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<td>Abacavir</td>
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<tr>
<td>AFASS</td>
<td>Acceptable, feasible, affordable, sustainable and safe</td>
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<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<tr>
<td>KS</td>
<td>Kaposi’s Sarcoma</td>
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<tr>
<td>MNCH</td>
<td>Maternal, Neonatal and Child Health</td>
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<tr>
<td>MSL</td>
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<td>MTCT</td>
<td>Mother-to-child Transmission of HIV</td>
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<td>MUAC</td>
<td>Mid-upper arm circumference</td>
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<td>Non-governmental Organisation</td>
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<td>NNRTIs</td>
<td>Non-Nucleoside Reverse Transcriptase Inhibitors</td>
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<tr>
<td>NRTIs</td>
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<td>Nelfinavir</td>
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<tr>
<td>NVP</td>
<td>Nevirapine</td>
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<td>OIs</td>
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<td>OPD</td>
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<td>OVC</td>
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<td>PCP</td>
<td>Pneumocystis jiroveci Pneumonia</td>
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<td>PCR</td>
<td>Polymerase Chain Reaction</td>
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<td>PEP</td>
<td>Post Exposure Prophylaxis</td>
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<td>PIs</td>
<td>Protease Inhibitors</td>
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<td>Provider Initiated Testing and Counselling</td>
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<td>RDA</td>
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<td>RNA</td>
<td>Ribonucleic Acid</td>
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<tr>
<td>RT</td>
<td>Reverse Transcriptase</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<td>sdNVP</td>
<td>Single dose Nevirapine</td>
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<td>Skin-fold-thickness</td>
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<tr>
<td>SOPs</td>
<td>Standard Operating Procedures</td>
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<td>SQV</td>
<td>Saquinavir</td>
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<td>STIs</td>
<td>Sexually Transmitted Infections</td>
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<td>RFT</td>
<td>Renal Function Test</td>
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<td>Ritonavir</td>
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<td>Tuberculosis</td>
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<td>TDF</td>
<td>Tenofovir</td>
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<tr>
<td>TLC</td>
<td>Total Lymphocyte Count</td>
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<td>TMP/SMX</td>
<td>Trimethoprim/Sulfamethoxazole</td>
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<td>TST</td>
<td>Tuberculin Skin Test</td>
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<td>UNAIDS</td>
<td>Joint United Nations Programme on AIDS</td>
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<td>University Teaching Hospital</td>
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<td>Voluntary Counselling and Testing</td>
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<tr>
<td>ZDV</td>
<td>Zidovudine</td>
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ACKNOWLEDGEMENT

On behalf of the Ministry of Health (MOH) I wish to acknowledge the significant contribution made by the Directorate of Clinical Care and Diagnostic Services for the leadership in putting together this training manual. Despite advances in the management of HIV infection, a significant number of children have not accessed timely care, support and treatment, in part due to inadequate health care worker capacity and low uptake of infant diagnosis of HIV. It is hoped that this training package will help develop this capacity to comprehensively manage children living with HIV.

I also wish to express my sincere gratitude to the following editorial team for their expertise and dedication: Dr. Gloria Munthali (Ministry of Health); Dr. Chipepo Kankasa, Dr. Mwiya Mwiya and Dr. Racheal Thomas (University Teaching Hospital Paediatric Centre of Excellency); Dr. Mwangelwa Mubiana and Dr. Muntanga Mapani (Centre for Infectious Disease Research in Zambia); Ms. Hilda Shakwelele, Ms. Rachel Thomas and Ms. Nakululombe Kwendeni (Clinton Health Access Initiative); Dr. Susan Zimba-Tembo (World Health Organisation); Dr. Lastone Chitembo (UNICEF); Dr. Rokaya Ginwalla (U.S. Centers for Disease Control and Prevention) and Dr. Ernest Mwila (Churches Health Association of Zambia); Dr. Msangwa Sinjani (AIDSRelief Transition); Dr. Jean Desire Kabamba (Levy Mwanawasa General Hospital); Dr. Lango Simbeye (Kabwe General Hospital); Musenge Matibini (FHI360); and Dr. Jack Menke (Elizabeth Glaser Pediatric AIDS Foundation).

Dr Davy Chikamata  
Permanent Secretary  
Ministry of Health
Introductory Module
Purpose of the Course

Even though children living with HIV respond very well to treatment with antiretroviral therapy, to date few of them have access to ART mostly due to a lack of cheap feasible diagnostic tests for infants, lack of affordable child-friendly antiretroviral (ARV) drugs and lack of trained health personnel. This course on paediatric HIV management aims to address the issue of lack of trained personnel. With an ever increasing burden of HIV and a high percentage of children infected, health workers urgently require accurate, up to date training and information on assessment and management of HIV in children. The paediatric HIV management course is designed to equip healthcare workers with the knowledge, skills and attitudes for provision of comprehensive care, support and treatment of children living with HIV.

Knowledge and skills acquired will ensure placement of more children on treatment by expanding ART initiation eligibility criteria to all children under 15 years old regardless of WHO Clinical Stage and CD4 Count. In addition, a family-based approach to HIV testing and counselling (HTC) encourages testing of all children and adolescents of unknown HIV status in the community and at the health facility irrespective of individual risk factors.

Course Methods and Materials

This course will use a variety of methods of instruction, including reading, written exercises, discussions, role plays and practicum in the in-patient and out-patient wards. Small groups of participants will be lead and assisted by facilitators as they work through the course modules. The facilitators are not lecturers in the traditional classroom sense. Their role is to answer questions, provide individual feedback on exercises, lead discussions and structure role plays. The course is organised into 12 modules as outlined in table 1. Some of the essential course materials and forms are also listed in the same table.

<table>
<thead>
<tr>
<th>Module</th>
<th>Topics</th>
<th>Course Materials</th>
<th>Course Forms</th>
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<tbody>
<tr>
<td>Module 1</td>
<td>Overview of HIV in children</td>
<td>Copt of Zambia</td>
<td>a) Sample PCR Request Form</td>
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<tr>
<td>Module 2</td>
<td>Diagnosis and staging</td>
<td>Consolidated Guidelines for Treatment and Prevention of HIV Infection Reference Cards:</td>
<td>b) Paediatric Initial History and Physical Form</td>
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<td>Approach to care of an HIV-exposed/infected infant or child</td>
<td>a) Weight-for-height reference card b) ART dosing chart</td>
<td>c) Adherence Form d) Paediatric Clinical Follow-up Form e) Summary Sheet</td>
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<tr>
<td>Module 4</td>
<td>Nutritional assessment and support</td>
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<td>Module 5</td>
<td>Antiretroviral drugs</td>
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<td>Module 6</td>
<td>Antiretroviral drug therapy</td>
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<td>Paediatric HIV related diseases</td>
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<td>Module 8</td>
<td>Palliative care</td>
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<td>Module 10</td>
<td>Psychosocial issues in paediatric HIV</td>
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<td>Module 12</td>
<td>Setting up comprehensive HIV services for children</td>
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Course Schedule
This is a five-day course including practicum starting at 08:00hrs and ending at 17:00hrs daily with in-built breaks. It may be expanded or shortened depending on the group’s learning needs, priorities and resources. Exceptionally it can be tailored into a three day intensive course for clinicians with previous HIV management experience.

Performance Assessment and Certification
There will be a pre-course and post-course test. In addition there will be continuous evaluation including written assignments as well as oral and clinical assessments. A certificate of attendance will be awarded upon successful completion of the course.
Module 1: Overview of HIV in Children
Learning Objectives
At the end of this module the participant will be able to:

• Describe the epidemiology of HIV infection
• Discuss HIV-1 and HIV-2 sub-types distribution and the structure and biology of the human immunodeficiency virus.
• Explain the pathophysiology, natural history and progression of HIV disease in children.

Listen to the presentation or read your modules on “Epidemiology of HIV” and then do Exercise A

Unit 1: Epidemiology of HIV

Zambia faces significant challenges to maternal, infant, and young child survival. Although the country recorded a decline in young child mortality according to the 2007 Demographic and Health Survey, the neonatal, infant, and under-five rates still remain unacceptably high at 34, 70, and 119 per 1,000 live births for deaths, respectively. There has been no decline in neonatal mortality in the past two decades. Leading causes of death among children under five include pneumonia, malaria, diarrhoeal diseases, and HIV. HIV is a generalised and mature epidemic in Zambia. The results of the last representative sample survey on HIV prevalence conducted in 2007 revealed that one of every seven (14.3 %) Zambians in the 15-to-49 year age group was infected with HIV. The 2012 Antenatal Care Sentinel HIV Surveillance indicated that 16.4 percent of pregnant women attending antenatal clinics were living with HIV.

The scale-up of prevention of mother-to-child transmission of HIV (PMTCT) programme has reduced the rate of infants contracting HIV from a peak of 7.72% in 1997 to 1.99% in 2011. Death rates due to HIV among infants have also reduced from a peak of 1.51% in 1997 to 0.33% in 2011, a reduction of about 78.1%. The estimated number of new infections in infants and children aged 1-4 years were 9,726 and 2,946 respectively in 1997 and 2011 (UNGASS 2012).

A total of 160,000 children aged zero to 14 were estimated to be living with HIV in 2012; of these, more than 89,000 needed antiretroviral therapy (ART). By the end of 2013 only 49,416 children aged zero to 14 were receiving antiretroviral therapy. Without treatment, one third of infants living with HIV die before their first birthday, and half before their second birthday as a result of opportunistic infections and intercurrent common diseases such as pneumonia, diarrhoea, malnutrition and malaria.

Modes of Transmission in children

• Mother-to-child-transmission (MTCT): 95 percent of childhood infections occur as a result of vertical transmission from infected mothers. Infants may acquire HIV from their mothers during pregnancy, at the time of delivery, or postnatally through breastfeeding. Without any intervention, between 30 and 40 percent of breastfeeding HIV-positive women transmit HIV to their newborns. With optimal care and support, this transmission can be brought down to less than 1-2 percent making it essential to confirm the HIV status of all antenatal women at the earliest possible moment.

• Child sexual abuse: The role of child sexual abuse as a source of HIV infection in children, although undocumented, is seen in our daily practice.

• Transfusion of infected blood or blood products is another possible source.

• HIV can also be transmitted to children by using unsterile injection needles and instruments.

![Figure 1: Risk of MTCT](image)
Exercise A
1. What is the national HIV seroprevalence?
2. What percentage of pregnant women attending antenatal clinics was living with HIV?
3. What is the infant and under-five mortality rate?
4. What is the predominant mode of transmission in children?
5. What are other possible modes of transmission in children?

When you finish this exercise discuss your answers with your facilitator, thereafter the facilitator will make a presentation (or advice you to read your module) on “Biology and Pathophysiology” and then do Exercise B.

Unit 2: The Biology of HIV

Basic Virology
The Human Immunodeficiency Virus (HIV) is a retrovirus from the lentivirus family. There are two types of HIV: HIV-1, which is found worldwide and is responsible for the worldwide pandemic, and HIV-2, found mainly in West Africa, Mozambique, and Angola. HIV-2 is less pathogenic, makes little or no contribution to paediatric AIDS. All discussion in this manual refers therefore to HIV-1.

Figure 2: HIV Structure

HIV has many subtypes. Subtype C is responsible for over 90% of infections in southern Africa including Zambia. Subtype C seems to be more virulent than the other subtypes and is associated with faster disease progression. It also has an increased risk of Nevirapine resistance.

HIV Life Cycle
The HIV life cycle in the host cell can be divided into several steps: binding, fusion, entry, transcription, integration and replication, budding, and maturation.
ARV target sites: Primary target cells for HIV

Cells with CD4 receptors or markers are the primary target cells for HIV. These receptors are found on:

1. T-helper lymphocytes also known as CD4+ cells
2. Macrophages which are found in:
   - Brain
   - Kidneys and other organs
   - Monocytes

Mode of Action of Antiretroviral Drugs

ARV drugs work at different stages of the HIV replication cycle. They interfere with the essential enzymatic steps in the cycle thus preventing the development of new infectious HIV particles. As a result, further destruction of CD4 cells is prevented.

Unit 3: Pathophysiology

Components of the immune system

<table>
<thead>
<tr>
<th>Non-specific immunity or innate immunity</th>
<th>Specific immune system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural barriers to infection:</td>
<td>Cellular immunity:</td>
</tr>
<tr>
<td>• Skin</td>
<td>• T-lymphocytes</td>
</tr>
<tr>
<td>• Nasal cilia</td>
<td>• CD4+</td>
</tr>
<tr>
<td>• Mucus</td>
<td>• CD8+</td>
</tr>
<tr>
<td>Phagocytes:</td>
<td>Humoral immunity:</td>
</tr>
<tr>
<td>• Neutrophils</td>
<td>• B-lymphocytes</td>
</tr>
<tr>
<td>• Macrophages</td>
<td>• Antibodies</td>
</tr>
</tbody>
</table>
Effect of HIV on the immune system
HIV targets CD4+ T-lymphocytes and destroys them. The CD4+ T-lymphocytes coordinate immune function of:
- the non-specific immune cells
- the specific CD8+ and B-lymphocytes

HIV causes profound immunodeficiency as a result of depletion of CD4+ T-lymphocytes and this is the hallmark of HIV infection. The CD4+ T-lymphocyte dysfunction is twofold:
- Reduction in numbers
- Impairment in function

Reduction in the CD4 cell number and the effects on their function reduces the capacity of the body to fight infectious diseases. Individuals with HIV infection are therefore increasingly susceptible to many infections especially at later stages of HIV infection. Absolute CD4 count higher in healthy children than in adults and varies with age. It slowly declines to adult levels by age 5. CD4 percentage does not change significantly with age. In children ≤5 yr CD4 percentage is the preferred immunological parameter for monitoring disease progression.

Figure 4: CD4 count/percentage and disease progression

The CD4 count/percentage declines with disease progression. There is a rapid increase in risk of developing AIDS or death as CD4+ cell percentage decreases below 15–20%. Prognosis is poorer in infants <12 months than in older children.

HIV Viral Load in Infants and Children
Definition: Viral load is the number of copies of HIV per ml. Viral load in perinatally infected infants differs from infected adults. The HIV RNA pattern in perinatally infected infants differs from the pattern in infected adults. The viral load levels are low at birth, and then increase to high values (>100,000 copies/ml) by two months of age, remain high throughout the first year of life, and then decline slowly over the next few years to set point. This pattern probably reflects the inability of the infant’s immature immune system to contain viral replication and, possibly, the greater number of HIV-susceptible cells. The viral set point is higher in children.
Host Immune Response to HIV

HIV attaches to cells of the immune system with special surface markers called CD4+ receptors. Cells with CD4+ receptors are found in many organs of the body: blood (T lymphocytes, monocytes and macrophages), brain (dendritic cells), liver, spleen and bone marrow (resident macrophages). *The basic effect of HIV on the immune system is CD4+ cell depletion and dysfunction.* The functional defects can occur before cell numbers decline.

Clinical Course of Illness

There are critical differences between the disease progression in children and in adults. These differences result in much more rapid disease progression and a much shorter duration for each stage. The higher mortality in HIV-infected children in Africa may result from inter-current infections, malnutrition, and lack of access to basic healthcare, lack of or delayed definitive diagnosis, and lack of access to primary HIV care and ART. Experience indicates that children perinatally infected with HIV fit into one of three categories:

- **Category 1: Rapid Progressors**, who die in the first year of life and who are thought to have acquired the infection in utero or during the early perinatal period (about 25–30%)
- **Category 2**: children who develop symptoms early in life, followed by a downhill course and death between the ages of three and five (about 50–60%)
- **Category 3: Long-term survivors**, who live beyond age eight (about 5–25%)

Predictors of Disease Progression in Infants include:

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

Maternal Predictors of Infant Disease Progression include:

- Maternal viral load at time of delivery
- Maternal CD4 cell count (<200)
- Rapidly progressive maternal disease
- Maternal death, which is associated with a two to fivefold increase in infant mortality compared to infants born to mothers who survive

Clinical presentation of rapid progressors

- The early severe Form is characterised by:
  - LBW
  - Early stunting
  - Developmental delay
  - Persistent oral candidiasis
  - Recurrent/persistent diarrhoea
  - Recurrent bacterial/fungal infections
  - Hepatosplenomegaly
  - Severe encephalopathy before 18 months
  - High viral load at birth
  - Rapidly decreasing CD4 counts
Clinical presentation of slow progressors includes:

- Opportunistic Infections after 2 - 10 years
- Growth stunting common
- Lymphoid interstitial pneumonitis (LIP)
- Parotitis
- Recurrent bacterial and fungal infections
- Skin problems
- AIDS related cancers
- Low viral loads at birth, stable CD4 counts for 2 - 10 years then slow decline

Exercise B

1. What are the steps of the HIV life cycle?
2. What is the clinical course of illness in children?
3. What are the predictors of disease progression in infants?

When you finish this exercise discuss your answers with your facilitator, thereafter you will be advised on when to proceed to Module 2 on “Diagnosis and Staging of Paediatric HIV”.
Module 2: Diagnosis and Staging of Paediatric HIV Infection
Learning Objectives
At the end of this module the participant will be able to:

• Describe the laboratory diagnosis of HIV infection in children.
• Describe the common clinical presentation of HIV infection in children.
• Define the clinical staging of paediatric HIV infection using the World Health Organisation (WHO) staging system.

Listen to the presentation/read about “Diagnosis of HIV infection in children” and then do Exercise A.

Unit 1: Laboratory Diagnosis of Paediatric HIV Infection

While the diagnosis of HIV in adults is relatively straightforward, establishing the HIV infection status of an infant or young child is more complex. The identification and follow-up of infants born to women known to be HIV infected is a necessary first step in infant diagnosis.

Specialised tests are required to determine whether a baby is infected with HIV or not. Laboratory tests are divided into two categories:

1. Antibody tests - which are relatively easy to perform (as in adults), provided that trained qualified personnel are available,
2. Virologic tests - which are expensive and involve complex laboratory methods.

Passive transfer of maternal antibodies across the placenta means that babies born to HIV-infected women will have circulating maternal antibodies in their systems up to the age of 18 months. Therefore, for children younger than 18 months, virologic tests must be done to detect the virus directly. Breastfeeding further complicates diagnosis in infants. HIV-exposed infants who are breastfed are at risk of acquiring HIV infection throughout the breastfeeding period, a factor that must be taken into account when requesting or interpreting HIV test results in children. Diagnosis of HIV infection facilitates the access for the infected child and the whole family to comprehensive HIV care.

It is recommended that provider initiated testing and counseling (PITC) be offered to all children who come into contact with a healthcare worker. This is especially important where high rates of HIV exposure are anticipated but have not previously been identified for various reasons (e.g. low coverage of maternal antenatal care [ANC] testing, lack of testing facilities and other infrastructure, or where testing was not previously accepted by the community).

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

• Serological or Antibody tests: for children aged >18 months. These include Enzyme-linked Immunosorbent Assay (ELISA), Rapid (used on blood or saliva); Western Blot.
• Virologic tests: for children <18 months of age. These include DNA or RNA PCR (Polymerase-Chain Reaction); P24 Antigen; viral culture.
• Currently, we use DNA-PCR testing in Zambia for Early Infant Diagnosis.

Antibody Tests
Antibody tests are the most widely used HIV diagnostic tests and provide evidence of HIV infection in adults and children who are older than 18 months. Sero-reversion refers to the time for the maternal antibodies to be eliminated from the infant. This period may vary from 6-18 months with uninfected non-breastfed children sero-reverting by 18 months of age.
Any child 18 months or older with a positive HIV-antibody test is infected with HIV. A child 18 months or older who has not breastfed for the past three months and whose HIV antibody test is negative is not infected with HIV.

HIV disease may progress very rapidly in infants – mortality at two years approaches 50 percent if HIV is not treated. Therefore, early identification and treatment of paediatric HIV disease can have a dramatic impact on outcome, and should be a priority whenever possible.

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

**Virologic Tests**

Virologic tests are used to differentiate the infected from the uninfected baby during the first 18 months of life. HIV DNA polymerase chain reaction (PCR) and HIV RNA PCR are two tests that detect HIV in blood; currently DNA PCR is recommended for early infant diagnosis. The sensitivity and specificity of virologic tests is generally excellent. False positive and false negative tests can occur. However, a single negative virologic test done after six weeks of age has sufficient negative predictive value to exclude HIV infection in a non-breastfeeding infant, and will only need a second antibody test at 18 months to confirm that the infant is not HIV-infected.

The sensitivity of HIV DNA PCR is low during the first two weeks of life because this test is not able to detect very low levels of HIV DNA in babies infected a few minutes/hours/days earlier, during delivery and early breastfeeding. After six weeks of life, the sensitivity and specificity of HIV DNA PCR tests approach 100%. DNA detection is unaffected by maternal ART or use of ARV in the mother or child for prevention of mother-to-child transmission of HIV.

**Positive Test Results**

One positive virologic test is strongly suggestive that the child is infected with HIV; in such cases, the child should be referred for ART initiation and have a confirmatory virologic test performed immediately.

**Negative Test Results: Children who have never Breastfed**

A single negative virologic test done after six weeks of age has sufficient negative predictive value to exclude HIV infection in a non-breastfeeding infant, and will only need a second antibody test at 18 months to confirm that the infant is not HIV-infected.

**Negative Test Results: Children who have ever Breastfed or who are currently Breastfeeding**

In an infant who recently stopped breastfeeding, a negative virologic test only rules out infection if performed at least 6 weeks after cessation. In an infant who continues to breastfeed, a single negative virologic test does not provide definitive diagnosis of the child’s infectious status since the child continues to be exposed to breast milk infected with HIV.
Figure 5: Algorithm for HIV virologic testing in children <18 months old

HIV-exposed infant or child <18 months old

Virologic (DNA PCR) test at 6-8 weeks old, 6 months old, and (if stops breastfeeding <12 months old) at 6 weeks after cessation of breastfeeding

- Positive test result: Likely HIV-infected
  - Immediately start cART
  - Repeat virologic test immediately to confirm HIV infection

- Negative test result
  - Breastfeeding remains HIV-exposed until cessation of breastfeeding
  - Never breastfed or no longer breastfeeding
    - HIV-uninfected
      - Refer to next level for HIV virologic testing
        - Monthly clinical monitoring

No virologic test available

<12 months old

- Well until 12 months old
- Symptomatic
  - Screen for presumptive severe HIV disease*

≥12 months old

- Well
  - If confirmed severe HIV disease, start cART immediately
- Symptomatic*

Serologic test at 12 months old and if stops breastfeeding <18 months old, at 6 weeks after cessation of breastfeeding

- Positive test result: Likely HIV-infected
  - Await virologic test results to start cART as indicated

- Negative test result
  - No longer breastfeeding
    - HIV-uninfected
    - If >18 months old, go to algorithm for serologic testing
### When to do DNA-PCR test in children <18 Months who are exposed and of unknown exposure

*Table 2: When to do DNA-PCR test in children <18 Months*

<table>
<thead>
<tr>
<th>Maternal HIV Status</th>
<th><em>Recommended Actions</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Known maternal HIV positive status</td>
<td>PCR testing of infant at six weeks of age or at first contact with health facility if after six weeks of age. Ensure that mother is enrolled in an ART clinic and is receiving appropriate care support and treatment</td>
</tr>
<tr>
<td>Known maternal HIV negative status</td>
<td>Ascertain that mother had repeat serological test during pregnancy. Offer antibody testing to mother if repeat testing was not done during pregnancy</td>
</tr>
<tr>
<td>Unknown maternal HIV status</td>
<td>Mother available for testing: Offer antibody test to mother. If she tests positive, offer PCR testing to infant if six weeks of age or more and also ensure that mother is enrolled in an ART clinic is receiving appropriate care support and treatment</td>
</tr>
<tr>
<td></td>
<td>Mother not available for testing (e.g. mother died or does not consent to be tested): Offer antibody test for infant. If positive, do follow up PCR testing at six weeks of age. Counsel mother on need for her to access HIV testing services to ascertain her status</td>
</tr>
</tbody>
</table>

### Timing of HIV testing and counselling in Children (0 to <10 years old)

*Table 3: Timing of HIV testing*

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Whom to test</th>
<th>When to test</th>
<th>HIV testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children &lt;18 months</td>
<td>Well, non-breastfed HIV-exposed infant (HEI)</td>
<td>6–8 weeks old</td>
<td>Virologic (DNA PCR) test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18 months old</td>
<td>Serologic test; follow with virologic (DNA PCR) test for positive serologic test in child &lt;18 months old</td>
</tr>
<tr>
<td></td>
<td>Well, breastfed HEI</td>
<td>6–8 weeks old</td>
<td>Virologic (DNA PCR) test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 months old</td>
<td>Virologic (DNA PCR) test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 months old</td>
<td>Serologic test; follow with virologic (DNA PCR) test for positive serologic test in child</td>
</tr>
<tr>
<td></td>
<td>Infant or child who has completely stopped breastfeeding</td>
<td>18 months old and/or ≥6 weeks after breastfeeding cessation</td>
<td>Serologic test; follow with virologic (DNA PCR) test for positive serologic test in child &lt;18 months old</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic infant with unknown HIV exposure</td>
<td>At first contact, as early as 6 weeks old</td>
<td>Maternal serologic test and/or infant serologic test; follow with virologic (DNA PCR) test for positive serologic test in child &lt;18 months old</td>
</tr>
<tr>
<td></td>
<td>Infant or child symptomatic for HIV infection</td>
<td>Immediately regardless of age</td>
<td>Serologic test; follow with virologic (DNA PCR) test for positive serologic child in child &lt;18 months old</td>
</tr>
<tr>
<td></td>
<td>Positive serologic test in child &lt;18 months old</td>
<td>At first contact</td>
<td>Virologic (DNA PCR) test</td>
</tr>
</tbody>
</table>
**Testing in symptomatic children**
If a child develops symptoms suggestive of HIV infection, repeat virologic testing should be performed immediately. Because symptoms of HIV and AIDS overlap with those of other common childhood diseases, efforts should be made to exclude other diagnoses.

**Testing in asymptomatic children**
Infants whose virologic test is negative and who remain **asymptomatic** should have a repeat virologic test done at 6 months; if still negative, antibody testing should be performed at 12 months of age. If the antibody test is negative, HIV infection is highly unless they are still breastfeeding, and a confirmatory antibody test should be done at 18 months or 6 weeks after cessation of breastfeeding.

**Presumptive diagnosis of Severe HIV disease in children <18 months**
Presumptive diagnosis is the diagnosis of HIV is recommended in children <18 months where there is no access to virological testing, or reporting of results is delayed, but the child has symptoms suggestive of HIV infection. It facilitates decision making regarding the initiation of ART which is potentially life-saving. It is not recommended in children >18 months because in this age group it is recommended to use adult national protocols to confirm HIV infection -antibody testing.

**Criteria for Presumptive Diagnosis of Severe HIV Disease in children <18 months of age**
A presumptive diagnosis of severe HIV disease should be made when the following are met:

**Table 4: Presumptive Diagnosis of Severe HIV Disease**

<table>
<thead>
<tr>
<th>The child is confirmed as being HIV antibody-positive and/or either</th>
<th>1. The child is symptomatic with two or more of the following:</th>
<th>2. A diagnosis of any AIDS-indicator condition(s) is made</th>
</tr>
</thead>
<tbody>
<tr>
<td>oral thrush</td>
<td>severe pneumonia</td>
<td>severe sepsis</td>
</tr>
</tbody>
</table>

A diagnosis of severe HIV disease in an HIV-seropositive child who is <18 months could be supported by a history of a recent HIV-related maternal death or advanced maternal HIV disease and the finding of a CD4 of <25% in the child. Once a diagnosis of presumptive severe HIV disease is made it is imperative to confirm the diagnosis of HIV infection as soon as possible using age-appropriate tests.

**Exercise A**
1. What does diagnosis of HIV infection facilitate?
2. What types of tests can one use to diagnose HIV infection?
3. What do we use virologic tests for?
4. How many PCR tests are required to interpret an HIV negative result in an infant?
5. How many PCR tests are required to make an HIV positive diagnosis in an infant?
6. Is DNA PCR affected by maternal ARVs (HAART or for prevention of mother-to-child transmission of HIV)?
7. At what age do you conduct a confirmatory antibody test?
8. When would you perform an antibody test on an asymptomatic child whose initial early virologic test was negative?
9. What test would you perform on a symptomatic child whose initial early virologic test was negative?

*When you finish this exercise discuss your answers during group feedback, thereafter the facilitator will make a presentation (or advise you to read your module) on “Clinical assessment of HIV infected children” and “Staging of Paediatric HIV infection. You will then do you an exercise.*
Unit 2: Common Clinical Presentation of HIV Infection in Children

Approach to Clinical Diagnosis
A rational approach requires a high index of suspicion. Paediatric HIV presents with conditions that are also found in HIV- children. Clinical features are more reliable in children with severe disease. These conditions are broken down as:

- Common in both HIV+ & HIV- children
- Common in HIV+ but less common in HIV- children
- Specific to HIV infection

WHO clinical staging is a standardised method for assessing disease progression and for making treatment decisions. Clinical staging should be used once HIV infection has been confirmed (i.e. once there is serological and/or virological evidence of HIV infection). Staging provides guidance on the prognosis of individual patients and to interventions needed at the different stages and for monitoring the response to ART.

Clinical signs & conditions suggestive of HIV infection in a child

Common in both HIV+ and HIV- children
- Otitis media - persistent or recurrent
- Diarrhea – persistent or recurrent
- Severe pneumonia
- Tuberculosis
- Failure to thrive
- Bronchiectasis
- Marasmus

Common in HIV, uncommon in HIV uninfected child
- Recurrent severe bacterial infections
- Persistent or recurrent oral thrush
- Parotid enlargement
- Generalized lymphadenopathy
- Hepatosplenomegaly (non-malaria areas)
- Persistent or recurrent fever
- Neurological dysfunction e.g. encephalopathy
- Persistent generalized dermatitis

Very specific for HIV infection:
- Recurrent invasive bacterial infection, excluding pneumonia (e.g. empyema, pyomyositis etc)
- Esophageal candidiasis
- Herpes zoster (multidermatomal)
- Invasive salmonella infection
- Pneumocystis jirovecii (formerly carinii) pneumonia
- Extra pulmonary cryptococcosis
- Lymphoma
- Kaposi’s sarcoma
- Lymphocytic Interstitial Pneumonitis (LIP)
Unit 3: Clinical Staging of Paediatric HIV Infection

WHO clinically classifies children into four stages (1, 2, 3 and 4) representing progressively more severe disease and worsening prognosis. This staging system is easy to use and is dependent upon clinical diagnoses rather than laboratory diagnosis. It is well suited for settings with limited diagnostic capabilities. In its simplicity, however, the system does not always account for the wide variety of disease manifestations seen in paediatric HIV infection thus making it difficult to classify some children. It is recommended that clinical staging should be consistently done for every child at every visit.

You use clinical staging only where HIV infection has been confirmed (i.e. serological or virological evidence of HIV infection). It is informative for assessment at baseline or entry into HIV care and can also be used to guide decisions on when to start Co-trimoxazole and monitor response to treatment. Therefore, the clinical stage indicates the urgency with which to start ART.

Table 5: WHO Staging of HIV-associated Clinical Disease

<table>
<thead>
<tr>
<th>Classification of HIV-associated clinical disease</th>
<th>WHO clinical stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>1</td>
</tr>
<tr>
<td>Mild</td>
<td>2</td>
</tr>
<tr>
<td>Advanced</td>
<td>3</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
</tr>
</tbody>
</table>

For detailed WHO clinical staging of paediatric HIV infection check Annex A.

How to Stage

Table 6: How to Stage

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Confirm the child’s status using the appropriate definitive test for age</td>
<td>If a child is &lt;18 months and is rapid test positive but virologic test is not available, then make a presumptive clinical diagnosis of HIV infection.</td>
</tr>
</tbody>
</table>
| 2    | Collect a comprehensive history | • At baseline include antenatal, birth and postnatal history  
• For subsequent visits, history is collected for time since last visit. |
| 3    | Conduct a physical examination: Stage the child using a symptom in the most advanced stage. |  |
Example
Wezi is a four year-old boy who has been referred from Kalingalinga Clinic to UTH because of poor appetite, loss of weight and overall failure to thrive. From the history, you learn that he tested HIV positive two weeks ago by rapid test, has just finished nine months of TB treatment for presumed TB adenitis (persistent generalised lymphadenopathy) with little response. You examine Wezi. His weight is 10kg, height is 85cms. He has extensive oral thrush and flat wart lesions on the face and neck and hepatosplenomegaly. His %CD4 is 10%. How would you stage Wezi?

WHO Clinical Staging Criteria:
Persistent generalised lymphadenopathy  1
Weight for age     4
Extensive oral thrush    3
Flat warts on face and neck   2
Hepatosplenomegaly    2

Wezi has unexplained severe malnutrition and is therefore classified as WHO stage 4.

There are differences in the levels of CD4 counts between adults and children. In children the:
• Absolute CD4 count varies with age
• Absolute CD4 count is higher in healthy children than in adults.
• CD4 percentage is a more constant/reliable indicator of immunosuppression for children < 5 years

Calculating CD4%

Table 7: Calculating CD4%

<table>
<thead>
<tr>
<th>Step</th>
<th>Calculation</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>Total WBC count (cells/mm$^3$) x % Lymphocytes</td>
<td>Equals Absolute Lymphocyte Count</td>
</tr>
<tr>
<td>Two</td>
<td><em><strong><strong>CD4 Count</strong></strong></em> X 100 Absolute Lymphocyte Count</td>
<td>Equals % CD4</td>
</tr>
</tbody>
</table>
Common Clinical Scenarios

Example 1: Negative Early Virologic Test in an Asymptomatic Infant who is Breastfeeding

Table 8: Negative Early Virologic Test in an Asymptomatic Infant who is Breastfeeding

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Repeat Virologic Test at 6 Months; if still Negative, go to Step 2</td>
<td></td>
</tr>
</tbody>
</table>
| 2    | Antibody Test at 12 Months of Age | 1. If negative, HIV infection is unlikely unless the child continues to breastfeed – go to step 3  
2. If positive, do virologic test  
   a. If virologic test is positive, child is infected  
   b. If virologic test is negative, go to step 3 |
| 3    | Repeat Antibody Test at 18 Months of Age | If child continues to breastfeed after 18 months of age, antibody testing should be repeated again 6 weeks after cessation of breastfeeding. 
NOTE: For children who have recently stopped breastfeeding, testing should ideally be done 6 weeks after cessation. |

Example 2: Negative Early Virologic Test in a Symptomatic Infant

If a child whose virologic test was negative at 6 weeks subsequently develops symptoms consistent with HIV infection, efforts should be made to exclude other diagnoses, and repeat virologic testing with PCR. If the repeat test is negative and an explanation for the child’s symptoms cannot be found, a consultation with an expert in paediatrics is recommended where available. (If the DNA-PCR result will be delayed consider screening the child for presumptive diagnosis).

Example 3: Positive Early Virologic Test

In this instance, the infant has had an initial virologic test at six weeks or soon after. This infant should be considered to be HIV-infected, whether or not he has symptoms of HIV. Care for the HIV-infected child is described in module 3.

Example 4: Discordant Tests

On rare occasions, a child will have an initial positive virologic test which, when repeated, is negative. This is a rare occurrence and can be due to errors in:  
- Handling or labelling specimens  
- Laboratory procedure  
- Reporting of result

In this case, address the above and repeat the test, check CD4 count, assess patient clinically and consult expert in paediatric HIV disease.
Exercise B

1. Which laboratory tests can confirm HIV infection in a 14 month old child with very low weight, persistent diarrhoea, oral thrush and recurrent pneumonias?

2. When do you use WHO clinical staging?

Case Studies

1. Mubiana is a 4 year old boy weighing 16kg. Presented to the clinic with a history of persistent generalised lymphadenopathy, there is no other complaint. The mother is worried about the swellings in the neck and armpits, which are now tender. You have HIV rapid tests and the child is HIV positive. What is Mubiana's clinical stage?

2. Theresa is a 7 year old girl. This is her first presentation to your clinic. Her weight is appropriate for age. The mother is however worried because she has persistent lymphadenopathy, dark skin patches from an earlier generalised itchy rash and has unexplained parotid enlargement. She is HIV positive. In what WHO clinical stage is Theresa?

3. Mumba is a five year old little boy with extensive flat wart infection on the forehead. The mother also says that he was treated for pulmonary tuberculosis a year ago. On examination he is underweight and has oral thrush. The child is HIV positive. In what WHO clinical stage is Mumba?

4. Chile is a 13 year old girl, grossly stunted (Tanner stage 1) and has unexplained parotid enlargement, abdominal examination reveals unexplained hepatosplenomegaly. The child is HIV positive. In what WHO clinical stage is Chile?

5. Maria, a three year old girl weighing 14kg, has persistent lymphadenopathy previously treated as TB adenitis with little success. A lymph node biopsy confirms Kaposi sarcoma (KS). She is HIV positive. In what WHO clinical stage is Maria?

6. Taonga is a healthy well-nourished two year old weighing 12 kg. She was admitted for an acute febrile illness confirmed to be malaria. She is HIV positive by rapid test. In what WHO clinical stage is Taonga?

When you finish the exercise discuss your answers during group feedback, thereafter the facilitator will advise you to read your module on “Interpretation of Test Results” and then you do the exercise that follows.

Interpretation of Test Results

For children >18 months, the antibody test will either confirm or exclude the diagnosis of HIV, however, for those <18 months, where DNA PCR is not available, a presumptive clinical diagnosis of HIV infection may be made to allow decision making regarding the need for initiation of potentially life-saving ART. Confirm the diagnosis at the earliest possible time depending on the age of the child.

Frequently Asked Questions

Is it always necessary to have two positive tests in order to be confident that a baby has HIV infection?

Yes. While a single positive virologic test performed at > 6 weeks of age is strongly suggestive of HIV infection, a repeat virologic testing is recommended. However, initiation of ART should not be delayed while awaiting the repeat test results.

When are you sure a child is HIV-infected?

- In a child 18 months of age or older, a positive rapid test result indicates that s/he is HIV-infected.
- In a child younger than 18 months, any of the following criteria indicate s/he is HIV-infected:
  1. Confirmed HIV virologic test (two positive tests)
2. The following scenarios are highly suggestive of HIV infection:
   a) One positive HIV virologic test.
   b) Symptoms consistent with HIV infection in an HIV-exposed child with evidence of immunodeficiency (CD4% of <25).

When are you sure a child is not HIV-infected?
In a child 18 months of age or older, who has not breastfed for the past six weeks (or who never breastfed), one negative HIV rapid test at 18 months indicates that s/he is not HIV-infected. A single negative virologic test performed at ≥ 6 weeks and less than 18 months of age in a child who never breastfed also excludes HIV.

In settings where virologic testing is unavailable, how should the diagnosis of HIV in infants and young children be approached?

A definitive diagnosis of HIV infection in a child < 18 months of age cannot be made without virologic testing. In settings where virologic testing is unavailable, a diagnosis of presumptive severe HIV disease can be made in a child who is HIV antibody positive and who either: a. has an AIDS-defining condition; or b. has 2 or more of the following: oral thrush; severe pneumonia; severe sepsis. Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive infant include: recent HIV-related maternal death or advanced maternal HIV disease; and child’s %CD4 < 25%.

Exercise C: State whether the child is HIV infected or not
1. Child is four years old and is HIV positive by rapid test.
2. Infant is 11 months and is HIV positive by rapid test.
3. Child is 12 months, HIV positive by rapid test and has lymphadenopathic KS.
4. Child is nine months old, asymptomatic, has never breastfed, is DNA PCR negative.
5. Child ten weeks old, positive by rapid test, CD4 22%, has severe pneumonia and oral thrush.
6. Child is 20 months old, HIV positive by rapid test and is asymptomatic.
7. Child 16 months old, HIV negative by rapid test and stopped breastfeeding five months ago.
8. Infant eight months old, DNA PCR HIV test negative and has never breastfed.
9. Child is four weeks old and DNA PCR for HIV positive.
10. Child is six months old, DNA PCR negative and is still breastfeeding.
11. Child is 11 months; HIV positive by rapid test, has PCP, no virologic test available, no CD4 counts available

When you finish the exercise discuss your answers during group feedback, thereafter the facilitator will advise you when to proceed to Module 3 on “Approach to Care of HIV-exposed and HIV-infected Children”.
Module 3: Approach to Care of HIV-exposed and HIV-infected Children
Learning Objectives
At the end of this module the participant will be able to:

- Comprehensive Paediatric HIV Care
- Approach to perinatally exposed infants regardless of whether they are HIV infected or not
- Approach to an infant or child with a confirmed diagnosis

Listen to the presentation or read your modules on “Comprehensive Paediatric HIV Care” and “Care for HIV-exposed Children” then do Exercise A.

Unit 1: Comprehensive Paediatric HIV Care

When a woman with HIV becomes pregnant, her infant is at risk of infection in utero, during labour and delivery and throughout the duration of breastfeeding. The risk of transmission for a child born to an HIV-infected mother without PMTCT interventions is about 30-40%. The majority of infants born to HIV-infected mothers, although they are not infected, have a two- to fivefold risk of mortality as a direct consequence of the mother’s HIV disease compared to children born to HIV-uninfected mothers. Differentiating HIV-infected from HIV-uninfected babies is challenging in the first year of life.

Table 9: Package for Comprehensive Paediatric Care

<table>
<thead>
<tr>
<th>Package for Comprehensive Paediatric Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Confirm HIV status as early as possible.</td>
</tr>
<tr>
<td>2. Monitor the child’s growth and development.</td>
</tr>
<tr>
<td>3. Ensure that immunisations are started and completed according to the recommended schedule.</td>
</tr>
<tr>
<td>4. Provide prophylaxis for opportunistic infections.</td>
</tr>
<tr>
<td>5. Offer ARV prophylaxis according to national guidelines</td>
</tr>
<tr>
<td>6. Actively look for and treat infections early.</td>
</tr>
<tr>
<td>7. Counsel the mother and family on:</td>
</tr>
<tr>
<td>a) Optimal infant feeding to minimise MTCT, prevent malnutrition and promote growth and development.</td>
</tr>
<tr>
<td>b) Good personal and food hygiene to prevent common infections, and encourage them to seek prompt treatment for any infections or other health related problems.</td>
</tr>
<tr>
<td>c) When the child should be followed-up according to national guidelines.</td>
</tr>
<tr>
<td>8. Conduct disease staging for the infected child.</td>
</tr>
<tr>
<td>9. Offer ART for the infected child.</td>
</tr>
<tr>
<td>10. Provide psychosocial support for the infected child and mother.</td>
</tr>
<tr>
<td>11. Refer the infected child for higher levels of specialised care if necessary, or to other social or community based support programmes.</td>
</tr>
</tbody>
</table>

When following the national PMTCT diagnostic algorithms, babies will be found to have HIV in the first few months of life via early virologic testing and HIV infection may be excluded early in a few children who are not breastfed. But a number of infants will fall into a category in which HIV infection has neither been definitively established nor completely excluded. Because paediatric HIV disease can progress very rapidly, both HIV-infected babies and those whose HIV status has yet to be determined require special care and attention during the first years of life. This module will provide a framework for comprehensive programmatic interventions (primarily clinical) that cater to the needs of children exposed to or infected by HIV within the broader context of other child health strategies.
Unit 2: Approach to Perinatally Exposed Infants

Care for HIV-exposed infants centres around three basic goals:
1. Preventing post-natal HIV transmission
2. Identifying the HIV-infected child: Virological testing will help distinguish which HIV-exposed infants are HIV-infected.
3. Preventing opportunistic infections: all HIV-exposed infants should receive prophylactic Cotrimoxazole to prevent Pneumocystis pneumonia (PCP). Isoniazid preventive therapy can reduce the risk of tuberculosis.
4. Maximising family health and well-being: enhanced healthcare services for infants born to HIV positive women on ART programmes can lead to improved health outcomes for both HIV-infected and HIV-exposed, uninfected children.

Health workers should provide the following elements of comprehensive care as a minimum to these children, inclusive of de-worming them every six months as soon as they are 12 months old.

