



THE REPUBLIC OF UGANDA

Ministry of Health

The Integrated National Guidelines on Antiretroviral Therapy, Prevention of Mother to Child Transmission of HIV and Infant & Young Child Feeding

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Integrated National Guidelines on Antiretroviral Therapy,
Prevention of Mother to Child Transmission of HIV and on
Infant & Young Child Feeding

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Errors and omissions expected.

Every effort has been made to ensure that drug dosages and treatment schedules are correct and in accordance with current medical practice. However, medical knowledge is constantly and rapidly changing, particularly in relation to HIV/AIDS. Thus, when using an unfamiliar drug, clinicians are urged to confirm that information (especially with regards to drug usage) complies with the latest standards of practice.

Hence these guidelines will need regular updating based on new knowledge, experiences and practices. We would welcome feedback and comments from the users and experts addressed to:

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Acronyms and abbreviations:

| | | |
|--------|---|---|
| 3TC | - | Lamivudine |
| ABC | - | Abacavir |
| ACP | - | AIDS Control Program |
| AFB | | Acid-Fast Bacilli |
| AIDS | - | Acquired Immuno-Deficiency Syndrome |
| ANC | - | Antenatal Clinic |
| APV | - | Amprenavir |
| ART | - | Antiretroviral Therapy |
| ARVs | - | Antiretroviral drugs |
| ATV | - | Atazanavir |
| CDC | - | Center for Disease Control |
| CMV | - | Cytomegalovirus |
| CNS | - | Central Nervous System |
| CTX | - | Cotrimoxazole (trimethoprim-sulfamethoxazole) |
| d4T | - | Stavudine |
| ddC | - | Zalcitabine |
| ddI | - | Didanosine |
| DLV | - | Delavirdine |
| DNA | - | Deoxyribonucleic acid |
| DOT | - | Directly Observed Therapy |
| DRESS | - | Drug Rash, Eosinophilia, and Systemic Syndromes |
| EFV | - | Efavirenz |
| ELISA | - | Enzyme-Linked Immunosorbent Assay |
| FDC | - | Fixed Dose Combination |
| FTC | - | Emtricitabine |
| HAART | - | Highly Active Antiretroviral Therapy |
| HB | - | Haemoglobin |
| HBV | - | Hepatitis B Virus |
| HCT | - | HIV Counseling and Testing |
| HCV | - | Hepatitis C Virus |
| HSV | - | Herpes Simplex Virus |
| IND | - | Indanavir |
| IMCI | - | Integrated Management of Childhood Illness |
| IRIS | - | Immune Reconstruction Inflammatory Syndrome |
| JCRC | - | Joint Clinical Research Centre |
| LPV/r | - | Lopinavir-ritonavir |
| MoH | - | Ministry of Health |
| MTCT | - | Mother-To-Child Transmission (of HIV) |
| MU-JHU | - | Makerere University – Johns Hopkins University |
| NFV | - | Nelfinavir |
| NNRTIs | - | Non-Nucleoside Reverse Transcriptase Inhibitors |
| NsRTIs | - | Nucleoside Reverse Transcriptase Inhibitors |
| NtRTI | - | Nucleotide Reverse Transcriptase Inhibitor |

| | | |
|---------|---|--|
| NVP | - | Nevirapine |
| OI | - | Opportunistic Infection |
| PCR | - | Polymerase Chain Reaction |
| PCR-DNA | - | Polymerase Chain Reaction-Deoxyribonucleic acid |
| PCP | - | Pneumocystis <i>carinii</i> pneumonia now <i>P. jiroveci</i> pneumonia |
| PGL | - | persistent generalized lymphadenopathy |
| PEPFAR | - | US President's Emergency Plan for AIDS Relief |
| PIs | - | Protease Inhibitors |
| PLWHA | - | People living with HIV/AIDS |
| PMTCT | - | Preventing Mother to Child Transmission |
| /r | - | low-dose ritonavir |
| RLS | - | Resource Limited Setting |
| RNA | - | Ribonucleic Acid |
| RPV | - | Rilpivirine (Edurant) Formerly TMC-278 |
| RTC | - | Routine Testing and Counseling |
| RTV | - | Ritonavir {as PI pharmacoenhancer} |
| SQV | - | Saquinavir |
| STD | - | Sexually Transmitted Diseases |
| TB | - | Tuberculosis |
| TDF | - | Tenofovir (Disoproxil Fumarate) |
| TEN | - | Toxic Epidermal Necrolysis |
| UN | - | United Nations |
| UVRI | - | Uganda Virus Research Institute |
| VCT | - | Voluntary Counseling and Testing |
| VL | - | Viral Load |
| WBC | - | White Blood Cells |
| WHO | - | World Health Organization |
| ZDV | - | Zidovudine |

Foreword

Since the first case of HIV was reported in the 1982, HIV has spread to all regions of the country and remains a leading cause of death with serious demographic, social and economic consequences. Currently about 1.2 million Ugandans are living with HIV and AIDS and over one million people have died as a result of the epidemic. Although, the overall national adult HIV prevalence has stabilized between 6-7% over the past decade, the number of new HIV infections remains unacceptably high, with over 124,000 new infections reported in 2009. This is attributed to poor alignment of HIV interventions to drivers of the epidemic and risk factors and insufficient programme intercessions to make significant public health impact.

Over the past decade, Ministry of Health in collaboration with partners has rolled out comprehensive HIV prevention, care and treatment with a sizable focus on Prevention of Mother to Child Transmission (PMTCT) and Infant and Young Child Feeding (IYCF). Ministry of Health believes that integration of these services into the existing health care system is the sustainable way to go. By March 2011, 274,208 people were accessing Antiretroviral Therapy (ART) from over 432 health facilities, giving coverage of 47% of the 577,000 people that need ART at a CD4 cut-off of 350 cells/ μ l. There is adequate evidence from HIV treatment programmes and research that ART has reduced AIDS-related illnesses and deaths and therefore prolongs and improves the quality of life of HIV-infected individuals. Mother to child transmission of HIV contributes 20% of new HIV infections in Uganda. PMTCT services have been rolled to over 1,300 sites in the country and is annually reaching 60% of pregnant women living with HIV with ARV prophylaxis. This is however, still far below the UNGASS target of 80%. The country has adapted and is rolling out the new PMTCT Guidelines aimed at elimination of new paediatric HIV infection resulting from MTCT. Nutrition has been incorporated as an integral component of comprehensive HIV care. Data obtained from HIV clinics in Uganda, indicate that 12% of PLHIV were diagnosed as acutely malnourished. This demonstrates the importance of integrating nutrition into HIV/AIDS care treatment and support.

For the first time in the history of HIV in Uganda, Ministry of Health has decided to combine guidelines for ART, PMTCT, PEP and Infant and Young Child Feeding into one integrated document. This document therefore contains the revised guidelines for ART, PMTCT, PEP, Nutrition Care and Support for PLHIV and Infant and Young Child Feeding in the context of HIV. Paediatric and Adolescent HIV care is comprehensively dealt with in the guideline. The integrated document is also meant to facilitate integration of these services and promote a family-centred approach to HIV prevention, care and treatment.

This document has been developed for use by health workers at the primary level up to the tertiary level and will assist them to provide quality and standardised HIV prevention, care and treatment services including the delivery of integrated nutritional care, treatment and support of people infected and affected with HIV. It's the hope of Ministry of Health that this document will contribute tremendously to quality health care service delivery.

Dr. Jane Aceng
Director General Health Services

1.0 Introduction

In 1982 Dr. Anthony Lwegaba, then working as a Medical Officer in Kalisizo Health Center, Rakai District, described the first cases of HIV disease in Uganda. Now, almost thirty years later, HIV is the commonest cause of death among the young adults aged 20-45 years. Although the overall HIV prevalence has been reduced from over 18% of the early nineties to below 6.4% (2004.2005), it is estimated that over one million people (including about 100,000 children under 15 years) are currently infected and, probably a million have already died from HIV/AIDS. Over the last 25 years, the MOH in collaboration with local and international partners established a care program for HIV infected people. In the past six years, the program integrated antiretroviral therapy (ART) into the comprehensive response to HIV prevention, care and support. Currently, 230,000 out of the 550,000 patients estimated to be in need of ART are already accessing it (January 2011). This has been possible through initiatives such as the World Health Organization (WHO), the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and the United States President's Emergency Plan for AIDS Relief (PEPFAR). In addition, in the past two years, Government of Uganda provided an additional 30 billion shillings to supplement the international contribution.

ART delivery is feasible in a resource-limited setting (RLS) for adults, adolescents and children and its effectiveness in Uganda patients is similar to that elsewhere. However, challenges that may limit effectiveness of ART in Uganda include: 1) late initiation of treatment in advanced HIV with resultant increased early mortality 2) prevalent concurrent infections like TB, 3) ensuring uninterrupted ARV drug supply 4) loss to follow-up with treatment interruptions, 5) poor nutritional guidance particularly for the infected infant and young child, 6) monitoring ART efficacy and safety, and 7) limited health infrastructure with inadequate human resources. The experience gained during the ART program rollout coupled with new scientific evidence have necessitated a revision of the guidelines. The public health approach to delivery of comprehensive HIV care remains the basis for the Uganda ART guidelines. This focuses on maximizing survival at the population level through standardized sequencing of the available ARVs, delivered to individuals by means of simplified approaches and supported by clinical and basic laboratory monitoring.

It has become necessary to revise the 2009 Edition guidelines in order to incorporate the new knowledge and experiences that have accumulated to date. The new guidelines have also taken into account the 2010 Revision of the WHO global ART recommendations. However, the basic concepts of the earlier 2003 edition have been retained: a standardized formulary for first and second-line ART, with the use of two NRTIs and an NNRTI as the first-line approach; maintenance of the Protease Inhibitor (PI) class as the mainstay of second-line regimens; and simplified patient management with standardized laboratory monitoring to indicate when to Start, when to Substitute for toxicity, when to Switch for failure or Stop therapy (the “four Ss” of simplified clinical decision-making). Stavudine (d4T), has now been replaced with tenofovir for first-line regimens, particularly for the adult and adolescent patient, mainly because of its long-term toxicities. Tenofovir-containing regimens have a low toxicity profile and the once-daily administration possibility with the potential for improved adherence. The revised integrated guidelines provide detail on the use of ART in adults, adolescents, and children as well as on the

prevention of mother to child transmission, including general principles on related ART problems, comprehensive care services and infant and young child feeding approaches.

The revised National guidelines on antiretroviral therapy, prevention of mother to child transmission of HIV and on infant and young child feeding contribute to the National Strategic Plan (NSP) and are targeted to reach all health providers who take care of HIV infected patients either directly or indirectly through counseling and appropriate referral.

1.1 Objectives of the Integrated National ART Guidelines

- To provide a standardized and simplified guide to the use of antiretroviral drugs in a comprehensive HIV/AIDS service delivery setting for adults, adolescents and children
- To maintain a standard delivery of ART with evidence-based, safe and rational use of antiretroviral drugs
- To provide a standardized and simplified guide to the use of antiretroviral drugs in the prevention of mother to child HIV transmission
- To provide a standardized and simplified guide on infant and young child feeding for those who are HIV infected or exposed
- To serve as a training tool and reference material for health service providers, program managers, and people living with HIV/AIDS.

2.0 General Principles

Effective management of HIV infected patients requires that the health worker appreciates and understands all the relevant issues that surround HIV/AIDS. Giving antiretroviral drugs is only a small component of HIV/AIDS care. Under this section, some of these issues will be addressed before the specific guidelines are discussed.

2.1 Diagnosing HIV infection and Disease

When considering initiating antiretroviral therapy (ART):

- No one, except infants under 18 months with presumptive diagnosis of HIV/AIDS and where there is no access to PCR facilities, should be considered for ART without a confirmed diagnosis of underlying HIV infection. The diagnosis of HIV must be clearly documented by the health provider. In case of infants started on ART on suspicion, they should have their HIV status confirmed as soon as they are 12-18 months when an HIV antibody test can be offered or as soon as the PCR facilities become available.
- Individuals who do not know their serostatus but have signs and symptoms suggestive of underlying HIV infection should receive HIV counseling and testing as part of the integrated services of the health facility.

2.1.1 HIV counseling

HIV counseling is the confidential dialogue between a person and a care provider aimed at enabling the person to cope with stress and make personal decisions related to HIV/AIDS.

Counseling is an important component of HIV diagnosis, care and follow-up care for people living with HIV/AIDS [PLWHA] including those receiving antiretroviral therapy.

2.1.1.1 Approaches to HIV counseling and testing (HCT)

Voluntary counseling and testing (VCT) is an approach where counseling and testing is initiated by a client or patient who wishes to know their HIV status. Unfortunately a number of HIV infected individuals frequently go through health units without proper diagnosis and linkage to care because they have not volunteered to test. As a result of this omission, the diagnosis of HIV infection and subsequently that of AIDS is made very late. In the VCT model, detailed risk assessment and risk reduction counseling are provided. This requires specialized training, skills and is resource (time, personnel and space) intensive. VCT remains a very important model of HCT. However, because of these and other limitations associated with the VCT model, health care provider-initiated approaches have been adopted for HIV testing in health units (Ref Uganda HCT policies).

2.1.1.2 Health care provider-initiated HIV testing approaches

Health care provider-initiated approaches include routine HIV testing and counseling (RTC), and diagnostic testing. In RTC and diagnostic HIV testing, health care providers initiate the HIV counseling and testing process as is the case for all other investigations. In RTC, HIV testing is offered to all patients or clients presenting to a health facility, irrespective of the presenting complaint. RTC is frequently referred to as the “opt out” approach because all patients are offered HIV testing but have the right to decline the test. In the diagnostic approach on the other hand, HIV testing is offered to patients on clinical suspicion of HIV infection. In both RTC and diagnostic testing brief pre- and post-test information is provided to ensure informed consent, risk reduction, partner notification and testing, and linkage to HIV/AIDS care for infected individuals. With health care provider-initiated approaches, information and disclosure of results are done in privacy by trained health workers. This provides an opportunity for immediate linkage to care for HIV infected individuals: screening and treatment for opportunistic infections or even preparation for ART can be initiated at the time of diagnosis. It also offers spouses opportunity to test together or shortly after the other.

Whenever possible all patients especially those attending high prevalence clinics for example medical (adult and pediatric) patients, TB, STD clinics, ANC etc should be routinely offered HIV testing as part and parcel of any other care provided. This is particularly important in the case of pediatric patients since these are often the index PLWHA in the family. If this is not possible, HIV testing should at a minimum be offered to all patients with signs and symptoms of HIV infection. Once a woman with young children is noted to be HIV infected, all her children should be offered an HIV test since many slow progressors are commonly seen in pediatric HIV clinics.

Whenever possible, family members of HIV infected individuals should also be offered HIV testing so that they too can receive care and treatment if infected. Additionally, counseling and testing of family members of HIV patients improves the support for adherence to ART and other care interventions.

The benefits of testing and counseling for the HIV in individuals include:

- Improved health through education, appropriate referral to specialized HIV clinics and nutritional advice, particularly on infant and young child feeding.
- Early access to care (including use of ARVs) and prevention of HIV-related illnesses
- Emotional support and better ability to cope with HIV-related anxiety
- Awareness of safer options for reproduction and infant feeding
- Motivation to initiate or maintain safer sexual behaviors.
- Motivation for accessing PMTCT services

2.1.2 Laboratory diagnosis and assessment of HIV infection

HIV infection is usually diagnosed by testing for antibodies against HIV-1 and HIV-2 using an enzyme-linked immunosorbent assay (ELISA) test or a simple/rapid test and confirmed using a supplementary test. Supplementary tests should be another ELISA or simple/rapid test based on a different antigen preparation or a different test principle.

2.1.2.1 Tests to detect the virus itself

Viral load estimations can be done in only a few limited centers, although the number of these centers is growing, and its cost is still prohibitive but is likely to improve soon. However, the test helps to determine the degree of viral replication as well as the aggressiveness of the disease. The higher the viral load, the more aggressive the HIV disease. The test can be used also to monitor the effectiveness of ART. Undetectable viral RNA-PCR does not exclude HIV infection. The test uses different cut off points e.g. <50 or <400 viral copies. Generally, viral load should be undetectable in the blood after 6 months of effective ART regimen.

2.1.2.2 Measuring immune suppression

The degree of immunosuppression can be established by determining the CD4 cell count. The level then can be used to decide when to start ART. Similarly it can also be used to monitor the effect of the treatment on the repairing of the immune system.

2.1.2.3 Clinical evaluation for HIV disease

The diagnosis of HIV disease can be made on careful clinical evaluation along with the presenting signs and symptoms of the patient. This is a very common practice particularly where facilities for HIV serology are not readily available. However, an HIV test is required before starting ART. The WHO clinical staging system is useful in clinically deciding the seriousness and severity of the disease and when to start ARVs even when CD4 cell count results are available. Details of the staging system are given in **Appendix 1 & 2**.

2.2 HIV Prevention

Highly active antiretroviral therapy (HAART) has been around since 1996. In Uganda, through the accelerated access program spearheaded by the MoH, over 250,000 people are on HAART with remarkable improvement in the quality and quantity of life. Unfortunately for every patient put on ART, there are two to three new HIV infected cases, thus undermining our success on

putting patients on ART. This means that as we scale up access to ART we should also treble our efforts on HIV prevention in order to eliminate HIV transmission in Uganda. There is a fear that as people become aware of the availability and effectiveness of ART, there will be a tendency to relax on HIV prevention strategies particularly by the most vulnerable group, the young ones (age 18-30 yrs), as they become sexually active.

2.2.1 Biomedical interventions

2.2.1.1 Vaccines

An effective, affordable vaccine would be the best hope to control and eradicate HIV infection. Vaccines have been used to eradicate smallpox, another viral disease, and to reduce the occurrence of other viral infections like polio and measles. Unfortunately development of an HIV vaccine has been a big challenge due to a number of reasons:

- Poor understanding of the immune response that is protective and therefore needed to be induced by the vaccine,
- High mutation rates by the virus
- Lack of a good animal model among others.

There are however scientific reasons to believe that a vaccine can be found. These reasons include:

- Studies in animal models using related viruses protected against infection after vaccinations and challenge,
- Identification of potential protective immune responses in individuals exposed to the virus but remain uninfected or those infected but are able to control the virus load to very low levels among others.

Many candidate vaccines have gone through the different phases of testing which include preclinical testing in animal models, small size clinical trials in humans to evaluate the safety and immunogenicity. These are called phase I and phase IIa trials. Only 5 candidate vaccines have progressed to phase IIb or III trials aimed at testing protection or efficacy of the vaccine. Of all these candidates only one has resulted in a very modest protective effect of about 31% over three years follow up. This trial was conducted in Thailand between 2003 and 2009. This level of protection is not good enough and in addition this one trial cannot lead to the licensure of this vaccine, so more trials will be needed and probably with a higher protective effect before it could be considered for being licensed.

So as we write these guidelines in 2011, there is no effective HIV vaccine. This further emphasizes the importance of other prevention strategies if we have to overcome the HIV epidemic.

2.2.1.2 Antiretroviral drugs for HIV prevention

The use of an antiretroviral drug (drugs) by HIV uninfected individuals for HIV prevention has progressively gained momentum since this concept was first extensively discussed in 2001. Research efforts are currently underway to find the right drugs, in the right combinations and by

the right route of administration to form the mainstay of ARV use for HIV prevention. Currently, anti-retroviral drugs (pills/tablets) taken orally constitute what is termed as Oral Pre-Exposure prophylaxis (PrEP), while topical use of an anti-retroviral or combinations of various anti-retroviral drugs constitutes what is termed as Microbicides. We will focus our discussion on the more advanced oral and topical formulations, but there are also additional research efforts towards development of a long acting injectable formulation of a PrEP agent.

2.2.1.2.1 ART for prevention

There is a biological basis for the use of antiretroviral drugs for prevention of HIV infection in that effective antiretroviral therapy decreases the level of plasma HIV viraemia and has been associated with reduction in levels of HIV viraemia in seminal and vaginal fluids.

It is now accepted in practice that through a reduction in maternal plasma viraemia, antiretroviral drugs given to a pregnant woman reduce the risk of HIV transmission to her unborn baby.

A person with HIV infection who has a sustained undetectable viral load as a result effective antiretroviral therapy and who has no other co-existing sexually transmitted infection, is also unlikely to transmit HIV infection to their sexual partner. The use of antiretroviral drugs to reduce sexual transmission of HIV has thus been extensively investigated over the past few years. On the population level, scientists working in Rakai district in Uganda had earlier observed that the risk of HIV transmission to the negative partner of a serodiscordant couple was inversely related to the plasma viral load of the HIV positive partner. Subsequently, further evidence linking antiretroviral treatment to a reduced risk of HIV transmission within serodiscordant couples became available from cohort studies. One of these studies was carried out in Rwanda and Zambia and reported a 79% reduction in risk of HIV transmission associated with antiretroviral treatment of the HIV positive partner. A similar cohort study carried out in South Africa reported a 97% reduction in risk of HIV transmission when the HIV positive partner was on antiretroviral therapy. The most compelling evidence for this principle has become available this year, through the recent early release of results from the HPTN 052 trial. HPTN 052 was a randomized controlled trial designed to evaluate whether immediate versus delayed use of antiretroviral therapy would reduce transmission of HIV to HIV-uninfected partners in a serodiscordant couple and potentially benefit the HIV-infected individual as well. Among the 877 couples in the delayed ART group, 27 HIV transmissions occurred; in contrast, only one (1) transmission had occurred in the immediate ART group at the time this study was terminated. This means that earlier initiation of combination antiretroviral treatment led to a 96% reduction in HIV transmission to the HIV-uninfected partner.

The clear message here is that:

- All those who are HIV infected and have a CD4 cell count of <350, are identified and put on antiretroviral therapy, HIV transmission will be significantly reduced at population level.
- This reduction in HIV transmission will further be improved by additional use of other HIV prevention strategies which should be used concurrently by both those who are HIV positive and negative

2.2.1.2.2 Oral Pre-Exposure Prophylaxis (PrEP)

The goal of oral PrEP is to deliver the right drug in the right place and at the right time. What this simply means is that we need an antiretroviral agent or combination agents which is highly potent against a variety of HIV-1 subtypes and HIV-2 (thereby conferring very low risk for development of drug resistance in case of breakthrough HIV infections), with fewer side effects and low pill burden and one which can preferably block HIV infection early in its replication cycle.

The two drugs currently being studied in a number of HIV prevention studies as oral PrEP agents (Tenofovir and Truvada) favorably measure up to this above description. There are three large studies currently ongoing on oral PrEP; the Thailand Bangkok Tenofovir safety study among Intravenous Drug Users, the Partners PrEP study among HIV discordant couples in Kenya and Uganda and the VOICE/MTN 003 study among high risk women in Uganda, South Africa and Zimbabwe.

Prior to licensure of any drug for a new indication such as use of an anti-retroviral drug by an HIV negative individual for HIV prevention, we need the strength of two positive studies or a single study demonstrating very high levels of efficacy of the drug, hence the need for these different studies.

One oral PrEP study, the iPrEX study using Truvada for HIV prevention among men who have sex with men (MSMs) in Brazil, Ecuador, Peru, South Africa and the USA has already been completed and its finding reported at the AIDS conference in the New England Journal. This study showed 44% efficacy of Truvada against HIV infection in this population group and since there are no studies currently underway in the MSM population, processes are underway in the USA for review and possible registration of Truvada as a drug for HIV prevention among gay men who are HIV negative.

2.2.1.2.3 Microbicides (Topical PrEP)

The scientific community is also working tirelessly to avail a product on the market that women at risk of HIV infection can apply topically within the vagina to prevent themselves from HIV infection once exposed to an HIV infected partner. One study has already been completed among high risk HIV negative women in Durban South Africa using a gel formulation of the anti-retroviral drug Tenofovir. Women in this study applied the gel vaginally before and after sexual intercourse and the study showed a 39% effect on HIV prevention. Confirmation of this finding will be determined once the VOICE study ends, but there is also an additional study being planned to further confirm this finding among a wider grouping of women across the whole of South Africa and not just in Durban. This study is called the FACTS study and will likely start by the end of 2011.

As most of the sexual activity is rarely planned or anticipated, adherence to these study drugs remains a problem. Research efforts are currently under way to develop new formulations intended for slow release of drug. This will help to remove the user-dependent barrier (i.e.

individuals having to remember to apply the gel every time, to simply inserting say a ring or film or receive an injection once a month.

2.2.1.3 Male circumcision

Results from three Randomized Controlled Trials conducted in Uganda (Rakai), Kenya and South Africa showed that medical male circumcision (MMC) reduces the risk of HIV acquisition among HIV negative men by 50-60%. In March 2007 WHO and UNAIDS recommended MMC as one of the components of a comprehensive HIV prevention package.

The studies conducted at Rakai Health Sciences Program, Uganda have also shown that MMC reduces the risk of herpes simplex virus type 2 (HSV-2), decreases acquisition and increases clearance of high-risk human papillomavirus (HPV) in HIV-negative men, reduces transmission of HPV to HIV-negative women, and reduces genital ulcer disease (GUD) in men.

Operations research conducted in Rakai has also shown that MMC can be safely provided to both HIV negative and HIV positive men with CD4 counts above 350, does not negatively affect sexual function and satisfaction in both men and women, and that it can be safely provided by clinical officers .

The Ministry of Health launched the MMC policy in July 2010 that promotes and advocates roll out MMC across the country using financial support both from the ministry and other support agencies such as PEPFAR, GFATM, etc. This support includes infrastructure development, commodity/supplies, MMC communication, HCT, capacity building (training and support supervision for providers), and MMC service provision through Models for Optimization of Volume and Efficiency (Task sharing, task shifting, mobile surgical camps etc). The ministry targets to circumcise ~4.2 million men in the next 5 years (~900,000 men per year) in order to reach MMC prevalence of 80% and avert HIV infection by 20%.

