



Guidelines for the Management of HIV in Children

2nd Edition 2010

**National Department of Health
South Africa**



FOREWORD

It is with pleasure that I present the new guidelines for the management of HIV-infected children.

Government has adopted a new outcome based approach to accelerate attainment of the objectives outlined in the MTSF (Medium term Strategic Framework) 2009-2014; one of the objectives being to improve the health profile of all South Africans.

The 10 point plan of the Health Sector is aimed at creating a well functioning health system capable of producing improved health outcomes. Priority 7 of the 10 point plan alludes to Accelerated implementation of the HIV & AIDS plan and the reduction of mortality due to TB and associated diseases.

On the 1st December 2009, on World AIDS Day, the Honourable President Jacob Zuma announced the new key interventions to improve ART access to special groups in order to decrease the disease burden, to address maternal and child mortality and y to improve life expectancy.

Based on the presidential announcements, children who are less than 1 year of age and test positive for HIV will be initiated on treatment, irrespective of their CD4 count. This intervention will directly contribute towards the reduction of infant mortality due to HIV and AIDS.

This document serves as a new guidance to health practitioners with regard to the comprehensive management of HIV infected children. The new ART regimens are described as well as laboratory and clinical monitoring at diagnosis, at initiation of antiretroviral treatment and whilst on treatment. It prioritizes integration of HIV with TB, other MCH services such as EPI, nutrition, adolescent health and PMTCT.

The important, but often forgotten area of psychosocial care and support of HIV positive children is also addressed in the guideline.

The many comments, additions and involvement from internal and external stakeholders is commended and has contributed to the excellence of the guidelines.

I would like to thank them all for the development of these guidelines despite their busy schedules.

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DATE:

ABBREVIATIONS AND ACRONYMS

ABC	Abacavir
AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
AZT	Zidovudine
BCG	Bacillus Calmette-Guérin
CB	Chart Booklet (IMCI)
CCMTS	Comprehensive Care, Management, Treatment and Support
CMV	Cytomegalovirus
CSF	Cerebrospinal Fluid
ddI	Didanosine
D4T	Stavudine
DNA	Deoxyribonucleic Acid
ELISA	Enzyme-linked Immunosorbent Assay
FDC	Fixed Drug Combination
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
HSR	Hypersensitivity reaction
IMCI	Integrated Management of Childhood Illnesses
IRIS	Immune Reconstitution Inflammatory Syndrome
LIP	Lymphocytic Interstitial Pneumonitis
MAC	<i>Mycobacterium Avium</i> Complex
MTCT	Mother to Child Transmission
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
ORS	Oral Rehydration Salts
PCP	<i>Pneumocystis Jiroveci</i> Pneumonia
PCR	Polymerase Chain Reaction
PEM	Protein energy malnutrition
PEP	Post-exposure prophylaxis
PHC	Primary Health Care
PI	Protease inhibitors
PMTCT	Prevention of Mother To Child Transmission
RNA	Ribonucleic Acid
SMX	Sulfamethoxazole
TMP	Trimethoprim
TB	Tuberculosis
VL	Viral Load
VTP	Vertical Transmission Prevention
WHO	World Health Organization
3TC	Lamivudine

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SECTION 1: INTRODUCTION

1.1 ANTIRETROVIRAL THERAPY IN SOUTH AFRICA

The South African Antiretroviral Therapy (ART) programme, known as the Comprehensive Care Management, Treatment and Support (CCMTS) programme was launched in 2003. Although the programme achieved much success, ongoing high mortality from HIV and AIDS indicated that substantial changes were required in order to improve access to HIV care and the overall success of the programme. On World AIDS Day in 2009, His Excellency President Zuma announced changes to the HIV and AIDS programme which aimed to reduce mortality from HIV and AIDS through strengthening of both prevention and treatment efforts. Improving access to ART formed an important component of South Africa's revitalized response to the HIV and AIDS epidemic.

The **goals** of the new ART programme, as outlined in these guidelines, are to:

- Achieve best health outcomes in the most cost-efficient manner
- Implement nurse-initiated ART
- Decentralize service delivery to primary health care (PHC) level and to ensure that ART is available at all PHC facilities
- Ensure that HIV and TB services are provided as part of integrated maternal and child health, and sexual and reproductive health services
- Diagnose HIV infection earlier
- Prevent HIV disease progression
- Avert AIDS-related deaths
- Retain patients on lifelong ART
- Prevent new infections among children, adolescents and adults
- Mitigate the negative impact of the HIV and AIDS epidemic

The **objectives** of the ART programme are to:

- Contribute to strengthening of the public and private health sectors capacity to deliver high quality integrated health and wellness services
- Ensure timely initiation of ARVs for treatment and prevention in line with the changes outlined by the President
- To minimize unnecessary drug toxicities

The **specific objectives** of the ART programme are to:

- To prioritize ARVs for:
 - Patients with CD4 counts < 200 cells/mm³ OR with severe HIV disease irrespective of CD4 count
 - Patients co-infected with HIV and tuberculosis (TB) with CD4 ≤ 350 cells/mm³
 - Pregnant women with CD4 ≤ 350 cells/mm³ for lifelong ART and CD4 > 350 cells/mm³ for prophylaxis
- To test all HIV-exposed children, and to initiate ART in all infants under one year of age who are found to have HIV infection
- To standardize first and second line therapy for children, adolescents and adults in the public and private sectors
- To reduce the use of Stavudine
- To expand the use of fixed dose combinations (FDCs) and co-packaged formulations
- To enable nurses to initiate ARVs for treatment and prevention
- To enable PHC facilities to initiate, manage, monitor and refer patients on ART

1.2 PRINCIPLES OF HIV MANAGEMENT IN CHILDREN

As signatories of the United Nations Convention of the Rights of the Child, health care providers in South Africa are obliged to comply with the following four principles, namely that each child has a right to:

- Life, survival and development
- Equitable treatment and care
- Participation in activities and decisions that affect him/her
- All actions should be based on the best interests of the child

HIV infection is not curable, and should be managed as a chronic disease. There are interventions which can significantly improve quality of life and prolong survival time

- Most care and support can be provided at primary care level. When referring, provide the caregiver with a clear explanation of the illness, a referral letter and a follow-up plan.
- Common childhood infections are the most frequent cause of illness and should be managed according to Integrated Management of Childhood Illness (IMCI) guidelines. When illness persists or is very severe, appropriate management is urgent.
- Caregivers of all children receiving ambulatory care must know how to tell when the child is becoming dangerously ill and needs the urgent attention of a health care provider.
- ART suppresses HIV activity and should be given to children who meet the criteria (see Section 6).
- An ill child is likely to suffer pain. Make every effort to keep the child comfortable and pain-free, and ensure that children with end-stage disease receive well managed terminal care.

In managing HIV-infected children and their caregivers, the following principles of palliative care medicine should be applied:

- Do not discriminate
- Be compassionate and show empathy
- Maintain confidentiality at all times
- Establish and maintain clear communication between all levels of the health care system (clinics and hospitals) regarding management of the child
- Involve all health care personnel and parents/caregivers in important patient care decisions
- Alleviate pain and suffering, and preserve quality of life for as long as possible, particularly in the later stages of the illness

1.3 HIV INFECTION AND THE HUMAN IMMUNE SYSTEM

The immune system includes:

- Neutrophils: White cells that protect against invading organisms, particularly bacteria
- Lymphocytes: These are a type of white cell which attack other organisms, such as viruses, tuberculosis and fungi. CD4 lymphocytes form a subgroup of these white cells
- Monocytes: These are similar to lymphocytes but have slightly different functions
- Antibodies are produced by the B subgroup of lymphocytes in response to an antigenic stimulus, such as vaccination or infection
- Lymphoid tissue: An aggregation of a large number of lymphocytes which form structures, such as regional lymph nodes or 'glands'

THE PATHOGENESIS OF HIV

The Human Immunodeficiency Virus (HIV) has unusual characteristics, which are responsible for the clinical and laboratory manifestations of HIV infection and AIDS. HIV has all its genetic material in two single strands of ribonucleic acid (RNA). The virus survives and replicates in CD4 lymphocytes. CD4 positive lymphocytes, monocytes and macrophages are the most important cells to be targeted by the virus. They have receptor sites to which the virus can attach itself and then penetrate the lymphocyte.

Once the virus is in the cell, its RNA is converted to a double strand of Deoxyribonucleic acid (DNA) by the reverse transcriptase enzyme. Viral DNA then enters the nucleus of the cell and is incorporated into the host DNA using the integrase enzyme. During cell-activation viral genetic material is replicated, proteins are made; and then extruded into the cytoplasm. These particles are cleaved by the protease enzyme and are then assembled and packaged using the cell membrane to bud off new viruses. Many millions of viruses can be made daily. Eventually infected CD4 lymphocytes are destroyed by this process.

EFFECT ON THE IMMUNE SYSTEM

CD4 lymphocytes play an important role in protecting the body against infection. When a large proportion of these lymphocytes have been destroyed, the immune system can no longer function normally and the child becomes immune deficient. As the CD4 count drops, immunodeficiency becomes more severe.

The lymphocyte count in the blood declines normally with age until adult levels are reached at 5 years of age. In adults, the absolute CD4 count indicates the degree of immune suppression. In children, the percentage of CD4 cells as a total of all lymphocytes is the best indicator of immunodeficiency (provided that the lymphocyte count is not very low). In children over 12 months of age a CD4 percentage over 25% means that there is minimal immune suppression; 15 – 24% indicates moderate suppression and a CD4 percentage less than 15% indicates severe immunosuppression. The CD4 count is a reliable marker of progressive immunodeficiency.

The immune system of young infants is immature and the risk of serious morbidity and mortality with HIV infection in this age group is especially high. HIV-infected infants (< 1 year of age) are particularly vulnerable and should receive special and frequent attention during this early phase of life.

1.4 MODES OF TRANSMISSION

- Mother to Child Transmission (MTCT) also known as vertical transmission accounts for the vast majority of HIV infection in children (Table 1)
- Sexual abuse
- Transmission by blood transfusion: rare when donor blood is carefully screened
- Insufficiently sterilized instruments, traditional scarification

Table 1: Risk Factors for MTCT

Maternal Factors	Infant Factors
High viral load *	Prematurity
Low CD4 count	Breastfeeding
Advanced AIDS	Mouth lesions
Chorioamnionitis	Invasive foetal monitoring during labour
Prolonged rupture of membranes	
Cracked nipples or other breast condition	

*HIV re-infection may be one of the factors responsible for high viral load during the perinatal period or subsequently

1.5 DISEASE PROGRESSION

HIV exposure occurs during pregnancy, at birth and during breastfeeding. Without intervention MTCT occurs in about 30% of infants. Interventions designed to reduce MTCT will reduce the incidence of HIV infection in children considerably.

In the absence of any intervention most of the children that are infected at the time of birth will develop features of the disease by six months of age. HIV disease progresses much more rapidly than in adults, with opportunistic infections becoming apparent. This rapid progression of the disease is largely determined by the immature immune system. There are additional contributory factors that may lead to rapid demise, such

as high maternal viral load at birth and maternal illness. A child whose mother has died of AIDS has a four-fold risk of early death, even if the child is uninfected.

Evidence suggests that 40% of HIV-infected infants die before they reach the first year of life and most of this mortality appears to occur within the first six months of life. Data indicate that regardless of CD4 % there is a 75% increased risk of mortality in children deferring ART in the first few months of life. Because of this, every effort should be made to identify infants as early as possible. Even after starting ART, young infants appear to have an excess mortality within the first year of life, so regular follow-up is required.

Rapid progression is more likely in the presence of:

- In utero infection
- Maternal high viral load and low CD4 count at time of delivery
- Maternal death
- Co-infections
- Malnutrition

1.6 PREVENTION OF PAEDIATRIC HIV INFECTION

Effective methods of prevention of paediatric HIV infection are well demonstrated both in resource rich and resource poor countries. Primary prevention of HIV infection (in adolescents and adults) and prevention of Mother-to-Child (MTCT), also known as Vertical Transmission Prevention (VTP), are effective ways of reducing the number of children who are infected with HIV.

PREVENTION OF PRIMARY INFECTION

Interventions to prevent HIV infection in adults and adolescents include:

- Reducing heterosexual transmission and involving men in interventions to reduce transmission
- Addressing gender issues especially reducing violence against women and children
- Keeping adolescent girls and boys in school, and delaying sexual activity
- Providing youth-friendly services at health facilities
- Integrating of sexual and reproductive health services, and providing comprehensive management of Sexually Transmitted Infections (STIs)
- Counselling regarding the dual risk of unintended pregnancies and STI's and HIV

ESSENTIAL COMPONENTS OF THE PMTCT PROGRAMME

Essential components of the South African comprehensive approach to PMTCT are shown in Table 2. The PMTCT programme is complex, difficult to implement and involves more than simply dispensing ART. It is a comprehensive service package with interventions and care/management services throughout the antenatal, labour and delivery, and postnatal periods. Case managers and mentorship provided through non-government organizations such as 'Mothers to Mothers to Be' will improve uptake and implementation of the PMTCT package.

Table 2: Essential components of the PMTCT Programme

AT ALL TIMES	<ul style="list-style-type: none"> - Primary prevention of HIV - Prevention of unintended pregnancy - Protection of children, and promotion of child survival
ANTENATAL	<ul style="list-style-type: none"> - Comprehensive antenatal services - Group information session on HIV infection and PMTCT - Routine offering of counselling and testing (rapid HIV testing). Women who test HIV negative need repeat testing at around 34 weeks - Individual post-test counselling - Routine CD4 cell count on ALL HIV-positive women - ARVs to prevent mother-to-child transmission of HIV - Lifelong ART for mothers with CD4 \leq 350 OR clinical Stage 3 or 4 - AZT from 14 weeks plus single dose NVP during labour and single dose TDF and FTC after delivery
LABOUR AND DELIVERY	<p>Optimal obstetric practices including:</p> <ul style="list-style-type: none"> • Avoid prolonged rupture of membranes • Avoid assisted instrumental delivery • Avoid invasive monitoring procedures • Avoid episiotomy and prematurity • Only suction the baby's nose and airway when there is meconium stained liquor • Wipe the neonate carefully at birth
POSTNATAL	<ul style="list-style-type: none"> - Postnatal infant feeding counselling and support for exclusive breastfeeding or exclusive replacement feeding - Early initiation of exclusive breastfeeding or exclusive formula feeding - ARVs to infants to prevent mother-to-child transmission of HIV - All HIV-exposed infants should receive single dose NVP post-delivery, and then low-dose NVP for six weeks - Stop at six weeks if mother is on lifelong ART or if baby is not receiving any breast milk - Otherwise continue NVP for as long as infant is receiving any breast milk - Early infant testing (PCR testing at six weeks). Refer infant for ART if PCR positive - Ongoing follow-up care and support for mothers and infants including early initiation of cotrimoxazole - Family Planning - Community support services

SECTION 2: IDENTIFYING CHILDREN WITH HIV INFECTION

It is important to identify children that are HIV-infected at an early stage to ensure that they and their families obtain optimal care. The disease progresses more rapidly in children than in adults and therefore children may be the first in the family to fall ill.

Early identification/diagnosis makes it possible to:

- Plan regular follow-up
- Initiate ART when indicated
- Ensure that children receive routine preventive health interventions e.g. immunization, growth monitoring and promotion, Vitamin A supplementation
- Provide additional preventative measures which can prevent the development of opportunistic infection in HIV-infected children – the most important interventions is provision of cotrimoxazole prophylaxis
- Identify and treat intercurrent illnesses early and effectively
- Establish whether others in the family are HIV-infected and provide appropriate treatment
- Provide psycho-social support to the family/caregiver through counselling and support
- Facilitate access to social grants, income generation opportunities and other support structures

Constant vigilance is essential in order to ensure that all children with HIV infection are identified as early as possible. The possibility of HIV infection should be considered during every contact with the health system, whether at PHC, district hospital or referral level.

Pro-active steps to detect children with HIV infection include:

- PMTCT records should identify all HIV-exposed and HIV-infected children
- Children in whom maternal HIV status is unknown should be tested for HIV
- The IMCI case management process includes consideration of possible HIV infection in all children who present to PHC facilities. Correct application of the IMCI case management process would therefore result in identification of almost all HIV-infected children
- Children with pneumonia (especially severe pneumonia), malnutrition and TB must be tested for HIV
- Siblings of children diagnosed as HIV-infected should be tested
- Orphans and abandoned children are at special risk of HIV infection, and their HIV status should be established

It is obligatory to identify all children with possible HIV-infection as part of routine primary care.

2.1 CLINICAL FEATURES OF HIV INFECTION IN CHILDREN

SIGNS AND CONDITIONS COMMON IN HIV-INFECTED CHILDREN BUT UNCOMMON IN UNINFECTED CHILDREN

- Severe pneumonia
- Severe bacterial infections esp. if recurrent
- Persistent or recurrent oral thrush
- Bilateral painless parotid swelling
- Generalized lymphadenopathy other than inguinal
- Hepatosplenomegaly
- Persistent or recurrent fever
- Neurologic dysfunction
- Herpes zoster – single dermatome
- Persistent generalized dermatitis not responding to treatment

SIGNS AND CONDITIONS COMMON IN HIV-INFECTED CHILDREN, BUT ALSO COMMON IN ILL UNINFECTED CHILDREN

- Anaemia
- Chronic ear infection
- Persistent or recurrent diarrhoea
- Severe pneumonia
- Tuberculosis
- Bronchiectasis
- Failure to thrive
- Marasmus

SIGNS AND CONDITIONS VERY SPECIFIC TO HIV INFECTION

- *Pneumocystis jiroveci* pneumonia (PCP)
- Oesophageal candidiasis
- Extrapulmonary cryptococcosis
- Invasive salmonella infection
- Lymphoid interstitial pneumonitis (LIP)
- Herpes zoster affecting several dermatomes
- Kaposi's sarcoma
- Lymphoma
- Recto-vaginal or recto-vesical fistula

2.2 CLINICAL STAGING HIV INFECTION

The WHO has developed a 4-stage system (Appendix 1).

Stage I: Asymptomatic

Stage II: Mild symptoms

Stage III: Moderate severity

Stage IV: Severe

The clinical staging is important because:

- It helps to determine the prognosis
- It strengthens the clinical diagnosis when laboratory testing is unavailable or delayed
- It guides decisions regarding initiation and success of ART

Confirmation of the diagnosis depends on laboratory investigations discussed in the next section.

Some opportunistic infections and illnesses are frequently seen in association with HIV infection and are rare in HIV-negative persons. These are referred to as AIDS defining illnesses.

SECTION 3: HIV TESTING IN CHILDREN

3.1 WHICH CHILDREN SHOULD BE TESTED FOR HIV INFECTION?

The following groups of children should be offered HIV testing.

- All HIV-exposed infants
- Children with:
 - Clinical features suggestive of HIV infection
 - Acute illnesses, especially if severe
- All children with the following IMCI classifications: Suspected symptomatic HIV infection or possible HIV infection
- All children diagnosed with TB or who have a history of TB treatment
- Family and social history:
 - Parental request to test the child
 - Father or sibling with HIV infection
 - Death of mother, father or sibling
 - When the mother's HIV status is unknown and her whereabouts are unknown
- When the child may have been wet-nursed or breastfed by a woman of unknown or positive HIV status
- When the child may have experienced or been at risk of sexual assault
- When it is in the best interest of the child where the child is being considered for foster or adoption placement

3.2 LABORATORY TESTS

Currently available tests include:

- HIV antibody detection tests e.g. HIV ELISA test and rapid tests
- HIV viral detection tests e.g. HIV DNA PCR (polymerase chain reaction) and viral load tests

CHILDREN UNDER 18 MONTHS OF AGE

HIV antibody detection tests cannot distinguish between the mother and the baby's antibodies. Maternal HIV antibodies are transferred via the placenta to the baby during pregnancy so that all vertically exposed babies will be born with HIV antibodies, and will test positive on antibody detection tests.

These antibodies can remain in the baby's blood for up to 18 months. If antibodies to HIV are found in children under 18 months of age, the child is **HIV-EXPOSED** (i.e. born to an HIV-infected mother) and a viral detection test such as an HIV DNA PCR is required to establish the infection status of the child.

The viral detection test currently used is the HIV DNA PCR, which detects HIV genes in human cells. It is highly sensitive (98.8%) and specific (99.4%) at 6 weeks of age, and detects virtually all infants infected during pregnancy (in-utero), labour and delivery. An HIV-exposed but uninfected child will test PCR negative and an HIV-exposed infected child will test PCR positive.

The PCR test is highly accurate in determining the HIV infection status of an infant provided that all infants that test PCR positive have a confirmatory viral detection assay on a second blood sample as soon as possible. Currently, the recommended confirmatory viral detection assay is a baseline viral load (VL). A VL above 10 000 copies/mL (> 4 log) is regarded as confirmation of HIV infection. If the VL is not > 4 log, additional viral detection tests are indicated. Initiation of ART should not be delayed while awaiting the result of the confirmatory viral detection assay.

A negative antibody detection test at any age excludes HIV infection provided the child was last breastfed 6 or more weeks before the test and has no clinical signs of HIV infection. However antibody tests should only

be used in children less than 18 months of age in order to determine whether or not the infant is HIV-exposed e.g. if the child is abandoned or the mother is not available.

CHILDREN OLDER THAN 18 MONTHS OF AGE

In children above 18 months of age, HIV antibody detection tests can be used to diagnose or exclude HIV infection as in adults.

If the rapid test is negative, the child is not infected provided there are no clinical features of HIV and breastfeeding ceased more than 6 weeks before the test was done.

