in life, followed by a downhill course and death by age 3 to 5 years (about 50–60%)
  - Category 3: Long-term survivors, who live beyond age 8 (about 5–25%)
- There are several reasons for the higher mortality of HIV-infected African children as compared to their counterparts in developed countries: intercurrent infections, malnutrition, limited access to care and treatment and, above all, lack of access to ART, which has led to dramatic improvements in survival of children in developed countries.

Epidemiology

Historical Perspective

Adult AIDS, and particularly the syndrome "Slim disease," was first described in Africa in the early 1980s. Paediatric HIV cases were first observed in clinical services in the East Africa region in the early to mid-1980s.

In Rwanda and Democratic Republic of Congo (in Kinshasa) the first cases of paediatric AIDS were identified in 1983–1984 in the clinical services and later in seroprevalence and perinatal studies. In Uganda, reports of paediatric HIV were documented in 1985 and in a specialist clinic started in 1988.

In the mid-1980s, longitudinal cohort studies were started in the cities of Kigali, Kampala, Kinshasha, Nairobi, and Blantyre, among others, to study the MTCT rate and the natural history of HIV-exposed and -infected children.

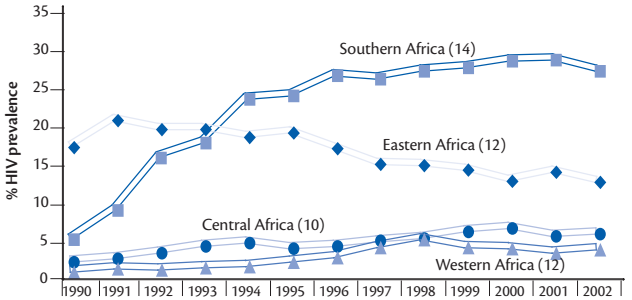
Magnitude of HIV/AIDS Epidemic in Children in Sub-Saharan Africa

The high HIV infection rate in children in Africa results directly from (1) the high HIV infection rate in women of childbearing age and (2) the efficiency of MTCT.

Of close to 40 million people living with HIV at the end of 2003, 70% live in sub-Saharan Africa, and 60% of those infected in sub-Saharan Africa are women. Infection rates among pregnant women in Africa range from 1% in Senegal to over 40% in Botswana (see **Figure 2.1**).

Of the 2.1 million children under the age of 15 years living with HIV worldwide, at least 90% live in sub-Saharan Africa. UNAIDS estimated that in 2003 there were 630,000 new paediatric HIV infections. It is currently estimated that in developing countries 1,600 children are infected daily by their HIV-infected mothers.

Figure 2.1. Median HIV Prevalence (%) in Antenatal Clinics in Urban Areas, by Sub-Region, in Sub-Saharan Africa, 1990–2002



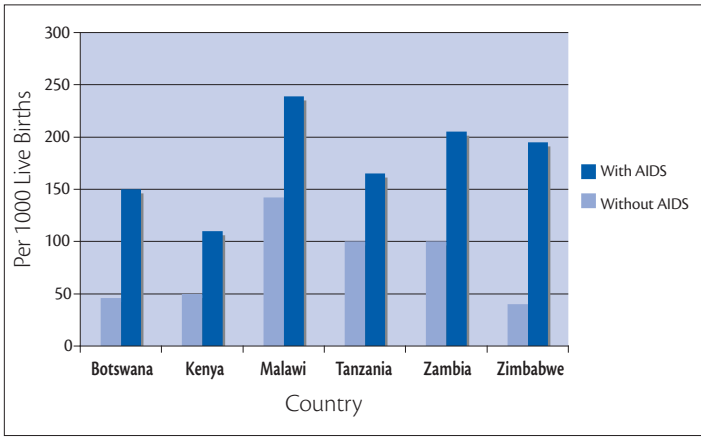
Source: Adapted from WHO AFRO 2003 Report, 2004 Report on the Global AIDS Epidemic (Fig 8)

Impact of the AIDS Epidemic on Children

AIDS affects children in many ways:

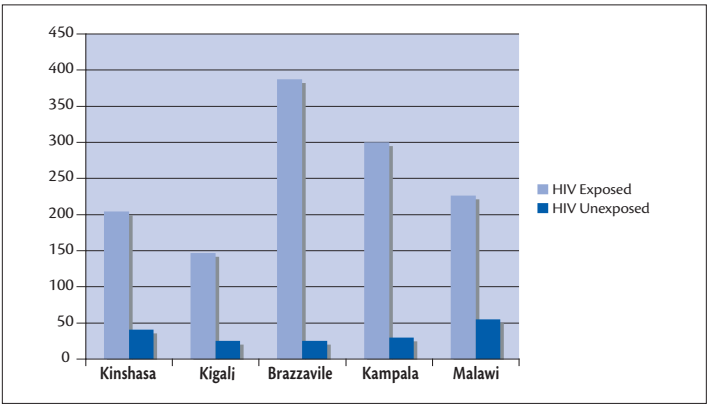
- In Africa, more than 400,000 children under 15 died of AIDS in 2003 alone. Demographic data from sub-Saharan Africa clearly show the estimated impact of HIV on childhood mortality (**Figure 2.2**).
- Maternal ill health, especially HIV-related, has a negative effect on infant survival. Infant and early childhood mortality among children of HIV-infected mothers (HIV exposed) is 2 to 5 times higher than that among children of HIV-negative mothers (HIV unexposed).

Figure 2.2. Estimated Impact of AIDS on Under-Five Child Mortality Rates, Selected African Countries



- There are over 13 million orphans worldwide who have lost one or both parents from AIDS. It is projected that by 2010 the number of children orphaned by AIDS will increase to more than 25 million. In 2001, 10 countries in sub-Saharan Africa had orphan rates higher than 15%, with at least half of the orphans resulting from AIDS (see **Figure 2.3**).
- The impact of AIDS on families and communities also affects non-orphaned children. With the deepening poverty that results from sick and dying parents, children are the first to suffer. They suffer mental, psychological, and social distress and increasing material hardships. The children may be the only caregivers for their sick or dying patients, may drop out of or interrupt school, and are at risk of discrimination and abuse, both physical and sexual.

Figure 2.3. Infant Mortality Rates in HIV-Exposed and Unexposed Babies: Data from 5 Different Cohort Studies



Modes of HIV Transmission

There are several potential modes of transmission of HIV to children, including MTCT, sexual transmission among adolescents, sexual abuse of children, transfusion of infected blood or blood products, unsterile injection procedures, and scarification.

More than 95% of HIV-infected infants in Africa acquire HIV from their mothers during pregnancy, at the time of delivery, or postnatally through breast-feeding. Without any intervention, between 30 and 40% of breast-feeding HIV-positive women transmit HIV to their newborns. The risk factors that increase MTCT are detailed in chapter 3.

Sexual transmission is a significant mode of transmission among adolescents.

The role of child sexual abuse as a source of HIV infection in children is undocumented, but this mode of transmission is of particular concern in countries where both HIV and child sexual abuse are major

public health concerns. Orphans are particularly vulnerable to sexual abuse.

Transfusion of infected blood or blood products is another possible source of HIV infection in children, but this mode of transmission has been greatly reduced by national blood safety programmes and improved blood transfusion services.

HIV can also be transmitted to children by using unsterile injection needles and procedures, but this is considered rare, even in Africa. WHO estimates that unsafe injections account for about 2.5% of HIV infections in both adults and children.

Scarification from traditional healers may also be a source of infection to children. While scarification may be more frequent in HIV-infected children, the process may represent desperate attempts by mothers and guardians to treat recurrent illnesses in the child, rather than being a source of the HIV infection. However, communal traditional rituals and therapeutic procedures that involve bleeding are potential modes of transmission, and communities must be educated about the potential dangers of these practices.

HIV Virology and Pathogenesis

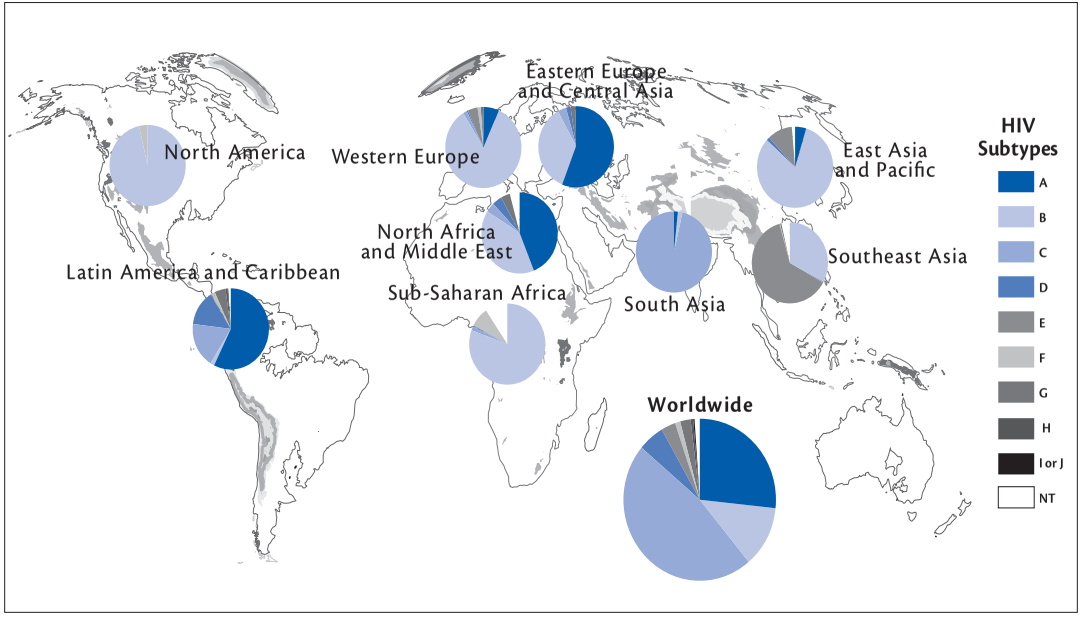
Basic Virology

There are two types of HIV: HIV-1, which is found worldwide and is responsible for the worldwide pandemic, and HIV-2, found mainly in West Africa, Mozambique, and Angola. HIV-2 is less pathogenic and makes little or no contribution to paediatric AIDS; therefore, all discussion in this handbook refers to HIV-1.

HIV-1 has many subtypes: A, B, C, D, E (see **Figure 2.4**, which shows subtypes by region). Africa has mainly subtypes A and D (East and Central), C (Southern Africa), and A recombinants (West Africa). Subtype C is responsible for over 90% of infections in southern Africa.

Subtype C seems to be more virulent than the other subtypes. It has higher transcription rates; it is associated with faster disease progression and with higher MTCT rates than subtypes A and D.

Figure 2.4. Estimated Prevalence of HIV-1 env Subtypes by Region (2000)



Osmanov, S et al. Estimated Global Distribution and Regional Spread of HIV-1 Genetic Subtypes in the Year 2000. JAIDS *2002:29*

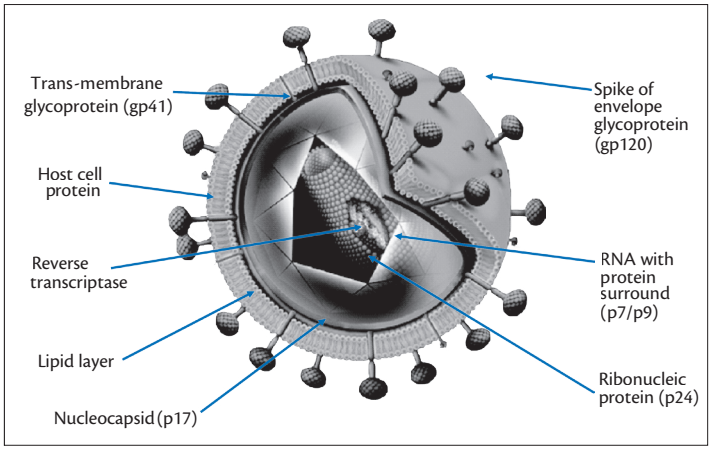
HIV Structure

HIV is a spherical ribonucleic acid (RNA) virus particle with a diameter of 80–100 nanometers (nm) (**Figure 2.5**). The particle has an outer double lipid layer derived from the host cell membrane. Within the lipid layer is the surface glycoprotein (gp120) and the trans-membrane protein (gp41), which mediate the entry of the virus into the host cell.

The core (capsid) is made of several proteins: p24 (the main protein), p17, p9, and p7. Within this capsid are two single strands of identical pieces of RNA, which are the genetic material of the virus (virion). The virion contains a number of enzymes, the most important of which are reverse transcriptase (RT), protease, and integrase. Reverse transcriptase converts viral single-strand RNA into double-strand deoxyribonucleic acid (DNA), which is then easily incorporated into host cells as proviral DNA.

Integrase enables integration of the newly formed double-strand DNA into the host chromosomal DNA. Proteases split the generated proteins so that they can be incorporated into the new virions.

Figure 2.5. HIV Structure



HIV Life Cycle

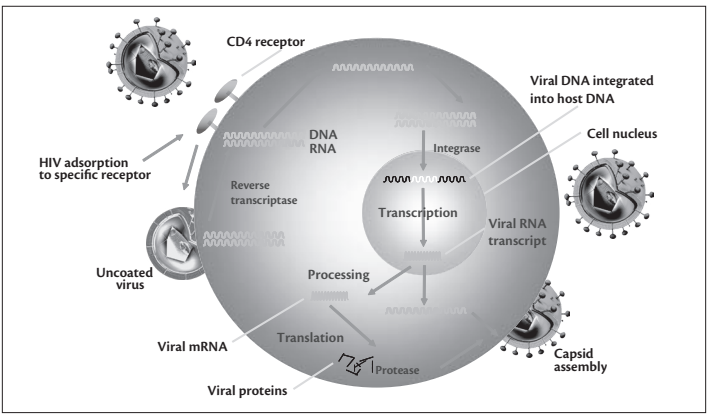
The HIV life cycle in the host cell can be divided into several steps (**Figure 2.6**): binding, fusion, entry, transcription, integration, replication, budding, and maturation.

Binding. HIV binds to cells via interaction between the HIV envelope glycoprotein and the host cell receptors (CD4 molecule) and co-receptors. The receptors are the CD4 antigen found on some T lymphocytes, macrophages, monocytes, glial cells of the brain, and Langerhan cells. The major co-receptors are CCR5 and CXCR4. These receptors and co-receptors determine which cells the HIV virus will infect.

Fusion. The HIV envelope protein gp120 binds to the host cell receptors and co-receptors on the outside of the cell. This results in insertion of gp41 into the cell membrane of the host cell, with fusion of the two membranes.

Entry. The virus particle leaves its membrane behind (uncoating) and the core of the virus is released into the cytoplasm of the host cell. The host cell enzymes interact with the core of the virus, resulting in the release of viral enzymes.

Figure 2.6. HIV Replication Cycle



Reverse Transcription

For the virus to multiply, the viral (single-strand) RNA must first be converted into (double-strand) DNA. This is done by the viral enzyme reverse transcriptase, which changes the single-strand viral RNA into double-strand DNA.

Integration and Replication

The viral DNA is then able to enter the host nucleus and the viral enzyme integrase is used to insert the viral DNA into the host cell's DNA. This is called *integration*. Once a cell is infected, it remains infected for life because the viral genetic material is integrated into the cell's DNA. The host cell is then used as a machine to produce more viral DNA (*replication*).

Budding

The many viral DNA particles (provirus) that are produced using the host cell machinery gather at the membrane of the CD4+ cells. The proviral particles push through the cell membrane by budding, taking the lipid bilayer with them, ready to form new virus particles.

Maturation

The gp160, embedded in the cell membrane, is cleaved by the enzyme protease to produce functional gp41 and gp120 to form a mature virus, which is then ready to infect a new cell.

HIV Viral Load in Infants and Children

In the initial stages of HIV disease in adults, the immune system can contain viral replication. Use of polymerase chain reaction (PCR) to detect either the viral DNA or viral RNA can reveal the HIV virus in the blood of HIV infected individuals. Several methods can be used to quantify HIV ribonucleic acid. The most commonly used assays have a lower limit of detection of 50 copies/ml.

The HIV RNA pattern in perinatally infected infants differs from the pattern in infected adults. HIV RNA levels increase to high values (>100,000 copies/ml) by 2 months of age, remain high throughout the first year of life, and then decline slowly over the next few years. This pattern probably reflects the inability of the infant's immature immune system to contain viral replication and, possibly, the greater number of HIV-susceptible cells.

Effect on Immune System

The basic effect of HIV on the immune system is CD4+ cell *depletion* and *dysfunction.* The functional defects can occur before cell numbers decline. Other immunological defects caused by HIV include lymphoid tissue destruction, CD8+ cell dysfunction, B-cell abnormalities, thymic dysfunction, and autoimmune abnormalities.

Non-HIV-infected infants and young children normally have higher CD4+ counts than adults. The normal CD4+ count varies with age

(and probably with region), reaching adult levels around 5 or 6 years of age.

The CD4+ T-cell absolute count identifies a specific level of immune suppression, but changes with age. The CD4+ T-cell % that defines each immunologic category does not change; CD4 >25% is normal, while CD4 <15% defines severe immune suppression (**Table 2.1**). CD4 % is thus the preferred immunologic marker for monitoring disease progression in children.

Table 2.1. Immunologic Classification for HIV-Infected Infants and Children

Immunologic Category	Age of Child		
	< 12 months	1–5 years	6–12 years
	Cells/µL (%)	Cells/µL (%)	Cells/µL (%)
1: No evidence of suppression	≥1500 (≥25)	≥1000 (≥25)	≥ 500 (≥ 25)
2: Evidence of moderate suppression	750–1499 (15–24)	500–999 (15–24)	200–499 (15–24)
3: Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

Source: CDC, 1994

Mechanism for Decline in CD4 Count

Several mechanisms are involved in causing the decline in CD4 count. These include:

- CD4 T-cell depletion through single-cell killing caused by accumulation of HIV DNA in the cell or by inhibition of cell function.
- Cell membranes of infected cells fusing with cell membranes of uninfected cells (syncitium induction), resulting in giant multi-nucleated cells that are readily destroyed by the immune system.
- Programmed death (apoptosis) also contributes to T-cell depletion. It is postulated that cross-linking of the CD4 molecule with gp120-

anti-gp120 antibody complexes programmes the cell for death without direct infection of the cell with HIV.

- HIV infection induces neutralizing antibodies against regions of the HIV envelope; these antibodies may play a role in mediating antibody-dependent cellular toxicity after binding to natural killer (cell killing) cells.
- HIV specific cytotoxic T-cells (CD8 cells) also play a role in killing HIV-infected cells.

These events contribute to depletion of CD4 cells and deteriorating immune function.

Natural History

Clinical Course of Illness

There are critical differences between the disease progression in children and in adults. Stemming largely from the lower efficiency of a child's immature (but developing) immune system, these differences result in much more rapid disease progression and a much shorter duration for each stage.

Perinatally acquired HIV infection in Africa, as in industrialised countries, demonstrates defined modes of expression of disease (see **below**), but with a poorer prognosis in Africa. The higher mortality in HIV-infected children in Africa may result from intercurrent infections, malnutrition, lack of access to basic health care, lack of or delayed definitive diagnosis, and lack of access to primary HIV care and ART.

With no interventions, the majority of perinatally HIV-infected children in Africa develop HIV-related symptoms by 6 months of age.

There are limited data on clinical and biological indicators of disease progression in HIV-infected children in Africa. Some reports and clinical experience indicate that children perinatally infected with HIV fit into one of three categories:

- Category 1: Rapid progressors, who die by age 1 and are thought to have acquired the infection in utero or during the early perinatal period (about 25–30%)
- Category 2: Children who develop symptoms early in life, followed by a downhill course and death by age 3 to 5 (about 50–60%)
- Category 3: Long-term survivors, who live beyond age 8 (about 5–25%)

Factors Predicting Prognosis

Factors used to predict a prognosis are derived mainly from studies performed in industrialised countries; however, these predictors are also useful in the African context. HIV RNA and CD4 % provide complementary and independent information about the prognosis for HIV-infected children. Using the two markers together, at baseline and with changes over time, provides a more accurate prognosis.

Predictors of disease progression in infants include:

- Infecting viral dose (maternal viral load at delivery)
- Any infection before 4 months of life
- Infant peak viremia
- Low CD4 count and percent
- Rapid decline in CD4 count
- Clinical AIDS
- p24 antigenemia

Maternal predictors of infant disease progression include:

- Maternal viral load at time of delivery
- Maternal CD4 cell count (<200)
- Rapidly progressive maternal disease

- Maternal death, which is associated with a 2- to 5-fold increase in infant mortality when compared to infants born to mothers who survive

Knowledge Gaps

- There are limited data on the natural history of paediatric HIV infection in Africa and other resource-constrained settings beyond the first 3 years of life.
- There are limited data on the biological markers of HIV disease among infants and children in sub-Saharan Africa—current assumptions that these are similar to infants and children in industrialised countries have not been validated.

Additional Reading

Pizzo, P. and C. Wilfert, eds. *Pediatric AIDS: The Challenge of HIV Infection in Infants, Children and Adolescents*. Williams & Willaims, 3rd edition, 1998.

Essex, M. et al. 2002. *AIDS in Africa*. Kluwer Academic Publishers.

Obimbo, E. et al, eds. *Pediatr Infect Dis J*, 23 (6):536–543, June 2004.

Chapter 3
Preventing Paediatric HIV Infection

Summary

- Mother-to-child transmission of HIV accounts for over 95% of childhood paediatric HIV infections in sub-Saharan Africa.
- There have been many scientific and operational advances in strategies to prevent MTCT. These include testing for HIV during pregnancy, modified obstetric practices, preventive ARV drug regimens, and modified infant feeding practices; however, these continue to be limited in both reach and scope.
- Widespread use of these effective interventions reaffirms that paediatric HIV infection is preventable, as demonstrated by the dramatic decline in the annual number of new paediatric infections in industrialised countries.
- In resource-limited settings, the most feasible regimens currently are an zidovudine (AZT) short-course therapy started during pregnancy between 32 and 36 weeks of gestation and/or a single-dose nevirapine (NVP) to the mother at the onset of labour and to her infant within the first week after birth.
- PMTCT programmes provide opportunities not only to prevent infection but also to identify and provide care for HIV-exposed and -infected children, their mothers, and their families.
- Early identification of at-risk and infected children is particularly critical because infants and children in general experience faster progression of HIV disease and experience high rates of morbidity and mortality early in life.

- Providing care to an infected mother not only improves her health and well-being, but also significantly impacts her infant's health and survival.
- Adolescents remain a high-risk group (for both HIV infection and pregnancy) and have specific issues that those planning prevention and care programmes for children must address.
- Post-exposure prophylaxis should be considered in cases of rape, exposure to contaminated blood, and human bites from an infected individual.

HIV Transmission Modes in Children

Mother-to-Child HIV Transmission

Infants who acquire HIV infection from their mothers do so during labour and delivery or after birth through breast-feeding. The absolute transmission risk is 5–10% during pregnancy; 10–20% during labour and delivery, and 10 to 20% during breast-feeding. (**Table 3.1**).

Table 3.1. Estimated Timing of Transmission and Absolute Transmission Rates

Time of Transmission	Absolute Transmission Rate (%)
During pregnancy	5–10
During labour and delivery	10–20
During breast-feeding	5–20
Overall without breast-feeding	15–30
Overall with breast-feeding through 6 months	25–35
Overall with breast-feeding through 18 to 24 months	30–45

Source: JAMA, 2000, 283:1175-1182

Risk Factors for Mother-to-Child HIV Transmission

The risk factors associated with MTCT include the following maternal and infant factors:

Maternal Factors

- Women with high viral load are more likely to transmit HIV to their infants, but there is no clear cut-off point below which transmission does not occur.
- Women with severe immunosupression (CD4 counts below 200) and those with advanced disease have an increased risk of transmitting HIV to their infants.
- Maternal micronutrient deficiencies increase the risk of MTCT of HIV significantly.

- Prolonged rupture of amniotic membranes, chorioamnionitis, and STIs significantly increase the risk of MTCT.
- During breast-feeding, cracked nipples and breast abscesses significantly increase the risk of MTCT.
- HIV-1 is more readily transmitted from an HIV-infected woman to her infant than is HIV-2. Subtype C has been associated with increased risk of MTCT.

Infant factors

- Infant risk factors for MTCT include:
  - Prematurity
  - Breast-feeding
  - Oral thrush and oral ulcers
  - Invasive fetal monitoring during delivery
  - Birth order (first twin) in twin pregnancies

Table 3.2 presents interventions to reduce the risk of MTCT and mitigate against infection.

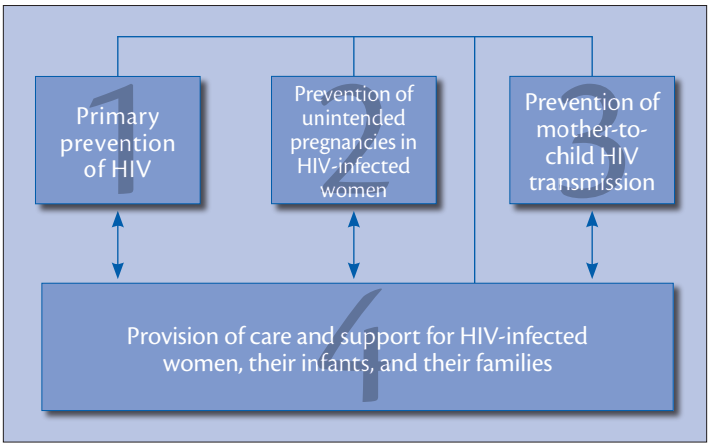
Table 3.2. Risk Factors and Mitigating Interventions

Risk Factor	Prevention/Mitigating Interventions
High viral load	Antiretroviral therapy in pregnancy
Low CD4 count	As above, provide pneumocystis pneumonia (PCP) prophylaxis
Advanced disease	Antiretroviral therapy, PCP and tuberculosis (TB) prophylaxis, OI treatment
Chorioamnionitis	Identify and treat sexually transmitted infections (STIs); Intermittent preventive therapy (IPT) for malaria
Malaria	Provide malaria prophylaxis during pregnancy
Low vitamin A	Maternal vitamin A supplementation does not reduce the risk of MTCT
Cracked nipples, abscesses	Counselling on optimal breast-feeding practice and breast care
Breast-feeding	Counselling on infant feeding options: exclusive breast-feeding, early and rapid cessation, replacement feeding options, and so on
Prematurity	Comprehensive antenatal care, identify at-risk mothers, provide PCP prophylaxis
Prolonged rupture of membranes	Comprehensive antenatal care, safer delivery practices, and modified obstetric care
Invasive infant procedures	Discourage scalp vein monitoring, vacuum extraction, episiotomy, and nasal suction

Preventing Paediatric HIV Infection

A four-pronged approach has been suggested for PMTCT of HIV. (**Figure 3.1**.)

Figure 3.1. Four-Pronged Approach to Paediatric HIV Infection (UN/WHO)



Prong 1: Primary Prevention of HIV Infection

Primary prevention of HIV infection in men and women reduces the risk of heterosexual transmission and so directly affects MTCT. Targeting pregnant and lactating women is a particularly pertinent strategy for preventing paediatric HIV infection.

Prong 2: Preventing Unintended Pregnancy Among HIV-Infected Women

Adolescent females in Africa have a six-fold increased risk of HIV compared to males of the same age. This high risk of HIV acquisition stems from the young women's social, biological, and emotional vulnerabilities.

Measures that may reduce HIV infection in adolescents include training in life skills and communication as a strategy to empower them to

delay sexual debut and engage in less risky sexual behaviours. The establishment of youth-friendly sexual, reproductive, and VCT services is also an important way to increase access to services.

PMTCT efforts to date have focused almost exclusively on preventing transmission after an HIV-positive woman is already pregnant. PMTCT programmes could be made more effective by increasing contraceptive use among non-pregnant, non-contracepting HIV-positive women who do not want to get pregnant (including those identified during pregnancy and followed up post-pregnancy) through integrating family planning and PMTCT services.

There is a tremendous potential—including marshalling the current good will and support for VCT and PMTCT programmes—for strengthening and promoting family planning services to support all women and integrating family planning information and counselling into VCT services. The feasibility and acceptability of such a strategy has been demonstrated in resource-constrained settings in Uganda and Kenya.

Integrating family planning into PMTCT programmes and vice versa will require reorienting toward protection against the dual risks of unintended pregnancies and of HIV infection. Service providers and HIV-infected clients both need to promote dual protection, (especially by the use of condoms), to guard against unintended pregnancies as well as STIs.

Prong 3: Preventing Mother-to-Child HIV Transmission

Specific interventions used to prevent HIV transmission from an infected mother to her child include use of ARV drugs, safer delivery practices, infant feeding, counselling, and support. These interventions present real opportunities to improve services for all women and children, and healthcare providers should provide them as part of routine pregnancy, maternity, and post-pregnancy care for mothers and their infants.

Essential Antenatal Care

Establishing PMCT programmes provides an opportunity to strengthen and improve the quality of antenatal care for all women. Antenatal care for all women should include regular routine visits to check for complications such as hypertension, diabetes, and pre-eclampsia that could lead to maternal death and/or poor infant outcomes.

Nutritional Support

Nutritional education and support (including multivitamin supplementation) is critical for all women and is associated with a decrease in the incidence of low birth weight and congenital defects. Micronutrient supplementation (excluding vitamin A) during pregnancy and lactation has a positive impact on the pregnancy outcomes of HIV-infected women.

Infection Prevention and Treatment During Pregnancy

Malaria during pregnancy is one of the most common causes of low-birth-weight infants, and intermittent preventive therapy for malaria significantly reduces malaria-related adverse outcomes. Dual infection with HIV and malaria is associated with increased risk of maternal, perinatal, and early infant death compared with the risks of either disease alone. Chorioamnionitis from malaria has been associated with increased MTCT, further emphasising the importance of intermittent preventive malaria therapy.

Sexually transmitted infections (STIs) and urinary tract diseases also precipitate premature delivery and increase an infant's risk of HIV infection. Healthcare professionals should routinely screen for syphilis. Because STIs are usually asymptomatic in women, health workers should actively seek symptoms by taking a clinical history and carrying out a genital examination.

To reduce the occurrence of neonatal tetanus, women should receive immunisation during pregnancy.

Counselling and HIV Testing

Effective PMTCT depends on providing routine, on-site antenatal counselling and HIV testing to all pregnant women and testing all women presenting with an unknown status at delivery.

Integrating counselling and testing services in maternal and child health settings requires significant planning and, often, reorganisation of services to ensure counselling capacity and services. This will include: creating private space, re-designing client flow, as well as orienting, training, and sometimes hiring additional service providers.

The need to introduce and maintain such services, particularly in the face of typically crowded and understaffed antenatal care (ANC) clinics, is a significant limiting factor to scaling up PMTCT interventions. Over time this has led to the development of multiple approaches to counselling and testing in MCH settings.

The ideal approach is to integrate HIV testing into routine antenatal care, with women reserving the right to refuse testing. HIV testing is the entry point for specific PMTCT interventions that include ARV prophylaxis, modified obstetric practices, and infant feeding counselling and support. Women who are HIV negative receive counselling about remaining negative and the high risk of infant transmission associated with becoming infected during pregnancy and lactation.

Infant Feeding Counselling

Counselling and support on infant feeding choices for HIV-positive women is a complex and challenging intervention requiring additional factual knowledge and understanding of postnatal HIV transmission (see **chapter 12**).

Antiretroviral Therapy for PMTCT

In 1994 the Pediatric AIDS Clinical Trials Group (PACTG) in the United States published the first randomised controlled trial demonstrating that prophylactic ART can reduce perinatal transmission. In the PACTG 076 study an intensive AZT regimen—starting at the end of the first trimester in the mother and for 6 weeks to the infant—re-

duced transmission from 25.5% to 8.3%. Since then several successful trials have shown that a combination of interventions may reduce transmission rates significantly. A summary of published studies from African trials is shown on **Table 3.3**.

Table 3.3. Early MTCT Rates in Breast-Feeding Populations Where Women Received Antepartum and/or Intrapartum and/or Postpartum Regimens

Regimen	Studies	Mother	Infant	Evaluation Time	Transmission Rate (%)
AZT* alone	RETROCI	From 36 wks antepartum to delivery	None	3 mths	16.5
	DITRAME	AZT from 36 wks antepartum and 1 week postpartum to mother	None	6 wks	12.8
NVP alone	HIVNET 012	Single dose in labour	Single dose	6–8 wks	11.9
	SAINT	Single dose in labour + one dose postpartum 24–48 hrs	Single dose	8 wks	13.3
AZT + NVP	DITRAME	AZT from 36 wks antepartum plus single-dose NVP in labour	Single dose NVP plus 1 wk ZDV	4–6 wks	6.2
AZT + 3TC	PETRA A	From 36 wks antepartum to 1 wk postpartum	1 wk	6 wks	5.7
	PETRA B	From onset of labour to 1 wk postpartum	1 wk	6 wks	8.9
	SAINT (= PETRA B)	From onset of labour to 1 wk postpartum	1 wk	8 wks	9.3
ddI + AZT	SIMBA	From 36 wks antepartum to 1 week postpartum	BF period 3TC or NVP	4 wks	6
AZT + NVP	Taha	No treatment for mother	NVP alone vs NVP + AZT for 1 wk	6–8 wks	20.9 15.3

*AZT=Zidovudine

- The decision about which regimen is appropriate should be made locally, and should take into account the feasibility, pattern of use of maternal and child health (MCH) clinics, efficacy, acceptability, ease of dosing, availability and cost, safety and logistical issues, and the stage of the disease and history of the mother's use of ARV drugs.
- In resource-constrained settings such as Africa, the most widely used regimens are the least complex single drug ones such as single-dose nevirapine and/or short course AZT.

Single-Dose NVP Regimen (HIVNET 012)

Nevirapine 200 mg given to the mother at onset of labour and 2 mg/kg single dose to the infant within 1 week.