2.2.2 Non-Biomedical interventions

2.3 General HIV care

These guidelines are specifically addressing antiretroviral therapy. However, ART should always be seen as one component of general HIV care. The other components, like Home based care, PMTCT, have been described in details in the appropriate guidelines that are published by the AIDS Control Program of the Ministry of Health. Health workers are strongly advised to use them hand in hand with these ART guidelines.

2.3.1 Comprehensive care for HIV patients

Although ARVs are becoming increasingly available, providers should not forget that patients need comprehensive HIV care services. One way to achieve this is through the “Family Based

Care” concept. Family based care involves targeting of the entire family as opposed to individuals, as the focus for HIV care and treatment services. All services including HIV testing, prevention, care and treatment for those who are infected are offered to the entire family including children that may be left out. This approach addresses the complex issues of disclosure and partner testing, condom use and uptake of reproductive health including PMTCT services. It also increases support for the HIV infected individuals, improves treatment adherence, and reduces sharing of drugs as all HIV infected individuals in the household are able to access care and treatment.

A non-ART basic HIV Preventive Care package has been defined in Uganda and should be given to all HIV infected patients irrespective of whether they are taking ART or not. In **Table 2.1**, we have listed some basic interventions for HIV-infected adults, adolescents and children focusing primarily on those that have been associated with the prevention of illness, mortality and HIV transmission. These can improve the health of patients and households with minimal cost and infrastructure.

- For the individual patient;
 - General basic hygiene practices such as washing your hands with soap and water before eating food or after the use of a toilet; Cotrimoxazole (trimethoprim-sulfamethoxazole, CTX) prophylaxis; isoniazid prophylaxis; Micronutrients;
 - Counseling on reduction in HIV transmission risk either sexually (through abstinence, faithfulness and condom use) or through PMTCT services.
- For the entire household or family;
 - Use of Insecticide-treated mosquito bed nets (ITNs) for malaria prevention; Safe drinking water, and HIV testing and counseling to family members

As part of comprehensive HIV care, it is now routinely recommended that those who test HIV positive with or without signs and symptoms should take daily CTX prophylaxis (160 mg trimethoprim/800 mg sulfamethoxazole for adults and equivalent dose per kg for children) irrespective of their CD4 cell count. This should also include those patients who initiate ART with CD4+ count of <250. This treatment has been associated with reduction in mortality, and reductions in malaria, diarrhea, and hospitalization. It is also the mainstay of prevention of *Pneumocystis jiroveci* pneumonia (PCP). There is evidence of effectiveness even in areas with high bacterial resistance to CTX. Cotrimoxazole prophylaxis might benefit even those persons with higher CD4+ counts (>250), and potentially reduce the rate of decline in CD4+ count and stabilize viral load.

Table 2.1: Potential basic care and prevention interventions for persons with HIV/AIDS

| Intervention | Impact | | Comments |
|---------------------------|---|---|--|
| | Individual with HIV | Household | |
| Cotrimoxazole prophylaxis | <ul style="list-style-type: none"> • Reduction in mortality, malaria, diarrhea, clinic visits, hospitalizations' • Possibly stabilizes viral load and slows CD4 | <ul style="list-style-type: none"> • Reduction in diarrhea, malaria, and mortality in children | <ul style="list-style-type: none"> • Reduction in morbidity for wide range of CD4 cell counts • Low rate of adverse events |

| | | | |
|------------------------------------|---|---|--|
| | cell count decline | | |
| Safe drinking water | <ul style="list-style-type: none"> Reduction in diarrhea | <ul style="list-style-type: none"> Reduction in diarrhoea and mortality | <ul style="list-style-type: none"> Efficacy data available among people with HIV on home-based disinfection with chlorine |
| Isoniazid prophylaxis | <ul style="list-style-type: none"> Reduction in incidence of TB Possible reduction in mortality | <ul style="list-style-type: none"> Theoretical benefit of reduced TB transmission | <ul style="list-style-type: none"> Questionnaire and through physical exam may be adequate to screen out persons with active TB Need to treat those diagnosed with active TB |
| Insecticide-treated bed nets (ITN) | <ul style="list-style-type: none"> Reduction in incidence of malaria | <ul style="list-style-type: none"> Reductions in malaria and mortality among children | <ul style="list-style-type: none"> Long-lasting insecticide-treated bed nets available that eliminate need for retreatment |
| Micronutrients and vitamin A | <ul style="list-style-type: none"> Reduction in morbidity, mortality, and disease progression in adults and children Possible beneficial effect on CD4 cell count and HIV viral load Vitamin A improves growth among HIV+ children | <ul style="list-style-type: none"> Micronutrient supplementation for pregnant or lactating women improves infant outcomes and may reduce rate of mother-to-child transmission of HIV | <ul style="list-style-type: none"> Pregnant women may benefit more from vitamin B complex, vitamin C, and vitamin E rather than Vitamin A alone |
| Family HIV counseling and testing | <ul style="list-style-type: none"> Psychological benefits of HIV-status disclosure Reduction in HIV transmission | <ul style="list-style-type: none"> Opportunity for HIV diagnosis in the family and early access to care and prevention efforts | <ul style="list-style-type: none"> High uptake with home-based counseling and testing |
| Family Planning and Condoms | <ul style="list-style-type: none"> Protection against STD and HIV super infection Prevention of unwanted/unplanned pregnancies | <ul style="list-style-type: none"> Protection of the partner and reduction of risk of MTCT | <ul style="list-style-type: none"> Family Planning options should be presented to both men and women. |

2.4 Antiretroviral Therapy (ART)

2.4.1 Goals of ART

The goals of treatment with antiretroviral drugs are to inhibit viral replication while minimizing toxicities and side effects associated with the drugs. The inhibition of virus replication permits restoration of the immune system. Viral eradication from the host genome is not achievable at the moment. However, there is a lot of research going on with the intent to eradicate the virus from the reservoir cells which will then make HIV cure a possibility. By using highly active antiretroviral therapy (HAART), it is possible to promote growth in children and prolong the survival of all HIV infected patients, reduce their morbidity and improve their quality of life. In summary the goals of ART are:

- The suppression of HIV replication, as reflected in plasma HIV concentration, to as low as possible (less than 50 copies/ml) and for as long as possible

- The preservation or enhancement of the immune function (CD4 restoration), thereby preventing or delaying the clinical progression of HIV disease
- Improvement in quality of life
- Reduction in HIV related morbidity and mortality
- Promotion of growth and neurological development in children

HAART may be defined as therapy which is potent enough to suppress HIV viraemia to undetectable levels (<50 copies/mL), as measured by the most sensitive assay available, and which is durable in its virologic effect. HAART conventionally includes three or more drugs from at least two classes. On the other hand, known sub optimal regimens, e.g. monotherapy, double nucleoside, or certain triple nucleoside combinations are not HAART and are contraindicated in HIV disease.

Tools to achieve the goals of therapy

- Maximization of adherence to ART. This may require getting a treatment buddy who will support the patient to adhere to his treatment.
- Disclosure of HIV serostatus reinforces patient adherence to ART.
- Rational sequencing of drugs so as to preserve future treatment options
- Use ARV drug resistance testing when appropriate and available
- Use of viral load estimates for monitoring if available

2.4.2 Principles of ART

Antiretroviral therapy is part of comprehensive HIV care. The guiding principles of good ART include:

- Not to start ART too soon (when CD4 cell count is close to normal) or too late (when the immune system is irreversibly damaged)
- Efficacy of the chosen drug regimens
- Freedom from serious adverse effects
- Ease of administration including no food restrictions.
- Affordability and availability of drugs and drug combinations
- Ongoing support of the patient to maintain adherence

2.4.3 Limitations of ART

Antiretroviral drugs are not a cure for HIV. However, when properly used by both patients and health care providers they are associated with excellent quality of life. They are relatively expensive, require an adequate infrastructure and knowledgeable health care workers. Training of health care personnel in the use of ARVs is critical to safe and effective use of these drugs.

Even when all these are in place, ART has its own limitations in several ways;

- Drug interactions and drug resistance may decrease the potency of these drugs
- Patients on ART may develop adverse drug reactions
- The HIV drugs are still relatively expensive even though their prices have significantly reduced

- Patients have to take at least 95% of their pills in order to respond well (adherence is key to successful therapy)
- The medications have to be taken for life. At present, eradication of HIV in the body is not yet possible
- Some patients may not respond (benefit) to treatment and continue to progress with their HIV disease in spite of doing everything right.
- Children are dependent on adults for adherence to ART

2.4.4 Available agents for ART

At present antiretroviral drugs come in six classes, each of which attacks a different site (NNRTIs, NsRTIs, NtRTIs all work at the same site) or stage of the HIV life cycle thereby interfering with its reproduction (**see Figure 2.1**):

- Entry inhibitors also called HIV fusion inhibitors (e.g., enfuvirtide or T-20) prevent the HIV virus particle from infecting the CD4 cell.
- CCR5 antagonists (e.g., Maraviroc) block the CCR5 core receptor molecules that HIV uses to infect new target T cells. Some forms of HIV use a different core receptor and thus some patients may not benefit from maraviroc.
- Nucleoside reverse transcriptase inhibitors (NsRTIs) incorporate themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and cannot create new virus.
- Nucleotide reverse transcriptase inhibitors (NtRTIs) e.g. Tenofovir which also work in similar fashion as above
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) stop HIV production by binding directly onto the reverse transcriptase enzyme thus preventing the conversion of RNA to DNA.
- Integrase inhibitors (e.g., Raltegravir) interfere with the ability of the HIV DNA to insert itself into the host DNA and thereby copy itself.
- Protease inhibitors (PIs) work at the last stage of the virus reproduction cycle. They prevent HIV from being successfully assembled and released from the infected CD4 cell. Boosted Protease inhibitors are combinations of low-dose Ritonavir (RTV) with a PI for pharmacoenhancement.

There are currently over 30 approved antiretroviral agents for the treatment of HIV-1 infection by Food and Drug Administration (FDA), a US Drug Regulatory Agency. Most of these drugs are also included on the list of WHO pre-qualified HIV medicinal products. These agents encompass all the possible target sites shown in **figure 2.1**. See **table 2.2**.

Figure 2.1: The Life Cycle of Human Immunodeficiency Virus Type 1 (HIV-1) and Major Antiviral Targets.

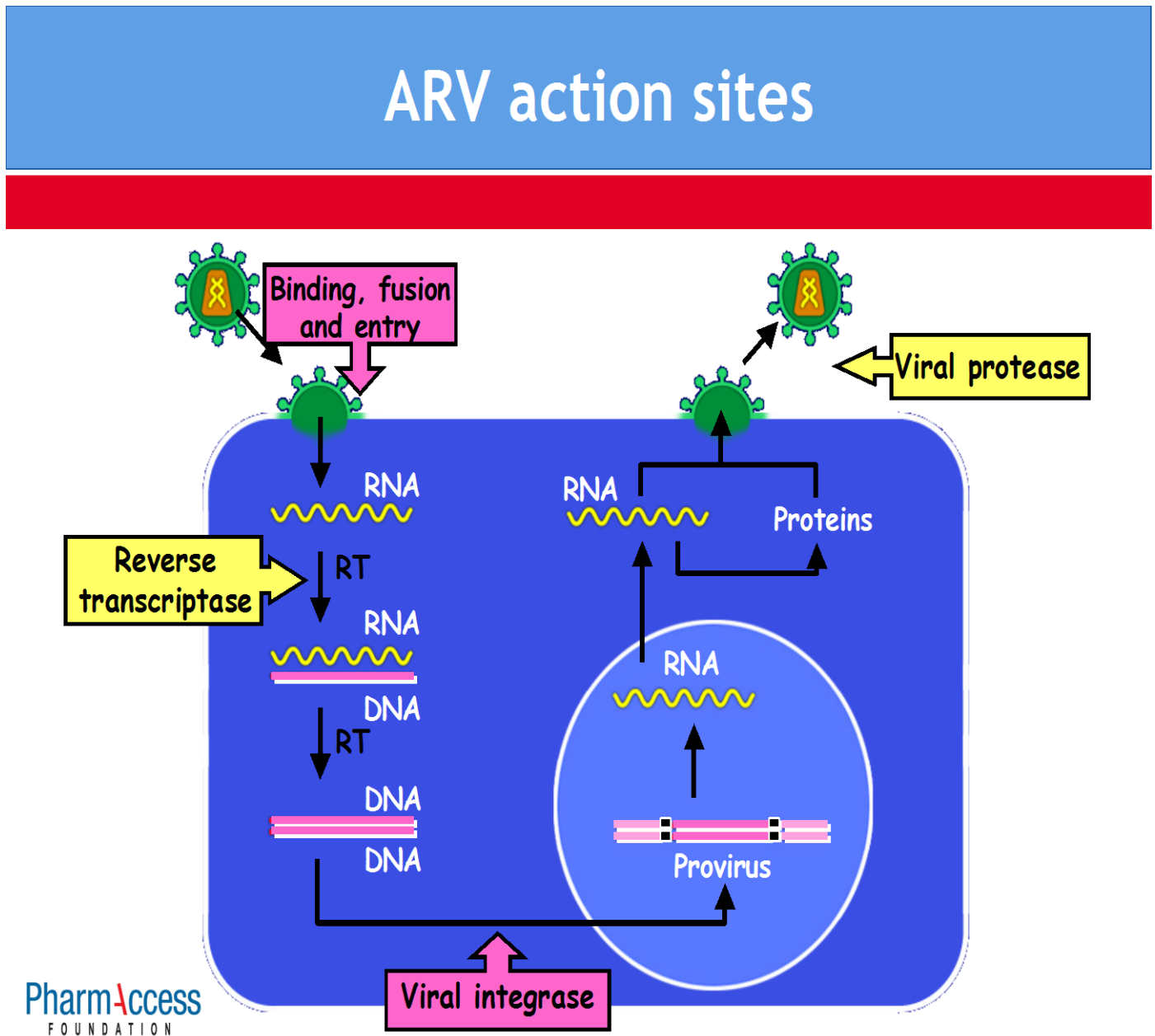


Table 2.2: Drugs Used in the Treatment of HIV Infection/ Available Antiretroviral Agents

| | Generic name | Brand/Trade name (s) |
|---|--|--|
| Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) | | |
| Single Drug Medicines (SDMs) | Abacavir (ABC) | Ziagen |
| | Didanosine (ddI) | Videx |
| | Emtricitabine (FTC) | Emtriva |
| | Lamivudine (3TC) | Epivir, Lamivir, Lamivox, avolam, Virolam |
| | Stavudine (d4T) | Zerit, Stavir, Stag, Atavex, Avostav, Virostav |
| | Tenofovir disopropryl fumarate (TDF) | Viread |
| | Zalcitabine (ddC) | Hivid |
| | Zidovudine (AZT) (ZDV) | Retrovir, Zidovir, Zido-H, Zidovex |
| Fixed Dose Combinations (FDCs) | Abacavir + Lamivudine (ABC/3TC) | Epzicom |
| | Abacavir + Zidovudine + Lamivudine (ABC/AZT/3TC) | Trizivir |
| | Stavudine + Lamivudine (d4T/3TC) | Zidolam, Stavex L, Virolis, |
| | Tenofovir + Emtricitabine (TDF/FTC) | Truvada |
| | Zidovudine + Lamivudine (AZT/3TC) | Combivir, Duovir |
| Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) | | |
| Single Drug Medicines | Delavirdine (DLV) | Rescriptor |
| | Efavirenz (EFV) | Sustiva, Stocrin, Efavir, Estiva, Viranz |
| | Nevirapine (NVP) | Viramune, Nevipan, Nevimune, Nevirex |
| | Rilpivirine (RPV) | Edurant (TMC-278) |
| | Etravirine (ETV) | Intelence (TMC-125) |
| Protease Inhibitors (PIs) | | |
| Single Drug Medicines | Amprenavir (APV) | Agenerase |
| | Atazanavir sulfate (ATV) | Reyataz |
| | Darunavir (DRV) | Prezista |
| | Fosamprenavir calcium (FOS-APV) | Lexiva |
| | Indinavir (IDV) | Crixivan |
| | Nelfinavir mesylate (NFV) | Viracept |
| | Ritonavir (RTV) | Norvir |
| | Saquinavir mesylate (SQV) | Invirase |
| | Tipranavir (TPV) | Aptivus |
| FDC | Lopinavir/Ritonavir (LPV/r) | Kaletra, Aluvia |
| Fusion Inhibitors | | |
| SDM | Enfuvirtide (T-20) | Fuzeon |
| Integrase inhibitors | | |
| SDM | Raltegravir | Isentress |
| CCR5 antagonist | | |
| | Maraviroc | Selzentry |
| Multi-class Combination Products | | |
| Fixed Dose Combinations (FDCs) | Stavudine + Lamivudine + Nevirapine (d4T/3TC/NVP) | Triomune, Virolans, Nevilast, Stavex LN |
| | Zidovudine + Lamivudine + Nevirapine (AZT/3TC/NVP) | Combipack, Duovir-N |
| | Tenofovir DF + Emtricitabine + Efavirenz (TDF/FTC/EFV) | Atripla |

2.4.5 When and how to start ART

2.4.5.1 Institutional requirements for starting ART

All health institutions that administer ART should be prepared to offer quality and dedicated services. This is because ART is life long and complicated. In our setting, the Ministry of Health has provided policy guidelines on the minimal infrastructure and staffing requirement for any health facility to administer ART. However, in the process of scaling up ART across the country, even health providers in institutions that may not be offering ART should know enough about it in order to sustain an effective referral network as described in the implementation guidelines.

2.4.5.1 ART initiation in general

Initiating ART should be based on the level of HIV immune suppression as assessed by WHO HIV stage (presence or absence of certain HIV related symptoms), and CD4 cell count. A baseline CD4 cell count not only guides the decision on when to initiate ART, it is also essential if CD4 counts are to be used to monitor ART. Viral load testing is still costly at the moment so it should not be part of screening algorithms for initiating ART in Uganda unless it is available at the facility where it can be used as an optional test to provide a baseline viral load. It is recommended that ART should be started **only** in those who are symptomatic and/or have evidence of significant immune system damage.

If a patient fulfils the above criteria, certain patient-specific factors should also be considered before starting ARVs. These factors include:

- Interest and motivation in taking therapy
- Presence of co-morbidities especially tuberculosis. Patients must have a screening history, physical exam and if necessary, laboratory tests, to rule out active infection. The treatment of co-existing infection takes priority over starting ART.
- Psychosocial barriers
- Financial barriers in those eligible but do not want to use the free ARV program
- Possible religious barriers (some who will be told to throw away their ART and ‘be healed by faith’ etc.)
- Potential for adherence (willingness to participate in ARV educational sessions and peer support ARV groups, and to complete a personal adherence plan with a counselor; willingness to disclose to family members; ability to travel to the clinic on a regular basis)

Before starting ART the patient should make the final decision regarding acceptance of treatment. This should be made after discussing with the health care providers all issues about the therapy and how they relate to the patient’s own situation. **Table 2.3** summarizes a baseline checklist for patients starting ART.

Antiretroviral therapy should not be started when patients:

- Are anemic (Hb below 8g/dl). These patients should be transfused with blood before starting ART. If transfusion is not available, use TDF instead of ZDV in the treatment regimen.
- Have symptomatic liver (e.g., severe jaundice) or kidney disease. They should be sent to a referral ART unit where additional investigations like excluding viral hepatitis will be done before an appropriate ART program is initiated.
- Are on chemotherapy for non-HIV related cancers with drugs that are likely to have an additive toxic effect with ARVs

2.4.5.1.1 Baseline clinical assessment

Before any patient is started on ART they should undergo baseline clinical assessment to include:

- A medical history
- Physical examination
- Laboratory investigations
- Counselling

The baseline medical history should include essential demographic characteristics; the past medical history including major illnesses and along the WHO staging scheme (including TB), hospitalisations and surgeries; the length of time since the diagnosis of HIV infection, current medications and symptoms. In the case of women, current or planned pregnancy and the access to contraceptive services should be reviewed. In case of children, the history of HIV status of the parents, particularly the mother, participation in the PMTCT program and who is taking care of the child.

The baseline physical examination should include vital signs, weight, and detailing of any abnormalities of the skin, oropharynx, lymph nodes, lungs, heart, abdomen, extremities, nervous system, eyes (including fundi if possible), and genital tract. Baseline investigations should include those outlined in **Table 2.4**.

The preparation of the patient for ART should start with baseline counselling. The issues discussed should include:

- A review of the expected benefits and potential side effects of the regimen chosen, and what other options are available at the treatment site
- A review of possible drug interactions (such as with oral contraceptives)
- The concept of partnership between patient and caregiver
- The life-long commitment to treatment that is being made, the follow up schedule, what laboratory tests are necessary and why
- The critical need to maintain safe sexual practices to prevent HIV transmission and re-infection with HIV
- The importance of drug adherence to a successful outcome and the need to report any perceived side effects of the medications
- The importance of disclosure of status to spouse and other family members for adherence support
- The importance of food hygiene, availability and nutritional supplements for the infant and young child

- What to do to avoid pregnancy if unwanted, and what to do if pregnancy is suspected or confirmed

Table 2.3: Baseline Clinical Evaluation Checklist for Patients Starting ART

| Assessment | |
|-------------------|---|
| 1 | <p>History:</p> <ul style="list-style-type: none"> • Level of understanding of HIV/AIDS; the length of time since the diagnosis of HIV infection; • Demographics and lifestyle: whether employed & nature of work • History of previous ART, prior use of nevirapine during pregnancy; • Pregnancy risks: Contraception options and choices, current or planned pregnancy, access to contraceptive services. • Sexual risks and disclosure: Willingness to practice safer sex, disclosure of HIV serostatus, use of condoms, HIV counseling and testing of sex partners and children. • Symptoms of chronic pain and depression • History of opportunistic infections & other significant illnesses e.g. TB & STIs, hospitalizations and surgeries; • Current medications (including anti TB drugs, traditional therapies etc.) |
| 2 | <p>Physical Exam:</p> <ul style="list-style-type: none"> • Weight • Height in infants/children • Nutritional status • Functional capacity and level of disability • Examination of vital signs, skin, eyes, oropharynx (presence of thrush), lymph nodes, lungs, heart, abdomen, genital tract (STIs), extremities, nervous system |
| 3 | <p>Baseline Laboratory tests to assess immunosuppression and disease aggressiveness</p> <ul style="list-style-type: none"> • Confirming HIV serostatus • CD4 testing, • Viral load if available and affordable • Full blood count particularly for patients starting on a ZDV-containing regimen • Pregnancy test for women of child bearing potential starting on EFV-containing regimen |
| 4 | <p>Baseline investigations to assess general health and diagnose any pre-existing HIV complications.</p> <ul style="list-style-type: none"> • A sputum smear for AFB for patients who have coughed for more than 2-3 weeks and a chest X-ray for patients who have unproductive cough or whose AFB smears are negative • Urine analysis for proteinuria, etc, particularly for patients starting on TDF containing regimen • Syphilis screening • Serum chemistries (liver and renal function tests), if available <ul style="list-style-type: none"> ➤ If ALT is elevated, do Hepatitis B surface antigen test, if available or refer • Symptom directed lab tests to diagnose pre-existing illnesses. |
| 5 | Staging of disease using WHO clinical criteria (See Appendixes 1 and 2) |
| 6 | Counselling and assessment of patients' readiness to start therapy including assessment for specific education/information/counselling support needs |

2.5 Co-infections and cancers in HIV infection

2.5.1 People co-infected with tuberculosis

HIV co-infection with tuberculosis is very common. In Mulago Hospital, 55-65% of patients admitted with TB are also HIV+. HIV increases the risk of TB infection by 5-10 times, and up to 1/3 of all HIV infected may develop TB. On the other hand, TB accelerates HIV progression. Co-management of TB and HIV is complicated by drug interactions between rifampicin and both the NNRTI and PI class of drugs, IRIS, pill burden, overlapping toxicities, stigma and adherence issues. Active TB may be present when ART needs to be initiated or develop during treatment. For patients with active TB in whom HIV infection is diagnosed and ART is required the first priority is to initiate standard anti-TB treatment.

NNRTI levels are reduced in the presence of rifampicin. There is however no benefit in increasing the dose of EFV from 600 to 800mg in patients weighing less than 60kg. EFV should not be used in women of childbearing potential without adequate contraception or in women in the first trimester of pregnancy. NVP is an alternative option but carries the risk of hepatotoxicity, in women with higher CD4 counts above 250 cells/mm³. Therefore NVP containing regimens should only be considered as a last option in such women and regular laboratory monitoring of liver enzymes is advised.

Triple NRTI regimens are considered an alternative regimen in patients undergoing TB treatment. ZDV+3TC+ABC and ZDV+3TC+TDF can be used safely with rifampicin. Both regimens can be used safely in patients with higher CD4 cell counts where the risk of toxicity for NVP is increased, and in HBV/HIV co infection. Pregnant women can take ZDV+3TC+ABC safely.

2.5.1.1 TB in patients on ART

In patients that develop active TB within six months of initiating first line ART, one has to consider modification of treatment and the possibility of ART failure. Although ART decreases the incidence of TB by at least 80%, the risk of developing TB is still higher than in the HIV negative population. Previously undiagnosed TB may present within the first six months as part of IRIS. If TB occurs during the first six months following the initiation of ART, this should not be considered as a treatment failure and the ART regimen has to be adjusted for co-administration of a rifampicin containing TB regimen.