Preventing Postnatal HIV Infection
With use of combination antiretroviral therapy in pregnancy to preventing HIV transmission, risk of the baby acquiring HIV is reduced to a minimum. In addition, use of antiretroviral drugs after the baby is born further reduces this risk. Current recommendations are to give the new born baby nevirapine as soon as possible after birth and to continue this for 6 weeks. Babies born to mothers with recent diagnosis of HIV and have not received ART or are considered not virologically suppressed due to short duration of ART should be given nevirapine for 6 months to prevent breast-milk transmission. If a baby has toxicity due to nevirapine, lamivudine can be substituted.

Confirm HIV Infection as Early as Possible
You should counsel every HIV-infected pregnant or postpartum mother on the need to confirm her child’s infection status as early as possible. Explain when and where to bring the child for HIV testing, depending on the availability of particular HIV tests in the locality.

Mother
• Provide routine testing for HIV antibodies for all pregnant women in ANC clinic and provide ART to HIV-infected women and prophylaxis to their infants.
• Offer HIV testing to women who deliver with unknown HIV status immediately after delivery and provide post-exposure prophylaxis to the infants of the HIV-infected women (see national guidelines).

Child
Early identification allows for appropriate care and can prevent/reduce early morbidity and mortality.
• Provide routine virologic testing for HIV through the PMTCT programme for all perinatally exposed children at six weeks of age or first contact thereafter and at six months of age.
• Provide routine testing for HIV for all children brought in sick to a health facility.
• Any child of any age and unknown HIV status who presents to a health facility with or without clinical signs and symptoms suggestive of HIV infection should be provided with diagnostic HIV testing to confirm or exclude HIV infection as early as possible.
• When virologic tests are not available, the clinician should always have a high index of suspicion and use clinical criteria to make a presumptive diagnosis of HIV infection in infants.
• Offer HIV test and PEP to those who have been sexually assaulted or those exposed to potentially infectious bodily fluids.
Growth and Development Monitoring and Promotion
Growth and development monitoring and promotion are critical child survival strategies in resource-poor settings, especially in areas with high rates of both childhood malnutrition and HIV, particularly for children in households directly affected by HIV and AIDS. We know that growth failure is greater in HIV-infected children than in uninfected children.

Nutritional Management
Poor nutrition weakens the immune system and predisposes children to common infections and, for those who are HIV-infected, to opportunistic infections (OIs). Both HIV-exposed and -infected children are at increased risk of malnutrition. For the strategies to prevent malnutrition and promote good nutrition refer to the module on nutrition.

Immunisations
Studies indicate that there is impaired passive transfer of maternal antibodies against common infections from HIV-infected mothers to their infants, and there may be impaired response following immunisation with a variety of antigens. All HIV perinatally exposed or infected infants should undergo the recommended EPI programme with the following modification:

• When considering BCG vaccination at a later age (re-vaccination for no scar or missed earlier vaccination), exclude symptomatic severe HIV disease.
• Give live measles vaccine to children, including those with symptoms of HIV and AIDS. HIV-infected children experience much more severe disease with wild measles virus, which outweighs the risks of vaccination.

Prophylaxis against Opportunistic Infections
Pneumocystis jiroveci Pneumonia (PCP)
PCP is a severe and rapidly progressive pneumonia with a fatality rate of 40 to 90 percent. HIV-infected infants are at a very high risk of this infection. It generally occurs between three and six months of age, sometimes as the first sign of HIV infection before the child is definitively determined to be HIV-infected. Prophylaxis of all HIV-exposed infants with Trimethoprim/Sulfamethoxazole (TMP/SMX) significantly reduces the incidence and severity of PCP.

Additional benefits of Cotrimoxazole include protection against common bacterial infections, toxoplasmosis, and malaria. A Zambian study (CHAP study) demonstrated an overall 45% reduction in mortality among HIV-infected children who received Cotrimoxazole prophylaxis, regardless of their CD4 count. The recommendation is that all infants born to HIV-infected mothers should receive prophylaxis against PCP from six weeks of age through the first year of life, or until they are proven to be uninfected.
Table 10: Who needs PCP Prophylaxis?

<table>
<thead>
<tr>
<th>Who needs PCP Prophylaxis?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All infants born to HIV-infected women, irrespective of ARVs taken during pregnancy and labour. Prophylaxis should continue until the child is confirmed to be HIV negative using an appropriate test for age.</td>
</tr>
<tr>
<td>• All children &lt; 24 months identified as HIV-infected by an age-appropriate test.</td>
</tr>
<tr>
<td>• Children aged 24 months and above, with symptomatic HIV disease (WHO stage 2, 3 or 4) or with CD4 &lt;25%.</td>
</tr>
<tr>
<td>• Any child with a history of PCP should continue with secondary prophylaxis (daily CTX) until age 5 when WHO clinical staging 1 and CD4 % ≥ 25 should be considered.</td>
</tr>
</tbody>
</table>

Note: All HIV-infected children who begin Cotrimoxazole prophylaxis, irrespective of whether Cotrimoxazole was initiated in the first year of life or thereafter, should continue until the age of five when they can be re-assessed. Adult clinical stage and CD4 thresholds for Cotrimoxazole initiation (WHO 2, 3 or 4 or CD4 < 350 regardless of clinical stage) apply to children older than five years; consider discontinuation when CD4 is above 350 for at least 6 months on ARV therapy or where there is no CD4 monitoring, when patient has no stage 2, 3 or 4 events with good adherence on treatment for at least 1 year.

For ease of administration, a once daily dose of TMP/SMX is recommended (trimethoprim component 8mg/kg/day). TMP/SMX is generally well tolerated in infants. Rash and fever are rare but are reported side effects. Bone marrow suppression can also be seen, most commonly in HIV-infected children receiving multiple medications.

You should clearly inform HIV-infected mothers at delivery that their children need prophylaxis against PCP starting at six weeks of age until it can be established that the child is not HIV-infected. For dosing refer to Table 6: Dosing Recommendations for PCP Prophylaxis

Dapsone is an alternative drug for use if CTX is contraindicated:
• Children >1 month 2 mg/kg/24 hours orally once daily with a maximum of 100mg per day
• Adults 100 mg/24 hours once daily (or twice daily)

Preventing Tuberculosis
In general, INH prophylaxis against TB should be given to children younger than five years who are exposed to smear-positive TB in their household but have no active TB (HIV-uninfected or -exposed). ALL HIV-Infected children ≥ 12 months old with or without exposure to smear-positive TB in the household should be given INH prophylaxis against TB after ruling out active disease. HIV-infected children < 12 months old should only be given INH prophylaxis if exposed to smear-positive TB and active TB is ruled out. INH for TB prophylaxis is given as a single oral daily dose of 10 mg/kg for six months.

Treatment of Acute Infections and other HIV-Related Conditions
HIV-exposed children are susceptible to common infections and OIs. HIV may alter the incidence, presentation, and response to conventional therapy. In some cases more aggressive and longer treatment courses may be necessary, as treatment failures are more frequent.

Clinical Assessment of the HIV-exposed Infant
HIV-exposed infants should be seen monthly until HIV has been definitively excluded. Because HIV disease progression can be very rapid during the first year of life, a baby who appears well at two months may have many abnormal findings when examined a month later. Each visit should include a history,
physical examination, the provision of PCP and ARV (where applicable) prophylaxis, and an assessment and plan.

History
A history should be obtained at all follow-up visits. A comprehensive birth history should be obtained during the first evaluation of the HIV-exposed infant. Information about the mother’s health, medical history, and use of cART may help identify infants at higher risk for infection.

Key questions should be asked each time the child is seen and should include:
- History of illness since last review
- Growth and nutritional assessment: Mothers should be asked about frequency, duration and adequacy of milk supplies for infants who are breastfed. Details of preparation and volume of feeds should be reviewed when formula is used
- Developmental assessment: Delayed acquisition of normal developmental milestones or loss of previously acquired skills can be the first sign of HIV encephalopathy. Simple questions should assess four critical developmental domains: cognitive, motor, language, and social. Much of the assessment will be done through observation during the physical examination. Use the developmental checklist.
- Parental concerns
- Possible household tuberculosis contact

Examining the HIV-exposed Infant
When HIV-exposed but uninfected infants are compared to HIV-infected infants, differences in weight and height are detectable within the first months of life. Careful monitoring of growth is an essential part of each medical encounter since weight gain can be a sensitive indicator of changes in health status. Weight, height, and head circumference should be measured at each visit and plotted on growth curves. The physical examination should include the usual components of paediatric care with special attention to physical findings common in HIV infection such as oral candida, rashes and lymphadenopathy.

Assessment and Plan
Each visit should conclude with an assessment of the child’s health, including his/her likely HIV infection status. Reviewing the following points would be helpful:
- What is the child’s HIV status?
- Are there clinical and/or laboratory findings suggestive of HIV infection?
- Does the child have any new problems?
- Is the child receiving required prophylaxis?
- Does the child require any laboratory studies?
- Has the child received the proper vaccination? Are any new ones due today?
- When should the child return for the next visit?

Regular Follow-up, Care and Referrals
Regular follow-up is the backbone to caring for HIV-exposed children and ensures optimal healthcare and psychosocial support to the family. Recommendations on frequency of follow-up are shown below. A well-informed mother who is aware of the follow-up schedule is the best way to ensure adequate follow-up care.

The paediatric ART programme supports the coordination of HIV-specific and routine Paediatric care in line with the EPI programme. HIV-exposed infants should be seen every four weeks during the first year of life when the risk of disease progression is greatest; more frequent visits may be necessary if indicated.
Table 11: Follow-up of HIV-exposed Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Visit Interval -clinical</th>
<th>Other concurrent activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-24 months</td>
<td>Monthly</td>
<td>At birth give ART prophylaxis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initiate Cotrimoxazole prophylaxis at six weeks or any time thereafter at first contact</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HIV DNA PCR testing (6 weeks and 6 months of age or at first visit thereafter)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immunisation according to Zambian guidelines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infant feeding and nutrition counselling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anthropometric measurements</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neurodevelopment assessments</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rapid HIV-test at 12 months and confirmatory test at18 months</td>
</tr>
</tbody>
</table>

Maximising Family Health and Well-being

Families will benefit from an open and honest exchange of information about the child’s health status.

- Use simple language to explain the difference between exposure to HIV and HIV infection to help parents and caregivers understand complex scientific concepts.
- Repeating information at each visit is helpful to ensure comprehension. Families may also greatly benefit from psychosocial support during this period of uncertainty.
- Exchange of information with members of a multidisciplinary team can provide important information about the care of the child.
- Use a family centered approach to identify all infected family members

Exercise A

1. A nine month old infant of unknown HIV status has come for measles vaccine. On examination, he has no BCG scar despite having received BCG at birth. He has unexplained severe failure to thrive. You are giving vaccines today. What is your decision?
2. A six month old infant of unknown HIV status is admitted with a second bout of pneumonia, has oral thrush, and is failing to thrive. The mother says that the child was born prematurely and she was advised by her mother-in-law not to have the child vaccinated secondary to chronic illness. What vaccines will you give?
3. A 12 month old child of unknown HIV status has been admitted with measles. She has only received BCG (no scar), OPV₀, DPTHib1, and OPV1. What vaccinations are recommended for this child?
4. A four month old perinatally exposed child was admitted and treated for septicaemia. Does he need PCP prophylaxis?
5. An infant has come for his ten week visit for vaccination. His DBS for DNA PCR was collected four weeks ago and it is negative. He has never breastfed. Should he continue receiving PCP prophylaxis?
6. You have just treated a six month old infant for PCP. Is he eligible for PCP prophylaxis?
7. You have a 17 month old breastfeeding child, HIV exposed, with WHO stage two conditions. Is she eligible for PCP prophylaxis?
8. Mrs. Banda is HIV positive and underwent PMTCT. Draw up a recommended follow-up plan for care and referrals for her perinatally exposed child.

When you finish the exercise discuss your answers during individual feedback, thereafter a role play will be conducted. Thereafter the facilitator will make a presentation (or ask you to read the module) on “Care of HIV-infected Children” and then do Exercise B.
Unit 3: Approach to an Infant or Child with a Confirmed Diagnosis

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

Evaluation of an HIV-infected Child (Staging)

1. History

   Initial History
   A comprehensive initial history will facilitate the development of a clinical profile for children entering the programme.

   The initial history should include a review of:
   - The birth history, including the use of antiretroviral drugs for perinatal prophylaxis.
   - The medical history, including HIV-related hospitalisations, illnesses, and medication.
   - Previous and/or current antiretroviral treatment, exposure to TB vaccines (e.g. BCG), tuberculosis treatment and prophylaxis for opportunistic infections.
   - Developmental history is also crucial as HIV infection frequently affects the central nervous system and can cause neurological manifestations, developmental delays, and cognitive as well as motor disabilities.

   Interim History
   A history should be obtained at each follow-up visit. This will help the clinician to determine whether there have been changes in the child’s health status or changes in the home setting that may affect the child’s health.

   Key questions should be asked each time the child is seen (refer to section on “Care of an HIV-exposed child”). In addition, ask on medication being received and drug adherence as well as academic performance and attendance for school going children.

2. Physical Examination

   Each visit should include an assessment of growth. Weight, length, and head circumference for children younger than two years of age should be measured at each visit and plotted on age-appropriate growth curves. The height and weight of older children should be recorded and charted regularly. Growth is a very sensitive indicator of disease severity. Weight loss or inadequate weight gain can be the first indication of HIV disease progression.

   Clinical Staging
   The initial physical examination should be comprehensive and subsequent exams can be guided by findings on the symptom checklist. Stage according to WHO criteria. This evaluation and staging should be done at every clinical visit and will help clinical monitoring of Paediatric HIV disease.

3. Laboratory and Immunologic Evaluation

   Once the diagnosis of HIV infection has been confirmed, a complete blood count and CD4 (count and percent) should be obtained. CD4 cell count and percentage will provide an assessment of the child’s level of immune suppression (see module 2).
Complete blood count (which can detect anaemia which is frequent in children with HIV) should be done as clinically indicated and CD4 cell number and percent should be measured at regular intervals for all HIV-infected children according to the follow-up schedule.

4. Prophylaxis for Opportunistic Infections

Pneumocystis Pneumonia

As noted earlier, Pneumocystis pneumonia (PCP) can occur during the first months of life and is often fatal in young infants. HIV-infected children and those whose HIV status has not yet been determined should be given Cotrimoxazole if they meet the criteria stipulated in the table "Who needs PCP prophylaxis" in Unit 1 of this module. Discontinuation criteria are described in the same table. Cotrimoxazole can contribute to hepatic dysfunction particularly when administered with other hepatotoxic drugs. It is generally well tolerated in children, though those with advanced HIV disease are often most likely to develop toxicities. Dapsone can be dispensed to children (>1 month of age) who are intolerant to Cotrimoxazole. The appropriate dose is 2mg/kg/day with a maximum dose of 100mg/day.

<table>
<thead>
<tr>
<th>Table 12: Dosing Recommendations for PCP Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Once Daily Dose by Age</strong></td>
</tr>
<tr>
<td><strong>Suspension</strong></td>
</tr>
<tr>
<td><strong>Single Strength Adult Tablet</strong></td>
</tr>
<tr>
<td>&lt; 6 months</td>
</tr>
<tr>
<td>100mg Sulfamethoxazole/20mg Trimethoprim</td>
</tr>
<tr>
<td>2.5mls</td>
</tr>
<tr>
<td>¼ tablet</td>
</tr>
<tr>
<td>6 months to 5 years</td>
</tr>
<tr>
<td>200mg Sulfamethoxazole/40mg Trimethoprim</td>
</tr>
<tr>
<td>5mls</td>
</tr>
<tr>
<td>½ tablet</td>
</tr>
<tr>
<td>6 years to 14 years</td>
</tr>
<tr>
<td>400mg Sulfamethoxazole/80mg Trimethoprim</td>
</tr>
<tr>
<td>10mls</td>
</tr>
<tr>
<td>1 tablet</td>
</tr>
<tr>
<td>&gt; 14 years</td>
</tr>
<tr>
<td>800mg Sulfamethoxazole/160mg Trimethoprim</td>
</tr>
<tr>
<td>n/a</td>
</tr>
<tr>
<td>2 tablets</td>
</tr>
</tbody>
</table>

Tuberculosis

Tuberculosis is the most common opportunistic infection in HIV-infected individuals as well as the leading cause of death. The risk of disease progression appears to be greater in children than in adults, and they are more likely to suffer severe complications including meningitis and miliary TB. Prompt diagnosis and correct treatment of HIV-associated TB disease are critically important.

The use of Isoniazid (INH) for treatment of latent TB significantly decreases the rate of active tuberculosis in TST-positive adults with HIV infection. Although there are few studies in infants and children, the success of this strategy in adults and the serious threat of TB disease in HIV-infected children, support its extension to the paediatric population.

INH should:
- Be given to all children (HIV- infected and –uninfected) under the age of five years who are in contact with an adult diagnosed with active tuberculosis, after ruling out active TB disease.
- Be given to ALL HIV-infected children with or without known contact with an active case of tuberculosis after ruling out active TB disease.
- Not be given to children who have contraindications to INH (e.g. active hepatitis) or who are suspected to have active tuberculosis.

Weight-based dosing for Isoniazid (10mg/Kg/day)
Table 13: Isoniazid Preventive Therapy

<table>
<thead>
<tr>
<th>Weight Range (kg)</th>
<th>Number of 100mg Tablets of INH to be Administered per Dose</th>
<th>Dose Given (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>½ tablet</td>
<td>50</td>
</tr>
<tr>
<td>5.1 to 9.9</td>
<td>1 tablet</td>
<td>100</td>
</tr>
<tr>
<td>10 to 13.9</td>
<td>1½ tablet</td>
<td>150</td>
</tr>
<tr>
<td>14 to 19.9</td>
<td>2 tablets</td>
<td>200</td>
</tr>
<tr>
<td>20 to 24.9</td>
<td>2½ tablets</td>
<td>250</td>
</tr>
<tr>
<td>&gt;25</td>
<td>3 tablets or 1 Adult tablet</td>
<td>300</td>
</tr>
</tbody>
</table>

For INH preventive therapy the child should be seen monthly

Note: previous history of TB is not a contraindication to IPT. Pyridoxine (vitamin B6) should be given during the time the child is taking isoniazid to prevent peripheral neuropathy.

Assessing of the HIV-Infected Child for ART.

1. Assessing for Antiretroviral Treatment
   Antiretroviral treatment (ART) is a crucial component of care for the HIV-infected child and is discussed at length in module 6. Although, all HIV positive children are eligible for cART, the decision to begin antiretroviral treatment is complex and requires a holistic approach (medical/psychosocial factors). HIV-infected children should be assessed at each visit.

2. Assessment and Follow-up Plan
   At each visit review a number of key questions as a way to synthesise information obtained during the evaluation:
   • Does the child have any new findings on history or physical examination?
   • Are there any acute problems that require immediate evaluation or treatment?
   • Is there evidence of HIV disease progression?
   • Are there any new laboratory results from the last visit to review?
   • Is the child due for CD4+ testing today?
   • Is the child eligible for PCP prophylaxis?
   • Is the child eligible for Isoniazid prophylaxis?
   • Is the child ready for ARV treatment?
   • Does the child or family need any referrals?
   • When is the next visit?

   The follow-up schedule will be determined by the child’s age, clinical stage and immune status. The patient should also have access to care between regularly scheduled visits. Parents and caregivers must have a way to contact a member of the team if the child falls ill between visits. This will allow them to seek advice and arrange to bring the child in for evaluation if needed. Enabling families to obtain both routine and urgent care within the same programme will enhance the overall management of the child’s disease.

Provide Psychosocial Support to the Infected Child and Caregiver
   This topic is discussed in module 10.
Exercise B
1. What is the main goal of care for an HIV-infected child?
2. What constitutes care for HIV-infected children?
3. What should constitute paediatric baseline evaluation?
4. What should the initial history in the evaluation of the HIV positive child include?
5. How is initial clinical staging conducted?
6. How is follow-up assessment done?
7. Who is supposed to receive PCP prophylaxis?
8. When should PCP prophylaxis be stopped?
9. Maybin is an eight month old infant. He was diagnosed with PCP two months ago. DNA PCR was done and he was reactive. His CD4 was 26%. Is he eligible PCP prophylaxis?

When you finish this Exercise discuss your answers with your facilitator. You will then be advised on when to proceed to Module 4 on “Nutrition and Paediatric HIV”.
Module 4: Nutrition and Paediatric HIV
Learning Objectives
At the end of this module the participant will be able to:
• Describe infant and young child feeding practices of an HIV-exposed infant/child.
• Describe the interaction between HIV infection and nutrition and management of nutritional problems of HIV-infected and affected children.
• Discuss growth monitoring in HIV-infected and affected children.
• Describe management of HIV-infected child with severe malnutrition.

Listen to the presentation/read about “Infant and young Child feeding practices in the context of HIV” and then do individual Exercise A.

Unit 1: Infant and Young Child Feeding Practices

Although prevention of mother-to-child transmission of HIV interventions can substantially reduce the risk of transmission during pregnancy, labour and delivery, the only proven way to prevent HIV transmission via breastfeeding is by totally avoiding breastfeeding and instead feeding the infant from birth with suitable replacements for breast milk.

Maternal factors such as recent HIV infection, advanced maternal disease, low CD4 count, high HIV RNA viral load, and mastitis are known to increase the risk of infection and suggest possible interventions. Recent evidence has shown that provision of ARVs either to the baby or to the mother during breastfeeding significantly reduces the risk of HIV transmission.

While breastfeeding of all types is associated with a higher rate of HIV transmission than replacement feeding, some studies have shown that exclusive breastfeeding is associated with a lower transmission risk than mixed feeding. It is thought that the introduction of foreign antigens may make it easier for HIV to cross the mucosal surface of the gastrointestinal tract, whilst breast engorgement - more likely to occur with mixed feeding - causes sub-clinical mastitis, a condition that increases the viral load in breast milk. Mixed feeding (earlier than six months of age) with both breast milk and other foods should be avoided since it brings with it both the risk of HIV infection and the risks of diarrhoea and other infectious diseases.

While breastfeeding is the primary guarantee of child survival in resource-poor settings, breastfeeding by HIV-infected women significantly increases the incidence of HIV infection among breastfed infants. Among women with established HIV infection, the estimated additional risk of transmission from breast milk, over and above the risk during pregnancy and delivery, is about 15% for an HIV-exposed baby who breastfeeds for up to six months and about 20% for babies who breastfeed into the second year of life.

Women who are newly infected during pregnancy or lactation have a much higher likelihood of transmitting HIV infection to their infants. The risk of transmission through breast milk among women with recent infection is about 29%. Babies continue to be at risk of HIV infection as long as they are exposed to HIV-contaminated breast milk. Breastfeeding problems (e.g. cracked and sore nipples, mastitis, and breast abscesses) significantly increase the risk of transmitting HIV by breast milk. Good breastfeeding techniques can reduce this risk considerably.

Infant Feeding Options for a Mother who is HIV Positive and whose Infant is HIV Negative or is of unknown HIV Status
• Exclusive breastfeeding for the first six months of life unless exclusive replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS).
• After 6 months, appropriate complementary food should be introduced and breastfeeding continued for up to at least 24 months.
• Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.
Infant Feeding Options for a Mother who is HIV Positive and whose Infant is known to be HIV Positive

Mothers who are HIV positive and whose infants are also HIV positive are strongly encouraged to breastfeed exclusively for the first 6 months of life and then introduce complimentary feeds at 6 months while continuing breastfeeding up to 2 years of age.

Table 14: Infant and Young Child Feeding Options

<table>
<thead>
<tr>
<th>Maternal HIV Status</th>
<th>Infant HIV Status</th>
<th>Recommended Feeding</th>
<th>Timing of Complementary Feeding</th>
<th>Recommended Timing of Complete Cessation of Breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive on cART</td>
<td>Negative or Unknown</td>
<td>Exclusive breastfeeding for 6 months (EBF). Replacement feeding only if AFASS</td>
<td>After 6 months</td>
<td>At 12 months if food security assured</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Up to 3 years if food security not assured</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>EBF for 6 months</td>
<td></td>
<td>Up to 2 years</td>
</tr>
<tr>
<td>Negative or unknown</td>
<td>N/A</td>
<td>EBF for 6 months</td>
<td></td>
<td>Up to 2 years</td>
</tr>
</tbody>
</table>

Infant Feeding: to Breastfeed or not to Breastfeed?
The decision to breastfeed or formula feed is based on societal norms, individual and family beliefs, and individual resources. There is no specific policy concerning infant feeding practices. Recognising that conditions are different with each family, the programmes’ goal is to support each mother’s chosen feeding option as per prevention of mother-to-child transmission of HIV guidelines that are consistent with WHO recommendations and which are appropriate to the community in which the family lives.

WHO Recommendations
“When replacement feeding is acceptable, feasible, affordable, sustainable and safe (AFASS), avoidance of all breastfeeding by HIV-infected mothers is recommended; otherwise exclusive breastfeeding is recommended during the first 6 months of life. To minimise HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account local circumstances, the individual woman’s situation and the risks of replacement feeding (including infections other than HIV and malnutrition)”.

Informed Choice
Infant feeding and support are key interventions for the prevention of mother-to-child transmission of HIV through breast milk. All HIV positive women need counselling that includes information about the risks and benefits of various infant feeding options, guidance in selecting the most suitable option for their situation and support to carry out their choice. Ideally, women should be counselled about infant feeding options during antenatal care. Infant feeding counselling in the context of HIV should not be given to HIV negative women or women of unknown HIV status.

HIV-infected mothers should receive counselling that includes general information about the risks and benefits of all infant feeding options, as well as guidance in selecting the option most likely to their specific individual and family circumstances. Mothers should understand that exclusive formula feeding remains the most effective method for preventing postpartum HIV transmission via breast milk. In areas where exclusive formula
feeding may be unsafe or unavailable, and in circumstances where a woman prefers to breastfeed, exclusive breastfeeding is preferable to mixed feeding. You should be able to discuss this difficult issue with confidence, answer questions and provide complete and non-judgmental support for each individual mother’s decision about what is best for her and her new baby. When HIV-infected mothers choose not to breastfeed from birth or stop breastfeeding later, they should be provided with specific guidance and support for at least the first two years of the child’s life to ensure adequate replacement feeding.

Potential Advantages of Breastfeeding
Breastfeeding is the societal norm in Zambia and advantages include the important bonding that takes place between infant and mother. Breast milk contains maternal antibodies to a wide variety of organisms and may provide protection to the infant from diarrhoea, pneumonia, neonatal sepsis and acute otitis media. Successful breastfeeding does not depend on availability of formula or clean water, and has been associated with a decrease in early deaths from infectious diarrhoea. In addition there may be child-spacing effects due to the decreased pregnancy rate during the breastfeeding period due to the lactation amenorrhea that may accompany it. An infant with a definite diagnosis of HIV should continue to be breastfed for as long as possible.

Potential Disadvantages of Breastfeeding
Although breast milk is generally considered nutritionally complete for the first six months of life, it is not clear that this is true in the case of a mother with poor nutritional health herself. It is also unclear that the protection that breastfeeding normally confers against the common childhood infections including infectious diarrhoea, applies to infants born to HIV-infected women.

Exclusive breastfeeding means giving only breast milk and no other liquids or solids – not even water – with the exception of vitamin drops, mineral supplements or medicine. Exclusive breastfeeding with early cessation (<6 months) is no longer recommended unless:
- An HIV-positive mother develops symptoms of AIDS.
- A woman is in a position to provide adequate and hygienic replacement feeding to reduce the cumulative risk of longer duration breastfeeding.
- An HIV-positive woman who finds it difficult for socio-cultural reasons to initially avoid breastfeeding completely, but can at a later stage provide and hygienically prepare adequate replacement foods after the infant is a few months old.

Women who chose to breastfeed should be supported to maintain breast health and minimise cracked nipples or abscesses. Mixed feeding should be discouraged as it risks introducing diarrhoea and other illnesses to baby and transmitting HIV, unless it is unavoidable during the transition phase, which should be done gradually over a period of one month.

Transition from Exclusive Breastfeeding to Replacement Feeding for Mothers who choose not to Breastfeed beyond 6 Months
Duration should be gradual over a period of about one month.
- While a mother is breastfeeding, teach her baby to drink expressed breast milk from a cup
- This milk may be heat-treated to destroy the HIV
- Once the baby is drinking comfortably, replace one breastfeed with one cup-feed using expressed breast milk.
- Increase the frequency of cup-feeding every few days and reduce the frequency of breastfeeding. Ask an adult family member to help cup-feed the baby.
- Stop putting her baby to the breast completely as soon as she and her baby are accustomed to frequent cup-feeding. From this point on, it is best to heat-treat her breast milk.
- If her baby is only receiving milk, check that he is passing enough urine - at least six wet nappies in every 24-hour period. This means that he is getting enough milk.
- Gradually replace the expressed breast milk with formula (if below 6months) or whole milk if above 6 months.
• If her baby needs to suck, give a clean finger instead of the breast.
• To avoid breast engorgement (swelling) express a little milk whenever her breasts feel too full. This will help her to feel more comfortable. Use cold compresses to reduce the inflammation. Wear a firm bra to prevent breast discomfort.
• Do not begin breastfeeding again once she has stopped. If she does, she can increase the chances of passing HIV to her baby. If her breasts become engorged, express the milk by hand and discard it.
• Begin using the family planning method of her choice, if she has not already done so, as soon as she starts reducing breastfeeds.

**Wet nursing** is acceptable in some cultures, however, if this is the only feasible way of feeding the infant, *make sure that the wet nurse is counselled and tested and is also counselled on practicing safe sex.* The wet nurse should be willing to be with the infant for 24 hours a day. Monitoring of a wet nurse may be difficult and it is not routinely recommended.

**Supporting the mother to carry out a chosen feeding option** may require her sharing her HIV status with the family and it is your responsibility to discuss with the woman the importance of disclosure, on steps to be taken and ways of doing this. If possible with permission from the woman, the health worker can discuss with the family the chosen feeding option. Couple counselling is useful in this context.

**Replacement Feeding**
Replacement feeding includes feeding with a commercial or home-prepared formula. *In the first six months of life, milk in some form is essential for an infant.* The family must also have other resources such as water, fuel, utensils, skills, and time to prepare it correctly and hygienically. Replacement feeding is often a new way for a mother to feed a baby, and it should not be assumed that mothers know how to do it. *Mothers and families should be counselled on proper food hygiene,* including:

• Washing hands with soap and water before preparing food.
• Cups should be used to give replacement feeds.
• Washing the feeding and mixing utensils thoroughly and boiling them to sterilise them before preparing the food and feeding the infant.
• Boiling water for preparing the child’s food and any necessary drinks.
• Avoiding storing milk or cooked food, or, if this is not feasible, storing it in a refrigerator or a cool place and reheating thoroughly (until it bubbles) before giving it to the infant.
• Storing food and water in clean, covered containers and protecting it from rodents, insects, and other animals. Keeping food preparation surfaces clean.
• Washing fruits and vegetables with water that has been boiled, peeling them if possible, and cooking them thoroughly before giving to the infant.

**Commercial Infant Formula** is regulated to meet nutritional specifications for the first six months of life, is often fortified with micronutrients including iron and it is usually in powder form to be reconstituted with water. However it is deficient in breast milk immune cells and immune globulin and is expensive. A baby who is not breastfeeding will need about 150 ml of milk per kg of body weight per day. Commercial infant formula is an option for HIV-positive women when the family has reliable access to sufficient formula for at least six months. Feeding an infant for six months requires an average of 40 x 500g tins (or 44 x 450 g tins) of formula. Commercial infant formula should be reconstituted according to instructions on the container.

*Note: Commercial infant formula is often prepared incorrectly and not safely; therefore, particular attention must be paid to address this. Where formula is subsidised or free, mothers turn to mixed feeding.*
Home-prepared formula is not routinely recommended and is only considered in special circumstances when exclusive breastfeeding is not possible and:

- Commercial infant formula is not available or is too expensive for the family to buy and prepare;
- There is a reliable supply of animal or other milk and the family can afford it for at least 6 months;
- The family has the resources to prepare it hygienically, and can make the required modification accurately.

However, animal milk should be modified to suit infants. It is not routinely recommended.

**Ingredients for making home-prepared formula**

**Table 15: Ingredients for Making Home-prepared Formula**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cows’ milk</td>
<td>100mls</td>
</tr>
<tr>
<td>Water</td>
<td>50mls</td>
</tr>
<tr>
<td>Sugar</td>
<td>2 teaspoons (10g)</td>
</tr>
</tbody>
</table>

Micronutrients can be added if available.

**Infant Feeding After Six Months of Age**

After the age of six months, breast milk and other forms of milk alone are not adequate to meet a baby’s nutritional requirements. Therefore, for both breastfed and replacement-fed infants, complementary foods in addition to breast milk substitutes, should be introduced when they are six months of age. If there is evidence of growth faltering or the mother has decided to wean before six months of age complementary foods could be introduced as early as four months of age.

*Milk should continue to be an important component of the diet, providing up to one-half or more of the nutritional requirements between the ages of six and 12 months and up to a one-third of the requirements between the ages of 12 and 24 months.* In addition, complementary foods made from appropriately prepared and nutrient-enriched family foods should be given three times per day up to the age of nine months; between nine and 12 months, four feedings should be given daily; thereafter, five times per day.

**Exercise A**

1. What constitutes an informed choice on infant and young child feeding counselling?
2. What are the steps involved in counselling an HIV positive mother on infant feeding?
3. What are the infant feeding options for HIV positive women?
4. Malaika is a five month old female baby born to an HIV positive mum. She is still exclusively breastfed, but the mother is worried that Malaika will soon be six months old. She has now come for nutritional counselling, because she knows that breast milk alone is not enough for Malaika. What recommendations are you going to give for infant feeding after six months?
5. Mrs. Justina Banda is a prime gravida. She underwent routine testing and counselling at her local antenatal clinic, and she tested HIV positive. She started taking cART from 28 weeks gestation age. She is very worried that she may infect her baby with HIV. She has come for infant and young child feeding counselling. She is an economist and can afford formula. What are your discussion points?
   a) After further conversation you find out that replacement feeding is acceptable, feasible, affordable, sustainable and safe. What would you recommend?
   b) You see her in the postnatal clinic six weeks after delivering her baby. She has not breastfed and she is giving her infant Lactogen 1. What points of discussion will you highlight?

*When you finish the Exercise discuss your answers with the facilitator, thereafter a role play will be conducted. The facilitator will then make a presentation (or advice you to read the module) on “Nutritional Management of the HIV-infected and affected Child” and then do Exercise B.*
Unit 2: Interaction between HIV infection and Nutrition

Nutrition and infection
It is important to understand the relationship between nutrition and infection in general as this is not so much different with HIV infection. Poor nutrition increases the body’s susceptibility to infections, and infections exacerbate poor nutritional state.

Inadequate and inappropriate dietary intake leads to poor nutrition and negatively affect the immune system functioning hence reducing the body’s ability to fight infections. This leads to an increase in the incidence, severity, and length of infections. Symptoms that accompany infections such as loss of appetite, diarrhea, and fever lead to reduced food intake, poor nutrient absorption, nutrient loss, and altered metabolism. All of these contribute to weight loss and growth faltering, which further weaken the immune system.

An adequate nutrient and energy-dense diet coupled with general hygiene and food safety are critical interventions to break the cycle of infection and poor nutrition.

Effects of HIV on nutrition
HIV infection progressively erodes the immune function, leading to recurrent opportunistic infections, debilitation, and death. Poor nutritional status is a major contributor to the disease progression. In resource-limited settings, HIV infected children are often already undernourished. Their weakened immune systems further increase their vulnerability to infection.

HIV affects nutritional status in three distinct ways, listed below. These effects can occur simultaneously in the same person.

Reduced food consumption
Symptoms of OIs can result in reduced food intake because of the following:
• Inability to eat or swallow because of nausea or painful sores in the mouth or throat.
• Loss of appetite because of fatigue, depression, and other changes in mental state.
• Side effects of medications including nausea, appetite loss, taste changes, diarrhea, vomiting, and abdominal cramps.

Increased energy needs
The body’s response to HIV infection and viral replication uses additional energy. As the disease progresses and OIs occur, infections and symptoms such as fever further increase energy expenditure. When infection is prolonged, muscle wasting occurs and muscle tissue is broken down. These processes increase energy requirements during the asymptomatic phase by 10 percent over those recommended for healthy, non-HIV-infected people of the same age, sex, and physical activity level.

During the symptomatic phase, energy requirements increase by 20–30 percent over those recommended for healthy, non-HIV-infected children of the same age, sex, and physical activity level. The range in the requirement reflects the fact that children with more frequent and severe symptoms need up to 20 percent more energy. Energy requirements for symptomatic children who experience weight loss increase by 50–100 percent (WHO 2003, 2005).

Reduced absorption of nutrients
HIV interferes with the body’s ability to absorb nutrients, an effect that occurs with many infections. Poor absorption is also caused by OI symptoms such as diarrhea and vomiting. Poor absorption can occur in any phase of HIV infection in both adults and children and leads to excess nutrient loss. Poor fat
absorption reduces the absorption and use of fat-soluble vitamins such as A and E, which can further compromise nutritional and immune status.

Nutrition care and support helps break this cycle by helping HIV infected children maintain and improve their nutritional status, boost their immune response, manage the frequency and severity of symptoms, and improve their response to antiretroviral therapy (ART) and other medical treatment. Illustrates how effective nutrition interventions can help transform the vicious cycle of HIV and undernutrition into a positive relationship between improved nutritional status and stronger immune response.

Poor nutritional status can affect HIV in the following ways:

- Weakened immune system
- Increased susceptibility to OIs
- Slower healing process
- Possibly faster progression of disease
- Poorer response to treatment
- Despair and worsening depression

**Figure 6: Interactions between HIV and Nutrition**

![Image of interactions between HIV and Nutrition](source: Adapted from RCQHC and FANTA 2003a.)

**Figure 7: Effects of Nutrition on HIV: The cycle of benefits from nutrition interventions**

![Image of effects of nutrition on HIV](source: Adapted from: RCQHC and FANTA 2003a.)

Improving and maintaining good nutrition may prolong health and delay the progression of HIV to AIDS. The impact of proper nutrition begins early in the course of HIV infection, even before other symptoms are observed.
Unit 3: Growth Monitoring in HIV-Infected and Affected Children

Periodic Nutrition Assessment and Growth Monitoring

Growth is a very sensitive indicator of HIV disease and disease progression in children. Growth and development monitoring and promotion are therefore critical child survival strategies in Zambia, a country with high rates of both childhood malnutrition and HIV and AIDS. Poor growth has been shown to precede CD4 decline and the development of OIs. A simple growth chart is an excellent tool for the primary care practitioner and all personnel must be carefully trained in the importance of, and the techniques for, accurate measurement of height, weight, and head circumference. Weight is the optimal nutritional indicator because it is a composite measure of the different nutritional changes.

Nutritional Assessment and Support for Infants and Children

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

Poor growth may be the first indication that an HIV-exposed child is infected, prompting further evaluation of the child’s infection status. For a child with known HIV infection, growth failure can warrant the initiation of antiretroviral therapy or a change of therapy for those already on treatment.

Routine nutritional assessment should be performed at every clinical visit. A more extensive evaluation may be required for children with growth failure or other evidence of malnutrition as described below. All clinicians working with children should be able to conduct a paediatric nutritional assessment. At sites where more specialised expertise is available, children with growth abnormalities or dietary problems may be referred to a clinical nutritionist or dietician.

Its components can be thought of as screening questions and include:

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

• Asking about symptoms that may prevent food intake and absorption. The symptom checklist should identify symptoms – such as fatigue, mouth pain, difficulty sucking or swallowing, nausea, vomiting, and diarrhoea – that can prevent adequate nutrition. Additional evaluation, described below, will be needed for children with poor growth.

• Measuring the infant (head circumference, length, weight) or child (height, weight) and plotting his/her growth on standardized and locally appropriate growth charts.

  a) Carefully measure the child’s length or height only once, on the first day. For children less than 85cms in length or too weak to stand, measure the child’s length while supine (lying down). For children 85cms or more, measure standing height.

  Note: length is usually greater than standing height by 0.5cms. This difference has been accounted for in the weight – for – height reference card. If the child is ≥85cms but cannot be measured standing, subtract 0.5cms from the supine length.

  b) Weigh the child without clothes and quickly dress and wrap the child thereafter

  Note: it is important to standardise stadiometer and scales daily and each time they are moved
Measurement of weight, length, and head circumference should be performed on children younger than 24 months and height and weight for older children. During an infant's first year, nutritional assessments should be carried out every month, and every three months (monthly, if there is altered nutrition) beyond infancy in keeping with recommendations. Because the rate of growth also provides useful information, growth curves should be used – it is not enough to know that the child weighs more than at the previous visit.

**Growth Failure**

**Definition of Growth Failure**

Significant growth failure for infants and young children is defined as the failure to sustain a normal velocity of weight gain. This is defined as crossing two major percentile lines on the weight growth curve. For children already less than the fifth percentile for age, this is defined as the inability to follow along their own upward curve. Growth failure can also be defined by the loss of greater than or equal to five percent of body weight. It is important to be able to distinguish between a short-term lack of growth due to intercurrent illness or circumstance, and the sustained lack of growth which defines failure. “Linear growth failure” is defined by low length or height for age and is particularly important to be recognised during the first three years of life. If adequate growth is not attained during this period, it is difficult to catch up even if nutritional interventions are subsequently introduced. Once growth failure has been identified, prompt evaluation is indicated. The underlying cause may be socioeconomic, biomedical, or a combination of the two. However, as noted above, growth failure may be the first sign that an HIV-exposed infant is infected or that an infected child requires HIV therapy. It is therefore crucial to rapidly identify the reason for the inadequate growth.

**Assessment of a Child with Growth Failure**

A detailed nutritional history will help differentiate the child with inadequate intake from the one experiencing excessive losses. It should be more extensive than the one taken at a routine clinical visit and should include a 24 or 72 hour dietary recall. Additional information should include eating behaviour – excessive vomiting or spitting after feeds may indicate gastro-oesophageal reflux, for example. Description of stools will identify those children with diarrhoea. Frequent watery stools may indicate gastrointestinal infection. Voluminous, foul-smelling or greasy stools may help to identify the child with malabsorption. Poor appetite and fatigue may be indications of systemic infection such as tuberculosis or HIV.

**Targeted Physical Examination**

A targeted physical examination, will confirm the extent of malnutrition, and may also identify the cause. Once the likely cause has been identified, the health care provider should develop a specific plan of action. Unless the history and examination reveal clear evidence of specific organ dysfunction, it is not unreasonable to consider HIV and/or TB as the aetiology of growth failure. This needs to be confirmed as soon as possible with appropriate tests. If the child is currently receiving antiretroviral therapy, poor growth may indicate that the current regimen is failing.

**Laboratory Assessment**

You should approach this decision in a logical way, based on information from the history and physical examination. Stool examination, including culture exam for parasites, may provide the diagnosis for a child with diarrhoea. Assessment of haemoglobin may find that anaemia is the reason a child lacks the energy needed to feed.

**How can Paediatric Nutrition be supported?**

All children should receive multivitamins. Additional support includes counselling mothers about breastfeeding, and all patients about food and water hygiene. You are strongly encouraged to maintain an inventory of local resources – food pantries, micro-finance programmes, and other community-based programmes that may provide support to individuals with HIV and AIDS.
In addition to caloric supplementation, selection of specific foods may ameliorate certain symptoms, such as nausea, sore mouth and throat, or diarrhoea.