To be effective, the woman must receive maternal NVP dosing more than 2 hours before delivery. If the maternal dose is taken less than 1 hour prior to delivery or if the mother misses her dose, then the infant is dosed as soon as possible after birth.

Infant dosing can be prior to discharge from the hospital, but if the baby is not born at the hospital, then the baby can receive a single-dose NVP syrup within the first 7 days of life, but preferably within the first 3 days.

Short-Course AZT Regimen (Modified Thai)

Regimen: Oral AZT starting at 32–34 weeks gestation, 300 mg every 12 hours during pregnancy and every 3 hours in labour, and for 1 week to the infant, 4 mg/kg/day every 12 hours.

The aim is to provide at least 4 weeks of AZT to the mother and 1 week to the infant. Health workers must make an effort to provide at least 4 weeks of maternal dosing during pregnancy (beginning at 32–34 weeks or as soon as possible thereafter).

Combination Regimens

Regimens that combine more than one drug have been found to be more efficacious in preventing mother-to-child HIV transmission.

PHPT-2 Regimen (2004 Thai Regimen)

The PHPT regimen combines AZT (starting at 28 weeks or as soon as possible thereafter) with the single-dose maternal and infant nevirapine (HIVNET 012). This regimen reduces transmission to below 3% in non-breast-feeding populations.

Triple Combination ART

Highly active antiretroviral therapy (HAART) in pregnancy is the most effective regimen for reducing MTCT. In places where HAART is available, make decisions to use HAART during pregnancy for prophylaxis against MTCT after discussion between the woman and her healthcare provider.

Where the mother requires HAART to treat her HIV disease, guidelines for particular regimens do not differ when used during pregnancy, but health professionals must consider the safety of particular drugs, such as efavirenz and abacavir, during the first 3 months of pregnancy.

There is no additional benefit from the single-dose NVP regimen when a pregnant woman is already well controlled on HAART because the viral load will be low or undetectable.

Appendix A at the end of the handbook presents detailed recommendations for the use of antiretroviral drugs in pregnant women—for their own health and to prevent HIV infection in infants.

Safer Delivery Practices

Most HIV transmission occurs around the time of labour and delivery and the risk increases with prolonged rupture of membranes, invasive procedures, and prematurity.

Chlorhexidine vaginal douches have been shown to reduce the incidence of neonatal infections but not of HIV transmission, unless the membranes are ruptured for longer than 4 hours.

Healthcare professionals should discourage invasive obstetric procedures such as artificial rupture of membranes before full dilatation, foetal scalp monitoring, vacuum extraction, and episiotomy. The infant should be wiped soon after delivery, but vigorous suctioning of the infant should be avoided.

Elective caesarean section (before the onset of labour or the rupture of membranes) may reduce the MTCT risk. Caesarean section is not advocated for PMTCT in resource-limited settings, where feasibility and safety are questionable. When HAART is used for PMTCT, caesarean section does not have an added benefit.

Infant Feeding

Breast-feeding increases the HIV transmission risk by 10 to 20%; however, lack of breast-feeding increases children's risk of malnutrition and infectious diseases other than HIV. The decision about feeding must be on a case-by-case basis and be accompanied by comprehensive counselling and support.

Multiple feeding options can be used to reduce HIV transmission by breast milk. These include using infant formula, exclusive breast-feeding with early cessation, heat-treating expressed breast milk, or using other breast milk substitutes, for example, cow's milk (see **chapter 12**).

Immediate Postpartum Period

Counsel mothers and assist them to initiate the infant feeding option they have selected as soon as possible after delivery. Tell those who opt to breast-feed about the appropriate latching-on technique; give those who opt for replacement feeding demonstrations about replacement foods such as formula and other replacement milks. Also counsel them on food hygiene and personal hygiene as well as issues related to maternal infant bonding, particularly for those whose infants receive replacement food or are weaned early.

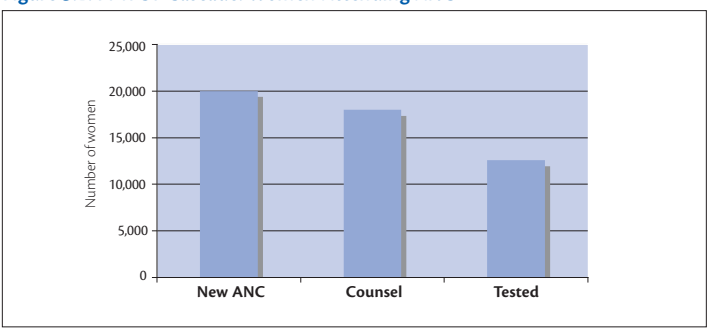
Immediate Newborn Care

Ensure appropriate newborn care: keeping the baby warm, wiping off the infant, and initiating feeding early.

Challenges of Implementing PMTCT

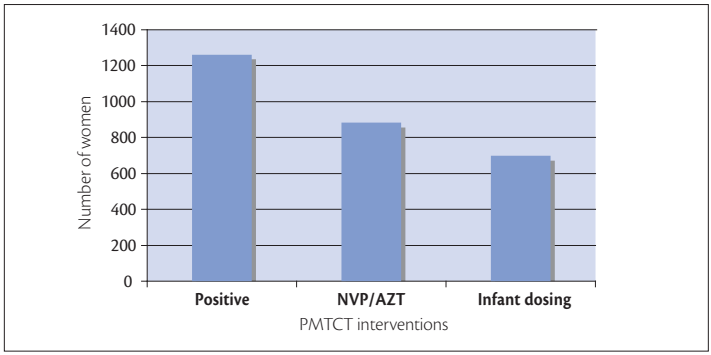
Low uptake of HIV testing by antenatal women (**Figure 3.2**) and low uptake of antiretroviral drugs by HIV-positive women identified during pregnancy (**Figure 3.3**) are having an adverse effect on the effectiveness of PMTCT programmes in the sub-Saharan African region. This can be attributed to institutional factors (such as client flow and low staff levels) that have a negative effect on service delivery and to inadequate community engagement (especially from male partners). There is an urgent need for strategies to improve programme impact.

Figure 3.2. PMTCT Cascade: Women Attending ANC



Source: Phillipa Musoke. Makerere University/Johns Hopkins University PMTCT programme services data, 2000-2003 (illustrative only)

Figure 3.3. HIV-Infected Women Accessing Services



Source: Phillipa Musoke. Makerere University/Johns Hopkins University PMTCT programme services data, 2000-2003 (illustrative only)

Prong 4: Providing Care and Support to HIV-Infected Women, Their Infants, and Their Families Synergy Between Prevention and Care

Prevention and care are mutually reinforcing elements of an effective strategy for dealing with the paediatric HIV epidemic. Access to care will enhance community support for PMTCT programmes and increase the uptake of important interventions, such as HIV testing. Psychosocial and nutritional support, treating OIs, and ART are important in both preventing and treating paediatric HIV infection.

A comprehensive approach to the paediatric epidemic involves treating the parents and other siblings to preserve the family unit, ensure a stable environment in which to nurture the children's growth and development, and reduce the prevalence of orphans.

Creating links between PMTCT programmes and those for the care and support of HIV-infected women, their infants, and their families will help to ensure that women themselves have access to the services they need. Furthermore, access to care and support services also enhances PMTCT services within communities. Such services include:

- Prevention and treatment of OIs
- Psychosocial and nutritional support
- Reproductive healthcare
- Control of STIs
- Family planning
- Antiretroviral therapy
- Young child care:
  - Diagnosis of HIV
  - Immunisations
  - Growth and development monitoring
  - Treatment of acute infections
  - Routine de-worming
  - Multivitamin supplementation
- Improved economic independence of women (poverty alleviation)

Non-Mother-to-Child Transmission

Sexual Abuse

Sexual abuse accounts for a relatively small proportion of infection in children. It is often difficult to tell if an older child was infected perinatally or by abuse. Orphans are especially vulnerable to sexual abuse.

Post-Exposure Prophylaxis

Initiate post-exposure prophylaxis (PEP) after rape or sodomy as soon as possible because it is most effective if begun within 24 hours of the assault and is probably ineffective after 72 hours. Also consider prophylaxis in other situations, such as exposure to contaminated

medical equipment, blood, or other bodily fluids and after human bites with disruption to the skin.

Points to keep in mind for post-exposure prophylaxis include:

- Administer AZT *plus* 3TC for a period of 28 days. On discharge from facility, issue children enough medication to complete the 28-day course (**Table 3.4**).
- Administer three-drug prophylaxis if parents can afford it or if significant exposure has occurred (e.g., penetrative sexual assault with perineal lacerations). Use nelfinavir in combination with AZT and 3TC for 28 days.
- Perform HIV testing at the time of initial contact (baseline test) after obtaining informed consent. Most seroconversions occur within 6 to 8 weeks after exposure. Repeat HIV testing at intervals of 6 to 8 weeks, 3 months, and 6 months after the assault.
- In children who were sexually assaulted, give consideration to preventing pregnancy and STIs and to collecting forensic evidence, including appropriate perineal swabs (local guidelines must be consulted).

Table 3.4. Drug Dosage for Post-Exposure Prophylaxis

Drug	Paediatric Dose	Adolescent Dose
AZT	180 mg/m^2/12 hours	200 mg 8 hourly
3TC	4 mg/kg/12 hours	≥50 kg 150 mg 12 hourly < 50 kg 2mg/kg 12 hourly
Nelfinavir	55 mg/kg/12 hours	750 mg 8 hourly

Transfusion of Blood Products

Routine donor screening has largely eliminated blood products as a route for transmission. However, a small number of such transmissions do occur where there is no safe blood supply or because HIV-infected donors were not detected during the *window period*. Children

in Africa are often transfused daily because of severe anaemia and every effort must be made to ensure safe blood supplies.

Other Modes of Transmission

In a small number of infants with seronegative parents, the mode of transmission is uncertain. However, nosocomial transmission can occur through contaminated or incompletely sterilised instruments at healthcare facilities, through traditional practices, and through contaminated expressed breast milk that is inadvertently given to hospitalized children. Wet-nursing could be another source of unexplained transmission.

Adolescents

Adolescents are vulnerable and often acquire HIV when they are involved in risky sexual practices, are sexually abused, or share needles when experimenting with illicit drugs.

Preventing Other Modes of Horizontal Transmission

Methods for preventing other modes of HIV transmission include:

- Instituting hospital infection control measures such as protective clothing (including gloves and eye protection), use of antiseptic techniques, sterilization of instruments and equipment, and adequate waste storage and disposal systems.
- Eliminating the reuse of needles and syringes.
- Taking special care with the administration of expressed breast milk. Do not use communal breast pumps. Place expressed milk into labelled bottles and check the labelled bottles before giving milk to any baby.
- Reviewing infection control measures regularly to minimise nosocomial infection. Pay attention to practices that are specific to each clinical discipline. For example, phase out nappy pins, which may facilitate the transmission of several viruses, including HIV.

Post-Exposure Prophylaxsis for Healthcare Providers

Post-exposure prophylaxis is critical for those exposed to HIV. Local institutional policy guidelines should be available for all healthcare providers. Some guidelines include:

- Start prophylaxis within 1 hour of exposure.
- Zidovudine 300 mg twice daily with lamivudine 150 mg twice daily for a total of 28 days is adequate for most exposures.
- For high-risk exposures (e.g., deep injury with a hollow needle from an HIV-infected patient, blood containing a viral titre, or a patient with end-stage AIDS), three-drug prophylaxis is recommended (i.e., zidovudine 300 mg twice daily, lamivudine 150 mg twice daily, and indinavir 800 mg) thrice daily for a total of 28 days.
- Test the source patient soon after the exposure, and review the need to continue prophylaxis when the HIV result of the source patient is known.
- When the source person's virus is known or suspected to be resistant to one or more drugs considered for the PEP regimen, then select drugs to which the source person's virus is unlikely to be resistant.
- Serial HIV enzyme-linked immunosorbent assay (ELISA) testing of the injured healthcare provider is essential to establishing whether seroconversion has occurred and for compensation claims. Perform a baseline HIV ELISA after obtaining informed consent. Most seroconversions occur within 6 to 8 weeks after exposure. Repeat ELISA testing 6 to 8 weeks, 3 months, and 6 months after the incident.
- Provide supportive counselling to the health worker. Advise him or her on the risk of infecting the sexual partner or on mother to child transmission if pregnant or breast-feeding.

Knowledge Gaps

- Effectiveness of PMTCT programmes in sub-Saharan Africa
- Implications of nevirapine resistance for future ARV therapy
- Role of HAART in sub-Saharan African PMTCT programmes

Additional Reading

Recommendations for the use of antiretroviral drugs in pregnant HIV-1 infected women. Available at: http://AIDSinfo.nih.gov

Preventing Mother-to-Child Transmission of HIV. A Strategic Framework. Family Health International, 2004.

Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: guidelines on care, treatment and support for women living with HIV/AIDS and their children in resource-constrained settings. World Health Organization, 2004.

Chapter 4
Approach to Care of HIV-Exposed or HIV-Infected Child

Summary

- Care providers can do more to improve the care and quality of life of HIV-exposed and infected children.
- Comprehensive care of HIV-exposed children that includes PMTCT, nutrition counselling, prevention of infections, and growth monitoring is feasible within resource-constrained settings and significantly improves the survival of these children.
- Early diagnosis ensures timely treatment and entry into ARV programmes.
- Establishment of follow-up services, and appropriate referral system for HIV-exposed children and their families are critical components of their care.
- Extending HIV care to mothers and other family members provides a support network for the affected child, and improves the survival of the child.
- Clear communication with the caregiver or parent and the affected child, and participatory planning for long-term care, increase the likelihood of treatment success.

Introduction

This chapter provides a framework for programmatic interventions (primarily clinical) that cater to the needs of children exposed to or infected by HIV, within the broader context of services for children affected by AIDS.

In most of sub-Saharan Africa there are limited paediatric HIV diagnostic facilities and therefore most HIV-infected children are diagnosed very late in the course of illness, or not at all.

The risk of transmission for a child born to an HIV-infected mother in an African setting without PMTCT interventions is about 30 to 40%. The other 70% of infants born to HIV-infected mothers, although they are not infected, have a 2- to 5-fold risk of mortality as a direct consequence of the mother's HIV disease, when compared to children born to HIV-uninfected mothers.

Expansion of PMTCT services leads to identifying greater numbers of HIV-exposed children and provides opportunities for early intervention and care.

Health workers need to integrate PMTCT services into the antenatal clinic and maternity and encourage pregnant women to use the services to reduce the numbers of new infant HIV infections and also as an entry point into their long-term care.

Comprehensive Paediatric HIV Care

Provide comprehensive care for the HIV-exposed or those infected with HIV in the broader context of other child health strategies and provide regular presumptive de-worming every 6 months. Health workers should provide the following, as a minimum, to these children.

Ten-Point Package for Comprehensive Paediatric AIDS Care

1. Confirm HIV status as early as possible.
2. Monitor the child's growth and development.
3. Ensure that immunizations are started and *completed* according to the recommended schedule.
4. Provide prophylaxis for opportunistic infections (PCP and TB) (see below).
5. Actively look for and treat infections early.
6. Counsel the mother and family on:
   a. Optimal infant feeding to minimise MTCT, prevent malnutrition and promote growth and development.
   b. Good personal and food hygiene to prevent common infections, and encourage her to seek prompt treatment for any infections or other health related problems.
   c. When the child should be followed up according to the WHO recommendations (see below).
7. Conduct disease staging for the infected child.
8. Offer ARV treatment for the infected child, if needed.
9. Provide psychosocial support to the infected child and mother.
10. Refer the infected child for higher levels of specialized care if necessary, or for other social- or community-based support programs.

In the context of providing child health services, a clinician is likely to encounter the following categories of children:

- Children born to HIV-infected women who may be infected but are of unknown HIV status and commonly referred to as *HIV-exposed children*
- Children with symptoms suggestive of AIDS

- Children known to be HIV-infected
- Children whose parents/guardians are sick with HIV/AIDS
- Children who have been orphaned by AIDS

Interventions Common to Both HIV-Exposed and HIV-Infected Infants

1. Confirm HIV Infection as Early as Possible

Healthcare workers should counsel every HIV-infected pregnant or postpartum mother on the need to confirm her child's infection status. Health workers should explain when and where to bring the child for HIV testing, which will depend on the availability of particular HIV tests in her locality.

For a child who has clinical signs and symptoms suggestive of HIV infection, or whose mother is known to be HIV-infected, it is important to confirm infection as early as possible because early identification allows for appropriate care and can prevent/reduce early morbidity and mortality.

Even without sophisticated laboratory tests, the clinician should always have a high index of suspicion and use clinical criteria to make a diagnosis of HIV infection. Where laboratory facilities are available, confirm clinical diagnosis as soon as possible.

When to Test

Provide routine testing for HIV antibodies for all sick children in high HIV prevalence areas.

Offer HIV testing to women who deliver with unknown HIV status immediately after delivery and provide post-exposure prophylaxis to the infants of the HIV-infected women.

If the mother is known to be HIV-positive and the child has clinical signs and symptoms suggestive of HIV/AIDS and is antibody positive, but PCR is not available, treat the child presumptively (see **chapter 8**).

The most widely available HIV tests are antibody-based tests (e.g., HIV rapid tests, ELISA), which are generally not useful for establishing a definitive diagnosis in HIV-exposed infants younger than 18 months of age. A positive HIV antibody test at a younger age may merely indicate passively transferred maternal antibodies. But a negative test at an earlier age in an HIV-exposed infant, particularly one who has never breast-fed or who was completely weaned at least 6 months previously, is a useful indicator of the absence of HIV infection.

HIV DNA PCR virologic testing, a test more appropriate for younger infants, is much more expensive and currently available only in research and referral laboratories. However, there is an urgent need to explore ways that HIV-antibody-positive children in primary care facilities can access these tests in referral laboratories.

2. Growth and Development Monitoring and Promotion

Growth and development monitoring and promotion are critical child survival strategies in resource-poor settings, especially in areas with high rates of both childhood malnutrition and HIV/AIDS, and particularly for children in households directly affected by HIV/AIDS. We know that growth failure is greater in HIV-infected children than in uninfected children. This may result from:

- Low birth weight (prematurity, small for age)
- HIV infection
- Other underlying disease, such as TB
- Inadequate macro/micronutrient intake
- A combination of any or all of the above

Growth monitoring is a tool that helps identify the vulnerable child and monitors the effect of interventions.

Nutritional Management

Poor nutrition weakens the immune system and predisposes children to common infections and, for those who are HIV-infected, to OIs.

Both HIV-exposed and -infected children are at increased risk of malnutrition for many reasons:

- Low birth weight
- Inappropriate/suboptimal infant feeding practices
- Poor weaning practices (timeliness, adequacy of foods, hygiene, meal frequency, feeding method)
- Household food insecurity
- Orphaning

HIV-infected children are additionally at risk from:

- Decreased intake because of oral disease (thrush)
- Anorexia associated with illness
- Increased loss of nutrients because of diarrhoea, malabsorption
- Increased metabolism because of HIV infection or other infections
- Inadequate child care, if the mother is sick or deceased

Strategies to prevent malnutrition and promote good nutrition include:

- Providing accurate information and skilled support to mothers and others responsible for feeding infants and young children
- Ensuring adequate nutrient intake based on locally available foods; providing universal (vitamin A) or targeted (e.g., iron, folate, zinc) micronutrient and mineral supplementation
- Providing food fortification and nutrient supplementation for the most vulnerable
- Providing prompt early treatment of common infections and OIs (e.g., candida)

- Ensuring the health and nutritional status of women and other caretakers of infants and young children

Emphasise good personal hygienic practices (e.g., oral, dental, nail, and skin care, and hand-washing and boiling drinking water).

Preventing HIV (from routes other than vertical) is critical for children, particularly those growing up in conditions of hardship imposed by loss of parents; those subject to sexual abuse, war, and conflict; and those adolescents who start sexual activity early in life (see **chapters 3 and 9**).

3. Immunisation

Studies indicate there is impaired passive transfer of maternal antibodies against common infections from HIV-infected mothers to their infants, and there may be impaired response following immunisation with a variety of antigens.

Children who are HIV-infected:

- Are more likely to experience progressive primary TB disease after exposure to TB. The clinician should give BCG at birth to children in Africa because tuberculosis is endemic.
- Experience more frequent episodes of Haemophilus influenza type b infection. Both the conjugate *Haemophilus influenza* and pneumococcal vaccines are effective, even in HIV-positive children, and are recommended in regions where these vaccines are affordable.
- Experience severe forms of disease with measles wild-type virus infection

Therefore, administer childhood immunisations as recommended by national Expanded Programmes on Immunisation (EPI) with the following modifications:

- When considering BCG vaccination at a later age (re-vaccination for no scar or missed earlier vaccination), exclude *symptomatic* HIV infection.
- Do not give yellow fever vaccine to symptomatic HIV-infected children; however, asymptomatic children in endemic areas should receive the vaccine at 9 months of age.
- Although measles vaccine is a live virus, do give it to children, even when symptoms are present, at 6 and 9 months. Studies from Uganda indicate that children experience much more severe disease with wild measles virus, which outweighs the risk of a milder illness from the vaccine.
- HIV-infected children can receive prophylactic measles immunoglobulin (0.5 ml/kg, maximum of 15 ml) within 6 days of exposure.
- Varicella immunoglobulin (0.15ml/kg) is advised within 3 days of exposure if children are exposed to chicken pox.

4. Prophylaxis Against Pneumocystis Pneumonia (PCP)

Pneumocystis pneumonia (PCP) is a significant cause of morbidity and mortality among young infants in Africa. Cotrimoxazole (CTZ) prophylaxis significantly reduces the incidence and severity of PCP. Additional benefits of cotrimoxazole include protection against common bacterial infections, toxoplasmosis, and malaria. A Zambian study recently demonstrated an overall 45% reduction in mortality among HIV-infected children who received cotrimoxazole prophylaxis, regardless of their CD4 count. Because early diagnostic tests (e.g., PCR) are not readily available, all children born to HIV-infected mothers should receive prophylaxis against PCP, at least during the first year of life, or until they are proven to be uninfected (see **Table 4.1**).

Table 4.1. Who Needs PCP Prophylaxis?

- **All** infants born to an HIV-infected mother irrespective of any antiretroviral during pregnancy and labour. Prophylaxis continues until infant is 12 months or is PCR negative or antibody negative whichever comes earlier.
- **All** infants identified as HIV infected during the first year of life by a PCR test or by a clinical diagnosis of HIV infection and a positive antibody test.
- Children older than 12 months, with symptomatic HIV disease or an AIDS-defining illness (WHO stage II and III- see chapter 5) or with CD4 <15% or TLC 1500/mm^3.
- Any child with a history of PCP, should continue with secondary prophylaxis (daily CTZ) for life.

Clinicians should clearly inform HIV-infected mothers at delivery that their children need prophylaxis against PCP starting at 6 weeks of age until it is established that the child is not HIV-infected. A practical way to ensure that mother and other health workers are informed is to make a note on the child's immunisation card at birth stating "Please give cotrimoxazole (5 mg/kg/day orally daily) from 6 weeks of age."

Table 4.2. Dose of Cotrimoxazole for PCP Prophylaxis

Weight of Child (kg)	CTZ tablets 20 mg TMP/100 mg SMX Paediatric strength (120 mg)[1]	CTZ suspension 40 mg TMP/200 SMX/ 5ml (240 mg)[2]	CTZ tablets 80 mg TMP/400 mg SMX Regular strength (480 mg)	CTZ Tablets 160 mg TMP/800 mg SMX Double strength (960 mg)
1–4	1 tab	2.5 ml	¼ tab	–
5–8	2 tabs	5 ml	½ tab	¼ tab
9–16		10 ml	1 tab	½ tab
17–50			2 tabs	1 tab
>50			2 tabs	1 tab

[1] Use other options for children over 9 kilograms
[2] Use regular or double-strength tablets for children over 16 kilograms

Alternative drugs for use if CTZ is contraindicated include:

- **Dapsone**
  - Children >1 month 2 mg/kg/24 hours orally once daily
  - Adults 100 mg/24 hours once daily (or twice daily)

If both CTZ and Dapsone are contraindicated (e.g., in children with G6PD deficiency who get haemolysis with CTZ and Dapsone) then use:

- **Pentamidine** (children >5 years)
  - 4 mg/kg/dose every 2–4 weeks IM/IV
  - 300 mg in 6 ml water via inhalation once monthly
  - Higher dose 45mg/kg/day for age 3–24 months
- **Atovaquone** 30mg/kg/day; higher dose 45mg/kg/day for age 3–24 months

Preventing TB

INH prophylaxis against TB should be given to children less than 5 years old who are exposed to smear-positive TB in their household (HIV-uninfected, -exposed, or -infected) whether the Mantoux test is positive or not. Active disease must be ruled out first. INH for TB prophylaxis is given as a single oral daily dose of 5 mg/kg for 6 months.

5. Treatment of Acute Infections and Other HIV-Related Conditions

HIV-exposed children are susceptible to common infections and OIs. HIV may alter the incidence, presentation, and response to conventional therapy. In some cases more aggressive and longer treatment courses may be necessary, as treatment failures are more frequent. TB must be ruled out as it is prevalent in most African settings (see **chapters 6 and 7**).

6. Regular Follow-up Care and Referrals

Regular follow-up is the backbone to caring for HIV-exposed children and ensures optimal healthcare and psychosocial support to the family. WHO has made recommendations on frequency of follow-up, as shown in **Table 4.3**, below. This is the minimum and more frequent contacts with the health care system are indicated for infected children and especially if they are on anti-retroviral treatment.

Table 4.3. WHO Recommendations for Follow-up of an HIV-Exposed Child

- At birth (for infants delivered at home)
- At age 1 to 2 weeks (mainly for infant feeding counselling)
- At age 6, 10, and 14 weeks (for immunization and infant feeding counselling)
- After age 14 weeks, monthly through age 12 months
- After age 12 months, every 3 months through 24 months
- After 2 years, a minimum of yearly visits
- At 18 months a confirmatory HIV laboratory test should be done (if there are no resources for an earlier antigen-based test)

Many PMTCT programmes lack mechanisms for follow up of HIV-exposed infants. A well-informed mother—who knows that at 6 weeks PCP prophylaxis should begin and that at 18 months the child should receive an HIV antibody test—is the best way to ensure adequate follow up care. A definitive laboratory HIV diagnosis (or clinical AIDS diagnosis) will differentiate a child who is HIV-exposed from a child who is infected.

HIV-infected children over the age of 24 months should be followed yearly if asymptomatic. Symptomatic children should be followed more frequently as needed.

Age	Monitor
6 weeks–12 months	Monthly
12–24 months	Every 3 months
24 months onwards	Yearly if not symptomatic
	If symptomatic, follow up as needed

Referrals

Referrals are an important part of managing an HIV-exposed or -infected child. This includes referrals to:

- Higher levels of specialized care for further investigations and treatment
- Social support programmes
- Community-based care programmes
- VCT sites for parents and siblings

Services Specific for HIV-Infected Children

1. HIV Disease Staging

Disease staging, with or without laboratory support, follows HIV diagnosis. Staging HIV disease provides a guide to the prognosis and interventions needed at the different stages (refer to chapters 5 and 8).

2. ARV Therapy

- Counsel for and provide ARV drugs. Give children ART according to international or national guidelines, which take into account that not all HIV-infected children are eligible for ART (see **chapter 8**).
- In the absence of laboratory confirmation of HIV, provide ARV drugs for HIV- exposed younger infants (less than 18 months, with a positive antibody test) only if there is evidence of immunodeficiency (CD4% < 20% or WHO paediatric stage 3 or 4). See **chapter 8**.
- In all cases where younger infants (<18 months) are started on ARV drugs in the absence of a virologic test, you must perform an antibody test at 18 months to determine whether to continue with ARV drugs.

Strategies to Increase Access to Paediatric ARV Services

Availability of ARV drugs is fairly recent in sub-Saharan Africa. Few clinicians have practical hands-on experience with ART in general,

and even fewer with ART in children. Healthcare providers need practical insights on how to set up a paediatric ART clinic. In general, the following strategies open up access for children:

- Provide services specifically for children (i.e., designated hours/days and/or designated providers) and make sure that potential users (e.g., people living with HIV/AIDS [PLHA] groups, providers who already are providing HIV-related care, and clinicians) know that these children-specific services are available
- Provide subsidies (or free services) for care and treatment for children, thus removing the biggest barrier to care and treatment
- Extend services to children whose parents and guardians are accessing HIV-related care services
- Advocate with interest groups already supporting OVC to integrate clinical care and treatment into their ongoing programmes

Communicating with Care-Provider and Psychosocial Support for the Child, Mother/Caregiver, and Family

An HIV diagnosis in a child has many direct implications for the other family members. MTCT is by far the most common HIV transmission mode to infants (95%) and, in the absence of other risk factors for HIV, assume maternal HIV infection until proven otherwise. Likewise, maternal HIV infection has direct implications for a child's well-being, even if that child is not HIV-infected.

Communicating with the caregiver is an important part of providing care and support to the child. At the earliest opportunity, health workers should discuss with the mother/caregiver the possibility of HIV infection in their child. This requires that health workers develop the skills necessary to effectively and positively provide counselling for women (and their partners), communicate bad news, and provide immediate and ongoing support.

Health workers should ensure that they provide adequate time for caregivers to ask questions so that they can fully understand the im-

plications of HIV and HIV testing, for themselves and for their child. When HIV is suspected in a child, the mother and family should be counselled and offered testing.

Communicating with the caregiver has direct benefits for the family, including:

- Helping the mother adopt a positive living attitude.
- Alerting the health worker to the possibility of treatable HIV-related conditions, such as TB, in the mother/family.
- Offering opportunity for mother/family to access other support services (e.g., peer support groups and post-test clubs), nutritional support, and ART.
- Providing relevant counselling to the mother on infant feeding options, and nutrition for herself and other family members.
- Providing support for mother/father to develop behaviour change to reduce HIV transmission.
- Counselling the mother to confirm the HIV infection status at a later age if the child is still young. This is particularly pertinent for PMTCT programmes, where a follow-up schedule and time point for infant testing must be carefully explained to the mother.

Parents and/or caregivers need to participate in making decisions and planning appropriate care for the child, including decisions about therapy and where the child should receive care. In this respect, health workers must ensure that the family considers the social needs of HIV-infected and -affected children.

In addition to providing practical and emotional support to caregivers, health workers should also deal with other specific issues, such as the importance of positive living and ensuring that the educational and recreational needs of children with HIV are met.

Care of the HIV-infected child should be child-focused, family-centred, and community-based, and the health worker must be aware

that the adolescent child has special considerations of denial, adherence, sexuality, peer pressure, school issues, and other responsibilities (e.g., child-headed families).

Other care and support services that may be available in MCH and family care centres include:

- HIV VCT for the mother, partner, and other children
- Sexual and reproductive health counselling and support, including family planning services
- Prevention and treatment of reproductive tract infections and STIs
- Mental health and psychosocial care and support
- Screening and treatment for TB
- Nutrition care and support services
- Prophylaxis and treatment of HIV-related infections and conditions
- ART for family members who meet treatment criteria

Children Whose Parents/Guardians Have AIDS or Who Are Orphaned by AIDS

Children often feel the impact of HIV/AIDS when their parents are first diagnosed with HIV, long before they become orphans because of AIDS. The poor understanding of the mental, emotional, spiritual, and social needs of children affected by HIV/AIDS has resulted in an extremely limited response to date.

HIV/AIDS-related illness or death in the family leads to:

- Mental, psychological, and social distress in the family and for the child
- Children left without adult love, adequate care, or protection
- Stigma and discrimination
- Exploitative child labour
- Sexual exploitation
- Life on the streets
- Child-headed household
- Withdrawal from, or interruption of, school
- Inadequate food, shelter, or fulfilment of other material needs
- Reduced access to health services

Regardless of which family member is first diagnosed with HIV/AIDS, comprehensive care for an exposed or infected child requires more than health care. The health worker should therefore enlist the early support of other sectors to link orphans and other vulnerable children (OVC) to programmes that provide psychosocial and socio-economic support and HIV prevention activities.

UNAIDS, UNICEF, and USAID provide the following guiding principles to respond to the needs of OVC (see **chapter 11** for details on psychosocial support):

- Strengthen the protection and care of OVC within their extended families and communities
- Strengthen the economic coping capacities of families and communities
- Enhance the capacity of families and communities to respond to the psychosocial needs of OVC and their caregivers
- Link HIV/AIDS prevention activities, care and support for PLHA, and efforts to support OVC
- Focus on the most vulnerable children and communities, not just those orphaned by AIDS
- Give particular attention to the roles of boys and girls and men and women, and address gender discrimination
- Ensure the full involvement of young people as part of the solution
- Strengthen schools and ensure access to education
- Reduce stigma and discrimination
- Accelerate learning and information exchange
- Strengthen partners and partnerships at all levels and build coalitions among key stakeholders
- Ensure that external support strengthens and does not undermine community initiatives and motivation

Knowledge Gaps

There are still critical gaps in the care of HIV-infected children related largely to the psychosocial support of the child:

- What is the best way to disclose HIV status to the child and siblings?
- What is the post-disclosure mental status of these children and how are they best supported?

- Older children (from as early as 5 to 7 years), based on their level of understanding, have communication and psychosocial needs related to their illness and/or that of their family members. What are these needs and how are they best met?
- What is the experience with family models of care to date?

Other gaps are related to the logistics of providing ARV in a poor resource setting. What are the best and most efficient mechanisms simultaneously to scale up ART for children and adults in resource-poor settings?

Additional Reading

Guidelines on HIV-Related Care, Treatment, and Support for HIV-Infected Women and Their Children in Resource-Constrained Settings [Draft for Review. December 2003]. Summary of Key Recommendations of WHO-UNICEF-UNFPA-World Bank-UNAIDS-FHI.

Children on the Brink 2004: A Joint Report on Orphan Estimates and Program Strategies. UNAIDS, UNICEF, USAID, July 2004.