If the rapid test is positive, a second, different rapid test is used for confirmation. If the 2nd rapid test is positive, the child is infected, and requires HIV care including assessment for possible lifelong ART. If the 2nd rapid test is negative, an HIV ELISA test should be submitted as a tie-breaker to establish the child's HIV status.

3.3 HIV TESTING GUIDELINES

Remember that counselling and consent from parents or primary caregivers is required before testing young children.

HIV-EXPOSED INFANTS

An HIV-exposed child is defined as a child born to a mother living with HIV until HIV exposure stops (6 weeks after the complete cessation of breast feeding) and HIV infection can be excluded. HIV-exposure status should be determined before birth as part of the PMTCT programme – where the mother's status is not known, this should be determined after birth.

Every HIV-exposed infant requires an HIV DNA PCR test at 6 weeks of age, or earlier if the child is ill or has symptoms suggestive of HIV infection. A confirmatory viral detection assay to confirm every positive PCR test is required. If the PCR is positive and the VL confirms HIV infection, the child should be started on ART.

HIV-uninfected breastfed infants must receive an age appropriate HIV test 6 weeks or more after stopping breastfeeding or if clinical features of HIV infection develop during breastfeeding. An age appropriate test refers to an HIV test that determines HIV status rather than HIV exposure i.e. a viral detection test in children younger than 18 months and an antibody detection test in children 18 months of age and older.

HIV-exposed infants who are PCR negative should have a confirmatory rapid test at 18 months of age.

ENSURING THAT ALL HIV-EXPOSED INFANTS ARE TESTED

Early infant diagnosis is vitally important and is closely linked to well baby care and particularly to the Expanded Programme on Immunization (EPI). Every contact with the health care service should be used to ensure that every child's HIV-exposure status is known and documented on the Road to Health Card.

6-week Immunization Visit

The optimum time for PCR testing of HIV-exposed infants is 6 weeks of age, coinciding with the 6 week immunization visit and establishing the maternal HIV status at this visit is integral to well baby care. Staff at immunization clinics should offer HIV testing to mothers and infants, and should check that HIV-exposed infants have been tested for HIV using DNA PCR, or will be tested on that visit. Appropriate responses based on the mother's HIV status are shown in Table 3. Remember that consent to test the child can be taken from the primary caregiver of the child.

Cotrimoxazole prophylaxis for all HIV-exposed infants must also begin at 6 weeks of age.

Table 3: HIV testing at six week visit

Mother's Status	Action
Positive maternal HIV status	All infants born to HIV-infected women require a PCR.
Negative maternal HIV status	Rapid test should be offered to mother to ensure she has remained HIV-uninfected.
Unknown maternal HIV status	Offer a rapid test to the mother. If she tests positive then her infant should have a PCR at the same visit. Provide the mother with the care she requires.
Unknown maternal HIV status and mother refuses testing	Offer an HIV rapid test (on the infant) to assess HIV-exposure. If the infant's rapid test is positive, perform a PCR test on the infant during the visit and counsel the mother to seek further HIV testing and care. NOTE: in the RTHC so that mother receives continued support during infant follow-up.

10 Week Immunization Visit

The next EPI visit is at 10 weeks of age when the PCR result should be available. Arrange for an earlier visit if the results are available, as the highest risk of infant death is between 2 and 3 months of age. Systems to trace PCR results and infants that default on their visits, and to fast-track positive PCR results to mother-infant pairs should be in place.

If the PCR is positive, a viral load must be sent immediately and the infant should be prepared to begin lifelong ART. If the PCR test is negative and the child is not breastfeeding, the infant is not infected. If the PCR test is negative, but the child is breastfeeding then repeat HIV testing will be required 6 weeks after breastfeeding has stopped or if the child develops clinical features suggestive of HIV infection. The repeat HIV test will be a PCR if the child is below 18 months of age and an antibody test if the child is older.

Remember that all children who have a PCR test should have a repeat HIV (antibody) test at 18 months of age.

BREASTFED CHILDREN

Postnatal transmission via breast milk can occur at any time during breastfeeding. If the breastfed infant tests PCR positive at any age then he/she is confirmed HIV-infected (and breastfeeding should continue). HIV infection can only be excluded by a negative PCR test 6 weeks after breastfeeding has stopped. Depending on the age of the child, a viral detection or antibody detection test to assess for postnatal transmission of HIV should only be done 6 weeks after breastfeeding has stopped.

All breastfed, HIV-exposed children should receive:

- a PCR test at 6 weeks of age
- a rapid test at 18 months of age
- an age-appropriate HIV test 6 weeks after breastfeeding has stopped

SICK CHILDREN OR CHILDREN WITH CLINICAL FEATURES OF HIV

Children of any age presenting with clinical features suggestive of HIV infection require an HIV test. The HIV results for sick children should be fast-tracked, particularly in young infants who have high morbidity and mortality rates unless they access early ART.

Symptomatic, HIV-exposed infants aged less than 6 weeks should have a PCR performed. If the PCR is positive, the infant is infected and requires urgent referral for a confirmatory viral detection test and ART initiation. If the PCR is negative, repeat at 6 weeks of age as in other HIV-exposed infants.

ABANDONED CHILDREN

The HIV status of abandoned infants less than 72 hours old should be established as soon as possible. An HIV rapid test should be used to establish whether the child is HIV-exposed, and if the test is positive, the child should be given nevirapine (stat dose plus daily until six weeks of age). If a rapid test result cannot be obtained within 1-2 hours, treatment with nevirapine should be commenced. HIV antibody testing should be performed as soon as possible. If the infant tests negative, nevirapine should be discontinued.

The HIV status of older abandoned children should also be established so that the child can receive other treatments such as cotrimoxazole for HIV-exposed infants and ART at six weeks if HIV-infected.

SECTION 4: CARE FOR THE CHILD WITH POSSIBLE OR CONFIRMED HIV INFECTION

Care of children with possible or confirmed HIV infection is considered under the following headings:

- PMTCT follow-up
- Confirmation of the HIV status and referral for ART if eligible
- Provision of regular follow-up and preventive care
- Provision of Cotrimoxazole prophylaxis
- Additional preventive care for HIV-infected children

4.1 PMTCT FOLLOW-UP (see PMTCT Guidelines for details)

Infant feeding counselling and support forms an important component of the PMTCT programme. In the past HIV-infected women were advised to choose between two infant feeding options, namely exclusive breastfeeding or exclusive replacement (formula) feeding.

However following the introduction of interventions to increase the safety of breastfeeding, exclusive breastfeeding is now the recommended option for HIV-infected mothers in South Africa, and health facilities should focus on ensuring that mothers adhere to the recommended ARV regimens and are supported to breastfeed. Mothers may still choose to replacement feed, although it is likely that they will be required to purchase their own formula.

Infants should be exclusively breastfed until six months of age. Exclusive breastfeeding means that the child takes only breast milk and no additional food, water, or other fluids (with the exception of medicines and vitamins, if needed). From six months of age, nutritious complementary foods should be added, as outlined in the IMCI chart booklet.

In order to make breastfeeding safer, all HIV-exposed children should receive prophylactic nevirapine from birth until six weeks of age (Table 4 for dosing requirements). Children who are receiving ANY breast milk should continue nevirapine until all breastfeeding stops, unless the mother is receiving lifelong ART. Although it is generally advised that mothers breastfeed for two years, HIV-infected mothers (not on lifelong ART) should consider cessation of breastfeeding their infants at one year of age, so that nevirapine can be stopped. However, if stopping breastfeeding would compromise the nutritional status of the child, then the mother should be advised to continue breastfeeding until two years of age (and the child should continue to receive nevirapine).

**Table 4: Prophylactic nevirapine for breastfed HIV-exposed infants
NVP Infant Dosing Guide**

Drug	Birth Weight	Dose	Quantity
NVP syrup (10mg/ml)	<u>Birth to 6 weeks</u> <2.5kg birth weight	10mg/d	1ml
	<u>Birth to 6 weeks</u> > 2.5kg birth weight	15mg/d	1.5ml
	For all: 6 weeks to 6 months	20mg/d	2ml
	6 months to 9 months	30mg/d	3ml
	9 months to end BF	40mg/d	4ml

HIV-exposed children should have a PCR test at six weeks of age. If the PCR is positive, a confirmatory viral assay (viral load) should be sent. If infection is confirmed, stop the nevirapine and initiate ART.

An age-appropriate HIV test should be done six weeks after breastfeeding has stopped. If this is negative, the child does not have HIV infection and does not require further HIV-related care – in other words, the child should receive routine preventive and curative health care.

Remember that all HIV-exposed infants should receive cotrimoxazole prophylaxis and routine preventive care as outlined.

4.2 CONFIRMATION OF HIV STATUS AND INITIATION OF ART

Early diagnosis and treatment are key to improving the outcome of children with HIV infection.

Therefore as soon as a child tests positive for HIV, the following steps should be followed:

- The child's HIV status needs to be confirmed. In young children this may require sending blood for a confirmatory viral assay (VL) test
- The child should be staged and baseline bloods (CD4 count and percentage, and VL) should be sent
- The child's eligibility for ART should be assessed using the criteria in Section 6.4
- If eligible, ART should be started as soon as possible, especially in infants
- If the child is not eligible for ART, the child needs regular follow-up. This must include regular reassessment of ART eligibility using staging and laboratory criteria. This must be done at least six monthly, and more frequently if the child is sick or is not thriving

4.3 ROUTINE FOLLOW-UP VISITS

Whilst initiation of ART is important, other aspects of care, such as ensuring that the child receives routine preventive care such as immunization and growth monitoring and promotion, should not be neglected. These should be provided through regular follow-up visits, the content of which is outlined below.

GROWTH MONITORING AND PROMOTION

- Growth faltering is an important indicator of disease progression in HIV-infected children. In children receiving ART it may be an early sign of treatment failure.
- Weight must be recorded on the child's Road-to-Health Chart or for children older than 5 years of life on their weight-for-age chart in the child's clinic file.
- Growth faltering must be assessed by means of careful examination for evidence of infections such as respiratory, gastrointestinal or urinary tract infections or TB.
- Feeding advice and food supplementation should be provided (Section 5).

IMMUNISATION

- HIV-infected and HIV-exposed children should be immunized according to the routine national immunization schedule.
- BCG should routinely be given at birth. However, if BCG is delayed because the mother has TB, the HIV-uninfected, exposed infant may receive BCG after completion of prophylaxis. The HIV-infected infant should not receive BCG until he is on ART and has some immune recovery.

ROUTINE TREATMENTS

It is important to ensure that HIV-infected children receive regular routine treatments such as Vitamin A supplementation, (Table 5) and deworming medication (Table 6).

Table 5: Vitamin A supplementation

Target group	Dosage	Schedule
All infants 6 to 11 months	100 000 IU	A single dose at the age of between 6 and 11 months (preferably at 9 months when child comes for immunization)
All children 1 to 5 years	200 000 IU	A single dose at 12 months and then every 6 months until the age of 5 years

Table 6: Routine deworming

Age	Weight	Mebendazole
12 up to 24 months	< 10kg	100mg twice a day for 3 days every six months
> 24 months	10 kg or more	500mg as a single dose every six months

4.4 COTRIMOXAZOLE PROPHYLAXIS

All HIV-infected and HIV-exposed infants must receive cotrimoxazole prophylaxis from six weeks of age as outlined in Table 7.

Table 7: Pneumocystis Jiroveci Pneumonia (PCP) Prophylaxis

Indications for cotrimoxazole	When to start	When to stop
All HIV-exposed newborns	Start from 4-6 weeks after birth	Stop when PCR negative \geq 6 weeks after full cessation of breastfeeding AND infant is clinically HIV negative.
All HIV-exposed Exclusive formula feeding children (EFF)	Start from 4-6 weeks after birth	Stop when PCR negative AND infant is clinically HIV negative AND EFF is expected to continue
All HIV-exposed breastfeeding children	Start from 4-6 weeks after birth	Stop when PCR negative \geq 6 weeks after full cessation of breastfeeding AND infant is clinically HIV negative.
HIV-infected infants < 12 months old	Start from 4-6 weeks after birth or as soon as possible after HIV diagnosis even if on ART.	All infants < 12 months should remain on prophylaxis.
For HIV-infected children 1-5 years with or without ART	All symptomatic children (WHO clinical stage 2, 3 or 4) or CD4 < 15% or < 500 cells/mm ³ .	Stop once ART-associated immune reconstitution has occurred for \geq 6 months i.e. CD4 percentage \geq 15% or CD4 count \geq 500 cells/mm ³ on \geq 2 occasions, 3-6 months apart.
HIV-infected children \geq 6 years of age with or without ART	Start if CD4 count < 200 cells/mm ³ or <15% OR WHO clinical stage 3 or 4 disease (including TB).	Stop once ART-associated immune reconstitution has occurred for \geq 6 months in children over 1 year of age: CD4 \geq 15% or \geq 200 cells/mm ³ on \geq 2 occasions, 3 – 6 months apart.
Any HIV-infected child with high risk for bacterial infections or at risk of malaria	Start cotrimoxazole prophylaxis even with ART immune-reconstitution.	Do not stop until risk has been eliminated and all CD4 cell percentage or CD4 cell count criteria listed above have been met
HIV –infected child with previous PCP infection	Start as soon as first PCP episode has been treated	Stop at age 5 years

*NOTE: Any one of the criteria could be used for starting therapy

Recommended doses of cotrimoxazole by age or weight of child are shown in Table 8.

Oral suspension or tablet administered once daily SMX = sulfamethoxazole; TMP = trimethoprim

Table 8: Recommended doses of cotrimoxazole for prophylaxis

Age or weight of child	Dose	Suspension (200 mg SMX / 40 mg TMP / 5mL)	Single strength tablet (400 mg SMX /80 mg TMP)	Double strength tablet (800 mg SMX /160 mg TMP)
< 6 months or < 5 kg	100mg SMX/ 20 mg TMP	2.5 mL	¼ tablet	–
6 months – 5 years or 5–15kg	200mg SMX/ 40 mg TMP	5 mL	½ tablet	–
6-14 years or 15–30 kg	400mg SMX/ 80 mg TMP	10 mL	1 tablet	½ tablet
> 14 yrs or > 30 kg	800mg SMX /160 mg TMP	–	2 tablets	1 tablet

Cotrimoxazole can cause erythema multiforme and Stevens-Johnson syndrome. If this occurs, stop the cotrimoxazole.

Dapsone should be used in cotrimoxazole intolerant patients. The recommended dose is 2 mg/kg/day or 4 mg/kg/week. The maximum daily dose is 100 mg (1 tablet).

4.5 ADDITIONAL PREVENTIVE CARE FOR HIV-INFECTED CHILDREN

Normal transplacental transfer of antibodies from the HIV-infected mother to the child may be impaired and neutrophil function depressed. The infant is therefore at greater risk of developing measles, TB and infections due to encapsulated organisms (*Haemophilus influenzae* and pneumococcal) at a young age.

This can be addressed by:

- Giving additional immunoglobulins to children who have been exposed to measles (measles immunoglobulin is not presently available). HIV-infected children who are admitted to hospital should receive measles vaccine. This is an additional dose and the child should still receive routine doses at 9 and 18 months of age.
- Varicella immunoglobulin (VZIG) is recommended for children who have been exposed to chickenpox. VZIG should be given as soon as possible after exposure to chicken pox or shingles, but within 96 hours for maximum efficiency. The varicella vaccine can be used both as prevention and as post-exposure prophylaxis if given within 3 days post-exposure.
- The influenza vaccine should be given yearly.

4.6 COUNSELLING AND SUPPORT

Appropriate counselling is ultimately the responsibility of the attending health care provider, and should be provided at all health facilities. Although the counselling can be delegated to a lay counsellor, health care workers remain responsible for overall psycho-social wellbeing of children and their caregivers.

Many non-governmental organizations (NGOs) traditional healers and community-based organizations (CBOs) play an increasingly important role in the care of people living with HIV, including assisting with counselling). Health care workers should be aware of local support organizations and resources, and refer patients to these organizations whenever appropriate.

SECTION 5: NUTRITIONAL SUPPORT

HIV disease in children often leads to multiple nutritional deficiencies and general malnutrition. Decreased food intake, impaired absorption and increased nutrient requirements all contribute to this.

5.1 NUTRITION INTERVENTIONS

Interventions include the provision of nutrition counselling, care, and support in order to:

- Protect and improve the nutritional status of HIV-infected individuals and HIV-affected households/or families
- Promote continuity of care
- Promote and improve adherence to treatment
- Improve birth outcomes and promote HIV-free survival in children
- Support growth and development in children
- Support symptom management

HIV infection can impair the nutritional status of infected children from soon after infection. Length/height and weight are reduced in almost all infected children and growth faltering often occurs, before opportunistic infections or other symptoms present. Growth failure is indeed a sign of possible undiagnosed HIV infection. HIV causes increased energy requirements in the infected child. This initially results in the wasting of lean body tissue and then of fat mass. Lean body tissue is the total amount of muscle and non-fat tissue in the body. Children with severe growth failure and loss of muscle (lean body tissue) are at an increased risk of mortality. ART improves weight, growth and development of infected children and improves their survival.

Besides weight and length/height, another good indicator of a child's general nutritional status is the mid-upper arm circumference (MUAC).

5.2 NUTRITIONAL SUPPORT

ASSESSING THE NUTRITIONAL STATUS OF CHILDREN

The nutritional needs of HIV-infected children vary according to age, stage of disease, the presence of acute and/or chronic infections and the treatment they receive. Nutritional needs are best met through balanced and varied diets in adequate quantities. When these are not available, or demands are high, additional support may be needed.

Appropriate and adequate nutrition is needed to achieve the full benefits of ART. Children often gain weight and height gain when ART is initiated, although height gain is generally much slower than weight gain. Monitoring of weight while on treatment is important as growth failure is often an indicator of treatment failure.

While ART can change the way the body uses fats, proteins and energy, these metabolic changes can generally be managed by nutrition counselling without the need to discontinue ART.

Refer to the "South African National Guidelines on Nutrition for People Living with TB, HIV, AIDS and Other Chronic Debilitating Conditions" for more information on nutritional management of HIV -infected children.

The ABCDE of nutritional care should be followed when assessing HIV-infected children:

Anthropometry:

Regular and careful assessment of a child's growth helps monitor HIV disease progression, can identify complications early, and so offer the opportunity to intervene. Plot the child's growth on the relevant growth chart (Road-to-Health Card or clinic chart). Use the chart to assess the child's growth. Classify the child's growth as:

- Normal growth
- Wasted (weight-for-height < 3rd centile)
- Stunted (height-for-age < 3rd centile)
- Underweight (weight-for-age < 3rd centile)

Biochemistry:

Consider the following tests in children on ART:

- Total cholesterol
- Serum triglycerides
- Serum glucose
- Haemoglobin (Hb)

Clinical:

The nutritional needs of HIV-infected children for growth; development and immunological function depend on the stage of disease and history of recent complications such as persistent diarrhoea or opportunistic infections. An HIV-infected child has increased energy needs due to the infection itself, but a child that has other opportunistic infections will have even higher requirements.

Dietary:

Children should be fed with care and patience. Before offering information and suggestions, first find out who the main caregiver is and who else is involved in feeding and care. This helps to understand the quality and consistency of care practices.

A brief diet history can be obtained to assess the preparation methods, amount and type of food consumed by the child. HIV-infected children often have loss of appetite and opportunistic infections that interfere with the absorption of the nutrients. Parents may not be able to admit their inability to feed the child with what they know the child needs. Questions about household income, recent job losses, the death of a pensioner and sole breadwinner are proxy indicators of household food security and should be included when talking to the caregiver.

If a child is given infant formula, careful examination of the methods of sterilization of utensils and mixing of the formulas should be performed.

If it is apparent that the child has food insecurity or is not meeting her/his energy requirement, she/he should be referred to a dietician and also a social worker to ensure access to child grants and other support.

Evaluation:

When a patient has returned for follow up visits, determine if the patient was seen by the other health worker(s) they were referred to and assess whether they have improved. Continue to refer until the patient is no longer classified as malnourished or food insecure.

5.3 GUIDELINES FOR FEEDING CHILDREN WITH ASYMPTOMATIC HIV INFECTION

Many caregivers are worried about their child's growth and eating patterns. Basic guidelines in the form of the South African food based dietary guidelines can be given to the caregiver. Caregivers should receive appropriate nutritional advice with consideration of cultural and financial constraints. Provide information on food preparation, hygiene, improving energy and nutrient density of meals and give examples of nutritious low cost foods. Adequate nutrition must be established early on as it will help to protect against malnutrition and it will improve and maintain growth and quality of life by avoiding infections such as diarrhoea. Preventive measures such as good hygiene, immunizations and regular vitamin A supplements help protect the child against infections and under nutrition.

FOOD-BASED DIETARY GUIDELINES

As soon as a child is infected with HIV they have an increased energy requirement of 10%. This needs to be taken into consideration when counselling the caregiver. It is always better to be able to give the nutritional advice to the caregiver that prepares the food and feeds the child (Table 9).