If TB develops more than six months after the initiation of ART, the decision as to whether the TB diagnosis represents ART failure depends on the CD4 count and viral load if available or whether the TB is pulmonary or extra pulmonary, or whether there are other non-TB clinical stage 3 or stage 4 events. The development of TB after six months of ART initiation without other clinical and immunological evidence of disease progression should not be regarded as representing ART failure. However, extra pulmonary TB should be considered as indicating treatment failure.

2.5.2 People co infected with Hepatitis and HIV

Hepatitis B infection is endemic in many resource-limited settings including Uganda where the seroprevalence ranges between 3-10%. The presence of HIV infection in patients with HBV is associated with higher rates of progression to advanced liver disease like cirrhosis. These patients are at an increased risk of hepatotoxicity during HIV treatment.

Hepatitis B is one of a few known non-retroviral viruses which use reverse transcription as a part of its replication process. Therefore, replication can be inhibited with NRTIs. However, treatment of chronic hepatitis B can be problematic in co-infected patients because of impaired immune function.

Co-infection with HIV and HCV occurs frequently, due to the fact that they are transmitted via the same pathways (parenteral, sexual, vertical). As HCV is ten times more infectious than HIV via blood-to-blood contact, intravenous drug users and recipients of blood products are particularly susceptible to co-infection. Nevertheless, the probability of transmission from occupational needle stick injuries after exposure to HCV contaminated blood is very low (about 0.3%)

2.5.3 People with cancer and HIV

2.5.3.1 Kaposi's Sarcoma

2.5.3.1.1 Epidemiology

Kaposi's sarcoma (KS) is the most common diagnosed malignancy among untreated HIV-infected people including children in many parts of sub-Saharan Africa, including Uganda. Its high frequency among HIV-infected persons accounts for it also being the most common malignancy amongst the overall adult population in many parts of the region. Although KS incidence has sharply declined amongst HIV-infected persons on antiretroviral therapy (ART) in Western settings, the occurrence of KS in the ART era in Africa is not yet established. Among HIV-infected persons not on ART, cumulative mortality is about 60% one year after KS diagnosis.

2.5.3.1.2 Etiology

KS is caused by a virus called human herpesvirus type 8 (HHV-8), which is also known as Kaposi's sarcoma-associated herpesvirus (KSHV). In Uganda, between 40% to 60% of adults are infected with HHV-8, with most becoming infected in childhood. Saliva is the body fluid that most commonly harbors HHV-8, but the exact mechanisms by which saliva spreads the virus are not understood.

2.5.3.1.3 Clinical features

KS is a complex malignancy at the cellular level originating from the lining of blood and/or lymphatic vessels. Although KS can affect any organ system except for the brain, it most typically involves the skin and mucous membranes. On the skin of dark-skinned persons, KS lesions appear dark black or brown; lesions may appear more purplish on lighter skin. KS lesions on the skin are typically multiple in number, painless, range from flat discolorations

(macules) to bulky nodules. While they have a predilection for the extremities, they can appear anywhere. On the mucous membranes, KS lesions appear reddish-brown or purple. Bulky lesions in the oral cavity may interfere with chewing, swallowing, or breathing. Among the internal organs, KS most commonly involves the lungs and gastrointestinal tract (GIT). In the lungs, symptoms of KS include cough, hemoptysis, and shortness of breath. In the gastrointestinal system, symptoms range from early loss of appetite (from gastric outlet obstruction) to upper or lower GIT bleeding. Because KS can diffusely involve the lymphatic system, oedema in the genitals or extremities is common. KS typically does not cause the “B” symptoms of fever, night sweats, or weight loss unless the patient is co-infected with other conditions like TB

2.5.3.1.4 Diagnosis

Clinical diagnosis of KS is very easy to anyone familiar with the condition. However, because a number of dermatologic conditions can mimic KS, the cornerstone of KS diagnosis is a biopsy of the suspicious lesion followed by histological examination by a pathologist. Biopsies can be performed by trained nurses with inexpensive disposable core punches if available. In many parts of Africa, the vast majority of KS is diagnosed in late/advanced stage when prognosis is worst and efficacious therapy scarcely available. In order to ensure the best chance for favorable response to therapy KS must be detected early and so the attending clinicians should routinely:

- a) Encourage patients to examine their own skin and report suspicious lesions;
- b) Ask patients if they have noticed suspicious lesions;
- c) Perform complete skin exams.

The KS status of the patient should be recorded at each visit.

2.5.3.1.5 Treatment

Treatment should ideally be limited to patients with biopsy-confirmed KS. If biopsies are not available, clinical diagnoses may suffice but should be made in consultation with experienced practitioners. All patients with AIDS-associated KS have an indication for ART. Patients with more advanced KS should be started on anti-KS chemotherapy at the earliest opportunity in addition to ART.

Immediate indications for chemotherapy include:

- Oral lesions that interfere with chewing, swallowing or breathing;
- Proven or suspected lung or gastrointestinal tract involvement;
- Painful or disabling edema;
- Presence of sizeable bulky lesions;
- Substantial degree of ulcerated and/or superinfected lesions.

Patients who need chemotherapy should be referred to the specialized units such as the Cancer Institute at Mulago Hospital or any other that offer oncology services. For patients who need immediate chemotherapy, the optimal timing of ART initiation is unknown, but until further data are available, ART should be initiated as soon as possible.

For patients who do not have an immediate indication for chemotherapy, ART should also be initiated as soon as possible. It is not yet precisely clear which patients will respond to ART

alone other than, in general, persons with less advanced KS. Therefore, all patients without indications for immediate chemotherapy should be started on ART alone and observed closely for progression.

2.5.3.1.6 KS-associated Immune Reconstitution Inflammatory Syndrome (KS-IRIS)

Some patients with KS experience worsening of the manifestations of their KS within the first 12 weeks of ART. Some of this represents the natural progression of refractory KS and some represents the phenomenon of KS-IRIS; prospectively distinguishing between the two etiologies is very difficult. When worsening is limited to the skin and not causing disability, it may be managed without stopping ART with the hope that it will spontaneously resolve. When there is evidence of visceral involvement or other disability, chemotherapy is indicated but ART should be continued. While there are no data to prove efficacy of chemotherapy for KS-IRIS, ample anecdotal reports support its use.

2.5.3.1.7 The role of corticosteroids

Corticosteroids have been associated with worsening of KS among untreated patients and should therefore be avoided. This contraindication of corticosteroids in KS should only be suspended in situations where the use of steroids have proven survival benefit (e.g., as adjunctive therapy in pneumocystis pneumonia). The role of corticosteroids in KS-IRIS is not known but should only be attempted after seeking expert opinion.

2.6 ART monitoring

2.6.1 Follow-up and monitoring patients on ART

Patients on ART need close monitoring to assess their adherence to the prescribed regimen, tolerance and side effects of the medications and efficacy of the treatment. Once someone starts on ART a schedule for follow-up and monitoring should be drawn up. It usually includes a first visit two weeks or earlier after initiation (which may be useful to also evaluate and reinforce adherence to ART), then monthly for 6 months and thereafter every three months. Monthly visits should be combined with those of drug dispensing, as they provide useful opportunities to reinforce adherence. However, after 6 months, the drug dispensing visits may not correspond with those for clinical follow-up. In this case the patient should be encouraged to report any problem to the ART clinician when they come for their drugs and not to wait for the scheduled clinical visit. At all clinic visits, HIV 'prevention with positives' messages should be reinforced. These should include partner HIV testing, condom use for the sexually active, encouragement regarding faithfulness and abstinence, and prevention of mother to child transmission of HIV (PMTCT), including promotion of family planning.

2.6.2 Clinical guidelines for monitoring ART

Regular patient evaluation and monitoring of ART is important to assess effectiveness of this intervention and to ensure safety.

2.6.2.1 Clinical assessment

Clinical assessment should include thorough history on all events that may have taken place since the patient started on ART. These may include any illnesses or new infections, hospitalisations and any other medications including traditional herbs and remedies. In the case of women the health worker should enquire for any missed menstrual periods to detect early pregnancy. This is then followed by physical examination including vital signs, weight, and any abnormalities that may be related to drug toxicity or development of new opportunistic infections. Also at each visit the patient should have access to a counsellor to evaluate and reassert adherence and HIV prevention issues. The clinical assessment should include evaluations of other potential individual risks, such as sexual transmission of HIV and pregnancy.

2.6.2.2 Clinical monitoring for toxicities

Patients should be informed about the symptoms of ARV drug toxicities and what to do when they do develop. They should be advised to seek medical care whenever they develop any skin rash or stop therapy if they develop severe skin eruptions and/or jaundice.

For the skin rash, the health worker should decide if the rash is dry or wet. A dry skin rash is without any blistering. In this case the patient should be monitored closely while he/she continues with the drugs. A wet skin rash is where there are blisters. All medications should be stopped, patient admitted and closely monitored in case he/she requires additional treatment such as steroids. If in doubt a more experienced clinician should be consulted for advice. **See Appendix 3 & 4**

2.6.2.3 Clinical assessment of ART effectiveness

Whether CD4 cell monitoring is available or not, clinical evaluation of the effectiveness of ART is important and helpful. The evaluation should be done at every opportunity when a patient meets with the health worker, be it at a health facility or in the community. The basic parameters examined should include:

- The patient's perception of how he/she is doing on treatment;
- Improvement in appetite
- Changes in body weight over the course of therapy
- Changes in the frequency and/or severity of HIV-associated symptoms (e.g., fevers, diarrhoea)
- Physical findings (e.g. oropharyngeal or vulvovaginal candidiasis);
- Signs and symptoms of IRIS or HIV-related disease progression

2.6.3 Laboratory guidelines for monitoring ART

2.6.3.1 Basic laboratory tests for monitoring toxicity & treatment response of antiretroviral therapy

Certain laboratory investigations are recommended as the absolute minimum to manage patients on ART. These should either be available on site or by transportation of specimens to a local reference laboratory (in which case results should rapidly be returned to the requesting clinician). Such tests are needed to identify potential toxic reactions e.g. anemia due to ZDV, and then to trigger changes in drug regimes according to recommended protocols; or as adjuncts to

monitoring the effectiveness of ART. **Table 2.4** summarizes the recommended investigations for patients on ART that can also be used monitoring.

Other tests may be indicated based on the suspicion of a drug toxicity or clinical disease progression. Sometimes it may even be better to refer the patient to a better-equipped facility for more advanced evaluation.

Table 2.4: Recommended Investigations for ART

| Investigation | | Level available | Objective | Frequency |
|--------------------------------|--|---------------------------------------|---|---|
| Absolute minimum tests | HIV antibody test | All levels | Diagnose HIV and initiate ART | Once before ART |
| | Haemoglobin or hematocrit | All levels | Monitor degree of anaemia – if severe transfuse before ART or use TDF instead of ZDV | When indicated or if on ZDV, at 4, 8 & 12 weeks and thereafter when indicated |
| | Urine analysis for those put on TDF | | | |
| Basic recommended tests | Total WBC + differential | All levels | Monitoring neutropenic side effects | 6-12 monthly & when indicated |
| | CD4 cell count | All ART participating units | Monitoring immune response to therapy | 6 monthly or when suspect failure |
| | LFTs: alanine or aspartate aminotransferases | District hospitals | Monitor hepatitis co-infection and hepatotoxicity | When indicated. For women who start ART with CD4 250-350, that include NVP 4, 8, 12 wks |
| | Serum creatinine and/or blood urea | District hospitals | Monitor renal function | When indicated. For pts on TDF, before start and every 6 months |
| | Serum glucose | District hospitals | Monitor hyperglycaemia in patients on Protease Inhibitors | When indicated |
| | Pregnancy test | All levels | Change therapy to appropriate regimen when pregnant Assess pregnancy status among adolescent girls since they may not reveal that they are sexually active | When indicated |
| Desirable tests | Bilirubin | District hospitals | Monitor hepatitis co-infection and hepatotoxicity | When indicated |
| | Serum lipids | Referral hospitals | Monitoring hyperlipidaemia for those on Protease Inhibitors | When indicated |
| | Serum lactate | Referral Hospitals | Diagnosing lactic acidosis when on NRTI e.g. d4T or ddI | When symptoms suggest lactic acidosis |
| | Hepatitis B antigen tests | Referral Hospitals | Diagnose and initiate appropriate treatment for viral hepatitis | At baseline and/or when symptomatic |
| Optional tests | Viral load | Referral Hospitals & Research Centres | Monitoring viral response to therapy & diagnosing HIV in children <18 months | Every 12 months or when suspect failure |

2.6.3.2 CD4 lymphocyte counts

In addition to regular clinical evaluation, the CD4 lymphocyte counts are one of the most useful and reliable ways of assessing whether a patient on ART is responding to therapy. In those who respond by suppressing their VL, rises of >100 CD4 cells/mm³ are to be expected in the first 6-12 months in the ARV naïve, adherent patient with drug susceptible virus. Higher elevations can be seen and the response often continues in subsequent years in individuals with maximum virological suppression. Immunologic failure on therapy can also be assessed. In adults, a useful definition of immunological failure is a return to the pre-therapy baseline or a fall of $>50\%$ from the peak CD4 cell count. It is essential not to base a significant clinical treatment decision on a single CD4 result, rather use serial measurements to see the trend.

2.6.3.3 Plasma HIV-RNA levels (Viral Load)

When available, plasma HIV-1 RNA is a useful indicator of the activity of an ARV regimen in individual patients. However, due to its high cost and technical demands, such facility is only available in a few referral hospitals and research centres. The lack of availability of viral load monitoring implies that treatment failure will need to be assessed immunologically and clinically, rather than virologically. One of the implications of this is that diagnosing treatment failure may be delayed until clinical features do develop. As with CD4 cell count, it is hoped that inexpensive and implementable methods for viral quantification in plasma or serum will become available in Uganda soon in order to improve the effectiveness of ARV programmes and the care of individual patients.

2.6.4 Follow-up at ART implementing centers

In the past few years, 450 health units have been accredited by the MoH to be able to participate in the national ART program. These units include hospitals, (both public, NGOs and private), health centers 4 and 3. The staff working at these units have received ART related training and new ones are being trained. Bigger units like regional and teaching hospitals and research centers like Joint Clinical Research Center (JCRC) are routinely providing support to the smaller units. All these units play a major role in ART follow-up which should include:

- Monitoring patients' response to ART
 - Symptom checklist to detect intercurrent illness, HIV disease progression or adverse events to ART. The severity and likely relationship of events to ART, should be documented by the attending clinician.
 - Weight; this should be recorded at every visit. Any unexplained loss should prompt careful re-evaluation of the patient.
 - Haematology (Hb and FBC) and biochemistry investigations should be done whenever there are symptoms of intercurrent infections and when there are symptoms suggestive of severe toxicity to ARV drugs. For patients on ZDV, a haemoglobin should be done more frequently, at 4, 8 and 12 weeks after initiation of ART in order to detect anemia early.
 - CD4 cell count should be done once every 6 months or earlier if patient is not clinically responding to ART

- Changes in ART, OI prophylaxis and other concomitant medications based on clinical and laboratory assessment. Record any drugs given for prophylaxis (e.g. cotrimoxazole, fluconazole)
- For females of child bearing age, ask about pregnancy (missed periods)
- Provide continuous counseling to ensure adherence to ART
 - Assessment of adherence by pill counts, 3-day recall, or nurse administered questionnaires: even the very young are able to give a clue to their adherence (always chat with them about the subject), reports from the treatment supporter or relatives
 - Discuss the role/action of the treatment supporter
 - Healthy living including abstaining from alcohol intake
- Identifying patients that need more sophisticated investigations and refer them to better equipped facilities
- Assess sexual transmission risk of the individual and provide ‘positive prevention’ counseling that includes safer sex practices, partner testing, disclosure of HIV status, PMTCT and reproductive health
- Screen for TB at every visit

2.6.5 Follow-up at community level

Community based organizations are important in providing continuous support to patients on ART. This demystifies ART and ensures better adherence to treatment. However, there should be an effective referral network between these organizations and other ART service providers in order to deal with possible complications without much delay. Where such organizations do have outreach care services, they could also include monitoring ART adherence, HIV testing for sexual partners of index clients and their household members. They should also reinforce HIV prevention messages, address stigma and social support for people living with HIV infection. This requires the ART implementing centers working hand in hand with these organizations.

To ease collaboration between ART implementing centers and the community organizations or networks, standard operating procedures (SOPs) or memoranda of understanding should be put in place to guide and inform the collaborations. Also the MOH Community Based care guidelines should be consulted for additional guidance on community follow-up.

2.6.6 ART data management and reporting

As more health units in Uganda provide ART services, there is need to collect relevant data that will help the health units to monitor their patients. This information will also assist the Ministry and stakeholders to monitor the performance of the ART program and the emergence of early warning indicators of HIV drug resistant strains. The patient monitoring system comprises of a minimum set of data elements that are collected and reported using standardized forms. The various forms comprise of:

- The Facility held HIV care/ART card that maintains a record of the client’s basic information and their follow up chronic AIDS care/ART
- Patient held ART card is a short summary record of the client and follow-up appointments

- The Pre-ART register lists all clients who are enrolled in chronic HIV/AIDS care including ART at the facility.
- The ART register maintains a longitudinal record of the follow up care of clients who are enrolled into ART
- The quarterly cross sectional reporting form is completed at the end of every quarter to keep track of all clients on ART and chronic HIV/AIDS care.
- The cohort analysis form is used for summarizing treatment outcomes

The data should be collected by all those units providing ART services and chronic AIDs care and should include the following information:

- At all levels of the health care system (National, District and Health Facility) for program monitoring.
 - Information that is collected and reported on a quarterly basis includes:
 - ✓ Number of individuals receiving chronic AIDS care during the quarter
 - ✓ Cumulative number of individuals ever enrolled in chronic AIDS care by the end of the quarter
 - ✓ Number of individuals in chronic AIDs care who received cotrimoxazole prophylaxis at their last visit in the quarter.
 - ✓ Number of individuals enrolled in chronic AIDS care during the last quarter
 - ✓ Number of pregnant females enrolled in chronic AIDS care in the last quarter
 - ✓ Percentage of infants born of HIV-infected women started on cotrimxazole prophylaxis within 2 months of birth
 - ✓ Number of individuals receiving HIV care/ART who were screened for TB at their last visit in the quarter
 - ✓ Number of individuals receiving HIV care/ART who started TB treatment during the quarter
 - ✓ Number of individuals who are eligible for ART but have not yet started treatment during the quarter.
 - ✓ Percentage/Number of adults with advanced and all children with HIV infection receiving ART during the quarter
 - ◆ Percentage of adults and children receiving first-line regimen
 - ◆ Percentage of adults and children receiving second line regimen
 - ◆ Percentage of adults and children receiving other regimens
 - ✓ Cumulative number of individuals ever started on ART by the end of the quarter
 - ✓ Number of ART naïve individuals who started ART during the quarter
 - ✓ Percentage of individuals still alive and known to be treatment 6, 12 months and annually after initiation of therapy
 - Information collected annually for monitoring HIV drug resistance Early Warning Indicators
 - ✓ Percentage of individuals starting ART who are prescribed an appropriate standard first-line regimen (target should be 100%)
 - ✓ Percentage of individuals who are still prescribed a standard first-line regimen 12 months from initiation of treatment (target should be >70%)
 - ✓ Percentage of individuals who attended all clinic appointments on time during the first year of ART (target should be >80%)

- ✓ Percentage of individuals lost to follow up during the first 12 months on ART (target should be <20%)
- ✓ Percentage of months in the year where there were no drug stock outs at the health facility (target should be 0)
- Information collected annually during special surveys and ART data quality assessments
 - ✓ Number of health workers in the health facility trained in ART service delivery in accordance with national standards
 - ✓ Percentage and number of health facilities offering ART that have access to laboratory services for monitoring ART
 - ◆ Percentage and number of health facilities that have access to CD4 cell count services.
- At the health facility level for patient monitoring
 - Information collected routinely for patient and programme monitoring at the health facility
 - ✓ Percentage of individuals receiving HIV care/ART whose immediate family members have been tested for HIV
 - ✓ Percentage of individuals referred by the health facility for HIV care at another facility
 - ✓ Distribution of care entry points of patients enrolled in chronic AIDS care at the facility
 - ✓ Percentage of patients who demonstrate $\geq 95\%$ adherence to their ARV medication
 - ✓ Reasons for poor adherence
 - ✓ Percentage of pregnant females linked with PMTCT interventions
 - ✓ Percentage of new mothers whose infants are linked to care
 - ✓ Reasons for ART treatment interruptions
 - ✓ Distribution of reasons for substituting, switching or stopping ART
 - ✓ Number, nature and frequency of side effects, opportunistic infections and other problems

The data collected should be forwarded to heads of health sub-districts, the district directors of health services and to the MoH headquarters at the AIDS Control Program (ACP) at the end of each quarter. It is anticipated that once the normal reporting mechanism of passing through established institutions at health sub-district and district to Ministry of Health has been established and functional, the reporting loop from health facilities to MOH will be phased out. At the health sub-district and district levels information should be used to inform the drugs, reagents and other logistics procurement processes, estimate staff requirements, identify bottlenecks in the ART program and find solutions. At ACP the data should be used to improve policies and guidelines on the program at national level and also allow for proper budgeting for the National ART Program.

2.7 Nutrition Care and Support for PLHIV

2.7.1 Introduction

Nutrition is an important component of comprehensive care for the HIV-infected individuals. The effect of HIV on nutritional status begins early in the course of infection, possibly even before the individual in question is aware of being infected. HIV infection affects nutritional status by putting extra demand on the immune system causing increased energy requirements, reduction in dietary intake, nutrient malabsorption, nutrient loss, and complex metabolic alterations that culminate in the weight loss and wasting.

Based on the evidence from the HIV/Nutrition project implemented by NuLife where nutrition was integrated into HIV/AIDS comprehensive care clinics, 12 % (21,000 PLHIV and affected clients) were diagnosed as acutely malnourished. Provision of nutritional therapy resulted into improved health and nutritional status. This finding demonstrates the importance of integrating nutrition into HIV/AIDS care treatment and support.

2.7.2 Objectives

The main objective of this section is to contribute to the improvement of nutritional status and quality of life of PLHIV. Specifically, this includes:

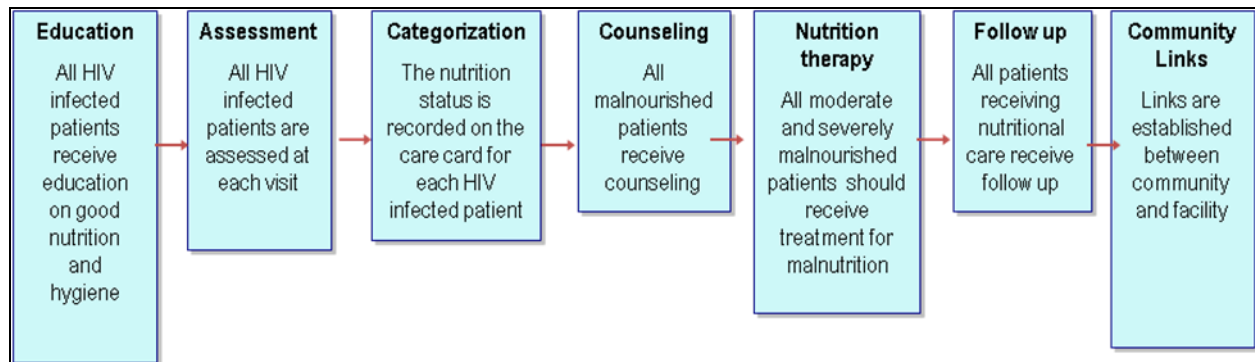
1. To aid health providers in the delivery of integrated nutritional care, treatment and support of people infected and affected with HIV.
2. To enable health providers diagnose and provide quality nutrition education, counseling, treatment and follow up.
3. To contribute to the adherence and compliance to HIV care through appropriate nutritional advice

Health workers providing nutrition care and support for PLHIV should endeavor to undergo training in Comprehensive Nutrition Care for PLHIV or Integrated Management of Acute Malnutrition (IMAM) offered by the MoH and partners

2.7.3 Implementation

Nutrition care can be integrated into HIV/AIDS care and treatment programs using the “The Seven Steps” approach

Fig 2.2: The seven steps to integration of Nutrition into the Health care service delivery system



2.7.3.1 Step 1: Health and Nutrition Education

All clients attending the pre- ART, ART, pediatric and PMTCT clinics should be educated on key nutrition practices using Nutrition and HIV job aids including the Nutrition Care and Support for PLHIV national counseling cards. Health and Nutrition education can be conducted in the waiting area. Topics need to be chosen carefully, in line with treatment and care package. Short, interactive, more practical sessions are readily accepted and absorbed than long lecture topics. Teach back sessions may be important to check on their understanding. Some of the important topics in nutrition include:

2.7.3.1.1 The importance of eating a variety of nutritious foods from the following food groups

Clients should be taught on the main food groups, their use and importance of eating one from each of the food groups daily. These groups include:

- STAPLE FOODS (Energy giving) includes Millet flour, sorghum flour, maize flour, potatoes, matooke, potatoes, yams
- LEGUMES (Body building from plant origin) which includes Beans, peas, grams, groundnuts, cowpeas, soya beans. The Legumes can be eaten more often
- ANIMAL SOURCE (Body building from Animal origin) which includes Milk, Meat, chicken, fish, and eggs. This group may be scarce as it is more expensive. Silver fish (Mukene/Omena/Muziri) is relatively inexpensive and highly nutritious.
- VEGETABLES (protective group): The dark green leafy vegetables such as pumkin leaves (Essunsa), cowpea leaves (Boo) Amaranthus (doodo/Ebbuga), Cassava leaves (Sombe) Nakatti, Ejjobyo, Hibiscus Cannabinus (Malakwang) Spinach and others; Tomatoes, Eggplant, Carrot, Bitter tomatoes (ntula), Okra leaves and pods, Katunkuma, Mushrooms (Obutiko).