Chapter 5
Diagnosis and Clinical Staging of HIV Infection

Summary

- The magnitude of HIV infection among children in sub-Saharan Africa (SSA) and the rapid progression of the HIV in this age group mean that there is a limited window of opportunity for effective intervention. Specific care and treatment interventions are linked to the certainty of diagnosis.
- Judicious use of clinical criteria and antibody tests can reliably diagnose HIV infection and confirm exposure status in many children in SSA. Every effort must be made to make an early and definitive diagnosis of HIV/AIDS as a first step to specific care, treatment, and support.
- HIV antibody testing continues to be the backbone of laboratory diagnosis, despite its limitation in children aged <18 months (who may still be carrying maternal HIV-specific antibodies).
- More complex (virologic) tests are needed to confirm HIV infection in children under 18 months of age. Particularly in this age group, additional laboratory tests (e.g., CD4 counts and CD4% and total lymphocyte counts) contribute enormously to critical care and treatment decisions.
- Combining clinical and laboratory criteria to stage HIV disease ensures timely and rational initiation of care, treatment, and appropriate counselling.

Introduction

Clinical signs and symptoms are useful parameters in making an HIV diagnosis, but in children clinical features of HIV infection overlap with those of other common childhood diseases (see **Table 5.1**). Clinical features are more reliable in children with severe clinical disease (AIDS).

Accurate diagnosis of paediatric HIV infection depends on laboratory tests, which can be divided into two categories: *antibody* tests, which are relatively easy to perform, provided that routine diagnostic laboratories staffed by qualified personnel are available, and *virologic* tests, which are expensive and involve complex laboratory methods.

Passive transfer of maternal antibodies across the placenta means that babies born to HIV-infected women will have circulating maternal antibodies in their systems up to the age of 18 months. Therefore, for children younger than 18 months, health workers must perform virologic tests, which detect the virus directly, to distinguish reliably the infant's HIV infection status from that of its mother.

If virologic tests are not available to confirm HIV infection, but CD4 cell assays or total lymphocyte counts are available, critical treatment decisions are necessary for infants who are HIV-positive and who have advanced disease (WHO Paediatric Clinical Stage III, see **Table 5.2**).

Breast-feeding may further complicate diagnosis in infants. HIV-exposed infants who are breast-fed are at risk of acquiring HIV infection throughout the breast-feeding period, a factor that must be taken into account when requesting or interpreting HIV test results in children.

Why Is It Important to Make a Diagnosis of HIV Infection?

HIV infection is common among children in sub-Saharan Africa and is a significant contributor to infant and childhood morbidity and mortality, with more than half of the HIV-infected children dying before their second birthday. Timely diagnosis of HIV enables timely

initiation of treatment. Furthermore, age is an important determinant of the rate of disease progression; the disease progresses much faster in infants and children than in adults. Resources for HIV care and treatment are slowly improving for adults in SSA; they must be similarly mobilised for the benefit of HIV-infected children.

Diagnosis of HIV infection facilitates the following:

- Access to currently available effective interventions, which reduce morbidity and mortality associated with infection.
- Access to needed interventions for other affected family members. Diagnosis of HIV in a child is often the first indication of infection among other family members and provides opportunities to provide care, treatment, and support to parents and siblings.
- Access to social and emotional support for the child and family.
- Appropriate healthcare and social welfare planning at the national, regional, and local levels.

Approach to Diagnosis

A rational approach to diagnosis of paediatric HIV infection requires health workers who have a high index of suspicion and are knowledgeable and skilled in diagnosis and management of HIV infection in children. Basic communication skills are essential to enable health workers to discuss and offer HIV testing to children and their parents.

Depending on available resources in a given setting, diagnosis may be

- Clinical (based on signs and symptoms), or
- A combination of clinical and laboratory-supported.

HIV-specific laboratory tests provide a definitive diagnosis, add to the strength of a clinical diagnosis (e.g., by confirming exposure), or can actively aid the exclusion of HIV disease, allowing clinicians to explore other differential diagnoses.

Other laboratory tests such as total lymphocyte count and CD4 count and percentage, provide further supportive evidence of HIV infection and an indication of the degree of immunodeficiency.

HIV/AIDS should be suspected among children with suggestive clinical signs or HIV-associated conditions (see **Table 5.1**). Health workers should extend diagnosis to children born to HIV-infected mothers, those who are sexually assaulted, or those exposed to potentially infectious bodily fluids. If HIV infection is suspected or confirmed, determine the exact clinical stage of disease using one of the two established staging systems (WHO or CDC system).

Clinical Diagnosis

HIV infection presents with conditions that are frequently found in children who are not HIV infected, making it difficult to make a clinical diagnosis. **Table 5.1** groups these conditions according to whether they are common in both HIV-infected children and uninfected children, common in infected children but less common in uninfected children, and whether they are very specific to HIV infection. The occurrence of these clinical signs or conditions may suggest HIV infection in a child and should alert the health worker to obtain other relevant additional history (such as maternal health), and laboratory data where possible.

Table 5.1. Clinical Signs or Conditions in Child That May Suggest HIV Infection	
Specificity for HIV Infection	**Signs/Conditions**
Signs/conditions very specific to HIV infection	• Pneumocystis pneumonia • Oesophageal candidiasis • Extrapulmonary cryptococcosis • Invasive salmonella infection • Lymphoid interstitial pneumonitis • Herpes zoster (shingles) with multi-dermatomal involvement • Kaposi's sarcoma • Lymphoma • Progressive multifocal encephalopathy
Signs/conditions common in HIV-infected children and uncommon in uninfected children	• Severe bacterial infections, particularly if recurrent • Persistent or recurrent oral thrush • Bilateral painless parotid enlargement • Generalized persistent non-inguinal lymphadenopathy • Hepatosplenomegaly (in non-malaria endemic areas) • Persistent and/or recurrent fever • Neurologic dysfunction • Herpes zoster (shingles), single dermatome • Persistent generalized dermatitis unresponsive to treatment
Signs/conditions common in HIV-infected children but also common in ill uninfected children	• Chronic, recurrent otitis with ear discharge • Persistent or recurrent diarrhoea • Severe pneumonia • Tuberculosis • Bronchiectasis • Failure to thrive • Marasmus

Diagnosis Using the IMCI Algorithm

The IMCI guidelines in most countries now include symptoms suggestive of HIV. Three countries (South Africa, Uganda and Ethiopia) have conducted studies on integrating HIV/AIDS into the IMCI algorithm, in which a child is classified as symptomatic HIV if the IMCI practitioner identified *any four* (or any three for South Africa) of the following:

- Recurrent pneumonia
- Oral thrush
- Present or past ear discharge
- Persistent diarrhoea
- Very low weight
- Enlarged lymph nodes
- Parotid enlargement

The studies found that these symptoms and signs have a high specificity but low sensitivity (except for South Africa), meaning that this approach would be very useful in identifying HIV infection when applied to an individual child in a clinical setting. However, because of the low sensitivity, many children would still be missed. Laboratory testing to confirm infection is therefore necessary.

Laboratory Assays (Tests)

Laboratory tests provide suggestive and/or confirmatory evidence of HIV infection. There are two types of laboratory tests:

- **Antibody tests:** HIV ELISA, rapid tests, and Western Blot
- **Virologic tests:** HIV DNA PCR assays, RNA assays including viral load, HIV immune complex-dissociated p24 antigen assays, and HIV peripheral blood mononuclear viral culture

Antibody Tests

Antibody tests are the most widely used HIV diagnostic test and provide reliable evidence of HIV infection in adults and children who are older than 18 months. The HIV antibody test is less reliable in infants aged less than 18 months because they may still be carrying HIV-specific antibodies acquired from the mother in utero. The time it takes for an HIV-positive mother's maternal antibodies to be eliminated from an infant's system (seroreversion) varies. The majority of uninfected non-breast-fed children will serorevert by age 15 months, but a smaller percentage (ranging from a low of 1% to a high of 18% in various studies) will not revert until age 18 months.

Despite these limitations, HIV ELISA and rapid tests are the most widely available tests, and do provide (or exclude) evidence of exposure.

Virologic Tests

HIV Immune Complex Dissociated p24 Antigen Assays

The p24 protein (antigen) is from the core proteins of the HIV virus (see **chapter 2**). Detection of p24 antigen is definitive evidence of HIV infection. The p24 antigen assays use techniques that can be performed in most routine laboratories. In addition, they can be used for diagnosis in children less than 18 months of age. Although the first-generation tests were highly specific, the sensitivity was lower than that of DNA PCR and RNA assays. The newer, ultra-sensitive p24 assays are more reliable, but require further evaluation for their use in infants.

HIV DNA PCR

DNA PCR assays amplify the HIV pro-viral DNA sequences within mononuclear cells present in peripheral blood and the results of such assays are the accepted standard for diagnosis of HIV infection during infancy in developed countries.

The sensitivity of HIV DNA PCR is low during the first 1 to 2 weeks of life because this test is not able to detect very low levels of HIV DNA in babies infected a few minutes/hours/days earlier, during delivery and early breast-feeding. After 4 to 6 weeks of life, the sensitivity and specificity of HIV DNA PCR tests approach 100%, except in babies who have continuing exposure to HIV through breast-feeding.

Some issues are associated with DNA PCR assays. Although the test can be completed within one day, blood samples from a number of patients are often tested in batches to reduce costs, delaying the availability of results for some individuals. HIV DNA PCR tests require specialized laboratory equipment and skilled personnel, and are therefore expensive. Also, samples may become contaminated with HIV DNA from other sources.

New technologies, such as real-time PCR technologies, could provide a good alternative because they are rapid, simple, cheap, and adaptable to the different clades of HIV. Their usefulness is still being evaluated.

HIV RNA Assays

HIV RNA assays detect viral RNA in plasma and other body fluids using a variety of methods (reverse transcriptase PCR, in vitro signal amplification nucleic acid probes [branched chain DNA], and nucleic acid sequence-based amplification [NASBA]).

RNA assays are more widely available than HIV DNA PCR tests, have a faster turnaround time, and require smaller blood volumes. RNA assays are also more sensitive for early detection of infection (first 2 months of life) than HIV DNA PCR tests.

Quantitative RNA (viral load tests) tests are used to determine the risk of HIV disease progression and to guide decisions for initiating ART.

HIV RNA assays require specialized laboratory equipment and skilled personnel and are, therefore, expensive.

HIV Peripheral Blood Mononuclear Viral Culture

The HIV peripheral blood mononuclear viral culture assay was the gold standard of HIV detection in the past, before the development of simpler and less expensive tests based on detection of HIV nucleic acid sequences DNA PCR or RNA PCR assays. This assay has a lower sensitivity than the other tests described above, and must be performed in protected laboratories (also called *P2 labs*). Current use is limited to research laboratories.

Where Laboratory Testing Is Available

Appropriate pre- and post-test counselling should be available and offered (see **chapter 11**). It is also important that health workers offer HIV counselling and testing to parents.

Pre-test counselling should include information about the limitations of the testing approach, the benefits of early diagnosis for the child, and the implications of a positive HIV antibody test results for the family.

Interpretation of Test Results

In children more than 18 months of age:

- HIV infection can be confirmed in those with positive antibody results
- HIV infection can be excluded in those with negative antibody results
- HIV-exposed children who continue to breast-feed should be retested 3 to 6 months after complete cessation of breast-feeding before HIV infection can be excluded

In children less than 18 months of age:

Virologic test available

- A negative test excludes HIV infection
- A positive test confirms HIV infection

Virological tests not available

- HIV infection can be excluded in those with negative antibody results (particularly if they had a previous positive result).
- Diagnose probable HIV infection in those with clinical features and positive antibody results. Confirm the result by repeat antibody testing after the child is more than 18 months of age.
- Retest HIV-exposed children who continue to breast-feed 3 to 6 months after complete cessation of breast-feeding, before HIV infection can be excluded.

In the presence of a clinical diagnosis, one HIV test is adequate to inform management. Children of HIV-infected women who are well and test positive should have a repeat test.

Staging HIV Infection and Disease in Children

Under current guidelines ARV treatment is initiated in patients with AIDS or those with rapidly progressive disease. Staging is a standardized method for assessing disease stage/progression and for making treatment decisions. It is important to stage children with HIV infection because staging:

- Clarifies the prognosis of individual patients
- May strengthen the clinical diagnosis of HIV infection when laboratory testing is unavailable
- Affects the type of treatment interventions, including indications for starting and/or changing ART

Clinical and laboratory parameters are used to stage HIV disease.

There are two international clinical staging systems that classify the severity of HIV infection in children: the U.S. Centers for Disease Control and Prevention (CDC) clinical staging and the WHO Paediatric Clinical Staging.

The CDC Clinical Staging System (**Appendix B**) divides infected children into one of four clinical categories: Category N (asymptomatic), Category A (mildly symptomatic), Category B (moderately symptomatic), and Category C or AIDS (severely symptomatic). Although the CDC staging system is more widely used in relatively advanced paediatric HIV care settings in Africa (e.g., Botswana, South Africa), the recently developed WHO paediatric staging, which relies more on readily identifiable clinical entities, may be more appropriate for the majority of HIV care settings in sub-Saharan Africa.

The WHO Paediatric Clinical Staging System (November 2004) also divides HIV-infected children into four categories.

Table 5.2. WHO Paediatric Staging of HIV/AIDS Disease	
WHO Paediatric Stage 1	• Asymptomatic • Persistent generalised lymphadenopathy (PGL) • Hepatosplenomegaly
WHO Paediatric Stage 2	• Papular pruritic eruptions • Seborrheic dermatitis • Fungal nail infections • Angular chelitis • Lineal gingival erythema • Extensive HPV or molluscum infection (>5% of body area/face) • Recurrent oral ulcerations (>2 episodes/6 mos) • Parotid enlargement • Herpes zoster (>1 episode/12 mos) • Recurrent or chronic upper respiratory infection (URI): otitis media, otorrhea, sinsusitis (>2 episodes/6 mos)
WHO Paediatric Stage 3	• *Unexplained* moderate malnutrition (-2 SD or Z score) not responding to standard therapy • *Unexplained* persistent diarrhoea (>14 days) • *Unexplained* persistent fever (intermittent or constant, >1 mo) • Oral candidasis (outside neonatal period) • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe recurrent presumed bacterial pneumonia (>2 episodes/12 mos) • Acute necrotizing ulcerative gingivitis/periodonitis • Lymphoid interstitial pneumonistis (LIP) • *Unexplained* anemia (<8 gm/dL), neutropenia (<1,000/mm^3), or thrombocytopenia (<30,000/mm^3) for >1 mo. • HIV-related cardiomyopathy • HIV-related nephropathy

Table 5.2. WHO Paediatric Staging of HIV/AIDS Disease	

WHO Paediatric Stage 4	Symptomatic HIV-antibody positive infant age <18 mos*
	• Two or more of the following:
	  • Oral candidiasis/rush
	  • Severe pneumonia
	  • Failure to thrive
	  • Sepsis
	* Presumptive diagnosis of Stage 4 disease in HIV-antibody positive infants <18 mos requires confirmation with HIV virologic tests when possible, or by antibody tests after age 18 mos.

WHO Paediatric Stage 4 (Any Age)	• *Unexplained* severe wasting or severe malnutrition (-3 SD or Z score) not responding to standard therapy • Pneumocystis pneumonia • Recurrent severe bacterial infections (>2 episodes/12mos, *excluding* pneumonia) • Chronic orolabial or cutaneous HSV (lasting >1 mo) • Extrapulmonary tuberculosis • Kaposi's sarcoma • Esophageal candidiasis • CNS toxoplasmosis • Cryptococcal meningitis • Any disseminated endemic mycosis • Cryptosporidiosis or isosporiasis (with diarrhoea >1 mo) • CMV infection of organ other than liver, spleen, lymph nodes (and onset age >1 mo) • Disseminated mycobacterial disease other than tuberculosis • Candida of trachea, bronchi or lungs • Acquired recto-vesico fistula • Cerebral or B cell non-Hodgkins lymphoma • Progressive multifocal leukoencephalopathy (PML) • HIV encephalopathy

Clinical AIDS and /or severe immune suppression define those children who need the most aggressive care and treatment interventions, including ART.

The older (1986) WHO Case Definition of AIDS in Children may be even more familiar to clinicians and health workers in many primary care settings. Despite its recognised weaknesses—it has a low sensitivity (but high specificity)—it is still of value in identifying children needing to be referred for treatment. Because it has a low sensitivity, these criteria may also identify children with primary malnutrition, tuberculosis or post-measles complications as having AIDS.

Table 5.3. 1986 WHO Case Definition of AIDS in Children

Major Signs (presence of at least 2 required):

- Weight loss or abnormally slow growth
- Chronic diarrhoea (>1 month duration)
- Prolonged fever (>1 month duration)
- Severe or recurrent pneumonia

Minor Signs (presence of at least 2 required):

- Generalized lymph node enlargement
- Oropharyngeal candidiasis
- Recurrent common infections (e.g., ear infections, pharyngitis)
- Persistent cough (in the absence of TB disease)
- Generalized rash
- Maternal HIV infection

AIDS is defined as the presence of at least 2 or more major signs and 2 or more minor signs if there are no other causes of immune suppression

Immunologic Staging

The CDC has also developed an immunological staging system based on CD4 counts by age: no evidence of immune suppression, moderate suppression, and severe immune suppression.

Table 5.4. Immunological Classification Based on Total and % CD4 Count

Immunologic Category	Age of Child		
	<12 months	1–5 years	6–12 years
	CD4/µL (%)	CD4/µL (%)	CD4/µL (%)
1: No evidence of suppression	≥1500 (≥25)	≥1000 (≥25)	≥500 (≥25)
2: Evidence of moderate suppression	750–1499 (15–24)	500–999 (15–24)	200–499 (15–24)
3: Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

In the absence of a CD4 count, a total lymphocyte count (TLC) can be substituted. A TLC of <3,500/mm³ for children <18 months, <2,300/mm³ for children 18 months to 6 years, or <1,200/mm³ for children over 6 years is indicative of immunosupression, especially when HIV-related symptoms are present.

Rationalizing Care

After doing diagnosis and staging, a plan for tailored care needs to be developed. It is important to note that *however limited the resources, there is always something to be done for an individual child*. **Table 5.5** provides an overview of how to proceed in different care settings.

Table 5.5. What Can Be Done for Different Levels of Resources and Certainty of Diagnosis?

IF there are:	AND:	THEN:
No laboratory facilities	HIV is suspected from clinical signs	• Monitor growth and development • Provide nutrition care and support • Control infections • Give PCP prophylaxis • Treat opportunistic infections (OIs)
	AIDS is suspected	• Provide all above, plus • Refer for ART
Simple tests (complete blood count) and child is HIV antibody positive	HIV is suspected for <18 months	• Monitor growth and development • Provide nutrition care and support • Control infections • Give PCP prophylaxis • Treat opportunistic infections (OIs) • Re-test at 18 months
	<18 months and has AIDS	• Provide all above, plus provide anti-retroviral therapy (see chapter 8)* • Re-test at 18 months
	HIV is confirmed for >18 months	• Provide all above, plus ART as indicated by clinical stage and CD4 or lymphocyte count
Virologic tests (PCR, p24 antigen tests)	HIV is confirmed	• Provide all above, plus ART where indicated

* Many experienced clinicians would not defer antiretroviral treatment in a young infant who has clinical AIDS and a high probability of mortality. If antiretroviral treatment is begun without a definitive HIV diagnosis, one should be sought at the earliest opportunity, if possible through referral of a dried blot sample to the nearest laboratory with PCR capacity.

Operational Challenges

- Improving access to inexpensive and simpler diagnostic tests for young infants at all levels of the health care system
- Promoting use of widely available HIV antibody tests for infants and children, especially where these are primarily available through VCT service points, which typically exclude child clients
- Improving basic laboratory diagnostics to include complete blood counts (CBC) at primary care levels and, where possible, CD4 counts, tests that are increasingly indispensable in the care of HIV-exposed and -infected infants

Chapter 6
Common Clinical Conditions Associated with HIV

Summary

- Babies are born with an immature and immunologically naïve immune system, predisposing them to an increased frequency of bacterial infections. The immunosuppressive effects of HIV are additive to those of an immature immune system and place HIV-infected infants at particularly high risk of invasive bacterial infections.
- Common childhood infections and conditions are more frequent in HIV-infected children and have a higher case fatality compared to uninfected children. These infections include diarrhoea, acute lower respiratory tract infections, acute suppurative otitis media, sinusitis, and failure to thrive.
- Immunisation and cotrimoxazole prophylaxis significantly decreases the frequency of invasive bacterial infections in HIV-infected children.
- There are few comprehensive studies documenting the etiological cause of infections and death in HIV-infected children in Africa.
- Viral opportunistic infections present significant challenges to management because diagnostic tests and therapies are not readily available.
- Highly active antiretroviral therapy induces immune reconstitution and is the most effective therapy for preventing OIs.
- This chapter addresses the following clinical conditions: diarrhoea, malnutrition, invasive bacterial infections, otitis media, malaria, anaemia, measles, neurological problems, skin conditions, oral, parotitis, persistent generalized lymphadenopathy, malignancies, and renal and cardiac complications of HIV infection.

Introduction

Babies are born with an immature and immunologically naïve immune system, predisposing them to an increased frequency of bacterial infections. Very early in HIV infection, the ability to respond to pathogens and other antigens and the ability of immune systems to recall the memory of past exposure is diminished. In addition, HIV causes a decline in neutrophils. The immunosuppressive effects of HIV are additive to those of an immature immune system and, therefore, the common conditions associated with HIV are frequently infectious in nature.

Common conditions experienced by HIV-infected children are diarrhoea, acute lower respiratory tract infections, septicaemia, acute suppurative otitis media, sinusitis, and failure to thrive. In young infants the earliest clinical signs and symptoms may be non-specific, such as failure to thrive, acute respiratory infections, and diarrhoea.

There are few comprehensive studies documenting the aetiological cause of infections and death in HIV-infected children in Africa. The published studies are frequently cross-sectional in nature and tend to focus on a single clinical condition or they are post-mortem studies biased towards the severest forms of disease, which result in death. It is therefore difficult to obtain a comprehensive picture of the common conditions over the course of HIV infection.

The aetiology of infectious disease changes significantly during the first few years of life, as the infant's immune system matures. Thus, studies on older children do not necessarily reflect events that occur in younger children. A good example is PCP, which is typically found in younger infants.

Diarrhoea

Acute diarrhoea is the most common cause of morbidity and the leading cause of death in HIV-infected children during the first year of life. Diarrhoea in HIV-infected children tends to be prolonged and is usually complicated by dehydration and malnutrition. There is also

an increased frequency of acute diarrhoea in HIV-exposed seronegative children whose mothers have symptomatic HIV or are dead, or following early introduction of complementary feeding

The infectious causes of diarrhoea in HIV-infected children are similar to the common causes in non-infected children. The leading cause of diarrhoea is rotavirus (RV), followed by bacterial causes that include *Enterobacter*, *Escherischia coli*, Shigella, *Salmonella* species, *Camphylobacter jejuni*, *Giardia lamblia*, *Entamoeba histolytica*, and *Candida albicans*. Children with RV infection tend to be younger, with 60–70% less than 1 year of age.

HIV-infected children with RV are more likely to present with respiratory symptoms at admission and are more frequently underweight when compared to uninfected children.

Malnutrition is a common co-morbidity in HIV-infected children, and this complicates their management.

In HIV-infected children, other infectious causes of diarrhoea include AIDS-defining illnesses such as cryptosporidiosis, isosporiasis, CMV infection, and atypical mycobacteria. HIV enteropathy is also a cause of diarrhoea, and *Strongyloides stercoralis*, *Tricuris tricuria*, cryptosporidiosis, atypical mycobacteria and CMV enteritis are commonly found in children with evidence of significant immune suppression. Because of the occurrence of unusual pathogens, healthcare workers should conduct standard stool microscopy and stool culture on all HIV-infected children with diarrhoea.

Persistent diarrhoea occurs with increased frequency in HIV-infected children (particularly those with significant immune suppression and failure to thrive) and infants of women with symptomatic HIV disease. Persistent diarrhoea is associated with a 11-fold increase in risk for death in HIV-infected children when compared to uninfected children. Up to 70% of diarrhoeal deaths in HIV-infected children result from persistent diarrhoea. Prolonged use of antibiotics and

drugs such as nelfinavir and ritonavir and can also contribute to HIV-related diarrhoea.

The principles of management of acute diarrhoea in HIV-infected children are the same as in other children and should follow IMCI guidelines, which include management and correction of dehydration, aggressive nutritional management to minimise the occurrence of persistent diarrhoea, and malnutrition and nutrition counselling, including a review of household hygienic practices, especially handling of the baby's water and food.

In management of acute diarrhoea, health workers should:

- Counsel mothers to begin administering available home fluids immediately upon onset of diarrhoea in a child.
- Treat dehydration with oral rehydration salts (or with an intravenous electrolyte solution in cases of severe dehydration).
- Emphasise continued feeding or increased feeding during and after the diarrhoeal episode.
- Use antibiotics only when appropriate, that is, in the presence of bloody diarrhoea or shigellosis, and abstain from administering anti-diarrhoeal drugs.
- Provide children with 20mg/day of zinc supplementation for 10-14 days (10 mg/day for infants under 6 months old).
- Provide mothers or caregivers two 1-litre packets of oral rehydration salts for home use until diarrhoea stops.

Source: WHO/UNICEF Joint Statement on Clinical Management of Acute Diarrhoea, May 2004

Management of Persistent Diarrhoea

- Manage as acute diarrhoea (see **box above**), including continued feeding and zinc supplementation.
- Examine child for non-intestinal infections and treat as appropriate.

Children with persistent diarrhoea should be managed as in-patients using the IMCI guidelines for the management of children with severe malnutrition: correct the hydration status and any electrolyte imbalances, take measures to prevent hypothermia and hypoglycae-

mia, and, where possible, conduct a full septic screen (blood, urine, and stool cultures, CXR, and CBC, as well as blood urea, electrolytes, and blood sugar estimation). Children with persistent diarrhoea should receive empiric broad-spectrum antibiotic cover according to national IMCI guidelines.

Malnutrition

Childhood malnutrition is high among HIV-infected children and the magnitude is even higher in developing countries, where it is already endemic.

HIV-infected children are at increased risk of malnutrition for many reasons, including:

- Decreased food intake because of anorexia associated with illness, mouth ulcers, oral thrush
- Increased nutrient loss resulting from malabsorption, diarrhoea, HIV enteropathy
- Increased metabolic rate because of infections, OIs, and the HIV infection itself

Release of cytokines (TNF alpha, cachetin) into plasma or tissues may mediate weight loss in HIV-infected children.

The effects of malnutrition are compounded by the high burden and recurring infections and infestations in HIV-infected children. In addition, HIV-positive mothers have higher rates of low-birth-weight babies and premature birth, which are risk factors for malnutrition.

Characteristics of HIV-infected children associated with malnutrition include:

- Micronutrient deficiencies (low serum levels of zinc, selenium, vitamins, A, E, B6, B12 and C) are common among HIV-infected children, reduce immunity, and predispose them to more infections and worsening nutritional status

- Characteristically, deviations in linear growth and weight are apparent as early as 3 months of age in HIV-infected children.
- Stunting or low height for age is more prominent than wasting
- Malnutrition and cachexia are characteristic symptoms of AIDS

The clinical presentation of diseases in HIV-infected children is similar to that in HIV-negative children. However, marasmus is more common than kwashiorkor among HIV-infected children.

Clinical indicators of malnutrition in HIV-infected children are listed below, and any one of these can be used, depending on the resources available to the clinician:

- Weight or weight-for-height less than 90% of the National Center for Health Statistics (NCHS) median
- Weight for height < 5%
- Serum albumin < 3 gm/dL

Children with severe malnutrition must be admitted for in-patient care. The presence of any of the following features, which are significantly correlated with increased mortality, is an indication for admission (weight-for-age is not a good indicator of the child at risk of death).

- Weight for height less than 70% of the NCHS median
- Bipedal oedema
- Visible wasting

On admission, clinicians should:

1. Assess for dehydration and ensure good hydration

- Oral hydration is the preferred method, with intravenous (IV) hydration for children with signs of impending shock.

- For oral hydration use a solution that has lower amounts of sodium and higher amounts of potassium compared to the WHO standard rehydration salts.
- For IV rehydration use Ringer's Lactate solution with 5% glucose, half-strength normal saline with 5% glucose, or half-strength Darrow's solution with 5% dextrose. Give this as 15 mls/kg over 1 hour and possibly repeat if there is a good response.

2. Prevent and treat hypoglycaemia

- Treat all children admitted with severe malnutrition presumptively for hypoglycaemia by giving a bolus of intravenous 10% dextrose (5 ml/kg), followed by 50 ml of 10% dextrose by nasogastric tube. To prevent hypoglycaemia, feed the child every 3 hours with a high calorie liquid diet. In the initial resuscitative stage, give it orally or by nasogastric tube if the child is taking poorly. To avoid metabolic stress, do not give the child too much food during the first few days. During the recovery phase, increase the calorie and protein content up to 3 to 4 gm/kg body weight per day to achieve weight gain of approximately 100 gm/day.
- Initiate micronutrient supplements other than iron immediately at a dose of 200% the normal RDA. Micronutrients include vitamins, potassium, magnesium, zinc, copper, selenium, and iodide. Initiate iron supplementation after the child's appetite improves and infections have been treated.

3. Evaluate for the presence of infections

- Investigate the patient for occult infections. Laboratory investigations should include a complete blood count (CBC), liver function tests, stools and urine microscopy and culture and sensitivity, and a chest x-ray to look for evidence of TB. Centres with more advanced laboratories may measure pancreatic enzyme levels and/or carry out an upper gastrointestinal tract series and endoscopy.

- Presumptive antibiotic therapy: Characteristics of infection in the severely cachexic/ malnourished child are lethargy, hypothermia, hypoglycaemia, inability to feed, or looking sick. Treat the severely malnourished child presumptively with broad-spectrum antibiotics for the first 7 days of admission.

Full recovery occurs when a child achieves weight-for-height that is 90% of the median. The health resources in many sub-Saharan Africa settings do not allow for the prolonged admission of malnourished children. Children can be discharged once they have achieved >10 gm/day weight gain, are taking a solid diet, have a good appetite, show no oedema, and the mother is the primary care provider.

After returning home, the child should be fed at least five times per day, with the usual home foods modified to contain approximately 460 kilojoules and 2 to 3 gm/kg proteins per 100 gm of food. High-energy snacks should be given between meals along with electrolyte supplements.

Invasive Bacterial Infections

Invasive bacterial infections occurring with greater frequency and severity are one of the early manifestations of HIV disease in children. Common infections include bacterial pneumonia (see **chapter 7** for discussion of pneumonia), meningitis, and sepsis. Aetiology and clinical presentations may be similar to those in other children but the presence of occult infections is more frequent. Fever (axillary temperatures >37.5C) may be the only symptom of serious infections. HIV-infected children with fever therefore need careful clinical and laboratory assessment to identify the cause of fever. The treatment of infections in HIV-infected children is the same as in other children. However, recovery in HIV-infected children is often slower and treatment failures are more frequent. Presumptive treatment for these conditions should be according to age-appropriate local recommendations and should consist of broad-spectrum antibiotics (penicillin and an aminoglycoside). Treatment for malaria should also be included in malaria endemic areas.

Otitis Media

Ear infection is one of most common infections in HIV-infected children. Acute otitis media refers to ear infections that have lasted for less than 14 days. Suppurative otitis media is more common in infected children in the first year of life. By age 3 years, most HIV-infected children will have had one or more episodes of acute otitis media. Signs and symptoms are similar to those in other children and include ear pain, pulling on the ears, excessive crying, ear discharge, and irritability. At otoscopy the eardrum is hyperaemic bulging and immobile and there may be perforation. Management includes ear wicking 8 hourly when there is discharge and appropriate antibiotic cover.

Chronic suppurative otitis media occurs with increased frequency in HIV-infected children and is associated with chronic ear discharge, which is usually painless, and a perforated eardrum. Frequent ear wicking is the main mode of management; additionally you may syringe the ear using dilute vinegar 1 ml to 4 mls of clean water and instillation of antibiotics. It is preferable that experienced ENT practitioners do the ear syringing.

Malaria

Malaria is a major cause of morbidity and mortality in most countries of sub-Saharan Africa. Infants born to HIV-infected women are more likely to suffer from congenital malaria than children born to uninfected women. Likewise, an increased frequency of malaria has been noted in HIV-infected children, with associated higher levels of parasitaemia than in other children. Additionally HIV-infected children are more likely to be anaemic during an episode of malaria compared to uninfected children.

Clinical presentation and response to treatment is similar to uninfected children and treatment recommendations should follow the guidelines provided by the national malaria programme.

Because in many areas it will not be possible to differentiate cerebral malaria and meningitis at admission, you should treat all children

in malaria endemic areas with a presumptive diagnosis of cerebral malaria presumptively for bacterial meningitis. This is particularly relevant for HIV-infected children who have increased frequency of both conditions.

Prevention: Take standard measures for preventing malaria in HIV-infected children living in endemic areas (wearing long sleeves and pants in the evenings, impregnated mosquito nets, and topical insect repellents with DEET, as long as child does not have dermatitis or other skin problems).

Anaemia

Anaemia is a common condition in HIV-infected children and contributes significantly to morbidity. The prevalence of anaemia in HIV-infected infants is determined to a large extent by the prevalence of other conditions that cause anaemia, such as malaria and helminthic infections. The prevalence of malnutrition, and especially micronutrient malnutrition, also contributes significantly to the prevalence of anaemia.

HIV-infected children have an equal prevalence of anaemia compared to uninfected children but have a higher case fatality rate. A study in Abidjan found an equal frequency of anaemia in HIV-infected and uninfected children. In the same study, the case fatality rate (CFR) from anaemia was 13% in HIV-infected children (third commonest cause of death) compared to a CFR of 8% in uninfected children (fifth commonest cause of death).