Table 9: Food-based dietary guidelines

6 months to < 12 months	> 1 to 7 years	Children > 7 years, adolescents, adults
<ul style="list-style-type: none"> - Enjoy time with your baby - Teach your baby to drink from a cup - From 6 months start giving your baby small amounts of solid foods - Increase your baby's meals to five times a day - Offer your baby clean safe water regularly - Take your baby to the clinic every month 	<ul style="list-style-type: none"> - Feed your children five small meals a day - Encourage children to enjoy a variety of foods - Offer clean safe water regularly - Take children to the clinic every 3 months - Encourage children to be active every day - Make starchy foods the basis of a child's main meals - Children need plenty of vegetables and fruits every day - Children need to drink milk every day - Children should eat chicken, fish, eggs, beans, soya, or peanut butter every day - If children have sweets treats or drinks, offer small amounts with meals 	<ul style="list-style-type: none"> - Enjoy a variety of meals - Drink lots of clean safe water - Be active - Make starchy foods the basis of most meals - Eat plenty of vegetables and fruit every day - Eat dry beans, peas, lentils, and soy regularly - Chicken, fish, milk, meat or eggs can be eaten daily - Eat fats sparingly - Use salt sparingly - If you drink alcohol, drink sensibly - Use foods and drinks that contain sugar sparingly and not between meals

Enriching staple foods to increase the energy content

Most staple foods are low in energy and must be eaten in large amounts in order for energy requirements to be met. HIV-infected children require an increase in energy intake but often have reduced appetite or are not able to consume staple foods in large quantities. In order to increase the energy content of the staple while keeping the volume low the following can be done:

- High energy foods like-cooking oil, eggs, peanut butter, avocado, mayonnaise, milk, milk powder, sour milk, cream, beans, sugar, soya proteins or tinned fish can be added to foods
- Foods that allow for the addition of high energy foods are: porridge, soups, sandwiches, mashed potato, mashed vegetables like butternut or pumpkin, rice, pasta sauces, mealie rice, sauces for staple foods
- Homemade soups will have a higher energy and nutrient content than soups from a packet. Add protein sources, fats or oils and vegetables to increase the energy content
- When adding eggs or other protein sources to foods make sure that they are cooked well. For example if an egg is added to soft porridge, the egg must be added at least 8 minutes before the porridge is cooked to ensure that the egg is well cooked

GENERAL ADVICE

- If there is space at home, plant a vegetable garden, to help ensure that vegetables are more available.
- Home cooked food is better than pre-cooked food in tins or packets, which are expensive and may not be very healthy.
- "Take-away" foods like fried chicken are expensive and not very healthy.

- Sweets, chocolates and crisps are allowed but should not be eaten in place of food. If these snacks are eaten too often, the child will have no appetite for nutritious food like enriched pap, cereals, vegetables and meat.
- Dental hygiene is important. Clean the child's teeth after every meal.
- Milk is an important part of the child's diet. Children over 1 year of age should drink 2-3 glasses every day of fresh full cream milk, full cream powdered milk, sour milk or yoghurt.
- Physical activity and play help children to develop and maintain muscle bulk and a sense of well-being.

5.4 GUIDELINES FOR FEEDING CHILDREN WITH SYMPTOMATIC HIV INFECTION

The WHO recommends that children that have symptomatic HIV need an additional 30% energy while symptomatic children with severe malnutrition require up to 100% more energy. It may be difficult to reach an additional 100% of energy requirements, thus the use of nutritional supplement may be required.

5.5 FEEDING PROBLEMS

The IMCI Chart Booklet provides information on managing feeding problems in infants and young children.

NAUSEA AND VOMITING

- For the exclusively breastfed child, continue exclusive breastfeeding.
- For the older child (> 6 months) and formula fed infant
 - Teach the caregiver how to maintain good hydration by using oral rehydration solution (see diarrhoea)
 - Encourage small frequent meals. Serve the food on a small plate
 - Give food that the child likes
 - Allow fluids between meals and not with meals
 - Offer cold foods e.g. jelly if preferred to warm cooked foods
 - Give the child high energy drinks as they may be better tolerated than solid meals. Example of high energy drinks are Milo made with full cream milk, sour milk, liquefied enriched soups. Avoid thinned porridge that has not been enriched
 - Eat before taking medication
 - Dry toast, rusks, ginger biscuits and dry crackers may relieve nausea
 - Avoid food that is too sweet or fatty, tea and coffee and very salty or spicy foods

SORES IN THE MOUTH

- Continue exclusive breastfeeding where applicable
- Continue exclusive cup feeding where applicable
- Give paracetamol half an hour before solid feeds
- Try topical anaesthetic (Teejel or Bonjela)
- Avoid: acidic (sour) cold drinks or foods like orange juice, vinegar, hot curried food or foods containing chillies
- Give: sour milk and porridge soft and mashed food, cold custard (with added egg), ice cream, ice lollies and ice cubes
- Give cold puree enriched soups that are bland in taste
- Can feed with a straw to avoid the sores in the mouth
- Treat for oral thrush & Herpes simplex

POOR APPETITE

- Children with a poor appetite should be encouraged to drink frequently during the day and not with their meals; for example, sour milk, milk, custard, yoghurt, drinking yoghurt, soup or fruit juice.
- Make the food look and taste good, using colour and different texture to make the food more interesting.
- A child can be encouraged to eat by offering different foods and by making eating fun and a family occasion. Children that are left alone to eat do not eat as well as children that have company.
- Offer small, frequent meals to the child as often as needed throughout the day. Meal times do not need to be adhered to.
- High energy snack can be offer to the child e.g. fruit, dried fruit, peanuts, yoghurt or Mageu
- Limit the intake of fatty, oily and fried foods, sweet foods e.g. sweets, chocolates, puddings and caffeine (found in normal tea, coffee, and cola drinks).

ENCEPHALOPATHY

- Monitor child's feeding skills by watching the child eat and noting whether swallowing is adequate
- Adjust the consistency of the food to the deteriorating developmental level
- Modify eating techniques and utensils
- Refer to speech therapy for assistance with feeding

5.6 FOOD SUPPLEMENTATION

As part of the Integrated Nutrition Programme the Protein Energy Malnutrition (PEM) Scheme addresses the problem of malnutrition in children. Food supplementation is provided for children whose weight has been monitored on the Road-to-Health Chart and is found to be below the 3rd percentile.

The programme is administered at Primary Health Care facilities. Parents/caregivers must also be informed about IMCI feeding recommendations and referred to any community support agencies.

5.7 MANAGEMENT OF SEVERELY MALNOURISHED CHILDREN WITH HIV

DANGER SIGNS IN CHILDREN WITH SEVERE MALNUTRITION

Children with severe malnutrition and danger signs must be hospitalized and receive urgent treatment including daily assessment by a doctor (also during weekends). They should be nursed in a high care area until they are feeding well, infections are under control and diarrhoea has stopped.

In addition to the IMCI danger signs, any of these signs indicate the need for increased vigilance and intensive management of severe malnutrition. Carefully investigate for these danger signs when taking the history and when assessing the child:

- Hypothermia or fever
- Hypoglycaemia
- Jaundice
- Refusing feeds/ not feeding well
- Weeping skin lesions
- Diarrhoea for more than 7 days

TREATMENT

The stabilization phase aims to prevent or treat the following serious complications:

- Hypoglycaemia
- Hypothermia
- Dehydration

- Electrolyte imbalances
- Micronutrient deficiencies
- Infections

Initiation of ART is not an emergency, and priority should be given to preventing and managing the complications of severe malnutrition. The physiological and metabolic changes which occur must be corrected before ART is started.

Step 1: Prevent and Treat Hypoglycaemia and Initiate “Start-up” Feeding

The common cause of mortality and morbidity is hypoglycaemia, which can be prevented with frequent (3 hourly) regular feeding, both day and night (never missing a feed), prevention of hypothermia and aggressive treatment of infections.

Step 2: Prevent and Treat Hypothermia

Hypothermia is present when the underarm temperature is below 35°C and indicates the need to immediately warm and feed the child.

Step 3: Treat and Prevent Dehydration

Many children with severe malnutrition also suffer from diarrhoea, and are at risk of dehydration. To treat and prevent dehydration in the child with diarrhoea:

- Give oral zinc supplementation for 2 weeks:
 - 10mg daily for 0-6 months of age
 - 20mg daily if > 6 months of age
- Replace approximate volumes of stool losses with ORS after each stool is passed:
 - < 2yrs old 50-100mL of ORS
 - > 2yrs old 100-200mL of ORS
 - Give in small frequent sips using a cup and spoon especially after a loose stool or vomiting
- Children with the following signs need more aggressive therapy:
 - increase in pulse rate by 25 beats per minute and respiration by 5 breaths per minute
 - increased oedema and puffy eyelids
- In children receiving oral rehydration, monitor for signs of ongoing dehydration e.g. decreased urine output, excessive thirst, persistent diarrhoea and vomiting, sunken eyes and fontanelle. Monitor for signs of overload at least every hour and stop if necessary. Consider the need for more aggressive treatment if dehydration fails to resolve
- Monitor for shock

SECTION 6: ANTIRETROVIRAL THERAPY (ART)

Every HIV-infected child has the right to comprehensive therapy, which includes ART. ART can improve the morbidity and age-related mortality from HIV infection and in addition can dramatically improve quality of life.

Antiretroviral drugs (ARVs) inhibit the process of replication at the level of the enzymes involved.

- Nucleoside Reverse Transcriptase Inhibitors (NRTI) attach to the RNA strand and shorten the transcription of DNA from RNA by the reverse transcriptase enzyme
- Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI's) inhibit the reverse transcriptase enzyme directly
- Protease inhibitors (PI) prevent the new formation of viral particles by inhibiting the protease enzyme

These antiretroviral drugs work best if used in combination of three, e.g. two NRTI's and either an NNRTI or a PI. ART is an ARV combination regimen that can reasonably be expected to reduce the viral load to undetectable levels (i.e. < 25 copies/mL) when treating patients with no prior use of ARVs (also referred to as ARV-naïve). Absolute eradication of the virus is not achievable as it is also harboured in lymphoid tissue or the central nervous system, where the ARVs might not reach it.

If the treatment is stopped or adherence to medication is poor, the virus will replicate to high levels again. Viral genetic material can readily change (mutate) during replication, particularly if the blood level of the ARV is too low to be effective. Consequently there is a strong possibility that the virus then becomes resistant to that drug.

It is essential to ensure that adequate levels of the drugs are maintained in the body to prevent the development of resistant strains. Hence it is extremely important that patients are adherent to their medication.

6.1 PRINCIPLES FOR ART

- Clinical criteria and CD4 counts need to be considered when deciding to start children on ART (except for infants < 1 year of age). It is unwise to start ART too early (for example, when the CD4 count is normal and the child is asymptomatic) or too late (when the immune system is irreversibly changed)
- Use standard drug regimens – these drugs have proven efficacy, and seldom have serious side-effects. Some children will need non-standard regimens, but these should only be initiated by experienced clinicians
- Constant availability of ARVs must be assured
- It is important to be vigilant for drug interactions and resistance which may reduce the potency of ARVs. Patients should be monitored for adverse reactions
- For a good response at least 95% of the ARVs need to be taken. Adherence is therefore the key to successful therapy. Ensure that ongoing support is provided to the patient and family in order to maintain adherence
- A minority of patients may not respond to ART and continue to progress in spite of good adherence (This may occur especially in those who are severely ill prior to commencing ART. Underlying opportunistic infections should be sought)

6.2 DELIVERY OF ART

In the initial rollout of ART, children with HIV and AIDS considered to be candidates for ART were cared for in accredited units. These were units (at primary, secondary or tertiary institutions) where expertise in managing children on ART was available.

As the ART programme has expanded, and the pool of expertise increased, PHC facilities are now expected to be able to initiate and provide ART for both adults and children. Care for an increasing number of children should be provided at PHC level and by nurses.

The original CCMT unit should as resources to train members of staff from other units, and where more complicated cases can be managed.

Ongoing care for children on ART includes:

- Monitoring treatment adherence
- Providing the necessary ARVs on a monthly basis
- Regular clinical and laboratory monitoring of response to ART
- Assessment for drug side-effects or other complications
- Provision of routine care e.g. immunization
- Management of intercurrent infections and illnesses
- Counselling and support of the parents/caregivers
- Arranging for palliative care where appropriate with the support of NGOs
- The child's home is an important unit that must not be overlooked
- Home visits together with a social worker must be encouraged

REQUIREMENTS BEFORE ART IS IMPLEMENTED

Within the health care system:

- Supplies of treatments are assured
- Staff have the training and skill to manage children on ART
- Systems are in place to ensure that patients can be referred to the next level of care
- Supportive supervision is in place and health care workers have access to advice from more experienced clinicians
- A functional health information system is in place
- Effective and informative counselling services are in operation
- Management, clinical staff and pharmacists at primary care level and at first referral level must have received adequate and appropriate training

Within the child's family/environment, parents/caregiver/children should understand:

- That a responsible individual and a treatment supporter are identified to administer the drugs every day on a long-term basis
- That ART is lifelong therapy
- The prognosis of the condition
- ARV side-effects.

6.3 GOALS OF ANTIRETROVIRAL THERAPY

The goal of ART for children is to increase survival and decrease HIV related morbidity and mortality. On ART:

- The child's CD4 count should rise and remain above the baseline count
- The child's viral load should become undetectable (< 400 copies/mL) and remain undetectable

In some children, a suppressed though detectable viral load, with sustained elevation in CD4 count and absence of intercurrent and/or opportunistic infection, may be the best achievable goal.

6.4 ELIGIBILITY FOR ART

Patients must satisfy clinical and social criteria before being accepted for treatment.

Clinical Criteria

Confirmation of diagnosis of HIV infection AND:	
Age	Eligibility for Treatment
Child less than 1 year	All children should be started on ART
1 – 5 years	Symptomatic (stage III or IV) or CD4 \leq 25 % or absolute count $<$ 750 cells/mm ³
\geq 5 years	Symptomatic (stage III or IV) or CD4 $<$ 350 cells/ mm ³

Social criteria

These criteria are extremely important for the success of the programme and need to be adhered to – the principle is that adherence to treatment must be at least probable.

- At least one identifiable caregiver who is able to supervise the child for administering medication (all efforts should be made to ensure that the social circumstances of vulnerable children, e.g. orphans, are addressed so that they too can receive treatment)
- Disclosure to another adult living in the same house is encouraged so that there is someone else who can assist with the child's ART

6.5 INITIATING ART IN CHILDREN

BASELINE CLINICAL AND LABORATORY INFORMATION

The following information should be clearly documented:

- Child's weight and height
- WHO Clinical Staging
- Presence of symptoms suggesting TB
- Developmental level (Appendix 2)
- CD4 count and percentage
- VL
- Recent Full Blood Count (or Hb)
- ALT if starting on NVP based regimen

REGIMENS

Standard starting regimens for children initiating ART are shown in Table 10. Doses are based on the child's weight (see Antiretroviral Dosing Chart for Children, Appendix 4). It is important to regularly check that children receive the correct dose based on their weight. In older children or adolescents ensure that maximum doses are not exceeded.

Table 10: First line regimens for ART initiation

< 3 years or < 10 kg	Over 3 years and > 10 kg
Abacavir Lamivudine Lopinavir/ritonavir	Abacavir Lamivudine Efavirenz
For all children on Stavudine with no side-effects, Stavudine may be continued. Abacavir should be substituted once any lipodystrophy is suspected.	

6.6 ROUTINE MONITORING

Children on ART should initially be seen at least monthly for regular follow-up and monitoring. Follow-up visits provide an opportunity to:

- Check for and manage any intercurrent illnesses
- Monitor response to ART based on weight gain, development assessment, staging and laboratory results
- Assessment of adherence
- Assessment and management of side-effects
- Provision of ART and other HIV-related treatment e.g. cotrimoxazole
- Provision of routine care e.g. immunization
- Counsel the caregiver and provide psychosocial support
- Ensure that other members of the family are receiving care and treatment

Table 11: Routine Monitoring tests in children on ART

Test	Timing
CD 4 count and percentage	At initiation After six months, after one year, then annually
VL	At initiation After six months, after one year, then annually See recommended action (Table 12)
FBC	For all children – baseline If child on Zidovudine, then – baseline, 1 mo, 2mo, 3mo and then annually
LDL cholesterol triglycerides	Children on Lopinavir/ritonavir Annually
ALT	For a child on nevirapine, baseline, and repeat if child develops rash or jaundice

6.7 SECOND LINE REGIMENS

Changing from first to second-line ARV is a decision, which should only be undertaken after careful consideration. Second line treatment is generally used following treatment failure, as reflected by a VL greater than 1000 copies/mL (despite good adherence).

General considerations prior to defining treatment failure:

- Allow reasonable trial on therapy (at least 24 weeks) before concluding that a regimen is failing
- Always attempt to improve adherence before switching regimens as poor adherence to treatment is the commonest cause of virological failure
- Treat any intercurrent opportunistic infections
- Exclude Immune Reconstitution Inflammatory Syndrome (IRIS) – (Section 7.8)
- Ensure adequate nutrition
- First check adherence: if it is not possible to improve adherence, attempt directly observed therapy (DOT) with a health care worker or the trusted ‘other’ family member or friend identified under ‘social criteria’ above

Table 12: Viral load monitoring and recommended action

Viral load (VL)	Response		
< 400 copies/mL	-6 monthly viral load monitoring and routine adherence support		
400-1000 copies/mL	-Repeat viral load in 6 months -Begin step-up adherence package if VL still between 400 – 1000		
> 1 000 copies/mL	<table border="1"> <tr> <td>-Begin step-up adherence package -Repeat viral load in 3 months</td> <td> -If < 400, return to routine 6-monthly monitoring -If between 400 and 1 000, continue step up adherence and repeat VL after 6 months -If > 1 000, despite stepped up adherence support, AND child is on a NNRTI-based regimen, switch to second-line therapy only if adherence is > 80%. -If > 1000 and child is on a PI-based regimen: <ul style="list-style-type: none"> • Reinforce adherence (it is very difficult to fail a PI-based regimen unless the child ever received an unboosted PI)* • Switch to second-line therapy if VL > 5000, only if adherence is > 80% and consider drug resistance testing if available. -If child received an unboosted PI (e.g. ritonavir alone) in the past, do resistance testing if available and change to second line if VL > 1000 </td> </tr> </table>	-Begin step-up adherence package -Repeat viral load in 3 months	-If < 400, return to routine 6-monthly monitoring -If between 400 and 1 000, continue step up adherence and repeat VL after 6 months -If > 1 000, despite stepped up adherence support, AND child is on a NNRTI-based regimen, switch to second-line therapy only if adherence is > 80%. -If > 1000 and child is on a PI-based regimen: <ul style="list-style-type: none"> • Reinforce adherence (it is very difficult to fail a PI-based regimen unless the child ever received an unboosted PI)* • Switch to second-line therapy if VL > 5000, only if adherence is > 80% and consider drug resistance testing if available. -If child received an unboosted PI (e.g. ritonavir alone) in the past, do resistance testing if available and change to second line if VL > 1000
-Begin step-up adherence package -Repeat viral load in 3 months	-If < 400, return to routine 6-monthly monitoring -If between 400 and 1 000, continue step up adherence and repeat VL after 6 months -If > 1 000, despite stepped up adherence support, AND child is on a NNRTI-based regimen, switch to second-line therapy only if adherence is > 80%. -If > 1000 and child is on a PI-based regimen: <ul style="list-style-type: none"> • Reinforce adherence (it is very difficult to fail a PI-based regimen unless the child ever received an unboosted PI)* • Switch to second-line therapy if VL > 5000, only if adherence is > 80% and consider drug resistance testing if available. -If child received an unboosted PI (e.g. ritonavir alone) in the past, do resistance testing if available and change to second line if VL > 1000		

Second line regimens are shown (Table 13). Ensure that second-line therapy does not include any drugs used in first-line therapy.

Table 13: Second line ART regimens

Regimen which has failed	Action
Any regimen containing Lopinavir/ritonavir OR Child is younger than 3 years	Refer
Abacavir Lamivudine Efavirenz	Change to: Zidovudine (AZT) Didanosine Lopinavir/ritonavir
Zidovudine or Didanosine based regimen (providing Lopinavir is not part of the regimen)	Change to: Abacavir Lamivudine Lopinavir/ritonavir

Children may occasionally need to change a drug from the first-line regimen to one from the second-line regimen, because of intolerance or a serious adverse reaction. Switching limits the patient's second-line treatment options. The decision to switch must be made by a doctor with ARV experience. Switching of one drug should only be done if there is full viral suppression, failing which the whole regimen may need to be altered.

6.8 SALVAGE TREATMENT

Children who fail second line treatment should be referred to a specialist centre where treatment with third line agents can be considered.

6.9 SINGLE DRUG SUBSTITUTION OF STAVUDINE WITH ABACAVIR

The new ART guidelines aim to decrease the use of Stavudine, and children will no longer be initiated on Stavudine. However children who are currently stable on regimens that contain Stavudine should continue to take it. A high index of suspicion should be maintained for possible lipodystrophy. Children who develop lipodystrophy or others toxicity to Stavudine and are virologically suppressed should have a single drug substitution to Abacavir.

Toxicity warranting a switch:

- Lactic acidosis
- Peripheral neuropathy
- Metabolic syndrome including insulin resistance, hyperglycemia, hypertriglyceridaemia, hypercholesterlaemia and low HDL levels
- Lipodystrophy - Lipoatrophy/Lipohypertrophy

HIV-associated lipodystrophy can present with:

- Lipoatrophy (fat loss): including facial fat loss with or without involvement of the buttocks and limbs
- Lipohypertrophy (fat accumulation): including increased fat around abdomen, buffalo hump and breast hypertrophy
- Metabolic syndromes: insulin resistance, hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia and low HDL levels. These individuals are at risk of type 1 diabetes mellitus and coronary artery disease
- Lipodystrophy occurs in 18-33% of patients on ART and is associated with a longer duration of therapy (> 1 year) and the use of Stavudine, Didanosine and protease inhibitors

Lipodystrophy may result in permanent disfigurement. Early substitution of Stavudine to Abacavir will prevent clinical progression of lipodystrophy.