- **FRUITS** (protective group): Passion fruit, mango, pawpaw, orange, banana, watermelon, sweet melon, pineapple, avocado, Jackfruits, custard apple (Ekitafeeri), sugarcane, Jamun fruit (Jambula), Gooseberries (entuntunu)
- **FATS AND OIL** (High Energy giving source). Can be derived from Vegetable origin and considered the best (Groundnut oil, Sesame oil, sunflower oil, Olive oil, shea nut oil/butter, palm oil and margarine) or from animal source (ghee, Lard). Under normal circumstance, Fats and Oil should be eaten in moderation as too much may lead to storage in the body as fat leading to over weight and obesity.
- **Water** (Body hydration) Clean and safe water is very important to the body, a normal person should drink at least 8 glasses of water daily. Water intake should be increased during hot weather, fever or diarrhea/vomiting.

2.7.3.1.2 The importance of observing environmental, personal and food hygiene in preventing infections.

This topic cuts across prevention and protective measures and should be well understood by the clients as they are more vulnerable to infections. Emphasis should be placed on clean and safe water, hand washing, safe waste and faecal disposal.

2.7.3.1.3 Dietary management of HIV/AIDS related complications.

The clients need to be aware of symptoms that can affect their nutrient and energy intake and lead to/worsen their nutritional status. Refer to the **table 2.5** below on caring for Symptoms Associated with HIV/AIDS when educating client on this topic

Table 2.5: Dietary management of HIV/AIDS related complications.

| Symptom | Dietary management | Care and nutrition practice |
|--------------------------|---|--|
| Anorexia (appetite loss) | Stimulate appetite by eating favorite foods. Eat small amounts of food more often more energy-dense foods. Avoid strong-smelling foods | If appetite loss is a result of illness, seek medical treatment |
| Diarrhea | Drink plenty of fluids (soup, fruit, juice, boiled water, light tea) to avoid dehydration. Avoid strong citrus fruits (oranges & lemons), which may irritate the stomach. Eat foods rich in soluble fibre (millet, bananas, peas) to help retain fluids; fermented foods such as porridges & yoghurt; easily digestible foods such as rice, bread, millet, maize porridge, Irish or sweet potatoes. Eat small amounts of food but frequently. Continue to eat after illness to recover weight & nutrients lost. Soft fruits & vegetables cooked and mashed matooke, sweet potatoes, carrots; | Prevention Drink plenty of clean, boiled water. Wash hands with soap & water Before handling, preparing, serving, or storing food. After using the toilet/latrine or cleaning a child after defecation. Treatment Drink more fluids to prevent dehydration. Prepare rehydration solutions using oral rehydration salt packets (show packet) Go to a health facility if you have symptoms such as severe dehydration (low/no urine output), fainting, |

| | | |
|---------------------|--|---|
| | <p>eggs, chicken, or fish for protein. Boil or steam foods.</p> <p><u>Avoid the following foods:</u> Dairy products such as milk Caffeine (coffee & strong teas), Alcohol, Fried foods, butter, or margarine, Gas-forming foods (cabbage, onions, & soda beverages)</p> | <p>dizziness, shortness of breath, bloody stools, high fever, vomiting, severe abdominal pain, or diarrhea for > 3 days.</p> |
| Fever | <p>Eat soups with energy & nutrient-rich foods such as maize, potatoes, and carrots.</p> <p><u>Drink</u> more, plenty of liquids, lemon or guava tea.</p> <p>Continue to eat small, frequent meals as tolerated.</p> | <p>Drink fluids, especially clean boiled water, to prevent dehydration.</p> <p>Bathe in cool water & Rest.</p> <p>Take paracetamol, if available, with meals three times a day.</p> <p>Go to a health facility if you have a fever for several days that is not relieved with paracetamol, loss of consciousness, severe body pain, yellow eyes, severe diarrhea, convulsions, or seizures.</p> |
| Nausea and Vomiting | <p><u>Eat</u> small and frequent meals soups; unsweetened porridge & fruit such as bananas; lightly salty & dry foods to calm the stomach. Drink lemon juice in hot water, clean boiled water.</p> <p><u>Avoid</u> spicy or fatty foods, caffeine (coffee and tea) and alcohol.</p> | <p><u>Avoid</u></p> <p>An empty stomach, which makes nausea worse.</p> <p>Lying down immediately after eating (wait at least 20 minutes)</p> <p>Rest between meals.</p> |
| Thrush | <p><u>Eat</u></p> <p>Soft mashed foods such as sweet potatoes, Irish potatoes, carrots, bananas, scrambled eggs, soup and porridge.</p> <p>Eat cold foods or foods at room temperature.</p> <p><u>Avoid</u> spicy, salty, or sticky foods that can irritate mouth sores.</p> <p>Strong citrus fruits & juices that can irritate mouth sores.</p> <p>Sugary foods that cause yeast to grow.</p> <p>Avoid alcohol & Drink plenty of liquids.</p> | <p>Seek medical treatment.</p> <p>Eat small frequent amounts of food.</p> <p>Tilt your head back when eating to help you swallow.</p> <p>Rinse your mouth with warm boiled salty water after eating to reduce irritation and keep infected areas clean.</p> |
| Anemia | <p><u>Eat</u></p> <p>More iron-rich foods such as eggs, meat, fish, and liver; green leafy vegetables such as spinach; legumes (beans, peas, G.nuts); nuts; sesame seeds; and fortified cereals.</p> <p>Take iron and folate supplements</p> | <p>If available,</p> <p>Take one iron tablet daily with food and vitamin C (tomato or orange juice) to help with absorption.</p> <p>Seek treatment for malaria & hookworm.</p> <p>Drink plenty of fluids to avoid constipation.</p> |
| Muscle | <u>Eat</u> | Do regular weight-bearing exercises |

| | | |
|---------------------------------|--|--|
| wasting | Small frequent meals. Improve the quality and quantity of your diet by a variety of foods. More protein, starchy foods (cereals & staples). | to build muscles. |
| Constipation | Eat High-fibre foods such as maize, whole wheat bread, green vegetables, washed fruits with the peel. Avoid processed or refined foods. Drink plenty of liquids. | Avoid using enemas & medications to cleanse the bowels. Drink plenty of liquids, including boiled water. |
| Bloating or Heartburn | Eat small, frequent meals. Avoid gas-forming foods (cabbage, onions, & Soda beverages). Drink plenty of fluids. | Eat long enough before sleeping to let food digest. |
| Tuberculosis | Eat foods high in protein, energy, vitamins. | Seek medical attention immediately. Ask health workers about taking Medication with food. If taking Isoniazid for treatment, take a vitamin B6 supplement to avoid deficiency. |
| Loss of taste or abnormal taste | | Enhance the flavour of food with salt, spices, herbs or lemon. Chew food well and move it around your mouth to stimulate taste receptors. |

2.7.3.1.4 Management of medicine and food interactions.

Clients on ARVs or prophylaxis may experience problems when eating certain foods or the foods may cause the drugs they are taking to be less effective. They need to be made aware of common drug-food interactions and how they can reduce these effects:

- I. Food can affect drug efficacy.
- II. Drugs can affect nutrient utilization.
- III. Drug side effects can affect food intake or nutrient absorption.
- IV. The combination of certain drugs and foods can create unhealthy side effects.

Details of the drug food interaction can be provided during individual counseling.

Refer to the table on National guidelines on drug-food interactions when educating/counseling clients

2.7.3.2 Step 2 & 3: Assessment and Categorization

It is important to screen all clients attending pre- ART, ART, pediatric and PMTCT clinics (at the entry point/ registration) for malnutrition at each visit using color coded Mid-Upper Arm Circumference (MUAC) tapes. This is a simple and effective screening method in busy and understaffed HIV/AIDS/ART clinics. This activity can be relegated to lower staff cadre or expert clients/Community volunteers/VHT.

- The interpretation of the screening colour code: Green = Normal nutrition status; Yellow= Moderate Acute Malnutrition (MAM); Red= Severe Acute Malnutrition (SAM). The findings should be record in the clinic register and client care card.
- Only Clients with Yellow or Red MUAC code should be referred to a trained and skilled health worker/nutritionist for further examination and confirmation of the diagnosis of acute malnutrition. Such measures reduce on workload and congestion. Clients with pale palms and pale conjunctiva, extreme weakness or overweight/ abnormal fat distribution (Lipodystrophy) should also be referred for further assessment and investigation.

2.7.3.3 Step 4: Nutrition Counseling

Nutrition counseling should be provided by a staff/counselor trained in nutrition/IMAM/comprehensive Care and Support for PLHIV. Particular attention should be given to the following:

- Clients diagnosed with malnutrition (SAM, MAM Obesity, micronutrient deficiency)
- Clients not improving on nutritional therapy
- Clients defaulting on Nutrition care
- Clients who are ready for discharge from Nutrition care
- Clients s whose nutritional status requires inpatient care

In addition, counseling topics should include:

- Management and treatment of malnutrition
- Adherence to nutrition therapy
- Importance of returning for follow-up care
- Eating a variety of nutritious foods

2.7.3.4 Step 5: Nutrition Therapy

Clients diagnosed with Acute Malnutrition should receive appropriate nutrition therapy in accordance with the IMAM guidelines. The common nutrition therapy in form of foods includes:

- Ready-to-Use-Therapeutic-Food (RUTF/RUTAF),
- Commercial or locally prepared milk Formula-75 (F75) and Formula-100 (F100).
- Fortified Blended Food (FBF) e.g., Corn Soya Blend

The choice of therapy will depend on whether the client is enrolled to outpatient therapeutic care (OTC) inpatient therapeutic care (ITC), or supplementary feeding program (SFP). More information can be found in the IMAM guidelines. However, most cases of acute malnutrition (SAM, MAM) without medical complications can be treated on outpatient basis with RUTF.

Therapeutic foods should be made available in the same pharmacy as ARVs and other treatment; this will ensure comprehensive care of an individual, reduce client waiting time, improve compliance and consequently, the health and nutrition outcomes.

2.7.3.5 Step 6: Follow up Care

It is important to follow up the progress of clients on nutritional therapy in order to prevent relapse, check for adherence, monitor progress and identify medical complications.

- Encourage clients to return for follow-up visits

- Synchronize return dates with ART, YCC and ANC visits to reduce on the number of clinic visits
- Minimize client waiting times through integration of services
- At follow-up visit, check on the progress and compliance to treatment by taking MUAC and weight
- Provide continuous counseling where necessary

2.7.3.6 Step 7: Community linkages

It is important to build continuum of care at the community level through engaging expert clients and Village Health Teams (VHT) trained in nutrition care and support/ IMAM. Continuum of care involves case finding, referral, counter-referral, health and nutrition education and follow-up of clients.

2.7.4 Vitamins and Minerals

Vitamins and minerals are sometimes called micronutrients. Our bodies need them, in small amounts, to support the chemical reactions our cells need to live. Different nutrients affect digestion, the nervous system, thinking, and other body processes.

Micronutrients can be found in many foods. Healthy people might be able to get enough vitamins and minerals from their food. People with HIV or another illness need optimal micronutrients to help repair and heal cells. Also, many medications can create deficiencies of the micronutrients. Some nutrients are antioxidants, important for PLHIV as the infection leads to higher levels of substance (free radicals) that damage tissues. Likewise, the free radicals can worsen the disease. Therefore, higher levels of antioxidants can slow down the virus and help repair some of the damages.

PLHIV may benefit from taking supplements of the following vitamins and minerals:

- **B Vitamins:** Vitamin B-1 (Thiamine), Vitamin B2 (Riboflavin), Vitamin B6 (Pyridoxine), Vitamin B12 (Cobalamin), and Folate (Folic Acid).
- **Antioxidants**, including beta-carotene (precursor of Vitamin A), selenium, Vitamin E (Tocopherol), Vitamin C and **Zinc**

2.7.5 Other Supplements

In addition to vitamins and minerals, PLHIV may use supplements below:

- **Acidophilus**, a bacterium that grows naturally in the intestines, helps with digestion.
- **Alpha-lipoic acid** is a powerful antioxidant that may help with neuropathy and mental problems.
- **Carnitine** (also called acetyl-L-carnitine) may help prevent wasting and provide other immunologic and metabolic benefits,
- **Coenzyme Q₁₀** may help with immune function.
- **Essential fatty acids** found in evening primrose oil or flaxseed oil can help with dry skin and scalp.
- **N-Acetyl-Cysteine**, an antioxidant, can help maintain body levels of glutathione. Glutathione is one of the body's main antioxidants.
- **Omega 3 fatty acids** can help decrease triglycerides
- **Niacin** can help increase good cholesterol and decrease bad cholesterol

2.7.6 Safety of the Nutrients

Most vitamins and nutrients appear to be safe as supplements, even at levels higher than the Recommended Dietary Allowances (RDAs). However, some can cause problems at higher doses, including Vitamin A, Vitamin D, copper, iron, niacin, selenium, and zinc.

A basic program of vitamin and mineral supplementation should be safe. This would include the following, all taken according to prescription:

1. A multiple vitamin/mineral (without extra iron),
2. An antioxidant supplement with several different ingredients, and
3. A trace element supplement including chromium, copper, cobalt, iodine, iron, selenium, and zinc.

DO note that some multivitamins also include these trace elements.

It is important to remember that higher price may not mean better quality. Simple vitamins may work as well.

Any other program of supplements should be based on discussion with a doctor or nutritionist/dietician.

2.7.7 Dietary and herbal Supplements

A dietary supplement must meet all of the following conditions:

- It is a product that is intended to supplement the diet and that contains one or more of the following: vitamins, minerals, herbs or other botanicals, amino acids, or any combination of the above ingredients.
- It is intended to be taken in tablet, capsule, powder, softgel, gelcap, or liquid form.
- It is not represented for use as a conventional food or as a sole item of a meal or the diet.
- It is labeled as being a dietary supplement.

Clients should be counseled to get information on supplements that are based on the results of rigorous scientific testing, rather than on testimonials and other unscientific information. These are a type of dietary supplement that contains herbs, either singly or in mixtures. A herb (also called a botanical) is a plant or plant part used for its scent, flavor, and/or therapeutic properties.

Many herbs have a long history of use and claimed health benefits. However, some herbs have caused health problems for users.

1. It's important to know that just because a herbal supplement is labeled "natural" does not mean it is safe or without any harmful effects.
2. Herbal supplements can act in the same way as drugs causing medical problems if not used correctly/ taken in large amounts.
3. Women who are pregnant or nursing should be especially cautious about using herbal supplements, since these products can act like drugs. This caution also applies to treating children with herbal supplements.
4. Some herbal supplements are known to interact with medications in ways that cause health problems. It is important for the client to consult health care providers before using

an herbal supplement, especially if they are taking any medications (whether prescription or over-the-counter), see appendix x

5. If a client use herbal supplements, it is best to do so under the guidance of a medical professional.
6. The Food and Drug Authority (FDA) are working towards the regulation of dietary supplements including Herbal supplements.

2.8 Challenges of ART

When patients adhere to ART they benefit from a good quality of life almost similar to those who are HIV negative. However, there are many challenges patients and their carers face in order to achieve this status. Some of these challenges will be discussed below.

2.8.1 Immune Reconstitution Inflammatory Syndrome (IRIS)

Soon after initiating HAART some patients may experience symptoms and signs of inflammation. Patients may present with painful and swollen lymph nodes, chest symptoms, and unexplained fevers among others. These observations usually are due to a phenomenon termed the Immune Reconstitution Inflammatory Sndrome or ‘IRIS’. Other names for IRIS include Immune Restoration Disease (IRD) and paradoxical reactions. IRIS occurs when the immune response against a particular antigen increases after the start of ART, leading to an inflammatory reaction. Initiation of ART can also unmask previously undiagnosed infections by improving the inflammatory response due to the repair of the immune system.

Common IRIS related diseases in Uganda include *Tuberculosis* (TB), *Cryptococcal meningitis*, CMV retinitis, genital ulcers from Herpes Simplex, and Kaposi’s sarcoma.

IRIS events may occur in up to 40% of patients treated for TB who start ART and up to 5% in those with cryptococcal disease. The risk is higher in those with advanced HIV disease with low CD4 counts. IRIS events often occur between 2-8 weeks of ART initiation and less commonly after many months of ART. The diagnosis of IRIS should be considered by ART providers when a patient who has recently started ART (last 3 months) develops new symptoms when they should be getting better. This is particularly the case in patients with a known co-infection such as TB or cryptococcal meningitis who seemed to be responding well and adhering to treatment but then deteriorate within weeks after starting ART.

2.8.1.1 Examples of specific IRIS events

Tuberculosis: TB IRIS presents with worsening clinical symptoms after initial improvement and may occur in up to 40% of persons with TB who initiate ART. Patients with pulmonary TB may develop worse chest symptoms, new infiltrates on chest film, and enlarged lymph nodes that may become tender or form abscesses. TB meningitis and/or tuberculomas may present with confusion, fits and/or new focal neurological features. Abdominal TB may present with intestinal obstruction or even bowel perforation. TB IRIS is more common if ART is started early in the course of TB treatment and in patients with low CD4 counts. Most cases resolve without any intervention and ART can be safely continued. However, serious reactions like

tracheal compression from massive lymphadenopathy or respiratory difficulty may require use of corticosteroids.

Cryptococcal meningitis: IRIS events against cryptococcal meningitis may cause dangerous clinical deterioration with increased intracranial pressure and therefore increasing headache and/or vomiting, confusion and fits and visual disturbance.

2.8.1.2 Principles of Management of IRIS

The management of IRIS should be based upon the following questions:

1. *Is the responsible antigen being treated appropriately (e.g. TB, cryptococcal meningitis)?*
 - If the TB or Cryptococcal infection is being adequately treated then it will not be necessary to alter this treatment.
 - If the treatment has not been adequate or the adherence of the patient to the prescribed treatment has been poor, then treatment failure must be considered. In this case, appropriate specimens should be sent for culture and re-treatment of the infection initiated.
 - If the infection was unknown/undiagnosed/untreated and has only been 'unmasked' by ART, then appropriate therapy should be initiated immediately.
2. *Should the ART be continued or stopped?*
 - Once the diagnosis of IRIS has been made, patients should continue with their ART. Stopping should only be considered if there is a strong suspicion of drug toxicity.
3. *What other treatment can be used to treat IRIS patients?*
 - IRIS reactions are typically self-limiting, although may require the use of a brief course of corticosteroids to reduce inflammation for central nervous system or severe respiratory symptoms.

2.8.2 Patient adherence

ARV drug adherence is well recognized to be one of the key determinants of success of therapy. Conversely, poor adherence can lead to treatment failure, development of drug resistance and subsequent immunologic and clinical failure. Factors that contribute to good adherence include;

- Use of simplified, well-tolerated regimens involving as fewer pills as possible administered no more than two times per day.
- Patient counseling and education both before ART and during treatment. It is important to counsel patients carefully in advance of initiating therapy. This is typically a coordinated effort involving physicians, nurses, counselors and other health care providers including a treatment supporter or a close relative or friend if involved. ART should not be started at the first clinic visit. A period of education and preparation to try to maximize future adherence is important.
- Directly observed therapy (DOT) may be introduced with caregivers' or family members' assistance or treatment supporter. This maybe more useful for an initial 'training' period for patients but may not be sustainable for very long periods.
- Personal adherence plans that are integrated into patient routine activities. The plans should be regularly reviewed to incorporate changes in life style and job/work

requirements. They should be shared with the ART health unit who should make appropriate adjustments, e.g. scheduled treatment visits.

- Health systems that ensure availability of drugs, supplies and human resources at all times (see **2.8.3**).

Ongoing attention to, and reinforcement of, adherence throughout the entire course of ART is an essential part of any successful treatment program. Once treatment has begun, continued monitoring of adherence is essential. These monitoring tools include:

- Pill counts, but is subject to error and manipulation.
- Validated patient questionnaires that are easy to administer in the outpatient setting.
- Three day recall during clinic visits
- Spot checks at home

It is recommended that each patient recruited into a treatment program should complete a personal adherence plan. The adherence plan should include the identification of a treatment supporter (or companion) that will assist the patient to adhere to his/her drugs. The treatment supporter will be charged with checking on the patient at least once a week that the daily markings of the tablets taken by the patient on the treatment record. In order for this strategy to succeed, each treatment supporter should receive sufficient orientation to ARV adherence at least once. This should be preferably before the patient starts on ART and if not feasible at least in the next three months of ART.

2.8.3 Sustainable ARV drug supplies and delivery systems

The key to successful ART program is having a continuous supply of drugs for patients among other things. The participating health units in the ART program should ensure that they don't run out of any item of the recommended ARV drugs. Ordering drugs should be based on the consumption rate and done in plenty of time. Procurement and delivery procedures should be agreed upon with the relevant authorities at the beginning of the program.

Health units participating in the ART program should be aware of the following possible problems:

- Drug requirements will keep increasing every month depending on the number of new patients put on ART
- The ever increasing volume of procured drugs and other ART related supplies will add strain on storage facilities, security, revenue collection system and transport requirements

3.0 Guidelines on ART for Adults

3.1 HIV counseling for ART in adults

There are many patients who know their HIV serostatus through HCT but have yet to consider using ART. When a decision is reached that they should start ART, additional counseling is required to address the following issues and any other that may be considered important:

- That ARV drugs do not provide a cure. HIV may be suppressed but is not eradicated from the body. The individuals on ARVs may be infectious and transmit HIV and therefore HIV prevention is still a necessity (e.g. abstinence, condom use, partner HIV testing and disclosure, reduction in sexual partners, PMTCT...). However, for the majority of people who use ARV drugs properly, they are associated with much improved quality of life, reduced HIV transmission risk, and longer survival.
- The ARV drugs should be taken daily for life as there is no evidence to date that treatment interruption has any benefit. However, under special circumstances e.g. life-threatening toxicity, the clinician may stop the patients ART and reinstate it when the offending condition has improved.
- The ARV drugs, like any other medication, are associated with side effects. These may include anemia, neuropathy, liver damage, and physical bodily changes. However, regular monitoring of the patients can enable early detection of these adverse events.
- Regimen specific counseling should be provided once a suitable regimen is identified
- The best results from ART are obtained with complete adherence to the treatment regimen.
- Some patients may fail to respond to treatment and may require several changes of their drugs with or without success.
- All patients should be counseled on nutrition and lifestyle (e.g. cessation of alcohol and smoking)
- Patients should be advised to seek treatment whenever they suffer from any ailment

In addition, HIV prevention counseling interventions should be integrated into HIV care and treatment including:

- Prevention counseling, disclosure and partner testing
- Sexual and reproductive health, including family planning
- Prevention of mother to child transmission (PMTCT)

These issues should be thoroughly discussed by the counselor and any health worker who is directly involved with the patient. Also they should be repeated during follow-up.

However, counseling should not unnecessarily delay the start of ART especially in people with advanced immunosuppression ($CD4 < 50$). The recent trials presented at CROI-2011 showed a mortality benefit when ART is started within 2 weeks in people with advanced HIV disease.

3.2 ART initiation in adults

We now recommend that anyone with a CD4 cell count of 350 and below should be initiated on ART whether symptomatic or not. Those with a count above 350 should start on ART as provided below.

It is recommended to initiate Antiretroviral Therapy in Adults with documented HIV infection and;

- CD4 cell count of 350 cells/mm³ and below
- CD4 cell count above 350 cells/mm³ in those:
 - Who are co-infected with tuberculosis (TB),
 - Who are co-infected with HBV
 - Women who are pregnant (prophylaxis use only)
- WHO Stage III and IV disease irrespective of CD4 cell count

Tables 3.1a and 3.1b outline the criteria for initiating antiretroviral therapy.

Table 3.1a. WHO clinical staging and immunological criteria for initiating ART

| Clinical Stage (see revised WHO clinical staging, Appendix 1) | CD4 cell count | Comments |
|---|----------------|---------------|
| I | CD4 guided | Treat if ≤350 |
| II | CD4 guided | Treat if ≤350 |
| III | Treat | Treat |
| IV | Treat | Treat |

Table 3.1b. CD4 cell count criteria for initiation of ART

| CD4+ count (cells/uL) | Actions |
|-----------------------|--|
| <350 | Treat irrespective of clinical stage |
| 350-500 | Consider treatment in patients who are symptomatic (WHO Stage III or IV), have TB, HBV co-infected or are pregnant (prophylaxis) |
| >500 | Do not initiate treatment unless TB-co-infected, HBV co-infected or pregnant (prophylaxis), or stage III or IV |

A CD4 count is essential for ART initiation and subsequent monitoring of the patients. The decision to initiate ART is based on clinical staging and CD4. Fortunately in Uganda CD4 testing is now more readily available and accessible, particularly at all the sites that are participating in the various ART national programs, including Health Center 4s. So anyone who is put on ART **must have blood drawn for a baseline CD4 cell count within 3 months of initiation.**

3.3 Recommended starting (first line) regimens in adults

We recommend that the first-line regimen for adults and adolescents contain two NRTIs plus one NNRTI. The recommended combinations are;

Table 3.2: Recommended First Line Regimens Combinations

| | | |
|---|------|----------------|
| Preferred | | |
| | Plus | NVP or |
| TDF/3TC or | | |
| | | EFV |
| Alternative | | |
| AZT/3TC | Plus | NVP or EFV |
| ABC/3TC* | | |
| For women who have received SD NVP in the last 6 months | | |
| Preferred | | |
| TDF/3TC | Plus | ATV/r or LPV/r |
| Alternative | | |
| AZT/3TC | Plus | ATV/r or LPV/r |

Note: Combinations containing a PI are more expensive and should be preserved for 2nd line treatment.