**Table 16: Symptomatic Nutritional Counselling**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Nutrition Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>Encourage the child to drink throughout the day. If no longer breastfeeding, encourage soups, diluted fruit juice, water, or oral rehydration solution. Foods that are soft, mashed, and moist – such as porridge from cereals, rice, bananas, potatoes, and other soft vegetables - may be best tolerated. After diarrhoea has ceased give an extra meal for 2 weeks.</td>
</tr>
<tr>
<td>Sore mouth or throat</td>
<td>Encourage soft, mashed, or smooth foods such as avocados, squash, pumpkins, papaw, bananas, yogurt, soups and minced foods. Chewing small pieces of mango, or pawpaw may help to relieve pain. Avoid spicy and salty foods such as chillies and curries, as well as acidic or very sour foods such as oranges, lemons, vinegar, and tomatoes.</td>
</tr>
<tr>
<td>Nausea</td>
<td>Encourage dry foods. Eating small amounts more frequently is often easier than eating large meals. Avoiding fatty and greasy foods may help.</td>
</tr>
</tbody>
</table>

Adapted from “Living Well with HIV and AIDS” *Note: nutrition counselling should always be individualised.*

**Provide Nutritional Supplementation and Rehabilitation**

Caregivers should ensure adequate nutrient intake based on locally available foods and provide universal (vitamin A) or targeted (e.g. iron, folate, zinc) micronutrient and mineral supplementation. HIV-infected children have been shown often to be deficient in two essential micronutrients: vitamin A and zinc.

**Early Nutritional Supplementation**

Early nutritional supplementation in HIV-infected children and adults helps preserve lean body mass (LBM) and slows disease progression. One should not wait until there are signs of malnutrition to support nutrition in HIV-infected children. HIV-infected children should receive 150% of the Required Daily Allowances (RDA) for their age and sex. Multivitamin supplements are recommended daily. Give vitamin A according to our national guidelines.

**Table 17: Vitamin A Oral Dosing**

<table>
<thead>
<tr>
<th>Child’s age</th>
<th>Vitamin A oral dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 months</td>
<td>50,000 IU</td>
</tr>
<tr>
<td>6-12 months</td>
<td>100,000 IU</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>200,000 IU</td>
</tr>
</tbody>
</table>

**Other Nutrition Interventions**

- Perform presumptive de-worming on the child every six months starting from 12 months of age.
- Provide an extra meal per day after episodes of illness to allow for catch-up growth (see IMCI guidelines).
- Households should have a safe water system, point-of-use water treatment or filtration, or should use boiled water.
- Hygiene, particularly hand washing, and sanitation are important factors in prevention of infections.
- All households should use iodised salt.
**Strategies to Prevent/Treat Malnutrition**

- Prevent Low Birth Weight; ensure maternal wellbeing
- Prevent Mother-to-child transmission of HIV
- Institute appropriate infant feeding practices
- Prevent common childhood infections
- Ensure prompt and appropriate treatment of infections
- Monitor Growth. Provide micronutrient and food supplementation
- Encourage family planning and child spacing
- Provide antiretroviral treatment

**Exercise B**

1. What is paediatric nutritional assessment? Why is paediatric nutritional assessment important?
2. How often should paediatric nutritional assessment be conducted?
3. Who should perform paediatric nutritional assessment? How should paediatric nutrition be assessed?
4. How is growth failure defined?
5. Violet is a 20 month old female child. She is HIV positive and she has come for a follow-up visit. Her weight has remained static at 8kg compared to the previous weight two months ago. The mother says that she has had two bouts of diarrhoea, and has sores in the mouth. Upon examination, she is alert, with no signs of dehydration. Her temperature is 36.7ºC. How will you conduct symptomatic nutritional counselling? What early nutritional supplementation is required for Violet? What other nutrition interventions can be offered?
6. What are the strategies to prevent malnutrition in HIV-exposed and HIV-infected children?

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on “Care of the Severely Malnourished HIV-infected Child” and then do Exercise C.

**Unit 4: Management of HIV-Infected Child with Severe Malnutrition**

The severely malnourished child is likely to have more serious health problems in addition to malnutrition. In many cases these problems may not be clinically apparent. Characteristics of HIV-infected children associated with malnutrition include:

- Micronutrient deficiencies (low serum levels of zinc, selenium, vitamins A, E, B6, B12 and C) are common among HIV-infected children, reduce immunity, and predispose them to more infections and worsening nutritional status.
- Deviations in linear growth and weight may be apparent as early as three months of age in HIV-infected children.
- Stunting or low height for age is more prominent than wasting.
- Malnutrition with wasting is a characteristic symptom of AIDS.
- These children usually have anaemia and it is important to assess for palmar pallor.

The clinical presentation of malnutrition in HIV-infected children is similar to that in HIV-negative children, but severe wasting is more common than wasting with associated oedema (kwashiorkor) among HIV-infected children. Therefore you should look out for visible severe wasting especially of the trunk and buttocks, as well as oedema (swelling) of both feet.

**Severe Wasting**

A child with severe wasting has lost fat and muscle and appears like skin and bones, another term for this condition is marasmus. To look for severe wasting, remove the child’s clothes and look at the front and back view for loose skin, wasted areas and marked bony prominence.
Oedema
Oedema is a swelling from excess fluid in the tissues. It is usually seen in the feet and lower legs and arms. In severe cases it may also be seen in the upper limbs and face. To check for oedema, grasp both feet so that they rest in your palms with your thumbs on top of the feet. Press your thumbs gently for a few seconds. The child has oedema if a pit (dent) remains in the foot when you lift your thumbs.

To be considered a sign of severe malnutrition, oedema must appear in both feet. If the swelling is on one foot, it may be just a sore or infected foot. Any degree of oedema is considered significant. The degree of oedema is commonly rated in the following way:

Table 18: Rating of Degree of Oedema

<table>
<thead>
<tr>
<th>Rating</th>
<th>Oedema</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Mild</td>
<td>both feet</td>
</tr>
<tr>
<td>++ Moderate</td>
<td>both feet plus lower legs, hands, and lower arms</td>
</tr>
<tr>
<td>+++Severe</td>
<td>generalised oedema including feet, legs, hands, arms and face</td>
</tr>
</tbody>
</table>

Dermatosis
Dermatosis is a skin condition more common in children with oedema than in wasted children. A child with dermatosis may have patches of skin that are abnormally light, or dark in colour, shedding of the skin of the limbs, groin, behind the ears etc. There may be weeping lesions, and there may be severe rash in the nappy area. When the skin is raw and weeping, the risk is high for skin infections.

Table 19: Extent of Dermatoses

<table>
<thead>
<tr>
<th>Classification</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Mild</td>
<td>Discoloration or a few rough patches of skin.</td>
</tr>
<tr>
<td>++ Moderate</td>
<td>Multiple patches on arms and/or legs.</td>
</tr>
<tr>
<td>+++ Severe</td>
<td>Flaking skin, raw skin, fissures (opening in the skin).</td>
</tr>
</tbody>
</table>

Eye Signs

Table 20: Eye Signs

<table>
<thead>
<tr>
<th>Eye Signs</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bitot’s spots</td>
<td>• superficial foamy white spots on the conjunctiva (white part of the eye). These are associated with vitamin A deficiency</td>
</tr>
<tr>
<td></td>
<td>• Pus or redness are signs of eye infection</td>
</tr>
<tr>
<td>Corneal clouding</td>
<td>is seen as an opaque appearance of the cornea (the transparent layer that covers the pupils and iris). It is a sign of vitamin A deficiency</td>
</tr>
<tr>
<td>Corneal ulceration</td>
<td>is a break in the surface of the cornea. It is a severe sign of vitamin A deficiency. If not treated, the lens of the eye may push out and cause blindness. Corneal ulceration is an emergency and requires immediate treatment with vitamin A, atropine (to relax the eye), a topical antibiotic and an eye pad. Patients should be referred to an eye specialist where this service is available.</td>
</tr>
</tbody>
</table>
Identify the Child with Severe Malnutrition

Determine Standard Deviation Score (SD score) based on the Child’s Length or Height

An SD score is a way of comparing a measurement, in this case a child’s weight-for-length to an average. The averages used in this module are NCHS/WHO normalised reference values for weight-for-height and weight-for-length. A table is given on the weight–for-height reference card.

The SD scores may be loosely interpreted as follows:

• -1 SD approximately corresponds to 90% of the median weight-for-height
• -2 SD approximately corresponds to 80% of the median weight-for-height
• -3 SD approximately corresponds to 70% of the median weight-for-height

It is important to consider a child’s weight-for-height rather than simply weight-for-age. The latter is affected by stunting. Stunting may cause low weight – for age when a child is adequate weight-for-height. Feeding can correct wasting but cannot easily correct stunting.

To Use the Weight-for-Height Reference Table

1. First find the child’s length or height in the middle of the table, if the length or height is between those listed, rounds up as follows: if length /height is ≥ 0.5cm greater than the next lower length /height, round up, otherwise round down.
2. Then look in the left columns for boys or the right columns for girls, to find the child’s weight.
3. Look at the top of the column to see what the child’s SD score is.

The child’s weight might lie between two SD scores. If so indicate that the weight is between these scores by writing less than (<). For example, if the score is between -1SD and -2SD, write <-1SD.

Examples of SD scores:

1. A boy is 80cm in length and weighs 9.2 kg. His score is -2SD (roughly 80% of the median weight for his length)
2. A girl is 76.5cm in length and weighs 7.4kg. Round her length to 77cm. Score is -3SD (roughly 70% of the median weight for her length)
3. A girl is 90cm and weighs 10.3kg. Her weight is between -2SD and -3SD. Record her SD-score as <-2SD.

Exercise C

Refer to the SD-score reference card and indicate SD score for each child.

<table>
<thead>
<tr>
<th>Height and Weight</th>
<th>SD Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mumbi, girl, length 63 cm, weight 5 kg.</td>
<td></td>
</tr>
<tr>
<td>Chalwe, boy height 101 cm, weight 11.8 kg</td>
<td></td>
</tr>
<tr>
<td>Tanya, girl, length 69.8 cm, weight 6.3 kg</td>
<td></td>
</tr>
<tr>
<td>Peter, boy, length 82 cm, weight 8.5 kg</td>
<td></td>
</tr>
<tr>
<td>Chaife, boy, height 130 cm, weights 16.5 kg</td>
<td></td>
</tr>
<tr>
<td>Wabei, girl, height 105 cms, weighs 12.1 kg</td>
<td></td>
</tr>
<tr>
<td>Katai boy height 99 cm, weighs 11.8 kg</td>
<td></td>
</tr>
<tr>
<td>Katowa, girl, height 120 cm, weighs 16 kg</td>
<td></td>
</tr>
<tr>
<td>Sibeso, girl is 85 cm long and weighs 9.7 kg</td>
<td></td>
</tr>
<tr>
<td>Temwani, girl is 93 cm long and weighs 13.6 kg</td>
<td></td>
</tr>
</tbody>
</table>
When you finish the Exercise discuss your answers with the facilitator, thereafter you will be advised to read the module on “Recommended criteria for admission or referral for severe malnutrition” and then do Exercise D.

Recommended Criteria for Admission or Referral for Severe Malnutrition

Admit or refer to the severe malnutrition ward children who have:

- Weight-for-length/height less than -3SD (less than 70%) or visible severe wasting and/or
- Oedema of both feet

If the child is <-3SD or 70% weight-for-height, he/she is severely wasted. If there is oedema of both feet (and worse), the child is severely malnourished even though retained fluid may add to the child’s weight, making the height-for-weight greater than -3SD.

All severely malnourished children should be referred to the severe malnutrition ward, regardless of other presenting symptoms. Children with severe malnutrition are in danger of death from hypoglycaemia, hypothermia, fluid overload, and undetected infections. Their feeding and fluids must be controlled, or they could die. To ensure the proper feeding and treatment routines, it is critical to keep these children in a specialised ward. Other health problems and infections should be treated on the severe malnutrition ward.

Exercise D

1. Elaine is 22 months old. She is 67cm in length, weighs 7 kg and has oedema of both feet. Should she be referred to the severe malnutrition ward? Why or why not?
2. Promise is a two year old child. His height is 72cm and his weight is 7.2kg. He has no oedema. Should he be referred to the severe malnutrition ward? Why or why not?
3. Charity is six months old. She weighs 6.4kg and her length is 65cms. Should she be referred to the severe malnutrition ward? Why or why not?
4. Patrick is 18 months old. He is 65cm in length and weighs 4.8kgm. Should he be referred to the severe malnutrition ward? Why or why not?
5. Mweshi is a girl, five years old. Her height is 110 cm and her weight is 14.5 kg. Should she be referred to the severe malnutrition ward? Why or why not?

When you finish the Exercise discuss your answers with the facilitator, thereafter a presentation will be made on Emergency Care for Severely Malnourished HIV-infected Children

Emergency Care for Severely Malnourished HIV-Infected Children

- Assess for dehydration and give ReSoMal
- Prevent and treat hypoglycaemia by feeding the child or giving 50mls of 10% glucose orally or by NG tube if child unable to feed
- Evaluate for hypothermia (temperature below 35°C) and keep the child warm
- Address possible presence of infection

Long-term Solutions needed for Vulnerable Communities

Malnutrition in a person with HIV and AIDS is a multifaceted problem requiring multiple interventions, both short-term and long-term, applied simultaneously to break the vicious cycle of malnutrition, depressed immunity, infections and malnutrition. In particular, links to community and social services are required to address household food insecurity and other issues.
Exercise E
1. What constitutes pre-referral treatment for severely malnourished children?
2. Lena is an 18 month old girl whose arms and shoulders appear very thin. She has moderate oedema (both feet and lower legs). She does not have diarrhoea and vomiting, and her eyes are clear. She weighs 6.3 kg and her temperature is 35.5°C.
   a) What is Lena’s weight-for-height SD score?
   b) Should she be referred to hospital for severe malnutrition? Why or why not?
   c) Is Lena hypothermic?
   d) What two things should be done for Lena immediately based on the above findings?

When you finish this Exercise discuss your answers with your facilitator, thereafter you will be advised on when to proceed to Module 5 on “Antiretroviral Drugs”.
Module 5
Antiretroviral Drugs
**Learning Objectives**

At the end of this module the participant will be able to:

- Identify the different classes of ARVs, their sites and modes of action and formulations available for children
- Describe ARV drug regimens used in children
- Enumerate and manage adverse effects of ARV drugs

*Listen to the presentation or read your module 5 units 1 and 2 then do Exercise A.*

**Unit 1: Antiretroviral Drug Classes, Sites, Action and Formulations**

The main classes of antiretroviral drugs currently available in Zambia are: nucleoside analogue reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and Entry Fusion Inhibitors. Resistance to single or dual agents is quick to emerge and so single drug regimens are contraindicated. At least three fully active drugs, usually from two different classes, are the recommended minimum standard for all settings. WHO currently recommends that first-line regimens should be based upon two nucleoside analogue reverse transcriptase inhibitors (NRTI) plus one non-nucleoside drug (NNRTI). The use of triple NRTI as first-line therapy is used in special cases.

**Table 21: Classes of Antiretroviral Drugs**

<table>
<thead>
<tr>
<th>Classes of Antiretroviral Drugs</th>
<th>Sites and Modes of Action of ART</th>
<th>Drugs</th>
</tr>
</thead>
</table>
| Nucleoside Analogue Reverse Transcriptase Inhibitors| Inhibit reverse transcription of viral RNA into DNA by competitively blocking reverse transcriptase enzyme activity | • Zidovudine – AZT
• Lamivudine – 3TC
• Emtricitabine - FTC
• Abacavir – ABC
• Tenofovir Disoproxil Fumerate - TDF
• Zalcitabine - ddC
• Stavudine – d4T (no longer recommended) |
| Non-Nucleoside Reverse Transcriptase Inhibitors     | Inhibit reverse transcription by directly blocking reverse transcriptase enzyme activity          | • Nevirapine (NVP)
• Efavirenz (EFV)
• Etravirine (ETR)
• Delavirdine (DLV) |
| Protease inhibitors                                 | Inhibit the processing of large precursor proteins to form functional viral proteins              | • Ritonavir (RTV)
• Lopinavir/Ritonavir - (LPV/RTV)
Kaletra®
• Atazanavir/Ritonavir – (ATV/r)
• Saquinavir (SQV)
• Amprenavir (APV)
• Fosamprenviral (FPV)
• Atazanavir (ATV)
• Darunavir (DRV)
• Tipranavir (TPV) |
| Integrase Inhibitors                                | Inhibit the HIV enzyme integrase, thus preventing integration of HIV DNA into the host cell genome | • Raltegravir (RAL) |
| Entry Inhibitors                                    | Block important CD4 co-receptors or the fusion of the virus to the CD4 cell membranes and hence prevent binding and entry | • Maraviroc (MVC) (Co-receptor inhibitor)
• Enfuvirtide (fusion inhibitor) |
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

The NRTIs were the first class of antiretroviral drugs available for the treatment of HIV infection. Once they are converted intracellularly to active nucleoside metabolites they are potent inhibitors of the HIV reverse transcriptase enzyme, which is responsible for the reverse transcription of viral RNA into DNA. The drugs from the NRTI class are described below.

Abacavir

Abacavir (ABC), a guanosine analogue, is an alternative NRTI in first-line therapy and it is available in paediatric formulation. There is a similar safety profile in children to that in adults, with very little haematological toxicity.

Adverse Drug Reactions for Abacavir

The most serious adverse effect associated with ABC is an acute hypersensitivity reaction. Fewer than five percent of children starting ABC will develop signs and symptoms consistent with this syndrome, most within the first 6 weeks of initiation of therapy. Symptoms include flu-like symptoms, fever, cough, chills, malaise, rash, vomiting, diarrhoea, respiratory distress, headache and bone/joint pain. If a hypersensitivity reaction is suspected, ABC should be discontinued immediately. The syndrome is generally reversible while continuation of treatment can lead to death. Reintroduction of ABC at a later point can be fatal. Families should be counselled about these potential side effects and instructed to contact the healthcare team if any such symptoms occur and are aware of the need to immediately consult their care provider if signs or symptoms of a hypersensitivity reaction occur.

Of all the NRTI drugs, ABC has the least effect on mitochondrial DNA, and is the preferred substitute for d4T in a child who developed lactic acidosis or lipoatrophy while receiving a d4T-containing regimen. ABC could also be substituted for AZT in the event of intolerance.

Formulations for Abacavir

ABC is available in 20mg/ml solution and 300mg tablets, tablets may be swallowed whole or crushed and dispersed in water or onto a small amount of food and immediately ingested. A new fixed dose combination (FDC) crushable tablet containing ABC and 3TC is now available. Refer to Annex K for dosing chart.
Emtricitabine

Emtricitabine (FTC) is a cytidine analogue NRTI that is recommended for first-line regimens for adults as an option. FTC is structurally related to 3TC and shares its resistance profile. Where available, it can be used in children older than three months of age as an alternative to 3TC.

Lamivudine

Lamivudine (3TC) is a cytidine analogue, is a potent NRTI with an excellent record of efficacy safety and tolerability in HIV-infected children. It is a core component of the dual NRTI backbone of therapy. 3TC is an extremely well tolerated agent with minimal toxicity. It is contained in the following paediatric combinations (FDCs): AZT/3TC/NVP; AZT/3TC; and ABC/3TC;

Adverse Drug Reactions for Lamivudine

3TC is associated with minimal toxicity. Pancreatitis has been reported rarely in children, and other mitochondrial toxicities such as lactic acidosis and hepatic steatosis are much more common with drugs such as d4T and ddI.

Formulations for Lamivudine

It is available as:

- 150mg tablets,
- Fixed dose combination (FDC) crushable tablet containing ABC and 3TC or AZT and 3TC.

Lamivudine has few adverse effects. In children, the dose is calculated at 4mg/kg weight and is generally well tolerated.

Dosing: Refer to Annex K for dosing chart.

Tenofovir

Tenofovir (TDF), an adenosine nucleotide analogue, is another drug that has been incorporated by the WHO as an effective option for first-line regimens in adults and children over the age of 5. There is need for close monitoring of renal toxicity and bone mineralisation for the age group 5 – 10.

Dosing: Refer to Annex K for dosing chart.

Zidovudine

Zidovudine (AZT) is a thymidine analogue in the NRTI class and is generally well tolerated in children.

Adverse Drug Reactions for Zidovudine

Initial drug-related side effects are common with AZT. Headache, nausea, and fatigue can occur in some children. These symptoms are often transient and AZT should not be discontinued unless they are severe. Bone marrow suppression can also occur. Anaemia usually occurs within four to six weeks and neutropenia can be seen within the first six months. Haemoglobin monitoring before and during the first 3 months of treatment with AZT is thus useful. This is particularly important in Zambia, a country with stable malaria where anaemia is highly prevalent in young children. Anaemia should thus be considered in patients who develop pallor fatigue, shortness of breath or weakness while on Zidovudine. Macrocystosis is almost universal and is not an indication to switch agents or to conduct further diagnostic evaluation. Less common toxicities include cardiomyopathy, myopathy and lactic acidosis.
AZT has also been associated with metabolic complications of therapy, including lipodystrophy. Large volumes of AZT liquid formula are often poorly tolerated. ABC can be substituted for AZT in the event of intolerance to the latter and vice versa. As noted above, AZT should never be administered in combination with d4T a drug that has been phased out.

**Formulations for Zidovudine**
AZT is available in tablets of 300mg and as FDCs (AZT/3TC, AZT/3TC/NVP). Tablets may be crushed and dispersed in water or onto a small amount of food and immediately ingested.
Dosing: Refer to Annex K for dosing chart.

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
NNRTI-based regimens are now the most widely prescribed combinations for initial therapy. They are potent, i.e. they rapidly reduce viral load, but a single mutation can induce cross-class resistance. The NNRTIs Efavirenz (EFV) and nevirapine (NVP) both have demonstrated clinical efficacy when administered in appropriate combination regimens in children. However, differences in toxicity profile, the potential for interaction with other treatments and use of EFV in young children are factors that need to be taken into consideration when choosing an NNRTI.

**Efavirenz**
Efavirenz is generally well tolerated in children.

**Adverse Drug Reactions for Efavirenz**
It is associated with side effects/toxicities related to the central nervous system (CNS), and rash. Children experience vivid dreams, disrupted sleep, agitation, hallucinations, feelings of dissociation, depression and other mood changes. The CNS symptoms typically abate after 10 to 14 days in the majority of patients and can often be alleviated by taking the medication before bedtime. Some patients cannot tolerate these side effects and require a change of treatment.

The most common side effect of EFV in children is rash. It is generally a mild to moderate maculopapular pruritic rash and is seen more frequently in children than adults and usually does not require discontinuation of therapy. In Zambia EFV is recommended for use in children 5 years and above. EFV is metabolised via the cytochrome P450 pathway, but liver dysfunction is not generally associated with EFV use in children. EFV should be avoided in children with a history of psychiatric illness.

**Formulations for Efavirenz**
Efavirenz is available in 200mg (scored) and 600mg tablets. Tablets (200 mg) can be cut in half with a pill cutter.
Dosing: Refer to Annex K for dosing chart.

**Nevirapine (NVP)**
NVP is highly lipophilic and widely distributed in the body. As with EFV, NVP is metabolised via cytochrome P 450. This makes the drug less suitable for treating children who use other hepatotoxic medication, or drugs that can cause rash, or both, such as Rifampicin for the treatment of tuberculosis. NVP is currently the only NNRTI syrup available for infants. It also exists as part of the three-drug FDC (Duovir-N – i.e. AZT/3TC/NVP).

**Adverse Drug Reactions for Nevirapine**
The most common toxicity in adults and children receiving nevirapine is rash. NVP has a higher incidence of rash than other ARVs. Rash may develop in up to 20% of those taking the drug. Skin manifestations are
generally mild to moderate, but two to five percent may need to discontinue therapy because of this side effect. Skin rash can include systemic reactions and can progress to a severe and life-threatening Stevens-Johnson syndrome. Skin manifestations generally occur within the first two to six weeks of treatment. Rash can be minimised by introducing the drug at a reduced dose for 14 days and then increasing to full dose, and this “dose escalation” is the standard of care in the Government of the Republic of Zambia ART programme. If rash occurs, the dose should not be escalated until resolution and the child should be evaluated for systemic symptoms. If rash persists at four weeks of once daily treatment then a single drug substitution should be done. Liver function should be evaluated for rash ≥ grade 2. In general, nevirapine treatment can be continued for grade 1 and 2 toxicities, but should be discontinued for grade 3 or greater.

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

Symptomatic NVP-associated hepatic or serious rash toxicity, while uncommon, is more frequent in women than in men, and more likely to be seen in antiretroviral-naive women with higher CD4 cell count (>250 cells/mm³). NVP should therefore be used with caution in adolescent girls with CD4 count between 250-350 cells/mm³. If used in such adolescent girls, careful monitoring is needed during the first 12 weeks of therapy, ideally including liver enzyme monitoring.

Limited data indicate that both EFV and NVP may interact with oestrogen-based contraceptive pills. It is recommended that sexually active adolescent girls receiving EFV consistently use barrier methods to prevent pregnancy in addition to or instead of oral contraceptives. It is not known if use of preparations such as medroxyprogesterone acetate depot injection, which provide higher blood hormone levels than oral contraceptives, would have contraceptive efficacy compromised. Studies are under way to evaluate interactions between medroxyprogesterone acetate and selected PI and NNRTI drugs.

**Formulation for Nevirapine**

Nevirapine is available in tablet form as 50mg (dispersible), 200mg and syrup. The 200mg tablet is scored and may be divided into equal parts. Tablets may be crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature.

**Dosing:** Refer to Annex K for dosing chart.

**Note:** NVP is always initiated at half the full daily dose for 14 days to minimise the risk of toxicity. If no toxicities (rash, hepatitis) develop, the dose is escalated after two weeks.

**Protease Inhibitors (PIs)**

**Lopinavir/ritonavir**

Lopinavir/ritonavir is a ritonavir boosted protease inhibitor (Lopinavir) that is used as a first-line ARV in infants and young children under the age of 5 years but is used as second-line in older children and adults. It is metabolised through the hepatic cytochrome P450 and is an enzyme inhibitor. Co-administration with rifampicin reduces the levels by 75%.
**Adverse Drug Reactions for Lopinavir/ritonavir**
Lopinavir/ritonavir is generally well tolerated in children. It has been associated with *diarrhoea, nausea and headache*. Like most drugs of the same class LPV/r use can lead to hyperglycaemia, lipid elevations and lipodystrophy.

**Formulations for Lopinavir/ritonavir**
Lopinavir/ritonavir is available as an oral solution 80mg/20mg/ml (Kaletra®), and in tablet form -200mg/50mg and 100mg/25mg (Alluvia®).
The oral solution should be taken with food to increase bioavailability and must be refrigerated until dispensed. After removing from refrigeration, it is stable for 60 days at room temperature (up to 25°C). Where temperatures are expected to exceed 25°C, the feasibility of dispensing smaller amounts and giving more frequent refills should be considered. Dose is calculated based on the Lopinavir component. *The syrup has a bitter taste and burning sensation to the lips.* Oral solution contains Propylene glycol and 42% alcohol. The amount of solution should be rounded up to the nearest ½ ml for easier measurement. Consider using liquid for children in lower weight range. The tablet form is heat stable and can be taken with or without food.

Dosing: *Refer to Annex K for dosing chart.*

---

**Atazanavir/ritonavir**
A protease inhibitor boosted with ritonavir. Metabolized by hepatic cytochrome P450. Requires gastric acidity therefore dose separation is required if using anti-acids, H2 blockers or proton pump inhibitors.

**Adverse drug reactions for Atazanavir/ritonavir**
Causes indirect hyperbilirubinaemia and jaundice which is reversible; nausea, vomiting and abdominal pain may occur.

**Formulations for Atazanavir/ritonavir**
Atazanavir is available as capsules in 100mg, 150mg, 200mg and 300mg. It should be taken with food. The drug is not recommended in children under 6 years.

Dosing is weight based:
- 15-20kg: ATV/r 150/100mg
- 20-40kg: ATV/r 200/100mg
- >40kg: ATV/r 300/100mg

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**Unit 2: ARV Drug Regimens used in Children**
Studies of ART in children demonstrate that similar improvements are seen in morbidity, mortality and surrogate markers with many different potent ARV regimens as in adults. The preferred option when choosing a first-line regimen for infants and children up to 5 years of age is a reverse transcriptase inhibitor (RTI)-based regimen, which consists of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one protease inhibitor (PI). For children above 5 years, the preferred first line regimens of two nucleoside reverse transcriptase inhibitors (NRTIs) plus one non-nucleoside reverse transcriptase inhibitors (NNRTIs).
Advantages
NRTI/PI-based regimens are efficacious and generally well tolerated. Generic formulations are more often available.

Disadvantages
Disadvantages include need for refrigeration (LPV/r), need for different half-lives and limitation to future options.

Initial ARV Regimens for Children
The first-line ARV regimens are all highly active. They balance efficacy, toxicity, and logical sequencing of treatments to maintain future options and cost-effectiveness. We have prioritised the use of NRTIs/PIs combinations as highly active regimen that is potent and has a well established, tolerable side effects profile. Lopinavir which is a PI is now the drug of choice for children < 5 years. For children 5 years and above, TDF/XTC/EFV once daily FDC is recommended if available. If there is no suitable preparation, stand-alone drugs should be given. If the paediatric TDF is not available, then the alternative first line using ABC should be used in its place.

Table 22: Summary of Recommended First-line ARV Regimens

<table>
<thead>
<tr>
<th>Specific Populations</th>
<th>Description</th>
<th>Preferred 1st line cART</th>
<th>Alternative regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children</strong> (6 weeks to &lt;3 months old)</td>
<td>First-line</td>
<td>AZT + 3TC + LPV-r</td>
<td>After 3 months substitute to preferred 1st line with ABC</td>
</tr>
<tr>
<td>HIV and TB co-infection</td>
<td>AZT + ABC + 3TC</td>
<td>After 3 months, switch to ABC+3TC+EFV; after completion of ATT, switch to preferred 1st line with LPV/r</td>
<td></td>
</tr>
<tr>
<td><strong>Children</strong> (3 months to &lt;5 years old)</td>
<td>First-line</td>
<td>ABC + 3TC + LPV/r*</td>
<td>AZT + 3TC + LPV-r</td>
</tr>
<tr>
<td>HIV and TB co-infection</td>
<td>ABC + 3TC + EFV</td>
<td>After completion of ATT, switch to preferred 1st line with TDF + XTC + LPV-r</td>
<td></td>
</tr>
<tr>
<td><strong>Children</strong> (5 to &lt;10 years old)</td>
<td>First-line (NO history of maternal sdNVP; maternal NVP monotherapy; mother unsure of tail coverage)</td>
<td>TDF + XTC + EFV (weight-based dosing)</td>
<td>TDF + XTC + NVP† (weight-based dosing)</td>
</tr>
<tr>
<td><strong>Adolescents</strong> (10 to &lt;19 years old) weighing &lt; 35 kg</td>
<td>First-line: A once-daily fixed-dose combination is recommended.</td>
<td>TDF + XTC + EFV</td>
<td>TDF + XTC + NVP† or ABC + 3TC + EFV</td>
</tr>
<tr>
<td><strong>Adolescents</strong> (10 to &lt;20 years old) weighing ≥ 35 kg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For NVP initiation, refer to section below: Practical Hints for EFV or NVP Initiation.

The use of a triple NRTI regimen (i.e. AZT/d4T plus 3TC plus ABC) can be considered as an option for simplifying initial therapy in special circumstances but has somewhat lower virological potency compared to a two-class triple drug combination in adult studies and therefore its use is currently restricted to special circumstances, in particular for infants and children receiving TB treatment.
NRTI Drug Combinations to be Avoided

**TDF +3TC + ABC** - these drugs are associated with high incidence of early virologic failures

**Notes**
Data from three clinical trials involving the combination of TDF +3TC +ABC demonstrated high rates of virologic failure and drug resistance. In light of these concerns, and the lack of clinical data, this NRTI backbone should not be used in treatment-naive patients. Another report confirms that ABC and TDF select for K65R mutation, which reduces susceptibility to both drugs.

**Exercise A**
1. How are ARVs classified?
2. What are the sites and modes of action of antiretroviral drugs?
3. What are the recommended first-line drugs?
4. A six month infant has both pulmonary TB and severe immune deficiency, what would be the choice of first-line ARVs?
5. A two year old girl with clinical WHO stage 2 condition has a CD% of 11%. Which ARV regimen would you recommend?
6. What would be the choice of first-line ARV regimen for a 15 year old adolescent?
7. What would be the choice of first-line ARV regimen for a severely immune compromised six year old with PTB?

*When you finish the Exercise discuss your answers with your facilitator; thereafter read your module on “Adverse effects of ARV drugs” and then do Exercise B followed by case studies.*

**Unit 3: Adverse effects of ARV drugs**
Differentiating between complications of HIV disease and toxicity (i.e. also known as adverse events) secondary to ARV drugs used for the management of HIV infection is sometimes difficult. Alternative explanations for the “adverse effects” must be excluded before it is concluded that they are secondary to the ARV drug. Alternative explanations for an observed toxicity could include a concurrent infectious process (for example, common childhood illnesses including hepatitis A virus infection in a child with symptoms of hepatitis, or malaria in a child with severe anaemia), or a reaction to a non-ARV drug that is being given concurrently with the ARV drugs (such as isoniazid-induced hepatitis in a child on tuberculosis treatment or Cotrimoxazole-induced rash in a child receiving Cotrimoxazole preventive therapy).

*Adverse reactions that have non-ARV drug aetiology do not require change of the ARV drug.* The full spectrum of ARV toxicities observed in adults has also been reported in children. However, some toxicities observed in adults are less common in children e.g. TDF renal toxicity is more common in adults than children.

**ARV Drug Adverse Effects**
Table 23: ARV Drug Adverse Effects

<table>
<thead>
<tr>
<th>Class</th>
<th>Adverse Effects</th>
<th>Overlapping Adverse Effects</th>
</tr>
</thead>
</table>
| NRTI  | Mitochondrial dysfunction; including lactic acidosis, hepatic toxicity, pancreatitis, and peripheral neuropathy (the NRTIs differ in their ability to affect mitochondrial function, with d4T having greater toxicity than AZT, and 3TC or ABC even less so) | Bone marrow depression  
• AZT  
• Ganciclovir  
• Cotrimoxazole  
• Peripheral neuropathy  
• d4T  
• Isoniazid |
| NNRTI | • Rash  
• Fever  
• Nausea  
• Diarrhoea  
• Hepatotoxicity | Bone marrow depression  
• AZT  
• Ganciclovir  
• Cotrimoxazole  
• Peripheral neuropathy  
• d4T  
• Isoniazid |
| PI    | • Lipodystrophy  
• GI intolerance  
• Metabolic abnormalities e.g. hyperglycaemia, hyperlipidaemia, insulin resistance, and diabetes mellitus osteopenia, osteoporosis, and osteonecrosis  
• Lipid abnormalities | Diarrhoea  
Co-trimoxazole |
| Non-Class-related | • Haematological adverse events from drug induced bone marrow suppression, most commonly seen with AZT therapy (anaemia, neutropenia, and more rarely thrombocytopenia).  
• Osteopenia, osteoporosis, and osteonecrosis)  
• Allergic reactions such as skin rashes and hypersensitivity reactions, more common with the NNRTI drugs but also seen with certain NRTI drugs, such as ABC. Once hypersensitivity reaction to ABC has occurred, it should not be used again |  

Table 24: Severe Toxicities Associated with First-line Antiretroviral Drugs

<table>
<thead>
<tr>
<th>First-line ARV drug</th>
<th>Most frequent significant toxicity for the ARV drug</th>
<th>Suggested first-line ARV drug substitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>Hypersensitivity reaction</td>
<td>AZT</td>
</tr>
<tr>
<td>AZT</td>
<td>Severe anaemia or neutropenia</td>
<td>ABC</td>
</tr>
<tr>
<td></td>
<td>Lactic acidosis</td>
<td>ABC</td>
</tr>
<tr>
<td></td>
<td>Severe gastrointestinal intolerance</td>
<td>ABC</td>
</tr>
<tr>
<td>TDF</td>
<td>Renal toxicity</td>
<td>AZT</td>
</tr>
<tr>
<td>LPV</td>
<td>Hyperlipidemia, hyperglycaemia, Severe gastrointestinal intolerance</td>
<td>RAL</td>
</tr>
<tr>
<td>EFV</td>
<td>Persistent and severe central nervous system toxicity</td>
<td>NVP</td>
</tr>
<tr>
<td></td>
<td>Potential teratogenicity (adolescent girl in 1st trimester pregnancy or of childbearing potential not receiving adequate contraception)</td>
<td></td>
</tr>
</tbody>
</table>
### NVP

<table>
<thead>
<tr>
<th>Hypersensitivity reaction</th>
<th>Severe or life-threatening rash (Stevens-Johnson Syndrome)</th>
</tr>
</thead>
</table>

**EFV**

- a third NRTI (disadvantage, maybe less potent) or
- PI (disadvantage, premature start of 2nd line ARV drug)

**Notes:**

- 3TC/FTC-associated pancreatitis has been described but is considered very rare in children.
- Exclude malaria in areas of stable malaria.
- Defined as severe haematological abnormality that can be life-threatening and that is refractory to supportive therapy.
- Defined as severe, refractory gastrointestinal intolerance that prevents ingestion of ARV drug regimen (e.g. persistent nausea and vomiting).
- ABC is preferred in this situation; however, where ABC is not available AZT maybe used.
- Defined as severe central nervous system toxicity such as persistent hallucinations or psychosis.
- Symptomatic NVP-associated hepatic toxicity is very rare in HIV-infected children prior to adolescence.
- EFV is not currently recommended for children <3 years of age or <10kg, and should not be given to post pubertal adolescent girls who are either in 1st trimester of pregnancy or are sexually active and not using adequate contraception.
- Severe rash is defined as extensive rash with desquamation, angioedema, or serum sickness-like reaction; or a rash with constitutional findings such as fever, oral lesions, blistering, facial oedema, conjunctivitis; Stevens-Johnson Syndrome can be life-threatening. For life-threatening rash, most clinicians would not substitute EFV due to the potential for NNRTI-class specific toxicity.
- The premature introduction of the PI class of drugs in first-line regimens leads to limitations in the choice of drugs in the event of treatment failure (i.e. second-line regimens; see Section XI).

### Table 25: WHO Grading of Adverse Effects

<table>
<thead>
<tr>
<th>Grade 1: Mild</th>
<th>Grade 2: Moderate</th>
<th>Grade 3: Severe</th>
<th>Grade 4: Life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema, Pruritus</td>
<td>Diffuse maculopapular rash or dry desquamation</td>
<td>Vesiculation or moist desquamation or ulceration</td>
<td>Any one of: mucous membrane involvement, suspected Steven-Johnson syndrome (TEN), erythema multiforme, exfoliative dermatitis</td>
</tr>
</tbody>
</table>

**Hepatotoxicity (ALT, AST)**

<table>
<thead>
<tr>
<th>Value</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.25-2.5 × ULN</td>
<td>&gt;2.5-5.0 × ULN</td>
<td>&gt;5.0-10.0 × ULN</td>
<td>&gt;10.0 × ULN</td>
<td></td>
</tr>
</tbody>
</table>

**Renal Impairment (Creatinine)**

<table>
<thead>
<tr>
<th>Value</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.0-1.5 × ULN</td>
<td>&gt;1.5-3.0 × ULN</td>
<td>&gt;3.0-6.0 × ULN</td>
<td>&gt;6.0 × ULN</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** for grading of other toxicities refer to Annex E.
Principles of Management of Adverse Drug Effects

Table 26: Guiding Principles in the Management of ARV Drug Toxicity

<table>
<thead>
<tr>
<th>Guiding Principles in the Management of ARV Drug Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Determine the seriousness of the toxicity.</td>
</tr>
<tr>
<td>2. Evaluate concurrent medication and establish whether</td>
</tr>
<tr>
<td>the toxicity is due to (an) ARV drug(s) or due to another</td>
</tr>
<tr>
<td>non-ARV medication taken at the same time.</td>
</tr>
<tr>
<td>3. Consider other disease processes (e.g. viral hepatitis</td>
</tr>
<tr>
<td>in a child who develops jaundice on ARV drugs) because</td>
</tr>
<tr>
<td>not all problems that arise during treatment are due to</td>
</tr>
<tr>
<td>ARV drugs.</td>
</tr>
<tr>
<td>4. Manage the adverse event according to severity.</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Severe life-threatening reactions (Annex E): immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy); reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when patient is stabilised;

Severe reactions: substitute the offending drug without stopping ART;

Moderate reactions: consider continuation of ART as long as feasible; if patient does not improve on symptomatic therapy, consider single drug substitutions (a)

Mild reactions are bothersome but they do not require change in therapy.

Stress maintaining adherence despite toxicity for mild and moderate reactions.

If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilised.

Toxicity can be monitored clinically on the basis of child/guardian reporting and physical examination, and assessed also through a limited number of laboratory investigation tests, depending on the specific ARV combination regimen that is utilised and the healthcare setting. Routine laboratory monitoring, although desirable, is not required and cannot be carried out in many decentralised facilities.

The decision about the potential need to stop drugs or to substitute a new ARV drug for drug associated toxicity largely depends on the ability to attribute the toxicity to a specific ARV drug in the treatment regimen and on the severity of the toxicity symptoms. Given the limited number of paediatric ARV drugs and drug combinations currently available in Zambia, it is preferable to pursue drug substitutions where feasible, so that premature switching to completely new alternative regimens is minimised and also to restrict drug substitutions to situations where toxicity is severe or life-threatening.

As a general principle, mild toxicities do not require discontinuation of therapy or drug substitution, and symptomatic treatment may be given (e.g. antihistamines for a mild rash). Some moderate or severe toxicities may require substitution of the ARV drug associated with toxicity with a drug in the same ARV class but with a different toxicity profile, but do not require discontinuation of all ART. Severe life-threatening toxicity requires discontinuation of all ARV drugs and initiation of appropriate supportive therapy (such as intravenous fluids) depending on the toxicity, with substitution of another drug for the drug associated with the toxicity once the patient is stabilised and the toxicity is resolved. NNRTI drugs have a much longer half-life than NRTIs, leading to a concern that stopping all drugs simultaneously leads to exposure to drugs from the NNRTI class only. However, if the child has a life-threatening toxicity, all ARV drugs should be stopped simultaneously until the patient is stabilised. Clinical examination can also detect toxicities that are not life-threatening and that may appear late (months to years after therapy has been started), such as lipodystrophy. In such cases, referral to district or provincial hospital ART centres or consultation with an HIV expert is recommended for management.
Regardless of their severity, adverse events may affect adherence to therapy and a proactive approach to managing toxicity is recommended. Discussing the potential side effects of the ART regimen, prior to therapy initiation and during the early stages of treatment, with the child and his/her caregiver, as well as support during minor and moderate adverse events, can increase the likelihood of adherence to therapy. Most ARV drug toxicities are time-limited and symptoms resolve while ART is being continued. Nevertheless, the child and his/her caregiver should be familiar with signs of toxicities that are serious and require immediate contact with the provider and potential drug discontinuation. This is particularly important for toxicities that can be life-threatening if the ARV drug is not discontinued, such as NVP-associated Stevens Johnson Syndrome or symptomatic hepatitis or ABC-associated hypersensitivity reaction. As part of management, all adverse effects requiring a change in ART, cessation of ART, significant disability or death should be reported in the adverse effects register.

Exercise B
1. How is monitoring of ARV drug toxicity carried out?
2. How is grading of ARV drug toxicity classified?
3. What are the general principles of managing ARV drug toxicities?

Case Studies
1. Mumba, a five year old boy, was staged as clinical WHO stage 3 and his absolute CD4 cell count was 180 cells/mm$^3$. He was started on TDF/FTC/EFV, and the caregiver was told to watch out for adverse effects if any. After five days of treatment he was brought in with severe rash.
   a) What steps will you take in evaluating this child?
   b) Upon examination you find that the rash is severe but not life-threatening what would be your next move?
2. Maria, a three year old girl weighing 14 kg with confirmed lymphadenopathic Kaposi sarcoma (KS) is staged as clinical WHO stage 4. You start her on ABC+3TC+ LPV/r. After a week on treatment, the child develops severe gastrointestinal intolerance. She is vomiting all food taken, including water. She has no diarrhoea and her temperature is 36$^\circ$C. The child is severely dehydrated.
   a) What do you think is wrong with Maria?
   b) What action do you take?

When you finish the Exercise discuss your answers with the facilitator, thereafter read your module on “Paediatric Standard Operating Procedures in Annex 1 and 2 covering the first and second visits to a paediatric ART clinic” in readiness for a role play to be conducted. Thereafter you will be advised on when to proceed to Module 6 on “Antiretroviral Drug Therapy for Infants and Children”.