MONITORING

- Advise caregiver to report changes in facial features/body contours
- Clinical examination for features of Lipodystrophy. Look for:
 - Anthropometry:
 - Waist to hip ratio
 - Abdominal circumference
 - Limb circumference

MANAGEMENT

- The most effective management of lipoatrophy is EARLY DETECTION (especially with subtle signs of facial wasting) and CHANGING the regimen to a non-lipodystrophy causing regimen. Delay in changing the regimen will result in irreversible lipoatrophy and permanent disfigurement of the patient.
- For patients on Stavudine and with an undetectable viral load, Stavudine must be substituted for Abacavir. Consult a specialist to decide on an appropriate regimen for patients with lipodystrophy and a detectable viral load.
- There are no established methods for treating lipodystrophy. Encourage exercise and healthy diet 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.
- Be aware of the possibility of Abacavir hypersensitivity reaction (Section 7.5).

6.10 ADMINISTRATION OF ARVs

- For dosage and frequency (Appendix 4).
- Most ARVs are currently available separately. However it is anticipated that fixed dose combinations and co-packaged formulations. This will facilitate dispensing of ARVs, and promote adherence by reducing the number of medicines that patients have to take.
- Stavudine solution requires refrigeration. If no 'fridge' is available, Stavudine capsules may be opened and dissolved, and the required amount administered to the child. The rest can be discarded.
- Switch to tablets or capsules from syrups or solutions as soon as possible.
- Lopinavir/ritonavir needs to be kept cool (< 25° C), and should be refrigerated prior to dispensing. It can be kept out of the fridge for 42 days.
- Didanosine must be taken alone, on an empty stomach, at least an hour before (or 2 hours after) a meal. Tablets should be dissolved in at least 30 mL of water. It is important to use 2 tablets of Didanosine to obtain sufficient antacid buffering e.g. if a child needs 100g, prescribe 2 x 50mg tablets.

6.11 CONCOMITANT TUBERCULOSIS

- If the child is on an EFV containing regimen, there should be no change to the ARVs and standard dose TB Treatment should be added to the regimen.
- If the child is on a Lopinavir/ritonavir solution containing regimen, added ritonavir should be added at a dose of 0.75x the volume of the Lopinavir/ritonavir dose (Appendix 4). TB treatment should be dosed at standard doses.
- In older children (taking Lopinavir/ritonavir tablets) the dose should be doubled to roughly 600 mg/m² of Lopinavir (this is similar to the adult guidelines).
- If the child is on nevirapine, ALT should be monitored according to Table 11. Children who develop signs or symptoms of hepatitis should be referred to a treatment expert immediately.
- If the child is unable to tolerate the large number of drugs, ART may have to be interrupted until TB therapy has been completed – however this should only be done if the child is stable and has a good CD4 count, and in consultation with a treatment expert.

SECTION 7: ADVERSE REACTIONS TO ART

ARVs commonly have side-effects and occasionally serious adverse events (SAEs) can occur. However, side-effects are far less common in children than in adults.

Side-effects or adverse events are those reactions to drugs that are known to occur and would be listed in the package insert e.g. nausea, abdominal pain and vomiting. Life threatening episodes would be referred to as serious adverse events.

Mild side-effects include:

- Mild nausea, vomiting, diarrhoea
- Dizziness (Efavirenz)
- General malaise
- Peripheral neuropathy
- Nail discolouration

Generally it is recommended that patients continue with the medication if the side-effects are mild.

Adverse events should be recorded and reported regularly to the National HIV AND AIDS Cluster. Serious adverse events (SAEs) should be reported within 48-72 hours (Grade 4 or death) to the Medicines Control Council. Adverse event forms on yellow paper will be made available at all centres.

After the patient has recovered from the adverse event it may be possible to recommence therapy with a different regimen. Decision to recommence therapy should be done in consultation with a treatment expert.

7.1 GRADING OF ADVERSE EVENTS

See Appendix 5, Table 20

7.2 RESPONSE TO ADVERSE EVENTS

GRADES 1 AND 2:

- Child remains on therapy
- Repeat the test
- Reassess clinically within 2 weeks

GRADE 3:

- Test should be repeated within 1 week
- If still Grade 3, stop ALL ARVs and refer for specialist advice

GRADE 4:

- Stop all drugs immediately and seek specialist advice
- If the patient restarts therapy after the event has resolved, and the same grade 4 event recurs, appropriate changes or withdrawal of ART may need to be made
- Decisions should be made on an individual basis, and discussed with a treatment expert

If there is a need to discontinue ART, it is advisable to discontinue all ARVs rather than continuing with one or two agents alone. When a patient discontinues a NNRTI-containing regimen, attempt to continue the NRTI component for 2 days after stopping the NNRTI (for example, if NNRTI-related hepatotoxicity suspected).

Remember to complete an Adverse Event form and to submit the form to the local pharmacy service (Appendix 6).

7.3 LACTIC ACIDOSIS

All nucleoside analogues have been associated with lactic acidosis. It is a rare but potentially life-threatening metabolic complication of treatment. The pathogenesis is believed to involve drug-induced mitochondrial damage. Initial symptoms are variable; cases have occurred as early as one month and as late as 20 months after starting therapy, and are usually associated with Didanosine or Stavudine.

NOTE: there are no good screening tests to detect lactic acidosis and a high index of clinical suspicion should be maintained.

CLINICAL FEATURES

- Generalized fatigue, weakness
- Gastrointestinal symptoms (nausea, vomiting, diarrhoea, abdominal pain hepatomegaly, anorexia, and/or sudden unexplained weight loss)
- Respiratory symptoms (tachypnoea and dyspnoea)
- Neurologic symptoms (including motor weakness)

LABORATORY ABNORMALITIES

- Hyperlactataemia (> 2mmol/L)
- Increased anion gap [(Na + K) - (Cl + HCO₃); normal < 15]
- Elevated aminotransferases, CPK, LDH, lipase, and amylase
- Microvesicular steatosis is seen on histology of the liver

MANAGEMENT

- Discuss with a treatment expert
- ART should be discontinued in patients with symptoms
- Symptoms associated with lactic acidosis may continue or worsen following discontinuation of ART
- Therapy is primarily supportive (fluid, bicarbonate administration and respiratory support)
- Administration of riboflavin, thiamine and/or L-carnitine has been reported by some to have benefit in case reports

7.4 HEPATOTOXICITY DUE TO NEVIRAPINE

Hepatotoxicity may occur mainly in the first 8 weeks after starting therapy. In the initial phases of therapy ALT should be done frequently (Table 11, page 32). The patient may present with nausea, vomiting, right upper quadrant tenderness, and jaundice if severe.

A rash in a child on nevirapine with mucosal involvement OR associated with fever/systemic symptoms /derangement in liver functions should be treated as a Grade 4 toxicity. All ARVs should be stopped immediately. Patients should be referred to a specialist for advice regarding restarting ARVs. The patient should never be rechallenged with nevirapine.

MANAGEMENT

- Grade the level of toxicity (Table 20, Appendix 5). ARVs should be stopped if the toxicity is Grade 3 or 4

NOTE: skin rash associated with nevirapine toxicity may occur in association with liver dysfunction. Always check liver function tests if skin rash occurs.

7.5 ABACAVIR HYPERSENSITIVITY REACTION (HSR)

This a multi-organ process manifested by signs or symptoms from at least two of the following groups:

- Fever is the most common manifestation occurring in 80% of cases. Chills have been reported to accompany fever.
- Rash is experienced by 70% of cases, pruritis can also occur. In contrast to non-NRTIs and sulphonamides, the rash is often mild and may go unnoticed by patients. When rash occurs in the absence of other features of HSR, Abacavir should not be discontinued.
- Gastrointestinal symptoms such as nausea, vomiting, diarrhoea and abdominal pain are all features of HSR but may also occur in the absence of HSR, particularly when Abacavir is used with Zidovudine. Therefore, as with rash, patients with isolated gastrointestinal symptoms should not discontinue Abacavir but should be followed closely.
- Constitutional symptoms include fatigue, myalgias and generalized malaise.
- Respiratory symptoms occur in 18% of cases and include dyspnoea, cough and pharyngitis. Symptoms may be difficult to distinguish from influenza and other respiratory viruses. Respiratory symptoms together with abdominal symptoms suggest HSR rather than influenza or other respiratory illness. Clusters and combinations of symptoms are important in the diagnosis of Abacavir HSR.

With Abacavir HSR, there is an accentuation of symptoms in the hours immediately after the dose and worsening of symptoms with each subsequent dose. Stopping therapy is followed by rapid improvement in the symptoms.

If Abacavir is not stopped or is restarted after temporary cessation, the HSR will progress to hypotension, renal dysfunction and bronchospasm and ultimately, death. Abnormal laboratory findings may include leukopaenia, anaemia and thrombocytopenia, as well as elevations in transaminases, urea, creatinine and LDH. Eosinophilia is usually absent. Patch testing is currently only a research tool.

Rechallenging with Abacavir leads to anaphylaxis and should be avoided even in cases where there was diagnostic uncertainty.

MANAGEMENT

- On commencement of Abacavir, patients should be counselled in detail about the possible signs of HSR and be advised to contact their care provider should any occur. If symptoms do occur, therapy should not be discontinued without discussing with the health care provider, as there may be several other causes for similar symptoms. Therapy should not be initiated in patients with intercurrent symptoms to avoid confusion.
- It is advisable for patients to discuss symptoms early with the clinician rather than terminating therapy without consultation. Where termination without consultation occurs, Abacavir cannot be reinitiated. Patients should also be made aware of the special “patient alert card” that comes in the packaging. This card should be presented to any health care provider who sees the child especially when care is not given by the usual provider. Providers at emergency facilities may be less familiar with this condition and where possible contact information for the usual care provider should be provided as well.
- Deciding whether to stop therapy in a patient with suggestive symptoms can be difficult given the very non-specific nature of the presentation. A detailed medical history should be obtained. The following should be considered:
 - When was Abacavir initiated? In the case of Abacavir HSR usually within the past 6 weeks
 - Are two or more systems involved?
 - Do the symptoms increase with each dose?
 - Do the symptom exacerbate just after the dose?
 - Do the symptoms fit into the well recognized clusters?
 - What other medications are used and what was the timing of their initiation?

If patients present with mild symptoms and it is not clear whether symptoms are due to HSR, the clinician may consider allowing an additional dose. The patient should be able to report back or else hospitalization may be required for observation. If symptoms worsen, Abacavir should be terminated immediately and permanently. If symptoms do not worsen, Abacavir can be carefully continued while other possible reasons for the patient's symptoms are investigated. In patients where the diagnosis is thought to be clear or where there is sufficient concern, Abacavir should be terminated immediately and permanently.

If Abacavir is discontinued for HSR, it should be replaced with AZT. Abacavir should never be used in any future treatment regimen for this child.

Hospitalization and special investigation will depend on severity of symptoms. Corticosteroids do not prevent or alter the natural history. The reaction usually improves within 48 hours.

7.6 LIPODYSTROPHY SYNDROME

HIV-associated lipodystrophy includes fat loss and/or fat accumulation in distinct regions of the body: increased fat around abdomen, buffalo hump, breast hypertrophy, and fat loss from limbs, buttocks and face.

Other manifestations: insulin resistance, hyperglycaemia, hypertriglyceridaemia, hypercholestromia and low HDL levels. These individuals are at risk of type 1 diabetes mellitus and coronary artery disease. The syndrome usually occurs in patients who have been on long-term ART and is more common in individuals taking Stavudine or protease inhibitors

MANAGEMENT

- At the first indication of lipodystrophy, Stavudine or Zidovudine should be changed to Abacavir to prevent further irreversible lipodystrophy changes.
- 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. A single drug substitution of Stavudine or Didanosine for Abacavir can be made if the viral load is suppressed.

Figure 1: Example of lipodystrophy



7.7 IMPORTANT DRUG INTERACTIONS

There are multiple opportunities for serious drug interactions. Therapists are advised to scrutinize package information and seek advice if uncertain.

7.8 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

This paradoxical clinical deterioration after starting ART is also known as Immune Reconstitution Inflammatory Syndrome (IRIS). It is due to the improving immune system interacting with organisms that have colonized the body during the early stages of HIV infection.

CAUSES

A wide range of pathogens may induce IRIS including *Mycobacterium tuberculosis* (MTB), BCG, *Mycobacterium avium complex*, *Mycobacterium leprae*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Aspergillus terreus*, *Candida albicans*, *Pneumocystis jiroveci*, CMV, Human Herpes viruses, Human Papilloma virus and Hepatitis B and C viruses.

PRESENTATION

IRIS usually presents during the first 6 weeks after starting ART. Clinical presentations vary and depend on the causative organism and the organ-system that is colonized. For example IRIS caused by MTB may present with high fever, lymphadenopathy, worsening of the original tuberculous lesion, and/or deteriorating chest X-ray features including the development of a miliary pattern or pleural effusion.

MANAGEMENT

Includes specific antimicrobial therapy e.g. TB treatment for IRIS caused by TB. In severe reactions glucocorticosteroids and/or temporary discontinuation of ART may help.

7.9 BCG ADVERSE EVENTS

PRESENTATION

Adverse events related to BCG immunization have also been reported during immune reconstitution. These include:

- Abscess at the site of injection 10-15mm
- Lymphadenitis (> 1,5cm) (lymphadenopathy may also occur at other sites e.g. supraclavicular and cervical)
- Suppurative lymphadenopathy in association with BCG injection
- Disseminated BCG disease (indicated by failure to thrive, fever, hepatosplenomegaly)
- Osteitis
- Skin and eye reactions including erythema nodosum, lupus vulgaris and iritis

MANAGEMENT

- If these adverse events are noted it is important to notify the authorities on a vaccine adverse event form. If an abscess is present this should be drained to avoid sinus formation.
- Pus may be sent for TB culture and PCR for detection of *Mycobacterium bovis*-BCG should be requested.
- Most infants with localized BCG reaction will get better without anti-mycobacterial drugs especially if it is part of an immune reconstitution inflammatory syndrome (IRIS).
- Dissemination of BCG disease should be looked for with sputum, abdominal sonar and other investigations as indicated.
- Only children with disseminated BCG disease should routinely receive treatment with INH (20mg/kg/day), rifampicin (15 mg/kg/day) and ethambutol (25 mg/kg) for a period of 6 months. BCG is inherently PZA resistant and the current strain of BCG used in South Africa has low-level resistance to INH, hence the choice of drug regimen. Single anti-TB drugs are usually only available at hospital level, and the patients should be referred appropriately.

SECTION 8: ANAEMIA IN HIV-INFECTED CHILDREN

Anaemia is common in HIV-infected children and may be due to acute illnesses i.e. malaria, nutritional deficiency, opportunistic infections, drugs (cotrimoxazole, Zidovudine and other ARVs), auto-immune haemolysis, parvovirus infections and the direct effects of HIV infection on the bone marrow. Sickle cell anaemia, thalassaemia and other congenital causes of anaemia may co-exist.

Establishing a cause for the anaemia depends on the clinical features and the ability to investigate and refer infants. In many settings it may be challenging to make an accurate diagnosis due to lack of available special investigations and the distance to referral centres.

Iron deficiency occurs commonly in HIV-infected and uninfected children. Geohelminths such as *Trichuris trichuria* (whipworm) and *Necator americanus* (hookworm) are prevalent and contribute towards anaemia.

Anaemia should not be assumed to be due to iron-deficiency anaemia. A therapeutic trial of iron can be attempted ONCE and only prior to referral for more investigations. It should be preceded by a baseline Hb and REPEATED after 3 weeks to document a response (expected response $\geq 2\text{g/dL}$). A base-line reticulocyte count is most useful in differentiating between haemolytic anaemia and marrow suppression.

TREATMENT FOR IRON DEFICIENCY ANAEMIA

Elemental Iron: 2mg/kg 8 hourly with meals for 3 weeks; if Hb increases $\geq 2\text{g/dL}$ then continue for 3 more weeks).

DIETARY MANAGEMENT OF IRON DEFICIENCY ANAEMIA

Iron deficiency can be caused by consuming diet poor in iron rich foods or high consumption of food that prevent the absorption of iron. Caregivers of children should be encouraged to feed their children diets rich in iron.

There are two types of iron. They are absorbed into the body differently and come from different sources. The first is called haem iron, it is found in meat and meat product. Calcium is the only nutrient to negatively affect the absorption of haem iron. Non-Haem iron is the main source of dietary iron. This iron is found in a variety of foods. The absorption of non-haem iron is affected by the amount of iron the body has in its stores and other nutrients that are eaten with the source of non-haem iron.

Caregivers should be encouraged to give as much animal (haem) iron sources as possible to the child. Not only does it supply iron that is easily absorbed but it also helps to absorb non-haem iron. They should also include foods that are rich in vitamin C. Vitamin C helps with the absorption of all types of iron. It also protects the iron from nutrients that decrease the amount of iron being absorbed. They should avoid giving dairy products, teas and brans with meals that are rich in non-haem iron.

Below is a list of foods that are rich in iron.

Animal sources (Haem iron)

- Liver, chicken
- Molluscs, clam any variety (not easily available)
- Giblets, chicken
- Liver and by products, beef
- Lean meat
- Fish, Sardines tinned
- Egg
- Fish, tuna, tinned in water
- Poultry

- Fish, Haddock

Plant sources (Non-Haem iron)

- Dried beans, kidney, red boiled
- Dried beans, baked, tinned
- Beans, Lima, boiled
- Dried beans, white, tinned
- Dried lentils, boiled
- Fortified infant cereal
- Spinach, boiled
- Potato, baked with skin
- Pumpkin, boiled
- Tomato, tinned puree
- Peas, green
- Peas, split
- Fortified foods

SECTION 9: RESPIRATORY COMPLICATIONS OF HIV/AIDS IN CHILDREN

Many common childhood conditions present in the same way, whether children are infected with HIV or not. Their management is covered in other guidelines such as the IMCI case management guidelines, and the knowledge and skills required to manage these conditions represent core competencies for health care workers.

GENERAL DANGER SIGNS

Every sick child must be screened for General Danger Signs. These are:

- Convulsions with this illness
- Lethargy or loss of consciousness
- Vomiting everything
- Unable to take any feeds

These children are seriously ill and require urgent stabilization and referral. Danger signs are frequently associated with pneumonia and diarrhoeal disease.

9.1 BACTERIAL PNEUMONIA

Respiratory problems are common in HIV-infected children, and are an important cause of death. Recurrent bacterial pneumonia suggests severe immune suppression (WHO Stage III).

The IMCI guidelines should be used to assess, classify and treat children with cough and difficult breathing at PHC level.

The algorithm below applies to children aged 2 months up to 5 years.

Severe pneumonia or very severe disease	
Any general danger sign OR Chest indrawing* OR Stridor when calm	Give first dose of ceftriaxone IM Give first dose cotrimoxazole Give oxygen If stridor: give nebulised adrenaline Test for low blood sugar, then treat or prevent Keep child warm, and refer urgently
Pneumonia	
Fast breathing	Give amoxicillin for 5 days Soothe the throat and relieve the cough If coughing for more than 14 days, consider TB Advise mother when to return immediately Follow up in 2 days
Cough or cold	
No signs of pneumonia or very severe disease	Soothe the throat and relieve the cough If coughing for more than 14 days, consider TB Advise mother when to return immediately Follow up in 5 days if not improving
Fast breathing	
If the child is:	Fast breathing is:
2 months up to 12 months	50 or more breaths per minute
12 months up to 5 years	40 or more breaths per minute

*Chest indrawing means subcostal or lower chest wall recession

MANAGEMENT

Any child with the IMCI classification of ‘Severe Pneumonia or Very Severe Disease’ requires referral for admission and oxygen supplementation. Pre-referral treatment includes: Ceftriaxone IM, oxygen (Table 16), check for hypoglycaemia. Urgent access to oxygen is life saving in severe pneumonia. Many of these children will have *Pneumocystis jiroveci* (*carinii*) Pneumonia (PCP) which causes severe distress and requires immediate management - a dose of Cotrimoxazole is therefore included in the pre-referral management of all children older than one month of age with severe pneumonia (Table 15).

Children with pneumonia who have no signs of hypoxaemia are given amoxicillin according to the schedule below (Table 14). These children need not be admitted to hospital, but the caregiver must be told that she should return to the clinic if the child’s condition deteriorates (refusal to take feeds, loss of consciousness, seizures). Children receiving ambulatory care for pneumonia must be followed up within 2 days of starting antibiotics.

In infants aged less than 2 months, any of the signs listed below suggest severe bacterial infection and warrant urgent referral:

- Fast breathing (60 or more breaths per minute)
- Severe chest indrawing
- Apnoea
- Convulsions
- Nasal flaring or grunting
- Lethargic or unconscious
- Movement less than normal
- Bulging fontanelle

Table 14: Amoxicillin doses for use in Pneumonia

Weight	Dose	Give three times a day			Age
		Syrup		Capsule: 250 mg	
		125 mg/5mL	250 mg/5mL		
≥ 3.5–5 kg	125 mg	5 mL	2.5 mL	–	≥ 1–3 months
≥ 5–7 kg	175 mg	7 mL	3.5 mL	–	≥ 3–6 months
≥ 7–11 kg	250 mg	10 mL	5 mL	–	≥ 6–18 months
≥ 11–14 kg	375 mg	15 mL	7.5 mL	–	≥ 18 months–3 years
≥ 14–25 kg	500 mg	20 mL	10 mL	2 capsules	≥ 3–7 years
≥ 25–35 kg	750 mg			3 capsules	≥ 7–11 years
≥ 35 kg and above	1000 mg				≥ 11 years – adult

Table 15: Cotrimoxazole doses – treatment of PCP

Cotrimoxazole Treatment for PCP*		
Given four times a day		
Weight	Age	Cotrimoxazole dose four times a day
Less than 5 kg	6 weeks-2 months	2.5 mL
5 – 9.9 kg	2 up to 12 months	5 mL
10 – 14.9 kg	12 up to 24 months	7.5 mL
15 – 21.9 kg	24 up to 60 months	10 mL or 1 tablet
> 22 kg	> 60 months	15 mL or 1½ tablets

Table 16: Ceftriaxone doses

Ceftriaxone given once daily			
Weight	Age	Ceftriaxone	Ceftriaxone
3 – < 6 kg	0 up to 3 months	250 mg	1.0 mL
6 – < 10 kg	3 up to 12 months	500 mg	2.0 mL
10 – < 15 kg	1 up to 24 months	750 mg	3.0 mL
15 – 25 kg	24 up to 60 months	1g	4.0 (give 2 mL in each thigh)

INPATIENT MANAGEMENT

Treat according to local hospital guidelines

INVESTIGATIONS

- Full blood count and differential
- Blood culture (optimal yield is +/- 30% in bacterial pneumonia)
- Tuberculin skin test (Mantoux)
- Gastric washings/ sputum for AFBs
- Chest X-ray

TREATMENT

- Oxygen
- IV fluids
- Paracetamol 10-15 mg/kg/dose 6 hourly
- Ampicillin 100 mg/kg/day IV 6 hourly, changing to amoxicillin as soon as possible
- Gentamicin IV
 - < 10 years old: 8mg/kg stat, and then 6mg/kg daily thereafter
 - > 10 years 7mg/kg stat, then 5mg/kg daily thereafter
- Total duration 7-10 day
- If *Staph. aureus* infection is suspected: ADD cloxacillin 150 – 200mg/ kg/day in 4 doses (cefuroxime 200mg/kg/day 8 hourly IV is an alternative – ampicillin then not necessary) as initial therapy

Have a high index of suspicion for PCP in children less than 1 year of age presenting with severe pneumonia. Initiate therapy with cotrimoxazole early as described below, in addition to the management described above.