*ABC/3TC is for patients with poor renal function and/or anemic

FTC may be used instead of 3TC. Indeed there is a generic fixed dose formulation of TDF+FTC+EFV now available in the country.

3.3.1 Rationale for Choice of Initial ART Regimens:

Currently the Initial Treatment Regimens that are widely used in resource limited settings (RLS) and recommended for Uganda are: non-nucleoside reverse transcriptase inhibitor (NNRTI): Efavirenz (EFV) or Nevirapine (NVP) plus a nucleoside reverse transcriptase inhibitor (NRTI) backbone: Tenofovir (TDF) + Lamivudine (3TC) or Zidovudine (AZT) + 3TC. These first line regimens prolong life, have a low pill burden, and are cost effective.

The choice of preferred regimens is based on:

- Efficacy,
- Durability,
- Tolerability (potential toxicities),
- Usage in women and taking into consideration high incidence of unplanned pregnancies (high fertility rates)
- Ease of use (availability of fixed dose combination)
- Frequent occurrence of co-infections (TB, hepatitis and Kaposi sarcoma)
- Prevalence of anemia among patients starting ART
- Availability of regimen and continuity of supply to meet demand
- Potential for maintenance of future treatment options (sequencing of ARVs)

3.3.2 NRTIs

Tenofovir (TDF) -containing regimens are the preferred first line therapy for the following reasons:

- It has a relatively low toxicity profile
- Once-daily administration: Currently TDF is co-formulated with 3TC. A single combination pill of EFV, TDF and 3TC is available. This combination allows for the possibility of a 1-pill/day regimen, with the obvious potential for improved adherence.
- Can be used in pregnancy, and concurrently with TB medication
- TDF is the preferred first-line regimen because it reserves the thymidine analogues (AZT) and PIs for 2nd line therapy.
- It is associated with renal toxicity in a small percentage. (Up to 3% is small but not insignificant. The good news is that it is reversible once it is detected and the drug is stopped). Ideally baseline urea/creatinine levels and monitoring of urine for proteinuria on 6 monthly basis is necessary. However, this has a cost implication, so we recommend that patients should be closely clinically monitored and renal function tests done in those who are symptomatic.

Zidovudine (AZT) is associated with anemia (3-5%), which may lead to blood transfusions and rarely to death. This is one of the reasons why TDF is now the preferred 1st line regimen. This anemia is most commonly seen during the initial 4 months of therapy.

Stavudine (d4T) use has been associated with progressive disabling peripheral neuropathy especially among patients with advanced HIV disease and those taking concomitant anti-TB drugs. The primary pathology of stavudine related complications are due to mitochondrial toxicity with early apoptosis that may manifest as stigmatizing facial lipoatrophy, limb fat loss, enlargement of breast and abdominal fat, and lactic acidosis (potentially fatal). d4T has been phased out of use for all patients.

3.3.3 NNRTIs

The use of an NNRTI as the third drug is preferable to the use of a PI, since an NNRTI-containing first line regimen:

- Is less expensive
- Preserves the option to use a PI at a later date
- Appears to be safe during pregnancy (NVP)
 - EFV is not recommended during the 1st trimester but is safe after 14 weeks of gestation.
- Allows treatment of TB co-infected patients who are on rifampicin (EFV, not NVP)

The recommended NVP dosing regimen starts with a lower lead-in dose of 200mg once a day for 2 weeks, followed by 200 mg twice a day thereafter. This schedule is less frequently associated with a rash. Starting a fixed-dose regimen of combination NNRTI-NRTI treatment without the "lead in" dose of NVP may therefore be associated with increased toxicity. In addition, NVP has a much longer half-life than the other drugs in the combination. When such a fixed combination is stopped, it is recommended that the other two NRTI drugs are continued for at least seven days to avoid the development of NVP resistance.

There is concern that the use of NVP monotherapy in the PMTCT programs may promote resistance to the drug should these mothers initiate ART. Recent studies indicate that this is less likely if the mothers initiate ART at least six months after the PMTCT program. This risk of developing NVP resistance progressively diminishes after six months and disappears by 24 months after exposure.

Either NVP *or* EFV should be chosen as the primary NNRTI but both should be available for mutual substitution for toxicity and for issues related to drug choice in pregnancy and TB. **See 3.5**

3.3.4 Protease Inhibitor (PI)-based Regimens

PI-based regimens are an accepted standard of care for initial regimens. However, their high cost relative to NNRTI-based regimens makes their use too costly. In general PIs should be reserved for second-line therapy. PIs as initial therapy with a standard dual NRTI backbone are an option for the treatment of pregnant women with CD4 counts of 250–350 cells/mm³, or for individuals for whom NNRTI drugs are severely toxic and triple NRTI therapy is not available or deemed inappropriate. ATV/r signature mutation I50L does not cause resistance to other PIs. Resistance to LPV/r also confers resistance to ATV/r through a number of accumulated mutations. However these mutations do not easily develop so the majority of patients currently on a LPV/r based regimen may be proactively switched to ATV/r.

3.3.5 Triple NRTI Regimens

Triple NRTI is a combination of three NRTIs. This used to be an option where there were complication to both NNRTIs and PIs were not easy accessible. However, because of the dangers triple NRTIs pose in terms of high virological rates we recommend that triple NRTIs should not be used except in viral hepatitis (HBV and HCV).

Table 3.3: Recommended First and Second Line Regimens in Adults

| 1 st Line Regimens | 2 nd Line Regimens | Comments |
|--|--|--|
| <i>Preferred</i> | | |
| TDF/3TC + NVP Or TDF/3TC + EFV | AZT + 3TC* +ATV/r^ Or AZT+3TC* + LPV/r | Use of TDF, 3TC and EFV has low toxicity, once daily administration, and effective against hepatitis B. This combination is the preferred first-line. |
| <i>Alternative</i> | | |
| AZT/3TC + NVP Or AZT/3TC + EFV | TDF + 3TC* + ATV/r^ Or TDF+ 3TC* + LPV/r | - Relatively inexpensive 1 st line regimen. -AZT may cause anemia -If patient is anemic start with TDF |
| <i>For women who started with PI based regimens as their first line</i> | | |
| TDF/3TC/ATV/r | AZT/3TC/LPV/r | LPV/r can be used by ATV/r experienced individuals |
| AZT/3TC/ATV/r | TDF/3TC/LPV/r | |
| <i>For patients with poor renal function and anemia</i> | | |

| | | |
|----------------------|--|---|
| ABC/3TC + NVP or EFV | Correct anemia and put on AZT/3TC* + ATV/r^ or LPV/r | This class of patients has limited options and if toxicities are not corrected they are candidates for 3 rd line or salvage ART regimens |
|----------------------|--|---|

**3TC can be considered to be maintained in 2nd line regimens to reduce the viral fitness*

^ All new 2nd line patients should be placed on ATV/r if available

The recommendation is to procure and stock a higher proportion of the preferred NRTI and NNRTI and a smaller amount of the alternative drug or regimen that will be used in case of toxicity and/or contraindication of the first choice. For example, TDF can be a substitute for AZT in patients with severe AZT-induced anemia, and EFV can be a substitute for NVP in cases of NVP-associated hepatotoxicity.

First line regimens are recommended at national level to cover the majority of patients. Some patients may be considered for different combinations for various reasons. For example:

- NVP is preferred in women of childbearing for whom effective contraception cannot be assured
- NVP should be avoided among patients requiring simultaneous ARV treatment and TB therapy containing Rifampicin
- NVP should be avoided in women with a pre-nevirapine CD4+ T cell counts >250 cells/mm³ because of the increased risk of symptomatic hepatotoxicity and Steven Johnson syndrome
- EFV should be avoided in persons with a history of severe psychiatric illness.
- PIs may be considered for first line therapy in patients with Kaposi's sarcoma and those who severe skin reactions or hepatic failure with EFV

3.3.6 Other remarks:

- The use of Abacavir (ABC) in adults is currently limited because of potency particularly in patients presenting with a high viral load $\geq 100,000$ copies.
- The use of Didanosine (DDI) in adults is no longer recommended for efficacy and mostly toxicity (neuropathy)
- Certain dual NRTI backbone combinations should not be used within HAART. These are: d4T + AZT (proven antagonism), d4T + ddI (overlapping toxicities) and 3TC + FTC (interchangeable, but should not be used together). Fortunately d4T has been phased out.
- TDF+ddI, TDF+ABC, or ABC+DDI are not durable ART options
- LPV/r and ATV/r are reserved for 2nd line treatment
- ATV/r and LPV/r are the two preferred PIs. The two are similar with respect to tolerability and potency. ATV/r has the advantage of being dosed once daily while LPV/r has the advantage of a co-formulated ritonavir and is more readily available at the moment.

Recommended dosages and other drugs for adults are listed in **Appendix 5**. Relevant drug toxicities and major drug interactions for the recommended agents and other drugs are listed in **Appendices 3 and 4**.

3.4 Recommended second line regimens

It is recommended that the entire regimen be changed if treatment failure occurs. The choice for 2nd line regimens depends on the first line choice. (See **Table 3.3**). The PI class is reserved for second-line treatments, preferably supported by one new NRTI and maintain 3TC.

For economic reasons and for the simplicity of administration, ATV/r and LPV/r are recommended as the PI for second line regimen for treatment failure. ATV and LPV combined with low dose RTV are potent and well tolerated. On the negative side, these drugs are incompatible with rifampicin. Compared to LPV/r, ATV/r is now cheaper (having been made available as a generic), has a lower pill burden and can be taken as once a day and is therefore recommended as the preferred 2nd line PI. We recommend continuing 3TC in the setting of treatment failure because maintaining 3TC can improve viral susceptibility to AZT or TDF.

Before changing to 2nd line, patients should be re-evaluated. A lipid profile and bilirubin levels should be done for monitoring hyperlipidemia and hyperbiliruninaemia respectively. In addition the patient should be further counseled to point out the following:

- The patient needs to know why they failed,
- That it may not have been their fault,
- To re-emphasize that the drugs can still work,
- To talk them through the new regimen especially as PIs have gastro-intestinal side effects
- To emphasize the need to monitor for lipidemia and development of diabetes mellitus.

3.4.1 What to do after 2nd Line Treatment Failure

Salvage regimens are not readily available on the public free ART program so no salvage therapy regimens have been recommended. Decisions to continue a failing 2nd line regimen should be made on a case by case basis and in consultation with experts in ART. Because a failing ARV regimen that contains NRTIs and a PI may still have a beneficial effect on the immune status of the patient, there is reason to continue with it if no other treatment option is available and no resistance profile to guide the clinician on the next regimen. This is particularly true if there is evidence of good clinical response. Stopping may be considered if a patient fails to tolerate available 2nd line regimen or has fulminant life threatening and incurable OIs. It is important to carefully evaluate the benefits, adverse effects and cost of continuing ART. Laboratory monitoring needs, pill burden, toxicity/drug interactions and drug costs generally increase progressively when patient moves from 2nd line to salvage regimens.

However, when the patient can afford the costs of salvage therapy, there are options of new generation drugs on the market that are being used for the highly treatment-experienced patient. These agents include PIs like darunavir, NNRTIs like etravirine, rilprvine, Integrase inhibitors like raltegravir and chemokine receptor (CCR5) blockers like maraviroc. Prior to the use of these agents every effort should be made to have HIV drug resistance profile tests done. Although very costly, these procedures form the standard of care in resource rich settings which may be affordable to a selected few patients in our setting. In this case, the patient should be referred to a specialized ART clinic where the doctors are familiar with salvage therapy.

3.5 ART recommendation for those with tuberculosis and HIV co-infections

Where there is HIV co-infection with other conditions, a number of challenges arise when treating the co-infected patient. These challenges include drug interactions, overlapping toxicities, pill burden. They have been dealt with in more details in **chapter 2**.

It is recommended that people co-infected with TB/HIV initiate on ART after stabilizing on their TB therapy which ranges from 2-8 weeks and continue on ART indefinitely irrespective of their initial CD4 cell count.

For those with CD4 $>350/\text{mm}^3$ they should start ART after the intensive TB treatment phase, which usually lasts for 2 months.

In cases where a person needs to initiate TB and HIV treatment concurrently, the recommended first line treatment options are TDF/3TC + EFV or the alternative AZT/3TC + EFV. For HIV and TB co-infected pregnant women, **see table 3.4**.

In the exceptional circumstances where CD4 cell counts cannot be obtained, ART should be initiated 2 - 8 weeks after the start of TB therapy when the patient has stabilized on TB treatment.

In severely immunosuppressed patients (CD4 less than 50) co-infected with TB, ART should be started immediately (within two weeks of determining eligibility).

Table 3.4: Antiretroviral Therapy for Individuals with Tuberculosis Co-Infection

| Situation | Recommendations |
|---|--|
| <p>Very sick with Pulmonary TB or extra pulmonary TB or WHO stage IV</p> <ul style="list-style-type: none"> Irrespective of CD4 cell count | <p>Start TB therapy and when stable (usually within 2 to 8 weeks) ADD one of these regimens:</p> <ul style="list-style-type: none"> TDF/3TC/EFV (alternative AZT/3TC/EFV)– not to be used in first trimester of pregnancy or in women of childbearing potential without assured contraception TDF/3TC/NVP, AZT/3TC/NVP, - <i>used only if in rifampicin-free continuation phase</i> |
| <p>Pulmonary TB</p> <ul style="list-style-type: none"> Clinically stable CD4 >350/mm³ | <p>Start TB therapy for 2 months THEN start one of these regimens:</p> <ul style="list-style-type: none"> TDF/3TC/EFV or NVP AZT/3TC/EFV or NVP |
| <p>Develops TB when already on ART</p> <ul style="list-style-type: none"> Consider IRIS Consider ART failure | <p>Add TB drugs and continue with ART but:</p> <p>Change NVP for EFV (except in first trimester) – or Use AZT+3TC+ABC Evaluate/assess for ART failure (adherence,</p> |
| <p>Tuberculosis and ART failure</p> <ul style="list-style-type: none"> Falling CD4 count Development of other OIs | <p>Continue with failing 1st regime until end of Rifampicin – then:</p> <ul style="list-style-type: none"> Change to 2nd line with PI |
| <p>HIV pregnant women with TB</p> | <p>Treat TB first and when stable introduce ART regimens:</p> <ul style="list-style-type: none"> CD4 ≤ 350: TDF/3TC (alternative AZT/3TC) + NVP (or EFV after 1st trimester) CD4 ≥ 350: TDF/3TC (alternative AZT/3TC) + EFV after 1st trimester |

3.5.1 Second line ART for patients with TB

There are significant drug interactions with PIs and rifampicin. Rifampicin lowers the blood levels of PIs and vice versa resulting in suboptimal effectiveness. The use of any current PIs with Rifampicin should be avoided. When available, Rifabutin may be used in place of Rifampicin, although it is more costly.

3.6 Recommended ART in People co infected with Viral Hepatitis and HIV

Antiviral agents with activity against both HBV and HIV e.g. TDF and 3TC or FTC are recommended as first line agents in patients co-infected with HBV. In situations where both

HIV and HBV require treatment, the ART regimens must contain TDF and 3TC or FTC. It is preferable to use TDF and 3TC together as both drugs have anti-HIV and anti-HBV activity and the use of TDF or 3TC as the only anti-HBV drug can result in more rapid development of resistance. EFV is the preferred NNRTI option as the use of Nevirapine is not recommended for those with marked elevations of ALT (grade 4 or higher). When these individuals fail 1st line, they should in as much as possible continue with 3TC or FTC+TDF in their second line regimen unless they have access to another anti-HBV drug. For example, a patient previously on TDF/3TC/EFV can continue on TDF/3TC because this is still active against HBV, while adding AZT and ATV/r or LPV/r. The new regimen becomes (TDF/3TC/AZT/ATV/r). Therefore the patient will be on four drugs. For patients failing on AZT/3TC/EFV switch to TDF/3TC (ATV/r or LPV/r)

Rapid increases in Hepatitis-B viremia may occur while on ART as part of IRIS and present with symptoms of acute hepatitis (fatigue, abdominal pain and jaundice). These reactions tend to occur in the first few months of ART and may be difficult to distinguish from ART induced hepatotoxicity. Drugs active against HBV should be continued during a suspected flare and if the patient is on 3TC monotherapy for the HBV treatment, TDF should be added. If it is not possible to distinguish a serious HBV flare from ART toxicity, all ARV drugs should be withheld until the clinical condition improves. HBV flares may also occur when anti-HBV active drugs are stopped and it is therefore recommended that in patients with chronic HBV, 3TC should be continued as part of second line ART following initial ART failure even if it has been used in first line.

For HCV infection, the optimal treatment is pegylated interferon alpha and ribavirin (RBV) but it is very expensive and not readily available. The initiation of ART in HIV/HCV co-infected patients should follow the same principles and recommendations as for the initiation of ART in HIV-monoinfected patients. However, the patients should be followed up more closely because of the major risk of drug-related hepatotoxicity. Specific interactions of some ARVs and anti-HCV drugs include

- Ribavirin and DDI – pancreatitis/lactic acidosis (do not give concomitantly)
- Ribavirin and AZT – anemia (monitor closely)
- Interferon and EFV – severe depression (monitor closely)

Concurrent treatment of both HIV and HCV may be complicated by pill burden, drug toxicities and drug interactions. In patients with high CD4 cell counts (>350) it may be preferable to treat HCV before HIV, while in those who need ART it may be preferable to initiate ART and delay HCV therapy in order to obtain better anti-HCV response rates after immune recovery. EFV is the NNRTI of choice in patients with HIV/HCV confection or a triple NRTI regimen maybe used. NVP should be used with care and requires close monitoring. Patients with abnormal liver enzymes at baseline before ART initiation should be screened for HBV or HCV by serology wherever possible or be referred to where this can be done. EFV should be introduced after withdrawal of NVP following hepatotoxicity.

4.0 Guidelines on ART for Adolescents

4.1 Introduction:

With the help of antiretroviral therapy, increasing numbers of children with vertical transmission of HIV are growing to adolescence and adulthood. HIV-infected adolescents include long-term survivors of mother-to-child transmission, those infected through sexual abuse occurring in childhood and those who contracted the disease during adolescence through sexual relationships. This is a heterogeneous group including those who are in school, out of school, heads of household, orphans and adolescents under the care of adult guardians. Some know their HIV sero-status while others are not yet disclosed to. Some of them are in long term relationships. To protect this patient population, health care providers need to commit time and effort to making adolescent services visible, flexible, affordable, confidential, culturally appropriate and universally available. In this era of HAART, programmes need to look beyond initiating patients on antiretroviral therapy, but they also need to look at issues regarding adherence to long-term therapy while preventing early treatment failure, and secondary transmission to uninfected partners.

Initiating and switching ART for adolescents will follow the adult recommendations.

4.2 Definitions:

An adolescent is that person aged between 10-19 years (WHO definition), or even up to 21 years. A young person is that aged between 10-24 years. There are three stages of adolescent development: Early adolescence 10-13 years; middle adolescence 14-16 years; and late adolescence 17-21 years. Adolescents are a unique group of people with special needs. Adolescence is a critical period which is characterized by rapid physical, emotional, cognitive and social changes. (See Table 4.1)

Table 4.1 Stages of Adolescent development:

| | <i>Early Adolescence (10-13)</i> | <i>Mid Adolescence (14-16)</i> | <i>Late Adolescence (17-21+)</i> |
|---------------|--|--|---|
| Physical | Sex drive begins. Rapid physical change | Maturation complete. Sex drive surges | Maturation complete |
| Social | Peer pressure. Separation from parents begins. | Peer group sets standards. Peak conflict with parents. | Close friendships. Intimacy. Beginning of rapprochement with parents |
| Psychological | Concrete thinking. Poor future orientation. Narcissism Body image | Focus on identity. Omnipotence Questioning mores. Introspection | Focus on role in society. Idealism. Future oriented. Refinement of values |
| Sexual | Interest usually exceeds activity | Increasing sexual behavior experimentation | Orientation consolidates |

4.3 Special issues of HIV infected adolescents:

These include linkage to care, adherence, dealing with disclosure, discrimination and isolation; high risk behaviors such as early and unwanted pregnancy; and drug and alcohol abuse. At the same time, the two groups of adolescents living with HIV, those infected perinatally and those who acquire HIV during adolescence, often have different, if overlapping, needs and challenges. Some of these needs and challenges include transitioning of HIV care, and specific psychosocial needs.

4.3.1 Linkage to Care and Youth Friendly Services:

The care of adolescents and young people with HIV needs to be driven by low cost and innovative approaches that contribute to attracting this group of patients into care, and retaining them once they have made contact with the health services.

High quality of care must be assured, which includes:

- Non-judgmental attitudes by service providers regardless of their own beliefs and values;
- Sensitization to issues of stigma, fear and discrimination;
- There is need to redress the power imbalance that exists between health care providers and patients.

While providing sexual and reproductive health and HIV services to the adolescents you need to have the skills to respond to HIV related stigma and discrimination to encourage testing and disclosure, and to the desire of young people living with HIV to have children.

- Adolescents prefer to be seen by the same providers for reasons of trust and confidentiality, both of which are essential for the provision of comprehensive care.
- They also prefer health care settings that are oriented to their age group and providers who are attuned to their needs. The state of the art for adolescent care is a ‘one-stop shop’, multidisciplinary model that integrates primary care with HIV, mental health, prevention, and case management services.

It is possible to create a provider team that understands adolescents, and wants to work with them. Availability of flexible appointments that do not conflict with school or work, attention to payment barriers, and walk-in opportunities for youth (who may not plan ahead) can facilitate adolescents’ participation in health services.

4.3.1.2 Legal Issues:

Health workers need to understand that young people have their right to health care, including testing for HIV. Health workers also need to understand the law of the land regarding age of consent, and age of consensual marriage, and be prepared to work with the social service to support the young people.

4.3.1.3 Treatment adherence:

HIV medication regimens require strict adherence to prevent the emergence of resistant HIV. When considering prescribing options for adolescents, health workers should provide the simplest and most efficacious regimens.

4.3.1.4 Psychosocial Issues:

Understanding adolescent development is crucial for viewing the adolescent as a health care client and participant in treatment. In addition to the physical changes of puberty, adolescence consists of a series of cognitive, emotional and psychosocial developmental phases. The five major psychosocial issues include:

4.3.2 Being informed of HIV status

In helping youth cope with their HIV infection, it is necessary to simultaneously instill hope and provide support for the challenging years ahead. Many adolescents are still concrete thinkers. They have difficulty comprehending the concepts of disease latency and asymptomatic infection. Young people without apparent symptoms must learn to strike a balance between unhealthy denial of their condition and morbid preoccupation.

Individual counseling should be offered to those youth with specific issues that are identified by the health caregivers. Age specific psychosocial support networks should be formed to help in the reduction in stigma, coping with the infection, and having hope for the future.

4.3.3 Disclosure and partner notification

As children with perinatally acquired infection grow into adolescents, it is of paramount importance that health providers begin the process of disclosing their HIV status to them if they have not already been informed of their diagnosis. Disclosure in this sense is essential if the adolescent is to become a partner in the therapeutic alliance. It helps to bring the adolescent to terms with their disease condition, promote adherence, increase risk reduction for reinfection, and decrease treatment failure. Even for adolescents who have acquired HIV through sexual and other means, many times they may not initially be informed of their status, and the disclosure process takes long. In both situations, it is preferable that someone who is emotionally close to the adolescent makes the first move to disclose, and this should be done with the assistance of a qualified counselor.

A major initial hurdle confronting HIV-positive adolescents is deciding when and to whom they should disclose their status. Although the involvement of a supportive adult (preferably a parent) is ideal, many youth fear losing the love of their parent or hurting them.

Disclosure becomes a particularly salient issue with advancing disease because it is difficult to conceal medications from the people with whom one lives. Disclosure to sexual partners is ethically compelling but complicated.

- The aim should be to ensure that HIV-positive adolescents inform any sexual partners and always engage in safe sex (i.e. consistent, correct condom use).
- Disclosure and partner notification should therefore be well planned.
- Health workers are encouraged to help the adolescent to 'play out the scenario' and offer to participate in the disclosure process.

A new compelling phenomenon among HIV-infected adolescents is that there is a growing desire to have children of their own, in order to 'propagate and pass on their genes' and often they will not disclose to their partners for fear of rejection. When adolescents become pregnant they must be facilitated to join the PMTCT program.(read page.)

4.3.4 Mental illness and substance abuse:

Mental illness and substance abuse are frequently seen co-morbidities for HIV-positive adolescents, and need to be identified early because failure to identify and address these issues will hobble a patient's ability to cope with his or her disease. Furthermore, adherence to antiretroviral treatment is likely to be problematic. Mental health practitioners should ideally be part of the clinical team and should intervene as needed with such therapies as medication and individual and peer group support. In any case every effort should be made to identify and refer patients who need specialized care.

4.3.5 Age transitions

Health workers should support the transition of the HIV infected patient from pediatric to adolescent services, and finally to adult care programs. Emerging adults require programs that address their specific needs. They face the concurrent challenges of health care maintenance,

medication adherence, and illness within the context of maturing sexuality and establishing an independent life.

4.3.6 HIV counseling and testing:

HIV-testing programs must be accessible to young people to have any chance of success. While adolescents engaging in high-risk behaviors often do not believe that they are at risk, it is a myth that adolescents are likely to refuse HIV testing or that they do not want providers to ask personal questions. In fact, many young people prefer clinicians to initiate such discussions. In addition to primary care sites, venues that should consider offering routine HIV counseling and testing include mobile units, school-based health clinics, drug treatment facilities, and family planning programs. Services need to be youth-friendly, flexible, free, or low cost, and help overcome barriers such as transportation. Young people need special help with the implications of partner disclosure.