M5-12
Module 6
Antiretroviral Therapy for Infants and Children
Learning Objectives
At the end of this module the health worker should be able to understand:
1. Goals of antiretroviral therapy
2. Initiation of antiretroviral therapy in children
3. Monitoring children on antiretroviral therapy
4. Principles of Substitution, Switching and Stopping of antiretroviral drugs
5. Drug Resistance
6. Adherence Counselling

Listen to the presentation or read your modules on “Antiretroviral Drug Therapy for infants and Children” and then do Exercise A.

Unit 1: Goals of ARV therapy

The use of combination antiretroviral treatment (cART) has dramatically reduced HIV-associated mortality and morbidity among children and adolescents and transformed paediatric HIV from being a debilitating and rapidly fatal infection of early childhood to a manageable chronic disease. Many children with perinatal HIV infection are growing into adolescence and early adulthood. However, the complexities of making a definitive diagnosis early delays the use of the potentially lifesaving ARVs. HIV has a rapid disease course with about 50% of children are dead by their second birthday without an intervention.

Several challenges in the use of ARVs in children include:
• Complexities of identifying the HIV-exposed child (infant HIV diagnosis)
• Weight/size-based dosing
• Limitations of paediatric formulations
• Limited paediatric expertise and experience
• Overwhelming burden of disease in adult population and few vocal paediatric advocates.

The goals of ARV therapy are to:
• Maximal and durable suppression of HIV replication
• Restoration and preservation of immune function
• Restore normal growth and development
• Improve quality of life
• Reduced morbidity and mortality

The first ARV regimen should be both potent and durable. If adherence is adequate, clinical and immunologic benefits should be long lasting. Changing ARV medication should be done with caution; resistance and cross-resistance are important considerations, and ARV sequencing can have significant impact on future options and premature changes also risk exhausting future options.

The underlying principles of antiretroviral therapy (ART) in children are largely the same as in adults.
• Use a combination of ARVs (minimum of three*) because the use of combinations of drugs have demonstrated to have durable treatment success. Dual and particularly mono-therapy should never be used
• Use drugs from more than one class – triple nucleoside combination is inferior to the standard two class recommended regimens
• Preserve future treatment options since treatment is life-long
• Use a regimen demonstrated to have durable treatment success
• Avoid drugs with overlapping toxicities and drug-drug interactions
• Starting ART is not an emergency.
a. Prior to initiation of ART, it is important to deal with, and stabilise present co-morbidities (e.g. TB, liver disease, malaria, pneumonia, severe anaemia etc) as a priority

b. Patient preparation is critical and maximum adherence is essential for successful ART

c. As much as possible, treatment should be planned and started in good time

- Maximum adherence is essential for successful ART
- The best chance of success with ARV therapy is the choice of the first-line regimen. The choice of drugs should take into account
  a) Efficacy
  b) Tolerability
  c) Dosing schedule
- ART is one component of comprehensive HIV care and it works best when the other components are also maximised (prophylaxis, nutrition etc).
- ARVs are not a cure

The regular follow-up and monitoring is essential. ARV drugs are associated with adverse events and drug-drug interactions; treatment should be stopped or changed when necessary. It is also very important to provide continued support to the patient (and family).

Key Issues in Paediatric ART
Patient Readiness

*Readiness for ART is especially complex because successful treatment requires the collaboration of both children and their caregivers.* Not only must a child agree to take (or cooperate with taking) the medication, an adult must administer or supervise administration once or twice daily. In some cases this requires little preparation. In others, a significant amount of patient support is needed before ART can be prescribed. Adherence is discussed in greater detail in Unit 5 of this module.

- *Children are not little adults and are not always supervised by their parents or primary caregivers.*
- *Involvement of children in their own care is critical to successful treatment.*

Minimising viral resistance

Providers can play an important role in minimising the occurrence of HIV resistance by assisting patients to optimise adherence and by maintaining good prescribing practices.

- Never prescribe ARVs to a child in the absence of adherence preparation and support (family preparedness). ART is never an emergency. Work with families to minimise barriers to medication adherence.
- Pay meticulous attention to other medication and treatments and their potential to interact with ARV therapies.
- Never prescribe mono-therapy or dual therapy for treatment of chronic HIV infection.
- Never add a single drug to a failing regimen.
- Follow protocols with care when switching or stopping ARVs.

ART dosing

Unlike adults, for whom standard doses are usually prescribed, dosing *requirements for children vary with age and size (weight and/or body surface area).* Children must be measured (weight and height) at each visit, and the dose of treatment recalculated as the child grows. Puberty is another time of changing metabolic requirements, as dosing moves from paediatric to adult guidelines.

*In infants and children it is also important to consider:*

- Availability of a suitable formulation that can be taken in appropriate doses
- Simplicity of the dosing schedule
- Taste/palatability and hence compliance in young children
Unit 2: Initiation of ART in children

All children <15 years of age are eligible for cART irrespective of WHO staging and CD4 count or CD4%.

ART should never be initiated without preparation of the child and family for the complex task of long-term therapy. Similarly, ART should never be prescribed without assuring a secure drug supply, as unplanned interruptions of treatment can lead to therapeutic failure. The decision-making process for initiation of ART in children relies on a confirmed HIV diagnosis. The decision about when to start ART should also involve an evaluation of the social environment of the child needing therapy. This should include the identification of a clearly defined caregiver who understands the prognosis of HIV and the implications of ART (i.e. the fact that it is a life-long therapy; the implications of non-adherence; administration, toxicity and storage of drugs). Identification of a secondary (back-up) informed caregiver is also important when making decisions about the initiation of ART.

A comprehensive evaluation of the patient will guide the health provider in ensuring that there are no contraindications to initiating the child on cART

Pre-initiation tasks

History Taking
- Confirm the presence of HIV infection if not already confirmed or documented
- Review previous ARV exposure (e.g. PMTCT prophylaxis)
- Assess for presence of infections
- Review concomitant medication
- Review nutritional history and refer for nutritional support as required

Social requirements prior to cART
- Identify and fully counsel caregiver; take time, allow questions
- Confirm availability of support systems; family, social etc.
- Discuss disclosure to the infected child and to significant others

Special considerations:
Sexually active adolescents: assess for pregnancy; contraception need and efficacy of contraception choice

Physical examination

Prior to ART, apart from the history taking do a physical examination and ensure to:
- Complete a clinical assessment by ticking on the WHO staging chart found in your child baseline/follow-up form
- Evaluate for any existing illness:
  a) Screen for TB and include a CXR if available
  b) STI screening if an adolescent
- Conduct a neuro-developmental assessment
- Assess the nutritional status: weight, length/height and head circumference, surface area. Chart growth
- Assess for presumptive severe HIV disease for children <18 months without a virologic diagnosis.
**Laboratory**
- Full blood count including differential
- Liver function test (ALT/AST)
- Renal function test (Creatinine) and calculate Creatinine Clearance (CrCl)
- CD4 count or CD4%
- Other tests as indicated by presenting symptoms

**Exercise A**
1. What are the goals of treatment with ARV drugs?
2. Write down the underlying principles of ART?
3. You are an ART Programme Manager, what factors are you going to consider when choosing an ARV regimen for infants and children?
4. What are the key issues in the use of paediatric ART?
5. A two year old child with WHO stage 4 has CD4% of 12%. Outline your activities prior to initiating treatment at baseline.

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on "Presumptive diagnosis of HIV infection in Infants and Toddlers " and then do Exercise B.

**Presumptive Diagnosis of HIV Infection in Infants and Toddlers**
For situations where access to virological testing is not yet available, HIV disease in a child younger than 18 months of age can be presumptively diagnosed using clinical criteria of severe HIV disease to allow appropriate management of the potentially HIV-infected child. Use of a presumptive clinical diagnosis of infection should be accompanied by immediate efforts to establish the HIV diagnosis. Collect a DBS and send the specimen to your nearest reference laboratory for DNA PCR. Decisions on further treatment should be adjusted at that time by the results. For infants and children started on ART based on a presumptive clinical diagnosis of severe HIV disease, therapy should be closely monitored. In those infants and children who are no longer exposed to HIV (i.e. through breastfeeding from an HIV-infected mother) and where HIV infection can be confidently ruled out ART should be stopped. Use of clinical criteria to make a presumptive diagnosis of HIV infection is not needed in children ≥18 months of age as antibody testing establishes HIV status.

**Table 27: Presumptive Diagnosis of Severe HIV Disease**

| A presumptive diagnosis of severe HIV disease should be made if: | • The infant is confirmed HIV antibody positive; and  
• Diagnosis of any AIDS-indicator condition(s) can be made; or  
• The infant is symptomatic with two or more of the following  
  a) Oral thrush  
  b) Severe pneumonia  
  c) Severe sepsis  
| Other factors that support the diagnosis of severe HIV disease in an HIV sero-positive infant include: | • Recent HIV-related maternal death; or advanced HIV disease in the mother;  
• CD4 < 25% |

Confirmation of the diagnosis of HIV infection should be sought as soon as possible.
Exercise B
1. When is a presumptive diagnosis of severe HIV disease made?
2. Mwika is a 10 month old baby whose mother died when Mwika was eight weeks old. She presented to the health facility with failure to thrive with delayed milestones and is hypertonic in all four limbs and has a marked head lag. She weighs 4 kg, cannot sit unsupported and has extensive oral thrush. Her rapid HIV test is positive but her clinic has no access to virologic test.
   a) What is the likely diagnosis and why?
   b) How would you treat Mwika?

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on “Combination ART, Contraindications to first-line ARVs and Switching of Regimens” and then do Exercise C.

Combination Anti-Retroviral Therapy

Table 28: Combination Anti-Retroviral Therapy

<table>
<thead>
<tr>
<th>Combination Antiretroviral Therapy (cART) is the combination of at least three or more ARV drugs from at least 2 classes:</th>
<th>Two Nucleoside Reverse Transcriptase Inhibitors (NRTI) PLUS One Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td>Two Nucleoside Reverse Transcriptase Inhibitors (NRTI) PLUS One Protease Inhibitor (PI)</td>
<td></td>
</tr>
</tbody>
</table>

The first-line RTI based regimen is preferred because it is:
- Efficacious; less expensive
- Cold chain is not required
- Potent PIs are preserved for failures

The principle of a combination selection is:
- Enhancing potency and durability
- Minimizing the chances of resistance

Primary First and Second Line ARVs

Table 29: Primary First and Second Line ARVs

<table>
<thead>
<tr>
<th>Nucleoside Reverse Transcriptase Inhibitors (NRTIs) &amp; Nucleotide Reverse Transcriptase Inhibitors (NtRTIs)</th>
<th>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</th>
<th>Protease Inhibitors (Pis)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTI</strong></td>
<td>Tenofovir (TDF)</td>
<td>Efavirenz (EFV)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>Nevirapine (NVP)</td>
<td>Atazanavir-r (ATV-r)</td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>Abacavir (ABC)</td>
<td></td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What to Start with for HIV-1

Table 30: What to Start with for HIV-1

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Preferred 1st line HAART</th>
<th>Alternative if contraindications to preferred HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0 to &lt;3 months old)</td>
<td>AZT + 3TC + LPV-r</td>
<td>(Defer until 3 months old)</td>
</tr>
<tr>
<td>Children (≥3 to &lt;59 months old)</td>
<td>ABC + 3TC + LPV/r*</td>
<td>ABC + 3TC + EFV or AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>During ATT only:</td>
<td>ABC + 3TC + AZT</td>
</tr>
<tr>
<td>Children (5 years to &lt;10 years old)</td>
<td>TDF + XTC + EFV (weight-based dosing)</td>
<td>TDF + XTC + NVP or ABC + 3TC + EFV (weight-based dosing)</td>
</tr>
<tr>
<td>Adolescents weighing &lt; 35 kg</td>
<td>TDF + XTC + EFV</td>
<td>TDF + XTC + NVP or ABC + 3TC + EFV</td>
</tr>
<tr>
<td>Adolescents (10 to 19 years) or weighing ≥ 35 kg</td>
<td>TDF + XTC + EFV</td>
<td>TDF + XTC + NVP or ABC + 3TC + EFV</td>
</tr>
</tbody>
</table>

What to start with for HIV-2

Table 31: What to start with for HIV-2

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Preferred 1st line HAART</th>
<th>Second-line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>ABC or TDF or AZT + 3TC* + LPV/r</td>
<td>AZT + 3TC* + RAL or DRV/r (consult ATC**)</td>
</tr>
</tbody>
</table>

Unit 3: Monitoring children on ART

Careful monitoring is an essential component of effective ARV use, permitting early detection of adverse effects, on-going reinforcement of adherence, and periodic assessment of treatment efficacy. The type and frequency of monitoring is dependent on local resources.

Dosing of ART

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

Infants and young children often metabolise medication very rapidly. For some medication, the daily dose is greater for children than for adults. It is generally recommended that children continue to receive paediatric dosing throughout the course of pubertal development. Paediatric dosing guidelines should be followed until full physical maturity is reached (Tanner stage IV-V), at which point standard adult dosing should be used.
The purpose for monitoring is to:
• Evaluate treatment response and diagnose treatment failure early
• Evaluate adherence
• Screen for pulmonary TB
• Detect toxicity to ARV drugs

Areas for monitoring therapy
• Clinical
• Laboratory
• Treatment adherence
• Appointment adherence
• Psychological

Clinical monitoring schedule

Clinical Reviews
• Every 2 weeks for the first 4 weeks
• Then every 4 weeks until week 12
• Thereafter:
  a) For children < 24 months – monthly
  b) For children ≥ 24 months – every 3 months once stable on therapy
  c)

Clinical monitoring
First visit after ARV initiation: family education
• Review understanding of HIV: disease process and adherence strategies
• Observe accurate dosing and administration of drugs by caregiver
• Full clinical assessment
• Return visit in two weeks if no problems, sooner if there are problems i.e. rash & other Adverse drug reactions

Monthly clinical monitoring

• Interval medical history, symptom check
  a) Weight, height, head circumference, physical exam, nutritional assessment
  b) Side effects/toxicity, immune reconstitution
  c) Assess adherence
• Ask for demonstration of dose and administration of medication at each visit
• Recalculate dose
• Dispense more doses
Monitoring Schedule

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Initiate ART. Dispense two weeks’ worth of medication.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ensure that patient/family know what to do in the event of new symptoms or problems</td>
</tr>
<tr>
<td>Week 2</td>
<td>Monitoring for toxicity and adherence</td>
</tr>
<tr>
<td></td>
<td>Adherence assessment and support</td>
</tr>
<tr>
<td>Week 4</td>
<td>Symptom checklist (and targeted physical examination if needed).</td>
</tr>
<tr>
<td></td>
<td>Adherence assessment and support</td>
</tr>
<tr>
<td></td>
<td>Dispense two weeks’ worth of ART</td>
</tr>
<tr>
<td>Week 8</td>
<td>Symptom checklist</td>
</tr>
<tr>
<td></td>
<td>Comprehensive physical examination – recalculate ART dosing based on new height/weight</td>
</tr>
<tr>
<td></td>
<td>Adherence assessment and support</td>
</tr>
<tr>
<td></td>
<td>Dispense one week’s worth of ART</td>
</tr>
<tr>
<td>Week 12</td>
<td>Symptom checklist</td>
</tr>
<tr>
<td></td>
<td>Comprehensive physical examination – recalculate ART dosing based on new height/weight</td>
</tr>
<tr>
<td></td>
<td>Adherence assessment and support</td>
</tr>
<tr>
<td></td>
<td>Dispense ART – if patient is doing well and adherence is excellent, consider dispensing two months’ worth of ART.</td>
</tr>
</tbody>
</table>

After the 12-week initiation period, children who are doing well may be seen once every two months or according to the schedule. Adherence should be reviewed with the parent/caregiver as well as the older child at every visit.

**Laboratory Monitoring**

With the exception of children who begin therapy with baseline laboratory abnormalities (elevated liver function, anaemia, neutropenia), laboratory monitoring for ART toxicity is not routinely recommended. Abnormal findings on history or physical examination should, however, prompt appropriate laboratory investigation at the discretion of the treating clinician. Furthermore, if a child begins therapy with baseline laboratory abnormalities (particularly elevated liver function tests) it may be prudent to monitor laboratory values until abnormalities resolve or are determined to be stable. Below is a recommended schedule.

**Table 33: Laboratory Recommendations**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Laboratory Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>At minimum</td>
<td>Haematocrit</td>
</tr>
<tr>
<td>Preferable</td>
<td>FBC (including total lymphocyte count), LFT’s, CD4 count</td>
</tr>
<tr>
<td>If available</td>
<td>Lipid profile, Blood glucose</td>
</tr>
<tr>
<td>Optional</td>
<td>Viral load</td>
</tr>
<tr>
<td>Special</td>
<td>Children on NVP</td>
</tr>
<tr>
<td>considerations</td>
<td>ALT at baseline, at 3 months; thereafter as clinically indicated</td>
</tr>
<tr>
<td></td>
<td>Children on AZT</td>
</tr>
<tr>
<td></td>
<td>Hb at baseline, at 4 weeks, at 12 weeks; thereafter as indicated</td>
</tr>
</tbody>
</table>
Calculation of Creatinine Clearance (CrCl)

• All creatinine orders to the laboratory should include age, sex and weight
• If unable to perform Creatinine, specimens should be sent to nearest facility where test can be performed,

Adherence

Adherence: single most important strategy for long term success and sustainability of patients on ART. It is important to control HIV infection and to prevent resistance to ART. Treatment failure is generally a failure with adherence and efforts to ensure good adherence from the onset of ART initiation must be mandatory.

Adherence refers to taking medicines as prescribed i.e. the correct medicine of acceptable quality, in the correct quantity at the same correct time(s) for the correct duration. The patient should not skip doses; stop and re-start treatment without medical advice and should adopt a health seeking behavior

Adherence principals for children include:
• Involving children in their own ART care is important
• Developmental changes of children and their effects in adherence should be anticipated and addressed.
• Primary care givers are the principal care givers for children and should therefore ensure adherence
• Dosing schedule should be simple and able to fit into the schedules of the primary care givers.
• Access to child friendly ARVs is crucial for adherence.

Psychological

The following psychological parameters should be monitored for all children to ensure normal development and identify risk factors for adherence:
• Progress at school
• Relationships with family members, friends
• Attitude to daily drug taking, adherence
• Progress of disclosure
• Development into adolescence – sexual awareness, behavioural issues

Possible events and outcomes in the first six months of Art

• Clinical response – clinical response can be measured by improving WHO staging, growth parameters, improving developmental milestones
• Allergic reaction – These can be in the immediate post ARV initiation period or can happen later. Therefore, physical examination is important.
• CD4 recovery - In most children, CD4 count rises with successful therapy, unless therapy was started with a high CD4. However, in some children, severe immunosuppression may persist. The lower the CD4 level at start of therapy, the slower the recovery
• ARV toxicity - Toxicities may be classified as early toxicities occurring in the first few weeks to months and late toxicities, occurring much later. Hypersensitivity reactions may be difficult to distinguish from acute clinical events.
• Immune Reconstitution Inflammatory Syndrome (IRIS) – this is an entity that has been observed in patients starting ART, particularly those with very low CD4 values. Symptoms are similar to those seen in opportunistic infections. They usually occur within the first three months after the start of a potent ART, concurrent with a rapid rise of CD4 values. It is also possible that this immunological reconstitution may lead to the development of atypical presentations of some opportunistic infections. Clinical disease progression should be differentiated from the IRIS.
IF Diagnosis of tuberculosis is in line with WHO recommendations is made before starting ART AND A good initial response to tuberculosis therapy is observed before the patient started on ART

Table 34: Clinical Diagnosis of TB-associated IRIS

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>The onset of tuberculosis-associated IRIS should be within three months of starting ART with at least one major criterion and two minor criteria:</th>
</tr>
</thead>
</table>
| **Major Criteria** | • New/enlarging lymph nodes or other focal tissue enlargement  
                          • New/worsening radiological features  
                          • New/worsening CNS tuberculosis  
                          • New/worsening serositis |
| **Minor Criteria** | • New/worsening constitutional symptoms such as fever  
                          • New/worsening respiratory symptoms such as cough  
                          • New/worsening abdominal pain |
| **Alternative Explanations for Clinical deterioration Excluded** | • Poor adherence to TB therapy  
                          • Failure to TB therapy due to TB drug resistance  
                          • Another OI or neoplasm  
                          • Drug toxicity or drug reaction |
| **Immunological Criteria** | Increase in CD4 count |
| **Virological Criteria** | Decrease in viral load copies since the start of ART |

Mortality - is high in the first six months of ART especially in children with advanced disease.

Unit 4: Principles of Substitution, Switching and Stopping of ARVs

Changing (substitution or switching) or stopping ARVs may be necessary where there is:
- Toxicity
- intolerance on the current therapy
- treatment failure
- Change in treatment guidelines.

**Substitution**
Substitution is the replacement of a drug by another within the same class. This may occur where there is toxicity to an identifiable drug in the regimen. The offending drug can generally be replaced with another drug that does not have the same adverse effect, e.g. substitution of ABC for AZT (e.g. for anaemia) or EFV for NVP (e.g. for CNS toxicity), in the event of toxicity with LPV/r substitute with a triple NRTIs.

Given the limited number of paediatric ARV drug options available in Zambia today, drug substitution should be limited to situations where toxicity is severe or life-threatening.

For NVP-associated Stevens Johnson Syndrome, avoid substituting with EFV due to the potential for recurrence. This would require a change to a protease inhibitor or if this is not feasible to a triple NRTI regimen (i.e. substituting a third NRTI, such as ABC, for NVP). In the case of toxicity, a single drug substitution is indicated. In the case of therapeutic failure, the entire regimen should be changed.
### Table 35: Toxicities and Medical Contraindications to Initiation of First-line ARV Regimen

<table>
<thead>
<tr>
<th>Indication</th>
<th>Definition</th>
<th>Comments</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe anaemia</td>
<td>Hb &lt; 8 g/dl</td>
<td>Contraindication to use of AZT</td>
<td>Use ABC or TDF</td>
</tr>
<tr>
<td>Severe neutropenia</td>
<td>Neutrophil count &lt; 500 cells/mm</td>
<td>AZT use requires close monitoring</td>
<td>Use ABC or TDF</td>
</tr>
<tr>
<td>Severe renal insufficiency</td>
<td>Creatinine &gt; 3 times normal</td>
<td>Contraindication to TDF and caution in AZT, 3TC</td>
<td>Use calculated creatinine clearance. Conduct diagnostic evaluation as per local guidelines and reassess renal function. Expert consultation recommended if available.</td>
</tr>
<tr>
<td>Severe hepatic insufficiency</td>
<td>LFTs &gt; 5 times normal</td>
<td>Contraindication to NVP use</td>
<td>EFV can be initiated in children &gt;3 months. PIs can be used for &lt;3months</td>
</tr>
<tr>
<td>History of prior ARV intolerance</td>
<td>If intolerant of AZT, use ABC Other substitutions may require expert advice.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of prior ARV use (other than PMTCT)</td>
<td>Use of any ARV for &gt;4 weeks</td>
<td>Potential for ARV resistance</td>
<td>Expert management required. Consult local expert, the Advanced Treatment Centre (ATC); for case-by-case advice.</td>
</tr>
<tr>
<td>Current use of rifampicin-containing anti-TB regimen</td>
<td>Use of rifampicin</td>
<td>Drug-drug interactions with NVP</td>
<td>EFV-containing regimen for children &gt;3months of age Consider the use of triple NRTIs in the duration of ATT. This is better done in consultation with senior staff</td>
</tr>
</tbody>
</table>

### Social contraindications

One purpose of multidisciplinary, psychosocial, and adherence assessments is to exclude non-medical contraindications to ARV use and to confirm that children and their families are prepared to take the medication consistently and correctly. While many patients will be ready to begin treatment, identifying modifiable barriers to adherence will enable providers to intervene for others prior to ARV initiation.

### Detection of toxicities

ARV-associated adverse events may be detected by symptoms or laboratory investigation. Some symptoms are mild and/or transient, while others require supportive therapy (such as anti-emetics or anti-motility agents) or more frequent clinical monitoring. Severe side effects may require interruption of ART. When serious toxicity appears to be caused by a specific ARV, a single-drug substitution can be made. In some rare cases however, the entire regimen will need to be changed.

**Drug changes based on laboratory values** should be carefully considered, guided by the clinician’s experience and judgment, and viewed in the clinical context of the patient’s care. No changes should be made on the basis of a single test, although if the laboratory abnormalities are severe (grade 4) the medication should be stopped pending laboratory confirmation. Intercurrent illness may create transiently abnormal laboratory values, as may concomitant medication. Repeat testing should be done and evaluated for trends over time. If a treatment change is indicated, new drugs should not be started until toxicities have resolved to ≤ grade 2.
### Table 36: Clinical Indications to Substituting ARVs due to Toxicity

<table>
<thead>
<tr>
<th>Clinical Indication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Severe discomfort or minimal intake for ≥ 3 days</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Severe vomiting of all foods/fluids in 24 hours or orthostatic hypotension or IV therapy required</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Diarrhoea with orthostatic hypotension or IV therapy required</td>
</tr>
<tr>
<td>Fever</td>
<td>Unexplained fever of &gt; 39.6 °C &gt; 1-2 weeks</td>
</tr>
<tr>
<td>Headache</td>
<td>Severe or requires narcotic therapy</td>
</tr>
<tr>
<td>Rash</td>
<td>Moist desquamation, ulceration, or mucous membrane involvement, suspected Stevens-Johnson (TEN), erythema multiforme, exfoliative dermatitis, or necrosis requiring surgery</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>Angioedema or anaphylaxis</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Severe discomfort, objective weakness, loss of 2–3 previously present reflexes or absence of 2–3 previously present sensory dermatomes</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Normal activity reduced ≥ 50 %</td>
</tr>
</tbody>
</table>

### Table 37: Laboratory Indications to substituting ARVs due to Toxicity

<table>
<thead>
<tr>
<th>Laboratory Tests</th>
<th>Parameter</th>
<th>Grade 3 toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematology</td>
<td>Haemoglobin</td>
<td>&lt; 7.5 g/dl</td>
</tr>
<tr>
<td></td>
<td>Absolute neutrophil count</td>
<td>&lt;500 cells/mm³</td>
</tr>
<tr>
<td>Chemistries</td>
<td>Bilirubin</td>
<td>≥ 3.0–7.5 x upper limits of normal</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>&gt; 1.2–1.5 (&lt;2 yr), 1.7–2.0 (&gt;2yr) x ULN</td>
</tr>
<tr>
<td>Liver Function Tests</td>
<td>AST (SGOT)</td>
<td>&gt; 5 upper limits of normal or rapidly increasing</td>
</tr>
<tr>
<td></td>
<td>ALT (SGPT)</td>
<td>≥ 5 upper limits of normal or rapidly increasing</td>
</tr>
<tr>
<td>Pancreatic Enzymes</td>
<td>Amylase, lipase</td>
<td>≥ 2–3x upper limits of normal</td>
</tr>
<tr>
<td></td>
<td>Lactate</td>
<td>2.5 – 5 mmol/L</td>
</tr>
</tbody>
</table>

### Switching an ARV Regimen in Infants and Children due to Treatment Failure

Switching is the changing of a combination of classes of an ARV regimen to another combination. It is indicated in treatment failure. Successful ARV therapy leads to suppression of HIV replication with associated clinical and immunologic improvements.

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

*Poor adherence, inadequate drug levels, prior existing drug resistance or inadequate potency of the drugs chosen can all contribute to ARV treatment failure.* Genetic differences in drug metabolism may also be important. Wherever possible, treatment failure that is suspected clinically or immunologically should be confirmed virologically. When treatment failure is confirmed, switching to a new second-line regimen becomes necessary.
It is reasonable to expect a symptomatic patient to show significant clinical improvement within three months of initiating treatment. Within six months, CD4 counts can be expected to rise, although the magnitude of the rise in CD4 cell count is dependent on the baseline value (in general, however, one can expect a significant increase in CD4 number/percent for children with adequate viral suppression).

Treatment failure can be defined by using different criteria:
- Virological
- Immunological
- Clinical

The usual sequence for treatment failure is initially virological, followed by immunological and then clinical.

**Virological Failure**

Virological failure is defined as persistent viraemia after 24 weeks (6 months) of cART in an adherent patient: i.e. a VL of >50 c/ml or if detectable after at least 24 weeks cART in a treatment-adherent child. Failure to suppress viral replication results in a detectable viral load.

In children viral load may be detectable at 6-9 months after initiation. This does not necessarily mean treatment failure. The VL should be repeated after 3 months and if still persistently detectable after 12 months consider virological failure. Targeted VL monitoring should be used to confirm suspected treatment failure from immunological and/or clinical criteria.

Since it may not be possible to perform viral loads at all health facilities, all efforts must be made to access it at the nearest reference laboratory however, its availability is not a prerequisite for switching to a second-line ARV regimen.

For the management of a patient with possible virological treatment failure, see figure below:

**Figure 9: Management of Patients with Possible Virological Treatment Failure**
Immunological Failure

Immunological failure is defined as *a drop of the CD4 to values at or below certain age-dependent values (see table 17) or a failure of the CD4 count to rise above these threshold values*. Treatment failure is usually characterised by the development of severe immune deficiency after initial immune recovery.

It is also possible that children on ART may persist at or below their age-related CD4 threshold despite an adequate therapy (at least six months of ART). Immunological criteria for defining treatment failure are supplemental to clinical criteria.

Table 38: Age-related Immunological and Clinical Considerations to Switching to Second-line

<table>
<thead>
<tr>
<th>Criteria</th>
<th>&lt; 2 years of age</th>
<th>≥2 years to &lt;5 years of age</th>
<th>≥5 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO Staging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4%</td>
<td>%CD4+ values fall to &lt;25%</td>
<td>%CD4+ &lt;15%</td>
<td>n/a</td>
</tr>
<tr>
<td>CD4 Absolute</td>
<td>n/a</td>
<td>≥200 cells/μm³ or 50% fall from on-treatment peak or Fall below the baseline CD4 count</td>
<td>≥200 cells/μm³ or 50% fall from on-treatment peak or Fall below the baseline CD4 count</td>
</tr>
</tbody>
</table>

*For children under two years, consultation with experienced clinician is required. Preferably, at least two CD4 measurements should be available. Use of %CD4+ in children <5 years and absolute CD4 counts in those ≥5 years of age is preferred. If serial CD4 values are available, the rate of decline should be taken into consideration.*

Clinical Failure

Clinical failure is the development of either a new or recurrent clinical stage 3 or 4 condition e.g. loss of developmental milestones, oesophageal candidiasis, oral thrush refractory to treatment, malignancies etc. The severe clinical symptoms appear in a child who should have had sufficient time on ART (at least 24 weeks/6 months), with adherence assessed and considered adequately met. The exception is pulmonary TB which may or may not be an indicator of clinical failure and may not require consideration for second-line therapy.

Growth failure is an important presentation of treatment failure. However, before considering changing treatment due to growth failure, it should be ensured that the child is receiving adequate nutrition.

The classification of the *clinical stage of treatment is designated T1-T4*.

The gold standard for diagnosis of treatment failure is a viral load. However, where it is not readily available the following can be used:

- Children with new clinical stage T4 conditions should be considered for switching therapy regardless of CD4 value,
- For children who develop clinical stage T3 conditions, CD4 values are useful in determining the need for switching ART. In such children, if CD4 values are at or below the age-related threshold for severe immunodeficiency following previous immune response to ART, it is recommended to switch to a second-line regimen.
- In children on ART who are clinically well (i.e. clinical stage T1 and T2), switching a regimen should only be considered if two or more CD4 values below the age-related threshold for severe immunodeficiency
are obtained. In such children, if the CD4 value begins to approach the age-related threshold for severe immunodeficiency, increased clinical and CD4 follow-up is warranted.

- CD4 is best performed once the acute phase of the presenting illness is at least 4 weeks post resolution. If there is a modest decline of CD4 %< 5% and no failure to thrive, do not change medication, but maintain close monitoring.

- A regimen switch is not recommended in children at clinical stages T1 - T3 where CD4 values drop but remain above their age-related threshold.

Table 39: WHO Staging System to Guide Switching to Second-line Therapy

<table>
<thead>
<tr>
<th>WHO clinical stage on ART a</th>
<th>Management options b</th>
</tr>
</thead>
</table>
| No new events or PGL T 1   | • Do not switch to other regimen  
• Maintain regular follow-up visits including CD4 |
| Stage 2 events or T 2      | • Treat and manage staging event  
• Do not switch to new regimen  
• Assess and offer adherence support  
• Assess nutritional status and offer support  
• Schedule earlier visit for clinical review and consider CD4 |
| Stage 3 events or T 3      | • Treat and manage staging event and monitor response c, d, e  
• Check if on treatment 24 weeks or more  
• Assess and offer adherence support  
• Assess nutritional status and offer support  
• Check viral load and CD4  
• Consider switching regimen  
• Institute more frequent follow-up |
| Stage 4 events or T 4      | • Treat and manage staging event  
• Check if on treatment 24 weeks or more  
• Assess and offer adherence support  
• Assess nutritional status and offer support  
• Check viral load and CD4  
• Switch regimen while waiting for results  
• Institute more frequent follow-up |

Notes:
Clinical stages in this table refer to a new or recurrent stage at the time of evaluating the infant or child on ART. Annex B provides more details about the revised WHO Paediatric Clinical Staging System. It needs to be ensured that the child has had at least 24 weeks (6 months) of treatment trial; adherence to therapy has been assessed and considered to be adequate prior to considering switching to second-line regimen.
Differentiation of opportunistic infections from immune reconstitution syndrome is important. In considering changing treatment because of growth failure, it should be ensured that the child is not failing to grow due to lack of adequate nutrition, and that any intercurrent infections have been treated and resolved.
Pulmonary or lymph node TB, clinical stage 3 conditions, may not be an indication of treatment failure, and thus not require consideration of second-line therapy; response to tuberculosis therapy should be used to evaluate the need for switching of therapy, if viral load testing is not available.
Table 40: Switching to Second-line Therapy Based on Availability of CD4

<table>
<thead>
<tr>
<th>WHO paediatric Clinical stage on ART&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Availability of CD4 measurements&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Management options</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 and T2&lt;sup&gt;d&lt;/sup&gt;</td>
<td>No CD4</td>
<td>• Do not switch regimen</td>
</tr>
</tbody>
</table>
|                                             | CD4                                         | • Consider switching regimen only if two or more values below age-related threshold for severe immunodeficiency<sup>e</sup> are available  
|                                             |                                             | • Increase clinical and CD4 follow-up if CD4 approaches age-related threshold for severe immunodeficiency |
| T3<sup>d</sup>                              | No CD4                                      | • Consider switching regimen<sup>f</sup> |
|                                             | CD4                                         | • Switching regimen is recommended if CD4 at or below age-related threshold for severe immunodeficiency and particularly if child initially had good immune response to ART |
| T4                                          | No CD4                                      | • Switch regimen, regardless of CD4 (viral load if available should guide decision) |
|                                             | CD4                                         | |

Notes:

a. It needs to be ensured that the child had at least 24 weeks of treatment trial; adherence to therapy has been assessed and considered to be adequate prior to considering switching to second-line regimen. Additionally, in considering changing treatment because of growth failure, it should be ensured that the child has adequate nutrition, and that any intercurrent infections have been treated and resolved.

b. Clinical stages in this table refer to a new or recurrent stage at the time of evaluating the infant or child on ART.

c. Where CD4 is available, at least two CD4 measurements should be compared.

d. Do not switch regimen if CD4 values are above age-related threshold for severe immunodeficiency.

e. As defined in table 17 above; if serial CD4 values are available, the rate of decline should be taken into consideration.

f. Some T3 conditions (i.e. pulmonary or lymph node tuberculosis and severe recurrent presumed bacterial pneumonia) may need to be treated and the need to switch regimens decided based on re-evaluation of the child in question.

The choice of secondary regimens balances potency, toxicity, formulation, and cost. As new data become available, it is likely that recommendations for second-line regimens will change.

Switching treatment

• Assess and review adherence
• Review patient medications
  a) Consider problems of drug administration and availability
  b) Pharmacokinetic reasons: drug – drug interaction, food
  c) Tolerability, taste, vomiting
• Change all the ARVs in the regimen if possible
• Consider overlap in resistance
• Counsel on each new drug
• Consider and discuss quality of life issues especially if complex new regimens to be used
If adherence is the problem:

- Refer for comprehensive adherence counselling
- Schedule regular appointments (48-72hrs) to assess adherence
- If child/caregiver is committed, then counsel and continue with ART, however, if commitment to continuation of ART is in doubt, a decision needs to be made about discontinuing ART altogether.

Exercise C

1. What are the contraindications to the use of first-line ARVs?
2. What is the clinical definition of treatment failure?
3. What are the common causes of treatment failure?
4. How does ARV treatment failure clinically manifest?
5. What measures should be taken prior to switching to second-line regimen due to treatment failure?
6. Dongo has been on ART for 2 years but lately it has been noticed that his growth rate has declined. After showing an initial response to treatment, he now has severe unexplained malnutrition. How will you stage Dongo? Is he having treatment failure?
7. Bunke is a 23 month old toddler who was started on ART at age six months. He now has persistent oral thrush refractory to treatment and regressed milestones. Is this clinical failure?
8. Melody is a five year old girl who has been on ART for three years. Last month she had oesophageal candidiasis and her CD4 had dropped to 7% after reaching a peak of 32% 20 months ago. Is this treatment failure?
9. How can you use Melody’s immunological findings for decision-making regarding switching ART?
10. Rusa is a seven year old on ART who has developed a lymphoma. How can you use Rusa’s clinical findings for decision-making regarding switching ART?
11. Thoko is nine years old and has been on ART for 12 months. She has now developed pulmonary TB. How can you use Thoko’s clinical findings for decision-making regarding switching ART?
12. Kalenga, an eleven year old male, has been on treatment for ten months. However his CD4 count remains at less than 200/mm³. How do you assess Kalenga?
13. Mabvuto, a ten year old male child, has been on treatment for 18 months. After twelve months of treatment, his absolute CD4 count had gone up from 180 cells at baseline to 580 cells/mm³. After 18 months it is 480 cells/mm³. Are you going to change his ART regimen? If yes why?
14. What guides decision-making regarding switching ART in the absence of CD4 measurement?

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on “Second-line Regimens” and then do Exercise D.

Recommended 2nd line regimens in Infants and Children with treatment failure of 1st-line regimens

In the event of treatment failure, the entire regimen should be changed from a first-line to a second-line combination. The new second-line regimen should include at least three new drugs, one or more of them from a new class, in order to increase the likelihood of treatment success, minimise the risk of cross-resistance, and be based upon drugs that retain activity against the virus strain. Designing potent and effective second-line regimens for infants and children is particularly difficult because of the current limited formulary available in the country today. This highlights the importance of choosing potent and effective first-line regimens and maximising their durability and effectiveness by optimising adherence.

Choice of Second-line Regimen Following a First-line Regimen of Two NRTI plus One PI

For children below 3 years failing on LPV/r, no switch improve adherence and refer to an Advanced Treatment Center. For those above 3 years, switch to EFV based regimen.

( Drugs currently recommended for third line regimens can be considered for use in children <3yrs of age. Paediatric formulations available for third line include Darunavir, Etravirine, and Raltegravir)
Choice of Second-line Regimen Following a First-line Regimen of Two NRTI plus One NNRTI
A regimen based on a protease inhibitor (PI), boosted with Ritonavir (RTV), combined with two new NRTI agents is recommended as the second-line treatment for children failing a regimen of 2 NRTIs with a NNRTI.

Choice of NRTIs
NRTI cross-resistance, especially in the presence of long-standing virological failure allowing accumulation of multiple drug resistance mutations, may compromise the potency of alternative dual NRTI components. Given the cross-resistance that exists where AZT is failing a second-line regimen that might offer more activity includes ABC and TDF. However, high level AZT/3TC resistance can confer diminished susceptibility to ABC. If ABC plus 3TC were used as first-line nucleoside combination, AZT plus 3TC would be the choice for an alternative regimen.

Choice of PIs
In the guidelines, LPV/r remains the preferred PI for use in children.

Atazanavir is available for use in adults. It is licensed for use in children >6yrs but currently not available in Zambia.

Choice of a Second-line Regimen Following an Alternative First-line Regimen with Triple Nucleosides
Treatment failure on an alternative, triple NRTI regimen can be managed with a wider choice of drug options because two important drug classes (i.e. NNRTIs and PIs) will have been spared. The PI component remains essential in constructing a second-line regimen.

(The clinical efficacy of continuing 3TC in a child who fails an initial first-line regimen that included 3TC has not been proven. Some data in adults suggest that continuing 3TC therapy even in the presence of multi-drug resistance (including the M184V mutation associated with 3TC resistance) may continue to provide additional antiviral activity, potentially due to decreased viral replicative fitness and increasing susceptibility of some ARVs).

Choice of a Second-line Regimen Following a PI-based Initial Regimen
Reintroduction of the NNRTI class in the second-line regimen is not considered safe if initially NNRTI was substituted with PIs in the first-line regimen because of severe toxicity and a triple NRTI regimen is not feasible. If PIs had been used as first-line with NRTIs, NNRTIs remain the only new drug class that can be introduced but the durability of such a regimen will be compromised by the inevitable and potentially rapid development of single point mutations with high-grade NNRTI resistance. In both of these circumstances, referral of the patient to a setting where specialised and individualised HIV care is provided is warranted, however, this may not be an option open to all patients. Any subsequent regimen will have to be based on the limited available formulary, including NNRTIs and NRTIs.
### Table 41: Recommended Second-line Regimens in Infants and Children

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Comment</th>
<th>Failing 1st line ART</th>
<th>2nd line ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (0 to &lt;10 years old)</td>
<td></td>
<td>ABC or TDF + XTC</td>
<td>AZT + 3TC</td>
</tr>
<tr>
<td>Children &lt;3 years old</td>
<td></td>
<td>AZT or d4T + XTC</td>
<td>ABC or TDF + XTC</td>
</tr>
<tr>
<td>Children ≥3 years old</td>
<td></td>
<td>NNRTI-based ART</td>
<td>LPV/r-based ART</td>
</tr>
<tr>
<td></td>
<td>Improve adherence and refer to next level</td>
<td>LPV/r</td>
<td>No switch</td>
</tr>
<tr>
<td></td>
<td>NNRTI non-exposed/naive</td>
<td>LPV/r-based ART</td>
<td>EFV-based ART</td>
</tr>
<tr>
<td>Adolescents (10 to &lt;15 years old)</td>
<td>2nd line should consist of 2 NRTIs + LPV/r</td>
<td>TDF + XTC + EFV</td>
<td>AZT + 3TC + LPV/r</td>
</tr>
<tr>
<td>Adolescents (15 to &lt;20 years old)</td>
<td>the alternative of 2 NRTIs + ATV/r</td>
<td>TDF + XTC + NVP</td>
<td>ABC + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ABC + 3TC + NVP</td>
<td></td>
</tr>
</tbody>
</table>

#### Important steps to consider in the Event of Failure of Second-line Regimens

All patients being considered for third line cART should have:
- Confirmed second line failure with a viral load test (after at least 6 months of using second line)
- Genotype (resistance) testing

All such patients should be referred to the Advanced Treatment Centres with a complete history of all previous drugs taken and the duration of use.

#### Stopping therapy

At some stage the option to stop ART may need to be considered; although prevention of opportunistic infections, symptom relief and pain management need to continue. Symptoms and pain are a major cause of discomfort and poor quality of life during the course of HIV infection in infants and children. Many of these symptoms can be prevented, treated or controlled with basic medication and therapies. Non-pharmacological methods are an important adjuvant to symptom management. Efforts to identify the cause of symptoms and pain should be pursued as much as possible, without adversely affecting the quality of the child’s life and within the limits of available resources. Symptoms and related pain should be anticipated and prevented to the extent possible.