TB should also be considered as part of the differential diagnosis of pneumonia.

If there is no improvement within 48 hours of admission, or if the child develops a nosocomial (hospital-acquired) pneumonia, change antibiotics to cover the main organisms responsible for nosocomial infections at the individual hospital.

9.2 PNEUMOCYSTIS JIROVECI (FORMALLY CARINII) PNEUMONIA (PCP)

PCP, which is an AIDS defining condition, accounts for a high proportion of mortality in HIV-infected infants. The majority of cases can be prevented with cotrimoxazole prophylaxis, whilst early and appropriate treatment significantly improves the outcome. PCP is characterized by the following features:

- Tachypnoea (fast breathing)

- Hypoxaemia - oxygen deprivation characterized by disorientation, confusion and with cyanosis if the child is not anaemic) – the infant appears to be “hungry” for air
- Absent or low-grade pyrexia – however sudden onset of fever may be a feature

Clinical findings on chest auscultation may be negligible and thus not in keeping with the degree of respiratory distress. On chest X-ray one might see a diffuse interstitial infiltrate. Early and appropriate treatment, significantly improves the prognosis.

Suspect PCP if the child:

- Is less than 12 months old and
- Has tachypnoea (fast breathing) i.e. 50 or more breaths/minute in infants 2 to 12 months, 40 or more breaths/minute in children 12 months up to 5 years
- Is dyspnoeic (with severe difficulty in breathing)
- Has few crackles relative to the degree of dyspnoea, and decreased breath sound intensity on auscultation
- Is hypoxaemic – many children who are anaemic may be profoundly hypoxaemic without appearing cyanosed

Begin treating for PCP immediately on suspicion (in addition to usual treatment of pneumonia) (Table 15), even if the HIV status of the child has not yet been established. All infants and children with suspected PCP should be treated in hospital.

INPATIENT MANAGEMENT OF SUSPECTED PCP (PNEUMOCYSTIS PNEUMONIA)

Treat aggressively. Palliative care principles with an emphasis on relieving respiratory distress should also be applied.

INVESTIGATIONS

- Check oxygen saturation: If PCP is present, oxygen saturation is usually less than 90% on pulse oximetry (in room air)
- Chest X-ray: Diffuse bilateral alveolar or interstitial infiltrate (findings can vary)

TREATMENT

- Oxygen
- Cotrimoxazole. Load with 250mg/m² of the trimethoprim component, then give 20mg/kg/day of trimethoprim component 6 hourly IV for 5 days changing to orally for 3 weeks if response adequate. NOTE: this is a higher dose than that used for prophylaxis.
- If PCP is confirmed or if child is hypoxaemic, give Prednisone (1-2mg/kg) daily for two weeks
- Consider adding clindamycin 30 – 40mg/kg/day for severe disease
- Paracetamol 10-15mg/kg 6 hourly for pain or fever > 37.5°C
- Morphine must be given if severe respiratory distress is not responding to other medical management, and admission to an intensive care unit is not an option
 - Morphine oral starting doses:
 - < 1 year: 0.2- 0.4 mg 4 hourly
 - 1 – 5 years: 0.5- 5 mg 4 hourly
 - 6 - 12 years: 5-7.5 mg 4 hourly
- PCP prophylaxis should continue after discharge as per guidelines (Table 8, page 21).

PREVENTION OF PCP

Most cases of PCP can be prevented through administration of routine prophylactic cotrimoxazole. All children with HIV infection must receive cotrimoxazole prophylaxis as outlined in Table 8.

9.3 TUBERCULOSIS

Diagnosing TB in children can be difficult. It is easy to overdiagnose TB, but it is also easy to miss it. Due to immune deficiency, HIV-infected infants and children are particularly susceptible to TB.

Suspect TB if the child has:

- Contact with an adult pulmonary tuberculosis source case – often the 1st indication of childhood tuberculosis
- If the child was the index case, then the mother/caregiver may be the TB source case
- Fever for more than a week
- A chronic unremitting cough (for more than 2 weeks)
- Ongoing weight loss or poor weight gain (crossing percentiles on the Road-to-Health Chart)
- Loss of playfulness

INVESTIGATIONS

- Mantoux tuberculin skin test:
 - An induration ≥ 5 mm represents a positive test indicating TB infection.
 - A negative test does not exclude TB.
- Gastric washings and/or induced sputum for culture of *M. tuberculosis*. Also culture other body fluids or tissue (e.g. fine needle aspiration of lymph nodes), if available. Culture positive specimens should also undergo drug susceptibility testing.
- Radiology: Chest X-ray features are the same in HIV-infected and HIV uninfected children. Interpretation is more difficult in HIV-infected children, because of other concurrent lung diseases/infections.

Radiological features suggestive of pulmonary TB in HIV-infected children: alveolar consolidation and/or hilar lymphadenopathy and/or cavitation/ “breakdown”, and/or atelectasis and/or pleural/pericardial effusion and/or miliary TB.

NOTE: Adequate analgesia should be given to prevent procedural pain e.g. for pleural tap, intercostal drains.

MANAGEMENT

- Children should be treated using the treatment regimens outlined in the National Treatment guidelines and EDL standard treatment guidelines. The doses may need to be altered for children who are receiving ART (see Section 6.11).
- All children with severe forms of TB, such as tuberculous meningitis, miliary TB, or other extra-pulmonary TB should receive inpatient hospital therapy initially and subsequently be considered for referral to TB hospitals for maintenance treatment. These children require 9 months of TB treatment and need 4 drugs (preferably additional ethambutol) during the intensive phase of treatment.
- Give paracetamol or tilidine to all children with meningitis for relief of headache (see pain management below).
- All HIV-infected children should receive pyridoxine if they are on TB treatment:
 - < 5 years 12.5 mg daily
 - > 5 years 25 mg daily
- HIV-infected children may need to be treated for TB for longer than 6 months if they do not respond well to treatment. Drug-resistant TB must also be considered if there is poor response to treatment.
- All HIV-infected children (on or off ART) on treatment for tuberculosis should receive prophylactic cotrimoxazole (at least until CD4 count is $> 25\%$).

SUPPORT

Caregivers need to receive accurate and detailed information about:

- the diagnosis
- the need to complete the full course of treatment
- the possibility of other family members or close contacts having TB

PROPHYLAXIS

- Routine TB prophylaxis for HIV-infected children is not currently recommended.
- All children who are HIV-infected regardless of age need to receive INH prophylaxis for 6 months if exposed to a close adult contact with pulmonary tuberculosis.
- If the source case is resistant to INH, rifampicin (10-15 mg/kg daily) prophylaxis should be given for 4 months.

BCG IMMUNIZATION

- BCG is given at birth to all infants regardless of HIV exposure, especially considering the high prevalence of TB in South Africa.
- However, there should be close follow-up of infants known to be born to HIV-infected mothers who receive BCG at birth in order to provide early identification and treatment of any BCG complication. Disseminated BCG-disease seems to be less likely if ART is started early in infancy.
- The diagnosis of BCG disease is difficult and treatment is specialized as *M. bovis* is resistant to Pyrazinamide and requires higher doses of other first-line TB medications (The Danish strain *M. bovis* BCG is resistant to INH at current phenotypic drug susceptibility testing concentrations and is also resistant to Ethionamide).

9.4 LYMPHOID INTERSTITIAL PNEUMONIA (LIP)

Lymphoid interstitial pneumonia (LIP) is a slowly progressive interstitial lung disease of unknown aetiology. LIP is often asymptomatic, but at times presents with symptoms. It is common and occurs in no less than 40% of perinatally infected children.

WHEN TO CONSIDER LIP

HIV-infected child aged more than one year with:

- Recurrent low-grade bacterial infections, chronic lung disease and bronchiectasis
- Slowly progressive hypoxia, tachypnoea and exertion fatigue
- Clubbing of fingers
- Enlarged parotid glands
- Hepatomegaly
- Suggestive Chest X-ray findings: Bilateral reticulonodular infiltrates and mediastinal lymphadenopathy

Children with LIP often have episodes of intermittent acute pneumonia necessitating antibiotic treatment or admission to hospital. Distinguishing this problem from TB can be difficult.

MANAGEMENT

- No therapy is required for asymptomatic children.
- If the child has any respiratory symptoms, ART should be initiated as these children can develop severe Chronic Lung Disease.
- Management of severe or progressive LIP should be carried out in consultation with a specialist HIV clinic, although there is seldom an indication for admission to hospital. Once treatment has been

initiated at the referral level, follow-up and maintenance treatment can be provided at the PHC clinic.

- Treatment with steroids in addition to ARTs is required for hypoxic children (oxygen saturation consistently $< 92\%$) and/or those developing signs of cor pulmonale (right sided heart failure). Prednisone 2mg/kg daily for 4 weeks for severe cases may also be of help. Thereafter wean to the lowest dose required to maintain oxygen saturation $\geq 92\%$.
- Exclude any acute lower respiratory tract infection and pulmonary TB prior to treating children thought to have LIP with steroids.
- The child will usually be able to be weaned off steroids once they have been on ART, but may need long term low dose steroids.
- All children started on steroids should also be given PCP prophylaxis for as long as they are on steroid therapy (Table 8).

SECTION 10: GASTRO-INTESTINAL CONDITIONS

10.1 ACUTE GASTROENTERITIS

Dehydration is a common cause of mortality and morbidity in children with an acute diarrhoeal episode. It is therefore recommended that the process of assessment and management follows the structure below: Viz. Assess dehydration => general history and examination → consider risk factors → consider special types of diarrhoeal illness.

Use the IMCI algorithm below and rehydrate immediately where indicated.

Assess hydration. Classify as “Severe dehydration”, “Some dehydration”, or “No visible dehydration”			
Hydration Classification	Severe dehydration	Some dehydration	No visible dehydration
Signs	2 of the following signs:	2 of the following signs:	
Level of consciousness	Lethargic or unconscious	Restless and irritable	Alert
Sunken eyes	Sunken	Sunken	Not sunken
Ability to drink	Poor or unable	Eager, thirstily	Normal, not thirstily
Skin Pinch (Turgor)	Very slow return > 2 secs	Returns slowly < 2secs	Returns immediately

TREATMENT

Zinc supplements – 10 mg daily for 2 weeks in age 0 to 6 months
– 20 mg daily for 2 weeks in age > 6 months

Severe dehydration:

- Give 20mL/kg Normal saline IV rapidly
- Repeat this twice if pulse remains weak or undetectable
- Then give 20mL/kg every hour for 5 hours (If IV treatment is not possible use a nasogastric tube)
- Refer urgently
- Offer ORS as soon as possible
- Assess 2-hourly while awaiting transport.
- If signs have improved after 4 hours move to ‘some dehydration’ and change therapy accordingly

Some dehydration:

- Start feeding as soon as rehydrated (about 4 hours).
- Give oral ORS 80mL/kg over 4 hours. Increase the amount if the child wants more.
- Encourage the mother to give the ORS by cup and spoon.
- Encourage the mother to continue breastfeeding, where applicable, or to give any other fluid.
- In case of vomiting: wait for 10 minutes, warm the ORS slightly if possible and resume rehydration.
- Reassess after 4 hours: if unchanged, continue. If signs have disappeared continue as for ‘no visible dehydration’. If worse, change to ‘severe dehydration’ management.

No visible dehydration:

- The aim is to prevent dehydration
- If exclusive breastfeeding, give more frequently and longer
- Give SSS* in addition
- If not on exclusive breast milk offer food-based fluids, e.g. soft porridge, maas (amasi), yoghurt, Sugar Salt Solution or ORS**
- Give ORS if the child has been rehydrated for ‘Severe dehydration’ or ‘Some dehydration’

*Sugar salt solution: 1 litre of clean or boiled water + 8 level teaspoons of sugar + ½ teaspoon of salt.

**ORS: dissolve the contents of one sachet into 1 litre of clean or boiled water.

Fluid intake:

- Up to 2 years: 50 – 100mL after each loose stool
- 2 years and over: 100 – 200mL after each loose stool

Step 2: Carry out the normal history taking and examination

Step 3: Look for special risk situations

The following groups of children should be managed as inpatients:

- Infants under 2 weeks old
- Malnourished children
- Children with signs such as:
 - Convulsions with this illness
 - Altered level of consciousness
 - Persistent vomiting
 - Respiratory distress
 - Persistent diarrhoea with dehydration
 - Hypothermia
 - Surgical abdomen
 - Dysentery in child < 12 months

These children should not be managed at PHC establishments, but should be referred. Pre-referral treatment should be given and rehydration started before referral.

Step 4: Look for special types of diarrhoea

Bloody Diarrhoea: Consider dysentery

Diarrhoea with high fever/very ill: Consider Typhoid and refer

Persistent diarrhoea (more than 14 days) must be carefully managed, as outlined below:

GENERAL MANAGEMENT

- Continue feeding
- Educate the family on hygiene
- Review in 5 days, or earlier if the child gets sicker
- Advise caregiver when to return immediately, and on home care and prevention of diarrhoea

FLUID MANAGEMENT FOR INPATIENT CARE

Knowledge about how much fluid is required is essential even when a child is not ill. Maintenance fluids can be given orally or intravenously. Usual fluid requirements for maintenance can be calculated from body weight. Provide 100mL/kg for the first 10kg of body weight, 50mL/kg for the next 10kg, and 25mL/kg/day thereafter.

NUTRITIONAL MANAGEMENT

- If breastfed, continue breastfeeding throughout rehydration and maintenance phases of treatment.
- If formula fed, restart formula feeds after completion of initial rehydration (after 4 hours).
- Restart complementary feeding and other foods after initial rehydration.

DRUG THERAPY

- Zinc is beneficial in that it lessens the period of diarrhoea as well as the stool frequency.
- Anti-diarrhoeal agents are not beneficial and may be harmful.

- Diarrhoea episodes do not require antibiotic treatment – except in cholera and typhoid.
- Antibiotic treatment may be required in the neonate, in cases of severe malnutrition, severe systemic illness (toxic) or if there is dysentery.

10.2 DYSENTERY

Dysentery presents with blood in the stool with or without mucus.

OUTPATIENT MANAGEMENT

- Refer for inpatient care if any of the following features are present:
 - Child is dehydrated
 - Child is < 12 months
 - Child unable to tolerate oral medication
 - No improvement after 2 days of antibiotic
 - Child is deteriorating
- Assess hydration and manage as outline above
- Continue feeding
- Send stools for microscopy and culture
- Give Zinc
 - 10 mg daily for 2 weeks in age 0 to 6 months
 - 20 mg daily for 2 weeks in age > 6 months
- Treat with ciprofloxacin as an outpatient
 - ciprofloxacin 15mg/kg/ dose 12 hourly for 3 days
- Educate the family on hygiene
- Review after 2 days but earlier if there is deterioration
- Advise caregiver when to return immediately, and on home care and prevention of diarrhoea

HOSPITAL MANAGEMENT

Ceftriaxone: 20–80mg/kg/day IM daily for 3-5 days

OR

Ciprofloxacin 5–10 mg/kg/dose for 3 days

10.3 PERSISTENT DIARRHOEA

This problem is associated with an 11-fold increase in risk of death. Up to 70% of diarrhoeal deaths in HIV-infected children are due to persistent diarrhoea.

OUTPATIENT MANAGEMENT

- Assess and treat for dehydration (see Section 10.1, Acute gastroenteritis).
- Continue feeding: Optimal nutritional therapy is a vital component of the management. Nutritional therapy consists of providing easily available, inexpensive and culturally acceptable foods.
- Give an additional dose of Vitamin A (Table 5, page 20). NOTE: omit additional dose if the child has had a dose during the previous month.

FEEDING RECOMMENDATIONS FOR PERSISTENT DIARRHOEA

- If still breastfeeding, give more frequent, longer breastfeeds, day and night.
- If taking other milk:
 - 1st choice is to: replace with increased breastfeeding
 - 2nd choice is to: replace with fermented milk products, such as amasi (maas) or yoghurt

- 3rd choice is to: replace half the milk with nutrient-rich semisolid food (like mashed fruit or vegetables)
- For other foods, follow feeding recommendations for the child's age
- Avoid very sweet foods or drink
- Give small, frequent meals at least 6 times a day
- After recovery give one extra meal a day for at least a week.

Follow-up after 5 days

Refer for inpatient management if:

- Child now shows signs of malnutrition or has lost weight
- Some or severe dehydration
- Diarrhoea has not improved despite the child being fed appropriate foods at home

HOSPITAL TREATMENT FOR PERSISTENT DIARRHOEA

Persistent diarrhoea in HIV-infected children is difficult to manage, particularly if the child is also malnourished. Children with any dehydration should be admitted for correction of dehydration, electrolyte or acid-based abnormalities.

Investigations

- Assess for infections elsewhere, e.g. urinary tract infection.
- Send a fresh stool for microscopy and culture to the laboratory, to identify a typical or unusual organisms;
- If there is:
 - Treatment failure **OR**
 - Blood in stool **OR**
 - Not responding to standard nutritional support
 - Then, do a Clinitest on stool water to detect lactose. NOTE: use a tablet and not a urine dipstick.

Feeding

- If reducing substance is present (> 0.5% on Clinitest), try a non-lactose containing feeds (e.g. a soya-based formula)
- Provide yoghurt (or a similar fermented milk product, e.g. maas) if available. This reduces by one-half the amount of lactose in the child's diet
- Give frequent small meals, at least six times a day (see Section 5)

10.4 CANDIDIASIS (THRUSH)

ORAL CANDIDIASIS

This is a very common problem in HIV-infected children. If it persists beyond the neonatal period despite treatment, it is strongly suggestive of HIV infection. It is at times accompanied by candidial napkin rash.

Description

This may be confined to the tongue and buccal mucosa and/or extend into the pharynx and/or oesophagus. If it is extensive it is painful and interferes with eating and swallowing.

Outpatient management

- Nystatin suspension (1mL of 100,000IU/mL suspension) after each feed for seven days
- Remember to continue for 48 hours after cure
- Relieve pain with paracetamol. Topical analgaesia may be of benefit
- Treat refractory oral candidiasis, and suspected oesophageal candidiasis with Fluconazole 3mg/kg/day for up to 21 days

Refer if:

- Appropriate medication is unavailable
- The child is unable to feed or vomiting all feeds

OESOPHAGEAL CANDIDIASIS

This is an AIDS-defining illness. Suspect oesophageal candidiasis if a child with oral candidiasis:

- Refuses feeds
- Has difficulty swallowing difficulty
- Drools
- Has a hoarse voice or stridor

Oesophageal candidiasis may occur in the absence of oral candidiasis

Treatment

- Fluconazole 3mg/kg/day for 21 days IV changing to oral Fluconazole if tolerating feeds
- Relieve pain

SECTION 11: COMMON SKIN CONDITIONS IN HIV-INFECTED CHILDREN

11.1 HERPES SIMPLEX VIRUS

This illness is usually part of an acute primary infection with extensive ulcers in and around the mouth. There may be recurrent infections and at times secondary bacterial infection.

DESCRIPTION

Painful ulcers 4-5 mm in diameter can be seen on the tongue, lips and all mucosal surfaces of the mouth. They cause severe pain and interfere with feeding. The child often salivates and drools excessively. Chronic extensive ulcers around mouth and/or nose may also occur.

OUTPATIENT MANAGEMENT

- Oral acyclovir:
 - 2 years and over give 400mg 8 hourly for 5 days
 - Under 2 years, give 200mg 8 hourly for 5 days
 - Repeated courses may be required
- If superinfected give Amoxicillin (10 -25mg/kg 8 hourly) and Flucloxacillin (12-25 mg/kg 6 hourly max 500mg per dose). Topical antibiotics may be indicated as well
- Provide pain relief
- Refer if:
 - appropriate medication is unavailable
 - disseminated infection suspected (pneumonia, jaundice, abnormal neurological findings)
 - the child is unable to ingest fluids
 - the child is dehydrated

Inpatient management

Aciclovir IV 5 – 10 mg/kg/dose 6 hourly for 10 – 14 days

Change to oral 10 – 20 mg/kg/dose 4 – 6 hourly

11.2 CHICKENPOX (VARICELLA)

Presents with vesicles, which start as papules and eventually become crusted, distributed over face, trunk and limbs. The child with immune suppression may have large and extensive vesicles. Vesicles appear in crops over several days. Mucosal surfaces may also be involved.