Health providers should establish the momentum for youth-sensitive follow-up, including treatment and counseling:

- To provide basic HIV information,
- Assess risk and obtaining consent during the pre-test counseling visit,
- Promote preventive healthy behaviors, assess substance use and discuss family planning issues.

The counseling session is an invaluable opportunity to educate teenagers about condom use and safer sex, whether or not testing occurs. Effective HIV counseling for adolescents should be culturally sensitive and tailored to the developmental needs of adolescents. Youth considered potentially self-destructive or impulsive require careful assessment before testing.

Counseling adolescents poses particular challenges, for example special sensitivity is required to address their level of sexual and emotional development. Even ensuring that adolescents return for a follow-up visit, when they receive test results, calls for special effort, such as telephone/sms reminders, or provision of transport reimbursement.

Beyond providing basic information, health facilities should use interventions that increase self-esteem, individual competencies and psycho-social skills. They should also incorporate a peer-support model, and take advantage of adolescents' inherent abilities to diffuse the information and skills they acquire into the community at-large.

4.3.7 Prevention and outreach:

For HIV-infected adolescents and youth, the term '*prevention*' must be looked at from the broad aspect of preventing early and unwanted pregnancies; preventing sexually transmitted infections; and preventing the development of a resistant viral strain while on treatment. In addition, 'positive prevention' should be encouraged to ensure that the adolescent does not become a driver of the HIV epidemic. Other basic preventive measures should also be part of the holistic care package, including provision of clean water and insecticide-treated mosquito nets. A comprehensive prevention strategy requires multiple levels that target young people's various

psychosocial and health care needs. The range of prevention can be briefly summarized as “ABC”: abstain, be faithful, and use condoms. Although each of these steps is important, none can stand alone or is perfect for all adolescents all of the time. We recommend the continued use of the abstinence and behavioral change for the youth strategy (ABY) for the adolescents and young people.

Community outreach is critical for programs focusing on HIV in young people. It is essential for raising awareness regarding HIV care and prevention services among at-risk youth, and their providers. Given that most adolescents living with HIV are unaware of their infection, linkages with agencies serving high-risk youth are crucial for the success of facility based services. These connections are not by themselves sufficient to identify HIV-positive youth and bring them into care, however. Social marketing campaigns that span the continuum from HIV prevention through testing and care can make a major contribution. In addition, using adolescents and youth as peer educators and distributors for the condoms makes it more acceptable for their peers.

5.0 Guidelines on ART for infants and children

5.1 Diagnosing HIV infection in infants and children

5.1.1 Introduction to early infant diagnosis

The vast majority (about 90%) of infants and children with HIV acquire the infection through mother-to-child transmission. Evidence has shown that HIV infection follows a more aggressive course among infants and children than among adults, with 30% dying by age 1 year, and 50% by age 2 years without access to life-saving drugs, including antiretroviral therapy and preventive interventions such as cotrimoxazole prophylaxis.¹ In addition, new evidence highlights early HIV diagnosis and antiretroviral treatment as critical for infants and indicates that a significant number of lives can be saved by initiating antiretroviral treatment for HIV-positive infants immediately after diagnosis within the first 12 weeks of life. The Children with HIV Early Antiretroviral Therapy (CHER) study from South Africa demonstrates a 76 % reduction in mortality at one year of age when treatment was initiated within this time period.² The high mortality rates of infected infants and significant number of lives saved by early treatment underscore the importance of early diagnosis as it catalyses access to life saving pediatric care and treatment services for vulnerable HIV exposed infants.

5.1.2 The determination of HIV exposure status in infants and children.

All infants should have their HIV exposure status established at their first contact with the health system, at or around birth, but always before 6 weeks of age. This may be ascertained in one of the following ways;

1. Preferably, by checking the Child health Card of the baby for the PMTCT codes of the mother if they were transferred to the card at birth.
2. If there is no indication in the Child health Card, determine whether the HIV status of the mother was assessed in this pregnancy by checking the Antenatal Care card for record of Mothers PMTCT code, or maternal or caregiver questioning.
3. If maternal HIV testing has not been done or the HIV status of the mother remains unclear for the duration of the pregnancy, then perform an HIV serological test on the mother after obtaining informed consent.
4. If the mother is unavailable or does not consent to maternal HIV testing, then perform HIV serological testing of the infant to determine HIV exposure status. Maternal or guardian consent is required for such testing.

Once the exposure status has been determined, then the appropriate HIV test can be done to diagnose HIV depending on the age of the infant.

5.1.3 Laboratory diagnosis of HIV infection in infants and children under 18 months of age

¹ Newell, Marie-Louise, et al., 'Mortality of Infected and Uninfected Infants Born to HIV-infected Mothers in Africa: A pooled analysis', *The Lancet*, vol. 364, no. 9441, 2–8 October 2004, pp. 1236–1243.

² Violari, A., et al., 'Children with HIV Early Antiretroviral Therapy (CHER) Study', presentation at the 4th IAS Conference on HIV Pathogenesis, Treatment and Prevention, Sydney, 22–25 July 2007.

5.1.3.1 Virologic testing

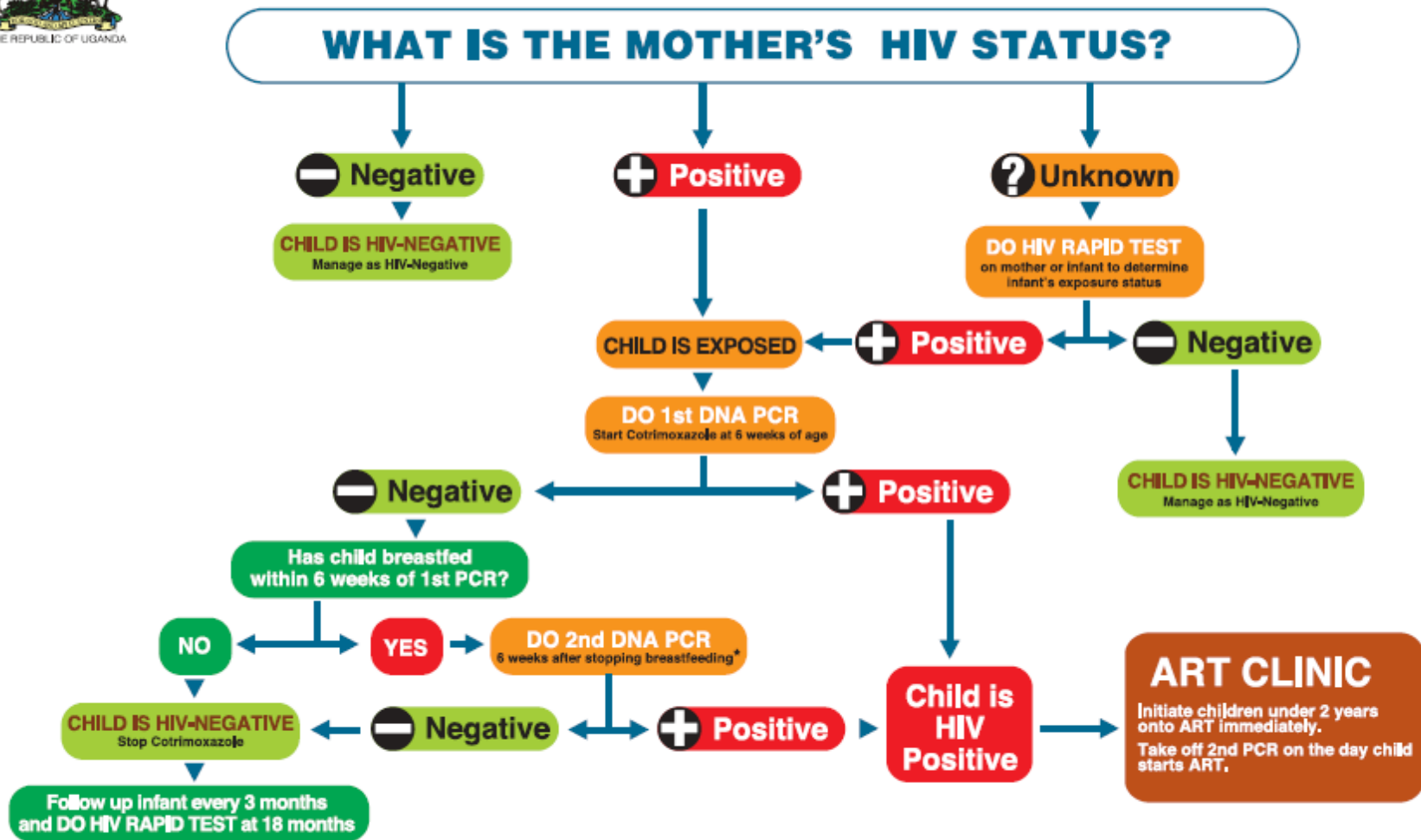
DNA PCR is the recommended test for confirming HIV status in infants and children less than 18 months of age.

1. It should be done at 6 weeks of age or the earliest opportunity thereafter.
2. If the DNA PCR test is positive, the infant should be referred to the ART clinic and started on ART. However a repeat test should be taken on the day a child is started on ART
3. If the test is negative and the child is breastfeeding or has breastfed in the 6 weeks before testing, the test is not definitive and there is need to repeat the test 6 weeks after cessation of breastfeeding.

See **testing algorithm** for details of HIV testing in Children less than 18 months.



TESTING ALGORITHM FOR HIV EXPOSED INFANTS



*If infant with negative 1st PCR is symptomatic, take off a 2nd PCR immediately even when still breastfeeding.
If the 2nd PCR is negative, still take a 3rd PCR 6 weeks after stopping breastfeeding.

5.1.3.2 The role of antibody testing in infants and children less than 18 months of age

Diagnostic testing for HIV-1 in infants younger than 18 months differs from that for older children, adolescents, and adults because of the presence of maternal antibodies. During pregnancy maternal HIV antibodies are transferred passively to the fetus and can persist for as long as 18 months. HIV antibody test like Rapids tests are positive in all newborns of HIV-infected mothers, including infants who are not infected. Even if an infant becomes infected and begins making his or her own antibodies, antibody tests cannot differentiate between antibodies from the mother and those from the infant.

Interpretation of antibody test results in infants and children less than 18 months of age

Negative antibody test means:

- The infant or child is not exposed to HIV.

HIV positive antibody test means;

- The infant or child is HIV exposed but may or may not be infected. It does not confirm HIV infection in the infant.
- Mother is or was HIV infected

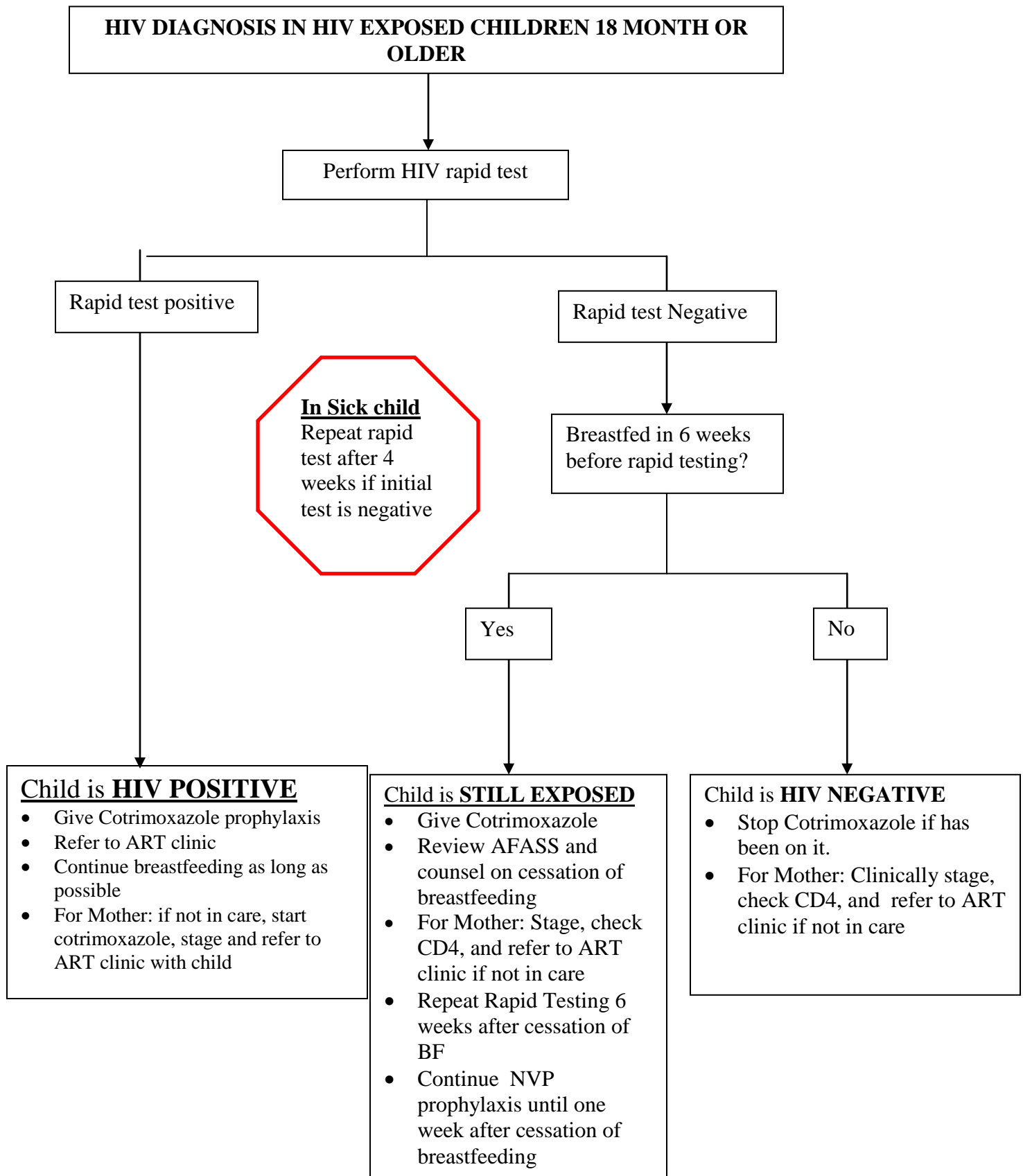
It's therefore recommended that confirming the HIV status of children less than 18 month should be done using virologic test like DNA PCR.

5.1.4 Laboratory diagnosis of HIV infection in children 18 months of age and older.

By 18 months of age, maternal antibodies that were transferred to the child during pregnancy would have completely disappeared. The presence of HIV antibodies in these children will therefore mean they are infected and are producing antibodies of their own.

Antibody tests should therefore be used for confirmation of HIV infection in children above 18 months of age. **(See Figure 5.1)**

Figure 5.1: Algorithm 1.



5.1.5 Presumptive diagnosis of HIV infection in infants and children under 18 months of age

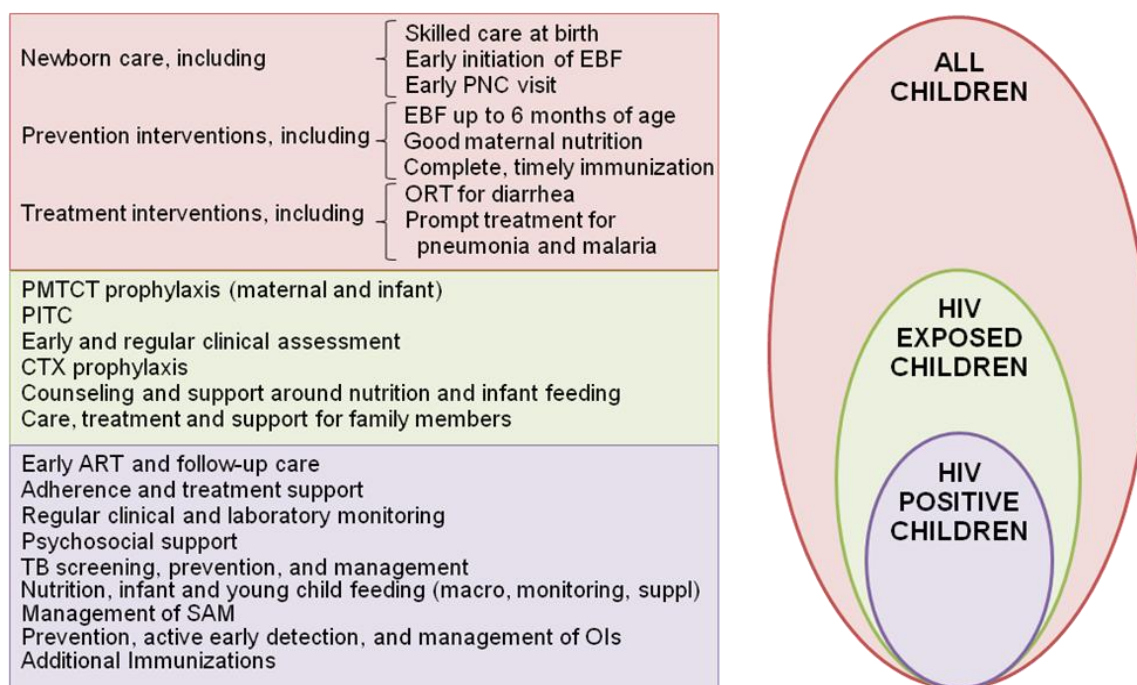
In facilities where there is no access to DNA PCR, a presumptive diagnosis of severe HIV disease can be made in infants and children who are less than 18 months of age with a positive serological HIV test (in either the mother or child), and who have specific symptoms suggestive of HIV infection (see section 5.4). An infant or child who meets these criteria has severe HIV disease and needs immediate ART. HIV serological testing should be repeated at 18 months of age to confirm HIV infection in the child.

5.2 Care and follow up of HIV exposed and infected infants and children

In Uganda, Malaria, Pneumonia, diarrhoea, and HIV account for approximately two-thirds of under-5 mortality, with malnutrition being an underlying cause of approximately 60% of all causes for child deaths. There exists strong evidence that a range of interventions provided to mothers and children, irrespective of HIV status, can effectively reduce child mortality by at least 60%. Therefore, at a minimum, HIV exposed and HIV-infected infants and children, who are immuno compromised and more susceptible to illness, should have access to these life-saving interventions as well.

To ensure that HIV-exposed and infected children have the highest chances of survival and optimal health outcomes, the Government of Uganda with its partners, as a critical step, have defined their essential package of child health services to include HIV-related services for prevention, testing, care, and treatment.

Figure 5.2: Care and follow-up of exposed Infant



5.2.1 Care and follow up of HIV exposed infants and children

HIV exposed infants should be regularly followed up. The infants should be followed up monthly until 6 months of age and there after 3 monthly until 18 months. These visits are synchronized with the immunization schedules for the infant. During every visit, specific care indicators must be monitored. These include;

5.2.1.1 Immunization

All HIV exposed infants should be immunized according to the national immunization schedule. The immunization status must be assessed at every visit and vaccines given according to schedule. Missed vaccines should be given before the child leaves the facility. Infants with symptomatic HIV should not be given live vaccines like yellow fever and BCG. However in Uganda BCG is given at birth and by this time most of the babies are either uninfected or asymptomatic, so BCG should be given. See table below for the national immunization schedule.

Table 5.1: Immunization schedules

| Age | Birth | 6 weeks | 10 weeks | 14 weeks | 6 months | 9 months | 12 month | 18 month |
|---------|--------------|---------------------------|---------------------------|---------------------------|----------|---------------------|--------------------|--------------------|
| Vaccine | BCG, OPV0 | DPT Hep Hib 1 OPV 1 | DPT Hep Hib 2 OPV 2 | DPT Hep Hib 3 OPV 3 | Vit A | Measles vaccines | Vit A Deworming | Vit A Deworming |

5.2.1.2 Growth

Anthropometric measures of weight (wt), height (ht), mid upper arm circumference provides an objective way of assessing growth and development of a child. Growth is one of the most sensitive clinical indicators of HIV infection in infants and children. All facilities providing care for infants and children should have wt scales and ht boards and should regularly monitor growth of the children. These measures should be taken at every visit and should be plotted on the child health card to determine whether the wt for age is normal.

5.2.1.3 Development Monitoring

Failure to develop or loss of milestones in infants is one of the signs of severe HIV infection in children. Assessment of developmental milestones and head circumference provides an objective way of assessing development in children. In development milestones assessment, motor and cognitive skills are assessed and this should be done at every clinic visit.

Table 5.2: Warning signs for delayed milestone development.

| Age | Warning Signs |
|----------|--|
| 6 weeks | no eye contact, no smile, Poor suck, Floppy / excessive head lag |
| 6 month | Cannot reach for objects with both hands, Floppy, no response to sound, Poor social response to people |
| 9 months | Unable to sit unsupported , hand preference, fisting, persistence of primitive reflexes |
| 1 year | Unable to bear weight on legs |

| | |
|-----------|---|
| 18 months | Not walking, no pincer grip, no single words with meaning |
|-----------|---|

5.2.1.4 Early Infant Diagnosis (DNA PCR)

DNA PCR should be done at 6 weeks of age or the earliest opportunity thereafter. All infants who are HIV positive should be referred to ART clinic and started on ARV's. If the test result is Negative and the child breastfed in 6 weeks of the test, a 2nd DNA PCR test should be done 6 weeks after cessation of the breastfeeding.

5.2.1.5 Nevirapine (NVP) Prophylaxis.

All HIV exposed infants should be given NVP prophylaxis from birth. Nevirapine Syrup should be refilled at every visit at the facility according to the prescribed visit schedule.

- For infants born to HIV positive mothers who received ARV prophylaxis (PMTCT option A regimen) and are breastfeeding, NVP prophylaxis should be given from birth until 1 week after cessation of breastfeeding.
- For infants born to HIV positive mother who are on ART during the entire period of breastfeeding NVP prophylaxis should be given until 6 weeks of age.
- For infants born to HIV positive mother who are on total replacement feeding, NVP prophylaxis should be given until 6 weeks of age.
- Infants whose mothers did not receive any ARV's for PMTCT should still be given NVP for prophylaxis and duration is guided by whether they are breastfeeding or on replacement feeding.
- HIV exposed infants who are identified later after birth but before 18 months of age, and are breastfeeding, should be started on NVP prophylaxis while a DNA PCR test is taken for diagnosis. If the test result is positive, Stop NVP prophylaxis and the infant should be started on ART with a PI containing regimen. If the test is negative and the child is continuing to breastfed, NVP prophylaxis should be continued until 1 week after cessation of breastfeeding.

Table 5.3: Infant NVP dosing

| Infant NVP dosing | Age | Birth to 6 weeks | | 6weeks-6 months | >6months-9month | >9mo to end of breastfeeding |
|-------------------|------------|------------------|--------|-----------------|-----------------|------------------------------|
| | | 2.0-2.5kg | >2.5kg | | | |
| | Daily Dose | 1ml | 1.5ml | 2ml | 3ml | 4ml |

5.2.1.6 Cotrimoxazole prophylaxis

Cotrimoxazole prophylaxis should be provided for infants from 6 weeks of age. This should be continued until the final HIV status is determined.

- For Infants whose final HIV status is negative, Cotrimoxazole prophylaxis should be stopped.
- For Infants whose final HIV status is positive, cotrimoxazole prophylaxis should be continued.

5.2.1.7 Counseling and support on nutrition and infant feeding

Infant feeding counseling should begin way before birth when the pregnant mother has been identified to be HIV positive. Decision on how she will feed the baby should be made before delivery. The mother should then be supported to implement the feeding option she has chosen.

This support and counseling should be provided from birth and at every visit. (*For more detail see Infant and Young Child feeding counseling – Chapter 7.0*).

5.3 When to start antiretroviral therapy in infants and children.

Although the pathogenesis of HIV and the underlying principles of ART are similar in adults and children, there are specific physiologic, clinical, practical and social issues to consider when treating HIV-infected children with ART. Data on the efficacy of ARVs in adults can generally be extrapolated to children, but issues of pharmacokinetics, formulations and ease of administration require special consideration. The differences in the natural history of HIV infection and the predictive value of surrogate markers between adults and children impact on decisions about starting and switching ART. Suitable formulations for children are not available for some ARVs (particularly the protease inhibitors) but the situation is rapidly improving. Further, as young children metabolize drugs differently from adults, caution should be taken when deciding on dosages for various age groups. Since children are growing and hence weights keep changing, ARV doses need to be adjusted from time to time. When in doubt, the attending clinician should consult or refer the child.