The care of the terminally ill child is a major challenge especially in resource-limited settings where there is a paucity of experience and replicable models of planned terminal care, both institutional and community-based. At the end-of-life there are typically more symptoms that must be addressed and there are poly-pharmacy guidelines to control multiple syndromes and treatment for multiple conditions. Terminal care preparation for children and their families is a long-term process and requires continuity in care providers and services. Critical factors in effective long-term planning include early and active communication and involvement with parents/guardians/caregivers and their on-going support, community-level support structures, a functional health infrastructure, knowledgeable human resources, and access to essential drugs and supplies. Terminally ill children are often placed in acute care facilities which may not be appropriate for the needs of the child. Home-based care is usually preferred. Families must be involved in decisions about the best place for care and the preferred place of death if the child has end-stage HIV disease.
Exercise D

1. Mwaba is an 11-year-old boy who started ART three months ago. His baseline CD4 was 54 cells mm$^3$, he now has overwhelming sepsis. Should the initial regimen be changed to second-line regimen? How will you manage Mwaba?

2. Daisy is a four-year-old girl who has been on ART for the past two years. She has responded extremely well to ART. Her growth and development is appropriate for age, however she now has a bad flu which has persisted for two weeks and mum is worried. Is this treatment failure?

3. Kablinga, a ten-year-old male child, has been on TDF/3TC/EFV for the past three years. His baseline absolute CD4 count rose from 45 cells at baseline to a peak of 360 at two years on ART. He came last month for a scheduled follow-up; his absolute CD4 count had dropped to 69 cells. Is he failing on ART? What would be your next move?

4. Elsie is a five-year-old girl who has been on ART for the past three years. She has suddenly developed a stage three illness. What will you do?

5. What decisions are supposed to be made in the event of treatment failure?

6. What is the choice of second-line regimen following a first-line regimen of two NRTI plus one NNRT? Which are the preferred drugs?

7. Musonda a 3-year-old boy who was started on AZT, 3TC and ABC at 8 months of age. At baseline he was failing to thrive, had miliary tuberculosis and his %CD4 was 1%. His CD4 rose to a pick of 22% after two years on treatment, he now has been diagnosed with non-Hodgkin’s lymphoma of the abdomen and his cell count is 14%. Would you change to second line? If yes what would be your choice of drugs?

8. What are the strategies in the event of failure of second-line regimens?

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module “Monitoring Paediatric Antiretroviral Therapy” and “Paediatric Standard Operating Procedures: Determination of Eligibility for ART in Annex 3 and then do Exercise E.

Unit 5: Drug Resistance

HIV drug resistance occurs when mutations in the viral genome enable the virus to continue to replicate even in the presence of antiviral medications. It can be specific for particular drugs, or can affect other similar antiretroviral drugs (cross-resistance). In order for resistance to occur, both ongoing viral replication and suboptimal antiretroviral levels are required. Factors that give rise to sub-therapeutic drug levels and subsequently rebound viraemia with resistant virus include:

- mono- and dual-therapy;
- inappropriate combinations of drugs;
- adding just a single drug to a failing regimen;
- interruption of treatment;
- Prolongation of a failing regimen is all likely to result in the development of increased drug resistance.

Development of HIVDR in children on ART is usually related to poor adherence, use of suboptimal regimens or PMTCT interventions, or problems with drug absorption or pharmacokinetics; drug resistant strains can be transmitted from the mother, develop due to administration of paediatric ART or maternal or infant ARVs used for PMTCT or maternal ART.

In children, factors contributing to HIVDR include:

- Poor adherence
- Use of sub-optimal regimens or dosages
- PMTCT interventions
• Problems with drug absorption or pharmacokinetics
• Transmitted resistance from mother

**Diagnosis of Drug Resistance**

It is important to understand that resistance tests are most accurate at identifying drug resistance to the current regimen; absence of detectable drug resistance to previously used drugs does not rule out the presence of reservoirs of virus harboring resistance to the previous regimens. Re-introduction of those previously used drugs is likely to result in the rapid re-emergence of drug resistance. It is therefore critical to interpret drug resistance test results in the context of the patient’s entire antiretroviral treatment history.

Two main types of resistance tests are currently available: genotypic testing and phenotypic testing. Genotypic tests have the following characteristics:

• They identify specific mutations in the viral genome associated with drug resistance
• They are less costly than phenotypes, though still costly in resource-limited settings such as Zambia
• Results can be obtained relatively quickly
• They do not directly measure susceptibility to ARVs
• Interpretation of results may be difficult, particularly when multiple mutations with differing effects on drug activity are present in the same virus

Genotypic tests are currently available in Zambia at a limited number of testing centers including the University Teaching Hospital.

Phenotypic tests:

• Report the susceptibility of the patient’s virus to specific drugs. Such susceptibility reports take into account all of the different mutations present in the virus and their impact on a particular drug’s activity
• Are very expensive
• Take longer to get the results
• Use more complicated technology, and are currently not available in Zambia

As a general rule, genotypes are most useful when testing for drug resistance in patients early in the drug treatment continuum, while phenotypes may be more useful for patients who have undergone multiple rounds of treatment and therefore are likely to have complicated resistance patterns.

**Preventing and Managing Drug Resistance**

Due to the limited availability of resistance testing, as well as the cost, complexity, and limited availability of drugs for highly treatment-experienced patients, the best approach to managing drug resistance in our setting is to prevent it from occurring in the first place.

**Minimizing the Emergence of HIV Drug Resistance (HIVDR)**

Multiple factors can prevent the emergence of drug resistance in patients receiving HAART. These include:

1. Use of potent, tolerable, and durable ART drug combinations as per current national guidelines
• Specific problems that should be considered in treating children include the need to change dose and formulations as children cross thresholds of weight or age, and limited availability of suitable paediatric ARV formulations
• To avoid emergence of HIVDR in the event of discontinuation of ARVs due to toxicity, it may be necessary to not discontinue all ARVs at the same time.

2. Ensuring full adherence to treatment by:
• Using child-friendly FDCs
• Ensuring that children and their caregivers are adequately counseled prior to initiation of treatment
• Ensuring that all caregivers understand how and when to give the medications appropriately
• Ensuring that adherence is monitored and assessed at each clinic visit
• Ensuring an uninterrupted supply of drugs for the patient
3. Timely identification and management of treatment failure when it occurs, including switching to an appropriate new regimen (if necessary) after the cause of treatment failure has been identified and addressed

**Monitoring HIVDR: Early Warning Indicators (EWIs)**

HIV is characterized by very rapid replication, a high mutation rate in the presence of drug-selective pressure, viral recombination, and the need for lifelong treatment. Because of these characteristics, some degree of HIVDR is anticipated to occur among persons on treatment even if appropriate ARV regimens are provided and optimal adherence to therapy is supported.

WHO has developed a generic monitoring protocol to monitor the emergence of HIVDR and associated programmatic factors in cohorts of infected children starting first-line ART. The survey is designed for implementation following a rolling three-year cycle in sentinel ART sites treating children. The survey identifies programmatic factors associated with the emergence of HIVDR, which can be adjusted to optimize patient care and minimize the emergence of preventable drug-resistant HIV.

ART site-based HIVDR EWIs are identifiable factors that may be associated with the emergence of HIVDR and which, if addressed at either the ART site or programme may prevent development of HIVDR. The Early Warning Indicators (EWIs) are reflected in the figure below.

**HIVDR Early Warning Indicators (EWI)**

*Figure 10: HIVDR Early Warning Indicators*
Hence, implementing an HIVDR EWI monitoring system allows ART programmes to assess the extent to which they are optimally preventing HIVDR. The EWIs should be monitored in all ART sites when feasible, or from a representative sample of ART sites. Achieving the best possible performance as measured by these indicators will help minimize the preventable emergence of drug-resistant HIV. Sites which do not achieve one or more of the EWI targets may require increased resources, staff training, or additional review to clarify the kind of support needed. Likewise, lessons may be learned from sites achieving and surpassing targets and applied to sites observed to be functioning less well.

**Surveillance for HIVDR in Newly Infected Treatment-naive Infants**

An unwanted outcome related to the use of ARVs for PMTCT is the development of drug-resistance in the small number of infants who do become infected. Administration of one or more ARVs, especially if one NNRTI is administered alone, can lead to the development of drug-resistance in the infant in the event that HIV is transmitted.

Maternal prophylaxis regimens with two or more ARVs are not only more effective in preventing transmission but are also less likely to result in maternal HIVDR and infant HIVDR if transmission occurs. Small research studies have evaluated the prevalence of drug-resistance among infants associated with various PMTCT regimens administered to mothers and infants. The very few infected infants exposed to combinations of NVP and one or more NRTIs have been seen to have resistance at rates between 13% and 57% [118-123] with lower rates (between 13% and 14%) seen in two other small studies (of 7 and 8 infants, respectively) among infants receiving two NRTIs (AZT/3TC).

However, nationwide surveillance systems have not yet been developed to evaluate the association between PMTCT and HIVDR among infants, largely because of the expense and difficulty of collecting specimens and performing resistance assays.

**Exercise E**

1. Lishomwa, a 4 year old male, is HIV positive and has been referred for ART to your health centre. No clinical staging labs have been done.
   b. What constitutes the baseline clinical assessment for him?
   c. What constitutes the laboratory assessment for him?
2. Kalolo is 5 years old. He is HIV positive and has a WHO stage 3 conditions when assessed at baseline. There is no CD4 machine available in his district. What should be done for him?
3. What are the important signs of infant and child response to ART?
4. Mubanga is a 3 year old child who has just been started on ART. How is he going to be followed up?
5. Memory, a two year old female patient, is on ART. What activities should be done on her scheduled visits for children receiving ART?

*When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on “Adherence counselling in children” and then do Exercise F followed by a case study and a role play.*
Unit 6: Adherence Counselling

Adherence to treatment is taking the correct number of doses at the correct time in the correct way for as long as prescribed. The client should take at least 95% of the doses prescribed to suppress the virus. Adherence to care is the keeping of all clinic appointment and other instructions given by clinic staff.

Adherence differs from compliance. Adherence is the act of sticking to something or steady devotion towards it (acceptance of an active role in one’s own health care). Whereas compliance is the act of conforming, yielding or acquiescing (lack of sharing in the decision made between provider and client).

Adherence can be particularly difficult for children and their caretakers. It requires both the commitment of a responsible adult and the involvement of an ill child. The child’s developmental stage will influence the extent to which s/he can or will cooperate with medication administration, as will the parent-child relationship. Paediatric formulations are not always suited for administration to infants and young children; they may taste bad or be difficult to swallow. Paediatric antiretroviral regimens are frequently complex, requiring caretakers to measure liquid formulations, crush pills, open capsules, or dissolve tablets in water; doses may increase as the child gains weight. Furthermore, if more than one caretaker (relatives, nannies, teachers etc) looks after sick children, this may complicate both administration and assessment of adherence, and provoke disclosure issues.

These factors should not discourage programmes from including children – after all, the lifesaving benefits of paediatric antiretroviral treatment dramatically outweigh the challenges. But they do mean that special attention to, and expertise in, paediatric adherence is an essential component of care. We recommend a four-part approach to paediatric adherence, focusing on education, preparation, on-going assessment, and support.

Adherence is key to successful outcomes in achieving viral suppression and preventing drug resistance

Issues surrounding adherence in children
- Children depend on caregivers for administration of medication
- Children’s developmental level influences ability and willingness to take medications
- Adolescents need special consideration

Adherence in adolescents
- Denial and fear of their HIV infection
- Misinformation
- Distrust of the medical establishment
- Fear and lack of belief in the effectiveness of medications
- Low self-esteem
- Unstructured and chaotic lifestyle
- Lack of family and social support

Adherence associated with the caregiver and the family
- Careful social assessment should always precede starting therapy
- Poor family circumstances compound the adherence difficulties.
- Families’ reluctance to disclose diagnosis may limit medication administration at daycare/school

Forms of non-adherence
- Missing one dose of a given drug
- Missing a dose of all the three drugs
- Missing multiple doses
• Missing a whole week of treatment
• Not observing the time intervals
• Not observing the dietary instructions

Consequences of poor adherence
• Incomplete viral suppression
• Continued destruction of the immune system and decrease of CD4 cell count
• Progression of disease
• Emergence of resistant viral strains
• Limited future therapeutic options and higher costs for individual and program.

How to assess adherence
• Caregiver/Child’s reports
• Caregiver/Child’s report using a 4 day, 1 week, 1 month or most recent recall of missing a dose
• Can be done using a series of non-judgmental questions at clinic visits
• Has a tendency to over estimate
• Self-report agrees well with actual medication (when a trusting provider/patient relationship develops)
• Easiest tool in clinic setting

Medication counts
• Providers count remaining medication during clinic visit

Problems:
• Caregiver/Child can dump pills prior to visit
• Caregiver can antagonize patient and provider
• Unannounced pill counts can be better, at the clinic or at home

Biological markers
• An increasing %CD4 and CD4 implies good adherence
• But in some cases CD4 counts may remain low even with good adherence:
• Detectable viral load and viral resistance

Pharmacy records
• Pharmacists keep record of drugs dispensed to each patient:
• Can inform the relevant doctor of lapses in patients collecting their medicines (esp. good for patients who buy their own medicines)

Problems:
• Is not a measure of ingestion
• Requires patients to always use the same pharmacy

How to promote adherence
1. Participation of the child in a plan of care. Do not rush to initiate ARV; ensure that the caregiver/child must be ready
2. Counseling: Individual or in group
3. Information/Education/Communication on ARV drugs:
   a) Provide simple written information (booklet, pamphlet, cartoons and bubbles)
   b) Warn the child and caregiver about common side effects
   c) Same adherence message by all health workers
   d) Buddy system (Caregiver and siblings reminds client to take medicines)
   e) Medication diaries, medication charts
   f) Incentives (transport, food etc)
g) Availability and affordability of ARV drugs
h) Directly Administered ART Therapy (DAART) or modified Direct Observed Treatment
i) Continuous education of the Caregiver and the Child

**Patient readiness assessment**
Caregiver/child’s knowledge on:
- Medical history
- Knowledge of HIV disease
- Opportunistic infections
- Social support

On drug regimen
- Action of ARV drugs
- Need for continued prevention
- Side effects and what to do

On adherence promotion strategies
- Siblings
- Medication diary
- Referral to Play groups or post-test clubs

**Family and community involvement**
- Identify a Family Care Giver or Buddy with the patient
- Familiarize them on ART and on adherence as they are your client
- Involve them during medical consultations and counseling sessions
- Home based care: educate Family Care Giver in recognizing side effects and referring to hospital if needed
- Community involvement and understanding in ARV care is important

**Non-disclosure as a cause of non-adherence**
- This is commonly seen in children
- Child is either left with the child-minder or granny – no idea about the child’s HIV status
- Only told that the medication is either for flu or cough
- Importance of continued medication not explained

*Figure 11: Four-part Approach to Paediatric Adherence*
1. Education

*Paediatric care is a partnership between clinicians, caregivers and children.* This collaboration is critical to the success of paediatric antiretroviral treatment. *Clinicians cannot simply write a prescription and recommend that an infant take his/her medication once or twice daily! An informed and committed adult, supported by an experienced multidisciplinary care team, is a mandatory part of the equation.*

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

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

**Defining adherence**

Adherence is the extent to which a client’s behaviour coincides with a prescribed health care regimen determined through a shared decision making process between the client and health care provider. There should be acceptance of active role in one’s own health care.

**Explaining the importance of adherence**

*Caretakers should know that the goal is to take every dose, every day, for life. Medication must be taken on schedule, in the right combination and at the correct dose.* Using simple terms, visual aids, and relevant analogies, health workers and that taking medication irregularly or should clearly explain why such high levels of adherence are required. Caretakers should understand that missing doses of medication can lead to treatment failure, intermittently may confer all of the risks and none of the benefits of antiretroviral treatment.

**Emphasising the need for communication**

It is important to develop trust, partnership, and honest communication with children and their caretakers.

2. Preparation and Practice

*Taking the time to prepare patients and families can make the difference between treatment success and treatment failure and should be a routine part of prescribing antiretroviral therapy.* It is important to consider:

**Who will administer the medication?**

*Ideally, everyone who cares for the child should know how to administer the treatments. Stigma and secrecy complicate adherence for children, as they do for adults,* and ART preparation will need to be personalised to the circumstances of each household.

**What medication will be given?**

While children and caregivers do not necessarily need to know the formal or technical names of each medication, they must be able to confidently identify each one, and know how it is to be stored, measured, and administered. Clearly labelling, marking, or colour-coding the medication can be enormously helpful, and a close partnership with the dispensing pharmacist is important.
When will medication be given?
Antiretroviral medication should be given at the same time every day. While our first-line regimens do not have stringent dietary requirements, some ARVs do need to be taken on an empty stomach, others with food. Caretakers should know when to give medication – a watch is not required, but some practical system of timekeeping (e.g. sunrise, sunset) will be important.

How will medication be given?
Caretakers must know how to measure the doses – do tablets need to be cut or crushed? Should syrups be measured with a specific measure or with a syringe? Should medicines be taken with or without food? Does the taste of a particular ARV need to be masked? Can the medicines be taken at the same time? What should be done if a child spits out or vomits the medication?

Useful strategies include practicing medication preparation and administration in the clinic. Written and pictorial information, videotapes, and tools such as pillboxes, blister packs and pre-marked syringes or measuring cups can also assist caretakers with the difficult task of supporting paediatric adherence.

The risk of non-adherence can be reduced by preparing caretakers for common problems. Offering hypothetical scenarios and role plays involving both adults and children – what would you do if the child vomits? Refuses one medication? Leaves home for the day without the medication? – can also be quite helpful.

3. Assessment
For many patients, formal and systematic assessment by a multidisciplinary team is the best way to identify problems with medication taking.

There is no perfect way to measure adherence in the clinical setting, at a minimum, families should be asked about adherence at every visit and pharmacy records should be reviewed on a regular basis. Asking patients to report on missed doses during the last week prior to the visit can be a useful way to assess adherence. Asking specific, open-ended questions about concerns with administration or tolerance of medication is often a good way to learn of adherence problems. Pill counts, home visits and parallel histories from different family members can also be helpful, although these will not be appropriate in all settings. As children age, they should be included in the discussion of adherence.

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

Measurement of Daily Doses
Paediatric dosing must be precise to ensure adequate therapeutic levels. When possible, caregivers should use syringes to measure and administer liquid medication. Caretakers should be discouraged from using household spoons as they may vary in size, which can lead to inaccurate dosing.

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

It is best to avoid high temperatures for all medication. Medication should not be stored in direct sunlight or in other spots likely to become very hot. Most drugs should be kept in a cool place. In particular, Lopinavir/Ritonavir (Kaletra®) needs to be stored in a cool place. If refrigeration is available, caregivers should be informed to keep this medication in the refrigerator. If not, ask where in the home cool items are stored – is there a cool pot, extra water jug, or cooler?

Lopinavir/Ritonavir liquid must be stored in a glass container, as the liquid may corrode plastic. The pharmacist will dispense this medication in a glass container, and patients should be advised to draw medication into the syringes only at the time of administration. A filled syringe should not be used to store or transport doses.

Masking the Taste of Medication

1. For liquid medication, first draw up the medicine in a syringe to measure the proper volume. Combine with 5-10 cc of tasty liquid such as juice, milk, or non-alcoholic beverage. Do not combine with large volumes. Mix vigorously. Be sure that the caregiver is aware the child must drink the full amount.

2. Alternatively, dip the syringe tip into something sweet to mask the initial taste or give small amounts of beverage pre- and post- medication administration.

3. For pills, crush with a mortar and pestle until fine. For capsules, open the capsule into a small bowl. Add 1-2 teaspoons of food (jelly, jam, crushed banana, cereal) and combine vigorously. Feed child all of the food to ensure that all medication is consumed.

4. Review which medication in tablet form can be broken in half and swallowed for older children. Hard tablets may be dipped and coated with sauce or any other viscous food product to help the older children swallow pills.

5. Immediately after administering medication, offer child a sweet-tasting food to mask the taste of the medication. Administration of sweet or tangy substance prior to giving medication may also be helpful.

6. Remember to give lots of praise after each dose!

Avoiding or Minimising Nausea

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

1. Offer the child a small meal of bland food (cereal, crackers, and bread). Shortly thereafter, administer medication.

2. Administer tablets and capsules with only enough water or beverage needed to swallow. Children have a tendency to drink much more water than necessary, which often leads to vomiting due to the large volume of liquid.

3. Reassure the caregiver that the nausea is usually temporary until the child’s body gets used to the medicine. Stress the importance of giving meds in a calm, unhurried manner, especially during the first few weeks.
Exercise F

1. Erica is John’s aunt. John is a male toddler whose mother died two weeks ago. John has been commenced on ART. How will you counsel Erica?

2. Thoko is an 18 month old child who has to take ARV syrups. The grandmother says she cannot read nor write. How will you assist grandmother to measure out her dosages correctly?

3. Lula was started on a first-line regimen two months ago. She is taking her ABC + 3TC very well but refuses to take Kaletra®. She says that it tastes horrible. It is true that Kaletra® is unpalatable and because of its bad test it is extremely difficult to convince Lula to take it. What is your advice to Lula’s grandmother on possible ways of masking the taste of medication?

Case Study for Group Discussion

Paul is three years old. His mother is a housewife and his father is a truck driver who travels quite often between South Africa and Zambia. The father is away from home for long periods, sometimes up to four months. Paul was started on ART eight months ago. Until last month, he was progressing very well. Two weeks ago he was brought in with an acute febrile illness, associated with severe oral thrush. You treated him with Nystatin® drops, an oral antibiotic and Coartem. Today he still has oral thrush but he now complains of pain when swallowing food and he has lost 1.5 kg over the past two weeks.

a) What do you think is wrong with Paul?

b) How will you evaluate and manage Paul?

When you finish the Exercise discuss your answers with your facilitator, thereafter you will have a role play. The facilitator will advise on when to proceed to Module 7 on “Paediatric HIV-related Diseases”.
Module 7
Paediatric HIV-related Diseases
Learning Objectives
At the end of this module the healthcare worker will be able to:

• Describe other common clinical conditions seen in HIV-infected children.
• Describe the clinical presentation, diagnosis, treatment and prevention of common opportunistic infections and illnesses seen in HIV-infected children.

Listen to the presentation on “Paediatric HIV related diseases” (or read your modules) on “Managing common infections in HIV-infected children” and then do Exercise A.

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

Common conditions experienced by HIV-infected children are diarrhoea, acute lower respiratory tract infections, septicaemia, acute suppurative otitis media, sinusitis, and failure to thrive. The aetiology of infectious disease changes significantly during the first few years of life as the infant’s immune system matures. A good example is PCP, which is typically found in younger infants.

Unit 1: Managing Common Infections in HIV-infected Children

Diarrhoea
Acute diarrhoea is a common cause of morbidity and mortality in HIV-infected children during the first year of life. Diarrhoea in HIV-infected children tends to be frequent and prolonged. Persistent diarrhoea is associated with an 11-fold increase in risk for death in HIV-infected children when compared to uninfected children. There is also an increased frequency of acute diarrhoea in HIV-exposed sero-negative children whose mothers have symptomatic HIV or are dead, or following early introduction of complementary feeding.

Table 42: Common Causes of Diarrhoea in HIV-infected Children

<table>
<thead>
<tr>
<th>Viral</th>
<th>Protozoa</th>
<th>Bacterial</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus (most common cause)</td>
<td>• Entamoeba histolytica</td>
<td>• Enterobacter</td>
<td>• HIV enteropathy</td>
</tr>
<tr>
<td></td>
<td>• Cryptosporidiosis</td>
<td>• Escherichia coli</td>
<td>• Candida albicans</td>
</tr>
<tr>
<td></td>
<td>• Isosporiasis</td>
<td>• Shigella</td>
<td>• Prolonged use of antibiotics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Salmonella</td>
<td>• Drugs such as ritonavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Atypical mycobacteria</td>
<td></td>
</tr>
</tbody>
</table>

The principles of management of acute and persistent diarrhoea in HIV-infected children are the same as in other children and should follow IMCI guidelines, including: management and correction of dehydration, aggressive nutritional management, nutrition counselling and a review of counselling on household hygienic practices, especially handling of the baby’s water and food.
Invasive Bacterial Infections
Invasive bacterial infections occurring with greater frequency and severity are one of the early manifestations of HIV disease in children. Common infections include bacterial pneumonia, meningitis, and sepsis. Aetiology and clinical presentations may be similar to those in other children but the presence of occult infections is more frequent. Fever may be the only symptom of serious infections. HIV-infected children with fever therefore need careful clinical and laboratory assessment to identify the cause of fever. The treatment of bacterial infections in HIV-infected children is the same as in other children but recovery in HIV-infected children is often slower and treatment failures are more frequent.

Otitis Media
Ear infection is one of most common infections in HIV-infected children. Acute otitis media refers to ear infections that have lasted for less than 14 days. Suppurative otitis media is more common in HIV-infected children in the first year of life. By age three years, most HIV-infected children who are not on ART will have had one or more episodes of acute otitis media. Signs and symptoms are similar to those in other children and include ear pain, pulling on the ears, excessive crying, ear discharge, and irritability. Management includes ear wicking until dry, when there is discharge, and appropriate antibiotic cover for acute infection (IMCI guidelines). Chronic suppurative otitis media occurs with increased frequency in HIV-infected children and is associated with chronic ear discharge, which is usually painless, and a perforated eardrum. Frequent ear wicking is the main mode of management (IMCI guidelines).

Malaria
Infants born to HIV-infected women are more likely to suffer from congenital malaria than children born to uninfected women. Likewise, an increased frequency of malaria has been noted in HIV-infected children, with associated higher levels of parasitaemia than in other children. Additionally HIV-infected children are more likely to be anaemic during an episode of malaria compared to uninfected children. Clinical presentation and response to treatment is similar to HIV-uninfected children and treatment recommendations should follow the guidelines provided by the national malaria programme.

In many areas, it is difficult to differentiate cerebral malaria and meningitis at admission; therefore, all children in malaria endemic areas who are on presumptive treatment for cerebral malaria should also be treated presumptively for bacterial meningitis. This is particularly relevant for HIV-infected children who have increased frequency of both conditions.

Measles
Measles is one of the major causes of morbidity and mortality and is a severe illness in children with HIV infection, particularly those with advanced immune deficiency. Severe cases can occur without the typical rash and may be complicated by pneumonia or encephalitis. HIV-infected children with measles have a high case fatality and should be treated in hospital. Measles may occur in early infancy in HIV-infected children because of inadequate transfer of maternal antibodies and infection may occur despite history of immunisation. Give measles immunisation to HIV-infected children at nine months. Follow IMCI and EPI guidelines for management.

Exercise A
1. Mutale is a four year old female child who has been on ART for the past 18 months. She has had diarrhoea for the past five days. She shows signs of some dehydration. How will you manage her?
2. Sungwe, a three year old boy weighing 7.5 kg, has had diarrhoea lasting for three weeks. Mother says that he has lost weight. Upon examination he has oral thrush. He has some dehydration. What will be your management?

When you finish the exercise discuss your answers with your facilitator, thereafter read your module on “Management of central nervous system and pulmonary conditions including management of children with opportunistic infections” and then do Exercise B.
Unit 2: Management of CNS and Pulmonary Conditions

Central Nervous System Conditions

1. Opportunistic Infections

Opportunistic infections are seen in cases of severe immune suppression (CD4 < 200/µL) in older children and adolescents. The most common CNS OI in children is reportedly CMV infection. Other viruses, especially herpes simplex and varicella-zoster virus, can also cause acute encephalitis. Fungal infections, particularly candida and aspergillus meningitis, are reported to be the second most common infection in children. Cryptococcal meningitis is rarely seen in young children with AIDS but has been reported among older children and adolescents. Toxoplasma encephalitis has rarely been reported in older paediatric patients. Referral to higher levels of care is appropriate if diagnosis cannot be established definitively. Table 19 provides details on various opportunistic infections.

2. Seizures

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

- Space-occupying lesions (most often cerebral toxoplasmosis or tuberculoma)
- Meningitis (most often bacterial in young children, cryptococcal in older children and adolescents)
- Metabolic disturbances
- Non identified cause other than HIV infection

Treatment is aimed at the underlying disorder and seizure control through standard anti-epileptic medication. Drug interactions may be a problem for patients on HAART; for those on HAART, the drug of choice is valproate. For patients presenting with focal seizures, consider treatment for toxoplasmosis if no other cause is apparent.

Table 43: Opportunistic Infections of the Central Nervous System

<table>
<thead>
<tr>
<th>Neurological Disease</th>
<th>Clinical Presentation</th>
<th>Diagnostic tests</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytomegalovirus</td>
<td>Presents with encephalitis, retinitis, radiculomyelitis or neuritis</td>
<td>CSF, PCR, MRI (if available)</td>
<td>Intravenous Gancyclovir 10mg/kg per day in two divided doses for 2-3 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Foscarnet 280mg/kg/day in 3 divided doses for 14-21 days may be used when there is sight-threatening CMV retinitis</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>Presents with fever, headache, seizures, change in mental status Focal neurological signs uncommon</td>
<td>CSF-Indian ink positive Cryptococcal antigen test, MRI (if available)</td>
<td>Induction with amphotericin B (0.4-1.0mg/kg/day) for 2 weeks followed by fluconazole 10-12mg/kg/day (max 800mg) for a minimum of 8 weeks, then 3-6mg/kg once daily maintenance therapy</td>
</tr>
</tbody>
</table>
Toxoplasmosis
Most common manifestations are encephalitis, mental changes, fever, headache and confusion
Serology, MRI (if available)
Do not lumbar puncture if there is a space occupying lesion (SOL)
Pyrimethamine loading dose 2mg/kg/day (max 50mg) for 2 days, then maintenance, 1mg/kg/day (max 25mg) plus sulphadiazine 50mg/kg every 12 hours/folinic acid 5-20mg 3 times weekly. Alternatively Cotrimoxazole can be used at 5mg/kg of the trimethoprim component BD for 30 days

Herpes simplex virus
Associated with fever-altered state of consciousness, personality changes, convulsions, and usually focal neurological signs particularly temporal lobe signs
Rising serum HSV titres and increased ratio of CSF-to-serum concentration of HSV antibody
Viral isolation
I/V Acyclovir 20mg/kg given 3 times a day for 21 days

3. HIV Encephalopathy
Neurological symptoms are widely prevalent, occurring at all stages of HIV infection and affecting any part of the nervous system. It is estimated that 40% to 70% of HIV-infected persons develop symptomatic neurological disturbances, but the brain is most commonly affected in children. However, neurological manifestations are infrequently diagnosed in children. HIV infection of the brain interferes with the process of growth and manifests as static, slowing, or regression of developmental milestones or as localized damage. This whole process is referred to as HIV encephalopathy. HIV encephalopathy and developmental delay are common in HIV-infected children and indicate advanced clinical disease.

Diagnosis of HIV encephalopathy is mainly clinical and depends on the presence of at least two of the following for at least two months:
• Failure to attain or loss of developmental milestones or loss of intellectual ability.
• Impaired brain growth or acquired microcephaly.
• Acquired symmetrical motor deficit manifested by two or more of the following: paresis, pathologic reflexes, ataxia, or gait disturbances.
• Cerebrospinal fluid is normal or has non-specific findings and CT scan shows diffuse brain atrophy.

Managing encephalopathy should include evaluating the child with the help of a neurologist, if possible. ART is possibly the only way to reverse the effects of HIV infection on the CNS and allow restoration of growth, development, and milestones. Depending on the severity, the patient will need a support system, which includes physical therapy, a social worker, and surgery to minimise contractures.

4. Neuropathy
HIV-related neuropathy is a troublesome condition that occurs in as many as one-third of patients with a CD4 count < 200/µL. In addition, ART and other medication used in the treatment can also have neurological side effects, the most common of which is peripheral neuropathy. Neuropathy in children is more difficult to diagnose and less well described than in adults. Diagnosis is based on clinical presentations such as pain or numbness that has a “glove and stocking” distribution. Treatment is mainly symptomatic. Pain due to neuropathies may respond to analgesics combined with amitriptyline, carbamezepine, and lamotrigine. Use morphine in end-stage disease.
Pulmonary Conditions

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

1. Bacterial Pneumonia

Pneumonia is the leading cause of hospital admissions and death in HIV-infected children. It is also the most common pulmonary condition and presents the same way in both infected and uninfected children. *Streptococcus pneumoniae* is the most common pathogen isolated in both HIV-infected and -uninfected children. Other organisms include *H. influenzae*, *Klebsiella* and *Staphylococcus aureus*. Recurrent bacterial pneumonia suggests immune suppression (WHO stage 4). Recurrent pneumonia should be investigated further to exclude other conditions such as tuberculosis, foreign body, bronchiectasis, LIP, and fungal pneumonias.

The clinical presentation of pneumonia includes fever, cough, fast breathing with or without chest in-drawing and crepitations or decreased breath sounds on auscultation. Diagnosis of pneumonia is largely on clinical grounds. Some laboratory tests may help in pointing towards an aetiological agent; an increased white blood count with a neutrophilia suggests bacterial pneumonia and growth on blood cultures may result from the causative organism. Because symptoms of pneumonia and those of malaria often overlap, a blood smear for malaria parasites should be done.

The management of pneumonia should follow the recommended IMCI guidelines. Severe pneumonia should be managed in a hospital or other in-patient facility and should include both supportive and specific therapy. In children below one year of age, clinicians must consider PCP as possible cause of severe pneumonia and treat accordingly.

2. Pneumocystitis Pneumonia

Pneumocystis pneumonia (PCP) is caused by a fungus called *Pneumocystis jiroveci* (formerly called *Pneumocystis carinii*). PCP is a major cause of severe pneumonia (15–30%) and death (30–50%) in HIV-infected infants who are not on ART; these infants are usually in a good nutritional state and may not have clinical features that indicate the presence of HIV and AIDS. The incidence of PCP is highest during the first year of life and usually peaks at three to six months of age. It can occur after one year of age, but with decreasing frequency.

**Clinical Features of PCP**

Clinical features of PCP in children include the following:

- Low-grade fever or afebrile
- Marked respiratory distress (chest in-drawing, cyanosis, inability to drink)
- Auscultation: clear chest or diffuse fine crepitations
- Poor response to standard antibiotic treatment
- Pulse oximetry: severe persistent hypoxia (paO2 <90%)
- Occasionally, associated HIV symptoms include oral thrush, lymphadenopathy, and/or weight loss

**Investigations**

Sputum induction with nasopharyngeal aspirates or bronchoalveolar lavage may help in diagnosing PCP. Radiological changes include hyperinflation of the lung fields although such are not specific to PCP. In cases where a definitive diagnosis of PCP cannot be made, a high index of suspicion of PCP is required and therapy must be initiated promptly, along with treatment for bacterial pneumonia.
Management of PCP

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

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

For **specific management** of PCP:

- Give intravenous high dose Cotrimoxazole (CTX) 20 mg/kg/day of trimethoprim administered every six hours for 21 days. Give the same dose orally if IV preparations are not available.
- Add prednisone at 2 mg/kg/day in two divided doses for 7 to 14 day if child is in severe respiratory distress then taper off thereafter at 1mg/kg/day for 7 days.

*After an acute episode of PCP, provide daily oral Cotrimoxazole (8 mg/kg/day of TMP). At the age of 5 years, reassess the CD4, if > 350 then can stop.*

3. Tuberculosis

Diagnosing TB in children is difficult and more so in HIV-positive children because an HIV-positive child may have many other pulmonary conditions and HIV-related chronic lung diseases that mimic the symptoms of TB.

<table>
<thead>
<tr>
<th><strong>Table 44: Evaluation for Tuberculosis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History (symptoms and signs of TB disease)</strong></td>
</tr>
<tr>
<td>• Unexplained weight or failure to grow normally</td>
</tr>
<tr>
<td>• Unexplained fever, especially if more than 14 days</td>
</tr>
<tr>
<td>• Cough of any duration</td>
</tr>
<tr>
<td>• Failure to respond to appropriate antibiotic treatment of presumed bacterial pneumonia or meningitis</td>
</tr>
<tr>
<td>• Exposure to an adult with probable or definite pulmonary or infectious TB</td>
</tr>
<tr>
<td><strong>Physical examination</strong></td>
</tr>
<tr>
<td>• Fluid on one side of chest (dullness on percussion, reduced air entry)</td>
</tr>
<tr>
<td>• Enlarged non tender lymph nodes or abscess, especially in the neck</td>
</tr>
<tr>
<td>• Signs of meningitis, especially if sub-acute and develop over several days</td>
</tr>
<tr>
<td>• Cerebrospinal fluid containing mostly lymphocytes and elevated protein</td>
</tr>
<tr>
<td>• Abdominal swelling, with or without palpable lumps</td>
</tr>
<tr>
<td>• Progressive swelling or deformity of a bone or a joint including the spine.</td>
</tr>
<tr>
<td><strong>Laboratory investigations</strong></td>
</tr>
<tr>
<td>• Microscopic examination for acid fast bacilli (Ziehl-Nielsen stain) and culture of specimen, such as early morning gastric aspirates for three consecutive days and pleural, ascites and cerebral spinal fluid as relevant</td>
</tr>
<tr>
<td>• Gene Xpert (where available)</td>
</tr>
<tr>
<td>• Chest radiograph for lobar opacity, pleural effusion, military pattern.</td>
</tr>
<tr>
<td>• PPD Tuberculin skin test (&gt;5mm is positive)</td>
</tr>
</tbody>
</table>

*Modified from WHO Treatment of TB Guidelines for National Programmes, fourth edition, 2010*
Diagnosis of Extra-pulmonary TB
Clinicians may use the following to diagnose extra pulmonary TB:

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

Treating TB in Children
In most instances, treatment of TB is usually presumptive because it is difficult to make an aetiological diagnosis. In treating children who are co-infected with HIV and TB, use our national guidelines (see Annex H). There exist drug/drug interactions between some TB drugs and antiretroviral drugs. Because of the interaction between protease inhibitors and rifampicin, treatment in patients who are co-infected with TB and HIV will have to be modified.

4. Lymphoid Interstitial Pneumonitis (LIP)
Lymphoid interstitial pneumonitis (LIP) is common in children (occurs in at least 40% of children with perinatal HIV) and usually occurs in children aged over two years. LIP is often mistaken for pulmonary TB (miliary) because of the chronic cough and the miliary-like pattern on chest x-ray; hilar/mediastinal lymph nodes also occur. The table below highlights similarities and differences between LIP and TB. Diagnosis of LIP is usually by exclusion.

Table 45: Similarities and Differences between LIP and TB

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Miliary</th>
<th>LIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory distress</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>Wasting</td>
<td>+++</td>
<td>+/-</td>
</tr>
<tr>
<td>Persistent fever</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Generalised lymphadenopathy</td>
<td>-/+</td>
<td>+++</td>
</tr>
<tr>
<td>Parotid enlargement</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Digital clubbing</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CXR features</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diffuse micronodular</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>• Diffuse reticulonodular</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>

Managing LIP includes the following:

- Steroids when children with LIP have significant respiratory distress (exclude TB first): Prednisone 2 mg/kg/day initially for four weeks daily then alternate day maintenance for two to three months and review.
- Oxygen therapy during episodes of hypoxia
- Bronchodilators (e.g. salbutamol) where wheezing is a problem
- Antibiotics during episodes of concurrent super-infection with pneumonia
- Chest physiotherapy and postural drainage if there is secondary bronchiectasis
- Refer for specialist care if resistant to therapy
5. Bronchiectasis
Bronchiectasis may occur as a complication of severe or recurrent pneumonia, TB, LIP, or measles. It involves damage to the bronchial lining because of recurrent infection and weakening of the bronchi with cystic formation and secondary infection.

The clinical presentation of bronchiectasis includes the following:
- Chronic cough, mainly in the morning
- Copious purulent sputum
- Halitosis
- Digital clubbing
- Recurrent pneumonia

Diagnosis involves clinical criteria noted above, a chest x-ray which may show localised infiltrates, cystic areas (honeycomb appearance) and dilated bronchi (persistent opacity in one area). Where possible, collect sputum and culture for bacteria and to exclude fungi and treat appropriately.

Treatment:
- Supportive treatment includes daily chest physiotherapy and postural drainage.
- Broad-spectrum antibiotics
- Bronchodilators such as salbutamol can be used when bronchospasms are present.
- Consider referral to a specialist. Surgery may be necessary in cases with segmental lung damage.

6. Viral Pneumonitis
Children with HIV may develop severe viral pneumonitis from a number of viruses, including respiratory syncytial virus (RSV), parainfluenza virus, influenza virus, adenovirus, varicella (chicken pox), measles, and cytomegalovirus (CMV). However, it is not possible to confirm the actual aetiological agent. The clinical presentation may be much more severe and case fatality higher than in non-HIV-infected children. Viral pneumonitis in HIV-infected children presents as pneumonia rather than bronchiolitis.

Specific treatment for CMV is Ganciclovir, but this is rarely available and very expensive. HAART may be useful in ameliorating severity. Varicella zoster immunoglobulin may reduce the severity of varicella pneumonitis if it is given within 72 hours of exposure. Alternatively, you may use oral acyclovir. Immunisation (measles vaccine) can prevent measles but you can also give measles immunoglobulin (0.5 ml/kg (maximum 15 ml) within six days of measles exposure, regardless of previous measles immunisation history.

7. Other Pulmonary Conditions
Kaposi’s sarcoma (KS) is the most common HIV-associated malignancy associated with the lungs. In addition to the mucocutaneous lesions and lymphadenopathy, patients present with progressive cough and rarely haemoptysis. Chest x-rays will show mediastinal lymphadenopathy, pleural effusion, or bilateral interstitial infiltrates. Diagnosis of pulmonary KS can be made at bronchoscopy, where multiple purplish lesions can be visualized. Intra-pulmonary biopsy should not be done, as it can lead to profuse haemorrhage. Treatment includes chemotherapy and needs referral to experienced centres of cancer treatment.

Lymphomas (both T- and B-cell) may present with non-specific symptoms and signs, and chest x-rays showing mediastinal lymphadenopathy, focal opacities, or pleural effusions. Refer patient to a level 3 hospital.
Exercise B

1. What are the common pulmonary conditions that occur in HIV positive children?
2. What is the aetiology of Pneumocystis Pneumonia?
3. When is the incidence of PCP at its highest?
4. Chimfwembe, a six month old infant weighing 7 kg is referred to UTH from Chelston Clinic with a diagnosis of severe pneumonia. He was admitted at Chelston Clinic for two days and was treated with crystalline penicillin and chloramphenicol with poor response. On examination there is:
   - Low-grade fever (37.9°C)
   - Marked respiratory distress (chest in-drawing, cyanosis, inability to drink)
   - Auscultation: clear chest
   - He also has extensive oral thrush
   - Chest X-Ray reveals non-specific radiological changes. The presumptive diagnosis is PCP. What will be your supportive, specific and long-term management of this child?
5. Mweshi is a female infant admitted as a case of severe pneumonia, her temperature is 39.2°C. How will you manage the child?

Role Play

Mother: You have brought your 2 year old daughter for her 3 month review on ART (ABC, 3TC, LPV/r). You are worried because Tombi has lost weight and over the past 3 weeks she has looked sicker than usual, she has low grade fever with associated night sweats. You took her to the local clinic 2 weeks ago and procaine penicillin was prescribed without improvement, in fact she is actually getting worse. You are worried that she might have TB, because her father died of TB 4 months ago. Her baseline %CD4 was 4%.

Doctor: You weigh the child, her weight is 8kg, her previous weight last month was 9.5kg, and upon physical examination you notice that, there is dullness on percussion with reduced air entry to the right lung. She has enlarged non tender lymph nodes in the neck... You conclude that the child has right sided pleural effusion. You admit, order early morning gastric aspirates for three consecutive days and you tap a little pleura fluid for microscopic examination for acid fast bacilli (Ziehl-Nielsen stain) and culture of specimen. Chest radiograph confirms right sided pleural effusion, gastric lavage and pleural aspirate are both negative for AAFB. How will you manage this child?

When you finish the exercise discuss your answers with your facilitator. Then proceed to read your module on “Other Medical Conditions” and then do Exercise C.

Unit 3: Other Medical Conditions

Dermatitis and other Skin Manifestations

The most common skin manifestation of HIV and AIDS in children is a non-specific generalised dermatitis. Viral, bacterial, and fungal skin infections are more common and are also more difficult to treat than in children who are not immune compromised. Other manifestations include flat warts and molluscum contagiosum which do not have specific therapy.