Child is infectious until all lesions have crusted completely, therefore he/she needs to be isolated for some weeks.

HIV-infected children, who have been exposed to Chicken Pox, should be given Varicella immunoglobulin

OUTPATIENT TREATMENT

- Acyclovir 80mg/kg per day orally in (3-4 divided doses) for 7-14 days
- If secondary bacterial infection develops add amoxicillin 10-25mg/kg 8 hourly and oral Flucloxacillin 12-25 mg/kg per dose 6 hourly, with a maximum of 500mg per dose
- Refer to higher level of care if:

- Appropriate medication is not available
- Disseminated infection is suspected (pneumonia, jaundice, abnormal neurological findings)
- The child is unable to ingest fluids OR
- The child is dehydrated

TREATMENT FOR DISSEMINATED INFECTION

- Acyclovir IV: 500 mg/m² per dose per day in 3 divided doses for 7-14 days or 10mg/kg/dose in 3 divided doses for 7-14 days
- Oral or intravenous antibiotics may be needed if vesicles have secondary bacterial infection

11.3 HERPES ZOSTER

This is a reactivation of varicella. Vesicular lesions usually occur in the region of a dermatome unilaterally and are associated with pain and fever. As zoster is uncommon in children one must suspect HIV infection. If more than one dermatome is affected it is an AIDS defining condition.

OUTPATIENT TREATMENT

- Aciclovir: 10 –20 mg/kg/dose 4 to 8 hourly for 7 days may hasten healing of lesions
- Pain control/relief with paracetamol
- Refer to a higher level of care if appropriate medication is unavailable or disseminated disease is suspected
- Treatment for disseminated infection is as above

11.4 SEBORRHOEIC DERMATITIS

This is characterized by eczematous lesions, often with diffuse scaling of scalp ('cradlecap'), erythema and scaling of the intertriginous folds and napkin areas. It tends to be severe in HIV-infected children. Secondary bacterial and candidial infection of the rash is common.

OUTPATIENT MANAGEMENT

- Aqueous cream (UEA) as soap
- 1% hydrocortisone cream twice daily to affected areas
- If more severe, try betamethasone valerate 1:10 or 1:4 in UEA and nystatin and terramycin ointment together with steroid cream
- If still unresponsive, add oral antibiotics or prednisolone

11.5 MOLLUSCUM CONTAGIOSUM

Papular umbilicated lesions usually occurring around eyes, but may be generalized. They may become severe or develop large forms if the child is immunosuppressed.

TREATMENT

- If mild, no treatment is required
- Tincture of iodine Bp, applied to the core of individual lesions using an applicator
- If severe refer to a specialist centre for treatments such as liquid nitrogen
- Extensive lesions will only respond to ART

11.6 WARTS

There are widespread common and plane warts. Large genital warts are frequent and extremely refractory to usual modalities of treatment (salicylic paint, cryotherapy, podophyllin, chloroacetic acid). Mild warts may be left alone, refer for management if severe.

TREATMENT

- Liquid nitrogen is the main therapy
- Topical retinoid gels (Adapalene®) for extensive flat warts
- Application of 50% trichloroacetic acid once monthly
- Genital warts: 25% podophyllin in TBCo applied every two weeks
- ART is indicated in severe cases, often resulting in clearing of the warts and decreasing the chance of recurrence

11.7 IMPETIGO

Crusting superficial sores usually occur around mouth or nose. Deeper lesions can be seen on the legs (ecthyma). They are usually caused by *Staph. aureus* or *Strep pyogenes*. In HIV-infected children, lesions may be more severe and recur more frequently. The underlying cause may be insect bites or abrasions which are scratched and become septic.

TREATMENT

- Oral erythromycin 10mg/kg/dose 6 hourly or cloxacillin 12-25mg/kg/dose 6 hourly orally
- Antiseptic soaps are helpful - especially for hand washing
- Clean short finger-nails
- Apply simple antiseptic to abrasions to prevent infection

11.8 TINEA (RINGWORM)

Tinea corporis presents as circular lesions with a raised edge and central clearing on the body. They are itchy at times. Tinea capitis: circular lesions on scalp with alopecia. Extensive infections are seen with HIV.

TREATMENT

- Whitfield's ointment is effective for Tinea corporis
- Oral griseofulvin 20mg/kg/day in two doses for 1-3 months
- Topical imidazole creams

11.9 DRY SKIN AND ITCHING

Aggravated by soaps

TREATMENT

- Use UEA or UE (emulsifying ointment) instead of soap
- Emulsified bath oils

11.10 DRUG RELATED SKIN REACTIONS

Lesions are very varied ranging from somewhat pigmented patches to extensive shallow ulceration or necrotic skin lesions. The conditions may be severe and life-threatening

TYPES

- Maculopapular erythema
- Urticaria
- Erythema multiforme major (Steven's Johnson syndrome) target lesions/bullae/skin sloughing, involves mucosal surfaces
- Toxic epidermal necrolysis – sloughing of epidermis
- Fixed eruption

CAUSATIVE AGENTS

- Antibiotics (cotrimoxazole, penicillin, sulphonamides, anti-TB drugs)
- Phenolphthalene laxatives
- NSAIDs
- Antiretrovirals
- Anticonvulsants

TREATMENT

- Depends on the severity and the need for the implicated drug.
- Discontinue suspected drug. Response to stopping drug should be seen within 3-5 days.
- Refer for admission if any of these occur: Erythema multiforme, Stevens Johnson Syndrome, Toxic epidermal necrolysis

OUTPATIENT TREATMENT

- Topical or oral steroids
- Promethazine 0.125 mg/kg 6 hourly orally as needed until the skin rash disappears

SECTION 12: OTHER COMPLICATIONS AND OPPORTUNISTIC INFECTIONS

12.1 CRYPTOCOCCAL MENINGITIS

This condition, which is more common in older children, presents with signs of meningitis, either acute or with a chronic headache or with cranial nerve palsy. Suspect cryptococcal meningitis when these signs occur in any HIV-infected child. It may also present as part of IRIS.

Always request laboratories to do Indian ink stain and cryptococcal antigen test (more sensitive than Indian ink stain) on all cerebrospinal fluid (CSF) specimens from HIV-infected children with suspected meningitis. Always measure CSF pressure.

Other investigations:

- Chest X-ray
- Ophthalmological assessment
- Fungal culture blood and urine

TREATMENT

- All children with suspected cryptococcal meningitis need to be treated initially as inpatients.
- Treat with Amphotericin B (1.0 mg/kg, IV, once daily) for 14 days or longer (limited by deteriorating renal function as indicated by rising serum creatinine).
- Thereafter change to oral Fluconazole (12 – 15 mg/kg per day, maximum 400 mg) for 8-10 weeks.
- The high mortality in cryptococcal meningitis is directly related to elevation of intracranial pressure, as cryptococcal polysaccharide antigen blocks CSF absorption. Serial spinal tap to relieve CSF pressure should be repeated daily for as long as the opening CSF pressure is elevated. CSF should be tapped until pressure is normalized (14 cm water). Thereafter repeat taps on alternate days until opening pressure is normal.
- Acetazolamide and furosamide are contraindicated in patients with cryptococcal meningitis as dehydration aggravates renal toxicity due to Amphotericin.
- Relapse episodes should be treated with Amphotericin B for 4-8 weeks, preferably until CSF culture is negative. Thereafter, change to oral Fluconazole.

PREVENTION OF RECURRENCE

After therapy, secondary prophylaxis with Fluconazole (6 – 10 mg/kg per day orally) should be continued. Until recently, lifelong secondary prophylaxis was recommended. However, discontinuation should be considered (after being on prophylaxis for at least 6 months) in asymptomatic children aged ≥ 6 years, on ART with a sustained CD4 count ≥ 200 cells/mm³.

12.2 CYTOMEGALOVIRUS (CMV) INFECTION

Disseminated disease can present with hepatosplenomegaly, generalized lymphadenopathy and respiratory involvement. Retinitis, CNS manifestations, and infection of the gastrointestinal tract are important additional manifestations and can also manifest as part of Immune Reconstitution Inflammatory Syndrome. Diagnosis can be difficult as presence of antibodies to CMV does not necessarily imply infection. Histological diagnosis is the most helpful.

TREATMENT

- All children with CMV infection need to be treated as inpatients (tertiary level). The decision whether to use Ganciclovir should be taken by a specialist team.
- Ganciclovir IV if available (10 mg/kg per day in 2 divided doses over 1-2 hours for 14 – 21 days, followed by lifelong maintenance therapy with 5 mg/kg per day, IV, 5 days per week).

12.3 DISSEMINATED INFECTION WITH MYCOBACTERIUM AVIUM COMPLEX (MAC)

MAC usually presents with disseminated disease in children with HIV infection. Patients may have pancytopenia from bone marrow depression and have non-specific signs. Isolated organ disease, especially pulmonary, gastrointestinal or skin disease occurs less commonly.

DIAGNOSIS

MAC may be isolated from blood, bone marrow, lymph node, other fluids and tissues.

TREATMENT

- All children need to be referred to a specialist centre for management
- Treatment: combination of at least two drugs e.g. Clarithromycin + Ethambutol or Azithromycin + Ethambutol (Clarithromycin 15 mg/kg/day orally 12 hourly, Azithromycin 20 mg/kg/day orally 12 hourly, Ethambutol 15-20 mg/kg/day orally once a day). Amikacin may be added. Ciprofloxacin may also be of additional benefit
- Use 3 or 4 drugs for disseminated disease

Most patients show substantial improvement within first 4 –6 weeks. Therapy should be continued lifelong, irrespective of the extent of improvement. However, once the patient has been on ART for at least 12 months, MAC therapy can be stopped if CD4 percentage has been more than 15% for 6 months and the patient is asymptomatic.

12.4 TOXOPLASMOSIS

This condition is rarely seen in children. Usually presents with encephalitis, with focal neurological abnormalities occurring in association with headache. Outside of the CNS, ocular and pulmonary involvement is the most common. PCP prophylaxis prevents toxoplasmosis.

DIAGNOSIS

- Diagnosis may be made on blood and CSF serology
- CSF PCR for toxoplasmosis may also be helpful
- Culture of the organism from blood or body fluids may also be helpful
- CT scan usually reveals multiple bilateral, focal hypodense ring-enhancing lesions
- If congenital toxoplasmosis suspected, placental histology is helpful in confirming the diagnosis

TREATMENT

- Depends on the extent of CNS involvement and should be individualized. In patients with extensive CNS damage palliative care is recommended.
- Specific treatment: specific treatment for paediatric toxoplasmosis is unavailable, thus a decision about management will need to be made by specialist team.
- Lifelong treatment is recommended for Toxoplasma encephalitis.

12.5 HIV ENCEPHALOPATHY

HIV-infected monocytes can cross the blood-brain barrier and thus infect the brain. Any part of the nervous system may be affected, but brain involvement predominates in children. It has been estimated that +/- 20% of HIV-infected children may be affected. HIV encephalopathy indicates advanced clinical disease (AIDS)

Diagnosis depends on the presence of at least one of the following findings for at least 2 months:

- Failure to attain or regression of developmental milestones or loss of intellectual ability verified by standard developmental scale or neuropsychological tests.
- Impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by CT scan.
- Acquired symmetric motor deficit manifested by two or more of the following: paresis, abnormal reflexes, ataxia, or gait disturbances.

MANAGEMENT

- Is multidisciplinary and includes the provision of a child dependency grant to support the caregiver.
- Initiation of ART may reverse some of the features of HIV encephalopathy.
- Seizures may occur – it may be necessary to exclude other pathologies.
- Attention deficit disorder and hyperactivity occur commonly. Specialist advice regarding management should be sought.

12.6 WASTING SYNDROME

Wasting syndrome indicates advanced clinical AIDS.

DIAGNOSIS

In the absence of concurrent illness other than HIV infection that could explain the following features:

- Persistent weight loss > 10% of baseline OR
- 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 and over OR
- < 5th percentile on weight-for-height chart on two consecutive measurements, more than 30 days apart

PLUS

- Chronic diarrhoea (i.e. at least two loose stools per day \geq 30 days) OR
- Documented fever (for \geq 30 days, intermittent or constant)

12.7 MALIGNANCIES

- Non-Hodgkin's lymphoma is the most frequent group of malignancies in children with HIV infection. These include CNS lymphoma and Burkitt's lymphoma.
- Kaposi's sarcoma is uncommon in children with HIV infection. However, it has been seen in infants and young children who present with generalized lymphadenopathy and with black/purple lesions on the mucosa of the mouth or on the skin.
- Other malignancies include leiomyoma and leiomyosarcoma.

MANAGEMENT

- Refer all children to a specialist centre if malignancy is suspected.
- Manage the child in association with a paediatric oncologist.
- Treatment may include ART and chemotherapy. Indicators of a good prognosis in NHL include a CD4 count > 0.1 x 10⁹/L, a near normal LDH level and no prior AIDS defining conditions.

SECTION 13: PAEDIATRIC PALLIATIVE CARE

Palliative Care is defined by the World Health Organization as the total active care of patients whose disease does not respond to curative treatment. In children this includes caring for the child's body, mind and spirit, and also giving support to the family. It begins when illness is diagnosed, and continues regardless of whether or not a child receives treatment directed at the disease. Health providers must evaluate and alleviate a child's physical, psychological and social distress. Effective palliative care requires a broad multidisciplinary approach that includes the family and makes use of available community resources; it can be successfully implemented even if resources are limited. It can be provided in tertiary care facilities, in community health centres and even in children's own homes".

The holistic approach and goal of improving quality of life means that it is relevant to the management of HIV-infected children at any stage of their disease regardless of whether they receive ART or not. In those children who for whatever reason require terminal care, a palliative approach ensures that suffering is minimized, death is dignified and the family supported.

13.1 PAIN IN HIV-INFECTED CHILDREN

Studies show that 21 -59% of paediatric HIV patients experience pain. Treating pain not only decreases morbidity, but can also influence mortality.

Causes of Pain in HIV

- HIV itself: peripheral neuropathy, cardiomyopathy, myositis, arthritis, osteonecrosis of the hip.
- Secondary and Opportunistic infections: e.g. meningitis, oral lesions (thrush, aphthous and herpetic ulcers), parotitis and lymphadenitis, skin conditions (shingles, severe scabies, nappy rashes, Stevens Johnson's syndrome), urinary tract infections.
- Iatrogenic causes: HIV monitoring bloods, diagnostic procedures (LP, thoracentesis, etc)
- Toxicities and adverse drug reactions: peripheral neuropathy.
- Psychosocial stressors/emotional pain: Living with a chronic illness, poverty, long periods of hospitalization, maternal separation, clinical depression, potential or actual loss (bereavement) of parent or other loved one.

13.2 MANAGING PAIN IN HIV-INFECTED CHILDREN

PAIN ASSESSMENT

- Assess all HIV-infected children for pain at each consultation (pain is the fifth vital sign)
- In non-verbal children behavioural and physiological indicators of pain (tachycardia, raised blood pressure, sweating etc) may help remembering that these disappear in chronic pain (Appendix 3 for behavioural indicators).
- Involve the parent/caregiver when assessing whether pain is present.
- Use developmentally appropriate pain rating scales where relevant (Appendix 3).
- Use common sense: if the child has a condition that is likely to cause pain in an adult assume that is painful for the child.
- When in doubt there is seldom harm in a trial of analgesia.
- Remember to continually re-assess and adjust treatment according to response.

PAIN MANAGEMENT

- Prevent procedural pain: Children do not get used to repeated painful procedures, anticipatory anxiety increases with each successive procedure. Pain associated with medical consultations is a significant cause of distress in HIV-infected children.

- Use EMLA cream where available for blood draws, venesection, lumbar punctures and supra-pubic aspiration of urine.
- Use conscious sedation and local anaesthesia for more invasive procedures (e.g. FNA, Bone marrow, and thoracocentesis).
- Apply the four broad principles of symptom control in palliative care:
 - Determine and treat the underlying cause (e.g. oral thrush) including non-physical causes (e.g. anxiety)
 - Use both drug and non-drug measures
 - Treat the symptom (pain) without causing new or unwanted side-effects (e.g. constipation)
 - Determine whether the treatment (of the underlying condition or the symptom) is in the patient's best interests (ethics: weigh burden vs. benefit of treatment)

OTHER PAIN SYNDROMES IN HIV

Three other “pain syndromes” that occur fairly commonly in HIV-infected children that may be difficult to manage and deserve special mention are peripheral neuropathy, abdominal pain and muscle spasms.

Peripheral neuropathy

Causes

- HIV itself (distal sensory neuropathy)
- Post herpetic neuralgia
- ART: Stavudine, Didanosine and Efavirenz
- Other treatments: INH, Chemotherapy (vincristine), metronidazole
- Vitamin B complex deficiencies (B1, B6 and B12) and foliate deficiency

Presentation

- Burning pain in hands and feet
- “Pins and needles”
- Numbness in fingers and toes
- Decreased ankle reflexes
- Loss of vibration sense (tested with tuning fork) in big toe

Management

- Remove offending agent if possible: change from Stavudine or Zidovudine to Abacavir and from Efavirenz to Ritonavir/Lopinavir
- Try multivitamins (B6, B12 and foliate)
- Treat Herpes Zoster early with Aciclovir to limit post herpetic neuralgia
- Use WHO ladder including NSAIDs and opioids as these have been shown to be helpful in managing neuropathic pain in combination with adjuvants
- Try an adjuvant: Amytriptaline has fewer interactions with ARVs than Carbamazepine although it is not effective in all cases

SECTION 14: CARING FOR THE TERMINAL CHILD

The management of a child who is imminently terminal (death expected to occur within a few days or weeks) should include:

- Relieving physical and emotional distress in the child
- Treating easily manageable complications
- Stopping all unnecessary drugs and focusing on medications assisting with the relief of terminal distress (pain and non-pain symptoms) only
- Limiting hospital admissions or reducing the duration of hospital stay
- Ensuring that parents / caregivers are adequately counselled, and that staff are sympathetic to individual needs
- Advance care planning: this is the process by which possible end of life events are predicted and plans are made to manage them to avoid unnecessary distress to the family and to limit crises
- Decision making as to preferred place of death (home, hospice, hospital) and referral to community based services where available (hospice palliative and home based care services)

The aims are as follows:

- Maintain quality of life
- Keep the patient as comfortable as possible
- Provide emotional support to a dying child and the grieving family
- Address the family's spiritual needs and assist them to perform culturally required rituals where necessary and non-invasive

14.1 SUPPORTIVE CARE OF TERMINALLY ILL CHILDREN

The decision to begin supportive (terminal) care is difficult and should be made on a case-by-case basis preferably by a team of professionals with the family's involvement. Once this decision has been made, it should be clearly communicated to other health care workers involved in the care of the child. This communication can take the form of a letter, which the family may be able to present to other health workers.

14.2 HOME CARE FOR TERMINALLY ILL CHILDREN

- Home care of the terminally ill child should be encouraged if the parent/s or caregiver/s are able to care for the child at home and where home conditions are comfortable for the child
- There should be no need for intravenous fluids or other intensive treatment
- Reassure the parents / caregiver(s) that the child has not been abandoned by the health services, and that they can re-visit the clinic and have the child readmitted to the hospital at any time
- Try to think of possible end of life scenarios and make pre-emptive plans to manage these to limit end of life crises (e.g. provide and instruct families to administer rectal Valium if seizures are a possibility)
- Refer the child and family to available palliative home based care services where available in the community
- Discussions and decisions regarding the institution of home care should be clearly recorded in the child's records
- The possibility of chronic/ terminal care at a hospice facility should be discussed with parents and/or caregivers if there are inadequate resources for the care of the child at home
- Provide or refer families for bereavement support and sibling care after the death of the child where necessary

SECTION 15: CONSIDERATIONS FOR ART IN ADOLESCENTS

Adolescence is defined as the period between 10 and 19 years of age. There are distinct groups of HIV-infected adolescents who may require ART.

- Adolescents who have been infected around birth
- Those who acquire HIV through unprotected sex

Adolescents with perinatal infection who began ART during early childhood because of rapid progression of HIV disease have some years of contact with health services and are likely to have experienced various ARV treatments. Challenges relate to disclosure if this has not been done by their parents, developmental and pubertal delay as well as stunting. Girls may experience delayed or irregular menstrual cycles. Wasting caused by progressive HIV illness may also be exacerbated by malnutrition.

STAGING

Children can transit to adult staging as both have four categories.

ART

Adult guidelines should be used for the initiation of ART in post-pubertal adolescents (over 15 years of age) or in pregnant adolescents. Those on paediatric schedules should be monitored closely because they are undergoing hormonal changes associated with the growth spurt.

ADHERENCE

Adherence is particularly difficult amongst adolescents. In addition to providing routine adherence counselling attention to other relevant issues is important. These include the adolescents' perception of being immortal, their desire for independence, lack of disclosure of HIV status and stigma. Their parents may find it hard to share the diagnosis of HIV with their children because of fear of stigma or blame from their own children.

It is therefore important that young people

- Are informed about their HIV status
- Are well educated on HIV – treatment, and adherence
- Have access to sexual and reproductive health services i.e. contraception, pregnancy testing, cTOP (choice on termination of pregnancy) etc.
- Clinics providing care should have support groups both at clinic and community levels

SECTION 16: POST-EXPOSURE PROPHYLAXIS AND SAFE WORKING PRACTICES

Most patient care does not involve any risk of HIV transmission. Each service requires a senior staff member responsible for universal precautions and handling accidental injuries.

16.1 UNIVERSAL PRECAUTIONS

Universal precautions are simple infection control practices used at all times in the care of all patients. The aim is to reduce the risk of transmission of blood borne infections.