Before a child is started on ART one has to assess the following;

- a) If the child is eligible for ART.
- b) Readiness of parents/caretakers or child (if older) to start ART in the child
- c) Do pre treatment baseline Assessment

5.3.1 Eligibility criteria for initiating art in infants and children

Three parameters guide the decision making process for initiation of ART in infants and children; these are the age, immunological status and WHO clinical Staging. However ART can also be started in children under 18 months of age presumptively (*as will be described in the next section.*) The following criteria is used to initiate infants and children on ART (see table a for summary of initiation criteria)

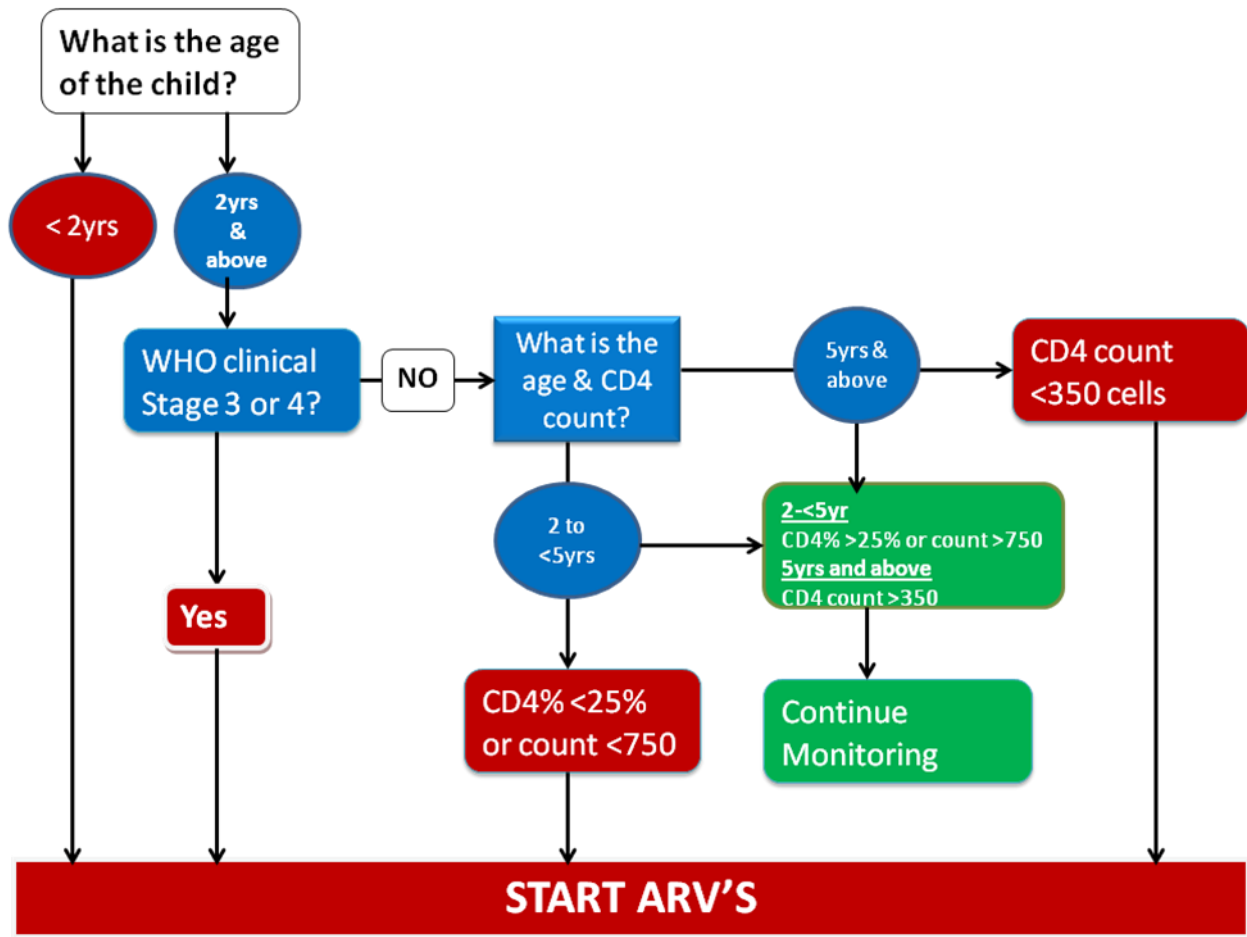
1. All infants and children under 2 years of age should be started on ART irrespective of WHO clinical stage or CD % or count. All children with WHO clinical stage 3 or 4 disease should be started on ART irrespective of the CD 4 count (**see appendix 2 for the WHO clinical staging Chart for guidance on how to stage**)
2. All children aged 2 years and under 5 years should be started on ART if the CD4 % is less than 25% or CD4 count is $<750 \text{ cells/mm}^3$
3. All children above 5 years should be started on ART if CD4 count is less than 350 cells/mm^3
4. All infants under 18 months of age with presumptive diagnosis of HIV

Table 5.4: When to Initiate ART in children.

| When to Initiate ART in Children | | | |
|--|--|-------|-----------|
| <i>All HIV-positive children should be clinically staged and receive a CD4 test when possible to determine the eligibility for ART, except for children under 2 years of age who should initiate ART immediately irrespective of clinical or immunological stage</i> | | | |
| Age | Criteria for Initiating ART | | |
| | WHO Clinical Staging | CD4% | CD4 Count |
| Under 2 years | Initiate ART if child is confirmed HIV Positive, regardless of CD4 or Clinical Staging | | |
| 2 to < 5 years | Initiate ART if Stage III or Stage IV | < 25% | < 750 |
| 5 years & above | | N/A | < 350 |

While at the clinic the clinician can follow the algorithm 2 below to assess children for eligibility and make decision on when to start ART.

Figure 5.3 Algorithm 2: Guide for assessing Children for Eligibility for ART



5.3.1.1 Criteria for starting ART in infants and children less than 18 months with presumptive diagnosis of severe HIV disease

For situations where access to virological testing is not yet available, WHO has developed clinical criteria for making a presumptive diagnosis of severe HIV disease in a child less than 18 months of age, in order to allow initiation of potentially life- saving ART (See **table 5.5**). Any presenting acute illness should be managed first followed by prompt initiation of Antiretroviral therapy.

- Treatment should be closely monitored
- Immediate efforts should be made to establish the HIV diagnosis with a DNA PCR, but at the latest with HIV antibody testing at 18 months of age.
- Decisions on further treatment should be adjusted at that time in accordance with the results.
- ART should be stopped in infants and children only where HIV infection can be confidently ruled out and when such children are no longer exposed to HIV (i.e. through breastfeeding from an HIV-infected mother).

- The initiation of ART on the basis of a presumptive diagnosis of severe HIV disease is not recommended for use by providers who are not appropriately trained in HIV care or the administration of ART.

Table 5.5 Criteria for presumptive clinical diagnosis

| A presumptive diagnosis of severe HIV disease should be made if: | |
|---|--|
| 1. The child is confirmed as being HIV antibody-positive AND | 2a. The infant is symptomatic with two or more of the following: <ul style="list-style-type: none"> • oral thrush • severe pneumonia • severe sepsis OR 2b. A diagnosis of any AIDS-indicator condition(s) as can be made |
| Other findings that support the diagnosis of severe HIV disease in an HIV- sero positive infant include: <ul style="list-style-type: none"> – Recent HIV-related maternal death or advanced HIV disease – Child's %CD4+ <20% | |
| Confirm the diagnosis of HIV infection as soon as possible. | |

- ***AIDS-indicator conditions include some but not all HIV paediatric clinical stage 4 conditions such as Pneumocystis pneumonia, cryptococcal meningitis, severe wasting or severe malnutrition, Kaposi sarcoma, extrapulmonary TB.***

As per the IMCI definition:

- **Oral thrush:** Creamy white-to-yellow soft small plaques on red or normally coloured mucosa which can often be scraped off (pseudomembranous), or red patches on the tongue, palate or lining of mouth, usually painful or tender.
- **Severe pneumonia:** Cough or difficult breathing in a child with chest indrawing, stridor or any of the IMCI general danger signs; i.e. lethargic or unconscious, not able to drink or breastfeed, vomiting, and presence or history of convulsions during current illness; responding to antibiotics.
- **Severe sepsis:** Fever or low body temperature in a young infant with any severe sign, e.g. fast breathing, chest indrawing, bulging fontanelle, lethargy, reduced movement, not feeding or sucking breast milk, convulsions.

It is unclear how often CD4 is lowered in the above conditions in HIV-uninfected children.

5.3.2 Determining readiness to start art

A child may be eligible for ART however the care takers may not be ready to start treatment immediately. The following is done to assess readiness and prepare the parent/caretaker;

5.3.2.1 Adherence Counseling

Adherence counseling must be done before a child is initiated on ART. The care taker must be prepared for the lifelong treatment. For treatment to be successful;

- The Parents/caregivers should understand that they must GIVE the medications

You must therefore understand – “what issues do the parents or caregivers have that might get in the way of them being able to attend to the needs of the child?”

- Parents/caregivers may be dealing with their own illness and medications
- Parents/caregivers may have job obligations
- Who gives the medicine: Relatives, daycare, babysitters
- Is there a treatment supporter (incase primary caretaker is not around who will be responsible.
- Myths/lack of understanding re: HIV
- Sometimes, if one parent has not disclosed to the other, it may be difficult to give ARV's to the child as it may disclose the status. The parent must be supported to disclose to the partner especially if they are living together.
- The Child must **TAKE** the medications
 - We must consider:
 - ✓ Previous medication history
 - ✓ Ability of child to swallow pills
 - ✓ Taste/texture
 - ✓ Volume of liquid needed
 - ✓ Developmental stage of child (special attention must be paid to older children and adolescents) **refer to section on adolescents – Chapter 4.0**
 - ✓ In older children, you must assess if the child has been disclosed to because it will affect their adherence to treatment.
- It must be explained to the parent/caretaker that this is lifelong treatment. He/she must be guided on the administration of the ARV's (How Much, How often and what time to give).
- At least 3 sessions should be given. In the event that the caretaker is on ART and is adhering well to treatment, the process of adherence counseling should not be prolonged since the parent/caretaker may already understand issues of ARV's.
- Adherence appointments should be on weekly basis. Don't give monthly appointment for adherence counseling as this will delay initiation of ART and the child may die before ART is initiated. Unnecessary delays must be avoided.

5.3.2.2 Doing a pre treatment assessment;

Pre treatment assessment provides a baseline for starting to monitor response to treatment as well as helps identify any infections that must be treated before ART is initiated. The following should be done before initiation of ART

- Full clinical assessment for infections & clinical staging. Any infections must be treated.
- Neuro developmental assessment (include Tanner staging)
- Weight, length/height, head circumference
- CD4+ count
- Viral load (where available)

Once all these have been done, the child can then be initiated on ART

5.4 Recommended first-line and second-line regimens for infants and children

5.4.1 Recommended first line regimens for infants and children

Most of the ARVs available for adults can also be used for children though not all of them have suitable formulations. AZT based regimens are the preferred 1st line ARV's for infants and children in combination with Lamivudine and Nevirapine or EFV. When AZT is contraindicated like in patients with anemia, ABC or D4T based regimen can then be used as 1st and 2nd alternative respectively. Use of EFV is not recommended in children under 3 yrs (or 15 kg), 1st trimester of pregnancy or sexually active adolescents. **See table 5.6 for summary of 1st line regimen.**

Dosages are based on either body surface area or weight. As these change with growth, drug doses must be adjusted in order to avoid the risk of under dosing. Weight based dosing for the ARV's has been summarized for ease of use by Health care providers. **(See Appendix 6)**

5.4.2 First line ART regimen for infants and children with nevirapine exposure

Protease Inhibitors (PI) are usually not used in first-line therapy. However, for infants and children <24 months who have been exposed to NVP or other NNRTIs, either directly or via maternal treatment before labor, during delivery or when breastfeeding, the PI LPV/r is now recommended as part of a first-line regimen. **See table 5.6** for summary of 1st line regimen in NNRTI exposed children.

Table 5.6: First and second line ART regimens in infants and children in Uganda

| 1st Line Regimens | 2nd Line Regimens | Comments |
|--|---|--|
| <i>Preferred</i> | | |
| AZT*/3TC/NVP or AZT*/3TC/EFV ¹ | ABC/3TC+LPV/r | *If a child is anemic (Hb <7.5g/dl) do not use AZT. Use ABC based regimen. ¹ Do not use EFV in children under 3 yrs (or 15 kg). |
| <i>1st Alternative</i> | | |
| ABC/3TC/ NVP or ABC/3TC + EFV ¹ | AZT/3TC+LPV/r | |
| <i>2nd Alternative</i> | | |
| D4T/3TC/ NVP or D4T/3TC + EFV ¹ | ABC/3TC+LPV/r | <ul style="list-style-type: none"> Should only be used if preferred or 1st alternative regimens are contraindicated or missing. All children above 5 years on this regimens should be switched to AZT based regimen |
| <i>For children exposed to NVP during PMTCT</i> | | |
| AZT/3TC/LPV/r | ABC/3TC/NVP or ABC/NVP/EFV ¹ | <ul style="list-style-type: none"> Children whose exposure to NVP is more than 24 months ago, the preferred 1st line ARV regimens can be used. |
| ABC/3TC/LPV/r | AZT/3TC/NVP or AZT/NVP/EFV ¹ | |
| D4T/3TC/LPV/r | ABC/3TC/NVP or ABC/NVP/EFV ¹ | |

Table 5.7: NRTI drug combinations to be avoided,

D4T + AZT, TDF + ddI^b both drugs work through common metabolic pathways
TDF + ABC^c -both drugs select for the K65R mutation
d4T + ddI^b -both drugs have overlapping toxicities

Notes:

- Based on data from studies performed in adults.
- Didanosine (ddI) is anadenosine analogue NRTI which is generally reserved for second-line regimens
- Data from 3 clinical trials involving the combination of TDF +ABC +3TC 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-naïve patients. Another report confirms that ABC and TDF select for K65R mutation which reduces susceptibility to both drugs.

5.4.3 Recommended second line ART regimens for infants and children

Second line therapy for children in the event of first-line regimen failure would include a change in nucleoside backbone (e.g., from ZDV/3TC to ABC/3TC) plus a PI (LPV/r), but for infants whose original first line regimen contained a protease inhibitor (LPV/r), an NNRTI (NVP or EFV) should be added to the nucleoside backbone chosen. **See Table.5.6.** Use of PIs other than LPV/r is more problematic in children due to lack of suitable pediatric drug formulations for IDV, SQV and ATV. ATV/r is not currently available as a pediatric formulation but when indicated can be given as separate entities.

5.4.4 Pediatric fixed combinations

Several manufacturers have developed pediatric versions of Fixed Dose Combination tablets (FDCs) which can be dosed more accurately in children than split adult FDCs and which are easier to prescribe and administer than individual single drug formulations and syrups. The tablets are scored, crushable and dispersible in water and may be dosed in children up to 24.9 kg including infants as small as 3kg. The currently available pediatric FDCs include: Triple FDC; AZT/3TC/NVP (60/30/50mg), D4T/3TC/NVP(6/30/50mg) baby, D4T/3TC/NVP (12/60/100mg) junior and duo FDC; AZT/3TC(60/30mg), D4T/3TC(6/30mg) baby,D4T/3TC (12/60mg) junior, ABC/3TC(60/30mg).

The triple FDC have a higher proportion of NVP which makes them better suited for dosing in children who metabolize Nevirapine more rapidly than adults. The pediatric FDCs are easier to prescribe and administer than individual single drug formulations and syrups. FDCs may lead to better adherence and therefore better outcomes with pediatric ART and therefore should be used more. Other advantages of FDC's include;

- Easier to dose, as you do not have to give instructions for multiple drugs
- They have more neutral taste
- Lower pill burden/volumes
- Easier to check adherence
- Easier to transport/store with no need for refrigeration
- Easier to order due to reduced number of formulations
- Better control in administration than oral solutions
- More versatile – can be crushed, dispersed in food or water, or swallowed as a pill

Children already on treatment with pediatric single drug formulations, syrups or adult split FDCs should be switched to pediatric FDC tablets.

See appendix 6 for the list of registered formulations as well as dosing for these formulations.

5.5 Clinical and laboratory monitoring

5.5.1 Introduction

Clinical and laboratory assessments should be performed at baseline (i.e. at entry into HIV care) for children, at initiation of and while on ART.

Clinical parameters should be used in conjunction with laboratory assessment, where available, for monitoring of children with HIV who are on ART. The inability to perform laboratory

monitoring, notably for CD4 or viral load, should not prevent children from receiving ART. This section describes recommendations for clinical and laboratory monitoring of Children on ART.

5.5.2 Baseline Clinical and Laboratory Assessments

The baseline evaluation of HIV-infected infants and children includes clinical assessment and basic laboratory tests, where available. One of the objectives of this initial assessment is evaluation for the presence of active opportunistic infections (OIs). This visit to the clinic also serves as an opportunity to provide counseling and support for children and/or caregivers regarding disclosure of their HIV status to others, nutrition and secondary prevention, as well as for identifying any other specific needs. See BOX 1 below for baseline clinical measures for children.

BOX 5. 1 Baseline clinical assessment for children

Following confirmation of HIV infection status, the baseline clinical assessment for children should include:

- Weight, height, head circumference and other measures of growth
- Clinical staging of HIV disease (Annex ...)
- Developmental status assessment
- Screening for malaria, TB disease, and exposure to TB
- Identification of concomitant medical conditions (e.g. hepatitis B or C infection, TB, other Co infections or OIs, pregnancy in adolescent girls)
- Details of concomitant medications, including co-trimoxazole and Anti TB's
- Nutritional status, including assessment of the quality and quantity of intake
- For those eligible for ART, assessment of the child's and caregiver's preparedness for therapy.

5.5.3 Routine Monitoring for children who are not yet on ART

Because of the rapid rate of disease progression in infants and young children, more frequent clinical and laboratory monitoring is indicated for them than for adults.

Once identified as HIV positive, infants and children should be referred to the nearest ART clinic where they will be followed up and treated.

- Children should be managed in the same clinic with mothers/parents and other family member who are HIV positive. Ensure that the appointment dates of the child are synchronized with that of the Mother/parents. This will enable the family to be reviewed on the same day. It will also reduce the number of visits to the facility as all can come once a week unlike when appointments are separate.
- HIV positive children should visit the HIV clinic every month to receive clinical care and refill their drugs.
- The clinical evaluation of HIV-infected children who are not yet eligible for ART should be performed every one to two months, at a minimum, and should include the same parameters as are used in the baseline evaluation (**BOX 1**) Clinical staging should be done at every visit and CD4 monitoring should be performed every six months; as these parameters are useful in determining whether the child has become eligible for treatment. Percent CD4 is preferred for children less than 5 years of age rather than absolute CD4 count.

5.5.2 Routine Monitoring of Children on ART

Once an infant or child is on ART, the frequency of clinical monitoring will depend on their response to ART. At a minimum, after starting ART, follow-up visits should occur:

- For infants, at weeks 2, 4, 8, and then every 4 weeks for the first year
- For children, at weeks 2, 4, 8, 12, and then every 2 to 3 months once the child has stabilized on therapy.

Routine clinical assessment should include addressing the child's and/or caregiver's understanding of and adherence to therapy, along with their need for additional support. Key signs of an infant's and child's response to ART include:

- Improvement in growth in infants and children who have been failing to grow
- Improvement in neurological symptoms and development in children with encephalopathy or those who have demonstrated delay in the achievement of developmental milestones
- Decreased frequency of infections (bacterial infections, oral thrush and/or other OIs).

See appendix 7 for a description of the routine follow-up visits for infants and children on ART.

5.5.3 Laboratory monitoring (see table 5.8 for summary of lab monitoring parameters)

5.5.3.1 CD4 Monitoring

CD4 monitoring should be done at a minimum of six months after the initiation of ART, and every six months thereafter. More frequent CD4 monitoring is indicated in cases of new or recurrent clinical staging events, growth faltering or neurodevelopment delay.

Where capacity for measuring CD4 is limited, monitoring should be targeted to the assessment of clinical events.

5.5.3.2 Viral Load monitoring

Routine monitoring for viral load is not essential where capacity and resources are constrained; however, viral load should be used whenever possible to confirm suspected clinical or immunological failure.

Table 5.8 Laboratory parameters for monitoring infants and children at baseline, before and during ART

| Lab test for diagnosis and monitoring | Baseline (entry into care) | Initiation of 1 st or 2 nd regimen | Every six months | As required or symptom directed |
|---------------------------------------|----------------------------|--|------------------|---------------------------------|
| HIV diagnostic testing | ✓ | | | |
| Hb | ✓ | ✓ | | ✓ |
| CD4% or Absolute CD4 count | ✓ | ✓ | ✓ | ✓ |

| | | | | |
|-------------------------------|---|--|--|---|
| WBC and differential | | | | ✓ |
| Pregnancy test in adolescents | | | | ✓ |
| Chemistry | | | | ✓ |
| Viral Load | | | | ✓ |
| OI screening | ✓ | | | ✓ |

5.5.4 What to expect in the first six months of therapy.

The first six months on ART are critical. Clinical and immunological improvement is expected but drug toxicities and/or immune reconstitution inflammatory syndrome (IRIS) may emerge. Some children fail to respond as expected or may even exhibit clinical deterioration during this time. Complications in the first few weeks following the initiation of ART are seen most commonly when therapy is started in children with severe immunodeficiency. Apparent failure to improve in a child with advanced HIV disease does not necessarily reflect a poor response to ART; it takes time for HIV viral replication to be controlled by ART and for the child's immune system to recover. It also takes time for the catabolism associated with HIV infection to be reversed, particularly in children with significant HIV-associated wasting. Additionally, as a child with advanced disease recovers immune function, exacerbation of previously subclinical coexisting infections (e.g. TB) may occur, resulting in apparent clinical deterioration. This is not attributable to failure of therapy but rather to its success and the resulting immune reconstitution. It is important to allow sufficient time on therapy before judging the effectiveness of a regimen and to consider the possibility of IRIS in children with worsening disease in the first few months of ART. Supporting adherence during this period is critical and, in such cases, switching of ARV regimen would be inappropriate.

5.5.4.1 CD4 Recovery

In most children, CD4 cell counts rise with the initiation of therapy and immune recovery. Generally, CD4 levels increase over the course of the first year of treatment, reach a plateau and then continue to rise further over the second year³. However, in some children, severe immunosuppression may persist. The lower the CD4 levels at the start of ART, the slower the recovery. At the same time, persistent failure to see a CD4 response should alert the clinician to potential adherence problems or non-response to ART. In this case, viral load determination can be useful.

5.5.4.2 Early ARV Toxicity

First-line drug toxicities fall into two categories: early toxicity, usually presenting in the first few weeks to months of therapy, and late toxicity. Section 5.7 provides more detail on identifying and managing toxicity.

5.5.4.3 Mortality on ART

³ Sutcliffe, C.G., et al., Effectiveness of antiretroviral therapy among HIV-infected children in sub-Saharan Africa. *Lancet Infect Dis*, 2008. 8 (8): p. 477-89.

While ART significantly decreases mortality overall, death rates are high in the first six months after initiation of ART, particularly when children start ART with stage 4 clinical events, severe immunosuppression, severe malnutrition or very low haemoglobin^{4,5}

5.5.4.4 Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome (IRIS) is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to antiretroviral treatment. While most HIV-infected children experience rapid benefit from ART, some undergo clinical deterioration. This is the result of either the unmasking of latent or subclinical infection or the reactivation of previously diagnosed and often treated conditions (infectious or non-infectious), sometimes termed “paradoxical” IRIS.

There are limited data on IRIS in infants and children and the causes are not clearly understood. The onset of IRIS in children most often occurs within the first weeks to months following the initiation of ART and is seen most often in children who initiate ART with very low %CD4+ levels (<15%) The most common OI associated with IRIS in children is TB, but those on treatment for Pneumocystis pneumonia (PCP) or cryptosporidiosis, or who have herpes simplex virus (HSV), fungal, parasitic or other infections may also develop IRIS. Where BCG immunization of infants and children is routine, BCG-associated IRIS (localized and systemic) is frequently observed (*Refer to section 2.7.1.2 for principles of management of IRIS*).

5.6 ARV drug toxicity

5.6.1 Introduction

Antiretroviral drugs can be responsible for a wide range of toxicities, from low grade intolerance that may be self limiting to life threatening side effects. Differentiating between ART toxicity (also known as adverse reactions) and complications of HIV disease is sometimes difficult. An observed toxicity could be due a concurrent infectious process e.g. common childhood illnesses, like Malaria in a child with severe anemia, or hepatitis A in a child with symptoms of hepatitis; or due to a reaction to medications other than ARVs e.g. Isoniazid – induced hepatitis in a child on treatment for TB or a rash induced by cotrimoxazole.

Although there are fewer data on ARV toxicity in children than in adults, the full spectrum of ARV toxicities observed in adults has also been observed in children. However some toxicities are less common in children than in adults e.g. the lipodystrophy associated with use of stavudine (d4T) or the symptomatic hepatotoxicity related to nevirapine (NVP) use, while others are more commonly reported in children than in adults e.g. tenofovir (TDF) –related loss of bone density or the efavirenz (EFV) related rash.

Drug related side effects while on ART can occur immediately (soon after a drug has been administered), early (within the first days or weeks of treatment) or late (after months or years of

⁴ KIDS-ART-LINC Collaboration, Low risk of death, but substantial program attrition, in pediatric HIV treatment cohorts in sub-Saharan Africa. *Journal of Acquired Immune Deficiency Syndromes*, 2008. 49 (5): p. 523-31.

⁵ Bolton-Moore, C., et al., *Clinical outcomes and cd4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. JAMA*, 2007. 298 (16): p. 1888-99.

treatment). Adverse reactions may be specific to a particular drug or they may be generic to the class of drugs in use.

5.6.2 Common ARV side effects in infants and children.

The most common toxicities include the following:

- **Hematological:** drug – induced bone marrow suppression most commonly seen with Zidovudine (AZT) leading to anemia, neutropenia, and more rarely thrombocytopenia.
- **Allergic reactions:** including skin rashes and hypersensitivity reactions, which are more common with the NNRTI class of drugs (NVP, EFV) but also seen with certain NRTI drugs, such as Abacavir (ABC).
- **Hepatotoxicity:** Because of the risk of potentially life threatening hepatotoxicity associated with NVP, hepatic dysfunction of any etiology in a child on NVP requires careful consideration of whether NVP should be discontinued.
- **Mitochondrial dysfunction:** primarily seen with the NRTI class of drugs and include lactic acidosis, hepatic toxicity, pancreatitis and peripheral neuropathy. The NRTIs differ in their ability to affect mitochondrial function: d4T and didanosine (ddI) are worse than AZT; lamivudine (3TC) and ABC have the least toxicity of all.
- **Lipodystrophy and other metabolic abnormalities:** primarily seen with d4T and the PI class of drugs and to a less extent the other NRTIs. Abnormalities include fat maldistribution and body habitus changes, hyperlipidaemia, hyperglycaemia, insulin resistance, diabetes mellitus, osteopenia, osteoporosis and osteonecrosis. *It should be noted however that lipodystrophy associated with d4T use occurs less frequently in children when compared to adults.*

5.6.3 Substituting drugs because of toxicity in infants and children

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.
- *Moderate or severe toxicities* may require substitution with a drug in the same ARV class but with a different toxicity profile, or with a drug in a different class, but don't require discontinuation of all ART.
- *Severe life threatening toxicities* require discontinuation of all ARV drugs and initiation of supportive therapy until the patient is stabilized and the toxicity is resolved.