Table 46: Common Skin Manifestations and Treatment

<table>
<thead>
<tr>
<th>Skin manifestation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scabies treatment</td>
<td>• 25% benzyl benzoate for 12 hours or gamma benzene hexachloride</td>
</tr>
<tr>
<td>children &lt; 1 year</td>
<td>• 2.5% sulphur ointment 3 x daily for 3 days</td>
</tr>
<tr>
<td></td>
<td>• Screen and treat other household contacts where appropriate</td>
</tr>
<tr>
<td></td>
<td>• Wash and iron bedding and clothing or hang them out in the sun</td>
</tr>
</tbody>
</table>
**Eczema treatment**
- Avoid soap and expose affected areas to sunlight
- Use aqueous cream and other moisturizers on dry areas
- Apply zinc oxide cream twice daily; if not responding, use 1% hydrocortisone cream twice daily
- Cut nails short

**Ringworm treatment**
- Apply Whitfield’s ointment (benzoic acid with salicylic acid) twice daily for 2-5 weeks for body lesions; if not successful try miconazole cream.
- For scalp lesions give griseofulvin 10mg/kg/day for 8 weeks; if not responding consider ketoconazole

**Herpes Zoster**
- Hospitalize all cases and treat; if possible with I/V acyclovir 30mg/kg/day divided into 3 doses (eight hourly) for a total of 7 days or 2 days after cessation of new lesion eruption, whichever is longer.
- Children who have been exposed to herpes zoster may receive prophylactic varicella-zoster immune globulin (VZIG) 125u per 10kg (max 625u) within 48-96 hours of exposure

### Oral and Dental Conditions

The most common oral condition in HIV-infected children is **candidiasis**, which may present as oropharyngeal or oesophageal candidiasis. Oral thrush is associated with difficulty or pain in swallowing or vomiting. *Children therefore present with reluctance to take food, excessive salivation, or crying while feeding.* Exclude other conditions that cause painful swallowing and are frequently found in HIV-infected children such as CMV, Herpes simplex, and lymphomas.

**Table 47: Treatment of Candidiasis**

<table>
<thead>
<tr>
<th><strong>Oral Candidiasis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nystatin 1-2 million u/day divided into 6 hourly doses for 14 days</td>
</tr>
<tr>
<td>• Fluconazole 3-6mg/kg once daily for 7-14 days</td>
</tr>
<tr>
<td>• Miconazole gel</td>
</tr>
<tr>
<td>• Ketoconazole 5-10mg/day once daily for 14 days; note that there are drug-drug interactions with antiretroviral drugs therefore avoid in children on ARVs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Oesophageal Candidiasis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fluconazole 3-6mg/kg once daily for 14 days</td>
</tr>
</tbody>
</table>

Other common dental conditions of HIV-infected children include:
- Dental caries
- Aphthous ulceration (Herpes simplex-related ulcer; if diagnosed early it will be amenable to acyclovir)
- Oral hairy leukoplakia
- Angular stomatitis
- HIV-associated gingivitis

### Cardiac and renal diseases in HIV

Clinicians should evaluate HIV-infected children for cardiovascular and renal symptoms and refer to specialist if patients are suspected or confirmed to have cardiac or renal disease.

### Anaemia

*Anaemia is a common condition in HIV-infected children and contributes significantly to morbidity. HIV-infected children have an equal prevalence of anaemia compared to uninfected children but have a higher case fatality rate.* Manage according to IMCI guidelines.
Malignancies
Clinical experience indicates that the frequency of occurrence of some malignancies is increasing. The major malignancies associated with HIV infection in African children are Kaposi’s sarcoma (KS) and non-Hodgkin’s lymphoma (Burkitt’s lymphoma, B-cell lymphoma). In Zambia we see both. *Treatment requires chemotherapy and ART and often leads to regression of the lesions. Refer to a level three hospital for initiation of treatment.*

Parotid Enlargement
Bilateral parotid gland enlargement is one of the most specific signs of HIV infection in children. Periodically the parotid glands may enlarge and regress over several months, and *intermittently they may become tender from bacterial supra-infection.* When they are tender, prescribe antibiotics and analgesics. *There should be no surgery.*

**Exercise C**

1. Lengwe, a ten year old girl, has been brought in for large bilateral parotid enlargement. Generally she is of good health, although she has a recurrent wheeze and the clinical officer at the clinic told the mother that she has asthma. She has been treated on two courses of ATT based on a non-resolving bad CXR. On physical examination she has respiratory distress, parotid enlargement, generalised lymphadenopathy, hepatosplenomegaly and finger clubbing. CXR reveals diffuse bilateral reticulonodular infiltrates appear similar to milliary TB and bilateral hilar or mediastinal lymph node enlargement.  
   a) What is your diagnosis?  
   b) How will you manage this child?

2. Anne is a 12 year old girl who looks quite small for her age. She weighs 25 kg and her height is 130cms. She is an orphan. She has been brought to the clinic because of a chronic productive cough of unspecified duration. She produces copious purulent sputum especially upon waking up in the morning, and she also has bad breath. Physical examination reveals halitosis and digital clubbing. Chest x-ray shows localised infiltrates, cystic areas, and dilated bronchi. How will you manage this child?

3. Chewa is a five year old boy with generalised lymphadenopathy. He was previously treated for TB adenitis with little improvement. The lymphadenopathy is so large that the clinic has decided to refer him for biopsy. The biopsy reveals lymphadenopathic Kaposi sarcoma. How will you manage this child?

4. Mulala is a seven year old boy with persistent generalised lymphadenopathy. What would be your differential diagnosis?

5. What are the most common skin manifestations of HIV and AIDS in children?

6. Lulu, a seven month old child, was growing well until two weeks ago, when her mother noticed reluctance to breastfeed even when hungry. The mother tried giving her cereal, she initially ate a little, but cried whilst being fed and eventually refused that as well. The mother looked in her mouth; there were a few white patchy lesions on the hard palate. She took her to the local clinic where amoxy and paracetamol were prescribed and mother was advised to do oral saline toilet twice a day. After two weeks of illness, the child is still vomiting all her feeds and she had lost 2kg. The mother has brought the child to the hospital. What is your diagnosis and how are you going to manage this child?

7. Seventeen month old Misodzi was referred to the hospital when her mother reported that she no longer smiled. Mother says the child had grown well up to 11 months of age, used to laugh, could sit unsupported and was able to stand, but has since regressed her developmental milestones. You examine the child. Her weight is 6.5kg, and she has a small head, stiff limbs with abnormal reflexes in all four limbs. You presume it is HIV and AIDS. Stage the disease and advise on management.

*When you finish the Exercise discuss your answers with your facilitator, thereafter you will be advised on when to proceed to Module 8 on “Palliative and End-of-life Care”.*
Module 8
Palliative and End-of-life Care
Learning Objectives
At the end of this module the health workers will be able to:
• Define and describe the goals of palliative care.
• Describe the management of symptoms and role of Home Based Care in palliative care.

Listen to the presentation (or read your modules) on “Palliative and End-of-life Care” and then do Exercise A.

Unit 1: Definition and Goals of Palliative Care

Palliative care is an active approach that aims to improve the quality of life of children and their families facing problems associated with chronic ill-health. Palliative care includes symptom management during both acute and chronic illness and end-of-life care.

The goals of palliative care are:
• Providing relief from pain and other distressing symptoms
• Integrating the psychological, medical, nursing, spiritual and social aspects of child care (holistic care)
• Ensuring continuum of facility-based with home-based care services
• Using a team approach to address the needs of the child and their families.

An HIV-infected child often has considerable discomfort; so good palliative care is essential. Take all decisions together with the mother or caregiver, and communicate them clearly to other staff. Consider palliative care at home as an alternative to hospital care. Some treatments for pain control and relief of distressing conditions (such as oesophageal candidiasis or convulsions) can significantly improve the quality of the child’s remaining life. Give end-of-life (terminal) care if:
• the child has had a progressively worsening illness
• Everything possible has been done to treat the presenting illness.

Ensuring that the family has appropriate support to cope with the impending death of the child is an important part of care in the terminal stages of HIV. Parents should be supported in their efforts to give palliative care at home so that the child is not kept in hospital unnecessarily.

Unit 2: Management of Symptoms in Paediatric Palliative Care

Pain Management
Pain as a symptom takes on special significance in children because it is very common and is often under-diagnosed and under-treated, even when effective and inexpensive medication are available. The management of pain in HIV-infected children follows the same principles as for other chronic diseases such as cancer or sickle-cell disease. A rational approach to pain management includes the following:
• assessment (history and physical exam to elicit potential causes and type of pain)
• Classification (is the pain mild, moderate, or severe?)
• treatment (depending on likely cause, type, and severity of pain)
• reassessment to ensure that optimal pain management is achieved and maintained

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

- Interviewing the older children
- Interviewing the caregiver (younger children in particular need adults to recognize and respond to their pain).

Observation:
  a) Crying and distressed facial expression.
  b) Persistent pain—also look for behavioral signs of pain:
  c) Irritability and restlessness
  d) Not wanting to move
  e) Lack of interest
  f) Decreased ability to concentrate
  g) Sleeping problems
  h) Changes in how the child moves
  i) Increased breathing rate or heart rate

To the extent possible, pain medication should be given:

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

Decisions about pain medication should be individualized for each child.

**Mild and Moderate Pain**

**Analgesics for mild to moderate pain (such as headaches, post-traumatic pain, and pain from spasticity) include the following:**

- Paracetamol
- Non-steroidal anti-inflammatory drugs, such as ibuprofen.

**Moderate and Severe Pain**

**Potent analgesics such as opiates are used for moderate to severe pain.**

- Codeine: give orally every 6–12 hours, combined with non-opioids to achieve additive analgesia.
- Morphine is an inexpensive and potent analgesic: give orally every four to six hours. Monitor carefully for respiratory depression. If tolerance develops, the dose will need to be increased to maintain the same degree of pain relief.
- Pethidine: give every four to six hours – for acute pain, i.e. post op pain

If pain is severe, provide the full four hourly dose of oral morphine, and in addition, give the next scheduled 4 hourly dose at the prescribed time. Add up all required additional doses provided in 24 hours, and increase the next day dose by this amount, spread evenly across the six four hourly doses. In general, one should allow 24 hours before considering a dose increase or oral morphine. It is important to note that there is no maximum dose for oral morphine, as long as pain is inadequately controlled. The right dose of oral morphine is the dose that achieves optimal analgesia, and this is determined through titrating dose against analgesia response. Pain is the natural antidote to morphine overdosing.

Figure 12 presents treatment guidelines for pain in children. They are based on the WHO analgesic ladder for the management of mild, moderate, and severe pain.
Figure 12: The WHO Analgesic Ladder

* Note that aspirin should generally be avoided in children (because of Reye’s syndrome
** If pain control is not achieved with usual therapeutic doses of step 1 medications, the logical step would be to move on to step 2 (rather than increasing doses of the step 1 drugs).

Opioids include codeine, morphine, and Pethidine.

Adapted from: Palliative Care: A community health approach to palliative care for HIV/AIDS and cancer patients in Sub-Saharan Africa, WHO, 2014

Other Pain Control Measures

**Table 48: Pain Control Measures**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>Apply on gauze to painful mouth ulcers before feeds (apply with gloves) it acts in two to five minutes. TAC (tetracaine, adrenaline, cocaine): apply to a gauze pad and place over open wounds; it is particularly useful when suturing.</td>
</tr>
<tr>
<td>Other drugs</td>
<td>Specific pain problems include diazepam for muscle spasm, carbamazepine or amitriptyline for neuralgic pain, and corticosteroids (such as dexamethasone) for pain due to an inflammatory swelling pressing on a nerve.</td>
</tr>
</tbody>
</table>

Non-pharmacologic approaches to relieve pain in children

1. Use distraction methods to help relieve pain
   a) Age-appropriate active distraction
   b) Older child can concentrate on games, conversation or special story
   c) Music
2. Other non-drug methods:
   a) Swaddling, carrying infant, warmth, breastfeeding, feeding.
   b) Stroking, rocking, massage.
   c) Avoid intramuscular injections in pain control.

**Management of Anorexia, Nausea and Vomiting**
Encourage caregivers to continue providing meals and to try:
- giving small feeds more frequently, particularly in the morning when the child’s appetite may be better,
- giving cool foods rather than hot foods,
- avoiding salty or spicy foods.

**Use metoclopramide 0.1-0.2 mg/kg q4-6h for severe nausea and vomiting**

**Skin care**
Children in palliative care are prone to rashes, some of which are itchy.
- Clean and cover moist areas with a dressing, or expose and apply GV solution if there are not too any flies around.
- Keep finger nails short and clean to help reduce scratched areas from getting infected.
- Give an anti-histamine for sleep at night if sleep is disturbed by scratching.
- Sometimes an oil-based cream or a short course of a weak steroid cream is helpful.

**Prevention and Treatment of Pressure Sores**
- Check predilection sites for pressure sores frequently
- Teach the caregivers to turn or change the position of the child at least once every two hours.
- If pressure sores develop, keep them clean and dry.
- Clean and cover sores with a dressing,
- Use local anaesthetics to relieve pain.

**Care of the Mouth**
- Teach the caregivers to wash out the mouth of the patient after every meal.
- Mouth ulcers: clean the mouth at least four times a day, using clean water or salt solution and a clean cloth rolled into a wick.
- Apply 0.25% or 0.5% gentian violet to any sores.
- Crushed ice wrapped in gauze and given to the child to suck may give some relief.
- Avoid bottle-feeding.
- Oral thrush: use antifungals
- Secondary bacterial infection: use penicillin plus oral metronidazole for seven days.
The Role of Home Based Care in Palliative Care

Table 49: Role of Home Based Care in Palliative Care

<table>
<thead>
<tr>
<th>Prepare for Treatment</th>
<th>Prepare household members, community leaders on treatment expectations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disclosure</td>
<td>Promote disclosure readiness at home. Identify treatment assistant in household.</td>
</tr>
<tr>
<td>Adherence</td>
<td>Strengthen adherence techniques in routine daily life (travel, work). Remind treatment appointments.</td>
</tr>
<tr>
<td>Recognize</td>
<td>Early recognition of side effects: rashes, numbness, weakness, jaundice and treatment failure: weight loss, opportunistic infections (OIs).</td>
</tr>
<tr>
<td>Refer</td>
<td>Assist clients/patients to attend counselling, testing and care in hospital</td>
</tr>
<tr>
<td>Organize</td>
<td>Design safe storage for drugs at home</td>
</tr>
<tr>
<td>Nutritional Support</td>
<td>Promote balanced food intake for all, including those on ART</td>
</tr>
</tbody>
</table>

Exercise A

1. At what point in the care of a child with HIV would you offer palliative care?
2. What are the steps to a rational approach to pain management?
3. Lillian, a 14 month old toddler, has severe gingivo-stomatitis. How will you manage this condition?
4. Misodzi, a five year old terminally ill child has no appetite and is refusing most meals. What will you advise the caregiver?
5. Simeza is a four year old terminally ill child who has extensive mouth ulcers. What will be your advice to the caregiver?

When you finish the exercise discuss your answers with your facilitator, thereafter you will be advised on when to proceed to Module 9 on “Adolescent HIV Services”.
Module 9
Adolescent HIV Services
Learning Objectives
At the end of this module the health workers will be able to:
• Explain adolescence and stages of development
• Explain adolescence and sexuality.
• Identify challenges of adolescents living with HIV
• Develop strategies to address the concerns of adolescence
• Explain life skills for adolescents
• Transition adolescents to adult services

Listen to the presentation (or read your modules) on “Adolescent HIV services” thereafter will be group work and plenary discussion on comprehensive services for HIV-infected adolescents for your health facility.

Unit 1: Adolescence and Stages of Development

WHO defines adolescents as individuals aged 10–19 years and young people as those aged 10–24 years. It is a stage of rapid physical growth and mental development and is recognised in many communities and cultures and marked with traditional rites of passage. At the same time, the adolescent is going through a process of acquiring knowledge and skills to enable them to live independently.

The HIV epidemic among young people is largely invisible to them and society. Infection rates among young women are at least twice as high as in young men. Adolescents (10-19 years) represent 26% of the Zambian population. An estimated 27,000 young people (15-24 years old) were newly infected with HIV in 2011 with 60% of them being girls. In 2013, it was estimated that 90,329 children living with HIV were in need of treatment.

Adolescents and HIV
All adolescents should be encouraged to test for HIV (consent and assent issues) and all HIV positive adolescents should be encouraged to commence treatment immediately if they are below 15 years while those above 15 years should follow the adult guidelines. ARV dosage is linked to Tanner staging and age while youth friendly services make access for adolescents much safer and easier.

Stages of Adolescence
The following are the different stages of adolescence:
• Early adolescence (10-13 years)
• Mid-adolescence (14-16 years)
• Late adolescence (>17 years)

The categories of adolescent changes are physical, social and psychological. General characteristics of adolescent changes include the following:
• Developing autonomy
• Establishing satisfactory relationships
• Developing an identity
• Developing moral reasoning
Physical Changes
The following physical changes will take place:
• Growth of pubic hair and arm pits hair
• Profuse sweating and body odor
• Acne on the face.
• Physical attraction to others

For boys, the following will happen:
• Deepening of voice
• Muscle development
• Wet dreams
• Growth of facial hair

While for girls, the following changes will take place:
• Enlargement of breasts
• Menstruation begins (menarche)
• Widening of hips

Social Changes
Social adolescent changes include the following:
• Friendship formation
• Attraction to opposite sex
• Formation and joining of peer groups
• Dress to fit fashion and peers
• Seeking for recognition
• Need for adventure

Psychological changes
Finally, the following psychological changes will manifest:
• Emotional and moody
• Rebellion
• Egocentric
• Increased sexual feelings
• Curious and inquisitive
• Sense of independence
• Creative and innovative.
• Seeking and doubting the meaning of life.

Table 50: Physical Development and Sexual Maturation (Tanner Classification)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Physical Development and Sexual Maturation</th>
</tr>
</thead>
</table>
| Early | Girls – breast bud, downy pubic hair near labia, peak growth velocity  
      | Boys – darkening and enlarging scrotal sac, testicular growth, downy pubic hair |
| Mid   | Girls – further growth of breasts, increased pigmentation of pubic hair, menarche  
      | Boys – further increase in size of testes, enlargement of penis, growth |
| Late  | Mature physical development               |
**Unit 2: Adolescence and Sexuality**

**What is Sex?**

Sex is the state of being male and female (maleness or femaleness). The gender roles that are associated with each sex (e.g. nurturing is left for women whereas security and breadwinner role is for men). It can also be described as the emotions associated with being a male or a female. Sex includes the anatomy of the female and the male and their functions.

**Definition of Sexuality**

Sexuality is the inter-play of physical, psychological, social and spiritual make up of gender, gender roles, gender identity, sexual orientation, sexual preference, and social norms as they affect physical, emotional and spiritual life.

**Social status of girls and women**

In many African societies, a girl’s status is only recognized when she enters into a sexual relationship and demonstrates the ability to have a baby. Older men usually seek younger sexual partners. In such a relationship the girl is vulnerable because she is not able to negotiate for safe sex with the older man who has a greater risk of infection. Her dependence on the older man makes her vulnerable.
Adolescent physical development and risk of STI's
Young adolescents have an immature genital tract which is more vulnerable to STI's and HIV. This is because of:
• Insufficient thickness of the vaginal wall
• Insufficient mucous protection
• Cervical cells (columnar epithelium) which are protective against infection are not yet fully developed.
• Early maturing adolescents may be at greater risk of peer pressure to engage in high risk behavior.

Environmental influences on risk taking behavior
Social and cultural environments are strong determinants of sexual risk taking. Poverty and isolation may increase an adolescent’s likelihood of becoming sexually active
Several studies on orphans in Kenya found that a significant percentage of girls aged 11-15 years had either had a baby, an abortion or were pregnant (Mutemi et al.)

Role of parents in sexual education
Parents play a very important role in their children’s sexual education. The ideal practice is for them to talk about sex and sexuality with their adolescent children. However parents experience many barriers to communicating about sexuality with their children including:
• limited knowledge about HIV/AIDS
• lack of information, lack of confidence with their own sexuality & history of not discussing these issues with their parents

Gender and peer Influences on sexuality.
Sexually active adolescent girls tend to rely on their male partners for sexual decision making and they will tend to have sex to please their boyfriends even when they themselves do may enjoy it. For boys to have sex - it is a sign to prove man hood.

Factors which influence sexual activity
Factors such as an adolescent’s attributes will influence sexual activity. These include:
• Values, attitudes, beliefs, perceptions, standards etc.
• Adolescents with a high sense of self-esteem and strong goal orientation are more likely to delay sexual activity.

Adolescent development
There are three stages of adolescent development: early, middle, and late adolescence. Tanner classification is used to stage sexual maturation, and physical growth and maturation. Table below summarises the changes that adolescents experience during different stages of development. It is worth noting that physical and sexual maturity does not mean there is emotional and cognitive maturity to anticipate the undesirable effects of sex such as pregnancy and STIs- since sexual maturation is completed well before emotional and cognitive development.
Table 51: Stages of Adolescent Development

<table>
<thead>
<tr>
<th>Emotional Development</th>
<th>Early (10-13 years)</th>
<th>Mid (14-16 years)</th>
<th>Late (≥ 17 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wide mood swings, Intense feelings, Low impulse control</td>
<td>Sense of invulnerability, Risk taking behavior peaks</td>
<td>Sense of responsibility for one’s health, Increasing sense of vulnerability, able to think of others and suppress one’s needs, less risk taking</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cognitive Development</th>
<th>Early (10-13 years)</th>
<th>Mid (14-16 years)</th>
<th>Late (≥ 17 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Concrete thinking Little ability to anticipate long term consequences of their action Literal interpretation of ideas</td>
<td>Able to conceptualize abstract ideas such as love, justice, truth and spirituality</td>
<td>Formal operational thought. Decision making tree can be made. Essential to understanding the consequences of various actions. Ability to understand and set limits. Can understands other’s thoughts and feelings</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relation to Peers</th>
<th>Early (10-13 years)</th>
<th>Mid (14-16 years)</th>
<th>Late (≥ 17 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increased importance and intensity of same sex relationships</td>
<td>Peak of peer conformity Increased opposite sex relations</td>
<td>Peers decrease in importance Begin to develop mutually supportive, mature, intimate relationships</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relation to Family</th>
<th>Early (10-13 years)</th>
<th>Mid (14-16 years)</th>
<th>Late (≥ 17 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estranged Need for privacy</td>
<td>Peak of parental conflict. Rejection of parental values</td>
<td>Improved communication Acceptance of parental values</td>
</tr>
</tbody>
</table>

Unit 3: Challenges around HIV/AIDS and the Adolescent

A large proportion of adolescents in Zambia are at risk of HIV infection. The social environment of adolescents influences their ability to access HIV-related services. Typically, adolescents have limited financial capability that restricts their access to HIV treatment services. Regardless of their social status, non-infected adolescents need preventive services, and those who are infected require care, treatment, and support. Essentially there are two groups of adolescents living with HIV:

**Adolescents face a lot of challenges including:**

- Limited knowledge about HIV transmission and prevention
- Limited access to health information and care
- Lack of adolescent-friendly health facilities
- Myths and misconceptions on sex and sexuality
- Issues of marriage and child bearing
- Conforming to cultural sexual roles and expectations.
- Disclosure
• Poverty
• Sex in exchange for money “sugar daddies and mummies”
• Growing up in dysfunctional families
• Peer influences
• Stigma and discrimination

**Risk taking**

Determinants of risk-taking behaviour in adolescents include their stage in development, biological and physiological characteristics, individual attributes, and their environment. A number of high-risk behaviours, such as alcohol and drug abuse, often lead to sexual risk taking. Adolescents tend to have a poor perception of their own risk of HIV and their perception of risk differs from adults. Studies among adolescents have shown that people with a high sense of self-esteem and direction are less likely to be involved in risk-taking behaviour such as sexual experimentation or substance abuse. Studies have also demonstrated that many adolescents lack in-depth knowledge about HIV. They do not internalise the biological explanation of disease causation.

Biological factors that put young women at risk include immaturity of the cervix in adolescence. The single layer of columnar cells in the cervix is more vulnerable to transmission of STIs, including HIV, than the multiple layers of squamous epithelial cells in the mature cervix.

**Strategies to support ALHIV include the following:**

• Develop support systems for adolescents.
• Address sexual issues among adolescents.
• Addressing of reproductive health issues among adolescents.
• Parenting seminars for caretakers
• Adolescents should be empowered to disclose their HIV status.
• The adolescents should be empowered with life skills
• Adolescents engage in activities without analyzing the consequences.
• Disclosure can be a challenge to intimate relationship.

**Unit 4: Communicating with and counseling adolescents**

**Challenges in communicating with adolescents**
Adolescents tend to not have pre-conceived ideas regarding the treatment process and tend to take time to build trust in therapist & to settle into counseling process. They are more likely to be non-compliant with medication or other treatments and they are less likely to seek health care from other sources, including health centers.

**Challenges and Issues**
Adolescents may be physically and sexually mature enough to engage in what is perceived as “adult” activities (smoking, taking alcohol, sex etc.)

However lack of cognitive maturation and experience makes it difficult for the adolescent to perceive today’s actions as directly related to tomorrow’s consequences.

Adolescents need positive responses from adults and a balance between structure and freedom to express their feelings in order to gain stability.

If adolescents receive a positive response, they are able to develop new inner resources such as identity, purpose in life, independence, responsibility and the ability to endure problems.
Counseling the adolescent

By the time they reach adolescence, many perinatally infected children have the stigmata of chronic illness, including stunted growth and development and poor school performance because of frequent absences. The delay in adolescent development often leads to poor self-esteem and a great sense of inadequacy.

Effective counselling for adolescents should be culturally sensitive, tailored to their developmental needs, and in accordance with local values and laws. Psychosocial care should revolve around disclosure of HIV status, family or partner notification, and understanding the disease and treatment modalities. Adolescents must be supported to cope with illness and death, their own as well as that of their parents.

The following tips may assist in the successful counseling of adolescents:

- Identify assets/strengths
- Be creative in counseling (take a walk together, listen to music)
- Encourage responsibility
- Understand adolescent “language”

Keys to Effective Counseling with Adolescents

- The most important instrument is you! The therapeutic alliance/relationship is crucial to moving forward and is key to all future stages of therapy.
- Attitude and behavior are critical.
- Adolescents are more likely to improve when treatment is integrated with warmth, genuineness, and empathy.

Unit 5: Life Skills

Definition:

Life skills are skills needed by an individual to operate effectively in society in an active and constructive way. Personal and social skills are required for young people to function confidently and competently with themselves, with other people and the wider community.

Having life skills helps adolescents be confident, knowledgeable, and able to take responsibility for their lives. It develops them into stronger, more aware and more caring human beings equipped to cope more with demand and pressure. It also helps them assess risk levels and to take only those risks which are likely to lead to a better life. The component of life skills are: self-awareness, coping with emotions, making decisions, different ways of communicating, assertiveness and negotiations.

Life skills are required to facilitate development of adaptive and positive behaviors as well as to enable adolescents to effectively deal with the demands and challenges of life.

Categories of Life Skills

There are different categories of life skills and these are discussed below:

a) The skills of knowing and living with oneself which includes:

- Self awareness
- Self esteem
- Assertiveness
- Coping with emotions
- Coping with stress
b) **The skills of knowing and living with others:**
- Inter personal relationships
- Friendship formation
- Empathy
- Peer pressure/resistance
- Negotiation
- Non – violent conflict resolution
- Effective communication

c) **The skills of making effective decisions:**
- Decision making
- Critical Thinking
- Creative Thinking
- Problem solving

Adolescents prefer healthcare settings that are oriented to their age group and providers who are attuned to their specific needs. The ideal facility is a one-stop centre with multidisciplinary providers for primary care, gynaecological services, OI prophylaxis, and ARV drugs; but often this is not available or immediately possible. The following principles should guide national policies and youth services in general. Every client has a right to:
- Information and access - regardless of sex, creed, colour, marital status, or location
- Choice
- Safety
- Privacy and confidentiality
- Dignity—to be treated with courtesy, consideration, and attentiveness
- Comfort—to feel comfortable when receiving services
- Continuity—to receive services/supplies for as long as needed
- Opinion—to express views on services offered

**Transitioning**
Taking on a greater role in self-care and self-advocacy may be challenging for the adolescent, depending on their level of development and maturation. Not all ALHIV will be ready to make the transfer to adult care at the same age. Healthcare workers must take into account their cognitive and physical development, their emotional maturity, their support at home and in the community, and their health status. It is possible for adolescents to have a smooth transition to adult care and receive adolescent-friendly services in the adult clinic.

Key factors that support successful transition include: an agreed transition plan that gives the ALHIV time to prepare for the transition and to take on more responsibility for self-care, an adult clinic that is willing to meet the special needs of adolescents and is staffed with healthcare workers who understand the special needs of ALHIV.
A Self-care and Transition Timeline for ALHIV

Table 52: Self-care and Transition Timeline

<table>
<thead>
<tr>
<th>Age</th>
<th>Advice</th>
</tr>
</thead>
</table>
| 10–12 years old | • Encourage caregivers to fully disclose to the child  
                         • Solicit direct conversation with the adolescent  
                         • Increase private meetings and counselling sessions with the adolescent  
                         • Begin to explain medications and adherence  
                         • Deal with early adherence issues and challenges  
                         • Link to support groups                                                                                                                                 |
| 13–16 years old | • Assist adolescent with a calendar for appointments and medicines  
                         • Ensure adolescent understands diagnosis, needed medications, adherence, health precautions, positive living, and positive prevention |
| 16–19 years old | • Enforce responsibility in making and keeping appointments  
                         • Provide ALHIV with copies of medical records and any other forms or documents required by the adult clinic  
                         • Review medical history with the client  
                         • Encourage questions about care plan and treatment regimen and possible changes  
                         • Transfer medical records to new provider, highlight key issues  
                         • Visit the adult clinic together with the adolescent client |


Group Work and Plenary session
Get into your working groups and list services that are required by the HIV-infected adolescents. Then plan for comprehensive services for adolescents that include non-ARV and ARV care for HIV-infected adolescents for your health facility.

a) Where and when will services be provided?  
b) By whom?  
c) What will be the non-clinical eligibility criteria?  
d) How will you cater for the disenfranchised adolescents

After discussion, have your rapporteur present in the plenary.

Take Home points
The following are key take home points:  
• Adolescence is a period of physical, emotional, social and cognitive changes  
• Sexual maturation is completed well before emotional and cognitive development  
• Adolescence is a “vulnerable” period that can result in risky behaviors and exposure to HIV infection.  
• HCW should be aware that adolescents living with HIV are faced with many challenges and should be able to address them.  
• Life skills for adolescents help in development of adaptive and positive behaviors to effectively deal with the demands and challenges of life  
• Preparing adolescents to take more responsibilities and transition to adult care is an important aspect
Module 10
Psychosocial Care in Paediatric HIV
Learning Objectives

By the end of the learning session, the healthcare workers will be able to:

- Explain the psychosocial problems in HIV affected children.
- Explain the psychosocial impact of HIV on children.
- Outline the types of psychosocial assessments and interventions.
- Describe communication and disclosure to children

Psychosocial support is an integral component of the holistic approach to caring for an HIV-infected child. “Psychosocial” refers to the dynamic relationship between social and psychological experiences where the effects of one continually influence the other. Psychosocial issues must be addressed from the perspectives of the child, the caregiver, and the healthcare provider. Support for a child and his/her family allows them to build on their strengths and adopt a positive outlook.

Unit 1: Psychosocial Problems in HIV affected Children

Causes of psychosocial problems can be at the individual child, family and community levels. See table below:

Table 53: Causes of Psychosocial Problems

<table>
<thead>
<tr>
<th>At Individual Child Level</th>
<th>At Family Level</th>
<th>At Community Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Poor Parenting</td>
<td>• HIV Illness in multiple family members</td>
<td>• Lack of knowledge of HIV</td>
</tr>
<tr>
<td>• Caring for both parents</td>
<td>• Poverty</td>
<td>• Lack of knowledge of children’s needs</td>
</tr>
<tr>
<td>and other siblings</td>
<td>• Stigma &amp; discrimination</td>
<td>• Worsening poverty</td>
</tr>
<tr>
<td>• Separation, from brothers and sisters</td>
<td>• Multiple losses</td>
<td>• Stigma and discrimination</td>
</tr>
<tr>
<td>• Chronic illness</td>
<td>• Dysfunctional relationships (abuse, Single parenting)</td>
<td>• Over stretched communities due to increasing numbers of orphans and vulnerable children</td>
</tr>
<tr>
<td>• Death or sickness of a parent</td>
<td>• Child-headed households</td>
<td></td>
</tr>
<tr>
<td>• Loss of home</td>
<td>• Elderly caregivers</td>
<td></td>
</tr>
<tr>
<td>• Abuse (sexual, physical, emotional)</td>
<td>• Chronic illness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Death and bereavement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Substance abuse, domestic violence</td>
<td></td>
</tr>
</tbody>
</table>

Stigma & discrimination are some of the major causes of psychosocial problems in children. Stigma may refer to:

- Negative labeling of a person/groups of persons in a way that reduces their dignity, self-image and self esteem
- Negative attitudes, reactions and actions from self or others due to HIV infection
- Bad feeling about self or others
Discrimination refers to:
- Stigma in action
- Stigmatizing thoughts, beliefs and derogatory attitude towards the affected individual.
- An act or behavior as a result of stigma
- Treating someone differently which include:
  a) Denial of rights and opportunities
  b) Social, psychological and physical abuse

Unit 2: Psychosocial Impact of HIV in Children

Children living with HIV may have the following psychosocial symptoms:

Table 54: Psychosocial Symptoms

<table>
<thead>
<tr>
<th>Physical symptoms</th>
<th>Behavioral symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Body pains (abdominal pain, headache chest pain)</td>
<td>• Restlessness</td>
</tr>
<tr>
<td>• General malaise</td>
<td>• Hyperactivity</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>• Withdrawal and self-neglect</td>
</tr>
<tr>
<td></td>
<td>• Aggressiveness</td>
</tr>
<tr>
<td></td>
<td>• Sleep disturbance</td>
</tr>
<tr>
<td></td>
<td>• Acting out</td>
</tr>
<tr>
<td></td>
<td>• Stealing</td>
</tr>
<tr>
<td></td>
<td>• Drug abuse and sexual promiscuity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emotional symptoms</th>
<th>Social symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Emotional neglect in infants from sick depressed mother</td>
<td>• Older children</td>
</tr>
<tr>
<td>• Irritability</td>
<td>• Avoidance and rejection by peers (due to effects of wasting, skin lesions etc)</td>
</tr>
<tr>
<td>• Lack of interest in surroundings</td>
<td>• Social withdrawal and isolation</td>
</tr>
<tr>
<td>• Depression, sadness and mood changes</td>
<td>• Antisocial behavior</td>
</tr>
<tr>
<td>• Suicidal tendencies</td>
<td>• Younger children</td>
</tr>
<tr>
<td>• Anxiety, fear and anger</td>
<td>• Difficult to identify</td>
</tr>
<tr>
<td>• Temper tantrums</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cognitive symptoms</th>
<th>Psychiatric symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inability to concentrate</td>
<td>(require referral to specialist services)</td>
</tr>
<tr>
<td>• Regression of milestones</td>
<td>• Confusion</td>
</tr>
<tr>
<td>• Forgetfulness or poor memory</td>
<td>• Forgetfulness</td>
</tr>
<tr>
<td>• Confusion</td>
<td>• Disorientation</td>
</tr>
<tr>
<td>• Poor academic performance</td>
<td>• Memory loss</td>
</tr>
<tr>
<td></td>
<td>• Personality changes</td>
</tr>
<tr>
<td></td>
<td>• Anxiety</td>
</tr>
<tr>
<td></td>
<td>• Seizures</td>
</tr>
<tr>
<td></td>
<td>• Agitation</td>
</tr>
<tr>
<td></td>
<td>• Aggression</td>
</tr>
<tr>
<td></td>
<td>• Hallucinations, Delusions</td>
</tr>
<tr>
<td></td>
<td>• Mood disorders</td>
</tr>
</tbody>
</table>
Unit 3:  
Psychosocial Assessment and Interventions

Definition of Psycho-social Assessment  
This is an in-depth investigation of the psychosocial dynamics that affect the client and the client’s environment.

The importance of assessment includes the following:  
• Identifying areas that promote and/or inhibit maximum independence and functioning  
• Developing an effective treatment plan that promotes maximum independence and functioning.  
• Poor assessment leads to poor treatment and assessment skills are a reflection of treatment skills.

Assessment of psychosocial problems should include the following areas:  
• Demographics  
• Surroundings  
• Living arrangements,  
• Family involvement/interaction  
• Extended family strengths and supports  
• Individual and family

Psychosocial assessment should be conducted at the first visit and should be an on-going activity at every subsequent visit. In addition the provider must be fully aware of all aspects of the patient’s treatment, stage of the illness and readiness for ARV.

Types and levels of psychological and social Intervention  
The various types of psychological and social interventions include play, family, group and support group therapy.

Table 55: Types of Psychological and Social Interventions

<table>
<thead>
<tr>
<th>Type of Therapy</th>
<th>Interventions</th>
</tr>
</thead>
</table>
| Play therapy    | • This is a therapy directed through play and games using toys and other tools or appropriate media  
• Art therapy is directed through drawings and paintings |
| Family therapy  | This is where the counselor works with the whole family for the benefit of the child taking into consideration the family systems, social and cultural values and the environment |
| Group Therapy   | • This is a therapeutic process between a counselor and a group with common problems.  
• The group benefits from sharing experiences, learning from others, counselor’s professionalism and personal interaction. |
| Support Groups  | • An informal group made of clients/patients with similar problems  
• Not necessarily structured  
• Can be open to new participants or closed  
• It is a common psychosocial intervention offered to willing participants (important to prepare the clients in advance) |
Psychotherapy

- This is a process between a therapist and a child where the child and his family are assisted to acknowledge, understand and adjust through their feelings, thoughts and behavior to handle a problem
- More intense, one-to-one intervention
- It’s also known as talk therapy, counseling, psychosocial therapy or, simply, therapy.
- Most forms of psychotherapy use only spoken conversation.
- Though some also use various other forms of communication such as the written word, art work, drama, narrative story, or therapeutic touch

All health care workers should be aware of the various organizations offering some of the following support services to which they can refer clients:

- Support groups for psychosocial and economic empowerment
- Psychologists for psychological interventions
- Psychiatrists for treatment of mental disorders
- Social workers/ NGOs and CBOs for contact tracing and case management
- Community health workers for home based care
- Religious leaders for spiritual care

Unit 4: Communication and Disclosure to Children

Communicating with Children

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

Communicating effectively with children requires skills in listening, observing, and understanding their messages. At least one person who is familiar with and normally cares for the child should be present. This is true for all children, but especially for young ones who often find it hard to trust and communicate with someone they do not know.

Different ways to communicate with Children

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

It is important to let children feel free to express themselves as they wish and not to criticise the techniques or their feedback, as such criticism may inhibit free expression. All children will continue to ask questions about a topic after explanations have been given to them. There are many reasons why it is sometimes difficult for us to communicate effectively with children. One is that we do not encourage them to talk about themselves. We often get information about children through third parties like caregivers, even when the child is present and able to provide the same information. Another reason is that a child who does not
know you well may find it hard to talk to you about his or her feelings. Cultural and traditional factors may also contribute to this difficulty in communicating. Other factors that tend to block communication with a child include being critical or judgmental, laughing or humiliating a child, and not respecting the child's beliefs.

Counseling for Children and Disclosure of HIV to Children

The counselling process begins with the first contact with the child; this may be in a clinic setting when the child is brought in sick, at home during home visiting, or at school. It is common for a child to be accompanied by a parent or other family member. As a general rule, interaction with the child should take place in the presence of a parent and, when appropriate, with other family members or siblings, until the counsellor has gained the confidence and trust of both the child and the caregivers.

Disclosure is the process of revealing to the child their HIV status and helping them to understand what this means. It may mean sharing the HIV status of the child with others (family members, friend, teacher, etc.)

It is usual to begin informing children about their HIV status when they are between five and seven years old, depending on the child’s ability to understand and on the parents’ consent. You should do this gradually.

Many parents may want to keep the diagnosis of HIV from the child; it is therefore often necessary to counsel the parents first, to help them understand the importance of having the child know his or her status. Carrying out discussions with children in the presence of parents or guardians ensures that the messages the children receive from counsellors and parents are consistent. Take parents’ viewpoints into account, even when they do not necessarily match those of the health worker, counsellor, or child.

Experience in counselling children about conditions not related to HIV, indicates that children cope better when told of these conditions at an early rather than later age. Ideally, parents should be the ones to disclose HIV results to their children. However, most parents do not know how to go about this and how to handle the emotional experience associated with disclosure. Parents need practical support to understand how to explain the results to their child. Also, parents should not inform their child about either their child’s HIV status or their own until they have themselves come to terms with it. Because sharing the diagnosis of HIV with children can be complicated and challenging, the subject should be a recurring theme of any family’s treatment plan.

Members of the multidisciplinary team – from clinicians to counsellors to peer educators – can be valuable conduits of shared experience and information, helping caregivers to learn from the experiences of others facing similar dilemmas. It is much easier to approach the topic if it is routinely and neutrally addressed early on, rather than during a health crisis or family change. Disclosure with children should never happen casually, inadvertently, or in the heat of anger or conflict. While each family will have different needs and questions, it may be helpful to begin the conversation by addressing the four domains listed below. Rather than attempting to answer all questions in one visit, it is more reasonable to pick a few topics each time, gradually constructing a picture of the unique circumstances and context of each family.

1. The Child (or Children)
   - Is the child symptomatic? Taking medication?
   - How old is the child? How verbal? Is s/he functioning as an adult?
   - Is the child living with a sick parent or sick family members?
   - Is the child asking questions about HIV?
   - Does the child appear distressed, anxious, or worried?
   - Is the child sexually active and at risk of contracting or spreading HIV?
2. The Parent/Adult Caregiver(s)
   - Has the parent/caregiver been tested for HIV?
   - Is the parent/caregiver infected? Symptomatic? Taking medication?
   - If the adult is ill, is s/he in need of help from children in the household?
   - Is the infected adult an important attachment figure for the child?

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

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

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

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

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

Benefits of disclosure
Disclosure helps the child and family adopt positive attitude, prolongs life, empowers, is educative, reassures and minimises psychological reactions. It also helps the child to adhere to treatment and should be done in the presence of a parent or close guardian who will provide support.
**Bereavement Counselling**

As children with HIV near the end of their lives, attention must be paid to helping these children and their families move through this time with the least amount of suffering and as much support and dignity as possible. Encourage open communication about what is happening among the children themselves, the parents, and the health workers. Reassure parents and help them understand that professionals are not giving up on their children, but rather that there is nothing more that can be done. All children continue to ask questions even after they have received explanations; this applies to questions about disease as well as to other matters. All children in the family require continuing counselling and help after the death of a loved one. Parents and caregivers also need support for their emotional reaction toward a dying child. And of course the dying children themselves need help. Using a supplement like the memory book is often useful for facilitating discussion about the child’s family history and preparing for the future. Details on child counselling can be found in a child counselling course.

**Exercise A**

1. How should psychosocial issues be addressed?
2. What are some of the effective ways of communicating with children?
3. What constitutes an opt-out approach?
4. Tombi is an eight month old infant with unknown HIV status presenting with clinical signs of HIV infection. Her mother died two months ago suffering from PTB. What steps are you going to use as basis for counselling her guardian?
5. Chebo is a 12 year old girl known to be HIV-infected and responding poorly to treatment. What counselling steps are you going to use as basis for counselling Chebo and her guardian?
6. Dalitso is known to be HIV-infected and responding well to treatment. What counselling steps are you going to use as basis for counselling her guardian?
7. Albert is a 12 year old boy who is HIV positive. His parents told him that he had a cardiac condition and needed to take drugs on a daily basis. He recently joined an Anti AIDS club at school and the first topic was on ARVs. He realised that he was on ARVs. Without permission from his parents, he came to the clinic and demanded to know from the counsellor what was wrong with him. The counsellor made an appointment for him to come with his parents the following week. Do you agree with this approach? If not, what could you have done differently?
8. Diana and Eddie are orphans aged 10 and 12 years and are both HIV positive. They know their status and are on ART. Their paternal aunt, a single woman, looks after them very well. Currently they are both healthy and going to school. Recently their aunt fell ill and they are concerned. They demand to know whether their aunt is HIV positive and whether she is going to die like their parents did. How will you counsel these children?