Measles

Measles is one of the major causes of morbidity and mortality in sub-Saharan Africa and is a severe illness in children with HIV infection, particularly those with advanced immunodeficiency. Severe cases can occur without the typical rash and may be complicated by pneumonia or encephalitis. HIV-infected children with measles have a high case fatality and should be treated in hospital. Management should include 2 doses of vitamin A, calculated on the basis of the child's age

(50,000 IU if aged <6 months; 200,000 IU in children aged 12 months to 1 year).

Measles may occur in early infancy in HIV-infected children because of inadequate transfer of maternal antibodies and infection may occur despite history of immunisation.

Give measles immunisation to HIV-infected children at 6 months and repeat at 9 months.

Neurological Manifestations

HIV is a neurotropic virus that invades the central nervous system by infecting monocytes, which cross the blood-brain barrier and establish HIV infection in microphages and microglial cells. Neurological symptoms are widely prevalent, occurring at all stages of HIV infection and affecting any part of the nervous system. It is estimated that 40% to 70% of HIV-infected persons develop symptomatic neurological disturbances, but the brain is most commonly affected in children.

Neurological manifestations are some of the most common modes of presentation of HIV/AIDS, but they are infrequently diagnosed in children. Delay in reaching developmental milestones, in particular, may be an early indication of HIV infection in HIV-exposed children. In general, however, neurological manifestations, especially peripheral neuropathy (and especially in children) are not considered, may be difficult to diagnose, and even when diagnosed, are inadequately managed. Encephalopathy and developmental delay are common in HIV-infected children and indicate advanced clinical disease.

ART is possibly the only way to reverse the effects of HIV infection on the CNS and allow restoration of growth, development, and milestones. However, ART and other medications used in the treatment can also have neurological side effects, the most common of which is peripheral neuropathy.

HIV Encephalopathy

Growth and development of the brain is outwardly manifested by achievement of childhood milestones (smiling, walking, talking, etc.). HIV infection of the brain interferes with this process and manifests as static, slowing, or regression of developmental milestones or as localized damage. This whole process is referred to as HIV encephalopathy.

HIV encephalopathy has been reported to be about 21% in HIV-infected African children. Age of onset of developmental delay is unpredictable, but the onset of encephalopathy may be related to the presence of other symptoms of HIV disease (e.g., hepatosplenomegaly and lymphadenopathy).

Diagnosis

Diagnosis is mainly clinical and depends on the presence of least two of the following for at least 2 months:

- Failure to attain or loss of developmental milestones or loss of intellectual ability
- Impaired brain growth or acquired microcephaly
- Acquired symmetrical motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbances
- Cerebrospinal fluid is normal or has non-specific findings and CT scan shows diffuse brain atrophy.

Management

Managing encephalopathy should include evaluating the child with the help of a neurologist, if possible. If nothing other than HIV is found, the treatment goal is to reduce viral load. Depending on the severity, the patient will need a support system, which includes physical therapy, a social worker, and surgery to minimise contractures.

Other Neurological Manifestations

Neuropathy

Several types of peripheral neuropathy affecting single or multiple nerves have been documented (e.g., axonal neuropathy, demyelinated neuropathy, polyradiculopathy, and radiculopathy). HIV-related neuropathy is a troublesome condition that occurs in as many as one-third of patients with a CD4 count < 200/μL. It presents with dysaethesias and numbness in a "glove and stocking" distribution.

Neuropathy in children is more difficult to diagnose and less well described than in adults. Diagnosis is based on clinical presentations such as pain or numbness that has a "glove and stocking" distribution.

Treatment is mainly symptomatic. Pain due to neuropathies may respond to analgesics combined with amitriptylne, carbamezapine, and lamotrigine. Use morphine in end-stage disease.

Seizures

Seizures are common non-specific manifestations of neurological illnesses associated with HIV. Seizures may result from:

- Space-occupying lesions (most often cerebral toxoplasmosis or tuberculoma)
- Meningitis (most often cryptococcal)
- Metabolic disturbances
- No identified cause other than HIV infection

Treatment is aimed at the underlying disorder and seizure control through standard anti-epileptic medication. Drug interactions may be a problem for patients on HAART; for those on HAART the drug of choice is valproate.

For patients presenting with focal seizures, consider treatment for toxoplasmosis, if no other cause is apparent.

Opportunistic Infections

CNS OIs are seen in cases of severe immunosuppression (CD4 <200/μL) in older children and adolescents (**Table 6.1**).

The most common OI in children is, reportedly, CMV infection. Other viruses, especially herpes simplex and varicella-zoster virus, can also cause acute encephalitis.

Fungal infections, particularly candida and aspergillus meningitis, are reported to be the second most common infection in children.

Cryptococcal meningitis is rarely seen in young children with AIDS, but has been reported among older children and adolescents. Toxoplasma encephalitis has rarely been reported in older paediatric patients.

Table 6.1. Opportunistic Infections of the Central Nervous System

Neurological Disease	Clinical Presentation	Diagnostic Tests	Management
Cytomegalo-virus	• Presents with encephalitis with retinitis, radiculomylitis, or neuritis	CSF, PCR, MRI, if available	Intravenous ganciclovir 10mg/kg per day in 2 divided doses for 2 to 3 weeks. Foscarnet 180mg/kg/day in 3 divided doses for 14 to 21 days may be used when there is sight threatening CMV retinitis.
Cryptococcus	• Presents with fever, headache, seizures, change in mental status • Focal neurological signs uncommon	CSF-Indian ink positive Cryptococcal antigen test, MRI, if available	Induction with amphotericin B (0.7–1.0 mg/kg/day) for 2 weeks followed by fluconazole 400mg/day for a minimum of 10 weeks, then 200mg/kg maintenance therapy.
Toxoplasmosis	• Most common manifestations are encephalitis, mental changes, fever headache, and confusion.	Serology, MRI, if available Do not do lumbar puncture if there is mass lesion.	Pyrimethamine loading dose 2 mg/kg/day (max 50 mg) for 2 days then maintenance, 1 mg/kg/day (max 25mg) plus sulphadiazine 50 mg/kg every 12-hours/folinic acid 5–20 mg 3 times weekly. Treat until 1–2 weeks beyond resolution of signs and symptoms.
***Herpes simplex* virus**	• Associated with fever-altered state of consciousness, personality changes, convulsions, and usually focal neurological signs, particularly temporal lobe signs	Rising serum HSV titres and increased ratio of CSF-to-serum concentration of HSV antibody Viral isolation	IV Acyclovir 20mg/kg given 3 times a day for 21 days.

Dermatitis and Other Skin Manifestations

The most common skin manifestation of HIV/AIDS in children is a non-specific generalized dermatitis. Other skin lesions are secondary infections and the frequency is related to the severity of immune suppression. Viral, bacterial, and fungal skin infections are more common, but also more difficult to treat than in children who are not immunocompromised. Treatments for some common skin manifestations are shown in **Table 6.2**.

Other non-infectious manifestations include:

- Seborrhic dermatitis
- Atopic dermatitis
- Eczema
- Psoariasis
- Drug eruptions
- Skin lesions associated with nutritional deficiency (more prevalent in children than in adults; drug eruptions are lower in children than in adults; cotrimoxazole can cause reaction in children who are immunocompromised)

Table 6.2. Common Skin Manifestations and Treatments	
Skin Manifestation	**Treatment**
Scabies Treatment **Children <1yr**	• 25% benzyl benzoate for 12 hours or gamma benzene hexachloride • 2.5% sulphur ointment 3x daily for 3 days • Screen and treat other household contacts where appropriate • Wash and iron bedding and clothing or hang it out in the sun
Eczema Treatment	• Avoid soap and expose affected areas to sunlight • Use aqueous cream instead of soap for washing; use moisturizer on dry areas • Apply zinc oxide cream 2x daily; if not responding, use 1% hydrocortisone cream 2x daily • Cut nails short
Ringworm Treatment	• Apply Whitfield's ointment (benzoic acid with salicylic acid) 2x daily for 2 to 5 weeks for body lesions; if not successful try 2% miconazole cream • For scalp lesions give griseofulvin 10m/kg/day for 8 weeks; if not responding consider ketoconazole
***Herpes zoster* Prophylaxis**	• Hospitalise all cases and treat, if possible, with IV acyclovir 30mg/kg/day divided into doses every 8 hours for a total of 7 days or 2 days after cessation of new lesion formation, whichever is longer • Children who have been exposed to herpes zoster may receive prophylaxis using varicella-zoster immune globulin (VZIG) 125U per 10 kg (max 625U) within 48–96 hours of exposure.
***Herpes simplex* Treatment**	• Local antiseptic (gentian violet) • Analgesia (paracetamol) • Admit all children with disseminated or severe herpes simplex and give acyclovir 5mg/kg intravenously 3 times a day or 200–400mg orally 5 times a day, for 7–10 days.
Impetigo Treatment	• Hygiene, proper washing, cut fingernails, soak crusts off in soapy water • Apply 10% iodine solution 3x daily or zinc oxide cream • Antibiotics indicated only if pyrexial, lymphadenopathy, or lesions are resistant to treatment (first-line = amoxycillin for 10 days; second-line = flocloxacillin or erythromycin for 10 days)

Oral and Dental Conditions

Oral and dental conditions are also common in HIV-infected children, particularly those who are malnourished. Therefore, good dental hygiene is important. The most common oral condition in HIV-infected children is candidiasis, which may present as oropharyngeal or oesophageal candidiasis. Oral thrush is predictive of HIV infection if seen after the neonatal period without prior antibiotic treatment, if lasting for more than 30 days, or if it is recurrent. Oral thrush is associated with difficulty or pain in swallowing or vomiting. Children therefore present with reluctance to take food, excessive salivation, or crying while feeding. Exclude other conditions that cause painful swallowing and are frequently found in HIV-infected children such as CMV, *Herpes simplex*, and lymphomas.

Treatment of Candidiasis

Oral Candidiasis

- Nystatin 1–2 million U/day divided every 6 hours until resolution

Oesophageal Candidiasis

- Fluconazole 3–6 mg/kg once daily or
- Amphotericin B, 0.3mg/kg/day

Other common dental conditions of HIV-infected children include:

- Dental caries
- Aphthous ulceration (*Herpes simplex*-related ulcer; if diagnosed early it will be amenable to acyclovir)
- Oral hairy leukoplakia
- Angular stomatitis
- HIV-associated gingivitis

Malignancy

The major malignancies associated with HIV infection in African children are Kaposi's sarcoma (KS) and non-Hodgkin's disease lymphoma (Burkitt's lymphoma, B-cell lymphoma). B-cell lymphoma is more prevalent in South Africa than Burkitt's lymphoma. Clinical experience indicates that the frequency of occurrence of some malignancies is increasing.

Kaposi's Sarcoma

Before the HIV pandemic, KS was rare in children, and adults tended to have the less aggressive endemic type. Currently, KS is more prevalent in East and Central Africa and less prevalent in West and South Africa.

KS can present as early as the first month of life. KS is associated with human herpes virus 8 and usually presents as generalised lymphadenopathy, black/purple mucocutaneous lesions (skin, eye, and mouth); the chest lesions may mimic those of TB.

Diagnosis is confirmed by biopsy of the lesion and histological examination. Treatment requires chemotherapy and radiotherapy, but ART also often leads to regression of the lesions.

Parotid Enlargement

Bilateral parotid gland enlargement is one of the most specific signs of HIV infection in children. Parotid enlargement is usually not tender and is commonly found in older children who are slow progressors; it may be associated with lymphoid interstitial pneumonitis. When parotid enlargement is exceptionally large, it may be disfiguring and lead children to be teased and/or emotionally distressed.

Periodically the parotid glands may enlarge and regress over several months, and intermittently they may become tender from bacterial super-infection. When they are tender, prescribe antibiotics and analgesics. There should be no surgery.

Persistent Generalised Lymphadenopathy

Persistent generalised lymphadenopathy is one of the most common early clinical presentations of HIV-infected children. It may also be associated with other parotid enlargement or hepatosplenomegaly. A biopsy may show non-specific inflammation of the nodes. It is important to remember that disseminated TB, Kaposi's sarcoma (KS), and leukaemia can also present with generalised lymphadenopathy. Other causes include acute toxoplasmosis, rubella, CMV, herpes, and syphilis.

Other Medical Conditions

Cardiac Disease and HIV

Studies from developed countries indicate that most HIV-infected children referred for cardiovascular assessment were found to have abnormalities that were often clinically non-apparent. Few similar studies have been reported for African children. One such study, in Uganda, involved 230 symptomatic HIV-infected children. Of these, 51% had abnormal echocardiographic changes. One-quarter of those with abnormal echocardiographic changes had cardiovascular symptoms. Therefore, clinicians should evaluate HIV-infected children for cardiovascular symptoms and manage appropriately (Lubega, unpublished data).

Renal Disease

Focal segmental glomerulopathy has been reported in up to 15% of U.S. patients. Focal segmental glomerular sclerosis was the most typical lesion associated with HIV. Such patients may present with proteinuria and haematuria. African data are lacking. Although randomised trials have not been performed, prednisone and sometimes ACE inhibitors may be useful.

Knowledge Gaps

- There are few comprehensive studies documenting the etiological cause of infections and death in HIV-infected children in Africa.

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Chapter 7
Pulmonary Conditions

SUMMARY

- Pneumonia is the leading cause of hospital admissions and death in HIV-infected children. Recurrent episodes of pneumonia suggest immune suppression, but this should be investigated further to exclude other conditions such as TB, foreign body, and lymphoid interstitial pneumonitis.
- In children less than 1 year, consider PCP a possible cause of severe pneumonia. Treat infants with severe pneumonia in areas of high HIV prevalence presumptively for PCP, until it is excluded or they are HIV antibody negative.
- PCP in an infant may be the first AIDS-defining condition in the child and an indication of HIV infection in the family. Therefore efforts should be made to provide counselling and testing for HIV for the mother and the family. All HIV-exposed children should receive prophylaxis against PCP from 6 weeks of age until it is established that the child is not HIV-infected.
- All HIV-exposed children should receive prophylaxis against PCP from 6 weeks of age until it is established that the child is not HIV-infected.
- Children who are co-infected with HIV and TB experience higher case fatality and it is important to look actively for TB in children with chronic cough and provide treatment as early as possible.
- Lymphoid interstitial pneumonitis (LIP), is common in children (about 40% with perinatally acquired HIV), is diagnosed by exclusion, and is often mistaken for miliary pulmonary TB because of chronic cough and *miliary-like* pattern on chest x-ray.

Introduction

Pneumonia and chronic lung diseases contribute to the increased morbidity and mortality of HIV-infected children. Most children present with recurrent bacterial pneumonias, but in children less than 1 year of age PCP also contributes to the high infant mortality. The incidence of TB in children depends on the prevalence of TB in the adult community, and other HIV-related chronic lung diseases often have a similar clinical presentation leading to over diagnosis of TB.

In treatment of different pulmonary conditions, it is important to remember that the standard therapy may need to be adjusted by increasing the length of treatment, using different antibiotics, and/or providing prophylaxis.

The different pulmonary conditions may be difficult to differentiate from each other and are often fatal in the immune-compromised child. The most common include:

1. Bacterial pneumonia
2. Pneumocystis pneumonia (PCP)
3. Tuberculosis
4. Lymphoid interstitial pneumonitis (LIP)
5. Bronchiectasis
6. Viral pneumonitis

1. Bacterial Pneumonia

Pneumonia is the leading cause of hospital admissions and death in HIV-infected children. It is also the most common pulmonary condition and presents the same way in both infected and uninfected children.

Streptococcus pneumoniae is the most common pathogen isolated in both HIV-infected and -uninfected children. Other organisms include *H. influenzae*, *Klebsiella*, *Staphlococcus aureus*, and enteric gram

negatives (*E. coli*, *Enterobacter*, *Salmonella*, *Citrobacter*, *Proteus*, and *Pseudomonas*). These bacteria generally colonize the nasopharynx before the child develops pneumonia.

Recurrent bacterial pneumonia suggests immune suppression (CDC class C, WHO stage 3, see **chapter 8**). Recurrent pneumonia should be investigated further to exclude other conditions such as tuberculosis, foreign body, bronchiectasis, LIP, and fungal pneumonias.

Clinical Presentation

Clinical presentation of pneumonia includes the following:

- History of fever, cough, and fast breathing (tachypnoea) with or without chest in-drawing (retractions), cyanosis, and lethargy
- On auscultation may hear crepitations, decreased breath sounds, or bronchial breathing (lobar pneumonia)
- When pulse oximetry is available, persistent hypoxia is demonstrated (oxygen [O_2] saturation less than 90%)

Diagnosis

Diagnosis of pneumonia is purely on clinical grounds (see **immediately above**). However some laboratory tests may help in pointing towards an aetiological agent.

- An increased white blood count (WBC) with a neutrophilia (granulocytosis) suggests bacterial pneumonia and growth on blood cultures (bacteraemia) may result from the causative organism.
- A chest x-ray is not necessary for diagnosis of acute pneumonia, but it may be done if there is poor response to appropriate treatment or when suspecting TB, foreign body, or tumour.
- Because symptoms of pneumonia and those of malaria often overlap, a blood smear for malaria parasites should be done in endemic areas.

Managing Bacterial Pneumonia

Outpatient Management (*for mild pneumonia*)

The management of pneumonia should follow the recommended national guidelines or IMCI guidelines. If there are no guidelines, or you are not aware of them, use the following:

- Oral amoxycillin or penicillin is adequate.
- Cotrimoxazole (CTZ) may be used as first-line therapy for outpatient pneumonia.
- If a child is already on CTZ prophylaxis, CTZ should not be used to treat pneumonia unless PCP is suspected. If PCP is suspected, then use a high dose of CTZ (see **management of PCP below**).
- Analgesics/antipyretics (e.g., paracetamol 15 mg/kg/dose every 6 to 8 hours) should be prescribed for fever and pain.
- Avoid using aspirin to treat children.
- If a child has recurrent pneumonia (more than three times in one year), the child should be investigated further to rule out TB, foreign body, or chronic lung disease.

Managing Severe Pneumonia

Severe pneumonia should be managed in a hospital or other inpatient facility and should include both supportive and specific therapy.

Supportive Care

Supportive care of severe pneumonia includes the following considerations:

- Use supplemental oxygen when a child presents with chest indrawing, cyanosis, and/or hypoxia.
- Correct severe anaemia (Hb <5 g/dL) by transfusion with packed red blood cells.

- Ensure adequate oral hydration and monitor fluid input and output (I/O chart). If respiratory distress is severe, pass an N/G tube and give food in small volumes to avoid aspiration during feeding. You may use IV fluids cautiously to avoid fluid overload, if the child is vomiting.
- Provide an analgesic (paracetamol) for fever and pain (avoid aspirin).
- Provide Vitamin A supplementation if the child has not received vitamin A in the last 3 months.

Specific Therapy

The specific antibiotic therapy depends on the sensitivity pattern of the common organisms in the region. However, if unknown, the recommended therapy is:

- First-line antibiotics include intravenous Chloramphenicol or Ceftriaxone/Cefotaxime, if available
- Alternatives include Ampicillin/Cloxacillin *plus* Gentamicin if cephalosporins are not available and there is a high level of resistance to chloramphenicol.

Other Considerations

Other considerations for treating pneumonia in children include the following:

- In children less than 1 year of age, clinicians must consider PCP a possible cause of severe pneumonia and treat accordingly (see **below**).
- If pneumonia is associated with typical *staphylococcal* skin lesions (e.g,. bullae), chest x-ray with pneumatoceles, a positive blood culture for staphylococcus (not contaminant), post measles, or with poor response to first-line antibiotics, then you must consider staphylococcal pneumonia and add cloxacillin or vancomycin to the treatment.

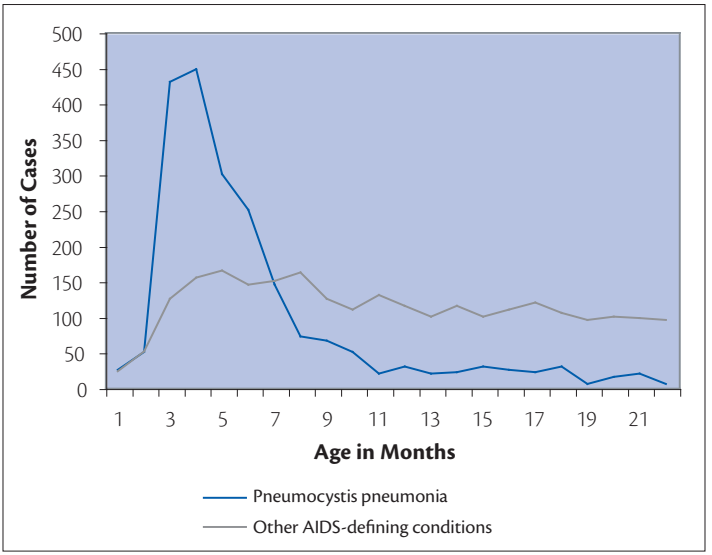
- If you suspect enteric gram negatives, then add Gentamicin or Ceftazidime to the regimen, if available. Suspect enteric gram negatives if the child has had repeated hospitalisations or repeated pneumonia with consolidation in the same lobe, poor response to first-line antibiotics, green mucoid sputum, underlying bronchiectasis, or chronic lung disease.

2. Pneumocystis Pneumonia

Pneumocystis pneumonia (PCP) is caused by a fungus called *pneumocyctis jiroveci (*formerly called *pneumocystis carinii).* PCP is a major cause of severe pneumonia (15–30%) and death (30–50%) in HIV-infected infants. Infants are usually in a good nutritional state and may not have clinical features that indicate the presence of HIV/AIDS.

The incidence of PCP is highest during the first year of life and usually peaks at 3 to 6 months of age. It can occur after 1 year of age, but with decreasing frequency. **Figure 7.1** below, although from the United States, probably reflects similar occurrence in Africa.

Figure 7.1. Threat of PCP: AIDS-Defining Conditions by Age at Diagnosis Perinatally-Acquired AIDS Cases through 1992, USA



Source: Prophylaxis against Pneumocystis carinii pneumonia among children with perinatally acquired human immunodeficiency virus infection in the United States. Pneumocystis carinii Pneumonia Prophylaxis Working Group, N Engl J Med, 1995. March 23:332(12):786-90.

Clinical Features of PCP

Clinical features of PCP in children include the following:

- Low-grade fever or afebrile
- Marked respiratory distress (chest in-drawing, cyanosis, inability to drink)
- Auscultation: clear chest or diffuse fine crepitations
- Poor response to standard antibiotic treatment
- Pulse oximetry: severe persistent hypoxia (paO_2 <90%)

- Occasionally, associated HIV symptoms include oral thrush, lymphadenopathy, and/or weight loss

Investigations

Sputum induction with nasophyaryngeal aspirates or bronchoalveolar lavage may help in diagnosing PCP. There are no radiological changes specific to PCP.

In cases where a definitive diagnosis of PCP cannot be made, but where there is a high index of suspicion of PCP, therapy must be initiated promptly, along with treatment for bacterial pneumonia.

Management of PCP

Management of PCP is both supportive and specific. In supportive management of PCP:

- Provide oxygen therapy
- Maintain and monitor hydration
- Provide paracetamol for pain
- Continue therapy for bacterial pneumonia

For specific management of PCP:

- Give intravenous high dose cotrimoxazole (CTZ) 20 mg/kg of trimethoprim per day OR 80 mg/kg/day of sulphamesoxazole given every 6 hours for 21 days. Give the same dose orally if IV preparations are not available.
- Add prednisone at 2 mg/kg/day for 7 to 14 day if child is in severe respiratory distress (taper if treatment >7days).

Follow-Up

After an acute episode of PCP, provide daily cotrimoxazole 10 mg/kg/day of TMP orally. This secondary prophylaxis is life-long.

PCP may be the first AIDS-defining illness in the child and the first indication of HIV infection within the family. Therefore, efforts must

be made to provide counselling and testing for HIV for the mother and the family. If the mother or another family member is identified as HIV-infected, refer to appropriate services for ongoing care and support.

Chronic Lung Disease

The primary causes of chronic lung disease are TB, LIP, bronchiectasis, and pulmonary Kaposi's sarcoma or lymphoma.

3. Tuberculosis

TB and HIV Co-Infection

The HIV pandemic has led to a resurgence of TB in both adults and children, and the burden of TB in children depends on the burden of the disease in the adult population.

Children also have an increased risk of developing primary progressive TB because of the associated severe immune suppression resulting from their young age and HIV. Extrapulmonary TB is seen more often in HIV-infected children.

There is a higher case fatality rate for children who are co-infected with TB and HIV. It is important to look actively for TB in children with a chronic cough and to provide treatment as early as possible.

The reported seroprevalence of HIV in children with TB ranges from 10 to 60%. The highest prevalence of HIV infection in children with TB has been reported in Southern Africa, the lowest prevalence in West Africa. In autopsy studies, the prevalence of TB seemed to be much less, but this may have been the result of selection bias in the studies.

Diagnosing TB in children was difficult even before the HIV/AIDS pandemic; now it is more difficult because an HIV-positive child may have many other pulmonary conditions and HIV-related chronic lung diseases that mimic the symptoms of TB.

Clinical Diagnosis

Table 7.1 below shows the evaluation of a child suspected to have TB.

Table 7.1. Evaluation of HIV-Exposed Infant for Tuberculosis Disease	
History (Symptoms and Signs of TB Disease)	• Unexplained weight loss or failure to grow normally • Unexplained fever, especially if more than 14 days • Chronic cough (more than 30 days) • Failure of response to appropriate antibiotic treatment of presumed bacterial pneumonia or meningitis • Exposure to an adult with probable or definite pulmonary infectious TB
Physical Examination	• Fluid on one side of chest (dullness to percussion, reduced air entry) • Enlarged, non tender lymph nodes or abscess, especially in the neck • Signs of meningitis, especially if subacute and develop over several days • Cerebrospinal fluid contains mostly lymphocytes and elevated protein • Abdominal swelling, with or without palpable lumps • Progressive swelling or deformity of a bone or joint, including the spine
Laboratory Investigations	• Microscopic examination for acid-fast bacilli (Ziehl-Nielsen stain) and culture of specimens, such as early morning gastric aspirates for three consecutive days and pleural, ascites and cerebrospinal fluid as relevant. • Chest radiograph for lobar opacity, pleural effusion, miliary pattern. • PPD tuberculin skin test (>5mm is positive).
Modified from WHO Treatment of TB; Guidelines for National Programs, Third Edition, 2002.	

Most TB diagnostic criteria (chronic symptoms, smear positive contact, positive Mantoux, response to treatment) have lower sensitivity and specificity in a co-infected child than in a non-HIV-infected child (**Table 7.2** below).

Table 7.2. Impact of HIV Infection on Value of Commonly Used Criteria for Diagnosis of TB

Diagnostic Feature of Pulmonary TB	Impact of HIV
Chronic symptoms >1 month	Less specific
Smear positive contact	Less specific
Malnutrition	Less specific
Positive Mantoux	Less sensitive
Characteristic chest x-ray	Less specific
Response to treatment	Less sensitive

Source: Graham et al. Int J Tuberc Lung Dis, 2001 Jan: 5 (1) 12-23.

Diagnosis of Extra-Pulmonary TB

Clinicians may use the following to diagnose extra pulmonary TB:

- When there are superficial enlarged lymph nodes, biopsy or fine needle lymph node aspirate may be diagnostic
- Body fluids—ascitic, pleural, or cerebrospinal—can be subjected to ZN stain and culture, but the yield is usually poor
- Bone marrow aspirate and culture may be diagnostic in disseminated TB with persistent fever and wasting
- Ultrasound can help differentiate loculated fluid and consolidation
- Computerised tomography (CT) scan, where available, may assist in diagnosing abdominal, pulmonary, and CNS disease
- Contrast CT scan can differentiate inflamed mediastinal lymph nodes from thymic shadows in younger children

Treating TB in Children

In most instances treatment of TB is usually presumptive because it is difficult to make an aetiological diagnosis.

In treating children who are co-infected with HIV and TB, use national guidelines. Where guidelines may not be available, the following table can be used:

Table 7.3. Treatment/Prophylaxis of TB in HIV-Exposed or HIV-Infected Infants

Treatment	• **Treat all confirmed or highly suspect cases** • **Treatment should be directly observed therapy**	
Smear-Negative Pulmonary TB or Non-Severe Disease[1]	• First 2 months: isoniazid + rifampicin + pyrazinamide daily or 3 times a week ***Followed by either:*** • Next 6 months: isoniazid + ethambutol ***or*** isoniazid + thioacetazone daily ***or*** • Next 4 months: isoniazid + rifampicin daily or 3 times weekly	
Smear-Positive Pulmonary TB or Severe Disease[1]	• First 2 months: isoniazid + rifampicin + pyrazinamide + streptomycin (or ethambutol) daily or 3 times a week ***Followed by either:*** • Next 6 months: isoniazid + ethambutol daily ***or*** isoniazid + thioacetazone daily ***or*** • Next 4 months: isoniazid + rifampicin daily or 3 times weekly	
Meningitis, Miliary TB or Spinal TB with Neurologic Signs (regardless of Smear Results)[1]	• First 2 months: isoniazid + rifampicin + pyrazinamide + streptomycin (or ethambutol) daily or 3 times a week ***Followed by:*** • Next 7 months: isoniazid + rifampicin daily	
Anti-TB Medication Doses	**Daily dosing** Isoniazid ..... 5 mg/kg (range 4–6) Rifampicin ..... 10 mg/kg (range 8–12) Pyrazinamide..... 25 mg/kg (range 20–30) Ethambutol..... 15 mg/kg (range 15–20) Streptomycin..... 15 mg/kg (range 12–18)	**Intermittent dosing (3 times weekly)** Isoniazid ..... 10 mg/kg (range 8–12) Rifampicin ..... 10 mg/kg (range 8–12) Pyrazinamide..... 35 mg/kg (range 30–40) Ethambutol..... 30 mg/kg (range 25–35) Streptomycin..... 15 mg/kg (range 12–18)
Prophylaxis (after active TB disease is excluded)	• Infants born to HIV-infected women diagnosed with TB disease who started treatment <2 months before delivery • Infants and children with exposure to an adult with active TB disease	
Prophylaxis Medication	• Isoniazid 5–10 mg/kg orally once daily for 6 months.	

[1] WHO recommendations for therapy (when national guidelines not available)

Source: Adapted from WHO

Drug/Drug Interactions

TB Treatment and Antiretroviral Drugs

Because of the interaction between protease inhibitors and rifampicin (in general, serum protease inhibitor levels are lowered substantially and rifampicin levels increased 2 to 3 times the usual concentration), treatment in patients who are co-infected with TB and HIV may have to be modified (see **chapter 8** for details).

4. Lymphoid Interstitial Pneumonitis

Lymphoid intersitial pneumonitis (LIP) is common in children (occurs in at least 40% of children with perinatal HIV), but rare in adults (occurs in about 3% of adults with HIV), and usually occurs in children more than 2 years of age. Various studies in Africa have documented a 30–40% prevalence of LIP in HIV-infected children, and up to a 60% prevalence in those with chronic lung disease. LIP is often mistaken for pulmonary TB (miliary) because of the chronic cough and the *miliary-like* pattern on chest x-ray.

Pathogenesis

Possible explanations for LIP include a co-infection of the lungs by HIV and Epstein Barr Virus (EBV), leading to immune stimulation with lymphoid infiltration and chronic inflammation.

Clinical Symptoms

Diagnosis of LIP is usually by exclusion. However the following may be helpful:

- Patient usually in good general condition despite respiratory distress
- Recurrent cough and dyspnoea
- Usually associated with parotid enlargement, generalized lymphadenopathy, and hepatosplenomegaly
- Finger clubbing may be present

- Poor response to TB therapy
- Terminally chronic lung disease with hypoxia

Radiological Picture

Radiological indicators of LIP include:

- Diffuse bilateral reticulonodular infiltrates may appear similar to miliary TB
- Bilateral hilar or mediastinal lymph node enlargement

The table below high lights similarities and differences between LIP and TB.

Table 7.4. Comparison of Miliary TB and LIP

Clinical Features	Miliary TB	LIP
Respiratory distress	-/+	+++
Persistent fever	++	++
Wasting	+++	-/+
Generalized lymphadenopathy	-/+	+++
Parotid enlargement	-	++
Digital clubbing	-	++
Hepatomegaly	++	++
CXR features		
• Diffuse micronodular	++	+
• Diffuse reticulonodular	-	++
Lymphadenopathy	-/+	++

Management

Managing LIP includes the following:

- Steroids when children with LIP have significant respiratory distress (exclude TB first). Prednisone 2 mg/kg/day initially for 4 weeks daily, then alternate day maintenance for 2 to 3 months and review.
- Oxygen therapy during episodes of hypoxia
- Bronchodilators (e.g., salbutamol) where wheezing is a problem
- Antibiotics during episodes of concurrent super-infection with pneumonia
- Chest physiotherapy and postural drainage if there is secondary bronchiectasis
- Refer for specialist care if resistant to therapy

5. Bronchiectasis

Bronchiectasis may occur as a complication of severe or recurrent pneumonia, TB, LIP, or measles. It involves damage to the bronchial lining because of recurrent infection and weakening of the bronchi with cystic formation and secondary infection.

Clinical Presentation

The clinical presentation of bronchiectasis includes the following:

- Chronic cough, mainly in the morning
- Copious purulent sputum
- Halitosis
- Digital clubbing
- Recurrent pneumonia

Management of bronchiectasis

Management includes diagnosis of bronchiectasis and its treatment.

Diagnosis

- With the above symptoms and signs, a chest x-ray may show localized infiltrates, cystic areas, dilated bronchi (persistent opacity in one area).
- Where possible collect sputum and culture for bacteria and to exclude fungi. If the sputum grows a specific organism, adjust treatment appropriately.

Treatment

- Supportive treatment includes daily chest physiotherapy and postural drainage. Caregivers should be trained in daily physiotherapy and postural drainage.
- Broad-spectrum antibiotics: chloramphenicol, augumentin, cefuroxime, azithromycin/clarithromycin or third-generation cephaolosporins (Ceftriaxone, Ceftazidime, Cefpodoxime), if available. Ciprofloxacin may be used as a last resort (be careful about prolonged use) for in-patients with possible enteric gram-negative and anaerobic organisms.
- Bronchodilators such as salbutamol/albuterol can be used when bronchospasms are present.
- Prophylactic antibiotics may be needed for several months if patient presents with recurrent pneumonia/bronchiectasis. Consider referral to specialist.
- Surgery may be necessary in cases with segmental lung damage.