Some preventive measures:

- Cuts and sores should always be covered.
- Whenever hands are contaminated with bodily fluids, they should be washed thoroughly with soap and warm water for at least 10 seconds.
- Gloves should be worn to prevent contact with blood or blood containing bodily fluids.
- Aprons should be worn in high exposure areas, e.g. trauma unit, labour ward.
- A solution of household chlorine bleach (e.g. Jik®) should be used as a disinfectant for surfaces and other inanimate objects.
- Spills of bodily fluids should be cleaned immediately with such disinfectant.
- Blood contaminated material or nappies should be disposed of in a plastic bag with a secure tie.
- Children with ongoing bleeding should be separated from the others until such bleeding has stopped.
- Human bites and sports injuries carry a very low risk for viral transmission, except if there is mixing of blood from both parties.
- Precautions need to be taken particularly by all health care providers to prevent needle-stick injuries.

16.2 PROCEDURE FOR “SHARPS INJURY” OR OTHER EXPOSURE

Each clinic or hospital should ensure that mechanisms to allow the procedure described below are in place before any accident occurs:

- Following a “sharps” injury, immediate first aid should be given, such as flushing the site with running water, hand washing with soap and water, and, where there is bleeding, allowing the site to bleed briefly.
- Any exposed mucous membranes should be flushed with large amounts of water.
- Antiseptic solutions can have a caustic effect and have not been proven to be effective. However, in the absence of water, antiseptic solutions can be used.
- Report injury to supervisor.
- Ensure that the Workman’s Compensation Act (WCA) form is filled in.
- Consult a doctor for assessment of injury and initiation of treatment.
- Voluntary confidential counselling should be available immediately, and HIV testing and follow-up counselling must be made available.
- Post-exposure prophylaxis (PEP) with ARVs can reduce the risk of becoming infected.
- Starter pack kits are available at government hospitals on a 24 hour basis, these include a 2-day course of AZT and Lamivudine.
- The rest of the medication can be received at the hospital dispensary.

NOTE: Many health providers find reporting and undergoing voluntary testing and counselling stressful, and some choose to remain silent. This silence is often due to the fear, stigma and discrimination associated with HIV. They will require sensitive support to avoid the very unpleasant consequences.

Table 17: PEP recommendations for occupational exposure

	Status of the source		
	HIV positive	Unknown	HIV negative
Percutaneous exposure to blood or potentially infectious fluids	AZT, 3TC, LPV/r	AZT, 3TC, LPV/r	No PEP
Mucocutaneous splash or contact with an open wound with blood or potentially infectious fluids	AZT, 3TC, LPV/r	AZT, 3TC, LPV/r	No PEP
Percutaneous exposure, mucocutaneous splash or contact with an open wound, with NON-infectious bodily fluids	No PEP	No PEP	No PEP

TIMING OF PROPHYLAXIS

- Start as soon as possible, preferably within 1-2 hours of exposure
- The exposure risk should be considered if there is a delay in obtaining prophylaxis
- Prophylaxis is of doubtful benefit if started 72 hours after injury

POST-HIV EXPOSURE PROPHYLAXIS

- Prophylaxis should continue for 28 days and should consist of AZT, 3TC and Lopinavir/ritonavir twice daily
- Counselling about potential side-effects from medication (especially gastrointestinal) should be given

16.3 POST-EXPOSURE PROPHYLAXIS FOLLOWING ALLEGED PENETRATIVE SEXUAL ABUSE

Start treatment as soon as possible, ideally within 1 hour after exposure, but not later than 72 hours post exposure

RECOMMENDED DRUG REGIMEN: (Appendix 4)

- Zidovudine 180mg/m²/dose twice daily (suspension 10 mg/mL)
- Lamivudine 4 mg/kg/dose twice daily (suspension 10 mg/mL)
- Lopinavir/ritonavir 300/75mg/m²/dose twice daily (suspension 80/20mg/mL) only if there has been significant exposure

For adolescents:

- Zidovudine 300 mg bd
- Lamivudine 150 mg bd
- Lopinavir/ritonavir 300/75mg/m²/dose twice daily. Only if there has been significant exposure.

Duration of prophylaxis is 28 days.

Counselling is an integral part of care for survivors of sexual assault.

INVESTIGATIONS

- One must be sensitive about taking blood from a child in a post-abuse situation
- Full blood count
- HIV ELISA on both the survivor and exposure source, where available
- It is useful to know the baseline HIV status; blood for HIV can be taken a few days up to 1 week post-exposure

- Follow up of HIV status at 6 weeks, 3 months and 6 months. The survivor can be reassured that the likelihood of sero-converting beyond this period is extremely small

Stop prophylaxis if:

- Survivor is HIV DNA PCR positive (baseline HIV test) or Survivor is over 18 months and is HIV ELISA positive
- Perpetrator is HIV ELISA negative

SECTION 17: PSYCHOSOCIAL SUPPORT

A child with AIDS usually identifies a whole family at risk of infection. HIV can overwhelm already weak coping capacities and push a family into complete disorganisation and crisis. More than one family member may be ill with AIDS at the same time. This puts strain on the family and increases vulnerability to psychosocial stress.

PERIODS OF PSYCHOSOCIAL VULNERABILITY

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

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. Infected or affected children may become aggressive, disruptive and/or restless. Other common problems are bedwetting, sleep disturbance, withdrawal and depression. Depression often goes unnoticed and /or untreated.

In conclusion, counselling and psychosocial support are integral components of the holistic approach to caring for an HIV-infected child.

SECTION 18: LEGAL ISSUES

HIV and AIDS present one of the greatest threats to the wellbeing of children and has a catastrophic effect on the lives of children living in poverty. The loss of many adults to AIDS-related illnesses has meant that children have lost teachers, health care workers and, most importantly, parents.

The provisions of the Children's Act have widened the scope of who may provide consent by introducing a definition of caregiver and giving this class of persons certain legal rights, which include the right to consent to medical treatment. The Act also lowers the age of consent to 12 years and in cases where a child has sufficient maturity, a child below the age of 12 years may also give consent.

18.1 HIV TESTING OF CHILDREN

HIV testing of any child may take place if it is in the best interest of the child and if a person legally capable of providing informed consent provides such consent. The primary caregiver of the child is able to give consent for testing regardless of parental whereabouts.

Subject to Section 132 of the Children's Act, children may be tested for HIV except when –

- It is not in the best interest of the child and no caregiver consent has been given
- HIV testing without consent may occur when the test is necessary in order to establish whether –
 - A health worker may have contracted HIV due to contact in the course of a medical procedure involving contact with any substance from the child's body that may transmit HIV; OR
 - Any other person may have contracted HIV due to contact with any substance from the child's body that may transmit HIV, provided the test has been authorised by a court

Consent for HIV-test on a child may be given by –

- The child, if the child is-
 - 12 years of age or older; OR
 - Under the age of 12 years and is of sufficient maturity to understand the benefits, risks and social implications of such a test;
- The parent or caregiver, if the child is under the age of 12 years and is not of sufficient maturity to understand the benefits, risks and social implications of such a test;
- The provincial head of social development, if the child is under the age of 12 years and is not of sufficient maturity to understand the benefits, risks and social implications of such a test;
- A designated child protection organisation arranging the placement of the child, if the child is under the age of 12 years and is not of sufficient maturity to understand the benefits, risks and social implications of such a test;
- The superintendent or person in charge of a hospital, if –
 - The child is under the age of 12 year and is not of sufficient maturity to understand the benefits, risks and social implications of such a test; and
 - The child has no parent or caregiver and there is no designated child protection organisation arranging the placement of the child; OR
- A children's court, if:
 - Consent in terms of paragraph (a), (b), (c) or (d) is unreasonably withheld; OR
 - The child or the parent or caregiver of the child is incapable of giving consent

HIV-testing for foster care or adoption purpose

If HIV-testing of a child is done for foster care or adoption purpose, the state must pay the cost of such tests where circumstances permit.

Section 129(9) of the Children's Act: A High Court or Children's Court may consent to the medical treatment or a surgical operation on a child in all instances where another person that may give consent refuses or is unable to give such consent.

SECTION 19: COUNSELLING

The following guidelines are provided to assist health workers for counselling of the mother or other caregiver in the absence of a parent:

19.1 PRE- AND POST-TEST COUNSELLING

A child must receive age-appropriate pre- and post-test counselling by a trained person, regardless of whether the child is able to provide consent in terms of the Child Care Act. Where the child is not legally able to provide informed consent, the person providing such consent must also receive appropriate pre- and post-test counselling.

19.2 CONFIDENTIALITY

Children above the age of 12 and who are legally able to provide informed consent to an HIV test are entitled to maintain the confidentiality of their HIV status. Consent to disclose the HIV status of such a child must be given by the child.

The same principle should apply to children below the age of 12, who are of sufficient maturity to understand the benefits, risks, social and other implications of the test. However, a strict interpretation of the law concludes that the parents and legal guardians of children below the age of 12 may have a legal right to have access to the results of the HIV test.

In the case of children below the age of 12 and who cannot consent to HIV testing, consent to disclosure must be given by the persons referred to above.

19.3 PRE-TEST COUNSELLING

- Choose a private area for counselling, where you will not be disturbed or overheard.
- Assure the client that everything said is confidential (You could have a poster on your wall making this clear and showing your commitment).
- Talk through the reasons for HIV testing of the child and/or the mother.
- Ask questions in a sensitive way to find out about current and previous risk behaviour. Remember that the client may not know about her/his partner's risk behaviour.
- Find out how much the client already knows and how much he/she wants to know
- Offer information about HIV and AIDS.
- Offer information about the HIV antibody test, including information about the 'window period' of infection.
- Go through the implications of a positive test result for the client and her/his family, and the emotional responses, e.g. fears, anger, loss, etc.
- Discuss the client's possible responses to a positive test result. He/she can think about whom he/she would tell and where they might get support.
- Be aware of what the client's concerns are and let these guide the discussion. For example, if a woman is being counselled and already has children, her major concern may be what will happen to her child and siblings if she is HIV-infected.
- Go through the implications of a negative test result.
- Provide information about how the test is done, how long before the results will be ready, and how the client could obtain the results.
- Give enough time for the client to consider whether he/she wants to have the test.
- If the client decides to have the test, obtain consent in writing on the clinic card.

19.4 POST-TEST COUNSELLING

- Counselling is essential after the result of the test has become available, irrespective of the result.
- Always meet with the mother or caregiver as soon as possible.
- Before speaking to the client familiarise yourself with the facts about the client.
- Find a private room where you will not be disturbed.
- Allow the client to express emotion.
- Allow for silence; time may be needed to absorb bad news.
- If an HIV ELISA was done in an infant this will reflect the mother's status but not necessarily that of the infant. In such a case the infant's HIV status will be determined by a PCR if < 18 months or an ELISA positive result thereafter (refer to section 3). The parents must therefore be counselled both about their own status and that of their child.

If the result is negative:

- Deal with the feelings arising from a negative result and explain about the 'window period'
- Discuss ways to prevent HIV infection through safer sex and the importance of remaining negative

If the result is positive:

- Tell the person as clearly and gently as possible. Deal with the immediate feelings
- Give the client time to understand and discuss the result.
- Provide information in a way that the client can understand, provide emotional support and help the person to discuss how he/she will cope.
- Discuss how the person plans to spend the next few hours and days.
- Identify what support he/she has.
- Discuss with whom the client wants to share the test result. Find out if the client intends to tell his/her partner. Help the person to decide whether or not to tell him/her immediately and, if appropriate, how to tell him/her.
- Go through the ways the client can take care of her/his own health and let her/him know about any available treatment.
- For a pregnant woman, go through the ways she may reduce the risk of MTCT during pregnancy, labour and after the birth.
- Discuss how she will feed the baby and the importance of exclusive feeding – whatever choice she makes. Discussion of cotrimoxazole prophylaxis for the infant and the mother needs to be initiated. Details of this must be discussed at a follow-up session.
- Identify what difficulties or problems the person foresees and discuss how to deal with them.
- Encourage the client to ask questions.
- Where possible and acceptable refer the client to a community organisation for support.
- Encourage the client to return for a follow-up session when he/she has had time to think about some of the information just provided.
- If appropriate, some information could be written down as the person is unlikely to be able to remember everything that was said.
- If the child is HIV-infected the parent or caregiver must be told, what to expect with regard to the health of the child, possible ART and how to care for the child.

SECTION 20: ADHERENCE

Although this section was originally written with adult patients in mind, the difficulties associated with ART for infants and children are highlighted. Adherence to ART is essential to avoid development of drug resistance. It is not possible for health care providers to reliably predict which caregivers or individuals will ultimately be adherent to their treatment plan, as adherence does not correlate with gender, cultural background, socio-economic or education level, or language barriers between provider and patient. It is therefore essential to provide all caregivers with a comprehensive plan to support adherence. Several strategies need to be applied and all members of the health care team, as well as family and possibly even community based support groups need to be involved.

20.1 ROLE OF THE HEALTH CARE TEAM

Experience has shown that adherence decreases as time progresses. Thus, monitoring and support of adherence is essential. See the list below for some factors affecting adherence to paediatric ART. A trusting relationship between the patient and caregiver with members of the health care team is essential. Optimal adherence requires full participation by the health-care team.

Every interaction with the patient and caregiver provides an opportunity for reinforcing the absolute need for adherence.

Some important factors diminishing adherence in children

- Drug side-effects and adverse events
- Intercurrent illness
- Caregiver illness or otherwise occupied
- Patient resistance to taking medicines – Ritonavir singly or in combination with Lopinavir has a very bitter taste
- Drug stock-out
- Change or absence of patient's nurse or doctor
- Frequent daily doses – e.g. twice or three times per day
- Cost of transport
- Lack of a single caregiver
- Substance abuse in the home

Supportive and non-judgmental attitudes and behaviours will encourage patient/caregiver honesty regarding adherence and problems. If adherence problems are noted at a regular follow-up visit, we need to try to contact the family between clinic visits to ensure that no problems have arisen regarding regular diarising of the treatment. Furthermore it is important to remind the caregiver to report any troublesome side effect or interim illnesses (e.g. investigate new barriers such as transport problems, more frequent visits, enlist support of family/friends, and review counselling).

ARV stock-out should never occur; this is an important disincentive for the patient to continue to collect drugs regularly. If the staff member who normally deals with the child is planning a move or vacation, the caregiver needs to be informed of that and reassured that the therapy will continue.

Sub-optimal adherence calls for intensified support and further counselling. This is best done by means of home visit. For all health care team members, specific training regarding ART and adherence should be offered and updated periodically.

20.2 ADHERENCE TO ART

- Success of ART hinges on tablet taking behaviour.

- Ideal adherence means a patient must take more than 95% of their doses (i.e. missing less than 3 doses in a month).
- If patients take less than 95% of doses, they are at risk of developing viral resistance and ultimately virological failure (Table 18).

Patients taking < 80% of their doses are unlikely to have any durable virological suppression and should be targeted for adherence improvement urgently. At every follow-up visit this must be reinforced.

20.3 STRATEGIES TO PROMOTE ADHERENCE

- Spend time and have multiple encounters to explain goals of therapy and need for life-long adherence.
- Consider monitoring of medications such as cotrimoxazole or any other drug that is being given prior to ART initiation.
- Negotiate a treatment plan that the patient can understand and to which he/she commits.
- Encourage disclosure to family or friends who can support the treatment plan.
- Inform patient of potential side-effects – severity, duration, and coping mechanisms.
- Establish ‘readiness’ to take medications before ART initiation.
- Provide adherence tools where available: written calendar of medications, pill boxes.
- Encourage use of alarms, pagers or other available mechanical aids for adherence. Link schedules to daily activities such as mealtimes and tooth brushing
- Avoid adverse drug interactions; full disclosure for over-the-counter drugs and traditional medicines.
- Anticipate, monitor and treat side-effects.
- Include adherence discussions in support groups.
- Develop links with community-based organizations to support adherence.
- Encourage links with support groups.
- Create links with patient advocates.
- Pill boxes with pill counts
- SMS reminders by cell phone

Table 18: Correlation between adherence and virological response to ART

Adherence to ART*	Viral Load < 400 copies/mL
> 95% adherence	78%
90% to 95% adherence	45%
80% to 90 % adherence	33%
70% to 80 % adherence	29%
< 70 % adherence	18%

*(number of doses dispensed minus tablets returned) over (number prescribed) e.g. (30-5)/28=25/28=0.9 (90%)

20.4 BASIC ADHERENCE PACKAGE AT INITIATION

PRE-TREATMENT:

- Pre-treatment information and education as per visit schedule.
- Caregiver and/or patient are introduced to therapeutic counsellor and patient advocate, if available and agreed to or nominated by patient, and home visit is arranged.

- Monitoring cotrimoxazole prophylaxis compliance for one month prior to commencing therapy (This is not to be used to exclude people from ART. It is meant to reinforce daily medication taking behaviour from the outset, and identify potential problems before starting ART).

ON TREATMENT:

At each visit:

- ART pill or syrup returned needs to be counted or estimated (% doses missed). This is the ideal but this depends on the clinic load and capacity to undertake this intensive activity. Adherence goal is > 95% doses taken. Patients with adherence < 80% require increased adherence support),
- Tablet/syrup count/estimate may be done before the patient sees the health care provider, and the count reviewed by the health care provider during the early/initial visits to evaluate adherence. This does take up time and might not be possible at all sites all the time,
- Missed or late clinic visits should trigger concerns about adherence,
- Routine adherence discussion/education with counsellor is of value. This should be an open-ended discussion, with time for questions and repetition,
- Feedback from therapeutic counsellors to the rest of team is important to get a better profile of patients and their environment,
- Encourage caregiver participation in a support group
- Continue monthly visit with therapeutic counsellors for first three months and quarterly thereafter, and
- Arrange regular community visits by patient advocates.

STEP-UP ADHERENCE PACKAGE FOR PEOPLE WITH REDUCED ADHERENCE OR VIROLOGICAL FAILURE

This applies to all those whose adherence is less than 80% at any visit.

- The therapeutic counsellor/nurse or doctor needs to re-educate the patient and caregiver (and their 'buddy') about the importance of adherence. The long-term benefits need to be re-emphasised.
- Evaluate the support structures in place. Are they appropriate? How can they be improved? What other options are there?
- Consider the use of pillboxes and/or daily dosing diary.
- Encourage participation in a support group or link with a patient advocate,
- Consider doing a psychological profile,
- Check family situation (through social worker and therapeutic counsellor),
- Increase home visits by therapeutic counsellors / patient advocates to daily or weekly at a minimum (spot pill counts to be done at home), and
- Consider directly observed therapy for an agreed period.

SECTION 21: DISCLOSURE TO CHILDREN

The United Nations Convention on the Rights of Children (Article 12) states that children have the right to participate in decisions about their own health care. The decision to disclose the HIV status to the child is a difficult one to make.

21.1 REASONS FOR DISCLOSING HIV STATUS TO CHILDREN

- As the age of children living with the disease steadily increases it will result in a population of sexually active young people with HIV infection.
- Keeping the secret is a burden.
- Disclosure should always be in the best interests of the child. This applies to the disclosure itself as well as the manner of disclosure.
- Benefits of disclosure include recognition of the child's autonomy, increased intimacy with those close to the child, and improved psychological adjustment.
- The child may need to prepare for tasks ahead (sickness, painful procedures etc)
- Children often know more than adults give them credit for.
- Children not told about their disease often have much more anxiety and distress.
- Disclosure needs to take place before adolescence.

21.2 GUIDELINES FOR THE DISCLOSURE OF HIV STATUS TO CHILDREN

Many parents/caregivers are afraid to tell their children. For the above reasons they will need encouragement and support to do this. However, it is inadvisable to disclose the status to the child against the wishes of the parent/caregiver.

Where possible enlist the help of trained child counsellors Try to balance the needs of the child and the parents. Disclosure is a process, not a once-off event; plan future visits to answer questions and assess how the child is coping with the information.

- Assess the child's readiness
- Offer the parents time, support and information
- Plan in advance the time, place and people who will be present for the disclosure
- There may be advantages to have a written plan of what should be disclosed to the child

WHAT IS THE RIGHT THING TO SAY?

- Find out how much the child knows about their illness and what he/she wants to know
- Children need to know that they are loved and will be cared for.
- Many children believe that sickness is their fault - they need reassurance that their illness or their parent's illness is not a punishment for a wrongdoing.
- Children need to learn how HIV is transmitted.
- The age of the child suggests what can be told to them, e.g. a 5 year old. may not need to hear the word HIV, while an older child can be given more information.
- Be honest. If you don't know the answer to the child's questions say so and then seek help.
- Be led by the child in terms of the amount of information he/she requires.
- Use language appropriate for the child's insight understanding, education and emotional readiness.
- Anticipate possible responses by the child and plan for the future; this may include follow-up sessions, counselling and support for the child and parent/family, or education about signs of emotional distress in children.
- Anticipate the impact of the disclosure on other family members, friends, the school and the community and plan for this.
- Once the disclosure has happened, monitor the child's behaviour (sleeping, school problems, and withdrawal). Changes in behaviour can indicate a need for more support and intervention. Despite the best planning, you cannot be certain how a child will respond.

- Be respectful of the child's needs, feelings and responses.
- Stories and books may be of assistance.