*Note: Disclosure about all things related to HIV and AIDS is a process that requires repeated continuous and attentive conversation with children. Once disclosure to a child occurs dialogue about the topic will need to continue again and again. The dialogue will change and evolve as children progress through different developmental stages and as treatments and circumstances change and transform. Revisiting the topic of disclosure frequently with a child and checking in with them about their worries and concerns can be a wonderful way to guide and facilitate a young person’s development as they learn about whom they are and who they have the potential to become. Children who are well informed about all aspects of HIV and AIDS will ultimately contribute to the strength of families and communities who are facing the epidemic. Youth who have experienced open and honest information will hopefully mature into adults who are equipped both to manage and prevent HIV and AIDS. By committing to honest and open discussion of the HIV and AIDS diagnosis and its consequences providers can model powerful messages of compassion acceptance and strength for the families that they serve.*
Module 11
Prevention of HIV Infection
Learning Objectives
At the end of this module the health worker should be able to:

- Describe modes of Mother to Child HIV Transmission and how to prevent them.
- Describe modes of horizontal HIV transmission in children and how to prevent them.

Listen to the presentation (or read your modules) on “Prevention of HIV infection” and then do Exercise A.

Unit 1: Prevention of Mother to Child Transmission of HIV

Mother-to-Child HIV Transmission (MTCT)
Infants who acquire HIV infection from their mothers do so during labour and delivery or after birth through breastfeeding. MTCT accounts for over 95% of childhood paediatric infection in Africa. The absolute transmission risk, without intervention, is 5–10% during pregnancy, 10–20% during labour and delivery, and 10 to 20% during breastfeeding. However effective interventions for PMTCT are now available and PMTCT programmes provide opportunities to identify and provide care for HIV-infected women, children and their families, and the majority of infants born to HIV-infected women are HIV free. The three objectives of the next five year PMTCT Scale-Up Plan which is called “Virtual Elimination of MTCT of HIV and Provision of Care and Treatment for Paediatric HIV” are:

- To reduce the transmission of MTCT of HIV to less than 5 percent by 2015.
- To reduce the unmet need for family planning by 50 per cent from the current levels of 27 percent by 2015.
- To provide antiretroviral therapy to at least 95 percent of HIV-positive children in need of treatment by 2015.

Table 56: Estimated Time of Transmission and Absolute Transmission Rates

<table>
<thead>
<tr>
<th>Time of transmission</th>
<th>Absolute Transmission Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>During pregnancy</td>
<td>5-10</td>
</tr>
<tr>
<td>During labour and delivery</td>
<td>10-20</td>
</tr>
<tr>
<td>During breastfeeding</td>
<td>5-20</td>
</tr>
<tr>
<td>Overall without breastfeeding</td>
<td>15-30</td>
</tr>
<tr>
<td>Overall with breastfeeding through 6 months</td>
<td>25-35</td>
</tr>
<tr>
<td>Overall with breastfeeding through 18-25 months</td>
<td>35-45</td>
</tr>
</tbody>
</table>

Source: JAMA, 2000, 283:1175-1182

Risk Factors for Mother-to-Child HIV Transmission
The risk factors associated with MTCT include: viral, maternal, infant and postnatal factors. The following factors have been associated with increased risk of MTCT:

Viral Factors:
- Virulence of the transmitted strain: HIV 1 is more virulent and more readily transmitted from an HIV-infected woman to her infant than HIV 2.
- Aggressiveness: Class C is more aggressive than other types
Maternal Factors
- Viral load: Women with high viral load are more likely to transmit HIV to their infants, but there is no clear cut-off point below which transmission does not occur.
- Stage of HIV disease: Severe immune suppression (CD4 counts below 200) and advanced disease.
- Maternal micronutrient deficiencies
- Prolonged rupture of amniotic membranes, abruptio placenta, chorioamnionitis, and STIs.
- Co-morbid diseases: The presence of diseases such as TB, malaria or STIs (syphilis, chancroid and bacterial vaginosis).
- High risk behaviour during pregnancy and lactation
- Breastfeeding: Cracked nipples and breast abscesses.

Obstetric Factors
- Mode of delivery: vaginal delivery in women with detectable viral loads (> 1000 c/ml)
- Intrapartum haemorrhage
- Obstetric procedures: Rupture of membrane, routine episiotomies, vacuum and forceps delivery.

Infant Factors
- Prematurity
- Small for gestation age
- Breastfeeding
- Oral thrush and oral ulcers
- Invasive foetal monitoring during delivery
- Birth order (first twin) in twin pregnancies

Postnatal
- Breast conditions i.e. mastitis, breast abscesses, cracked nipples
- Pattern of infant feeding (breastfeeding, mixed feeding).
- Infant infections i.e. oral thrush, gastritis

Preventing Paediatric HIV Infection
Comprehensive PMTCT services includes four prongs:

Prong 1: Primary Prevention of HIV Infection
The drivers of the HIV epidemic include low rates of HIV testing, multiple concurrent sexual partners, low rates of male circumcision, MTCT, commercial sex workers, and migrant workers. Adolescents, especially young female adolescents, are vulnerable to HIV infection. Primary prevention of HIV infection in young men and women reduces the risk of heterosexual transmission and so directly affects MTCT. Targeting pregnant and lactating women is a particularly pertinent strategy for preventing paediatric HIV infection.

The following interventions should be done in the health facilities and community:
- Counsel regarding STIs and HIV prevention, including post-test information on how to remain HIV negative or to live positively based on the outcome of the HIV test result
- Provide condoms or information on where to access condoms, including female condoms
- Refer to youth friendly services for more comprehensive sexual information, including HIV prevention
- Treatment of discordant couples
- Provide adherence support for adolescents on cART (prevention with positives)

Prong 2: Prevention of Unintended Pregnancies among HIV-Infected Women
Prevention of unintended pregnancies in HIV-infected women contributes to elimination of mother-to-child transmission. It includes counselling and provision of a variety of family planning methods. With timely initiation of cART and adherence to cART in the HIV infected non-pregnant women, planning for pregnancy is encouraged.
• Refer patients to Family Planning clinics, if needed, for further counselling and alternative methods
• Promote mixed methods, also known as dual protection, because condoms alone or hormonal methods alone when the woman is on cART have been associated with unintended pregnancies
• Offer condoms to all men and women ≥15 years old
• Offer long-term FP methods to all women ≥15 years old
• Depot medroxyprogesterone acetate (DMPA) 150 mg (1 vial) IM injection in deltoid muscle every 3 months
• Noristerat 200mg IM injection in deltoid or gluteal muscle, every 2 months
• Hormonal implant
• Intrauterine contraceptive device (IUCD)
• Sterilization (male or female) if child-bearing is complete

Patients have the right to choose their FP method, including declining all methods

Prong 3: Prevention of mother-to-child transmission of HIV using ARVs
Specific interventions used to prevent HIV transmission from an infected mother is defined as the “minimum package of care” which constitutes
• Provision of quality ANC
• Provision of routine HIV counselling and testing services with opt-out
• cART
• Safer delivery practices
• Infant feeding counselling to guide informed choice
• Daily NVP for 6 weeks in all HIV-exposed infants

Table 57: ED-NVP Dosing Table for Infants

<table>
<thead>
<tr>
<th>Infant age</th>
<th>Weight</th>
<th>NVP 10mg/ml daily dosing</th>
<th>Quantity in ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth – 6 weeks</td>
<td>Birth weight 2 – 2.499kg</td>
<td>10 mg once daily</td>
<td>1 ml once daily</td>
</tr>
<tr>
<td></td>
<td>Birth weight &gt; 2.5kg</td>
<td>15mg once daily</td>
<td>1.5ml once daily</td>
</tr>
</tbody>
</table>

Prong 4: Provision of appropriate treatment, care, and support to women, children, and families
A comprehensive approach to the paediatric epidemic involves treating the parents and other siblings to preserve the family unit, ensure a stable environment in which to nurture the children’s growth and development, and reduce the prevalence of orphans. Creating links between PMTCT programmes and those for the care and support of HIV-infected women, their infants, and their families will help to ensure that women themselves have access to the services they need. Furthermore, access to care and support services also enhance PMTCT services within communities. Such services include:

Infected Women
• Prevention and treatment of OIs
• Psychosocial and nutritional support
• Reproductive healthcare
• Control of STIs
• Family planning
• Antiretroviral therapy
• Improved economic independence of women (poverty alleviation)

Young Childcare
• Daily NVP for HIV-exposed infants
• Co-trimoxazole prophylaxis for all HIV-exposed infants
• Immunisations
• Growth and development monitoring
• Treatment of acute infections
• Routine de-worming
• Multivitamin supplementation
• Diagnosis and treatment of HIV

Table 58: Key activities to provide comprehensive PMTCT

<table>
<thead>
<tr>
<th>Prongs</th>
<th>Key activities to be considered</th>
</tr>
</thead>
</table>
| Primary prevention of HIV infection among women of reproductive age | • HIV information and education in antenatal, delivery and postnatal care settings  
• HIV testing and counselling (provider-initiated testing and counselling) – This includes couple HIV testing and counselling  
• Retesting of pregnant women in high prevalence settings (and where and when feasible)  
• Safer sex practices, including dual protection – Prevention of HIV and other sexually transmitted infections as well as preventing unintended pregnancies through the promotion and distribution of condoms  
• Screening and treatment for sexually-transmitted infections (especially in antenatal settings)  
• Prevention with positives (couple testing and counselling, condom promotion and distribution of condoms) |
| Prevention of unintended pregnancies among women living with HIV | • Family planning counselling and services (Point of service provision to be considered: antenatal and post-partum care settings, family planning clinics, HIV care/antiretroviral treatment centers/clinics)  
• Introduction of HIV testing and counselling in reproductive health and family planning services  
• Safer sex practices, including dual protection (condom promotion and distribution)  
• Positive health, dignity and prevention programs including prevention with positives (couple testing and counselling, condom promotion and distribution of condoms) |
| Prevention of HIV transmission from women living with HIV to their infants | • Good quality antenatal and delivery care (all components) – including prevention and treatment of malaria, diagnosis and treatment of tuberculosis, and congenital syphilis, and isoniazid preventive therapy after excluding active TB.  
• Provider initiated HIV testing and counselling in antenatal and delivery care settings.  
• Clinical (staging) and immunological (CD4) assessment of pregnant women testing HIV positive. (Where, when and by whom services will be provided?)  
• Antiretroviral treatment for pregnant women eligible for treatment for their own health.  
• Antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV for women not eligible for antiretroviral treatment. It is critical to ensure that the activities noted in the proposal are in keeping with the antiretroviral prophylaxis strategy selected by the national programme. For example, programmes that chose ‘Option A’ in a breastfeeding population should ensure that systems to follow infants exposed to HIV and provide continuous access to nevirapine are described clearly.  
• Safer obstetric practices, birth planning and emergency preparedness.  
• Infant feeding counselling and support. |
| Provision of appropriate treatment, care and support to women living with HIV and or syphilis, mothers, their infants and their families | Package of services for mother  
• Antiretroviral treatment for women eligible for treatment  
• Co-trimoxazole prophylaxis  
• Continued infant feeding counselling and support  
• Nutritional counselling and support  
• Post-natal care within 4-6 weeks  
• Sexual and reproductive health services including family planning | Package of services for children exposed to HIV  
• Routine child health care services:  
• Routine immunization and growth monitoring and support  
• Continued infant feeding counselling and support  
• Screening and management of congenital syphilis  
• Screening and management of tuberculosis  
• Prevention and treatment of malaria  
• HIV-related package of interventions:  
• Antiretroviral prophylaxis |
Exercise A
1. What are the risk factors for Mother-to-Child HIV Transmission?
2. Mrs Kabanda has come to book for antenatal clinic. She is 27 weeks gestational age. She undergoes routine counselling & testing and is found to be HIV positive. What interventions are you going to provide her to reduce the risk of MTCT?
3. You have recently graduated in midwifery and have been posted to a rural health centre. The World Bank is willing to fund your centre in order to prevent unintended pregnancies in young women living in your catchment area. What should be your focus?
4. After 12 months there is a mid-term review. The donors are very happy with the systems you have put in place. However, you have been so busy with your work in the adolescent and family planning clinic that you overlooked HIV positive pregnant women. You are now asked to set up a PMTCT service at your clinic. Describe the steps you will take to achieve this?
5. Veronica, a single mother, is pregnant with her second child. Her first child, three year old Mwamba, is HIV positive and currently on cART. Veronica wants to undergo PMTCT with a hope of having an HIV-free baby. She has booked in at 24 weeks. You have done her CD4 and it is 560. What is your plan for further management?
6. This week you are working in the labour ward and you recognise Veronica as she is wheeled into the labour suite. From her records you confirm that she has been taking cART. What will you do?

When you finish the Exercise discuss your answers with your facilitator, thereafter read your module on “Non Mother-to-Child (horizontal) Transmission” and “Prevention of HIV Transmission in the Healthcare Setting” and then do Exercise B.

Unit 2:
Horizontal (Non Mother-to-Child) Transmission

Modes of HIV Horizontal Transmission to Children and Adolescents:
- Sexual transmission (including sexual abuse)
  - Rape and defilement
  - High risk survival sex
  - Married adolescents

NB: Children under the age of 16 years cannot consent to sex and therefore any exposure to sexual activity is considered to be sexual assault.

- Use of contaminated needles and other skin piercing instruments:
  - Traditional scarification and needle sharing among intravenous drug users
  - Piercing with sharp instruments
  - Poor hygiene practices in health care settings

- Exposure to infected body fluids
- Transfusion with contaminated blood and blood products
### Management of non-Mother-to-Child (horizontal) Transmission

**Table 59: Management of non-Mother-to-Child (horizontal) Transmission**

<table>
<thead>
<tr>
<th>Prophylaxis against HIV, STIs and pregnancy in post-sexual assault</th>
<th>Offer PEP as appropriate</th>
</tr>
</thead>
</table>
|  | • Do a rapid test and start PEP if negative  
• If positive offer emotional support and supportive counseling, assess for ART eligibility and provide comprehensive care.  
• Empirically treat for bacterial STI's and vaccinate against HBV. |
|  | Offer Emergency Contraception to adolescents if they have any evidence of sexual maturation  
Offer trauma counseling to the child and parents |

**Management Steps of sexually assaulted child**
- Admit the child where possible  
- Take history to establish circumstances leading to the sexual assault.  
- Examine the child (under anesthesia or sedation) to determine the extent of injury and whether the assault is acute or habitual.  
- Ideally should be done by a female in the presence of a mother/caregiver  
- Collect blood for HIV, HBV, and syphilis screening and plan to repeat them at 6 weeks, 3 months and 6 months after the assault.  
- Collect specimens of genital secretions to be examined for sperm and seminal fluid  
- Take swabs for bacterial STIs and Trichomonas vaginalis if feasible.

**Support care to sexually assaulted child**
- Provide follow up HIV testing (after 6 weeks & 3 months) and supportive counseling  
- Alert authorities as appropriate  
- Refer as appropriate for legal services  
**NB:** Keep good records keeping in mind that sexual assault is a criminal offence.

**Figure 14: Algorithm for Evaluation and Treatment of Possible Horizontal HIV Transmission**

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**Figure 14: Algorithm for Evaluation and Treatment of Possible Horizontal HIV Transmission**

![Image of the algorithm](image_url)
Recommended Prophylaxis
No evidence indicates that any specific antiretroviral medication or combination of medications is optimal for use as PEP. However, on the basis of the degree of experience with individual agents in the treatment of HIV-infected persons, certain agents and combinations are preferred.

Table 60: Drugs for PEP

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>ARVs</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk: intact skin</td>
<td>Not recommended</td>
<td>NA</td>
</tr>
<tr>
<td>Medium risk/High risk</td>
<td>AZT + 3TC + LPV/r</td>
<td>28 days</td>
</tr>
<tr>
<td></td>
<td>(Refer to ARV module for dosing)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For older children &gt; 35kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF + XTC + LPV/r</td>
<td></td>
</tr>
</tbody>
</table>

Follow-Up of Exposed Persons
- An HIV blood test to be done on the day of the exposure; this test needs to be repeated at 6 weeks, 3 months and 6 months post exposure
- Evaluation by a MO or CO within 72 hours after starting PEP and monitoring for side effects for at least 2 weeks
- In children who were sexually assaulted, give consideration to preventing pregnancy and STIs and to collecting forensic evidence, including appropriate perineal swabs (local guidelines must be consulted).

Exercise B
1. How do children and adolescents acquire HIV infection horizontally (non-PMTCT)?
2. Patricia is a 13 year old girl who was sexually abused 24 hours ago by a neighbour. She is quite withdrawn and tearful. You are in the emergency room. How will you evaluate this child?
3. You have done the HIV test and it is negative. The mother informs you that she started her periods a year ago. What is your next step?
4. How will you administer the post-exposure prophylaxis?

When you finish this Exercise discuss your answers with your facilitator, thereafter you will be advised on when to proceed to Module 12 on “Setting up Comprehensive HIV Services for Children.”
Module 12
Setting-up
Comprehensive HIV Services
Learning Objectives
At the end of module 12, health care workers should be able to:
- Understand how to set up paediatric ART care services with follow up
- Explain the importance of data completion on clinical care
- M&E systems for paediatric ART care
- Describe the allocation of the Unique Patient Identifier (UPI)
- Demonstrate basic skills in and understand basic concepts of SmartCare
- Explain the process of Report and Requisition for antiretroviral drugs (R&R)

Listen to the presentation (or read your modules) on “Setting-up Comprehensive HIV services for children”.

Unit 1:
Setting up Comprehensive HIV Care Services

Entry Points into Paediatric HIV Care/ART
According to the Zambia Consolidated Guidelines for Treatment and Prevention of HIV infection (February 2014), children under the age of 15 years from pregnant and breastfeeding women who are on cART from MNCH that are tested positive should be initiated from MNCH as soon as possible. The figure gives an overview of entry points into Paediatric HIV care and ART.

Figure 15: Entry Points into Paediatric HIV Care/ART
In order for the above schema to work, referrals within the health facility need to be developed and agreed upon and each facility should be able to develop a health facility operational manual for linking children from different entry points to counselling and testing services with clearly developed referral forms.

Essential components of a continuum of care should have an efficient referral system within and between health facilities: MNCH, (PMTCT), OPD, IPD, TB and other paediatric clinics, malnutrition ward, VCT, adult care clinics and HBC. PITC should be provided in all these service areas after which they should be referred appropriately for continued care. There should also be a functional referral system between community care and social support programmes (e.g. for Orphans and Vulnerable Children) and health facility. M&E components should support the linkages between services.

A formalised meeting mechanism should be instituted between care, treatment and support partners in the district to make referrals functional and develop directory of services.

*Figure 16: Patient Flow Chart from Various Units to Paediatric ART*

*Figure 17: Paediatric HIV Services and Referral*
Note: PITC should be provided in all inpatient wards. It should also be provided in all the different outpatient clinics. However, for those outpatient clinics that are unable to do so, they should be linked to paediatric C&T.

Once these children have been identified, they should be followed up following the comprehensive package of care described in module 3.

Staff Requirements
Each health facility providing paediatric ART should have a functional ART team with defined roles and responsibilities for each team member contained in a clear management structure. Each facility should have facility specific SOPs, that can be adapted from the generic SOPs described in these training modules.

Staff support services include Regular multi-disciplinary team meetings (MCH/in-patients/ C and T etc.); measures for the prevention and management of staff burn-out and support from the management with supportive supervision. Continuous medical education (CME) should be an integral part of the programme with exchange programmes whenever possible

**Table 61: The Paediatric ART Team-Ideal**

<table>
<thead>
<tr>
<th>Nurses</th>
<th>Physiotherapist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians</td>
<td>Occupational Therapist</td>
</tr>
<tr>
<td>Laboratory</td>
<td>Nutritionist</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>Counsellor</td>
</tr>
<tr>
<td>Administrators</td>
<td>Record Clerk</td>
</tr>
<tr>
<td>Community Health Workers/home support givers/social workers/Adherence Supporters</td>
<td>Spiritual Caregiver</td>
</tr>
<tr>
<td></td>
<td>Volunteers</td>
</tr>
<tr>
<td></td>
<td>Psychologist</td>
</tr>
</tbody>
</table>

Though desirable, absence of any of above should not delay HIV service delivery for children

Health Systems Support for Comprehensive Care
There should be reasonable staffing in these health facilities and opportunities for capacity building should be created. There should be a supervision framework, built-in referrals, logistics and management systems and health management information systems. All these impact on HIV care services, therefore timely and appropriate planning for these services would strengthen these systems at all levels of care.

Appropriate ARV and Commodity Management
All health workers working in the paediatric ART clinic should be able to manage drugs and commodities for paediatric HIV services. They should know the drug and health commodity management cycle, product selection, procurement, storage, distribution and inventory. Commodity availability effects demand for HIV care services, it also affects the quality of care. However HIV commodities are costly to obtain and to manage and many of them i.e. laboratory reagents and some ARVs have a short life, requiring expert and timely management of the procurement and distribution processes in order to avoid stock-outs and expiry of drugs on the shelf.

*Timely and complete reports results in timely supplies; incomplete reports result in incomplete supplies. No reports result in no supplies and no ART products result in no ART programme.*
Unit 2: Importance of Data Completion on Clinical Care

M&E stand for Monitoring and Evaluation. Monitoring is the systematic and routine collection of information from projects and programmes for four main purposes:
• To learn from experiences to improve practices and activities in the future;
• To have internal and external accountability of the resources used and the results obtained;
• To take informed decisions on the future of the initiative;
• To promote empowerment of beneficiaries of the initiative.

Evaluation is assessing, as systematically and objectively as possible, a completed project or programme (or a phase of an ongoing project or programme that has been completed). Evaluations appraise data and information that inform strategic decisions, thus improving the project or programme in the future. Evaluations should help to draw conclusions about five main aspects of the intervention:
• relevance
• effectiveness
• efficiency
• impact
• sustainability

M&E can support management and engage stakeholders in understanding programme
• progress
• learning from achievements
• problems
• agreeing on how to improve both strategy and operations.

When it comes to record-keeping and monitoring, information is good only if it can be used. We are only collecting information for that reason. Data that cannot be used should not be collected. However, it is not uncommon that quite useful data goes unused.

Strategies for data utilization
• Quality assurance committee conduct monthly data audit at facility level.
• Discuss the indicators and program performance in clinical meetings
• Participation and presentation in district integrated meetings and share best practices

Quality data should be collected as frequently as needed. Data should be complete and should be frequently checked for completeness. It should be accurate, and the data should cover all areas of interest. It should be timely and easily accessible from each source and easy to retrieve. In other words, there should be excellent maintenance of registers and other standard tools used to collect information.
### Table 62: Data Quality

<table>
<thead>
<tr>
<th>Data Quality</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Degree of excellence exhibited by data in relation to the portrayal of the</td>
<td>• Reliability and effectiveness of data</td>
</tr>
<tr>
<td>actual situation on the ground</td>
<td>• Data Quality Assurance (DQA)</td>
</tr>
<tr>
<td>• Reliability and effectiveness of data</td>
<td>• Process of verifying the reliability and effectiveness of data</td>
</tr>
<tr>
<td>• Data Quality Assurance (DQA)</td>
<td>• Going through the data periodically and ‘scrubbing’ it (e.g. data audit)</td>
</tr>
<tr>
<td>• Process of verifying the reliability and effectiveness of data</td>
<td></td>
</tr>
<tr>
<td>• Going through the data periodically and ‘scrubbing’ it (e.g. data audit)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Challenges in getting quality data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Human resource constraints</td>
<td>• Completeness</td>
</tr>
<tr>
<td>• Changing faces of data tools</td>
<td>• Validity</td>
</tr>
<tr>
<td>• Inadequate understanding of M &amp; E systems</td>
<td>• Consistency</td>
</tr>
<tr>
<td>• Distances</td>
<td>• Timeliness</td>
</tr>
<tr>
<td>• Late reporting</td>
<td>• Accuracy</td>
</tr>
<tr>
<td>• Inadequate technology</td>
<td></td>
</tr>
<tr>
<td>• Lack of internet</td>
<td></td>
</tr>
<tr>
<td>• Late data tools update</td>
<td></td>
</tr>
<tr>
<td>Updates made after report is made</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factors of good quality of data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Completeness</td>
<td>• Capacity building</td>
</tr>
<tr>
<td>• Validity</td>
<td>• Understanding data tools</td>
</tr>
<tr>
<td>• Consistency</td>
<td>• Understanding indicators</td>
</tr>
<tr>
<td>• Timeliness</td>
<td>• Reporting structure and time periods</td>
</tr>
<tr>
<td>• Accuracy</td>
<td>• Feedback meetings</td>
</tr>
<tr>
<td></td>
<td>• Constant mentoring</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How to get quality data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Capacity building</td>
<td>• Understanding data tools</td>
</tr>
<tr>
<td>• Understanding data tools</td>
<td>• Understanding indicators</td>
</tr>
<tr>
<td>• Reporting structure and time periods</td>
<td>• Feedback meetings</td>
</tr>
<tr>
<td>• Feedback meetings</td>
<td>• Constant mentoring</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Flow of Data from Site to the National Level

There are registers in each ART clinic. Facilities with computers will enter information from the registers and patient files into the computer using the SmartCare software. Those without computers will use tally sheets to compile their numbers. After data has been collected at health facility level, again depending on the level of the health facility, first level will send their data to the district office for computing and analysis. The bigger hospitals can do their own data analysis, but are required to forward their data monthly to the DCMOs who in turn will send it to the provincial level, and from there to the central level.
Unit 3: Monitoring and Evaluation Systems for Paediatric ART Care

The M&E systems for pediatric care from the MNCH differ from those in the ART facility in the following aspects.

1. M&E systems in the ART facility concentrate on collection of data for initiation and follow-up (standardized at 12, 24, and 36 months after initiation).
2. M&E systems in the MNCH department belong to the prevention of the Mother to Child Transmission of HIV (PMTCT) M&E framework which is mainly interested in:
   a) initiation of the pregnant or breastfeeding woman on cART
   b) linkage of mother and child
   c) Early Infant Diagnosis
   d) Initiation of cART in the MNCH
   e) Linkage to ART care after 24 Months.

The Three Service Delivery models

Table 63: Service Delivery models

| Service Delivery Model 1 (SDM 1) | a facility where maternal health services (MNCH) and ART services take place in separate locations within the same facility. These are mostly larger facilities (e.g. in hospitals and large health centres). |
| Service Delivery Model 2 (SDM 2) | Sites where maternal health services (MNCH), OPD and other services take place in one location, often by the same HCW. These sites are the PMTCT only sites that will start offering ART under Option B+. These are mostly smaller facilities (e.g. urban and rural health centres) |
| Service Delivery Model 3 (SDM 3) | Facilities with advanced treatment services in large specialized facilities (e.g. referral hospitals like the Paediatric Centre of Excellence at UTH, Arthur Davison Children’s hospital in Ndola). |

In all SDMs children and partners who are found to be HIV positive are initiated from MNCH. In SDM1 children and partners are transferred to the ART facility immediately after initiation. In SDM2 women, partners, children below the age of 15 years are followed up from the MNCH until 24 months post-partum. In SDM3 pregnant and breastfeeding women, partners and children under 15 years are transferred as soon as the condition of the mother allows transfer to the referring facility.

M&E systems in the MNCH differ depending on basis of the presence of SmartCare. The healthcare provider in the MNCH department will establish a client file (medical record) for each HIV-exposed infant (HEI) in facilities without SmartCare. The baby information should be placed in a color-coded or specially marked file container in order to keep mother and baby information stored together (physically linked).
### Table 64: M&E systems in the MNCH

<table>
<thead>
<tr>
<th>Facilities Without SmartCare</th>
<th>HEI information is entered in the following cards and registers:</th>
<th>Information of women, partners and children started on ART in MNCH will be recorded in the following registers and cards.</th>
<th>Information of women, partners and children started on ART in MNCH is entered in an ART patient file.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• HEI and Mother Register</td>
<td>• HEI Monthly Register</td>
<td>• Patient Locator Form</td>
<td>• HTC Register/Daily Activity Register</td>
</tr>
<tr>
<td>• Under-five Card</td>
<td>• ANC Register</td>
<td>• Initial History and Physical Form (IH&amp;P)</td>
<td>• Patient Locator Form</td>
</tr>
<tr>
<td>• Safe Motherhood Card</td>
<td>• Delivery Register</td>
<td>• Clinical Follow-up Form</td>
<td>• HTC Register/Daily Activity Register</td>
</tr>
<tr>
<td>• DBS Tracking Register</td>
<td>• HEI &amp; Mother Follow-up Register</td>
<td>• Short Visit Pharmacy Form</td>
<td>• Patient Locator Form</td>
</tr>
<tr>
<td>• Community Register</td>
<td>• PNC Register</td>
<td>• HIV Care Summary Sheet</td>
<td>• Status Form</td>
</tr>
</tbody>
</table>

### Facilities With SmartCare

- In facilities with SmartCare it is real time data entry, there is no paper involved (SmartCare e-first). Information is entered into the computer while conversing with the client.
- Data entry into SmartCare is into the ART module either e-first (in model sites) or E-last (the majority of the ART facilities). In the e-first model site setup patient data is stored on the SmartCare Care Card.
- If SmartCare is in the ART facility the files are transported to the ART facility data room each day at the end of the day for entry into SmartCare by the data associated (e-last)

- Infants who are found to be HIV positive in the MNCH and not yet on treatment will be registered in SmartCare using the pediatric ART module.
- The infant goes home with two updated records - a Care Card and Safe Motherhood Card

### The IATT Recommended Enhanced Indicators
Enhanced data collection is a strategy to monitor a subset of clinics to ensure that implementation is sustainable, the quality of program services remains high, and the goal of eliminating mother to child transmission is met.
Table 65: IATT Recommended Enhanced Indicators

| Seven IATT Recommended Enhanced Indicators | 1. Enhanced monitoring indicators 1: Rapid Test Quality Assurance |
|  | 2. Enhanced monitoring indicator 2: ARV medicine and RTK stock outs |
|  | 3. Enhanced monitoring indicator 3: Retention on ART 1, 2 and 3 months after ART initiation |
|  | 4. Enhanced monitoring indicator 4: Retention for women who are pregnant or breastfeeding at initiation of ART at 6 and 9 months |
|  | 5. Enhanced monitoring indicator 5: Percentage of eligible HIV infected pregnant and breastfeeding women initiating Cotrimoxazole prophylaxis |
|  | 6. Enhanced monitoring indicator 6: HIV exposed infant retention on Cotrimoxazole |
|  | 7. Enhanced monitoring indicator 7: final status indicators |

| Set of indicators that measure retention of mothers and babies to the end of PMTCT | 1. Percent of mothers retained on ART until PMTCT discharge |
|  | 2. Percent of HIV-negative infants from PMTCT |
|  | 3. Percent of HIV-positive infants from PMTCT |
|  | 4. Percent of positive infants initiating ART |
|  | 5. Percent of HIV-exposed infants dying before 18 months |
|  | 6. Percent of HIV-exposed infants lost to follow up before 18 months |

Unit 4: Allocation of the Unique Patient Identifier

In order to estimate programmatic mother to child transmission rates, maternal and infant records must be linked. Each patient must be assigned a unique patient identifier which permits tracking over time, and across service delivery areas. The same system links a mother to her infant. The basis of the unique identifier is formed by the eight digit NUPD number which can be found on the SmartCare Care Card. The UPI number is allocated to a patient in the following way:

- A SmartCare Care Card is given to each pregnant and breastfeeding, each partner, each of the children accompanying the mother and to the HEI.
- Every SmartCare Care Card has an eight digit ID number.
- To this eight digit ID number, the province, district, and clinic ID are added resulting in the 15 numbers called the Unique Patient Identifier.
- The 15 digit unique identifier will always stay the same for this individual.
- The UPI will be used on all clinical forms, cards and registers.

A service numbers are added to the UPI
- A patient collects a sequential service number at every service delivery point ART/ANC/L&D or postpartum number.
- The Nurse or midwife issues the pregnant or breastfeeding woman her (service numbers) and adds this number to the unique 15 digit number.
- The MNCH nurse or Midwife writes the UPI on the Safe Motherhood Card and in the ANC Register (pregnancy) or HEI and Mother Follow-up Register/PNC Register (postnatal) or in the Delivery Register.
Unit 5: Basic Concepts of SmartCare

SmartCare is the Ministry of Health designated, national standard for electronic health records (EHR) and it is the only comprehensive electronic tool that can collect, store, report on and aggregate data from a large patient population. It provides health data reports in a timely manner at any level. All health and community facilities will issue a Care Card to each client, including new born babies and children through the use of the eight digit Care Card number as the Unique Patient Identifier. All sites and communities should stock enough Care Cards.

Figure 18: SmartCare Features
SmartCare Reports
SmartCare Users are given access to the system depending on their roles or the activities that they are required to perform. This ensures the security and confidentiality of patient privileged information. Reports are classified as:

- Facility level reports
- Administrative Services reports
- Clinical services reports

Transport Databases (TDB)
Transport Databases (TDB) are created for the purpose of aggregation of data as well as for the defragmentation (reconciliation or healing) of client records at the facility. TDB is created to enable facilities to roll up facility data to the district.

Entering Child in SmartCare
Below table illustrates steps, data elements, tools and who is responsible for data entry for partners and children (between 2 and 15 years of age) of pregnant/breastfeeding mothers.

Table 66: Entering Child in SmartCare

<table>
<thead>
<tr>
<th>Steps</th>
<th>What</th>
<th>Paper Record</th>
<th>Electronic Record</th>
<th>Who</th>
</tr>
</thead>
<tbody>
<tr>
<td>Register the client</td>
<td>Enter:</td>
<td>ART forms (Patient locator)</td>
<td>Smart Care Registration interaction</td>
<td>Health provider, Data clerk, Registry Clerk</td>
</tr>
<tr>
<td></td>
<td>• Date of Visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Provider details</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Address</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• client details</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Next of kin details</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial Visit</td>
<td>Enter:</td>
<td>ART forms</td>
<td>Smart Care: Adult ART module</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>• Client ART number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enter client conditions if the client is presenting any problems</td>
<td>ART forms</td>
<td>Smart Care: Adult ART module</td>
<td>Health provider, Data clerk</td>
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<tr>
<td></td>
<td>Enter Investigations done</td>
<td>ART forms</td>
<td>Labs orders and results module</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>Enter Regimen dispensations</td>
<td>ART forms</td>
<td>Smart Care: Pharmacy module</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>Enter prescriptions for drugs and dispensations</td>
<td>ART forms</td>
<td>Smart Care: Pharmacy module</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>Enter Referral details</td>
<td>ART forms</td>
<td>Smart Care: Referral Tab</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>Enter Notes about the client</td>
<td></td>
<td>Smart Care: Notes Tab</td>
<td>Health provider, Data clerk</td>
</tr>
<tr>
<td></td>
<td>Save the visit and enter Next Visit Date</td>
<td></td>
<td>Smart Care: ART module, SM Card</td>
<td>Health provider, Data clerk</td>
</tr>
</tbody>
</table>
**SmartCare Mother-Baby Link**

The mother baby pair link is created and made possible in SmartCare at delivery phase. The child is registered in SmartCare. Once a pre fill ID is clicked, a Care Card is issued to every child who is born.

<table>
<thead>
<tr>
<th>Steps</th>
<th>What</th>
<th>Paper Record</th>
<th>Where</th>
<th>Who</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>Add New born to link the baby to the mother</td>
<td>Mother and baby file are kept in a color coded folder.</td>
<td>Smart Care New Born: Delivery Tab</td>
<td>Nurse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Midwife</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clinician</td>
</tr>
</tbody>
</table>

**Table 67: SmartCare Mother-Baby Link Steps**

**The Five Rs**

Whenever there are problems with SmartCare that are not related to the central power supply and need attention from the National SmartCare team, follow the five Rs:

1. **R – Report**: Report any Smart Care incidents to the in-charge or person responsible when they happen
2. **R – Record**: Record all Smart Care incidents in the Smart Care incident log book (see form attached to the CPU)
3. **R – Remind**: Remind the person reported to if the incident is not resolved within 48hrs
4. **R – Resume**: Resume Smart Care operations when the incident is resolved
5. **R – Review**: Review why the incident happen and take any action to prevent it reoccurring in the future

Backlog of data entry negatively influences the quality of service delivery.

**Unit 6: Process of Report and Requisition for ARV drugs Logistics**

An effective paediatric ART program requires a logistic system that ensures that the right goods, in the right quantities, in the right conditions are delivered to the right place at the right time and at the right costs. To help you effectively carry out the logistic system at your health facilities;

- You should be trained in ARVs logistics system; i.e. types of records; reporting systems; logistics monitoring and evaluation.
- You should promote appropriate use of paediatric ART commodities i.e. paediatric dosing guidelines; special dispensing requirements for paediatric ART drugs; rational drug use; medication use counselling; storage conditions for paediatric drugs.

The importance of commodity management in paediatric ART includes:

- Commodity availability which in turn is affected by demand
- Commodity availability affects the quality of HIV care services
- HIV and AIDS commodities are costly to obtain and manage, they have a short shelf life and therefore overstocking should be avoided
- HIV and AIDS commodity stock-outs must be avoided for an effective program.

Common commodities needed to run an HIV clinic effectively are: HIV test kits, reagents gloves, swabs, needles, syringes etc, files, referral forms, patient ART forms, registers and other related stationary, clinic
equipment, X-ray, microscope, OI and ARV drugs. These should be available all the time. Since most, if not all activities are dependent on commodities, there is a need to know your commodity needs in order to provide your services.

**Role of the ART Team in Commodity Management**
The role of the paediatric ART team is to promote appropriate use of paediatric HIV and AIDS commodities including compiling and communicating service statistics i.e. numbers of children enrolled, on ART etc. They should be trained to rationally prescribe and dispense drugs and other supplies, which includes, using the correct drugs for a correct indication; using a correct dose dispensed correctly and patient compliance and adherence to treatment., ensure a functional system to monitor supplies and manage clinic commodity stocks i.e. HIV test kits, reagents, gloves etc. They should also ensure secure storage of clinic level stocks. Clinicians fit into the overall management of commodities through correct recording of statistics and reporting.

**The Report and Requisition Form (R&R Form)**
The Report and Requisition for antiretroviral drugs (R&R) form is filled at the end of every month by the pharmacists or the sister in charge. The R&R form is send to the District Community Health Offices (DCMO) together with the Transport Data base and the HIA1 and HIA2 forms. At the district the data is merged and send up to the Province every quarter to inform the national program.

**Uses of the ARV Drugs Report & Requisition**
- Ordering and Resupply of ARV Drugs
- Recording and reporting consumption of ARV drugs used at the national level for decision making:
- To forecast future needs.
- Monitoring logistics system performance
ANNEXES
Annex 1: SOPs: 1st Visit to Paediatric ART Clinic

**Entry points to paediatric ART clinic**
1. MCH (symptomatic if >18 months positive antibody test).
2. PMTCT (positive DNA PCR or perinatally exposed)
3. VCT (infected caregiver)
4. Paediatric out-patient units
5. Paediatric in-patient units routine testing (both symptomatic and asymptomatic)
6. Adult services (infected caregivers)
7. Community/primary care health facilities (HIV exposed and/or symptomatic infants and children)

The caregiver comes with a referral form to present to the registration and records unit

**Diagnosis of HIV infection**
May and may not have been documented. Confirmed HIV infection: DNA PCR for younger than 18 months and rapid test for children 18 months and older.

**Registration**
1. Interviewed by the registration clerk
2. Entered in the attendance and treatment follow-up register
3. Registration and records will establish a medical record including the patient’s health facility and ART numbers
4. Patient will be given an appointment card for recording dates of scheduled appointments for follow-up
5. The patient and his/her medical record are referred to the triage nurse

**First visit**
**The triage nurse will:**
1. Determine the reason for the visit
2. Identify caregivers accompanying the child
3. Obtain presenting data and vital signs
4. Complete the triage process
5. Direct patient and caregiver to the clinician for assessment

**The clinician (MO, CO, nurse) will:**
If the child does not have a definitive HIV diagnosis, test according to national guidelines. If positive:
1. Complete baseline assessment using the enrolment form (presenting symptoms, allergies, past medical history, systemic examinations).
2. Stage the child according to the WHO classification
3. Discuss ART with the patient/caregiver on existence of eligibility criteria and determine caregiver’s willingness in starting ART.
4. Initiate treatment for acute symptoms
5. Initiate prophylaxis with Cotrimoxazole, if child is <24 months, severely immune compromised or no contraindications i.e. CTX allergies, acute liver symptoms.
6. Collect blood for baseline laboratory testing (FBC, %CD4 and count, LFT, RFT)
7. Direct caregiver to registration and records to schedule a follow-up visit.
Annex 2: SOPs: 2nd Visit to Paediatric ART Clinic

The triage nurse will:
1. Collect the patient’s medical record and registration
2. Record new presenting symptoms and the vital signs on the paediatric visit form
3. Direct the patient/caregiver to the trained paediatric ART care provider (MO/CO, nurse).

The MO/CO/nurse will:
1. Assess the patient and include progress notes on the paediatric follow-up visit form.
2. Inform the caregiver of the laboratory test results from the last visit.

Patient will be referred for ART:
1. The HP will review the patient’s status and will complete the paediatric follow-up visit form
2. The MO will refer the patient to the adherence nurse for the first counselling session (pre-ART counselling).

All paediatric HIV infected patients:
- a) Discuss reasons for eligibility for ART
- b) Review information provided during the last visits about ART and the criteria for enrolling in the programme
- c) Counsel the caregiver about ART adherence, stressing that the first regimen has the best chance of long-term success.
- d) Assess the caregiver’s (patient’s) readiness to start ART
- e) If they agree to start ART, direct the patient to the adherence nurse for pre-ART counselling.

Annex 3: SOPs: Determination of ART Initiation

Purpose
The treating physician will assess the following before initiating ART:

Social criteria
- a) Proximity and accessibility to the health facility.
- b) Willingness by the caregiver to bring the child regularly and be contacted any time at home

Deferral criteria
- a) A patient with an acute opportunistic infection should be treated for the acute infection prior to starting ART
- b) A patient whose caregivers are not ready to begin ART or are unwilling to follow adherence counselling and monitoring visit schedule (they will need continued counselling to find ways of overcoming the barriers)

Exclusion criteria
- a) Severe or end stage liver failure
- b) Severe or end stage renal failure
- c) Severe cardiomyopathy or advanced stage cardiac disease

Post exposure prophylaxis
A child who has been sexually defiled will be eligible for PEP according to guidelines.
Annex 4: SOPs: Pre -ART Counselling

**Purpose**
1. To educate and counsel patients/caregivers about HIV and ART
2. To assess the readiness of the patient/caregivers to start ART and adherence to the prescribed drugs
3. To identify patient and family needs for additional medical and support services

**Procedures – first part or first session**
After the MO has discussed treatment initiation refer for the first pre-treatment adherence counselling (might need two visits).

The adherence nurse will:
1. Register the patient and gather additional socio-demographic data as needed
2. Assess caregiver’s knowledge of HIV and discuss goals of ART, reasons for combination therapy and the importance of medication adherence.
3. Identify any difficulties and potential barriers to keeping medical appointments, taking and adhering to the medication (personal, environmental, social, financial, nutritional)
4. Discuss the particular challenges for children i.e. disclosure, resistance by children to the medicine because of bad taste, frustration at having to take the medicine daily etc.
5. Identify the need for other services i.e. nutrition, legal aid, housing etc, and make appropriate referrals
6. Schedule the next appointment
7. Document the session

**Procedures - second part or second session**
If the caregiver reports to registration and records on another day from the first visit above, they will be directed to the triage nurse who will determine whether the patient has developed signs and symptoms that require assessment by MO/CO.