6. Viral Pneumonitis

Children with HIV may develop severe viral pneumonitis from a number of viruses, including respiratory syncytial virus (RSV), parainfluenza virus, influenza virus, adenovirus, varicella (chicken

pox), measles, and cytomegalovirus (CMV). However, in most African settings it is not possible to confirm the actual aetiological agent. The clinical presentation may be much more severe and case fatality higher than in non-HIV infected children. Viral pneumonitis in HIV-infected children presents as pneumonia rather than bronchiolitis.

Some reports indicate that CMV may be a co-pathogen in infants with PCP, and that using steroids to treat PCP may aggravate the CMV pneumonitis. Specific treatment is ganciclovir, but this is rarely available and very expensive. HAART may be useful in ameliorating severity.

Varicella zoster immunoglobulin may reduce the severity of chicken pox pneumonitis, if it is given within 72 hours of exposure. Alternatively, you may use oral acyclovir. Immunisation (measles vaccine) can prevent measles but you can also give measles immunoglobulin (0.5 ml/kg (maximum 15 ml) within 6 days of measles exposure, regardless of previous measles immunisation history.

Other Pulmonary Conditions

A child presenting with an unexplained sudden onset of dyspnoea or subcutaneous emphysema may indicate spontaneous pneumothorax, which may be associated with PCP, LIP, or other cause of pneumonia.

Asthma/reactive airway disease may occur in HIV-infected children, just like in their HIV-negative counterparts, and must be managed accordingly.

Fungal chest infections (e.g., aspergillosis, nocardia, cryptococosis, and rarely candida) in Africa are rarely reported. Where there are facilities, further investigation of patients with poorly responding chest infections should include fungal stains and cultures.

Kaposi's sarcoma (KS) is the most common HIV-associated malignancy associated with the lungs. In addition to the mucocutanoeus lesions and lymphadenopathy, patients present with progressive dyspnoea, cough, and rarely haemoptysis. Chest x-rays will show

mediastinal lymphadenopathy, pleural effusion, or bilateral interstitial infiltrates. Diagnosis of pulmonary KS can be made at bronchoscopy, where multiple purplish lesions can be visualized. Intra-pulmonary biopsy should not be done, as it can lead to profuse haemorrhage. Treatment includes chemotherapy (vincristine and bleomycin or liposomal preparations of danorubicin and doxorubicin). This needs referral to experienced centres of cancer treatment.

Lymphomas (both T- and B-cell) may present with non-specific symptoms and signs, and chest x-rays showing mediastinal lymphadenopathy, focal opacities, or pleural effusions.

Future needs

- Easier and more accurate diagnostic tests for pulmonary conditions
- Need to evaluate different treatment options for optimal efficacy among HIV- infected children with pulmonary conditions

Additional Reading

Graham, SM, JB Coulter, and CF Gilks. Pulmonary disease in HIV-infected African children. *Int J Tuberc Lung Dis* 2001 Jan: 5 (1): 12-23.

Chapter 8
Antiretroviral Therapy

Summary

- All HIV-infected children should have access to HIV comprehensive care, which includes antiretroviral therapy where indicated.
- There are specific issues to consider when treating HIV-infected children with ART, including establishing a definitive diagnosis, availability of appropriate formulations, palatability, adherence, accuracy of dosing and need to revise dose regularly, and pharmacokinetics issues.
- Adverse events are much less common in children than in adults.
- Generic antiretroviral drug preparations may reduce the overall cost of treating patients.
- In planning for antiretroviral therapy, tailor the best programme to local circumstances; keep it simple and doable.
- Presumptive ART should be provided for sick children under 18 months with positive HIV antibody tests when there are no facilities for PCR testing to confirm infection. In this case, antibody testing should be repeated at 18 months, and if results are negative, ART stopped.
- Access to treatment for children's parents and families is equally critical and has direct implications for treatment outcomes for the child.

Introduction

The treatment of HIV-infected children with ARV drugs depends on available local resources and infrastructure. Health workers must continually update their knowledge and skills on ART because it is a rapidly changing field and because it has benefits for child health.

This chapter aims to help healthcare workers in sub-Saharan Africa understand the basics of treating HIV-infected children with ARV drugs. Adapt the specifics of the treatments, however, to local circumstances.

The goals of treatment with ARV drugs are to:

- Prolong the survival of HIV-infected children
- Promote optimal growth and development
- Preserve, enhance, or reconstitute the immune system and therefore reduce opportunistic infections
- Suppress HIV replication and therefore prevent disease progression
- Reduce the morbidity of children and improve their quality of life

HAART is the only regimen potent enough drastically to reduce viral replication and prevent the emergence of resistance (which can ultimately result in treatment failure) for a significant amount of time. Such regimens, which are combinations of at least three ARV drugs, have been associated with immunologic restoration, slower HIV disease progression, durable therapeutic responses, improvements in quality of life, and reduction in the emergence of drug resistance. HAART can reasonably be expected to reduce the HIV viral load to undetectable levels (<50 copies/ml) in treating patients with no prior exposure to ARV drugs.

Tools to achieve these therapy goals include:

- Maximising adherence to ART
- Rationally sequencing drugs so as to preserve future treatment options

Principles of ART

ART is part of comprehensive HIV care. The guiding principles of ART include these:

- Do not start ART too soon (when CD4 cell count is normal) or too late (when the immune system is irreversibly damaged)
- Choose drug regimens with proven efficacy, freedom from serious adverse effects, and ease of administration
- Consider affordability and availability of drugs and drug combinations
- Provide ongoing support for the patient and family to maintain adherence

ARV drugs are not a cure for HIV; however, when both patients and healthcare providers use them properly they are associated with excellent quality of life. ARV drugs are expensive and their use requires an adequate infrastructure and knowledgeable healthcare workers.

ART does have limitations:

- Drug interactions and drug resistance may decrease the potency of ARV drugs
- Patients on ART may develop adverse drug reactions
- HIV drugs are expensive, even though prices have come down significantly
- Patients must take at least 95% of their pills to minimize the emergence of drug resistance, which may result in treatment failure. Adherence is key to successful therapy.

ART for Children

There are specific issues to consider when treating HIV-infected children with ART (**Table 8.1**).

Table 8.1. Specific Issues to Consider When Treating HIV-Infected Children with ART

Issue	Comment
Virological suppression	Although most children improve with ART, complete virological suppression is more difficult to achieve in children than in adults
Pharmacokinetic issues	The absorption of ritonavir, for example, is unpredictable in young children, and the optimal dose of efavirenz has not been established in young children.
Adverse events	Adverse events are much less commonly reported in children than in adults.
Drug formulations	Child-friendly formulations like suspensions are not available for all ARV drugs.
Cost	Paediatric suspensions are relatively more expensive than capsules or tablets.
Palatability	Ritonavir suspension is extremely unpalatable and may affect adherence.
Drug administration	For example, didanosine is problematic in young children because it must be administered on an empty stomach.
Drug storage	For example, refrigeration is not available in many settings, which precludes the use of preparations such as stavudine suspension.
Compliance	Infants and children depend on the compliance of their caregivers.
Concurrent administration of traditional medication	This is an under-researched area. Until evidence to the contrary emerges, the use of herbal therapies should be discouraged.

Organisational Issues

Planning is critical when setting up or strengthening an existing HIV clinical care programme to undertake ART for children, but you should balance the need to have all elements in place against the need to start services as soon as possible. Issues that should be considered include:

- Enlisting the support of policy makers and leadership at the Ministry of Health level and at the local level. Getting leaders to associate themselves with the programme, to talk about it, support it, and enlist yet more support for it.
- Planning with input from local leadership; establishing partnerships with existing AIDS service and support organisations and with organisations working with OVC.
- Identifying and establishing relationships with other accessible service points for services you are unable to provide.
- Estimating the potential demand for the service based on your knowledge of the HIV burden, existing referral patterns and relationships, availability of other ART centres in the locality, and whether these services are free, subsidized, or full cost recovery. Developing a plan for parents and caregivers.
- Systematically including parents and caregivers in the child's care.
- Orienting the staff at the health unit, bringing together all key stakeholders so that they can understand the implications of the programme.
- Training staff in HIV clinical care and ART and introducing to the national guidelines, if they exist. If there are no national guidelines, use international guidelines, while balancing the need for *excellence* against the urgency to provide ART for children.
- Obtaining staff consensus on standards and standard operating procedures for ART in the health unit (e.g., all children must be weighed at every visit) and using those standards to continuously improve the quality of services. Assigning and clarifying roles.

- Ensuring that the Ministry of Health has accredited the health unit as an ART treatment centre for children.
- Tailoring the best practical programme to the local circumstances. For example, multiple skills are needed to operate an ART clinic efficiently, yet lack of human resources is a real constraint. Staff can be trained to take on additional roles. Clinicians, for example, can be trained as counsellors, and less skilled staff can be trained to take and chart weights and heights, to retrieve and file medical records, etc.
- Mobilising volunteers without burdening them with unrealistic demands; keeping their work hours short; ensuring their safety (e.g., they should not handle medical waste); understanding their motivations and goals; and being clear about what they should expect.
- Providing simple and accurate information that will help the community access services and support those who use the services.
- Establishing a system for collecting, analysing, and using information for improving the programme. Being open to integrating lessons learned along the way.

Opportunities and Entry Points for ART in Children

There are already multiple opportunities to reach children who need HIV care and ART:

- *PMTCT programmes* identify HIV-exposed and -infected children.
- Depending on local HIV seroprevalence, between 10 and 70% of *hospitalised* children may be HIV-infected. In some situations, 30% of children with severe pneumonia and 44% with severe malnutrition are HIV-infected.
- Between 42 and 60% of children with *tuberculosis* may have HIV, and HIV-infected children are 5 to 15 times more likely to develop TB.

- Adults attending *infectious disease clinics* or diagnosed at *VCT* services often have children who may be sick and need care.
- *Siblings of children* enrolled in care may also be HIV-infected.
- Programmes targeting *OVC* often include children who need ART.

Indications for Starting ART in Children

WHO guidelines for starting ART in children should be used in conjunction with the WHO Paediatric Clinical Staging (see **chapter 5**). CDC clinical staging may be used instead of the WHO clinical staging

When to Start Treatment

The local healthcare team and the family should make the decision to treat a child with ART after considering all medical, family, and social factors. Beginning ART is not a medical emergency, and providers should take the time necessary to adequately prepare the parents/caregivers before treatment is started. Such preparation includes discussions about the drugs, the need for life-long therapy, the implications of suboptimal adherence, and ongoing care. Several preparatory visits may be necessary to ensure that the family is ready to undertake the child's ART.

Requirements Before Treatment Is Started

Do not start a child on ART before certain requirements are met:

- A clearly defined caregiver, who must understand prognosis of HIV infection, side effects of medicines, how to administer and store medicines, implications of non-adherence, and the fact that it is life-long therapy
- Accessibility of supportive processes, such as counselling services and family support groups
- Access to nutritional supplements and cotrimoxazole prophylaxis
- Clinical status and/or CD4% of child should be within acceptable treatment recommendations (refer to local guidelines or **Table 8.1**)

- Regular supply of OI drugs, ARV drugs, laboratory reagents, and other consumables
- Trained personnel

Treatment of infected parents and siblings should be considered to preserve family unit; good health of the mother is particularly important for survival of the child.

Table 8.1. WHO Recommendations for ART in Children When CD4 Testing Is Available:

Children with confirmed HIV infection with:

WHO paediatric stage 3 or 4, irrespective of CD4 cell %

Or

WHO paediatric stage 2, with:

- CD4 <20% for children less than 18 months of age ***or***
- CD4 <15% for children more than 18 months of age

Antibody-positive children <18 months with no virologic test* but with

- WHO paediatric stage 3 or 4, irrespective of CD4 cell %
- WHO paediatric stage 2 only if CD4 cell % <20%
- (WHO paediatric stage 1: don't treat if no virologic tests are available)

* Must have confirmatory test at 18 months to continue with ART

WHO Recommendations for ART in Children When CD4 Test Is Not Available:

Less than 18 months of age:

- WHO stage 3 or 4, irrespective of total lymphocyte count (TLC)
- WHO stage 2 only if TLC <3,400/mm^3 or mother has severe symptomatic disease (WHO adult stage 3 or 4) or died of AIDS
- WHO paediatric stage 1: don't treat if no virologic tests are available

More than 18 months of age:

- WHO stage 3 or 4, irrespective of TLC
- WHO paediatric stage 2 only if TLC <2,300/mm^3 if age 18 months to 6 years, or if over 6 years, if TLC <1,200/mm^3

Pre-Treatment Assessment

The following evaluations should be part of the pre-treatment assessment:

- Complete clinical assessment
- Neurodevelopmental assessment
- Weight, length/height, and head circumference
- Complete blood count (CBC) and differential count, including total lymphocyte count (TLC)
- Alanine aminotransferase (ALT)
- Chest radiograph
- CD4 count (where available)
- Viral load (where available)

These evaluations help in deciding patient's suitability for ART, and during treatment they are used for assessing clinical and biological response as well as monitoring adverse reactions to the drugs.

First-Line Therapy

Treatment for HIV-infected children should follow national recommendations. If there are no national recommendations, then the following first-line options may be considered (see **Table 8.2** for drug dosages and administration instructions):

- Less than 3 years of age and/or <10 kg—zidovudine/lamivudine/nevirapine
- More than 3 years of age and/or >10 kg—zidovudine/lamivudine/efavirenz
- Failed nevirapine prophylaxis—zidovudine/lamivudine/lopinavir and ritonavir co-formulation

Table 8.2. Antiretroviral Drugs in Paediatric Practice

Drug	Formulation	Dosage	Adverse Events	Comments
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Zidovudine *AZT, ZDV, or Retrovir*	Suspension 10 mg/ml Capsules 100 mg, 250 mg Tablets 300 mg	180 mg/m² bd Or 90–180 mg/m² tds Neonatal dose: 2 mg/kg qid	Neutropaenia, anaemia, headache; myopathy, lactic acidosis (rare)	Can be given with food Store at room temperature
Lamivudine *3TC*	Suspension 10 mg/ml Tablets 150 mg	4 mg/kg bd Neonatal dose: 2 mg/kg bd	Headache, abdominal pain, fatigue, pancreatitis, peripheral neuropathy; neutropaenia, ↑ LFTs, lactic acidosis (rare)	Can be given with food Store at room temperature
Stavudine *d4T, Zerit*	Suspension 1 mg /ml Capsules 20 mg, 30 mg, 40 mg	1 mg/kg bd	Headache, GI upset, rash; peripheral neuropathy, ↑ LFTs, pancreatitis, lactic acidosis	Can be given with food Keep suspension refrigerated
Didanosine *ddI, Videx*	Suspension 10 mg/ml Tablets 25 mg, 50 mg, 100 mg, 150 mg	90–120 mg/m² bd	Diarrhoea, abdominal pain, nausea; peripheral neuropathy, pancreatitis, lactic acidosis, ↑ LFTs	Give on empty stomach Keep suspension refrigerated
Abacavir *ABC, Ziagen*	Suspension 20 mg/ml Tablets 300 mg	8 mg/kg bd	Hypersensitivity rash (5%), fever, malaise, mucositis, pancreatitis, lactic acidosis	Can be given with food Store at room temperature *Do not rechallenge after hypersensitivity*
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)				
Nevirapine *NVP, Viramune*	Suspension 10 mg/ml Tablets 200 mg	Start with 120 mg/m² once daily for 14 days Increase to full dose (120–200 mg/m²) every 12 hrs (maximum 200mg every 12 hrs) if no rash or severe adverse events	Rashes, Stevens-Johnson Syndrome, ↑ LFTs; hypersensitivity and hepatitis	Can be given with food Store at room temperature *Watch for liver toxicity*

Table 8.2. Antiretroviral Drugs in Paediatric Practice

Drug	Formulation	Dosage	Adverse Events	Comments
Efavirenz *EFV, Stocrin*	Capsules 50 mg, 200 mg	Single daily dose 10–15 kg: 200 mg 15–20 kg: 250 mg 20–25 kg: 300 mg 25–32.5 kg: 350 mg 32.5–40 kg: 400 mg >40 kg: 600 mg	Rash (mild), somnolence, abnormal dreams, insomnia, confusion, hallucinations, euphoria, amnesia, agitation, abnormal thinking	Can be given with food Administer at night Store at room temperature No pharmacokinetic data <10 kg and <3 years of age
Protease inhibitors (PIs)				
Ritonavir *RTV, Norvir*	Suspension 80 mg/ml Capsules 100 mg	Initial dose of 250 mg/m^2 bd. Increase by 50 mg/m^2 bd at 2–3 day intervals to 400 mg/m^2 bd. If <2 yrs of age, maximum dose 450 mg/m^2 bd	GI intolerance, headache, anorexia, ↑ LFTs; Abnormal lipids (rare)	Give with food Palatability improved by mixing with milk, honey, ice cream, yogurt or chocolate milkshake Store in refrigerator or room temperature
Nelfinavir *NFV, Vira-cept*	Suspension 50 mg/1 gm spoon Tablets 250 mg	Paediatric: 55 mg/kg bd Adolescent: 750 mg tds or 1250 mg bd	Diarrhoea, vomiting, rash; Abnormal lipids, exacerbation of chronic liver disease (rare)	Administer with food. Suspension may be mixed with water, milk, pudding, ice cream, formula
Lopinavir / ritonavir *LPV/RTV, Kaletra*	Suspension 80 mg LPV and 20 mg RTV per ml Capsules 133.3 mg LPV and 33.3 mg RTV	230 mg/m^2 LPV/57.5mg/m^2 RTV bd up to a maximum of 400 mg LPV/ 100 mg RTV bd Increase dose with NVP or EFV co-administration (refer package insert)	GI intolerance, rash, headache; Abnormal lipids, hyperglycaemia, pancreatitis (rare)	Give with food. A high fat meal increases absorption Refrigerate suspension or keep at room temperature for 2 months
Fixed drug combinations				
D4T/3TC/NVP (Triomune)	Tablet 40mg/50mg/200mg	1 tablet twice daily depending on child's weight		Tablet broken up as per weight of child. Attainment of accurate dosage difficult with breakage of tablet.

bd=twice a day, tds=three times a day, qid=four times a day, m^2=body surface area (BSA) metre squared

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

Monitoring and Follow-Up

Clinical Monitoring

The frequency of visits for clinical monitoring is as follows:

- Ideally the first visit should take place 2 weeks after initiating therapy. This appointment should focus on ensuring that medicines are being correctly administered and stored.
- Monthly visits for the first 3 months should focus on the child's clinical progress and effects of the drugs.
- After 3 months, if the child is compliant and clinically stable, appointments may be spaced at 3 to 6 month intervals.

At each visit:

- Plot physical growth (weight, length/height, and head circumference).
- Determine physical condition of the child.
- Address ongoing medical problems, including skin and dental problems and organ-specific complications of HIV infection.
- Treat intercurrent infections, if present.
- Check the doses of the drugs.
- Monitor neurodevelopmental progress at 12-month intervals. Supply medications at monthly intervals, even though the clinic appointments are more widely spaced.

Laboratory Monitoring

The schedule for laboratory monitoring is as follows:

- Repeat the CD4 count and % and viral load (where available) at 6-month intervals.
- Repeat CBC and ALT after 1 month of treatment; if normal, repeat these tests at 6-month intervals. If protease inhibitors are used, test

fasting lipid profiles (cholesterol and triglycerides) at baseline and then annually.

- Where viral load evaluations are not possible, monitor the child using clinical parameters and serial CD4 count and % or total lymphocyte count. Children less than 18 months of age with a TLC <2500/mm³ have a 12-month mortality rate of 20%. Children more than 18 months of age with a total lymphocyte count of <1500/mm³ have a 12-month mortality rate of 20%.
- PCP prophylaxis may be discontinued when the CD4 is consistently >20% (i.e., >20% on at least two occasions, performed 6 months apart).

Adherence Monitoring

Greater than 95% adherence to the drug regimen will ensure a good virological response and prevent the emergence of viral resistance. For a child taking medication twice daily, omitting more than 1 dose in 10 days implies <95%, or suboptimal, adherence.

A good relationship between the healthcare providers (i.e., counsellors, nurses, and doctors) and the caregiver helps optimise adherence. Ideally, the same primary healthcare provider should continue to treat the patient so that a long-term relationship can develop with the family.

Regular education and support during each clinic visit can enhance and maintain good adherence. You may monitor adherence using diary cards, medication checks, and other improvised measures.

Long-Term Management

The long-term sustainability of ART depends on social, educational, and emotional support for the family, which may include involving the community and providing social assistance.

The long-term success of ART for children can be achieved only if the health and well-being of the entire family is ensured; this includes pro-

viding appropriate ARV drugs for infected adults. Long-term success also depends on well-trained health providers who can provide a first-line regimen to allow for better options later on, as the child grows.

Antiretroviral Therapy and TB Treatment

Because of the interaction between protease inhibitors and rifampicin (in general, serum protease inhibitor levels are lowered substantially and rifampicin levels increased 2 to 3 times the usual concentration), you may have to modify treatment in patients who are co-infected with TB and HIV.

If TB infection is present prior to ART initiation:

Complete TB therapy, if possible, before starting ART

or

Delay ART for at least 2 months

Use the following as the third drug: ritonavir (if <3 years and 10 kg)

or

efavirenz (if >3 years and 10 kg)

If TB develops while on ART:

Consider interrupting ART

If on nevirapine or lopinavir/ritonavir co-formulation, switch to ritonavir or efavirenz (if more than 3 years of age and 13 kg); discontinue ART if there is ritonavir intolerance.

Indications for Changing Therapy

There are certain clinical, immunological, and virological conditions that might indicate the need to change to second-line therapy.

Clinical Conditions

Clinical conditions indicating that a change to second-line therapy is warranted:

- Lack of growth response or decline in growth over a 6-month period, after excluding other causes, including TB

- Not meeting neurodevelopmental milestones
- Development of HIV encephalopathy in a child with no previous manifestations
- Recurrence of infections, such as oral candidiasis, that are refractory to treatment
- Advancement from one clinical stage to another or new evidence of stage III disease

Do not regard short intercurrent episodes of pneumonia, lower respiratory tract infections, and gastroenteritis as clinical failure. TB can present as a progression to stage III disease and must first be excluded.

Immunological Conditions

Immunological conditions indicating that a change to second-line therapy is warranted:

- Return in CD4 cell percentage (or in children >6 years of age, absolute CD4 cell count) to pre-therapy baseline or below, in the absence of other concurrent infection
- ≥50% fall from peak level on therapy of CD4 cell percentage (or for children >6 years of age, absolute CD4 cell count), in absence of other concurrent infection

Do *not* measure CD4 % during a concurrent infection. Measure it, preferably, 1 month (or more) post-resolution. If there is a modest decline in CD4 % (<5%) and if there is no failure to thrive, do not change medication, but maintain close monitoring.

Despite a good clinical and immunological response, viral resistance will occur in the absence of complete viral suppression. Many experts will delay changing therapy unless there are signs of clinical or immunological progression.

Virological Conditions

Virological conditions indicating that a change to second-line therapy is warranted:

- Persistently elevated viral load in the absence of poor adherence to medication
- Progressive increase in viral load after the beginning of treatment (changes greater than 5-fold [0.7 log] in children less than 2 years of age, and of at least 3-fold [0.5 log] in children 2 years of age or older, after tests confirmed in a second determination, will reflect a clinically and biologically relevant change)
- <1.0 log reduction in relation to the initial level after 24 weeks
- Repeated viral load detection in children with earlier undetectable levels

The viral load should *not* be measured during a concurrent infection; preferably, measure it 1 month (or more) post-resolution.

Second-Line Therapy

Issues to consider when introducing second-line therapy are as follows:

- Do not rush into second-line therapy.
- When changing therapy, determine whether poor adherence was responsible for the failure; if it is not possible to improve adherence, attempt directly observed therapy (DOT) with a healthcare worker, a family member, or friend.
- If the patient is adherent, assume that resistance has developed and change therapy. The new regimen should include at least three new drugs.
- When changing therapy, review all other medications for possible drug interactions.
- When changing therapy, consider the patient's quality of life.

Medications for second-line therapy include the following:

- Didanosine, stavudine, and lopinavir/ritonavir co-formulation
- Failed nevirapine prophylaxis: consider using didanosine, stavudine, and efavirenz

Further Therapeutic Revisions

Ideally, further revisions in therapy should be guided by resistance testing. Strategies include dual PI- or dual NNRTI-based combinations, and *Mega HAART*, in which four or more drugs from all three ARV classes are used together. These strategies are expensive. Until further significant reductions in the cost of drugs and monitoring occur, these strategies are not appropriate for resource-limited settings. Experienced providers at referral centres should make the decisions about second-line and subsequent changes in therapy.

Discontinuation of Therapy

Under exceptional circumstances it may be necessary to discontinue ART. Such circumstances include extremely poor adherence and cases where the administration of medication is repeatedly interrupted. Continuing suboptimal ART is not useful because it will lead to the emergence of viral resistance. Consider discontinuation only after exploring all potentially corrective measures, including intensive counselling, additional caregiver education, and family support.

Adverse Events

Adverse events are gross clinical or biochemical abnormalities that may arise from infections, ART, or other drugs and treatment. The following principles are used to manage such adverse events. (see **Table 8.3** for management and **Table 8.4** for grading of adverse events):

- Establish whether the adverse event is due to ARV agents or to other medication.

- Because not all problems that arise during treatment result from ARV drugs, consider other disease processes (e.g., consider viral hepatitis in a child who develops jaundice on ARV drugs).
- If there is a need to discontinue ART, it is advisable to discontinue all ARV drugs simultaneously rather than to continue with one or two agents alone.
- Continue ART if there are Grade 1 or Grade 2 (mild) reactions; single-drug substitution may occasionally be necessary.
- Consider terminating treatment if there are Grade 3 reactions, and halt treatments if Grade 4 reactions occur. Manage the medical event; then reintroduce ARV drugs using a modified regimen.

Table 8.3. Clinical Signs, Symptoms, Monitoring, and Management of Symptoms of Serious Adverse Effects of ART that Require Drug Discontinuation

Adverse Effect/Possible Offending Drug(s)	Clinical Signs/Symptoms	Management
Acute hepatitis Nevirapine (NVP); EFV less common; more uncommon with zidovudine (ZDV), didanosine (ddI), stavudine (d4T) (<1%), and protease inhibitors (PI); most frequently with ritonavir (RTV)	Jaundice, liver enlargement, gastrointestinal symptoms, fatigue, anorexia; NVP-associated hepatitis may have hypersensitivity component (drug rash, systemic symptoms, eosinophilia)	• If possible, monitor serum transaminases, bilirubin. • All ARV should be stopped until symptoms resolve. • NVP should be permanently discontinued.
Acute pancreatitis ddI; d4T; lamivudine (3TC) (infrequent)	Nausea, vomiting, and abdominal pain	• If possible, monitor serum pancreatic amylase, lipase. • All ART should be stopped until symptoms resolve. • Restart ART with change to different NRTI, preferably one without pancreatic toxicity (e.g., ZDV, ABC).
Lactic acidosis All nucleoside analogue reverse transcriptase inhibitors (NRTIs)	Initial symptoms are variable: a clinical prodromal syndrome may include generalized fatigue and weakness, gastrointestinal symptoms (nausea, vomiting, diarrhoea, abdominal pain, hepatomegaly, anorexia, and/or sudden unexplained weight loss), respiratory symptoms (tachypnea and dyspnea) or neurologic symptoms (including motor weakness).	• Discontinue all ARV; symptoms may continue or worsen after discontinuation of ART. • Supportive therapy. • Regimens that can be considered for restarting ART include a PI combined with an NNRTI and possibly ABC.

Table 8.3. Clinical Signs, Symptoms, Monitoring, and Management of Symptoms of Serious Adverse Effects of ART that Require Drug Discontinuation

Adverse Effect/Possible Offending Drug(s)	Clinical Signs/Symptoms	Management
Hypersensitivity reaction Abacavir (ABC); nevirapine (NVP)	ABC: Constellation of acute onset of symptoms including: fever, fatigue, myalgia, nausea/vomiting, diarrhoea, abdominal pain, pharyngitis, cough, dyspnea (with or without rash). While these symptoms overlap those of common infectious illness, the combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC is more typical of a hypersensitivity reaction. NVP: Systemic symptoms of fever, myalgia, arthralgia, hepatitis, eosinophilia with or without rash.	• Discontinue all ARVs until symptoms resolve. • The reaction progressively worsens with drug administration and can be fatal. • Administer supportive therapy. • Do not rechallenge with ABC (or NVP), as anaphylactic reactions and death have been reported. • Once symptoms resolve, restart ARVs with change to different NRTI if ABC-associated or to PI- or NRTI-based regimen if NVP-associated.
Severe rash/Stevens-Johnson syndrome Non-nucleoside reverse transcriptase inhibitors (NNRTIs); nevirapine (NVP); efavirenz (EFV)	Rash usually occurs during the first 2–4 weeks of treatment. The rash is usually erythematous, maculopapular, confluent, most prominent on the body and arms, may be pruritic and can occur with or without fever. Life-threatening Stevens-Johnson Syndrome or toxic epidermal necrolysis (SJS/TEN) has been reported in ~0.3% of infected individuals receiving NVP	• Discontinue all ARVs until symptoms resolve. • Permanently discontinue NVP for rash with systemic symptoms such as fever, severe rash with mucosal lesions or urticaria, or SJS/TEN. • Once resolved, switch ART regimen to different ARV class (e.g., 3 NRTIs or 2 NRTIs and PI). • If rash moderate but not severe and without mucosal or systemic symptoms, change in NNRTI (e.g., NVP to EFV) could be considered after rash resolves.
Severe peripheral neuropathy ddI; d4T; 3TC	Pain, tingling, numbness of hands or feet; distal sensory loss, mild muscle weakness, and areflexia can occur.	• Stop suspect NRTI and switch to different NRTI that does not have neurotoxicity (e.g., ZDV, ABC). • Symptoms usually resolve in 2–3 weeks.

Source: WHO

Lipodystrophy

HIV-associated lipodystrophy includes fat loss and/or fat accumulation in distinct regions of the body. Increased fat around the abdomen, buffalo hump, breast hypertrophy, and fat loss from limbs, buttocks, and face occurs to a variable extent.

Other manifestations include insulin resistance, hyperglycaemia, hypertriglyceridaemia, hypercholestrolaemia, and low HDL levels. There is an increased risk for diabetes mellitus and coronary artery disease.

Lipodystrophy is more common in individuals who are taking NRTIs or protease inhibitors.

Managing lipodystrophy:

- There are no established methods for treating lipodystrophy.
- Encourage exercise to reduce fat accumulation.
- Some patients improve if switched from a protease inhibitor to an NNRTI.
- Statins and/or fibrates are effective at lowering cholesterol and triglyceride levels. Insulin resistance can be improved with anti-diabetic agents.

Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome (IRIS) is defined as: paradoxical clinical deterioration after starting HAART, resulting from improving immune system interaction with organisms that have colonised the body during the early stages of HIV infection.

A wide range of pathogens causes IRIS. These include *Mycobacterium tuberculosis* (MTB), *Mycobacterium avium complex*, *Cryptococcus neoformans*, *Aspergill*, *Candida albicans*, *Pneumocystis carini*, CMV, human herpes viruses, and hepatitis B.

IRIS usually presents within 6 weeks of starting HAART. Clinical presentations vary and depend on the causative organism and the organ system that is colonised. For example, IRIS caused by MTB may present with high fever, lymphadenopathy, worsening of the original TB lesion, and/or deteriorating chest radiographic manifestations, including the development of a miliary pattern or pleural effusion.

Managing IRIS includes specific antimicrobial therapy (e.g., TB treatment for IRIS caused by MTB). In severe reactions, glucocorticosteroids and/or temporarily discontinuing HAART may help.

Knowledge Gaps

- Effectiveness of ART in HIV-infected children in sub-Saharan Africa
- Optimal drug selection in children exposed to perinatal nevirapine
- Simplified monitoring strategies

Additional Reading

WHO. *Scaling Up Antiretroviral Therapy in Resource-Limited Settings*. Available at: http://www.who.int

CDC. *1994 Revised Classification System for Human Immunodeficiency Virus Infection in Children <13 Years of Age*. Available at: http://www.cdc.gov/mmwr/preview/ mmwrhtml/ 0032890.htm

CDC. *Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis*. Available at: http://www.cdc .gov/mmwrhtml/rr5011a1.htm

Chapter 9
Adolescent Issues

Summary

- Sub-Saharan Africa has been hit harder by the HIV/AIDS pandemic than any region in the world. Children less than 18 years of age represent one-third of all new HIV infections occurring annually, estimated at 1 million annually. UNAIDS estimates that up to two-thirds of new infections occur in those younger than 25 years of age.
- Adolescence (ages 10 to 19 years) is a critical period in a person's life, in which rapid changes in physical, emotional, cognitive, and social characteristics take place.
- Adolescents are not a homogeneous group. Some are out of school, some have become parents themselves, some are orphaned and heading households, some have not yet been tested for HIV, and some have been tested but have not been informed that they are HIV positive. Health workers must take into account the special circumstances of each individual when caring for adolescents who are HIV-infected or affected by HIV/AIDS.
- There are two groups of HIV-infected adolescents: those who acquired HIV through vertical transmission and those who acquired HIV through horizontal transmission (largely sexual). As many as 5% of children with vertical transmission live to adolescence, even without ART.
- A conceptual framework for developing comprehensive, effective, integrated HIV/AIDS prevention and care programmes is urgently needed for the care of HIV-affected adolescents and young people throughout sub-Saharan Africa.