APPENDICES

Appendix 1: WHO Clinical Staging

CLINICAL STAGE 1

- Asymptomatic
- Persistent generalized lymphadenopathy

CLINICAL STAGE 2

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Fungal nail infections
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis or tonsillitis)

CLINICAL STAGE 3

- Unexplained moderate malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5°C intermittent or constant for longer than one month)
- Persistent oral candidiasis (after first 6–8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis or periodontitis
- Lymph node tuberculosis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (< 8 g/dL), neutropaenia ($< 0.5 \times 10^9$ per litre)
- And/or chronic thrombocytopenia ($< 50 \times 10^9$ per litre)

CLINICAL STAGE 4

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection or meningitis but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after one month of life)
- HIV encephalopathy
- Cytomegalovirus infection: retinitis or cytomegalovirus infection affecting another organ, with onset at age older than one month
- Extrapulmonary cryptococcosis (including meningitis)
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated non-tuberculous mycobacterial infection
- Cerebral or B-cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy
- HIV-associated rectovaginal fistula

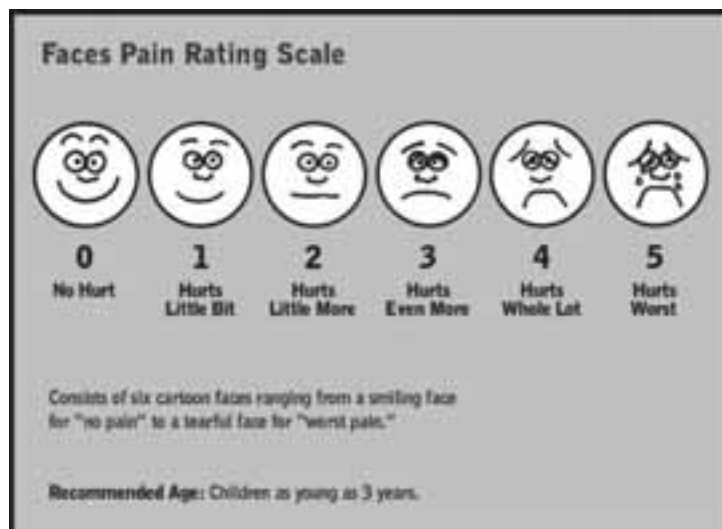
3 months	Prone: support on forearm lifts head buttock flat Rolls over	Holds object placed in hand Watches hands Pulls at clothes	Quietens to familiar sound Turn head towards sound	Excited when fed Reacts to familiar situation
6 months	Pull to sit: braces shoulder pulls to sit Prone: extended arms lifts head & chest Supine: plays with feet sits with support	Reaches for object Radial approach to toys Transfers Shadow reaction in other arm	Babbles Repetition Laughs aloud Turns to mother's voice	Puts everything in mouth Responds to image in mirror Starts to hold bottle Shows likes and dislikes
9 months	Sits without support Rolls Crawls Rocks on all four Pulls to stand	Holds a cube in each hand Points	Deliberate vocalisation Babbles Imitates sounds Understands "no"/"bye-bye"	Stranger anxiety Holds bottle Drinks from cup
12 months	Bear creep Walks around furniture sideways walks with feet apart and arms up	Pincer grasp Release on request Begins to cast Looks for toys when out of sight	Knows own name 2-3 words with meaning Understand simple commands	Finger feeds Pushes arms into sleeves Plays games
15 months	Walks alone Collapses backwards Stairs: creeps up, goes down backwards	2 cube tower Holds 2 cubes in one hand	Jabber with expression 2-6 words Points to objects on request	Picks up, drinks & puts down cup Spoon feeds with mess Indicates wet nappy
18 months	Walks with arms down Cannot turn unless still Pulls a toy Throws a ball Climbs onto a chair	3 cube tower Scribbles	6-20 words	Handles spoon well Looks at pictures Takes off shoes & socks
24 months	Runs Stairs: up & down 2 feet per step Kicks ball Squats & rises without hands	6 cube tower Obvious hand preference	< 50 words Short phrases Ask for food, drink, toilet	Spoon feeds without mess Clean and dry by day Pretend play
36 months	Rides tricycle Stairs: up-1 foot per step; down-2 feet per step Climbs Walks on tip toes	9 cube tower Copies circle Cuts with scissors Builds a bridge	Knows name & sex Uses pronouns Talks incessantly	Toilet trained Dress with supervision Eats with a fork Washes & dries hands
48 months	Stairs up & down 1 foot per step Stands on 1 leg for 3-5 seconds Hops	Copies cross Builds gate	Full name and age Recognise colours	Eats with spoon & fork Dresses & undresses Make believe play
60 months	Walks along narrow line Hops on each foot separately	6 cube steps Copies square & triangle Draws a man	Fluent speech Knows 3 opposites	Dresses and undresses alone Uses knife and fork Chooses own friends
72 months	Sits up without using hands Walks backwards along straight line	10 cubes steps Copies diamond	Learns comparatives	Cooperative play

Appendix 3: Scales for Assessing Pain in Children

FLACC Scale for Determining the Intensity of Pain of a Child who Cannot Speak (under 3 years or very ill)			
Score	0	1	2
Face	No particular expression or smiling	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (Awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by touching, hugging or being talked to, distractible	Difficult to console or comfort

Each of the categories (F) Face (L) Legs (A) Activity (C) Cry (C) Consolability is scored from 0-2, which results in a total score between zero and ten.

From *The FLACC: A behavioral scale for scoring postoperative pain in young children*, by S Merkel and others, 1997, *Pediatr Nurse* 23(3), p.293-297. Copyright 1997 by Jannetti Co. University of Michigan Medical Center. Reprinted with permission. <http://www.childcancerpain.org/content.cfm?=&assess13>



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Appendix 4: ARV dosages

Antiretroviral Drug Dosing Chart for Children (2009)

Target dose	Stavudine (d4T)	Lamivudine (3TC)	Zidovudine (AZT)	Didanosine (ddI)	Abacavir (ABC)	Efavirenz (EFV)	Nevirapine (NVP)	Lopinavir/ritonavir (LPV/r)	Ritonavir (RTV)	Co-trimoxazole	Multi-vitamins	Target dose
Available formulations	Sol. 1mg/ml Caps 15, 20, 30mg	Sol. 10mg/ml Tabs 150mg (scored)	Sol. 10mg/ml Caps 100mg Tabs 300mg (not scored)	Tabs 25, 50, 100mg (dispensable in 30ml water) Caps 250mg EC (not scored)	Sol. 20mg/ml Tabs 300mg (not scored)	Caps 50, 200mg Tabs 50, 200, 600mg (not scored)	Sol. 10mg/ml Tabs 200mg (scored)	Sol. 80, 200mg/ml Tabs 200, 500mg, 100, 250mg	Sol. 80mg/ml	Sol. 40, 200mg/5ml Tabs 80, 400mg (scored)	Sol. Tabs (B Co)	Available formulations
Wt. (kg)	Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg											
<3	6ml	3ml	6ml	avoid	3ml	Dosing = 10kg not established	5ml	1.5ml	**1ml	2.5ml	2.5ml	<3
3-3.9	6ml	3ml	6ml	avoid	3ml	Dosing = 10kg not established	5ml	1.5ml	**1ml	2.5ml	2.5ml	3-3.9
4-4.9	7.5mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	4-4.9
5-5.9	7.5mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	5-5.9
6-6.9	10mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	6-6.9
7-7.9	10mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	7-7.9
8-8.9	10mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	8-8.9
9-9.9	10mg: open into 5ml water; give 2.5ml & discard rest	4ml	9ml	2x250mg tabs	4ml	Dosing = 10kg not established	8ml	1.5ml	**1.2ml	3ml OR 1/4 tab	2.5ml	9-9.9
10-10.9	15mg: open into 5ml water	6ml	12ml	1x50mg+1x250mg tabs 2x250mg tabs 1x50mg+1x250mg tabs	6ml	200mg cap/tab	10ml	2ml twice daily OR 100, 250mg tabs: 2 tabs am, 1 tab pm	**1.5ml	10ml OR 1 tab	5ml	10-10.9
11-11.9	20mg: open into 5ml water	1/4 tab	2 caps 1 cap pm	2x50mg tabs am; 1x50mg+1x250mg tabs pm	7ml	200mg cap/tab + 50mg cap/tab	1 tab am; 1/2 tab pm	2.5ml twice daily OR 100, 250mg tabs: 2 tabs twice daily	**2ml	10ml OR 1 tab	5ml	11-11.9
12-13.9	20mg: open into 5ml water	1/4 tab	2 caps 1 cap pm	2x50mg tabs am; 1x50mg+1x250mg tabs pm	7ml	200mg cap/tab + 50mg cap/tab	1 tab am; 1/2 tab pm	2.5ml twice daily OR 100, 250mg tabs: 2 tabs twice daily	**2ml	10ml OR 1 tab	5ml	12-13.9
14-16.9	20mg: open into 5ml water	1/4 tab	2 caps 1 cap pm	2x50mg tabs am; 1x50mg+1x250mg tabs pm	7ml	200mg cap/tab + 50mg cap/tab	1 tab am; 1/2 tab pm	2.5ml twice daily OR 100, 250mg tabs: 2 tabs twice daily	**2ml	10ml OR 1 tab	5ml	14-16.9
17-19.9	20mg: open into 5ml water	1/4 tab	2 caps 1 cap pm	2x50mg tabs am; 1x50mg+1x250mg tabs pm	7ml	200mg cap/tab + 50mg cap/tab	1 tab am; 1/2 tab pm	2.5ml twice daily OR 100, 250mg tabs: 2 tabs twice daily	**2ml	10ml OR 1 tab	5ml	17-19.9
20-24.9	20mg: open into 5ml water	1/2 tab pm	2 caps	1x100mg tab+ 1x250mg tab twice daily OR 1x250mg EC cap once daily	10ml	200mg cap/tab + 2x50mg caps tabs	1 tab	3ml twice daily OR 100, 250mg tabs: 3 tabs am, 2 tabs pm	**2.5ml	10ml OR 1 tab	5ml	20-24.9
25-29.9	30mg	1 tab	1 tab	once daily	1 tab	200mg cap/tab + 3x50mg caps tabs	1 tab	3.5ml twice daily OR 200, 500mg tabs: 2 tabs am, 1 tab pm	**3ml	10ml OR 1 tab	5ml	25-29.9
30-34.9	30mg	1 tab	1 tab	once daily	1 tab	200mg cap/tab + 3x50mg caps tabs	1 tab	4ml twice daily OR 200, 500mg tabs: 2 tabs am, 1 tab pm	**3ml	10ml OR 1 tab	5ml	30-34.9
35-39.9	30mg	1 tab	1 tab	once daily	1 tab	2x200mg caps tabs	1 tab	5ml twice daily OR 200, 500mg tabs: 2 tabs twice daily	**3ml	10ml OR 1 tab	5ml	35-39.9
>40	30mg	1 tab	1 tab	once daily	1 tab	600mg tab	1 tab	5ml twice daily OR 200, 500mg tabs: 2 tabs twice daily	**3ml	10ml OR 1 tab	5ml	>40

* A lead-in dose of nevirapine is given for the first 14 days of treatment equivalent to half of maintenance dose i.e. usual maintenance dose but given once-daily. Increase to full maintenance dose after 14 days if no rash develops.

Compiled by J. Nuttall & S. Kaiman for the Paediatric HIV/TB Policy Reference Group, Westerns Cape. Adapted from World Health Organisation guidelines, 2006 & 2008.

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071 840 1572



Body Surface Area (BSA) m² = $\sqrt{\frac{\text{Mass (kg)} \times \text{Height (cm)}}{3600}}$

Appendix 5: ARVs for children: Side-effects Adverse Events and Grading

Table 19: Adverse effects of ARVs

Class	Drug	Side-Effects/Adverse Events
NRTI	Zidovudine	Anaemia, granulocytopenia Myopathy, Lactic acidosis
	Didanosine ddi	Common: abdominal pain, nausea and vomiting Uncommon: pancreatitis, peripheral neuropathy, lactic acidosis
	Stavudine	Common: abdominal pain, nausea and vomiting Uncommon: lipoatrophy, lipodystrophy, peripheral neuropathy, lactic acidosis
	Abacavir	Hypersensitivity reaction (with or without rash) – may be fatal in adults and children
	Lamivudine	Common: headache, fatigue and abdominal pain, Uncommon: pancreatitis and peripheral neuropathy, lactic acidosis
NNRTI	Nevirapine	Skin rash, sedative effect and diarrhoea. LIVER TOXICITY
	Efavirenz	Skin rash CNS – Sleep disturbance, confusion, abnormal thinking. Teratogenic in primates
PI	Ritonavir	Nausea, vomiting, diarrhoea Hypercholesterolaemia and hypertriglyceridaemia
	Lopinavir /Ritonavir	Nausea, vomiting, diarrhoea Hypercholesterolaemia and hypertriglyceridaemia

Table 20: Grading of Adverse Events

Feature	Grade 1	Grade 2	Grade 3	Grade 4
Haematology				
Haemoglobin Infant 1-21 days	12.0-13.0 g/dL	10.0-11.1 g/dL	9.0-9.9g/dL	< 9.0g/dL
Haemoglobin Infant 22-35 days	9.5-10.5g/dL	8.0-9.4 g/dL	7.0-7.9g/dL	< 7.0g/dL
Haemoglobin Infant 36-56 days	8.5-9.4g/dL	7.0-8.4g/dL	6.0-6.9g/dL	< 6.0g/dL
Hb ≥ 57 days (HIV-positive only)	8.5-10.0g/dL	7.5-8.4g/dL	6.5-7.4g/dL	< 6.5g/dL
Absolute neutrophil count Infant 1 day	4.0-5.0x10 ⁹ /l	3.0-3.9x10 ⁹ /l	1.5-2.9x 10 ⁹ /l	< 1.5 x 10 ⁹ /l
Absolute neutrophil count Infant 2 - 7 days	1.25-1.5x10 ⁹ /l	1.0-1.24x10 ⁹ /l	0.75-0.99x10 ⁹ /l	< 0.75x10 ⁹ /l
Absolute neutrophil count Children ≥7 days	1.0-1.3 x10 ⁹ /l	0.75-0.9 x10 ⁹ /l	0.5-0.7 x10 ⁹ /l	< 0.5 x10 ⁹ /l
Platelets (cells/mm ³)	100 000- 124 999	50 000-99 999	25 000 –49 999	< 25 000 or bleeding
Gastro-intestinal				
Bilirubin	1.1-1.5 x N	2.0 -2.9 x N	3.0 -7.5 x N	> 7.5 x N
AST	1.25-2.5 x N	2.6-5.0 x N	5.1-10.0 x N	> 10.0 x N
ALT	1.25- 2.5 x N	2.6-5.0 x N	5.1-10.0 x N	> 10.0 x N

Feature	Grade 1	Grade 2	Grade 3	Grade 4
γ GT	1.1 – 4.9 x N	5.0 – 9.9 x N	10.0 – 15.0 x N	> 15.0 x N
Pancreatic Amylase	1.1-1.5 x N	1.6 – 2.0 x N	2.1 –5.0 x N	> 5.0 x N
Diarrhoea Adult and paediatric \geq 1 year	Transient or intermittent episodes of unformed stools OR Increase of \leq 3 stools over baseline per 24-hour period	Persistent episodes of unformed to watery stools OR Increase of 4 – 6 stools over baseline per 24-hour period	Bloody diarrhoea OR Increase of \geq 7 stools per 24-hour period OR IV fluid replacement indicated	Life-threatening consequences (e.g., hypotensive shock)
Diarrhoea Paediatric < 1year	Liquid stools (more unformed than usual) but usual number of stools	Liquid stools with increased number of stools OR Mild dehydration	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR Hypotensive shock
Constipation	NA	Persistent constipation requiring regular use of dietary modifications, laxatives, or enemas	Obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction)
Nausea	Transient (< 24 hours) or intermittent nausea with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 – 48 hours	Persistent nausea resulting in minimal oral intake for > 48 hours OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
Allergic / Dermatological				
Acute systemic allergic reaction	Localized urticaria (wheals) with no medical intervention indicated	Localized urticaria with medical intervention indicated OR Mild angioedema with no medical intervention indicated	Generalized urticaria OR Angioedema with medical intervention indicated OR Symptomatic mild Bronchospasm	Acute anaphylaxis OR Life-threatening bronchospasm OR laryngeal oedema
Cutaneous reaction-skin rash*	Localized macular rash	Diffuse maculopapular rash OR morbilliform rash OR target lesions	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR Superficial ulcerations of mucous membrane limited to one site	Extensive or generalized bullous lesions OR Stevens-Johnson syndrome OR Ulceration of mucous membrane involving two or more distinct mucosal sites OR Toxic epidermal necrolysis (TEN)
Nervous system				
Developmental delay – Paediatric < 16 Years	Mild developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Moderate developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Severe developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Developmental regression, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting
Neuromuscular weakness (including myopathy & neuropathy)	Asymptomatic with decreased strength on exam OR Minimal muscle weakness causing no or minimal interference with usual	Muscle weakness causing greater than minimal interference with usual social & functional activities	Muscle weakness causing inability to perform usual social & functional activities	Disabling muscle weakness causing inability to perform basic self-care functions OR Respiratory muscle weakness impairing

Feature	Grade 1	Grade 2	Grade 3	Grade 4
	social & functional activities			ventilation
Neurosensory alteration (including paresthesia and painful neuropathy)	Asymptomatic with sensory alteration on exam or minimal paresthesia causing no or minimal interference with usual social & functional activities	Sensory alteration or paresthesia causing greater than minimal interference with usual social & functional activities	Sensory alteration or paresthesia causing inability to perform usual social & functional activities	Disabling sensory alteration or paresthesia causing inability to perform basic self-care functions
Other				
Clinical symptoms not otherwise specified above	No therapy, monitor condition	May require minimal intervention and monitoring	Requires medical care or possible hospitalisation	Requires active medical intervention, hospitalisation or hospice care

Appendix 6: Guidelines for adverse drug reaction reporting

National Pharmacovigilance Programme

The Medicines Control Council (MCC) has a responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The National Pharmacovigilance Programme is coordinated by the MCC and has two dedicated Units responsible for the monitoring of the safety of medicines. The National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town monitors the safety of all registered medicines in South Africa. In addition, a focused surveillance unit at MEDUNSA is responsible for monitoring the safety of anti-retroviral (ARV) medicines and complementary medicines. The unit at MEDUNSA is also responsible for monitoring the safety of unregistered medicines used during clinical trials.

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (i.e. adverse drug reactions or ADRs). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an Adverse Drug Reaction (ADR)?

The Medicines Control Council (MCC) defines an Adverse Drug Reaction (ADR) or adverse reaction as a response to a medicine which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine.

Who should report Adverse Drug Reactions?

All health care workers, including doctors, dentists, pharmacists, nurses and other health professionals are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is not in the package insert, potentially serious or clinically significant.

What happens to a report?

All ADR reports are entered into a national ADR database. Each report is evaluated to assess the causal relationship between the event and the medicine. A well-completed adverse drug reaction/product quality form submitted could result in any of the following:

- Additional investigations into the use of the medicine in South Africa
- Educational initiatives to improve the safe use of the medicine
- Appropriate package insert changes to include the potential for the reaction

Changes in the scheduling or manufacture of the medicine to make it safer

The purpose of ADR reporting is to reduce the risks associated with the use of medicines and to ultimately improve patient care.

Will reporting have any negative consequences on the health worker or the patient?

An adverse drug reaction report does not constitute an admission of liability or that the health professional contributed to the event in any way. The outcome of a report, together with any important or relevant information relating to the reaction, will be sent back to the reporter as appropriate. The details of a report are stored in a confidential database. The names of the reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information is only meant to improve the understanding of the medicines used in the country.

Is the event possibly an ADR?

The following factors should be considered when an adverse drug reaction is suspected:

1. What exactly is the nature of the reaction? (*describe the reaction as clearly as possible and where possible provide an accurate diagnosis*)
2. Did the reaction occur within a reasonable time relationship to starting treatment with the suspected medicine? (*some reactions occur immediately after administration of a medicine while others take time to develop*)

3. Is the reaction known to occur with the particular medicine as stated in the package insert or other reference? *(If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine)*
4. Did the patient recover when the suspected medicine was stopped? *(some reactions can cause permanent damage, but most reactions are reversible if the medication is stopped)*
5. Did the patient take the medicine again after the reaction abated (i.e. rechallenge). If so, did the same reaction occur again? *(In most situations it is not possible or ethical to rechallenge the patient with the same medicine. If such information is available or if such a rechallenge is necessary, recurrence of the event it is a strong indicator that the medicine is may be responsible)*
6. Can this reaction be explained by other causes (e.g. underlying disease/s; other medicine/s; toxins or foods)? *(It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is. A medicine-related cause should be considered, when other causes do not explain the patient's condition)*

What types of reactions should be reported?

The following adverse drug reactions should be reported:

- All ADRs to newly marketed drugs or new drugs added to the EDL
- All serious reactions and interactions
- ADRs that are not clearly stated in the package insert.
- All adverse reactions or poisonings to traditional or herbal remedies

Report even if you are not certain the medicine caused the event.

What Product Quality Problems should be reported?

The following product quality problems should be reported:

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labelling
- Therapeutic failures

How can ADRs be prevented from occurring?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines

How are adverse drug reactions reported?

An Adverse Drug Reaction/Product Quality Report Form is enclosed in this book and should be completed in as much detail as possible before returning it by fax or post to any of the addresses provided below. Additional forms can be obtained by contacting the MCC at these addresses. Report forms may also be accessed via the following website: <http://www.mccza.com>

1. The Registrar of Medicines
*Medicines Control Council, Department of Health, Private Bag X828
Pretoria, 0001
Tel: (021) 312 0295; Fax: (021) 3123106*
2. The National Adverse Drug Event Monitoring Centre (NADEMC) *C/o Division of Pharmacology,
University of Cape Town, Observatory, 7925
Tel: (021) 447 1618; Fax: (021) 448 6181*
- 5.4 MEDUNSA Pharmacovigilance Unit
Fax (012) 521 4335