Adherence nurse will:
1. Review the previous counselling session and answer the caregiver’s (patient’s) questions.
2. Emphasise the importance of adherence to the ARVs.
3. Obtain commitment from the patient/caregiver to ART.
4. Discuss that ART is not a cure.
5. Discuss the benefits, risks, side effects of ARVs.
6. Jointly develop strategies that will help the patient adhere to the ARV regimen.
7. Schedule an appointment for the next counselling session on the day when the patient will visit the MO to begin ART.
8. Document the session
Annex 5: SOPs: Initiating ART

Purpose
1. To prepare caregivers for ART including education on each individual drug, dose schedule, possible side effects, and drug adherence
2. To begin treatment by issuing the prescription for ARVs

Procedures
The patient/caregivers will report to registration and records and will then be directed to:

1. The triage nurse who will document new signs and symptoms and take vital signs, then refer to the Medical Officer.

2. The MO will:
   a) Assess symptoms since the last visit and treat as needed
   b) Review the laboratory results from the patient’s previous visit
   c) Counsel the caregiver/patient about the ARV regimen, ART adherence, possible medication side effects, when and where to report them, follow-up monitoring visits and lab schedule
   d) Provide a written schedule for the medication
   e) Complete ‘treatment’ section of the appropriate clinical form
   f) Instruct the patient/caregiver to schedule an appointment for clinical consultation in two weeks’ time
   g) Issue prescription for the ARV regimen
   h) Refer the patient/caregiver to adherence nurse

3. The adherence nurse will:
   a) Review the patient’s medication regimen including:
      • Schedule for each medication
      • Dose for each medication; for liquid formulation demonstrate measurement of the dosage for each medication and ask the caregiver to repeat demonstration
   b) Stress the importance of 100% medication adherence
   c) Discuss strategies to improve adherence for example
      if appropriate to the child’s developmental stage and maturity, involve the child in his or her medication by making calendars, marking syringes and devising reminder strategies
   d. Discuss possible side effects
      • Which side effects to report the clinic immediately
      • Which side effects can be managed at home and how to manage them
      • Not to stop taking the medication in spite of side effects
   e. Counsel the patient/caregiver not to give to or share ARVs with others
   f. Explore ways of living positively: social support, healthy food, positive attitude, play for young children and spiritual support
   g. Identify needs that have not been addressed before, provide referrals to appropriate services
   h. Discuss on-going prevention issues such as how to manage bleeding wounds
   i. Direct the patient/caregiver to the pharmacy to get ARVs
Annex 6: SOPs: Adherence Monitoring of Patients on ART

Adherence monitoring after starting ART

The adherence nurse will:

1. **Assess the patient for adverse drug effects.** If necessary the patient will be referred to MO for further assessment and symptom management

2. **Assess medication adherence:**
   a) Discuss the patient’s experience with medication.
   b) Identify difficulties reported by the patient (in taking) or caregiver (in administering) the medication.
   c) Develop strategies to manage these difficulties and achieve adherence.
   d) Review each medication, dose schedule, possible side effects and how to manage.

3. **Report any serious difficulties with adherence** or concerns about the patient’s or caregivers’ commitment to ART to the MO/CO

4. **Provide support and encouragement** and instruct the patient/caregiver to report any serious adverse events to the clinic, or if such events should occur as an emergency, to immediately see the MO for assessments or go to the emergency room if the clinic is closed

5. **Review prevention** and risk of HIV transmission whilst on ART

6. For families where more than one member is HIV-infected, but only one member is eligible for ART, explain the dangers of sharing medication with other infected members

7. **Schedule the next counselling visit** on the same day as the patient’s appointment with the MO/CO if there are no adherence concerns.
   a) If patient is not adhering, but caregiver wants to continue with ART, schedule an appointment after 48 hours for intensive follow-up.
   b) If the patient is adhering and can be contacted by phone, the adherence nurse can call the caregiver in five to seven days’ time to check on patient status and reinforce medication adherence.

8. **Document the session in the ‘ART adherence counselling form’**.
Annex 7: SOPs: Change or Interruption of ART

**Change of Therapy**

1. **Drug reaction criteria**
   a) When patient experiences severe reaction or intolerable side effects that have a high probability of association with one of the antiretroviral drugs
   b) When strategies to manage the severe reaction or intolerable side effect do not reduce the reaction, and the patient experiences increased morbidity, threat of mortality and/or reduced quality of life.

2. **Drug reaction protocol**
   a) The offending drug should be identified and discontinued
   b) Another drug in the same drug class and among the approved regimen will be started to replace the discontinued drug (single drug substitution).
   c) The patient/caregiver will be counselled about the new drug (dose, schedule, side effects).
   d) The change of therapy will be documented in the patient’s medical record.

**Interruption Therapy**

**Medication non-adherence**

a) Patients who do not adhere to their ARV regimen will be counselled by the adherence counsellor on the importance of adherence and strategies to overcome barriers to adherence.

b) If patient continues to be non-adherent with ARVs during the subsequent two weeks, the health worker will assess the caregiver’s commitment to the child’s continuation on ART. S/he will reinforce the importance of medication adherence.

c) If non-adherence to ARVs continues, ART will have to be withdrawn following consultation with a multi-disciplinary team including family members; continue intense adherence counselling; treatment can be recommenced when adherence is assured.
Annex 8: SOPs: Family Centred Care

Caring for the Family Unit
The parents and other immediate family members of HIV-infected children may be HIV-infected. Care, treatment and support should be made available to all members of the family to optimise positive health outcomes and reduce detrimental impact of HIV and AIDS upon the family. On-going care and support can help preserve and strengthen the relationships and the economic function of family members.

Family centred strategies
1. If parents or other family members do not know their HIV sero-status, the clinic staff will discuss the benefits of testing and how to access care and support services should the test result be positive. If negative, strategies to prevent infection and maintain this status will be emphasised.
2. The clinic staff should offer counselling and testing to the family members.
3. For a parent or other immediate family member who is known to be HIV positive, the clinic staff can offer the baseline investigation then refer them with results to the facility's unit providing care and treatment for HIV-infected adults. A formal referral will be made. With the individual’s consent, the adult unit will confirm whether the individual has registered for care and that an initial clinical assessment has been done.
4. On-going communication and coordination of services are needed to achieve an integrated approach to caring for the HIV-infected and affected members of a family. To develop a family plan of care, staff treating children should regularly meet with those treating adults to discuss health status and needs of family members. Strategies to care for and support the family will be developed during this care meeting. Family members will be informed about this approach to care at the time they register their children and they will be encouraged to be active participants in the care and treatment services.
5. Care and support interventions will be documented in the medical record of both the child and adult.
Annex 9: SOPs: Health Facility Referral Management

**Policy**
To assure that the patient’s clinical needs are fully met, the paediatric HIV care staff will refer the patients/caregivers to the following services within the health facility for specialised management:
1. In-patient department
2. Specialty departments (i.e. skin clinic, surgery etc)
3. Laboratory
4. Radiology

**Procedures**
1. The sister-in-charge will arrange the details of the referral as ordered by MO/CO
2. The nurse will document the referral; the form will be maintained in the patient’s medical record.
3. Documentation regarding the patient from the referral site will be included in the patient’s medical record.
Annex 10: SOPs: Community Care and Referral Management

Referral to community services will be provided for HIV-infected children and their guardians who desire assistance with, and access to, resources to maintain a positive health status and effectively manage the multiple dimensions of HIV disease.

Procedures

1. **Confidentiality**: Referral staff will maintain confidentiality about each patient and protect the confidentiality of the patient’s record.

2. **Designated staff** will assist the patient and caregiver in determining needs and how to best meet those needs. Some PLHA organisations will volunteer at the HIV care centre to assist patients/caregivers with referral arrangements to needed services, as well as education and support.

3. **Service areas**
   Referral staff will assist the patient and caregiver in determining needs and how best to meet the following areas:
   a) Healthcare, inclusive of preventing infections
   b) Nutrition
   c) Housing
   d) Home-based care
   e) Schooling
   f) Economic support
   g) Activities as part of daily living
   h) Mental health
   i) PLWHA association support
   j) Social relationships
   k) Recreation and leisure
   l) Transportation
   m) Legal assistance
   n) Spiritual support

4. **Referral process**
   a) The referral staff and caregivers will jointly develop a service plan that defines the patient/family needs and the steps to take to meet those needs. The plan will be updated in accordance with changing needs.
   b) The referral staff will make referrals and coordinate delivery of services to meet the patient’s/family’s needs.
   c) The referral staff will track referral requests and follow-up to ensure that the patient’s/family’s needs are met.
   d) The referral staff will maintain a record of meetings with the patient/caregivers.
Annex 11: SOPs: Record-Keeping

**Procedures**

Each patient will have a medical record on file at the paediatric HIV care centre. For patients with pre-existing records at the health facility, the old file will be integrated into the new one.

The following forms will be maintained in the patient’s medical record:

- initial paediatric assessment form and eligibility form
- paediatric clinical follow-up form
- ART adherence counselling form
- laboratory investigations result form
- serial anthropometric or growth monitoring form

The registration clerk in the registration and records department will facilitate the patient’s attendance or treatment and clinical review in the ART programme. S/he will ensure that the patient’s medical record is available for each patient visit and that the appropriate forms are included in the file.

At each visit, all attending healthcare workers need to review the clinical management forms and ensure completeness.

Annex 12: SOPs: Monitoring and Evaluation

**Clinical monitoring and mentoring**

1. The multidisciplinary care team will meet monthly to share insights, discuss issues pertaining to patient care and participate in brief care updates on topics of interest. All care staff will be invited - including physicians, clinical officers, nurses, adherence counsellors, nutritionists, pharmacy staff and laboratory staff.

**Care indicators**

1. Data on ART management and HIV comprehensive care will be maintained in the patient’s medical record on a continuous basis
2. On a quarterly basis, the data entry clerk will collect data on defined indicators in accordance with the ART programme and evaluation plan. The following are examples of process indicators:
   a) Number of children tested for HIV
   b) Number of children with definitive diagnosis of HIV (DNAPCR or HIV rapid test)
   c) Number of children started on CTX
   d) Number of children started on ART during the reporting quarter
   e) Number of children who stopped taking ARVs during the reporting quarter
   f) Number of children whose ARVs regimen was changed during the reporting quarter
   g) Number of children on ART who were lost to follow-up during the reporting quarter
   h) Number of children who received adherence counselling during the reporting quarter
   i) Number of children who died prior to starting ART
   j) Number of children who died whilst on ART
### Annex A: WHO Clinical Staging for Children with Established Infection

<table>
<thead>
<tr>
<th>Children (0 to &lt;10 years old)</th>
<th>Adolescents (15 to &lt;20 years old)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
</tr>
<tr>
<td><strong>Pregnant &amp; Breastfeeding Women</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adolescents (10 to &lt;15 years old)</strong></td>
<td></td>
</tr>
</tbody>
</table>

#### Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

#### Clinical Stage 2

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

- Moderate unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent oral ulceration
- Papular pruritic eruption
- Fungal nail infections
- Seborrhoeic dermatitis

#### 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 > 1 month)
- Persistent oral candidiasis (after 6 weeks old)
- Oral hairy leukoplakia
- Lymph node tuberculosis
- Pulmonary tuberculosis
- Severe recurrent bacterial pneumonia
- Acute necrotizing ulcerative gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl), neutropenia (<0.5 x 10⁹/l) or chronic thrombocytopenia (<50 x 10⁹/l)
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease, including bronchiectasis

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for longer than 1 month
- Unexplained persistent fever (intermittent or constant for > 1 month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl), neutropenia (<0.5 x 10⁹/l) and/or chronic thrombocytopenia (<50 x 10⁹/l)
### Clinical Stage 4

**Children (0 to <10 years old)**
- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis (jirovecii) pneumonia
- Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month’s duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs with onset at > 1 month old)
- Central nervous system toxoplasmosis (after the neonatal period)
- HIV encephalopathy
- Extrapulmonary cryptococcosis, including meningitis
- Disseminated nontuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Symptomatic HIV-associated nephropathy or cardiomyopathy
- Recurrent septicaemia (including nontyphoidal Salmonella)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis

**Adolescents (10 to <15 years old)**

**Pregnant & Breastfeeding Women**

**Adults**

- HIV wasting syndrome
- Pneumocystis (jirovecii) pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than 1 month’s duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis, including meningitis
- Disseminated nontuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)
- Lymphoma (cerebral or B-cell non-Hodgkin)
- Symptomatic HIV-associated nephropathy or cardiomyopathy
- Recurrent septicaemia (including nontyphoidal Salmonella)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis

Reference: *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children, 2006*
Annex B: Serious Toxicities that may require Therapy Modification

<table>
<thead>
<tr>
<th>Possible clinical manifestations (Most common ARV drug(s) associated with the toxicity)</th>
<th>Possible laboratory abnormalities</th>
<th>Implications for antiretroviral drug treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Serious Adverse Reactions</strong></td>
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</tr>
<tr>
<td><strong>Acute Symptomatic Hepatitis (NNRTI class, particularly NVP, more rarely EFV; NRTIs or PI class)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Jaundice</td>
<td>• Elevated transaminases</td>
<td>• Discontinue all ARV until symptoms resolve</td>
</tr>
<tr>
<td>• Liver enlargement</td>
<td>• Elevated bilirubin</td>
<td>• If possible, monitor transaminases, bilirubin</td>
</tr>
<tr>
<td>• Gastro-intestinal symptoms</td>
<td></td>
<td>• If receiving NVP, NVP should NOT be re administered to the patient in future</td>
</tr>
<tr>
<td>• Fatigue, anorexia</td>
<td></td>
<td>• Once symptoms resolve, either to restart ART with change to alternative ARV (if on NVP regimen, this is required); or</td>
</tr>
<tr>
<td>• May have hypersensitivity component (rash, fever, systemic symptoms), usually occurs within 6-8 weeks</td>
<td></td>
<td>• to restart current ART regimen with close observation; if symptoms recur, substitute an alternative ARV c</td>
</tr>
<tr>
<td>• May have accompanying lactic acidosis (see below) if secondary to NRTI drug</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Acute Pancreatitis (NRTI class, more rarely 3TC)**                                |                                  |                                             |
| • Severe nausea and vomiting                                                       | • Elevated pancreatic amylase     | • Discontinue all ARVs until symptoms resolve |
| • Severe abdominal pain                                                            | • Elevated lipase                 | • If possible, monitor serum pancreatic amylase, lipase |
| • May have accompanying lactic acidosis (see below)                                 |                                  | • Once symptoms resolve, restart ART with substitution of an alternative NRTI, preferably one without pancreatic toxicity |

| **Hypersensitivity Reaction (ABC or NVP)**                                         |                                  |                                             |
| • BC: combination of acute onset of both respiratory and gastrointestinal symptoms after starting ABC, including fever, fatigue, myalgia, nausea, vomiting, diarrhea, abdominal pain, pharyngitis, cough, dyspnoea; rash (usually mild) may or may not occur; progressive worsening of symptoms soon after receives ABC dose, usually occurs within 6-8 weeks | • Elevated transaminases          | • Immediately discontinue all ARVs until symptoms resolve |
| • NVP: Systemic symptoms of fever, myalgia, arthralgia, hepatitis, with or without rash | • Elevated eosinophil count       | • NVP or ABC should NOT be re administered to the patient in future |
| |                                  |                                  | • Once symptoms resolve, restart ART with substitution of an alternative ARV for ABC or NVP |
### Lactic Acidosis (NRTI class)

- Generalised fatigue and weakness
- Gastrointestinal features (nausea, vomiting, diarrhea, abdominal pain, hepatomegaly, anorexia, poor weight gain and/or sudden unexplained weight loss)
- May have hepatitis or pancreatitis (see above)
- Respiratory features (tachypnoea and dyspnoea)
  - Neurological symptoms (including motor weakness).
- Increased anion gap
- Lactic acidosis
- Elevated aminotransferase
- Elevated CPK
- Elevated LDH
- Discontinue all ARVs until symptoms resolve
- Symptoms associated with lactic acidosis may continue or worsen despite discontinuation of ART
- Once symptoms resolve, restart ART with substitution of an alternative NRTI with lower mitochondrial toxicity risk (e.g. ABC or AZT)

### Severe Rash/Stevens Johnson Syndrome (NNRTI class, particularly NVP, less common EFV)

- Rash usually occurs during first 6-8 weeks of treatment
- Mild to moderate rash: erythematous, maculopapular, confluent, most often on the body and arms, with no systemic symptoms
- Severe rash: extensive rash with moist desquamation, angioedema, or serum sickness-like reaction; or a rash with constitutional findings such as fever, oral lesions, blistering, facial oedema, conjunctivitis
- Life-threatening Stevens Johnson Syndrome or toxic epidermal necrolysis
  - Elevated aminotransferases
  - If mild or moderate rash, can continue ART without interruption but close observation
  - For severe or life-threatening rash, discontinue all ARVs until symptoms resolve
  - NVP should NOT be re-administered to the patient in the future
  - Once symptoms resolve, restart ART with substitution of an alternative ARV for NVP (note: most experts would not change to another NNRTI drug if patient had severe or life-threatening Stevens Johnson Syndrome with NVP)

### Severe, Life-Threatening Anaemia (AZT)

- Severe pallor, tachycardia
- Significant fatigue
- Congestive heart failure
- Low haemoglobin
  - If refractory to symptomatic treatment (e.g. transfusion), discontinue AZT only and substitute an alternative NRTI

### Severe neutropaenia (AZT)

- Sepsis/infection
- Low neutrophil count
  - If refractory to symptomatic treatment (e.g. transfusion), discontinue AZT only and substitute an alternative NRTI
### Chronic Late Serious Adverse Reactions

#### Lipodystrophy/Metabolic Syndrome (PIs)

<table>
<thead>
<tr>
<th>Fat loss and/or fat accumulation in distinct regions of the body:</th>
<th>Hypertriglyceridaemia;</th>
<th>Substitution of an NNRTI for a PI may decrease serum lipid abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Increased fat around the abdomen, buffalo hump, breast hypertrophy</td>
<td>▪ Hypercholesterolaemia;</td>
<td></td>
</tr>
<tr>
<td>▪ Fat loss from limbs, buttocks, and face occurs to a variable extent</td>
<td>▪ Low HDL levels</td>
<td></td>
</tr>
<tr>
<td>▪ Insulin resistance, including diabetes mellitus</td>
<td>▪ Hyperglycaemia</td>
<td></td>
</tr>
<tr>
<td>▪ Potential risk for later coronary artery disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Severe Peripheral Neuropathy (more rarely 3TC)

<table>
<thead>
<tr>
<th>Pain, tingling, numbness of hands or feet; refusal to walk</th>
<th>None</th>
<th>Stop suspect NRTI only and substitute a different NRTI that is not associated with neurotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal sensory loss</td>
<td></td>
<td>Symptoms may take several weeks to resolve</td>
</tr>
<tr>
<td>Mild muscle weakness and areflexia can occur</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Notes:

a. Alternative explanations for the toxicity must be excluded before it is concluded it is secondary to the ARV drug. Note: This table does not describe detailed clinical toxicity management, only management of the ART regimen.

b. All laboratory abnormalities may not be observed.

ARV - antiretroviral drug; ART - antiretroviral therapy; CPK - creatinine phosphate kinase; LDH - lactate dehydrogenase; HDL - high-density lipoprotein; NRTI - nucleoside analogue reverse transcriptase inhibitor; NNRTI - non-nucleoside reverse transcriptase inhibitor; PI - protease inhibitor
### Annex C: Severity Grading of Selected Clinical and Laboratory Toxicities

#### GENERAL GUIDANCE TO ESTIMATING SEVERITY GRADE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Severe, Potentially Life-Threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characterization of symptoms and general guidance on management</td>
<td>Symptoms causing no or minimal interference with usual social and functional activities a: No therapy needed, monitor</td>
<td>Symptoms causing greater than minimal interference with usual social and functional activities: May require minimal intervention and monitoring</td>
<td>Symptoms causing inability to perform usual social and functional activities: Requires medical care and possible hospitalisation</td>
<td>Symptoms causing inability to perform basic self-care functions c: Requires medical or operative intervention to prevent permanent impairment, persistent disability, or death</td>
</tr>
</tbody>
</table>

#### HAEMATOLOGY

Standard International Units are listed in italics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Severe, Potentially Life-Threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute neutrophil count</td>
<td>750 - &lt;1,000/mm³</td>
<td>500 - 749/mm³</td>
<td>250 - 500/mm³</td>
<td>&lt;250/mm³</td>
</tr>
<tr>
<td>Haemoglobin (child &gt;60 days of age)</td>
<td>8.5-10.0 g/dL</td>
<td>7.5-&lt;8.5g/dL</td>
<td>6.5-&lt;7.5g/dL</td>
<td>&lt; 6.5g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>100,000-&lt;125,000/mm³</td>
<td>50,000-&lt;100,000/mm³</td>
<td>25,000-&lt;50,000/mm³</td>
<td>&lt;25,000/mm³</td>
</tr>
</tbody>
</table>

#### GASTROINTESTINAL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Severe, Potentially Life-Threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (SGPT)</td>
<td>1.25-2.5xULN</td>
<td>2.6 - 5.0 x ULN</td>
<td>5.1 -10.0 x ULN</td>
<td>&gt;10.0 x ULN</td>
</tr>
<tr>
<td>AST (SGOT)</td>
<td>1.25-2.5xULN</td>
<td>2.6 - 5.0 x ULN</td>
<td>5.1 -10.0 x ULN</td>
<td>&gt;10.0 x ULN</td>
</tr>
<tr>
<td>Bilirubin (&gt;2weeks of age)</td>
<td>1.1 - 1.5xULN</td>
<td>1.6 - 2.5xULN</td>
<td>2.6 - 5.0 x ULN</td>
<td>&gt;5.0 x ULN</td>
</tr>
<tr>
<td>Lipase</td>
<td>1.1 - 1.5xULN</td>
<td>1.6 - 3.0 x ULN</td>
<td>3.1 - 5.0 x ULN</td>
<td>&gt;5.0 x ULN</td>
</tr>
<tr>
<td>Pancreatic amylase</td>
<td>1.1 -1.5xULN</td>
<td>1.6 - 2.0 x ULN</td>
<td>2.1 - 5.0 x ULN</td>
<td>&gt;5.0 x ULN</td>
</tr>
<tr>
<td>Condition</td>
<td>≥1 year of age</td>
<td>&lt;1 year of age</td>
<td>Nausea</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>--------</td>
<td>--------------</td>
</tr>
<tr>
<td><strong>Clinical Diarrhoea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 year of age</td>
<td>Persistent episodes of unformed to watery stools OR increase of 4-6 stools over baseline per day</td>
<td>Persistent episodes of unformed stools OR increase of ≤3 stools over baseline per day</td>
<td>Persistent nausea resulting in decreased oral intake for ≥24-48 hours</td>
<td>Symptomatic AND hospitalisation not indicated (other than emergency treatment)</td>
</tr>
<tr>
<td>&lt;1 year of age</td>
<td>Liquid stools (more unformed than usual) but usual number of stools</td>
<td>Liquid stools with increased number of stools OR mild dehydration</td>
<td>Persistent nausea resulting in minimal oral intake for &gt; 48 hours OR aggressive rehydration indicated (e.g. IV fluids)</td>
<td>Symptomatic AND hospitalisation not indicated (other than emergency treatment)</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>Liquid stools</td>
<td>Persistent nausea resulting in decreased oral intake for ≥24-48 hours</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>NA</td>
<td>Symptomatic AND hospitalisation not indicated (other than emergency treatment)</td>
<td>Symptomatic AND hospitalisation not indicated (other than emergency treatment)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>Frequent episodes of vomiting with no or mild dehydration</td>
<td>Persistent vomiting resulting in orthostatic hypotension OR aggressive rehydration indicated (e.g. IV fluids)</td>
<td></td>
</tr>
<tr>
<td>Neuromuscular weakness (including myopathy and neuropathy)</td>
<td>Asymptomatic with decreased strength on exam OR minimal muscle weakness causing no or minimal interference with usual social and functional activities</td>
<td>Muscle weakness causing greater than minimal interference with usual social and functional activities</td>
<td>M muscle weakness causing inability to perform usual social and functional activities</td>
<td>Disabling muscle weakness causing inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Neuromuscular weakness (including myopathy and neuropathy)</td>
<td>Asymptomatic with sensory alteration on exam OR minimal paraesthesia causing no or minimal interference with usual social and functional activities</td>
<td>Sensory alteration or par aesthesia causing greater than minimal interference with usual social and functional activities</td>
<td>Sensory alteration or par aesthesia causing inability to perform usual social and functional activities</td>
<td>Disabling sensory alteration or paraesthesia causing inability to perform basic self-care functions</td>
</tr>
</tbody>
</table>

**OTHER LABORATORY PARAMETERS** Standard International Units are listed in italics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (fasting, paediatric &lt;18 years old)</td>
<td>170 - &lt; 200 mg/dl 170 - &lt; 200 mg/dl 200 - 300 mg/dl 200 - 300 mg/dl &gt;300 mg/dl &gt;300 mg/dl 4.40 - 5.15 mmol/l 4.40 - 5.15 mmol/l 5.16 - 7.77 mmol/L 5.16 - 7.77 mmol/L &gt; 7.77 mmol/L &gt; 7.77 mmol/L NA</td>
</tr>
<tr>
<td>Glucose, serum, high:</td>
<td>No fasting</td>
</tr>
<tr>
<td>Lactate</td>
<td>&lt; 2.0 x ULN without acidosis</td>
</tr>
<tr>
<td>Triglycerides (fasting)</td>
<td>NA</td>
</tr>
<tr>
<td>------------------------</td>
<td>----</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Neuromuscular weakness (including myopathy and neuropathy) | Asymptomatic with decreased strength on exam OR minimal muscle weakness causing no or minimal interference with usual social and functional activities | Muscle weakness causing greater than minimal interference with usual social and functional activities | Muscle weakness causing inability to perform usual social and functional activities b | Disabling muscle weakness causing inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation |

### ALLERGIC/DERMATOLOGIC

| Acute systemic allergic reaction | Localized urticaria (wheals) lasting a few hours | Localized urticaria with medical intervention indicated OR mild angioedema | Generalised urticaria OR angioedema with medical intervention indicated OR symptomatic mild bronchospasm | Acute anaphylaxis OR life-threatening bronchospasm or laryngeal oedema |

| Cutaneous reaction œ rash | Localized macular rash | Diffuse macular, maculopapular, or morbilliform rash OR target lesions | Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to one site | Extensive or generalised bullous lesions OR Stevens-Johnson syndrome OR ulceration of mucous membrane involving two or more distinct mucosal sites OR Toxic Epidermal Necrolysis (TEN) |

### NEUROLOGIC

| Alteration in personality-behaviour or in mood | Alteration causing no or minimal interference with usual social and functional activities b | Alteration causing greater than minimal interference with usual social and functional activities | Alteration causing inability to perform usual social and functional activities b AND intervention indicated | Behaviour potentially harmful to self or others OR life-threatening consequences |

---

<table>
<thead>
<tr>
<th>Triglycerides (fasting)</th>
<th>NA</th>
<th>500 - &lt; 751 mg/dl</th>
<th>751 - 1,200 mg/dl</th>
<th>&gt;1,200 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5.65 - &lt; 8.49 mmol/L</td>
<td>8.49 - 13.56 mmol/L</td>
<td>&gt; 13.56 mmol/L</td>
</tr>
</tbody>
</table>

| Neuromuscular weakness (including myopathy and neuropathy) | Asymptomatic with decreased strength on exam OR minimal muscle weakness causing no or minimal interference with usual social and functional activities | Muscle weakness causing greater than minimal interference with usual social and functional activities | Muscle weakness causing inability to perform usual social and functional activities b | Disabling muscle weakness causing inability to perform basic self-care functions OR respiratory muscle weakness impairing ventilation |

### ALLERGIC/DERMATOLOGIC

| Acute systemic allergic reaction | Localized urticaria (wheals) lasting a few hours | Localized urticaria with medical intervention indicated OR mild angioedema | Generalised urticaria OR angioedema with medical intervention indicated OR symptomatic mild bronchospasm | Acute anaphylaxis OR life-threatening bronchospasm or laryngeal oedema |

| Cutaneous reaction œ rash | Localized macular rash | Diffuse macular, maculopapular, or morbilliform rash OR target lesions | Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR superficial ulcerations of mucous membrane limited to one site | Extensive or generalised bullous lesions OR Stevens-Johnson syndrome OR ulceration of mucous membrane involving two or more distinct mucosal sites OR Toxic Epidermal Necrolysis (TEN) |

### NEUROLOGIC

| Alteration in personality-behaviour or in mood | Alteration causing no or minimal interference with usual social and functional activities b | Alteration causing greater than minimal interference with usual social and functional activities | Alteration causing inability to perform usual social and functional activities b AND intervention indicated | Behaviour potentially harmful to self or others OR life-threatening consequences |
| Altered Mental Status | Changes causing no or minimal interference with usual social and functional activities b | Mild lethargy or somnolence causing greater than minimal interference with usual social and functional activities b | Onset of confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social and functional activities b | Onset of delirium, obtundation, or coma |

Source: Adapted from Division of AIDS, National Institute of Allergy and Infectious Diseases, Table for grading the severity of adult and paediatric adverse events, Bethesda, Maryland, USA; December 2004. Notes: a. Values are provided for children in general except where age groups are specifically noted. b. Usual social and functional activities in young children include those that are age and culturally appropriate (e.g. social interactions, play activities, learning tasks, etc). c. Activities that are age and culturally appropriate (e.g. feeding self with culturally appropriate eating implement, walking or using hands). ULN - upper limit of normal
### Annex D: Sexual Maturity Rating (Tanner Staging) in Adolescents

<table>
<thead>
<tr>
<th>Stage</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0-15</td>
<td>Pre-adolescent</td>
</tr>
<tr>
<td>II</td>
<td>8-15</td>
<td>Pre-adolescent testes (≤2.5cm)</td>
</tr>
<tr>
<td>III</td>
<td>10-15</td>
<td>10-15</td>
</tr>
<tr>
<td>IV</td>
<td>10-17</td>
<td>10.5-16.5</td>
</tr>
<tr>
<td>V</td>
<td>12.5-18</td>
<td>13-18</td>
</tr>
</tbody>
</table>

#### Female
- **Age range (year):**
  - I: 0-15
  - II: 8-15
  - III: 10-15
  - IV: 10-17
  - V: 12.5-18

- **Breast growth:**
  - I: None
  - II: Breast budding (thelarche); areolar hyperplasia with small amount of breast tissue
  - III: Further enlargement of breast tissue and areola with no separation of their contours
  - IV: Separation of contour; areola and nipple forming secondary mound above breast tissue
  - V: Large breast with single contour

- **Pubic hair growth:**
  - I: None
  - II: Long, downy pubic hair near the labia, often appearing several weeks or months later
  - III: Increase in amount and pigmentation of hair
  - IV: Further enlargement, especially in diameter
  - V: Adult in size

- **Other changes:**
  - I: Pre-adolescent
  - II: Peak growth velocity often occurs soon after stage II
  - III: Menarche occurs in 2% of girls late in stage III
  - IV: Menarche occurs in most girls in stage IV, 1-3 years after thelarche
  - V: Menarche occurs in 10% of girls in stage V

#### Male
- **Age range (year):**
  - I: Pre-adolescent
  - II: 10-15
  - III: 10.5-16.5
  - IV: Variable: 12-17
  - V: Adult in size

- **Testes growth:**
  - I: None
  - II: Enlargement of testes; pigmentation of scrotal sac
  - III: Significant enlargement, especially in diameter
  - IV: Further enlargement, especially in diameter
  - V: Adult in size

- **Pubic hair growth:**
  - I: None
  - II: Minimal or no enlargement
  - III: Increase in amount; curling
  - IV: Adult in type but not in distribution
  - V: Adult in size

- **Other changes:**
  - I: Pre-adolescent
  - II: Menarche occurs in 2% of girls late in stage III
  - III: Menarche occurs in most girls in stage IV, 1-3 years after thelarche
  - IV: Menarche occurs in 10% of girls in stage V.

Source: Adapted from (121)
### Annex D: Recommended tiered Laboratory Capabilities for ART Monitoring

<table>
<thead>
<tr>
<th>Diagnosis and monitoring laboratory tests</th>
<th>Primary care level</th>
<th>District level</th>
<th>Regional/Referral level</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Antibody testing a</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HIV virological diagnostic testing b</td>
<td>-</td>
<td>+</td>
<td>✓</td>
</tr>
<tr>
<td>Haemoglobin c</td>
<td>+</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>WBC and differential</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>CD4 (absolute count and %)</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Pregnancy Testing d</td>
<td>+</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ALT</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Full chemistry(including but not restricted to: liver enzymes, renal function, glucose, lipids, amylase and serum electrolytes)</td>
<td>-</td>
<td>-</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Diagnostic tests for treatable co-infections and major HIV and AIDS-related opportunistic diseases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic microscopy for TB and malaria (sputum smear for TB and blood film for malaria diagnosis)*</td>
<td>+</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Full cerebrum spinal fluid (CSF) aspirate examination (microscopy, India ink, Gram stain, Ziehl-Neelsen). Syphilis and other STI diagnostic tests.</td>
<td>-</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Diagnostic tests for hepatitis B, hepatitis C serology, bacterial microbiology and cultures and diagnostic tests and procedures for PCP, Cryptococcus, toxoplasmosis and other major OIs)</td>
<td>-</td>
<td>+</td>
<td>✓</td>
</tr>
<tr>
<td>HIV viral load measurement f</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Key: ✓ Essential test  
+ Desirable, but not essential test  
- Not essential test  
ALT œ alanine transaminase; CSF-cerebrum spinal fluid; WBC -white blood count; PCP - Pneumocystis pneumonia  

Notes:  
a. Rapid tests are recommended at primary level and conventional methodologies can be used at district and regional/central levels.  
b. Virological testing for establishing HIV diagnosis in infants and children less than 18 months of age; can be performed using dried blood spots (DBS).  
c. Should be available if AZT is being considered for use.  
d. Should be available if EFV is being considered for use.  
e. Referral if microscopy is not available.  
f. Viral load measurement is currently not recommended for decision-making on initiation or regular monitoring of ART in resource-limited settings. Technology for assessment of viral load can also be used to diagnose HIV infection although it is not yet standardized for this purpose.
**Annex E:**
**Tips for Giving Medicine to Children on ART**

### Tips: Giving medicine to children on ART

**Remind caregivers to keep all medicines away from children to avoid poisoning**

**How can we advise caregivers on the best way to give medicine to babies and toddlers?**

1. Prepare and measure medicine in a syringe/dropper
2. With baby on your lap, brace the child’s head close to your body and fix the head tilted back a little
3. Put the medicine into the corner of the mouth towards the back, along the side of the tongue. This makes it harder for the child to spit out. Give little amounts at a time to prevent choking and spitting
4. Gently keep the child's mouth closed until s/he swallows
5. Never yell or show anger. Speak softly and say kind things
6. When medicine is finished, hold the child up and cuddle and comfort the baby. Offer the child water or juice only after the procedure is finished.

**How can caregivers assist older children take their medicine?**

1. Try masking the taste with different foods until you find one that works
2. Offer your child choices i.e. what kind of food does the child want the medicine mixed with, what kind of cup or spoon does the child prefer? Which type of drink?
3. Some children prefer to take a deep breath and drink fast, some slowly with a sip of a drink in between, some prefer you to count-down, or cajole them along as they drink.
4. Offer a reward i.e. a sticker, something good to eat or a game to play afterwards
5. Never ask the child whether s/he wants to take the medicine, instead be firm and state that the child must take it without being harsh
6. Connect taking the Medicine to not only feeling better but also to a desired activity or outcome

### What problems arise with giving medicine

1. **Vomiting medicine:** if your child vomits within half an hour, you can repeat giving the medicine.
2. **Missing a dose:** if your child misses a dose, give it as soon as you remember and then continue the regular schedule. Do not give two doses at the same time.
3. **Refusing the medicine:** let your child know that you understand that taking medicine is not fun. Do not threaten, punish, hit or yell at your child if s/he has a hard time taking the medicine. This only makes the situation worse and could make your child feel bad about him or herself.

### How to mix medicines with food and drinks

Both liquid medicines and powders can be mixed with drinks or food. *Remember* to tell the caregiver not to put the medicine in a large amount of food or drink, because if the child does not drink the whole amount s/he will not get all the dose of medicine. i.e. don’t add medicine to a whole bottle of milk or juice or a bowl of cereal. Do not mix medicine with food that is essential to your child’s diet, like formula. The child may associate that bad taste with all formula and stop drinking it, even when it does not contain medicine.

Coat the tongue with a sugary, sweet thick substance. Good things to mix with are juice, ice cream, chocolate syrup and other flavourful foods. The taste of some medicines is very hard to cover-up and the caregivers should be taught *not to give up* and keep trying different methods until they find one that works.

*Adapted from NYU manual for Coast General Provincial Hospital, Mombasa, Kenya*
### Annex F: Recommended Treatment Regimens for Children (adapted from National TB guidelines)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>TB management</th>
<th>Recommended ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant, on ART and develops TB</td>
<td>Start ATT immediately</td>
<td>Continue EFV-based ART</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evaluate for failure and consider switching to 2nd line ART in consultation with next level</td>
</tr>
<tr>
<td>Pregnant, on ATT, and diagnosed with HIV</td>
<td>Continue ATT</td>
<td>Start ART immediately if ATT has been taken for at least 2 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/XTC + EFV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If renal insufficiency, ABC + 3TC + EFV</td>
</tr>
<tr>
<td>Children &lt;3 years old with TB-HIV co-infection</td>
<td>Start ATT (RHZ) immediately</td>
<td>ABC + 3TC + EFV (when available)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ABC + 3TC + AZ Alternative regimen:</td>
</tr>
<tr>
<td>Newly diagnosed TB (category I) and HIV co-infection</td>
<td>Start CAT I ATT immediately</td>
<td>Start ART as soon as ATT is tolerated (after at least 2-3 weeks) regardless of CD4 count or WHO stage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/XTC + EFV</td>
</tr>
<tr>
<td>TB retreatment case (category II) and HIV co-infection</td>
<td>Start CAT II ATT immediately</td>
<td>If renal insufficiency, ABC + 3TC + EFV</td>
</tr>
<tr>
<td>On ART and develops TB</td>
<td>Start ATT immediately</td>
<td>If NVP-based regimen, switch NVP to EFV and continue cART.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If on LPV/r, double dose of LPV/r or start Rifabutin (in place of rifampicin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evaluate for failure and consider switching to 2nd line ART in consultation with next level</td>
</tr>
<tr>
<td>On ATT and diagnosed with HIV</td>
<td>Continue ATT</td>
<td>Start ART as soon as ATT is tolerated (after at least 2-3 weeks) regardless of CD4 count or WHO stage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF/XTC + EFV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If renal insufficiency, ABC + 3TC + EFV</td>
</tr>
<tr>
<td>On 2nd line ART with LPV/r and develops TB</td>
<td>Start CAT I or CAT II ATT per guidelines immediately.</td>
<td>Increase LPV/r from 2 tabs BD to 3 tabs BD for 2 weeks and then to 4 tabs BD for the remainder of TB treatment. If Rifabutin available (in place of rifampicin), start at 150 mg Monday/Wednesday/Friday.</td>
</tr>
</tbody>
</table>
### PAEDIATRIC CATEGORY

1. **New cases:**
   
a. **Children 5 to 20 kg**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase months for new all cases 10 months for TB Meningitis &amp; Ostearticular/Spinal TB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rifampicin, Isoniazid, Pyrazinamide (60,30,150mg)</td>
<td>Rifampicin, Isoniazid (60,30mg) Ethambutol (100mg)</td>
</tr>
<tr>
<td>5-7</td>
<td>1 tab</td>
<td>1 tab</td>
</tr>
<tr>
<td>8-10</td>
<td>2 tabs</td>
<td>1 tab</td>
</tr>
<tr>
<td>11-14</td>
<td>2 tabs</td>
<td>2 tabs</td>
</tr>
<tr>
<td>15-20</td>
<td>3 tabs</td>
<td>3 tabs</td>
</tr>
</tbody>
</table>

b. **Children 21 to 25 kg**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase 4 months for new all cases 10 months for TB Meningitis &amp; Ostearticular/Spinal TB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rifampicin, Isoniazid, Pyrazinamide, Ethambutol (150,75,400,275mg)</td>
<td>Rifampicin, Isoniazid (60,30mg)</td>
</tr>
<tr>
<td>21-30</td>
<td>2 tabs</td>
<td>2 tabs</td>
</tr>
<tr>
<td>&gt;30 kg</td>
<td>Use adult dosing tables</td>
<td></td>
</tr>
</tbody>
</table>

2. **Relapse, retreatment**

c. **Children 5 to 20 kg**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase (10 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rifampicin, Isoniazid, Pyrazinamide (60,30,150mg)</td>
<td>Ethambutol (100mg) Streptomycin (mg) Rifampicin Isoniazid (60,30mg)</td>
</tr>
<tr>
<td>5-7</td>
<td>1 tab</td>
<td>1 tab</td>
</tr>
<tr>
<td>8-10</td>
<td>2 tabs</td>
<td>1 tab</td>
</tr>
<tr>
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<td>2 tabs</td>
</tr>
<tr>
<td>15-20</td>
<td>3 tabs</td>
<td>3 tabs</td>
</tr>
</tbody>
</table>
### Children 21 to 25 kg

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Intensive phase (2 months)</th>
<th>Continuation phase (10 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-25</td>
<td>Rifampicin, isoniazid, pyrazinamide, ethambutol (150,75,400,275mg)</td>
<td>Rifampicin, isoniazid (60,30mg)</td>
</tr>
<tr>
<td>25-30 kg</td>
<td>2 tabs</td>
<td>2 tabs</td>
</tr>
<tr>
<td>&gt;30 kg</td>
<td>Use adult dosing tables</td>
<td></td>
</tr>
</tbody>
</table>
## Annex G: Criteria for Initiating, Discontinuing and Monitoring Cotrimoxazole Preventive Therapy

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Whom to Start</th>
<th>When to Start</th>
<th>When to Stop*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant &amp; Breastfeeding Women</strong></td>
<td>Pregnant women</td>
<td>Start as early as possible. Do not give SP. If SP taken, start CTX after 14 days.</td>
<td>(Continue throughout pregnancy)</td>
</tr>
<tr>
<td></td>
<td>Breastfeeding women</td>
<td>Continue if CD4 count &lt;350 cells/mm³ or WHO stage 3 or 4</td>
<td>CD4 count ≥350 cells/mm³ for two consecutive values at least 6 months apart while on ART</td>
</tr>
<tr>
<td><strong>Children (0 to &lt;5 years old)</strong></td>
<td>HIV-exposed (e.g. breastfed) child</td>
<td>At 6 weeks old or first contact (if &gt;6 weeks old)</td>
<td>Confirmed HIV-uninfected after full cessation of breastfeeding</td>
</tr>
<tr>
<td></td>
<td>HIV-infected child &lt; 24 months old</td>
<td>Start regardless of WHO stage or CD4%</td>
<td>At 5 years old and CD4 ≥25% and Stage I</td>
</tr>
<tr>
<td></td>
<td>HIV-infected child &gt; 24 months to &lt;5 years old</td>
<td>WHO stages 2, 3 and 4 or CD4 level &lt;25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presumptive HIV diagnosis &lt;18 months old</td>
<td>Start (or continue) regardless of WHO stage or CD4 %</td>
<td>Stop if confirmed HIV negative; if infected, stop at 5 years old and CD4 level ≥25% and Stage I</td>
</tr>
<tr>
<td><strong>Children (5 to &lt;10 years old)</strong></td>
<td>Child with a history of PCP</td>
<td>Start regardless of CD4 count or CD4%</td>
<td>At 5 years old and CD4 level ≥25% and Stage I if 5 to &lt;10 years old, stop based on adult criteria</td>
</tr>
<tr>
<td><strong>Adolescents</strong></td>
<td>HIV-infected children ≥5 years old, adolescents, and adults</td>
<td>CD4 count &lt;350 cells/mm³ or WHO stage 2, 3 or 4</td>
<td>CD4 count ≥350 cells/mm³ for two consecutive values at least 6 months apart while on ART</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>