Introduction

WHO defines adolescents as individuals aged 10–19 years and young people as those aged 10–24 years. Adolescence is the transition between childhood and adulthood. It is recognised in many communities and cultures and marked with traditional rites of passage. During this process, adolescents learn about the expectations of their communities and, in a sense, receive the mandate to engage in adult roles.

Adolescence is characterized by major physical, emotional and cognitive changes as well as significant changes in the relationship between the adolescent and their family and peers. At the same time, the adolescent is going through a process of acquiring knowledge and skills to enable them to live independently. There are three stages of adolescent development: early, mid, and late adolescence. **Table 9.1** summarizes the changes that adolescents experience during the different stages of development. It is worth noting that physical and sexual maturity does not mean there is emotional and cognitive maturity to anticipate the undesirable effects of sex such as pregnancy and STIs.

Table 9.1. Adolescent Development

Area of Development	Early: 10–13	Middle: 14–16	Late: 17 yrs and older
Physical	Pubertal changes	End of pubertal changes	Sense of responsibility for ones health
Emotional	Wide mood swings Intense feelings Low impulse control Role exploration	Sense of invulnerability Risk-taking behaviour peaks	Increasing sense of vulnerability Able to consider others and suppress ones needs Less risk-taking
Cognitive	Concrete thinking Little ability to anticipate long-term consequences of their action Literal interpretation of ideas	Able to conceptualise abstract ideas such as love, justice, truth, and spirituality	Formal operational thought Able to understand and set limits Understands thoughts and feelings of others
Relation to family	Estranged Need for privacy	Peak of parental conflict Rejection of parental values	Improved communication Accepts parental values
Peers	Increased importance and intensity of same sex relationships	Peak of peer conformity Increase in relationships with the opposite sex	Peers decrease in importance Mutually supportive, mature, intimate relationships

Adolescents Requiring HIV-Related Services

There are different categories of adolescents requiring HIV services:

1. **HIV-infected adolescents:** This group includes long-term survivors of mother-to-child transmission of HIV and youths infected during childhood or adolescence through sexual exploitation or from their own high-risk behaviour.
2. **Youth engaging in high-risk behaviour:** Increasing poverty and dissolution of families as parents die can also lead to increasing numbers of female and male youth engaging in survival sex. These high-risk activities put the adolescents at risk of HIV infection.
3. **Youth in long-term relationships:** One of the ultimate tasks of adolescents' development is being able to have mutually supportive, mature, intimate relationships that naturally lead to long-term relationships, even marriage. Many adolescent women acquire HIV from their husbands.

A large proportion of adolescents in resource-poor communities are at risk of HIV infection, and a meaningful impact on the HIV epidemic is unlikely unless their specific needs are met.

The social environment of adolescents influences their ability to access HIV-related services. They may be living at home with their parents, with relatives, or on their own; they may be married; they may still be in school; or they may be out of school. Typically, adolescents have limited financial capability that restricts their access to HIV treatment services. Regardless of their social status, non-infected adolescents need preventive services, and those who are infected require care, treatment, and support.

Risk Factors for HIV Infection Among Adolescents

Determinants of risk-taking behaviour in adolescents include their stage in development, biologic and physiologic characteristics, individual attributes, and their environment. A number of high risk behaviours, such as alcohol and drug abuse, often lead to sexual risk

taking. Studies among adolescents have shown that young people with a high sense of self-esteem and direction are less likely to be involved in risk-taking behaviour such as sexual experimentation or substance abuse.

Adolescents are also an important economic force and have therefore become the target of aggressive advertising by the media, which often portray lifestyles that are at variance with societal norms, for example, aggressively marketing cigarettes and alcohol to youth in East Africa.

Studies have demonstrated that many adolescents lack in-depth knowledge about HIV. They do not internalise the biological explanation of disease causation; many youths revert to traditional models to explain the cause of disease and to the prevalent belief that the power of God and traditional medicines are effective cures for HIV. The dichotomy of belief systems presents challenges in conveying prevention messages and ensuring that the messages translate into reduced high risk behaviors. Adolescents tend to have a poor perception of their own risk of HIV, and their perception of risk differs from adults.

Behavioural factors, particularly sexual activity, increase the risk of transmission among adolescents. It is estimated that up to two-thirds of the new HIV infections occr in those younger than 25 years of age (UNAIDS). There is ample evidence that adolescents are engaging in sexual risk taking:

- On average one-third of first-born babies in the region are born to adolescent women.
- Half the women seeking abortion-care services in public hospitals are adolescent girls.
- Many girls continue to drop out of school because of unwanted pregnancies.

While boys tend to initiate sex earlier compared to girls, and rural youth are more likely to be sexually active than urban youth, girls are more vulnerable to heterosexual transmission of HIV than boys. This

and the gender imbalance that results in the inability to insist on safer sex practices make adolescent girls between 15 and 19 years of age up to 6 times more vulnerable to HIV infection than their male counterparts in some communities. Biological factors that put young women at risk include immaturity of the cervix in adolescence. The single layer of columnar cells in the cervix is believed to be more vulnerable to transmission of STIs, including HIV, than the multiple layers of squamous epithelial cells in the mature cervix.

Homosexual transmission is higher among boys, and this risk is worsened by the use of intravenous drugs and alcohol. Homosexuality is a highly stigmatised and largely unacknowledged in sub-Saharan Africa and therefore the extent to which it contributes to HIV infection among adolescents is largely unknown.

Adolescents involved in sex work, migrants and refugees, adolescents living in the street and in war situations, and adolescents who are marginalised and discriminated against are all vulnerable to HIV. Children orphaned by AIDS (of whom a large proportion are adolescents) are also more vulnerable, particularly to sexual exploitation, which is a significant risk factor for HIV transmission.

Cultural practices and expectations also put young people at risk of HIV. For example, in many African settings, a girl's status is recognised when she has a sexual relationship and demonstrates the ability to have a baby.

HIV Preventive Services for Youth

The international community has committed to the following prevention targets pertinent to young people:

- By 2005, reduce the proportion of infants infected by HIV by 20%, and by 2010, by 50% (see also **chapter 3**)
- By 2005, reduce HIV prevalence among young men and women aged 15–24 in the most affected countries by 25% and by 2010, by 25% globally (UNGASS, June 2001, New York)

No single strategy works best to prevent HIV transmission among young people. The best programmes have built on the synergy of multiple interventions. Interventions must target youth wherever they happen to be and at multiple levels—through policy, community (including schools, health services), and the media. They should aim at providing young people with youth-friendly information, counselling, skills, commodities, and services for prevention and treatment of sexually transmitted infections (STIs) and HIV.

Complete sexual abstinence is the most effective means of protecting against both pregnancy and HIV infection. Messages of abstinence are particularly appropriate for younger youth who are not yet sexually active. Youth who want to defer sexual activity should get support to do so and be reassured that abstinence is a healthy life-style choice; they should learn how to overcome pressure from others to become sexually active.

HIV has a young face...

- Everyday, an estimated 5,000-6,000 young people aged 15-24 become infected with HIV.
- Globally almost one fourth of those living with HIV are under the age of 25.
- Of the 15-24 year old young people living with HIV, 63% live in sub-Saharan Africa.

The young face is also often female...

- Globally, a third of women living with HIV are between 15-24 years old.
- In sub-Saharan Africa, young women are three times more likely to be HIV positive.
- In some countries at least one fourth of young women experienced coerced and unprotected sex which can result in significant HIV transmission.

Source: UNAIDS, 2004

HIV prevention efforts among sexually active youth should encourage youth to limit their number of sexual partners and promote secondary abstinence. Those who are sexually active need sexual health services that include screening, treatment, and prevention of STDs; they should receive counselling, as well as condoms and contraceptives. They should get information about where they can access the services.

School-based interventions rely heavily on teachers—the trusted *gatekeepers* of information. Teachers are often expected to provide sexual and reproductive health education for their students, but they may not be well equipped to undertake this task effectively.

Services for HIV-Infected Youth

An estimated 5% of children infected through mother-to-child transmission of HIV survive early childhood into adolescence (long-term survivors). As ART services begin to include HIV-infected youth, many will live longer and be well enough to start engaging in intimate sexual relationships. Sexual health services should be broadened to include HIV-infected youth, with added discussion of how HIV infection modifies such life choices as whether to get married or have a baby.

Organization of services for HIV-infected youth needs to take into account the social context in which the youth are living and their stage of development. Chronically ill children who have growth and developmental delay of adolescence may feel comfortable receiving follow-up in a paediatric clinic. On the other hand, those who are already undergoing the changes of adolescence may feel they do not fit in the children's clinic even though they are not able to cope with the impersonal nature of adult clinics.

HIV-infected youth are frequently marginalised and also have escalating health needs. Their survival will depend largely on their ability to communicate their needs and negotiate for services. Training in communication and negotiation will empower them to access services.

Ultimately, one of the most critical life skills will be their ability to take responsibility for their own treatment. The health worker can help the youth achieve this objective by providing information about their treatment; communicating clearly about follow-up; providing the opportunity for drop-in services between visits, as and when desired; and developing a warm relationship with the youth that supports communication and disclosure of sensitive problems.

Diagnostic Services, Including Voluntary Counselling and Testing

HIV testing, including pre- and post-test counselling, should be available to adolescents who are symptomatic or those who want to know their HIV status. VCT has traditionally been recognised as the key entry point for developing integrated prevention and care programmes for adults. The role of VCT in programmes for children and adolescents, however, has been more controversial.

Despite the desire of many adolescents to know their HIV status, many programmes and published guidelines discourage testing for this group. For example, the *Model Guidelines for VCT of the Southern African Development Community* recommends: "Youth between 15 and 18 years may receive services (only) if they are a 'mature minor,' already engaged in risk-associated behaviour(s)" (Futures Group International, 2002). Determining who is a "mature minor" allows health practitioners to introduce gender bias and discrimination, discouraging adolescents from seeking testing.

Even when adolescents do have access to VCT, the quality of the services is often unsatisfactory. One study of adolescents in Nairobi found that one out of four youth did not talk with a service provider either before or after an HIV test. These youths got their test results either as a written report or from a third person, such as a parent (Horizons, 2001). A related study in Uganda found that few care and support services were available for referral of adolescents (Horizons, 2001).

We do not know whether the current models of VCT sites (free-standing, integrated, mobile/outreach, community, located in youth centre) are appropriate for adolescents, especially the younger ones, whose cognitive development has yet to reach the point of linking current activities to future outcomes. Younger adolescents may not appreciate the seriousness of HIV disease because they cannot comprehend its long-term implications.

Health workers should treat adolescents who are pregnant or who are already parents as adults and allow them to consent to HIV testing. Counselling and testing services offered in the context of pregnancy

care (as part of PMTCT) should extend to adolescents and their partners; this includes screening for STDs and HIV/STD prevention counselling. Young women are more likely to present for antenatal care later in pregnancy and less likely to deliver at a health facility or have a skilled birth attendant at delivery.

It is important to ensure confidentiality during counselling and physical examination.

Disclosure of HIV Infection Status

Adolescents' Need for Privacy

Disclosure of HIV status to adolescents presents challenges. Preferably a young person attending a sexual health service will have the support of a parent or of a guardian. Often, however, young people do not want their parents or caregivers to know about the medical consultation or its outcome.

An adolescent girl faced with a diagnosis of HIV during pregnancy may find it difficult to disclose her status to her partner (especially if he is older) or to her own parents or guardians.

It is important for health workers to discuss the value of parental support with the young person; at the same time, they should respect the young person's wishes, views, and confidentiality, should he or she not want parental involvement. Adolescents who are parents should be treated as adults.

Where there is possible child abuse, disclosure presents a greater challenge. If sexual abuse is suspected or ascertained, the clinician must support the young person and respect views on disclosure.

Parents' Fears of Disclosure

Parents of vertically infected children may already know the child's HIV status. Frequently these children's caregivers may be too afraid to disclose this diagnosis to the adolescent for fear of being blamed or even rejected. Health workers should emphasise that disclosure is

advantageous because it enables adolescents to comprehend issues surrounding their illness and care.

There is controversy about the age of disclosure, with some people advocating for disclosure as early as the age of 5 to 7 years, assuming that older adolescents may not be able to deal with it. Disclosure is a continuing process (not a one-time event) and is different for each family. A good cue for beginning the process is questions from the adolescent, although one should not necessarily wait for these. Be alert to reactions or comments that may signal that the young person is not ready to hear the information. Typically the health worker's role is a supportive one, but in the absence of an appropriate family member or at the request of the family, the health worker may have to assume the primary role.

When a health worker is required to take the lead role in disclosure, the following exploratory questions may launch the process:

- Why do you think you are coming to the doctor?
- What is the blood test for?
- Why do you think you take medication?
- Do you have any questions you would like to ask me?

It is critical never to make any assumptions about what a child or adolescent does or does not know.

Prevention and Management of OIs and Antiretroviral Treatment

Adolescents diagnosed with HIV/AIDS need to receive the same care that is increasingly available to adults—including antiretroviral treatment. The U.S. Centers for Disease Control and Prevention (CDC) recommend that clinicians should calculate the drug dosage for adolescents who have not yet achieved Tanner stage II (see **Appendix C**) as per the paediatric schedule; otherwise, treat them as adults.

Dose drugs such as cotrimoxazole, and other antibiotics for the treatment of opportunistic infections, on a per/kg basis, until the adoles-

cent is over 60 kg, when they would typically graduate to adult dosing guidelines.

Adolescents who do not qualify for ARVs should receive regular follow-up to monitor disease progression and ensure timely initiation of treatment.

Drug Adherence

Adherence to long-term therapy poses a special challenge in adolescents. This age group tends to have thoughts ranging from immortality to self-destruction. A multidisciplinary team that includes social workers, psychologists, counsellors, nurses, and clinicians needs to address this challenge.

Among the factors affecting drug adherence among adolescents and needing attention are:

- **Depression:** Individuals who are depressed have little motivation for life's activities, including taking prescribed medications. Encourage adolescents to discuss their feelings with the doctors, nurses, or counsellors in the clinic.
- **Active substance abuse** (alcohol, cocaine, heroin) makes it difficult to adhere to drugs. Alcohol use increases the likelihood of having serious side effects from some antiretroviral drugs. Clinic staff should counsel youth on substance use and create an atmosphere that encourages disclosure of drug use.

Some strategies may improve adherence among youth:

- Help them to believe that they can take drugs as prescribed. This is the first step to successful antiretroviral drug adherence. It also improves adherence when they believe HIV medications will fit into their life-style. Help the adolescent adopt a positive attitude towards the medication.
- Before starting ARVs, help the adolescent to practice drug adherence by first ensuring that they take vitamin pills and CTZ prophy-

laxis well. Adherence with previous medication is well correlated with adherence to current medication. Encourage the adolescent to keep a diary and the reasons for forgetting to take the drugs.

- Let the adolescents know that they should continue taking the drugs even if they are feeling well. Remind them that HIV is a chronic disease, that antiretrovirals are not a cure, and that in order to continue to feel well they need to take the antiretrovirals every day, as prescribed.
- Develop a good relationship with the adolescents and let them know you are their partner in striving for good health. A good relationship increases the likelihood that they will be practice adherence to prescribed drugs.

Reproductive Health Services

Studies recommend a comprehensive *essential* package of sexual and reproductive health services for young people at all primary health care facilities and other youth care service points (IPPFAR, RHRU, 2002). These include:

- Information, education, and counselling on sexual and reproductive health
- Information, counselling, and appropriate referral for violence/abuse and mental health problems
- Contraceptive information and counselling; provision of methods, including oral contraceptive pills, emergency contraception, injectables, and condoms
- Pregnancy testing and counselling; antenatal and postnatal care
- Referral for post-abortion care and post-abortion contraceptive counselling
- Information on sexually transmitted infections (STIs), including information on the effective prevention of STIs and HIV; diagnosis; and syndromic management of STIs, including partner notification

- HIV/AIDS information, pre- and post-test counselling, and appropriate referral for voluntary testing, if services and not available

Ongoing Counselling and Psychosocial Care

By the time they reach adolescence, many perinatally-infected children have the stigmata of chronic illness, including stunted growth and development and poor school performance because of frequent absences. They may be orphaned or live in a household with chronically ill parents. The delay in adolescent development often leads to poor self-esteem and a great sense of inadequacy.

Communities may ostracize adolescents orphaned by AIDS. Some of these sick youth are heads of households and have to fend for themselves and their younger siblings, as well as deal with issues of having to mature socially too soon. They face complex physical and psychosocial problems.

Effective counselling for adolescents should be culturally sensitive, tailored to their developmental needs, and in accordance with local values and laws.

Psychosocial care should revolve around disclosure of HIV status, family or partner notification, and understanding the disease and treatment modalities. Adolescents must be supported to cope with illness and death—their own as well as that of their parents.

Training in Life Skills

Having life skills helps adolescents be confident, knowledgeable, and able to take responsibility for their lives.

As a first step, HIV-infected adolescents should be given information about their own bodies and the process of development, including why growth might slow and what can be expected with ARV therapy. The process should also discussions held one-on-one or in peer groups that help them to develop self-awareness, self-appreciation, and self-respect.

As family members die, the ability to build friendships and support networks will sustain adolescents. Spiritual development helps build resilience for coping with difficult major life events, such as loss of family members.

Adolescents also need skills to enable them to earn a livelihood. Services should make every effort to keep the young person in school and to provide vocational training.

Health workers are not necessarily the most skilled persons to provide this training to HIV-infected children. By providing a meeting space in the clinic and inviting skilled individuals, health care workers can help facilitate the process and foster the formation of a forum where adolescents can get together and through which they can develop some of these skills.

Support for Youth-Friendly Policies and Programmes

Advocacy and action are necessary to mobilise political will and resources for youth-friendly HIV care and treatment services. The lessons learned from implementing youth-friendly reproductive health and HIV primary prevention services need to inform national policies. Experience is much more limited in connection with youth HIV care and treatment, in part because adolescents are classified either as adults or as children.

Some early experiences with youth-friendly VCT corners show that it is indeed possible to reach young people without creating parallel systems of service delivery.

Adolescents prefer healthcare settings that are oriented to their age group and providers who are attuned to their specific needs. The ideal facility is a one-stop centre with multidisciplinary providers to for primary care, gynaecological services, OI prophylaxis, and ARV drugs; but often this is not available or immediately possible.

The following principles should guide national policies and youth services in general. Every client has a right to:

- Information
- Access—regardless of sex, creed, colour, marital status, or location
- Choice
- Safety
- Privacy
- Confidentiality
- Dignity—to be treated with courtesy, consideration, and attentiveness
- Comfort—to feel comfortable when receiving services
- Continuity—to receive services for supplies for as long as needed
- Opinion—to express views on services offered

Care for adolescents should be linked to other programmes that provide reproductive and other social and material support.

Beyond providing clinic-based services, the health sector has an important role to play in providing evidence for policies and interventions in other areas, for example, in schools, communities, and social welfare services.

Advocacy also plays an important role in countering the stigma and discrimination that often underlie the transmission and impact of HIV/AIDS among young people and that limit their access to available needed services.

Knowledge Gaps

- Currently in most of sub-Saharan Africa, health practitioners and health facilities, whether for children or adults, are not adequately

prepared to address the needs of HIV-infected adolescents and young people, particularly those who are recently diagnosed.

- Knowledge and experience of services for the mental and psychosocial needs of adolescents and young people living with HIV/AIDS is limited.

Additional Reading

"Preventing HIV Infections in Children and Adolescents in sub-Saharan Africa through Integrated Care and Support Activities: A Review of Literature." *African Journal of AIDS Research* 2002, 1: 143-149.

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Voluntary Counselling and Testing and Young People: A Summary Overview. VCT Toolkit. FHI. December, 2002. Also available at www.fhi.org

Standards for Youth Care. A Guide to the Youth-Friendly Services Initiative. International Planned Parenthood Federation Africa Region. July, 2002.

Chapter 10
Long-Term and Terminal Care Planning for Children Affected by HIV/AIDS and Their Families

Summary

- Children with HIV/AIDS in resource-constrained countries experience high rates of morbidity and mortality relatively early in their lives, with up to 75% mortality by 5 years of age.
- Improvements in basic HIV care, and more recently antiretroviral therapy, have improved survival among HIV-infected children in developed countries. On the other hand, HIV-infected children in resource-limited settings continue to have little access to even basic HIV and supportive care.
- Globally, but particularly in resource-constrained settings, the terminal care needs and services for children with life-threatening illnesses are poorly understood and poorly developed.
- Delivering basic HIV/AIDS care, antiretroviral treatment, and terminal care to HIV-infected children and their parents requires planning to ensure more than episodic contact with the healthcare system, at both the institutional and community levels.
- Continuity in provider and services is essential for ensuring optimal quality of life for the child and family.

Introduction

Children with HIV/AIDS have a variety of clinical care and psychosocial and socioeconomic needs, as well as the need to enjoy their rights as children. These needs vary with the stage of the illness and the availability of family and community support systems.

To achieve the best outcomes, children affected by HIV should be *enrolled* early and *retained* in care. To ensure such enrolment and retention in care requires a system for identifying these children, for monitoring their health on an ongoing basis, and for delivering appropriate interventions as dictated by the stage of the illness.

Where different groups of providers deliver these interventions, as is often the case, there is a need for functional referral linkages and effective communication channels to ensure a continuum of care.

Is Chronic Disease Management Relevant to Children Infected with HIV?

It is true that the life span of children infected with HIV in Africa is often very short. However, the effects of the disease on their families will often have predated their own birth and will likely continue after their death.

The current promise of improved access to effective therapies in resource-poor setting, including antiretroviral therapy, must be turned into a reality. These therapies have already revolutionalised paediatric HIV care in industrialised countries, resulting in survival of perinatally-infected children into early adulthood.

Chronic disease management is therefore as relevant for children and their families in resource-poor settings as it is for adults. Because palliative care as a whole—and especially terminal care—is so poorly developed and very context specific, every effort should be put into planning for the long- term care of an HIV-infected child.

What Is the Starting Point for Planning Long-Term Care?

There are three common (or potential) entry points into care for children affected by HIV:

- Children diagnosed with or suspected to have HIV because of symptomatic disease (inpatient and outpatient clinics)
- Children born to HIV-infected mothers (MCH clinics, through PMTCT programmes)
- Children of parents known to have HIV/AIDS (in home care settings; or adult care settings, with the child as the attendant)

Health workers should initiate a long-term care planning process regardless of the stage of illness or the point of contact with the health system. This should be with participation of the child (if the child is old enough) and the family, since they play a critical role in executing care plans for the child. Discharge planning should be a routine part of care and should detail the date of the next visit, where to report, what records to bring, and so on.

Generally, health workers do not take enough advantage of these entry points. Even when they do, there are often insufficient links with the next point of contact. Hence each visit is like a new visit. Where health workers are committed to providing good care, the benefits of documenting HIV positive status far outweigh concerns about possible stigmatisation and discrimination.

The broad categories of clinical care needs for HIV-exposed or -infected children are:

- *Well-child* (not symptomatic, exposed, or infected) needs
- *Sick-child* needs
- Terminal care needs

- Needs of the child with terminally ill parents; orphan; or sibling of a symptomatic infected child

The needs of an individual child will change over time, depending on family circumstances and the stage of illness. The continuing but evolving needs require multiple providers, a participatory care plan, and effective mechanisms of communication among all players.

Clinical records offer the most objective way to ensure continuity of care, but health management information systems are often weak and ineffective. PMTCT programmes, for example, are still struggling with mechanisms to identify infected women and their exposed infants post-delivery. Concerns about stigmatisation limit the acceptability of including HIV status on simple hand-held patient cards.

The need for continuity of care, however, dictates that comprehensive clinical records, including HIV status, be kept—with mechanisms to preserve shared confidentiality among the care team. An informed and empowered caregiver actively complements clinical records and follows through with the follow-up schedule and care plan. Continuity in care providers is much more challenging, given the high levels of attrition, transfers, and mobility of health care workers, and underscores the need to invest in training of all health workers in all aspects of HIV care.

Needs of the Well Child

More than any other child, an HIV/AIDS-exposed or -infected infant needs traditional *under five* child health services, including:

- Immunisation
- Growth and development monitoring
- Optimal infant feeding and nutrition promotion
- Observance of basic personal and environmental hygiene
- Prompt treatment for incidental illnesses

- Information, education, counselling, and skills development for caregivers

Such infants also need HIV diagnostic services and preventative therapies (CTZ prophylaxis; INH prophylaxis, where indicated).

Coordinate well-child care services for infants with care for their mothers in maternal and child health (MCH) clinics. A tracking system (linked over time and with provider) is required to signal which children need to go into a more intense system of follow-up (see **sick-child needs**). Different programmes have tried different mechanisms, for example, including on infants' immunisation cards such notations as: "Nevirapine administered"; "provide PCP prophylaxis at 6 weeks"; "special prenatal care".

Needs of the Sick Child

In developing countries many HIV-infected children die from common childhood illnesses even before they develop severe immunosuppression. Early diagnosis and prompt and correct management of common infections can prevent many unnecessary deaths. IMCI guidelines, especially where they have been adopted for HIV, are relevant and should be applied for the care of HIV-exposed or -infected child.

Nutrition guidelines for sick children (IMCI) also apply, with modifications to limit HIV transmission through breast milk for infants of HIV-infected mothers.

Discontinue preventive therapies for children until they are either not at risk for these infections or until they have completed the recommended duration of treatment (INH).

Assess all sick infants against specific criteria (national or international) for antiretroviral therapy (ART). Make ART available for eligible HIV-infected children wherever it is available for adults with HIV/AIDS.

Continue caregiver information, education, counselling, and skills-building to optimise adherence to prescribed therapeutic and other interventions and to access other available care in the community (home care, psychosocial support, spiritual support, community revolving-drug-funding mechanisms, long-term food security interventions, economic empowerment activities, and the like).

Needs of the Terminally Ill Child

Terminal care for children with life-threatening illnesses, including AIDS, is a major challenge globally, and especially in resource-poor settings. In these settings, there is a paucity of experience and culturally acceptable and replicable models of both institutional and community-based planned terminal care.

An HIV/AIDS diagnosis in a child creates difficulties beyond the physical sickness, because of the associated guilt and the possibility or likelihood that more family members are infected, sick, or dying.

The child and parents are often ill-prepared for the coming death because of late diagnosis, the reluctance or inability of health workers to discuss death with patients, the unpredictability of the disease progression, and denial.

Where parents and/or caregivers are aware of or suspect a child's imminent death, they may react by withdrawing emotionally. This contrasts sharply with needs at the end of life: for physical comfort, physical touching, emotional closeness, and spiritual health, all of which can have a major positive impact on the quality of remaining life.

In the African setting, there are complex belief systems and rituals surrounding death and dying, and these systems may be different for a child and an adult.

Terminal care preparation for children and their families is a long-term process that requires continuity in both care providers and services. This is often not guaranteed in many resource-poor settings and it *will not happen unless it is planned*.

Terminally ill children are often placed in acute care facilities, but they may receive inappropriate care in these facilities because they must compete for resources with patients who are more acutely ill.

What Can Be Done to Improve Terminal Care for Children?

Orientation and training of healthcare workers in terminal care is essential to enable them recognise terminal illness, prepare the child and family, manage multiple symptoms optimally, and recruit needed support from members of the team.

Alternatives to acute care facilities, including hospice-care institutions (where these exist) and homes, should be considered and discussed with the family.

Basic nursing care and help with Activities of Daily Living (ADL) are central to good terminal care in particular, because failure to manage symptoms appropriately (see **below**) can directly affect the quality of dying and may even hasten death.

The frontline health worker in terminal care is the family caregiver and, increasingly, home care teams are investing in the instruction and training of these caregivers to optimise care in the home setting.

Care should focus on the needs of the child and family. It usually includes the following:

- Relieve distress and ensure comfort, to the extent possible (manage symptoms, attend to positioning and mobilising, maintain hydration and, at a minimum, keep the mouth moistened, keep skin dry, etc.). Avoid the temptation to provide care in a dark closed environment.
- Assist with activities of daily living.
- Limit hospital admissions if family can provide care at home. Review admission options if the family is not comfortable providing care at home.
- Provide emotional support to the dying child and grieving family.

- Encourage recruitment of more family members to participate in the care of the child.
- Help the family to plan ahead.
- Communicate with the child and family and other caregivers; this is central to the success of terminal care. Answer questions as they come up; it is acceptable not to know the answer. Listen carefully. For children, give information appropriate to their age. Do not stop with one conversation.

Grief management requires special consideration in children. Develop practical guidelines that take into account local sociocultural factors.

Symptom Relief

Symptoms are a major cause of discomfort and poor quality of life during the course of HIV infection and AIDS in children. Many of these HIV-related symptoms can be prevented, treated, or controlled with basic medications and therapies.

HIV symptoms are a direct cause of social isolation. Chronic coughs and severe pruritic and disfiguring skin disorders are particularly problematic for older children who are attending school, because the symptoms are highly visible and both teachers and pupils are concerned about contagion.

Non-pharmacological methods are an important adjuvant to symptom management with medications (or can be used alone). They include distraction methods, massage, aromatherapy, and more traditional therapies, which vary from place to place.

It is important to try to identify the cause of symptoms, to the extent possible, without adversely affecting the quality of the child's life and within the limits of available resources, especially if the causes might alter management. However, empiric and symptomatic treatment should not be withheld while doing diagnostic workup or in situations where the underlying diagnosis cannot be established. Also, health

workers should try to anticipate and prevent symptoms, when possible (e.g., pressure sores).

At the end of life there tend to be symptoms that must be addressed. *Polypharmacy* is a real danger and should be avoided to the extent possible, especially where adverse drug-drug interactions are likely. A summary of common symptoms and their management is presented in **Table 10.1**.

Table 10.1. Other Common Symptoms, Causes, and Their Management		
	Causes	**Management**
Nausea and vomiting	Drugs, gastrointestinal infections, fever	Small frequent feeds, fluids between meals; offer cold foods, eat before taking medications, dry foods, avoid sweet, fatty salty, or spicy foods.
Sore mouth	Herpes simplex, apthous ulcers, thrush, gingivitis	Keep mouth clean; clean with soft cloth or gauze in clean salt water. Give clear water after each feed. Avoid acidic drinks and hot food. Give sour milk or porridge, soft and mashed. Ice cubes may help; ice cream or yoghurt, if available and affordable.
Chronic diarrhoea	Infections, malabsorption, malignancies, drug-related	Rehydration, diet modification (e.g. yoghurt rather than fresh milk), micronutrient supplements. Oral morphine can alleviate intractable diarrhoea.
Persistent cough	Infections, LIP, bronchiectasis	Nebulization with physiotherapy, low-dose morphine
Severe dermatitis	Infections and infestations, hypersensitivity, malignancies	Emollients, antihistamines, antiseptics, topical steroids. Keep nails short to minimize trauma and secondary infection from scratching
Convulsions	Infections and infestations, encephalopathy, malignancies, PMLE, metabolic disorders	Anticonvulsants, dextrose, mannitol, steroids
Wounds	Infections, pressure, malnutrition	Wound dressing, metronidazole powder to control odour, honey applications on clean wounds

Pain Management

Pain as a symptom takes on special significance in children because it is very common and is often underdiagnosed and undertreated, even when effective and inexpensive medications are available. A rational approach to pain management includes the following:

- Assessment (history and physical exam to elicit potential causes and type of pain)
- Classification (is the pain mild, moderate, or severe?)
- Treatment (depending on likely cause, type, and severity of pain)
- Reassessment to ensure that optimal pain management is achieved and maintained

Assessment

Assessment and classification of pain in children is different from that in adults and depends on the age of the child and the stage of development. There are several ways to assess pain in children:

- Interviewing the older children
- Interviewing the caregiver. (Younger children in particular need adults to recognise and respond to their pain.)
- Observation

By using a combination of these methods, you may be able to elicit or observe the following:

- Listlessness/lack of interest
- Irritability, crying, wincing
- Not wanting to move (pseudoparesis)
- Changes in mood
- Change in sleep pattern
- Poor appetite

- Loss/lack of concentration
- Loss/lack of interest (for example, in play)

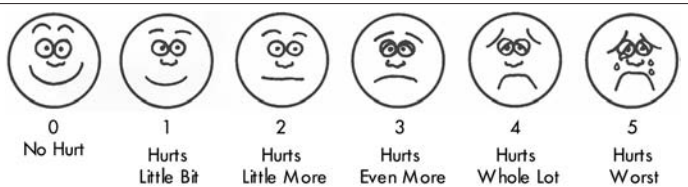
Common causes of pain among children with HIV disease include: severe infections (viral, bacterial, fungal, parasitic), abdominal pain (frequently of undetermined origin), spasticity secondary to encephalopathy, and procedural pain (spinal taps, blood draws, intravenous line insertion).

If you identify a cause of the pain, proceed with pain management along with specific treatment of the underlying cause, especially if this is reversible and the treatment does not compromise the child's quality of life (for example, consider aggressive chemotherapy for Kaposi's sarcoma in a child who is terminally ill).

Classification

In addition, depending on the age of the child, you can use different tools to grade the intensity of the pain.

For children aged 3 years and older, the **Wong-Baker Faces Scale** (below) is used.



To use the faces scale:

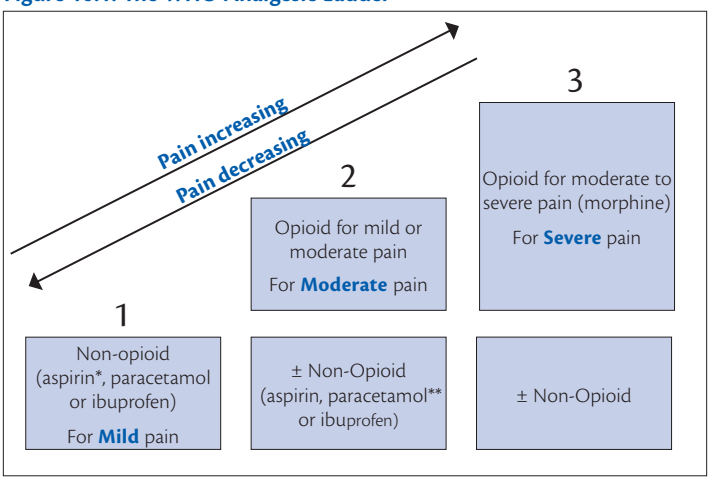
- Point to each face, in turn, and explain, in the child's language, what it portrays in terms of pain.
- Face 0 is happy because he or she feels no pain, all the way to Face 5, which portrays "it hurts as much as you can imagine" (although you may feel this bad and not cry).
- Now ask the child which face best describes how he or she feels. Record this number

Treatment

Figure 10.1, below, presents treatment guidelines for pain in children. They are based on the WHO analgesic ladder for the management of mild, moderate, and severe pain. To the extent possible, pain medications should be given:

- By mouth (orally). You may also give special preparations rectally although these may be less available an in some settings, less familiar and less acceptable.
- By the clock.
- By the WHO Analgesic Ladder.

Figure 10.1. The WHO Analgesic Ladder



* Note that aspirin should generally be avoided in children (because of Reye's syndrome), although often it is the only available option. In treating chronic pain in the terminal care setting, the need to alleviate pain and suffering often supersedes concern about Reye's syndrome.

** Note that rather than increasing the dose of paracetamol, for example, the logical step for uncontrolled pain would be to move on to step 2.

Adapted from: Palliative Care: symptom management and end-of-life care. Integrated Management of Adult Illnesses. Interim Guidelines for First-Level Facility Health Workers. WHO, 2004

Decisions about pain medication should be individualized for each child.

In the absence of codeine to manage moderate pain, aspirin every 4 hours can be alternated with paracetamol every 4 hours so that one or the other is administered every 2 hours.

Breakthrough pain (that occurs before the next regular dose of analgesia) can be managed as follows:

If pain is severe, provide the full 4 hourly dose of oral morphine, and *in addition, give the next scheduled 4 hourly dose at the prescribed time.* Add up all required additional doses provided in 24 hours, and increase the next day dose by this amount, spread evenly across the six 4 hourly doses.

Reassessing for optimal pain control: Regularly monitor pain control using the same methods above, and record breakthrough pain.

In general, one should allow 24 hours before considering a dose increase or oral morphine.

It is important to note that there is no maximum dose for oral morphine, as long as pain is inadequately controlled. The right dose of oral morphine is the dose that achieves optimal analgesia, and this is determined through titrating dose against analgesia response. Pain is the natural antidote to morphine overdosing.

Child with Terminally Ill Parents

Children with terminally ill parents are affected by HIV/AIDS in many ways and have a wide range of problems and needs such as the following:

- Psychological distress
- Anxiety about their security and safety
- Lack of parental nurturing
- Lack of basic needs
- Loss of inheritance
- Need to work
- Less education and skills
- Mental health needs
- Emergency and long-term childcare
- Bereavement and grief counselling

Responding to a dying parent's needs will also address many of the child's immediate concerns, including reassurance that the child will receive care when the parent is gone.

To respond to the needs of a child whose parent is dying in an appropriate way, it is important to understand how developmental stages affect children's perception of death and dying.

Table 10.2. Children's Perceptions of Death and Possible Interventions		
Age	**Perception of death**	**How to help the child**
1–3 years	Equate death with sleeping and expect people who have died to wake up. Fear separation from parent/caregiver.	Keep the child's daily routine as unchanged as possible. Make time each day to hold, talk to, and comfort the child.
3–4 years	Children this age do not accept death as final and think of it as a temporary separation. Child may believe that they are in some way responsible for the death because of powerful imaginations (magical thinking). Perhaps, if they wish hard enough, the dead person will come back.	Explain clearly why the person died: "X died because she was not well. It had nothing to do with you, with something that you did or didn't do".
5–8 years	Begin to accept death as final and view it as separation from loved ones. They have a great fear of a sick parent dying, and of being abandoned. They worry about their own death.	Reassure the child that minor illnesses and injuries can be treated. Reassure the child that it is okay to cry, to feel angry, sad, or frightened when someone dies. Reassure them that they are not responsible for the death.
8–10 years	Children learn that all living things must die; they begin to feel sorrow and loss. Interest in the mystery of death grows.	Answer questions as fully as possible. Do not discourage normal curiosity about death. Acknowledge the child's feelings. Allow the child to cry and talk about the loss.
9–11 years	React strongly to death. Interested in what happens after death. Death is accepted as a part of life.	Answer questions fully. Acknowledge and explore the child's feelings. Interventions may include: talking about memories; writing a daily journal; drawing pictures of how he or she feels; prayer; compiling a picture album of the loved one.

Adapted from: Manual. Maternal-Child HIV Training Course. *AIDS Research & Family Care Clinic. Coast Province General Hospital, Mombasa, Kenya. August, 2001.*

Although the above observations are based largely on what is known about the development of children in industrialised countries, there is every reason to assume that African children have comparable perceptions of death at the same ages.

The uninfected sibling of an infected or dying child similarly may have unmet psychosocial needs, as a result of the continuous attention demanded by the sick child. Secrecy and lack of communication may deter the child from asking questions. Resentment may occur because of feelings of deprivation and exclusion.

It is important for the family to set time aside for this sibling or siblings and to communicate what is happening, within the limit of each individual child's developmental stage and understanding.

Requirements to Ensure that Long-Term Care Is Planned and Executed

Critical factors in effective long-term planning include knowledgeable personnel, a functional health infrastructure, access to essential drugs and supplies, early and active communication and involvement with parents/guardians, community-level support structures, and ongoing efforts to support caregivers.

Personnel

Caregivers who are knowledgeable and skilled in a range of HIV care needs, including terminal care and symptom relief, and who understand the basic principles of managing chronic disease are critical for effective long-term care planning.

A Functional Health Infrastructure

To deliver basic HIV diagnostics and clinical care requires functional communication channels and referral relationships among care providers, hospital departments, other agencies and communities.

A Functional Information Management System

Written information is essential for tracking the patient through different services and monitoring document disease progression: registers, treatment notes, hand-carried patient cards with identifying number, and a treatment plan.

Access to Essential Drugs and Supplies

This is required for providing comprehensive care and services for children and their families.

Early and Active Communication and Involvement with Parents/Guardians

Communication with the child and parents or guardians is a critical component of care. It should include making care plans that include the preferred place of dying, where appropriate. This is a long-term process and it varies with the child's developmental age.

Community-Level Support Structures

Structures such as self-help groups are important in long-term care. Examples of skills building and services provided by such groups include:

- Building memories through deliberately planned activities with the child and family; these are important for a dying child and family members.
- Other options are documenting family experiences though diaries, albums, video footage—within the family's resources (for example, the Memory Book and the HIV/AIDS quilt).
- Community feeding centres for vulnerable children.
- Community revolving funds for economic empowerment activities.

Support for Caregivers

There must be continuing efforts to support caregivers by providing them with information, education, counselling, and skills building

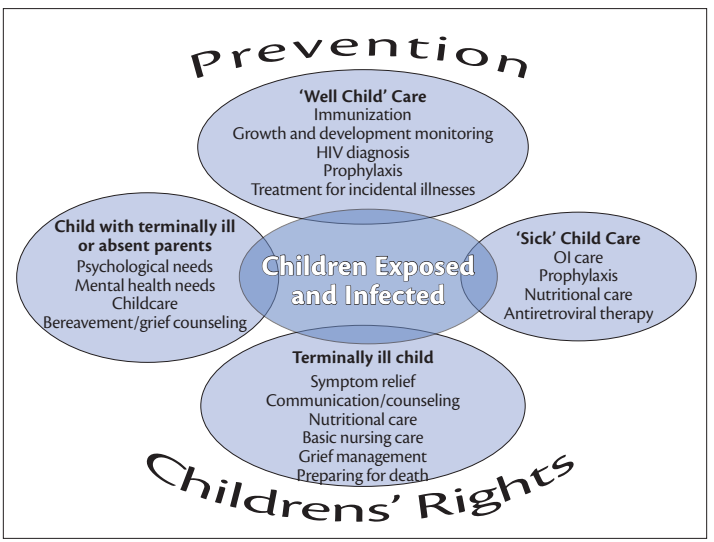
through community/home-based care providers, outreach workers, and institution-based counsellors and clinical care providers.

Clinician's Role in Long-Term Care Planning

The clinician's role in long-term care planning includes being a:

- Facilitator/catalyst of the process by mobilising a *care team* (in many settings it is limited in skills, skill sets, and number)
- Team leader, a monitor of the care plan
- Advocate for the child's rights
- Person to mobilise community and external resources to improve paediatric HIV care
- Liaison between child and parents and between parents and the rest of the care team, healthcare workers, and other disciplines

Figure 10.2. Long-Term Care Planning for Children with HIV



This handbook covers many of the needs highlighted above in detail in other chapters.

Knowledge and Operational Gaps

There is a dearth of knowledge about the terminal care needs and current practices in sub-Saharan Africa, particularly about culturally acceptable models of care. For example, is institutional hospice care an acceptable option for terminally ill children?

Operationally, how can we simultaneously improve both palliative care and antiretroviral therapy for children infected with HIV, given the enormous challenges of integrating paediatric HIV primary care into health care systems in Africa?

What are the beliefs and practices around the death of a child and how do these differ from those around adults?

How can we maximize symptom management in health facilities and in the community when drugs and consumables and their supply are difficult to assure, even in urban health centres?

Chapter 11
Counselling and Psychosocial Support

Summary

- Counselling aims to help the child and family cope with the many emotions of HIV/AIDS in the family.
- Problems that occur if the psychosocial needs of the child are not met include depression, which health workers often do not attend to.
- Communicating with children requires trying to understand their thoughts and feelings and responding in a way that is helpful.
- Children cope with disclosure of HIV results as effectively, if not better than, adults.
- Disclosure can start as early as 5 to 7 years of age, but it must be done gradually, in a culturally sensitive manner, and with the consent and participation of the parents or caregivers.
- Make every effort to link the health facility-related counselling for the child with other social and spiritual support services outside the health system.

Introduction

A child with AIDS usually identifies a whole family at risk of infection. AIDS disrupts the family balance by placing a dark cloud over the family's future.

Many families affected by AIDS are already burdened with poverty. HIV can overwhelm already weak coping capacities and push a family into complete disorganization and crisis. More than one family member may be ill with AIDS at the same time. This puts strain on the family—depleting economic reserves and increasing vulnerability to psychological stress and depression.

Care of the HIV infected child must be child-centred and family focused. This requires comprehensive care by a multidisciplinary team. The HIV infected child cannot be treated in isolation. A family-centred approach is crucial to strengthening the family's ability to cope with the child's illness and its consequences.

Counselling and psychosocial support are integral components of the holistic approach to caring for an HIV-infected child. Counselling is a continuous process that usually begins at the first point of contact in the health system and continues through non-health sector support services. Psychosocial issues must be addressed from the perspectives of the child, the caregiver, and the healthcare provider. Support for a child and his/her family allows them to build on their strengths and adopt a positive outlook.

Psychosocial assessments that identify each family's strengths and vulnerabilities are an essential component of the comprehensive care of an HIV-infected child. Such assessments help the health care team plan appropriate psychological interventions. An example of an assessment tool is provided in **Table 11.1**.

Table 11.1. Psychosocial Assessment of Anticipated Family Adaptation
• Child and family's knowledge and reactions to the disease • Beliefs, attitudes, and expectations regarding treatment and outcome • Coping ability during previous crises • History of depression and/or non-prescribed drug and alcohol use • Nature and stability of residential and occupational arrangements • Quality of relationships between family members and extended family members • Who is aware of the diagnosis and what was their reaction? • Socioeconomic status of the family • Socio-cultural factors or religious beliefs that might affect treatment decisions and adaptation • History of previous losses • Sources of emotional and financial support; availability of medical insurance • Health status of all family members
Source: Wiener L. and Septimus A. Psychosocial consideration and support for the child and family. In: Pediatic AIDS: the challenges of HIV infection in infants and children, and adolescents. Pizzo P.A, and Wilfert C.M., eds. Williams and Wilkins 1991.

Periods of Psychosocial Vulnerability

Psychological stresses are heightened at the time of initial diagnosis, during episodes of illness and during terminal illness.

Diagnosis

The family's response to the diagnosis of AIDS in a child includes shock, fear, guilt, disbelief, anger and sadness. Due to the implications of the diagnosis and a wish to reverse the outcome, it is not unusual for parents to request repetition of diagnostic tests. Once the HIV status is accepted, families experience grief reactions as they mourn the loss of their hopes and dreams for the future, and some family members may develop depression that requires intervention.

During Episodes of Illness

As the child has episodes of illness, parents struggle with feelings of helplessness, sadness and anger. It is during these episodes that the implications of the disease become an emotional reality.

Terminal Illness

Dealing with terminal illness is one of the most challenging tasks in the care of HIV-infected children. During this time parents need assistance to ensure that their child receives dignified end-of-life care in the hospital or at home.

Issues to Address in Psychosocial Support for Children Affected by HIV/AIDS

Issues from Infected or Affected Child's Perspective

HIV-infected children and uninfected children in families where there is HIV have to deal with many psychosocial issues, including:

- Dealing with chronic ill health, pain, and discomfort
- Being different from others
- Watching a parent battle a terminal illness and sometimes caring for them
- Bereavement and its consequences, such as separation from close family members or change in socioeconomic circumstances (e.g., having to leave school, having to do without basic necessities, having to get a job, having to look after younger siblings, being homeless)
- Asking questions that are not answered or getting evasive answers

Issues from Caregiver's Perspective

Regardless of how the child became infected, parents experience some degree of guilt. In sub-Saharan Africa where mother-to-child transmission is the main mode of HIV transmission in children, the

mother—who is invariably the primary caregiver—is also HIV infected. Psychological issues she will need to deal with include:

- Dealing with his or her own diagnosis
- Dealing with the child's illness and the related feelings of guilt, anger, and hopelessness
- Deciding whether or what to tell the spouse, child, relatives, neighbours, or school authorities
- Fear of disclosure and the need to lie to others
- Reproductive desires and decisions in the face of HIV
- Time away from work and implications for job security and earnings
- Concern about who will take care of the children after the caregiver's death
- Fear of her own death

Issues from Healthcare Provider's Perspective

Health providers who care for HIV-infected children often find it challenging to address the children's psychological needs. Challenges include:

- Not having the knowledge and skills to communicate effectively with children
- Not knowing what information is developmentally appropriate
- Not having the time to develop and nurture a relationship designed to make a child open up
- Not having or being aware of referral options

Psychosocial Needs of Children

All children need care, attention, security, love, nurturing, play, acceptance, a supportive home environment, and specific help to overcome their individual problems.

When children lose someone they love, they need simple and age-appropriate information about what has happened. They need to be listened to by someone who is prepared to answer the same question several times. Most importantly, they need reassurance that they will be taken care of and loved.

Problems that Can Occur in Infected or Affected Children

Infected or affected children may become aggressive, disruptive, and/or restless. Common problems are bed-wetting, sleep disturbance, truancy, or refusing to go to school, and bodily complaints with causes that may be difficult to ascertain. Other common problems include depression and withdrawal. Studies from Mildmay in Uganda indicate that many HIV-infected children are not told of their HIV status. Depression among these children (and even those who have been told their results) often goes unnoticed and/or untreated.

Communicating with Children

Effective communication with children means trying o understand the child's thoughts and feelings and trying to respond to the child in a way that is helpful. You need to understand the cultural environment in which the child lives because every culture has distinct ways of communicating, expressing feelings, and dealing with difficult circumstances—part of a child's social knowledge. Communication styles also vary according to social class, urban versus rural residence, and the age of the child.

To communicate effectively with children requires skills in listening, observing, and understanding their messages. At least one person who is familiar with and normally cares for the child should be

present. This is true for all children, but especially for young ones who often find it hard to trust and communicate with someone they do not know.

Different Ways to Communicate with Children

- Make-believe play
- Using stories
- Drawing pictures
- Music and dance
- Drama
- Writing about experiences

Children have many ways of communicating. They express themselves through play, drawing (sometimes even on the ground), making toys, and acting out situations through music, singing, dancing, and and sometimes writing. Play therapy is a powerful tool for young children to create a structure in which they can express and address feelings of fear, isolation, separation and abandonment. Playing while allowing children to talk freely can help build up their confidence.

Common themes that emerge through therapy include:

- Fear of others finding out their diagnosis
- Fear of rejection
- Concern about their parents' health status
- Being unable to talk openly with their parents about dying

It is important to let children feel free to express themselves as they wish and not to criticize the techniques or standards of the productions as such criticism may inhibit free expression. All children will continue to ask questions about a topic after explanations have been given to them; this holds for questions about disease as well.

Difficulties Communicating with Children

There are many reasons that it is sometimes difficult for us to communicate effectively with children. One is that we do not encourage them to talk about themselves. For example, in a healthcare setting or even

during home visits, we often get information about children through third parties, like caregivers, even when the child is present and able to provide the same information. Another reason is that a child who does not know you well may find it hard to talk to you about his or her feelings. Cultural and traditional factors may also contribute to this difficulty in communicating. Aa girl who was raped, for example, may feel comfortable talking about it only to her grandmother or, in her absence, to an older woman.

Other factors that tend to block communication with a child include: talking too much; being critical or judgemental, aggressive or bullying; laughing or humiliating a child; getting upset or arguing; being uncomfortable or embarrassed when a child is upset; or not respecting the child's beliefs. An adult who behaves in these ways may make the child may feel untrusting, suspicious, angry, or hostile.

HIV Testing for Children

HIV testing for children should follow national guidelines, where available. If guidelines are not available, it is important to ensure that children's rights are respected as much as possible. Testing symptomatic children in order to provide appropriate care can be done at any age as the health worker deems necessary, although the results may not be disclosed until the child is old enough to understand them.

Always seek consent for testing from the parent or caregiver. But older children (around 10 to 12 years of age) should also give their consent and then undergo pre-test counselling, so they know who will be involved in the testing process and who will receive the results. Sexually active children who require (or request) HIV testing may withhold their consent for disclosure of the results to their parents or caregiver.

Counselling and Disclosure

Counselling is intended to help the child and the family cope with the emotions and challenges they experience as a result of HIV infection in the family. Such counselling helps HIV-positive patients, including children, adopt a positive living attitude. This, in turn, can help them

prolong their life, improve their quality of life, and adhere better to a treatment regimen.

Which Child Requires Counselling/Help?

Basically, all HIV-affected children require counselling and help. The methods for communicating with children vary with the age group and socioeconomic circumstances. For example, a child who has never attended school may not be able to draw pictures as easily as a child who has attended school. Also, the younger a child is, the more likely he or she is to require the presence of a mother or caregiver during counselling. A counsellor should be familiar with the basic principles of counselling, which may be available in the form of national guidelines.

The counselling process begins with the first contact with the child; this may be in a clinic setting when the child is brought in sick, at home during home visiting, or at school. It is common for a child to be accompanied by a parent or other family member. As a general rule, interaction with the child should take place in the presence of a parent and, when appropriate, with other family members or siblings, until the counsellor has gained the confidence and trust of both the child and the caregivers.

Another reason for having more than one family member present is that it enables the counsellor to observe the reactions and interactions of both child and family. Older children can be counselled alone or with a family member present, as the child prefers. However, counsellors should not discuss issues such as sexuality without parental permission.

Parents should be continually informed and should participate in the decision-making and planning of appropriate care for their child, including decisions about where the child should be treated.

The counsellor must be sure to address the social needs of the HIV-infected and -affected child by referring the parents to appropriate organisations or institutions for socioeconomic and spiritual support.

At What Age Should Counselling Start?

It is usual to begin informing children about their HIV status when they are between 5 and 7 years old, depending on the child's ability to understand and on the parents' consent. You should do this gradually. Many parents may want to keep the diagnosis of HIV from the child; it is therefore often necessary to counsel the parents first, to help them understand the importance of having the child know his or her status.

Carrying out discussions with children in the presence of parents or guardians ensures that the messages the children receive from counsellors and parents are consistent. Take parents' viewpoints into account, even when they do not necessarily match those of the health worker, counsellor, or child.

Studies from Mildmay in Uganda indicate that children who are informed of their HIV status cope with disclosure as effectively, if not better, than adults. Experience counselling children about conditions not related to HIV indicates that children cope better when told of these conditions at an early rather than later age. It has been shown, for example (mainly in developed countries) that children who are told at an early age that they are living with foster parents develop fewer psychosocial problems than those who are told later and who grew up believing they were living with their biological parents. As children with HIV grow older, researchers should carry out investigations to understand more about the earliest age at which children should be informed of their status.

Who Should Tell Children About Their HIV Status?

Ideally, parents should be the ones to disclose HIV results to their children. However, most parents do not know how to go about this and how to handle the emotional experience associated with disclosure. Parents need practical support to understand how to explain the results to their child. Also, parents should not inform their child about either their child's HIV status or their own until they have themselves come to terms with it.

Sharing Results with Others

Many parents worry about other family members or the public knowing the HIV status of their child. They should receive counselling or other support to understand the benefits of informing specific people (e.g., close relatives or understanding school teachers).

Supporting Parents/Caregivers

Many parents need help to deal with the issues outlined above in the section *Issues from Caregiver's Perspective*. Support groups for parents and guardians of HIV-infected children provide a safe and comfortable environment for open discussion of issues. The feelings of isolation that are experienced by parents whose children have been diagnosed with HIV is often eased by talking to others in the same situation.

Supporting Siblings

Non-infected children are certainly going to be affected by their sibling's or parent's HIV status and become anxious about their illness or death. Parents may also *forget* non-infected siblings as they become absorbed in providing care to their infected child. Health workers should watch carefully for and help relieve anxiety, depression, and/or school difficulties in non-infected siblings.

Bereavement Counselling

As children with HIV near the end of their lives, attention must be paid to helping these children and their families move through this time with the least amount of suffering and as much support and dignity as possible. Encourage open communication about what is happening among the children themselves, the parents, and the health workers. Reassure parents and help them understand that professionals are not giving up on their children, but rather that there is nothing more that can be done.

All children continue to ask questions about any topic, even after they have received explanations; this applies to questions about disease as well as to other matters. All children in the family require continu-

ing counselling and help after the death of a loved one. Parents and caregivers also need support for their emotional reaction toward a dying child. And of course the dying children themselves need help. Using a supplement like the Memory Book is often useful for facilitating discussion about the child's family history and preparing for the future. See the following section for some practical steps for counselling children.

Steps for Counselling HIV-Infected Children

There are certain steps you can use as a basis for counselling HIV-infected children. These steps vary with the situation.

Child with unknown HIV status presenting with clinical signs of HIV infection and/or risk factors such as mother or sibling with HIV/AIDS:

- Ascertain child's and/or mother's or caregiver's understanding of HIV infection in general and, more specifically, of MTCT.
- Discuss the presumptive diagnosis of HIV infection in light of existing signs, symptoms, and risk factors.
- Explain the benefits of early awareness of HIV infection in the child's life and for the family.
- Where available and affordable, request permission to arrange for HIV test to be performed on the child's or mother's/parent's blood.
- If parents refuse to be tested or decide to postpone the test, accept their decision and reassure them that while their refusal will not compromise the management of the child's current illness, they and the health workers will be missing the opportunity to plan for optimum care and support if the child is HIV infected.

Child known to be HIV-infected and responding poorly to treatment:

- Ascertain child's and/or mother's or caregiver's understanding of HIV infection in general and, more specifically, of MTCT.

- Discuss the management of current problems and the reasons for poor response to treatment.
- Refer child to a higher level of care, for further investigations and/or community-based or home-based care programme, if necessary.
- Discuss psychological implications of HIV for the child, mother, father, and other family members.
- Provide continuing psychosocial support on coping with a chronic illness such as HIV.

Child known to be HIV-infected and responding well to treatment:

- Discuss follow-up, care, and risk factors for future illness.
- Discuss shared confidentiality and the social well-being of the child and the family.

Knowledge Gaps

- Age at which counselling should be initiated in children
- The appropriate age for disclosure to children
- The short- and long-term effects of disclosure

Additional Reading

National guidelines on counselling HIV-infected adults

Chapter 12
Nutrition and HIV

Summary

- Malnutrition is a significant cause of morbidity among children less than 5 years of age in Africa, and underlies two-fifths of childhood deaths. More than 80% of the children less than 15 years of age who are infected by HIV live in sub-Saharan Africa. (UNAIDS, 2003).
- There is a need to minimise the risk of HIV transmission to infants through breast-feeding while at the same time avoiding increasing their risk of morbidity and mortality from other causes.
- HIV-exposed and -infected children have an increased vulnerability to malnutrition.
- Caregivers should ensure adequate nutrient intake based on locally available foods; provide universal (vitamin A) or targeted (e.g., iron, folate, zinc) micronutrient and mineral supplementation.
- Growth is a very sensitive indicator of HIV disease and disease progression in children.
- Cachexia and growth faltering associated with HIV/AIDS respond well to ART, which is essential for managing severe cachexia.
- Malnutrition in a person with HIV/AIDS is a multifaceted problem requiring multiple interventions.

Introduction

Infants born to HIV-positive women are often small at birth and HIV-infected infants commonly develop failure to thrive. HIV-infected children in developing countries show a decline in length and weight within the first months of life, and eventually manifest a picture of chronic malnutrition. HIV-infected children tend to be stunted but not wasted: their weight-for-height z scores are often normal. This may result from:

- HIV infection
- Other underlying disease, such as TB
- Inadequate macro/micronutrient intake
- Combination of any or all of the above

At least 90% of HIV-infected children experience wasting and nutritional depletions during the course of their illness. High viral load in children is associated with increased risk of failure to thrive, while infections such as pneumonia, diarrhoea, and TB further exacerbate growth failure. Even in developed countries, where there is adequate food security, HIV-infected children manifest progressive loss of lean body mass, with relative preservation of subcutaneous fat tissues.

This chapter reviews the factors associated with increased vulnerability to malnutrition in HIV-exposed and -infected children and discusses strategies to prevent malnutrition; to reduce postnatal transmission of HIV through breast milk; to preserve lean body mass (LBM); and to promote child growth, development, and survival in the context of HIV.

Nutrition Management

The goals of nutrition management in the context of HIV include prevention or mitigation of factors associated with risk of malnutrition, appropriate infant feeding practices, nutritional supplementation and

rehabilitation, and preservation of lean body mass in HIV-infected children (ART).

1. Prevent or Mitigate Factors Associated with Risk of Malnutrition

Childhood malnutrition is prevalent worldwide. UNICEF estimated that in 2002 there were 149 million underweight children in the world and that nearly 3% of the world's children suffer from severe malnutrition. In sub-Saharan Africa, approximately one in every three children less than 5 years of age is undernourished.

Malnutrition increases a child's vulnerability to infection. It is currently estimated that malnutrition underlies 60% of all infectious disease morbidity. The case fatality rates for common childhood illnesses such as acute lower respiratory infection and diarrhoea are significantly higher in malnourished children.

Risk Factors for Malnutrition in HIV-Exposed and -Infected Children

Factors that significantly increase the risk of malnutrition during childhood include low birth weight (LBW), inappropriate feeding practices, repeated infections, and inadequate time set aside for infant feeding and child care. HIV-exposed and -infected children face a myriad of additional risks of malnutrition:

- **Maternal malnutrition:** HIV-infected women have higher prevalence of malnutrition compared to seronegative women and therefore have increased likelihood of delivering a LBW baby.
- **Repeated infections:** HIV-exposed and -infected children have frequent episodes of infections that make them more vulnerable to malnutrition. Repeated episodes of infection, oral candidiasis, dental problems, and medication can all contribute to loss of appetite and difficulty in eating.
- **Increased losses of nutrients:** HIV-infected children have increased loss of nutrients when they experience episodes of vomiting, diarrhoea, and gastrointestinal bleeding secondary to mucosal ulcerations.

- **Malabsorption:** Changes in the integrity of the intestinal mucosal membrane lead to malabsorption of macro and micronutrients. Certain antiretroviral drugs also interfere with absorption of nutrients.
- **Increased basal requirements:** Infections and chronic illness are characterized by increased basal metabolic needs. Cytokine mediators of inflammation such as TNF alpha and cachetin alter metabolism, leading to weight loss. In the African setting, where children have little access to HAART, the norm is frequent febrile episodes, back-to-back infections with high-energy demands for repair, alongside the normal needs for growth and development.
- **Psychosocial factors:** In nearly all instances, paediatric HIV is a family diagnosis that exerts social, psychological, and economic stress on the family. Psychosocial problems contribute to suboptimal nutrition of HIV-1 infected patients. An unstable family situation with inadequate emotional and social support is associated with poor growth in HIV-infected and uninfected children, particularly HIV/AIDS orphans.

2. Infant Feeding Practices in the Context of HIV

While breast-feeding is the primary guarantee of child survival in resource-poor settings, breast-feeding by HIV-infected women significantly increases the incidence of HIV infection among breast-fed infants. Among women with established HIV infection, the estimated additional risk of transmission from breast milk, over and above the risk during pregnancy and delivery, is about 15% for HIV-exposed babies who are breast-fed for up to 6 months and about 20% for babies who breast-feed into the second year of life.

Women who are newly infected during pregnancy or lactation have a much higher likelihood of transmitting HIV infection to their infants. The risk of transmission through breast milk among women with recent infection is about 29%.

Babies continue to be at risk of HIV infection as long as they are exposed to HIV-contaminated breast milk.

Breast-feeding problems (e.g., cracked and sore nipples, mastitis, and breast abscesses) significantly increase the risk of transmitting HIV by breast milk. Good breast-feeding techniques can reduce this risk considerably.

If a woman is infected with HIV, the only way to completely eliminate the risk of HIV transmission through breast-feeding is to feed her infant from birth with suitable replacements for breast milk, such as commercial infant formula or home-prepared formula made from modified animal milks.

Mixed feeding may be more risky for HIV transmission than exclusive breast-feeding, possibly because damage to the epithelial integrity of the intestine may facilitate entry of the virus and because breast engorgement, which is more likely to occur with mixed feeding, causes subclinical mastitis, a condition that increases the viral load in breast milk.

Infant Feeding During Period 0 to 6 Months

Given the need to minimise the risk of HIV transmission to infants while at the same time avoiding increasing their risk of morbidity and mortality from other causes, "when replacement feeding is acceptable, feasible, affordable, sustainable, and safe, avoidance of all breast-feeding by HIV-infected mothers is recommended. Otherwise, exclusive breast-feeding is recommended during the first months of life" and should then be discontinued as soon as feasible (WHO/UNICEF/UNAIDS).The recommendations further state that "when HIV-infected mothers choose not to breast-feed from birth or stop breast-feeding later, they should be provided with specific guidance and support for at least the first two years of the child's life to ensure adequate replacement feeding."

Safer Breast-Feeding

Where adequate replacement feeding is not possible, two strategies are proposed to reduce the risk of breast-milk transmission: (a) exclusive breast-feeding, with early cessation and (b) heat-treating breast milk.

Issues associated with exclusive breast-feeding with early cessation include:

- Allows infant to derive the benefits of breast-feeding during the most risky time for artificial feeding in environments with poor hygienic conditions (i.e., the first few months of life).
- Reduces risk of HIV transmission by reducing the length of time infant is exposed to HIV through breast milk and conserves the efficacy of ARV drug prophylaxis for PMTCT of HIV.
- Is an option for women who are not in a position to provide adequate and hygienic replacement feeding to their infants from birth to reduce the cumulative risk of longer duration breast-feeding.
- Optimum time for early cessation of breast-feeding is not known. It is advisable for an HIV-positive woman to stop breast-feeding as soon as she is able to prepare and give her infant adequate and hygienic replacement feeding. Family circumstances can also determine when the mother can stop breast-feeding and start replacement feeding.
- Early cessation of breast-feeding is advisable if an HIV-positive mother develops symptoms of AIDS.
- Early cessation of breast-feeding is an option for HIV-positive women who find it difficult for sociocultural reasons to avoid breast-feeding completely and who can provide and hygienically prepare adequate replacement foods after their infants are a few months old.

Replacement Feeding

Replacement feeding includes feeding with a commercial or home-prepared formula. From 0 to 6 months, milk in some form is essential for an infant. A baby who is not breast-feeding will need about 150 ml of milk per kg of body weight per day.

Commercial infant formula is an option for HIV-positive women when the family has reliable access to sufficient formula for at least 6 months. Feeding an infant for 6 months requires an average 40 x 500 g tins (or 44 x 450 g tins) of formula. The family must also have the resources—water, fuel, utensils, skills, and time—to prepare it correctly and hygienically. *Home-prepared formula* is a reasonable option for an HIV-positive woman in the following circumstances: commercial infant formula is not available or is too expensive for the family to buy and prepare; there is a reliable supply of animal or other milk and the family can afford it for at least 6 months; and the family has the resources to prepare it hygienically, and can make the required modifications accurately.

Particular attention must be paid to hygiene, correct mixing, and the feeding method. Even in the best situation, feeding newborn babies with any food other than breast milk increases the frequency of diarrhoeal disease and the family must make an effort to minimise this risk. Mothers and families should be counselled on proper food hygiene, including:

- Washing hands with soap and water before preparing food.
- Washing the feeding and mixing utensils thoroughly or boiling them to sterilise them before preparing the food and feeding the infant.
- Boiling water for preparing the child's food and any necessary drinks.
- Avoiding storing milk or cooked food, or, if this is not feasible, storing it in a refrigerator or a cool place and reheating thoroughly (until it bubbles) before giving it to the infant.

- Storing food and water in clean, covered containers and protecting it from rodents, insects, and other animals.
- Keeping food preparation surfaces clean.
- Washing fruits and vegetables with water that has been boiled, peeling them if possible, and cooking them thoroughly before giving to the infant.

Replacement feeding is often a new way for a mother to feed a baby, and it should not be assumed that mothers know how to do it. The best way to give replacement feeding is to cup-feed.

Infant Feeding After 6 Months of Age

After the age of 6 months, breast milk and other forms of milk alone are not adequate to meet a baby's nutritional requirements. It is recommended that an HIV-positive mother breast-feed for no longer than 6 months. Therefore, for both breast-fed and replacement-fed infants, complementary foods, in addition to breast milk substitutes, should be introduced when they are 6 months of age (as early as 4 months of age, if there is evidence of growth faltering or the mother has decided to wean before 6 months of age).

For breast-fed infants, the transition from breast milk to complementary foods and breast milk substitutes should be as short as possible to limit the duration of mixed feeding, but the transition should not be so short that it causes the undue traumatic effects that abrupt cessation of breast-feeding can have on both the mother and infant.

Milk should continue to be an important component of the diet, providing up to one-half or more of the nutritional requirements between the ages of 6 and 12 months and up to a one-third of the requirements between the ages of 12 and 24 months.

In addition, complementary foods made from appropriately prepared and nutrient-enriched family foods should be given three times per day up to the age of 9 months; between 9 and 12 months, four feedings should be given daily; thereafter, five times per day.

3. Periodic Nutrition Assessment and Growth Monitoring

Growth and development monitoring and promotion are critical child survival strategies in resource-poor settings, especially in areas with high rates of both childhood malnutrition and HIV/AIDS, and particularly for children in directly affected households. Growth is a very sensitive indicator of HIV disease and disease progression in children. Poor growth has been shown to precede CD4 decline and the development of OIs.

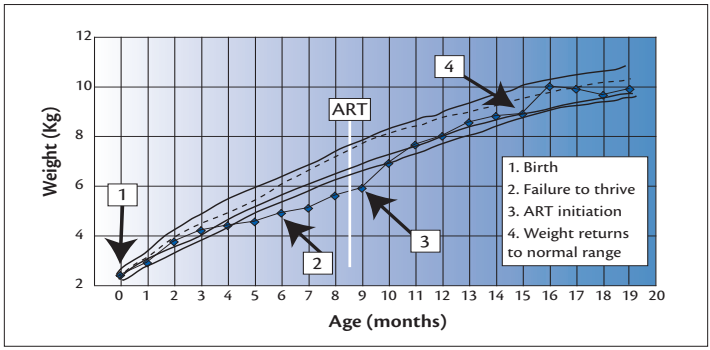
A simple growth chart is an excellent tool for the primary care practitioner; however, all staff must be carefully trained in the importance of and the techniques for accurate measurement of height, weight, and head circumference.

Growth monitoring begins with measuring and charting birth weight, length, and head circumference on child health cards. **The best clinic-based standards for growth monitoring are those from the National Center for Health Statistics (NCHS).** At the health-centre level, use the child health card to monitor a child's growth; at the community level, use the simple-to-use mid-upper-arm circumference (MUAC) tape method.

Subsequent measurements include weight, height, head circumference, triceps, skin-fold thickness (SFT), and MUAC; but weight is the optimal nutritional indicator, because it is a composite measure of the different nutritional changes. All health facilities should have an infant scale and workers should plot measurements on the growth monitoring child health card.

The growth chart below (**Figure 12.1**) depicts a typical pattern of weight gain in a perinatally-infected child. Many HIV-infected infants have a normal birth weight (Point 1). Some infants show failure-to-thrive (Point 2). When ART is initiated (Point 3), infants can gain weight and weight-for-age improves (Point 4).

Figure 12.1. Weight-for-Age Before and After Onset of ARV Therapy



Source: Perinatal HIV Prevention Trials, Thailand

During an infant's first year, nutritional assessments should be carried out every month in keeping with recommendations for all children. Thereafter, nutritional assessments should be carried out every 3 months (monthly, if there is altered nutrition). Dietary history and feeding practices should be carefully elicited, including other nutrition-related problems (e.g., poor appetite, chewing, swallowing, intolerance or aversion, food taboos, and history of nutritional supplementation).

4. Provide Nutritional Supplementation and Rehabilitation

Caregivers should ensure adequate nutrient intake based on locally available foods and provide universal (vitamin A) or targeted (e.g., iron, folate, zinc) micronutrient and mineral supplementation. HIV-infected children have been shown often to be deficient in two essential micronutrients: Vitamin A and zinc.

Early Nutritional Supplementation

Early nutritional supplementation in HIV-infected children and adults helps preserve lean body mass (LBM) and slows disease progression. One should not wait until there are signs of malnutrition to support

nutrition in HIV-infected children. HIV-infected children should receive 150% of the Required Daily Allowances (RDA) for their age and sex. Therefore, multivitamin supplements are recommended daily. Give Vitamin A according to national guidelines or following the International Vitamin A Consultative Group recommendation of three 50,000-international unit (IU) doses of Vitamin A—to be given at the same time as infant vaccines during the first 6 months of life. WHO also recommends iron supplements for HIV-infected children.

Other Nutrition Interventions

- Perform presumptive de-worming on the child every 6 months starting at between 6 to 9 months of age.
- Provide an extra meal per day after episodes of illness, to allow for catch-up growth (see **IMCI guidelines**).
- Households should have a safe water system, point-of-use water treatment or filtration, or should use boiled water.
- Hygiene, particularly handwashing, and sanitation are important factors in prevention of infections.
- All households should use iodized salt.

Strategies for Preventing Malnutrition in HIV-Exposed and HIV-Infected Children

Strategies for preventing malnutrition in HIV-exposed and -infected children require an integrated approach that addresses maternal and child health and prevention and care (**Table 12.1**).

Table 12.1. Strategies to Prevent and Treat Malnutrition in HIV-Exposed and HIV-Infected Children

Strategy	Action
Prevent LBW	• Prevent maternal ill health and malnutrition • Provide nutrition counselling to improve food intake • Monitor maternal weight gain during pregnancy • Screen for maternal anaemia, provide antihelminthic treatment • Provide micronutrient (e.g., iron and folate) and multivitamin supplements • Prevent and promptly treat infections in pregnant women (e.g., malaria, urinary tract infections, STIs, PCP, TB) • Manage complications of pregnancy (e.g., hypertension and diabetes)
Prevent mother-to-child transmission of HIV	• Adopt a comprehensive approach to PMTCT, including integrating PMTCT services into maternal and child health services for HIV-infected mothers who are already pregnant (see chapter 3)
Institute appropriate infant feeding practices	• Counsel mothers on infant feeding • Support mothers in their choice of feeding • Support timely institution of appropriate complementary food
Prevent common childhood infections	• Immunise against common childhood infections • Institute CTZ prophylaxis to prevent PCP and invasive bacterial infections • Provide health education and counselling on hygiene practices at household level • Provide vitamin A supplementation according to the national schedule • Ensure safe water supply, hygiene and sanitation in household

Table 12.1. Strategies to Prevent and Treat Malnutrition in HIV-Exposed and HIV-Infected Children

Strategy	Action
Ensure prompt and appropriate treatment of infections	• Empower families by training them to recognise illness in the baby and improving their health-seeking behaviour • Teach mothers to increase frequency of feeding after episodes of illness to allow for catch-up growth • Train primary-level health workers to manage common childhood infections (IMCI) and to suspect and manage HIV-related conditions
Monitor growth	• Weigh the child regularly and plot the weight on a growth chart • Detect and address early growth faltering
Provide micronutrient and food supplementation	• Provide vitamin A supplementation according to national guidelines • Provide multivitamin and iron supplementation if no contraindications
Encourage family planning and child spacing	• Promote family planning and child spacing to ensure maternal nutritional recovery between births and optimal child care practices
Provide antiretroviral treatment	• Advocate, promote, and implement ART for children. Strategies to facilitate equitable ART access for children include subsidies, family models of care, children-dedicated clinics (e.g., hours, space, and/or personnel), training of health workers to demystify paediatric ART, and so on.

Clinical Indicators of Malnutrition

Clinical indicators of malnutrition in HIV-infected children include the following (use any one of these parameters, based on the resources available to the clinician):

- Weight growth velocity <5% (or <3% for some child health cards) for more than 2 months
- Crossing a major percentile for weight line
- Weight or weight for height <90% of the NCHS median
- Weight for height <5%
- Loss of >5% lean body mass
- Serum albumin <3 gm/dl

If there is evidence of malnutrition, evaluate the following:

- Ongoing losses
- Nutrient intake
- Physical examination to look for evidence of thrush or oral ulcers, gastrointestinal bleeding, and signs of systemic infections
- Laboratory investigations that include a complete blood count; liver function tests; stools and urine microscopy, as well as culture and sensitivity; and chest x-ray to look for evidence of TB. In more sophisticated centres, clinicians may do pancreatic enzyme levels, upper GI series, and endoscopy.

For children with moderate and severe forms of malnutrition, nutritional rehabilitation is necessary (see **chapter 6**).

Table 12.2. Nutritional Management for Children With and Without Evidence of Malnutrition

Nutrition management of child with *no* evidence of malnutrition	Nutrition management of child with evidence of malnutrition
• Provide nutritional counselling and education, with an emphasis on the increasing nutrient needs with growth and chronic illness. • Care providers should give advice based on locally available and affordable foods. • Encourage families to maintain kitchen gardens to supplement the family's needs.	• As a general rule, early nutritional interventions are more effective than later interventions. • Initially try oral nutrition therapies. • Increase caloric density of foods that are familiar to the child by adding a high-fat supplement (e.g., cooking oil, butter, or margarine). • Treat underlying infection. • Initiate nutritional counselling and care and more intensive follow-up (initially 2 weekly and then monthly).

5. Preserving Lean Body Mass

Lean body mass, or fat-free mass, consists of muscle, bone, minerals, and other non-fat tissue. LBM contains approximately 73% water, 20% protein, 6% minerals, and 1% ash.

Cachexia is the preferential and inappropriate loss of lean body mass and is mediated by cytokines. Oral nutritional supplementation is the optimal approach, with enteral and parenteral alimentation indicated for patients unable to take their food orally (see **chapter 6** on nutritional rehabilitation).

Antiretroviral therapy is the definitive way to preserve LBM in HIV-infected children. Therefore, children who are HIV-infected and meet national (or WHO) criteria should be started on ART. In the face of extreme limitations in access to ARV drugs, health workers should definitely continue to advocate for access for HIV-infected children.

6. Additional Strategies

Additional strategies for addressing the needs of HIV-infected children include providing psychosocial and mental health care for depression and providing long-term solutions for vulnerable communities.

Psychosocial and Mental Health Care for Depression and Emotional Problems

Although all HIV-infected children are susceptible to severe forms of malnutrition, studies have found a differentially greater impact on orphans because of the effects of the virus on immunity, poverty, psychological and emotional factors, and inadequate childcare practices. Make appropriate links with social welfare services and to community-based groups for the continued support of OVC (see **chapter 11**).

It is important to identify children who have mental health problem (e.g., depression) and who need specific mental health care. When there is doubt as to the mental well-being of a child, the child should

be referred to the most experienced person on the team or to the closest mental health service, whichever is easier.

Long-Term Solutions Needed for Vulnerable Communities

Malnutrition in a person with HIV/AIDS is a multifaceted problem requiring multiple interventions—both short-term and long-term—applied simultaneously, to break the vicious cycle of malnutrition: depressed immunity, infections, malnutrition. In particular, links to community and social services are required to address household food insecurity and other issues.

Knowledge Gaps

- Little is known about the impact of micronutrient deficiencies on the natural history of HIV/AIDS among children.
- What are the daily RDA macro and micro requirements of HIV-infected children?
- What is the role of commercial food supplements in resource-poor settings (as these are currently diverting meagre resources from desperate families)?
- What is the impact of ARV treatment on the growth of HIV-infected children? Will they have catch-up growth? What do they need to ensure that they grow well?

Additional Reading

Miller, T. Nutritional aspects of pediatric HIV infection. In: Walker WA, and JB Watkins. *Nutrition in Pediatrics*. London: BC Decker Inc. 2nd edition, 1997.

Appendices

Appendix A

Clinical Situations and Recommendations for the Use of Antiretroviral Drugs in Pregnant Women and Women of Child-Bearing Potential in Resource-Constrained Settings

Clinical situation	Recommendation
A: HIV-infected women with indications for initiating ARV treatment[1] who may become pregnant	First-line regimens: AZT + 3TC + NVP or d4T + 3TC + NVP Avoid EFV in women of childbearing age, unless effective contraception can be ensured. Exclude pregnancy before starting treatment with EFV.
B: HIV-infected women who become pregnant while receiving ARV treatment	**Women** Continue with the current regimen[2] unless it contains EFV, in which case consider substituting NVP or PI if the woman is in the first trimester. Continue the same ARV regimen during the intrapartum period and after delivery. **Infants** Infants born to women receiving either first- or second-line ARV treatment regimens: AZT for one week and/or single-dose NVP.
C: HIV-infected pregnant women with indications for ARV treatment	**Women** Follow the treatment guidelines as for non-pregnant adults, except that you should not give EFV in the first trimester. First-line regimens: AZT + 3TC + NVP or d4T + 3TC + NVP Consider delaying the start of ARV treatment until after the first trimester, although for severely ill women the benefits of initiating treatment early clearly outweigh the potential risks. **Infants** AZT for one week and/or single-dose NVP.[3]

Clinical Situations and Recommendations for the Use of Antiretroviral Drugs in Pregnant Women and Women of Child-Bearing Potential in Resource-Constrained Settings	
Clinical situation	**Recommendation**
D: HIV-infected women without indications for ARV treatment[1]	**Women** AZT starting at 28 weeks or as soon as feasible thereafter: continue AZT during labour, plus single-dose NVP at the onset of labour **Infants** Single-dose NVP plus AZT for one week[3] **Alternative regimens (not in any order of preference)** **Women** Give AZT starting at 28 weeks or as soon as feasible thereafter; continue in labour. **Infants** Single-dose NVP plus AZT for one week.[3] ***or*** **Women** AZT + 3TC starting at 36 weeks or as soon as feasible thereafter; continue in labour and for one week postpartum. **Infants** AZT + 3TC for one week ***or*** **Women** Single-dose NVP **Infants** Single-dose NVP
E: HIV-infected pregnant women who have indications for starting ARV treatment[1] but treatment is not yet available	Follow the recommendations in **clinical situation D**, but preferably use the most efficacious regimen that is available and feasible .

Clinical Situations and Recommendations for the Use of Antiretroviral Drugs in Pregnant Women and Women of Child-Bearing Potential in Resource-Constrained Settings	
Clinical situation	**Recommendation**
F: HIV-infected pregnant women with active tuberculosis	If ARV treatment is initiated consider:[4] AZT + 3TC + SQV/r or D4T + 3TC + EFV can be considered. If ARV treatment is initiated in the third trimester, AZT + 3TC+ EFV or D4T + 3TC + EFV can be considered. If ARV treatment is not initiated, follow the recommendations in **clinical setting D**.
G: Pregnant women of unknown HIV status at the time of labour, or women in labour known to be HIV-infected who have not received ARV drugs before	If there is time, offer HIV testing and counselling to women of unknown status, and if positive, initiate intrapartum ARV prophylaxis. If there is insufficient time for HIV testing and counselling during labour, then offer testing and counselling as soon as possible postpartum and follow the recommendations in **clinical situation H.** **Recommended regimens (not in any order of preference)** **Women** Single-dose NVP; if imminent delivery is expected do not give the dose but follow the recommendations in clinical situation H **Infant** Single-dose NVP ***or*** **Women** AZT + 3TC in labour and AZT + 3TC for one week postpartum **Infant** AZT + 3TC for one week
H: Infants born to HIV-infected women who have not received any drugs	**Infants** Single-dose NVP as soon as possible after birth plus AZT for one week If the regimen is started more than 2 days after birth, it is unlikely to be effective.
Source: World Health Organization 2004 (Modified)	

[1] WHO recommendations for initiating in HIV–infected adolescents and adults. If CD4 testing is available it is recommended to offer ARV treatment to patients with: WHO IV disease irrespective of CD4 cell count, WHO Stage III disease with consideration of using CD4 cell counts less than

350 106 cell/L to assist decision-making and WHO stage I and II disease in the presence of CD4 cell count less than 200 106 cell/L. If CD4 testing is unavailable, it is recommended to offer ARV treatment to patients with WHO stage III and IV disease, irrespective of total lymphocyte count or WHO Stage II disease with a total lymphocyte count less than 1200 106 cell/L.

[2] Conduct clinical and laboratory monitoring as outlined in the 2003 revised WHO treatment guidelines.

[3] Consider continuing the infant on AZT for 4 to 6 weeks if the woman received ante partum ARV drugs for less than 4 weeks.

[4] ABC can be used in place of SQV/r; however, experience with ABC during pregnancy is limited. In the rifampicin-free continuation phase of tuberculosis treatment, an NVP-containing ARV regimen can be used.

Appendix B
CDC 1994 Revised Human Immunodeficiency Virus Paediatric Classification System: Clinical Categories[1]

Category N: Not Symptomatic

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

Category A: Mildly Symptomatic

Children with two or more of the following features but none of the conditions in category B or C.

Features: lymphadenopathy (at more than two sites); hepatomegaly; splenomegaly; dermatitis; parotitis; recurrent or persistent upper respiratory infection, sinusitis or otitis media

Category B: Moderately Symptomatic

- Anaemia (<8 gm/dL), neutropaenia (<1000/mm^3), or thrombocytopaenia (<100,000/mm^3) persisting ≥30 days
- Bacterial meningitis, pneumonia, or sepsis (single episode)
- Candidiasis, oropharyngeal, persisting (>2 months) in children >6 months of age
- Cardiomyopathy
- Cytomegalovirus infection, with onset before 1 month of age
- Diarrhoea, recurrent or chronic
- Hepatitis
- Herpes simplex virus (HSV) stomatitis, recurrent (≥episodes within 1 year)
- HSV bronchitis, pneumonitis, or oesophagitis with onset before age of 1 year

- Herpes zoster involving at least two distinct episodes or more than one dermatome
- Leiomyosarcoma
- Lymphoid interstitial pneumonitis or pulmonary lymphoid hyperplasia complex
- Nephropathy
- Nocardiosis
- Persistent fever (lasting >1 month)
- Toxoplasmosis, onset before 1 month of age
- Varicella, disseminated (complicated chicken pox)

Category C: Severely Symptomatic

- Serious bacterial infections, multiple or recurrent
- Candidiasis, oesophageal or pulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis or isosporiasis with diarrhoea persisting >1 month
- Cytomegalovirus disease with onset of symptoms at age >1 month (at a site other than liver, spleen, or lymph nodes)
- Encephalopathy (at least one of the following progressive findings present for at least 2 months in the absence of a concurrent illness other than HIV infection that could explain the findings): (a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard developmental scale or neuropsychological tests; (b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerized tomography or magnetic resonance imaging (MRI); (c) acquired symmetric motor deficit

manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbance

- Kaposi's sarcoma
- Lymphoma, primary, in brain
- Lymphoma, small, noncleaved cell (Burkitt's), or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
- *Mycobacterium tuberculosis*, disseminated or extrapulmonary
- *Mycobacterium avium* complex, or *Mycobacterium kansasii*, disseminated
- Pneumocystic pneumonia
- Progressive multifocal leukoencephalopath
- Salmonella (nontyphoid) septicaemia, recurrent
- Toxoplasmosis of the brain with onset at >1 month
- Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings: (a) persistent weight loss >10% of baseline *or* (b) downward crossing of at least two of the following percentile lines on the weight-for-age chart (e.g., 95th, 75th, 50th, 25th, 5th) in a child ≥1 year of age *or* (c) <5th percentile on weight-for-height chart on two consecutive measurements, ≥30 days apart *plus* (a) chronic diarrhoea (i.e., at least two loose stools per day for ≥30 days) *or* (b) documented fever (for ≥30 days, intermittent or constant).

[1] Centers for Disease Control and Prevention. 1994 revised classification for human immunodeficiency virus infection in children less than 13 years of age. *MMWR*, 1994. 43 (No. RR-12): pp. 1-10.

Appendix C
Sexual Maturity Rating

Sexual Maturity Rating (Tanner Staging) In Female Adolescents.*

Stage	Breast Growth	Pubic Hair Growth	Other Changes	Age Range (Year)
I	Pre-adolescent.	None	Pre-adolescent	0–15
II	Breast budding (thelarche); areolar hyperplasia with small amount of breast tissue	Long, downy pubic hair near the labia, often appearing with breast budding or several weeks or months later	Peak growth velocity often occurs soon after stage II	8 or 8½–15
III	Further enlargement of breast tissue and areola, with no separation of their contours	Increase in amount and pigmentation of hair.	Menarche occurs in 25% of girls late in stage III	10–15
IV	Separation of contour; areola and nipple form secondary mound above breast tissue	Adult in type but not in distribution	Menarche occurs in most girls in stage IV, 1–3 years after thelarche	10–17
V	Large breast with single contour.	Adult in distribution.	Menarche occurs in 10% of girls in stage V.	12½–18

* *Slightly modified and reproduced, with permission, from DE Greydanus and ER McAnarney: "Adolescence." In:* Survey of Clinica Pediatrics, *7th edition. E Wasserman and DS Gromisch (editors). McGraw-Hill, 1981.*

Sexual Maturity Rating (Tanner Staging) in Male Adolescents.*

Stage	Testes Growth	Penis Growth	Public Hair Growth	Other Changes	Age Range (Year)
I	Pre-adolescent testes ≤2.5 cm.	Pre-adolescent	None.	Pre-adolescent	0–15
II	Enlargement of testes; pigmentation of scrotal sac	Minimal or no enlargement	Long, downy hair, often appearing several months after testicular growth; variable pattern noted with pubarche	...	10–15
III	Further enlargement	Significant enlargement, especially in diameter.	Increase in amount; curling.	...	10 ½ – 16 ½
IV	Further enlargement	Further enlargement, especially in diameter.	Adult in type but not in distribution.	Axillary hair and some facial hair develop.	Variable (12–17)
V	Adult in size	Adult in size	Adult in distribution (medial aspects of thighs; linea alba)	Body hair continues to grow and muscles continue to increase in size for several months to years; 20% of boys reach peak growth velocity	13–18

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Appendix D
Safe Infant Feeding

To facilitate successful exclusive breast-feeding with early cessation:

- *Demonstrate to the mother how to place her baby on the breast* and to latch on correctly. The baby should face the mother without turning its neck; the baby's chin should be touching the mother's breast; and the baby should drag the nipple and areolar into the mouth.
- *Advise the mother how to care for her breasts so that she avoids the problems of cracked nipples and mastitis*, which increase a baby's risk of HIV infection. This includes having a once daily bath, wearing clean comfortable clothing, avoiding tight brassieres, and not applying abrasive creams and soaps on the breasts. If the mother has cracked nipples or mastitis, advise her to express the milk and heat treat it to make it safer for the baby before feeding (see section that follows on heat treating breast milk).
- *The weaning process* should be carried out over a period of a few days; the baby should be introduced to cup-feeding or expressed breast milk before being introduced to other foods. The period of mixed feeding should be minimised. Before weaning, demonstrate to the mother how to express breast milk, cup-feed her baby, and prepare nutritious weaning foods for her baby. Once weaning begins, demonstrate to the mother how to bind her breasts and apply compresses to stop lactation.
- In the first 6 months after delivery, a *woman who is exclusively breast-feeding is protected from conceiving because of lactational amenorrhea*. After she stops exclusive breast-feeding, however, she will start ovulating again and be able to become pregnant. It is important to provide the woman with adequate knowledge and an effective family planning method so that she can defer (or prevent) her next pregnancy

Issues associated with heat-treating breast milk include:

- Heat-treating expressed breast milk from an HIV-positive mother kills the virus in the breast milk. Heat-treated breast milk is nutritionally superior to other milks, but heat treatment also reduces the levels of anti-infective factors.
- Expressed breast milk should be heat-treated just before feeding the infant, to minimise contamination. If a refrigerator is not available, expressed breast milk should be kept in a clean container in a cool place and heat-treated just before feeding the infant.
- Expressing and heat-treating breast milk is time consuming and women may find that it is not a practical option for long-term infant feeding at home.
- Heat-treating breast milk may be most useful for sick and LBW babies in a hospital setting.

Teach the mother how to heat treat expressed breast milk using the following method:

- Express breast milk and place it in a glass that can withstand heat
- Place the glass of milk in a pot of water
- Heat the pot of water until it boils, with the glass of milk inside
- Remove the glass carefully and place it in a second pot of cold, previously boiled, water (*do not add cold water to the milk*)
- Check the temperature of the milk before feeding the infant
- To pasteurise the milk at home, bring the milk to a boil and then cool it immediately by putting it in a refrigerator or standing the container in cold water
- To minimise contamination, heat-treated breast milk should be put in a sterilised or very clean container and kept in a refrigerator or in a cool place

Feeding with bottles or artificial teats should be actively discouraged because:

- Cups are safer and are easier to clean with soap and water than bottles,
- Cups are less likely than bottles to be carried around for a long time; carrying bottles around for a long time gives bacteria more time to multiply; using feeding bottles increases the risk of diarrhoea, dental disease, and otitis media,
- Cup-feeding requires the mother or other caregiver to hold and have more physical contact with the infant; this means that the infant will receive more psychosocial stimulation than it would with bottle-feeding.
- Cup-feeding is better than feeding with a cup and spoon because spoon-feeding takes longer and often frustrates both the infant and the mother. This may result in the mother stopping the feeding before the infant has had enough.

Demonstrate to the mother how to cup-feed an infant:

- Hold the infant sitting upright or semi-upright on your lap and hold the cup of milk to the infant's lips.
- Tip the cup so the milk just reaches the infant's lips; the cup should rest lightly on the infant's lower lip and the edges of the cup should touch the outer part of the infant's upper lip.
- The infant should become alert and open mouth and eyes; a low-birth-weight infant will start to take the milk into the mouth with the tongue, while a full-term or older infant will suck the milk, probably spilling some of it.
- Do not pour the milk into the infant's mouth; just hold the cup to the lips and let the infant take it.
- When the infant has had enough, the infant will close its mouth and not take any more. If the infant has not taken the calculated

amount, it may take more the next time; otherwise, the mother should feed more often.

As mentioned previously, the mother can use either commercial infant formula or home-prepared formula as a breast milk substitute.

Commercial infant formula. Commercial infant formula is based on modified cow's milk or soy protein. The milk is modified to mimic the nutrient composition of breast milk and is usually adequately fortified with essential vitamins and minerals, including iron. The mother should follow the instructions on the tin for mixing the formula, to ensure that the formula is neither too concentrated nor too diluted. Over-concentrated milk formula overloads the infant with salts and waste amino acids, which can be dangerous for the kidneys. Over-diluted milk is dangerous because it exposes the infant to malnutrition. If the baby is receiving enough modified infant formula, it should not require complimentary foods until 6 months of age.

The correct mixing technique for modified infant formula follows:

- Review the instructions on the mixing of the replacement milk for the different milks available on the market (infant formula, animal milks, dried whole milk powder),
- Show the mother how to measure correctly the needed amount of milk powder (or liquid) and water for a feed. Use the containers available in her household to demonstrate the correct volumes of fluid to use in mixing the milk,
- Discuss with the mother how she should increase the amount of milk she is giving the baby as it grows.
- Review the instructions on the tin of milk and clarify any difficulties she has in following the instructions.
- Demonstrate how to make home-modified formula, in case she runs out of the commercial infant formula,

- On a follow-up visit, ask the mother to demonstrate preparation of the milk foods.
- Provide support when in the maternity (privacy to protect confidentiality, hot water to mix the food, and review of techniques for milk preparation).
- Review in the first 1–2 weeks after delivery, to monitor growth and deal with any difficulties the mother is experiencing with replacement feeding.

Home-prepared formula. Home-prepared formula can be made with fresh animal milks, dried milk powder, or evaporated milk. Animal milks have inadequate amounts of energy calories for a newborn and are deficient in many essential minerals and vitamins, including zinc, vitamins A and C, and folic acid. Thus, a baby who is fed animal milks will need multivitamin supplementation. A baby will require 92 litres of animal milk (500 ml per day) for the first 6 months of life. Cow, goat, and camel milk have more protein and higher concentrations of sodium, phosphorous, and other salts than breast milk. Goat milk is deficient in folic acid, which needs to be given to infants as a micronutrient supplement. Both sheep and buffalo milk have more fat and energy than cow milk. The protein content of sheep milk is high.

For an infant, use the full cream variety of dried milk powder or evaporated milk. Normally, reconstitution involves adding a specific amount of boiled water to a measure of powdered or evaporated milk, as instructed on the container or packet. Once the milk is reconstituted, it should be handled in the same manner as whole cream cow's milk.

Animal milk to be fed to a young infant must be modified. Dilute it with water to reduce the concentration of salts in the milk, add sugar to ensure adequate caloric content, and boil thoroughly to kill germs.

To make 150 mls of infant food from cow milk, mix 100 ml of boiled cow milk with 50 ml of boiled water, add 10 g (2 teaspoons) of sugar, and then boil the mixture. Cool the milk before feeding the baby.

To make 150 mls of food from sheep milk, mix 50 ml of sheep milk with 50 ml of water, add 5 g (1 teaspoonful) of sugar, and then boil the mixture. Cool the milk before feeding the baby.

Unmodified cow milk is an option for feeding an infant when (1) a woman is HIV-positive and commercial infant formula is unavailable or too expensive for the family or (2) the supply of cow milk is reliable, but the family lacks the resources to modify cow milk to make home-prepared formula.

The following foods are not recommended for replacement feeding of infants less than 6 months old: skim milk, sweetened condensed milk, fruit juices, sugar-water, and diluted cereal gruels; or milk products such as yoghurt and other acid milks.

Additional considerations for successful replacement feeding include vitamin supplementation, water requirements, and minimising risk of infection.

Babies being fed animal milk should receive a multivitamin supplement syrup once a day. If micronutrient supplements are unavailable, complementary foods rich in iron, zinc, vitamins A and C, and folic acid should be introduced at 4 months of age.

Babies who are fed on formula, home-modified animal milk, or unmodified animal milk require additional water. To ensure that the infant gets enough milk and that water does not displace milk, water should be offered to the infant after feeding.

Non-breast-fed infants are at increased risk of acute respiratory infections, diarrhoeal disease, and severe dehydration. Therefore, mothers and health workers must be vigilant about providing oral rehydration therapy when the baby has diarrhoea. Access to healthcare services is particularly important to ensure that infants who are receiving replacement feeding are attended in a timely manner.

Wet nursing

Consider wet nursing only when:

- The practice is culturally acceptable
- Potential wet nurse is informed of her risk of acquiring HIV infection, is offered HIV counselling and testing, voluntarily takes a test, and is HIV-negative
- Wet nurse is provided with information and is able to practice safe sex to ensure that she remains HIV-negative while she is breast-feeding the infant
- Wet nurse has access to breast-feeding support to prevent and treat breast-feeding problems such as cracked nipples

Appendix E
Grading of Adverse Events

Parameter / Feature	Grade 1	Grade 2	Grade 3	Grade 4
Haematology				
Haemoglobin (g/dL) ≥2 yr	10–10.9	7.0–9.9	<7.0	Cardiac failure 2° to anaemia
Abs neutrophil count (x 109/L)	0.750–1.200	0.400–0.749	0.250–0.399	<0.250
Platelets (cells/mm²)		50,000–75,000	25,000–49,999	<25,000 or bleeding
Gastrointestinal				
Bilirubin	1.1–1.9 X N	2.0–2.9 X N	3.0–7.5 X N	>7.5 X N
AST	1.1–4.9 X N	5.0–9.9 X N	10.0–15.0 X N	>15.0 X N
ALT	1.1–4.9 X N	5.0–9.9 X N	10.0–15.0 X N	>15.0 X N
γGT	1.1–4.9 X N	5.0–9.9 X N	10.0–15.0 X N	>15.0 X N
Pancreatic amylase	1.1–1.4 X N	1.5–1.9 X N	2.0–3.0 X N	>3.0 X N
Abdominal pain	Mild	Moderate–No Rx needed	Moderate–Rx needed	Severe–Hospital and Rx
Diarrhoea	Soft stools	Liquid stools	Liquid stools and mild dehydration, bloody stools	Dehydration requiring IV therapy or hypotensive shock
Constipation	Mild	Moderate	Severe	Distention and vomiting
Nausea	Mild	Moderate, decreased oral intake	Severe, little oral intake	Unable to ingest food or fluid for >24 hours
Vomiting	<episode/day	1–3 episodes/day or duration >3 days	>3 episodes/day or duration >7 days	Intractable vomiting
Allergic/Dermatological				
Allergy	Pruritis without rash	Pruritic rash	Mild urticaria	Severe urticaria Anaphylaxis, angioedema

Parameter / Feature	Grade 1	Grade 2	Grade 3	Grade 4
Drug fever (rectal)		38.5–40°C	>40°C	Sustained fever: >40°C, >5 days
Cutaneous		Diffuse maculopapular rash, dry desquamation	Vesiculation, ulcers	Exfoliative dermatitis, Stevens-Johnson or E. multiforme, moist desquamation
Nervous System				
Mental status and behaviour	Changes that do not affect function	Changes requiring pharmacologic or other therapy; or mild lethargy, sedation, or somnolence that resolves with rest	Changes not improved by drugs or other therapies; or onset of confusion, memory impairment, lethargy, sedation, or somnolence that does not respond to rest	Onset of delirium, obtundation, coma, or psychosis, or grade 3 toxicity that does not respond to dose reduction
Neuropathy/lower motor neuronopathy	None	Mild transient parathesia only	Persistent or progressive parathesias, burning sensation in feet, or mild dysethesia; no weakness; mild or moderate deep tendon reflex changes; no sensory loss	Onset of significant weakness, decrease or loss of DTRs, sensory loss in "stocking-glove" distribution, radicular sensory loss, multiple cranial nerve involvement; bladder or bowel dysfunction, fasciculations, respiratory embarrassment from chest wall weakness, grade 3 symptoms that do not resolve with dose reduction
Other				
Clinical symptoms not otherwise specified in this table	No therapy; monitor condition	May require minimal intervention and monitoring	Requires medical care and possible hospitalization	Requires active medical intervention, hospitalisation, or hospice care

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However limited the resources, there is always something that can be done for an individual child.

This handbook is also available at www.rcqhc.org

For additional print copies or more information about the African Network for the Care of Children Affected by AIDS (ANECCA), please contact:

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