NNRTIs (NVP, EFV) have a longer half-life than NRTIs, implying that stopping all first line drugs (involving NRTIs and NNRTIs) may result in exposure to sub-therapeutic levels of the NNRTI and subsequently to the development of NNRTI drug resistance. However, if a child has a life threatening toxicity, all ARV drugs should be stopped simultaneously until the patient is stabilized.

Regardless of their severity, adverse reactions may affect adherence to therapy. A proactive approach to managing toxicity is recommended. The potential side effects of the ART regimen before initiating therapy and during the early stages of treatment should be discussed with the child and his or her caregivers, and support should be offered during minor and moderate adverse reactions. The child and caregivers should be familiar with the signs of toxicities that are serious and require immediate return to the health facility, e.g. NVP – associated Steven Johnson

syndrome, drug induced hepatitis, lactic acidosis, pancreatitis or ABC – associated hypersensitivity.

The guiding principles for the management of ARV drug toxicity are shown in **(Box 2)** below.

| Box 2 Guiding principles for the management of ARV drug toxicity | |
|--|--|
| <ol style="list-style-type: none">1. Determine the seriousness of the toxicity.2. Evaluate concurrent medications and establish whether the toxicity may be attributable to an ARV drug or drugs, or to a non-ARV medication taken at the same time.3. Consider other disease processes. Not all problems that arise during treatment are caused by ARV drugs.4. Manage the adverse reaction according to its severity.5. In general:<ol style="list-style-type: none">a) Severe life-threatening reactions: Immediately discontinue all ARV drugs, manage the medical event and reintroduce the ARV drugs using a modified regimen (substituting the offending drug) when the patient is stabilized.b) Severe reactions: Substitute the offending drug without stopping the ART.c) Moderate reactions: Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single –drug substitution.d) Mild reactions: Reassure the child and caregiver that while the reaction may be bothersome, it does not require a change in therapy; provide support to mitigate the adverse reactions as well as counseling about the events.6. Stress the maintenance of adherence despite toxicity for mild and moderate reactions. | |
| | |
| | |
| | |
| | |
| | |

The guiding principles of substituting drugs because of toxicity in infants and children include:

- Drug substitutions should be limited to situations where toxicity is severe or life threatening, as there are few ARV drug options for children in resource limited settings.
- If toxicity is related to an identifiable drug, then the offending drug can generally be replaced with another drug from the same class that does not have the same adverse reaction.

For some life threatening toxicities, it may not be possible to identify an optimal substitute drug from the same drug class, e.g. one would not substitute NVP with EFV when the patient develops Steven Johnson syndrome; the recommendation changing to a triple NRTI regimen (i.e. substituting ABC for NVP) or substituting a PI (usually Lopinavir/ritonavir) for NVP.

Table 5.9 below lists the usual ARV substitution options for adverse reactions to particular drugs.

Table 5.9: Severe toxicities of ARV drugs in infants and children and the recommended drug substitutions

| Toxicity event | Responsible ARV drug | Suggested first line ARV drug substitution |
|---|-----------------------------|---|
| Acute symptomatic hepatitis | NVP | EFV |
| Hypersensitivity reaction | | A third NRTI e.g. ABC |
| Steven Johnson Syndrome (Severe or life | | Or |

| | | |
|--|-------|---------------|
| threatening rash) | | PI e.g. LPV/r |
| Lactic acidosis | d4T | ABC |
| Peripheral neuropathy | | AZT or ABC |
| Pancreatitis | | |
| Lipoatrophy/ metabolic syndrome | | ABC |
| Severe anemia or neutropenia | AZT | d4T or ABC |
| Lactic acidosis | | ABC |
| Severe gastrointestinal intolerance | | d4T or ABC |
| Persistent and severe central nervous system toxicity | EFV | NVP |
| Potential teratogenicity (applies to adolescent girls in first trimester of pregnancy) | | |
| Hypersensitivity reaction | ABC | AZT |
| Lipoatrophy/ metabolic syndrome | LPV/r | NNRTI |
| Dyslipidaemia | | |
| Severe diarrhea | | |

5.6.4 When to switch to 2nd line regimens

Poor adherence, inadequate drug levels or prior existing drug resistance can all contribute to ARV treatment failure. To identify treatment failure, it is recommended that one uses clinical criteria supported by immunological or virological confirmation where possible. When treatment failure is confirmed, switching to a new second-line regimen becomes necessary. Prior to switching therapy, it is essential to assess and address adherence issues.

Second line ART regimens tend to have a greater pill burden and are more expensive than first line regimens. A premature switch is therefore likely to be more costly for the patient and the program. However, a delayed switch to second line ART is likely to allow greater resistance to the first line NRTIs and has the potential to undermine the potency and durability of second line options.

When considering a switch on the basis of clinical criteria alone, the child should have been on the ART regimen for a reasonable period: the recommendation is that the child should have received the regimen for at least 24 weeks. Furthermore, adherence to therapy should have been assessed and found to be optimal, any intercurrent infection should have been treated and resolved, and immune reconstitution inflammatory syndrome (IRIS) excluded. Additionally, before considering a change in treatment because of growth failure, it should be ensured that the child is receiving adequate nutrition.

The determination of clinical, immunological or virological failure is summarized in **Table 5.10** below, and it is along these criteria that a patient should be switched to second line. ***It should be noted that a regimen should only be switched after at least 24 weeks on ART in a treatment adherent child.***

Table 5.10: Criteria for switching ART for treatment failure in infants and children

| | |
|------------------------------|---|
| Clinical criteria | <ul style="list-style-type: none"> • New stage 4 event or • New stage 3 event and no improvement with treatment |
| Immunological (CD4) criteria | <p>A drop in CD4 or failure of CD4 count to rise above these values</p> <ul style="list-style-type: none"> • <u>Child less than 5years:</u> CD4 count of <200 cells/mm³ or %CD4 $< 10\%$ • <u>Child 5years and above:</u> CD4 count of <100 cells/mm³ |
| Virological criteria | <ul style="list-style-type: none"> • Viral load $>5,000$ copies/ml |

5.6.5 Choice of 2nd line regimens in event of treatment failure

It is recommended that a regimen based on a PI, boosted with ritonavir (RTV), and combined with two NRTIs is the second line treatment for children who fail a regimen of two NRTIs with an NNRTI. New drugs that may be expected to have cross – resistance to drugs used in the first line should be avoided.

The recommended second line regimens following the various first line regimens in Uganda are shown in **Table 5.6 above**.

5.6.6 Strategies in the event of failure of second-line regimens

Beyond second line therapy, treatment strategies are expensive. Ideally, further revisions in therapy should be guided by viral resistance testing.

In formulating 3rd line or salvage regimens, newer NNTRIs e.g. etravirine and PIs e.g. tripranavir and duranavir, and newer classes of agents such as the CCR5 antagonist, maraviroc and the integrase inhibitor, raltegravir should be considered. Newer drugs should be used in combination with at least 1, and ideally 2 other active agents. Dual-PI strategies (e.g. saquinavir plus lopinavir/ritonavir) have been shown to be effective in children with extensive NNTRI plus NRTI resistance.

It may be possible to reintroduce previously prescribed drugs. In addition, continuation of lamivudine, despite the presence of lamivudine resistance mutations may contribute to virological suppression.

Empiric multi-drug regimens (including up to 3 PIs and / or 2 NNRTIs) have been promoted by some experts. Cost considerations, regimen complexity and potential drug-drug interactions may limit the use of this approach.

Experienced providers at referral or specialized centers should assist with decisions about advanced treatment regimens beyond second line.

5.7 HIV and TB co infection.

5.7.1 Introduction

HIV infected children are at increased risk of acquiring infection and progression to active TB disease following exposure to *M. tuberculosis* compared to those who are HIV negative. About 50 percent of HIV infected children with TB infection go on to develop the TB disease. Those who develop TB disease have a worse prognosis for severe disease. HIV infected children often have co-existing severe malnutrition which is also a risk factor for progression to severe disease. The prevalence of HIV in children with TB disease is about 50% in Uganda.

5.7.2 TB screening

All HIV-infected and exposed infants and children should be evaluated for TB symptoms using the MOH intensified case finding (ICF⁶) form at every visit to a health-care facility. **(See appendix 8 For ICF).** In addition, they should be evaluated for contact with a TB source case. Those reporting positive contact histories, poor weight gain⁷ or any symptoms on the ICF form should be investigated for TB. Infants and children have a wide range of pulmonary and extra pulmonary manifestations of Tuberculosis. The Pulmonary form is the commonest presentation. Diseases suggesting a possibility of TB include bronchopneumonia without improvement on a 7-14 day course of broad spectrum antibiotics, pleural effusion, asymmetrical peripheral lymphadenopathy, spinal deformity, abdominal peritonitis, ascites and meningitis in a setting of the above symptoms.

5.7.3 TB diagnosis

Diagnosis of TB in children is limited by the difficulty in obtaining bacteriological confirmation of the disease. However, this should always be sought whenever possible. Samples such as sputum (by expectoration, gastric aspiration or induction), fine-needle aspirates of enlarged lymph nodes, pleural fluid or ear swabs should be subjected to microscopy and other available bacteriological investigations. Gastric aspirates should not be undertaken in the absence of culture services.

Diagnosis of TB in children is presumptive and based on a suggestive clinical signs and symptoms, findings on Chest x-ray, Tuberculin Skin Testing (TST) and other investigations. Different scoring systems have been proposed but unfortunately these perform poorly in HIV-infected children. A “trial of TB treatment” should not be used as a diagnostic test for TB in children.

When making a diagnosis of TB among HIV infected infants and children, one needs to exclude HIV related fevers, weight loss, systemic and respiratory diseases which may mimic that of TB. The TST⁸ may be negative even in presence of TB disease. Radiological features in PTB are

⁶ ICF forms have cardinal symptoms of TB in adults : presence of cough for 2 or more weeks; blood stained sputum; persistent fevers for 3 or more weeks; noticeable weight loss and night sweats.

⁷ Poor weight gain is defined as: 1. reported weight loss, or 2. very low weight (weight-for-age less than -3 z-score), or 3. Under weight (weight-for-age less than -2 z-score), or 4. Confirmed weight loss (>5%) since the last visit, or 5. growth curve flattening).

⁸ In an HIV-infected child, induration of ≥ 5 mm diameter is read as a positive TST.

often non specific and/or similar to those seen in other HIV related Lung diseases. HIV related lung diseases include *bacterial pneumonia*, *viral pneumonia*, *Pneumocystis Jiroveci pneumonia*, *mixed lung infections*, *Kaposi's sarcoma*, *fungal lung disease* and *pulmonary lymphoma*.

The most important diagnostic clue for detecting TB in HIV infected children is a history of contact with an adult who has infectious TB. Since TB may not have yet been diagnosed in this adult, a prompt evaluation for TB in adults who care for the children is a critical part of the evaluation of the children.

5.7.4 TB treatment in HIV infected infants and children

The underlying principles for the treatment of TB in HIV-infected children are the same as for children who are not HIV-infected. However, the co-management of TB and HIV, and the treatment of HIV infection, is complicated by drug interactions, particularly between rifampicin and the NNRTI and PI classes of ARVs. TB treatment is based on standardized MOH treatment categories and doses summarized below: (See appendix 8 and appendix... respectively

5.7.5 First line ARV regimens for infants and children patients with TB disease.

The choice of ART regimen is guided by the need to minimize drug-drug interaction especially when Rifampicin is co-administered with NVP and PIs. Rifampicin induces hepatic microsomal enzymes leading to sub-therapeutic levels of these drugs. Rifabutin has minimal interaction with NNRTIs and PIs. When used in place of Rifampicin, the ART regimens need not be adjusted.

Table H. below summarizes ARV regimens used in TB/HIV co infection

Table 5.11 First Line ARV regimens for Infant and Children with Tb co infection

| | | | |
|---------------------------|-----------|-------------|-----------------|
| TB-HIV Co- infected | < 3 years | Preferred | AZT + 3TC + ABC |
| | | Alternative | AZT + 3TC + NVP |
| | ≥ 3 years | Preferred | AZT + 3TC + EFV |
| | | Alternative | ABC + 3TC + EFV |

5.7.6 Consideration for children diagnosed with TB while on first line ARV regimen

Anti -TB treatment should be initiated immediately upon diagnosis in these children while ART is continued. However, the ARV regimen should be reviewed and may need adjustment in order to ensure optimal treatment of both TB and HIV and to decrease the potential for toxicities and drug – drug interactions.

- For children 3 years and older who are NVP based regimen, it should be substituted with EFV.
- For children under 3 years maximize dose of NVP to 200mg/m² or give a triple NRTI regimen (AZT/3TC/ABC)
- For patients on a regimen containing LPV/r, adjust RTV dose to LPV: RTV ratio of 1:1.

5.7.7 Considerations for children diagnosed with TB but are not on ART.

All HIV infected children with active TB disease should begin TB treatment immediately, and start ART as soon as tolerated in the first 2-8 weeks of TB therapy, irrespective of the CD4 count and clinical stage.

5.7.8 Immune reconstitution inflammatory syndrome (IRIS) events in TB patients

IRIS is common in patients with advanced HIV disease (particularly those with a CD4 count less than 50 cells/mm³ or 10% in children) in the first few weeks of starting HAART. This is due to unmasking of a previously occult opportunistic infection by the improving immune function. Previously diagnosed disease may also get worse (Paradoxical IRIS). TB IRIS needs to be differentiated from drug failure or a side effect and non TB IRIS events (these may mimic or co-exist with TB). *Refer to section 2.7.1.2 for principles of management of IRIS*

Some cases of IRIS in HIV-infected children may in fact be TB (Unmasking of TB). Other cases may be localized or disseminated BCG disease in children who have received a BCG vaccination. BCG disease is difficult to treat as *M. bovis* is resistant to Pyrazinamide and requires higher doses of first line anti-TB medicines.

HIV-infected children suspected of having disseminated BCG disease should be referred to an appropriate expert for management, as the diagnosis of BCG disease is difficult and the treatment is specialized.

Management consists of continuing anti-TB treatment, assessing the child for new illness and in some cases, corticosteroids may be useful.

5.7.9 TB prevention

Protection of HIV infected infants and children from TB can be achieved through early detection and treatment of adult infectious cases and universal use of BCG at birth and IPT.

5.7.9.1 BCG vaccination is protective against severe forms of TB such as Millary TB and TB meningitis. It should not be given to infants and children with symptomatic HIV infection. However in Uganda BCG vaccine is given at birth and by then HIV infected children are unlikely to be symptomatic. So if given at the right time, most children will receive BCG vaccine.

5.7.9.2 Isoniazid preventive therapy (IPT)

IPT eliminates latent TB infection thereby reducing the risk of progression to active disease. Active TB disease must be routinely excluded before and during the course of IPT. IPT should be given for 6 months and the recommended dose of Isoniazid 10mg/kg (Max of 300 mg daily).



The following categories of children should receive IPT

It is indicated for:

- All HIV-infected infants and children exposed to TB through household contacts, but with no evidence of active disease irrespective of age
- Children living with HIV (>12 months of age and including those previously treated for TB), who are not likely to have active TB and are not known to be exposed to TB, should receive 6 months of IPT as part of a comprehensive package of HIV care.

Infants living with HIV, who are unlikely to have active TB and are not known to be exposed to TB, should not receive IPT as part of a comprehensive package of HIV care.

Appendix 2.....: WHO Paediatric HIV clinic Staging Chart

|  <div>  World Health Organization </div> | | | | |
|--|--|---|---|--|
| WHO Paediatrics HIV Clinical Staging | | | | |
| | WHO Clinical Stage 1 <i>Asymptomatic</i> | WHO Clinical Stage 2 <i>Mild Disease</i> | WHO Clinical Stage 3 <i>Advanced Disease</i> | WHO Clinical Stage 4 <i>Severe Disease (AIDS)</i> |
| Growth | | | Moderate unexplained malnutrition not adequately responding to standard therapy (very low weight for age, or low height for age, or low weight for height) | Severe refractory wasting or severe malnutrition unexplained and not adequately responding to standard therapy |
| Symptoms Treat common and opportunistic infections according to IMCI guidelines | No symptoms or only: • Persistent generalized lymphadenopathy | <ul style="list-style-type: none"> • Unexplained persistent enlarged liver and/or spleen • Unexplained persistent parotid enlargement • Skin conditions (e.g. chronic dermatitis, fungal infections or extensive molluscum contagiosum, extensive wart, seborrhoeic dermatitis, prurigo, herpes zoster) • Fungal nail infection • Recurrent or chronic (sinusitis, ear infections, pharyngitis, tonsillitis, bronchitis) • Mouth conditions (Recurrent oral ulceration, angular cheilitis, lineal gingival Erythema) | <ul style="list-style-type: none"> • Oral thrush (after the first six to eight weeks of age) • Oral hairy leukoplakia • Unexplained and unresponsive to standard therapy: <ul style="list-style-type: none"> – Diarrhoea >14 days – Fever >1 month (intermittent or constant, > 37.5 °C) – Thrombocytopenia* (<50,000/mm³ for > 1 mo) – Neutropenia* (< 5000/mm³ for 1 mo) – Anaemia for >1 month (Hb < 8 gm)* • Recurrent severe bacterial pneumonia • Pulmonary TB • TB lymphadenopathy • Chronic HIV-associated lung disease, including bronchiectasis • Symptomatic LIP* • Acute necrotizing ulcerative gingivitis/periodontitis | <ul style="list-style-type: none"> • Oesophageal thrush • More than one month of herpes simplex infection • Severe recurrent bacterial infections > 2 episodes in a year (e.g. muscle, bone or joint infection, not including pneumonia) • Pneumocystis pneumonia (PCP)* • Kaposi's sarcoma • Extrapulmonary tuberculosis • Toxoplasma brain abscess* • Cryptococcal meningitis* • HIV encephalopathy* |
| Prophylaxis | <ul style="list-style-type: none"> • Cotrimoxazole prophylaxis • INH prophylaxis, after excluding active TB | <ul style="list-style-type: none"> • Cotrimoxazole prophylaxis • INH prophylaxis, after excluding active TB | <ul style="list-style-type: none"> • Cotrimoxazole prophylaxis • INH prophylaxis, after excluding active TB | <ul style="list-style-type: none"> • Cotrimoxazole prophylaxis • INH prophylaxis, after excluding active TB |
| ARV therapy | Start ART if : <ul style="list-style-type: none"> • <2 Years treat all, irrespective of CD4 % or count • 2 to <5 Years CD4 < 25% (< 750 cells/mm³) • > 5years CD4 < 350 cells/mm³ | Start ART if : <ul style="list-style-type: none"> • <2 Years treat all, irrespective of CD4 % or count • 2 to <5 Years CD4 < 25% (< 750 cells/mm³) • > 5years CD4 < 350 cells/mm³ | Start ART irrespective of the CD4 count. | Start ART irrespective of the CD4 count and should be started as soon as possible. <ul style="list-style-type: none"> • If HIV infection is NOT confirmed in infants <18 months, presumptive diagnosis of severe HIV disease can be made on the basis of **: HIV antibody positive AND One of the following: <ul style="list-style-type: none"> – AIDS defining condition OR – Symptomatic with two or more of : <ul style="list-style-type: none"> • Oral thrush • Severe pneumonia • Severe sepsis |

6.0 Guidelines on Prevention of Mother to Child HIV Transmission (PMTCT) and improving Maternal, Newborn and Child Health (MNCH)

Scope of this section;

This section covers the Introduction, Vision and Goal, Specific Objectives and Targets, PMTCT Prongs, Basic integrated MNCH-PMTCT Package, recommended ARV regimens for PMTCT, community PMTCT as well as monitoring and evaluation of the PMTCT program.

6.1 Introduction

Mother to child HIV transmission (MTCT) still remains the second major mode of transmission of HIV in Uganda accounting for up to 18% of new infections (MOT Study) and the main source of HIV infection to children less than 5 years old. Without PMTCT the risk of transmission of HIV during pregnancy and delivery is estimated at 15-30% and the additional risk through breastfeeding is estimated at 10-20%. With the PMTCT intervention the risk in the breastfeeding population reduces to less than 5% and in the non-breastfeeding population is less than 2%. In line with the 2010 WHO guidelines, the program has developed a new scale up plan aimed at virtual elimination of MTCT.

The Global Virtual Elimination of Mother to child HIV transmission by 2015 involves;

- Reduction of new Pediatric infection by 90% from the 2009 baseline
- Reduction of transmission rate at population level among infants born to HIV positive mothers less than 5%
- 50% reduction in HIV incidence in reproductive age group by 50%
- Reduction of unmet need for family planning to Zero
- 90% reduction in HIV related maternal death
- 90% reduction in HIV related deaths among children less than 5years

This is only possible within a strengthened Maternal, Newborn and Child Health (MNCH) program. Integration of PMTCT and MNCH services therefore have the potential for increased synergy and efficiency across these programs and enhance maternal and child survival. Improved PMTCT and MNCH programs are very vital for keeping the HIV infected and affected women and their children alive.

6.2 Vision and Goal of the PMTCT Program 2010/11-2014/15

Vision: A generation free of HIV and AIDS in Uganda

Goal: To achieve virtual elimination of HIV transmission from mother to child and reduction of mortality and morbidity among women living with HIV and among HIV-exposed and infected infants

6.3 Specific Objectives:

The specific objectives are in line with the PMTCT scale up plan 2010-2015:

- To increase access and utilization of RH/HIV and STI prevention and treatment services to 80% of the women of reproductive age
- To increase access and utilization of family planning (FP) services to 80% of all women living with HIV
- To increase access and utilization of the recommended package for prevention of Mother-to-Child Transmission of HIV to 80% of HIV-infected women and their infants
- To increase access and utilization of family-centered HIV care and treatment to 80% of HIV-infected pregnant and lactating women and their children (if infected with HIV)

6.4 The 2015 Targets

These are coverage and population based targets.

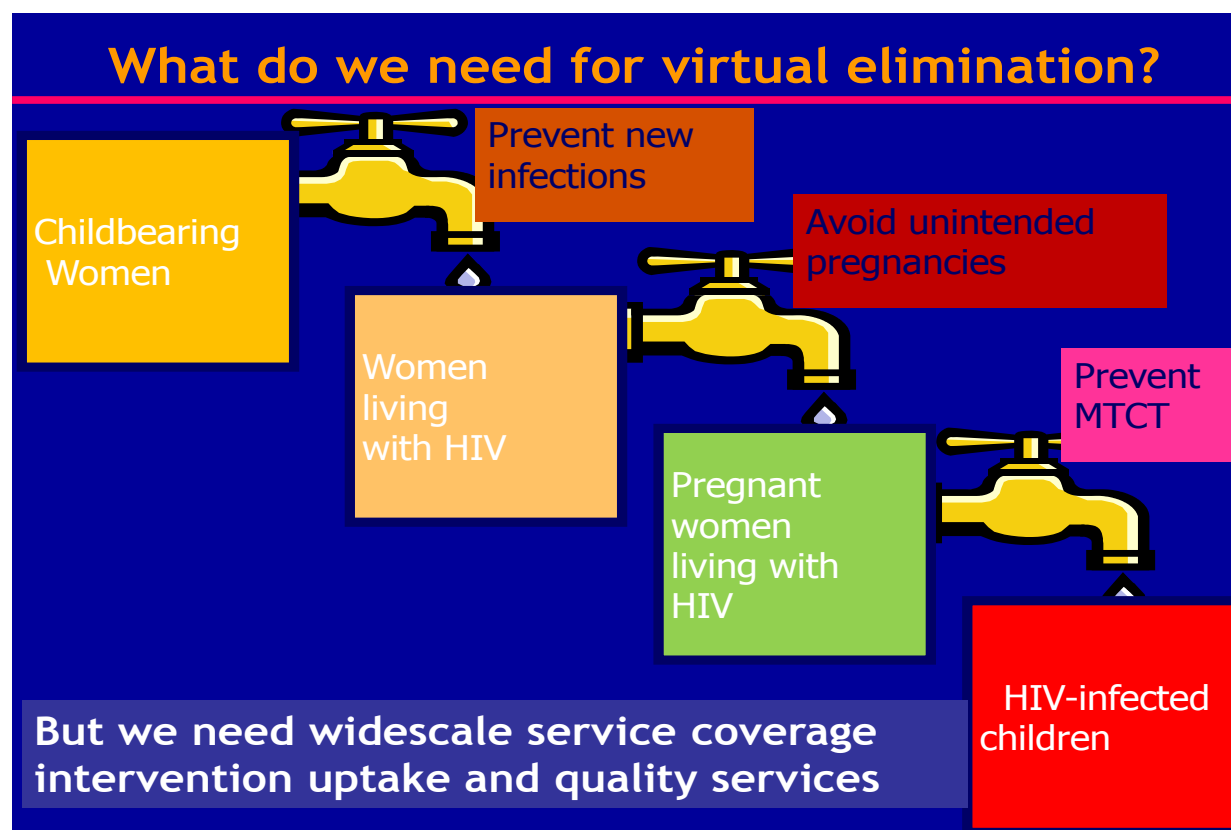
1. All health facilities up to HC III and in at least 30% of the functional HC II facilities providing integrated PMTCT services including care of HIV exposed infants.
2. Functional community PMTCT initiatives including psychosocial support groups available at 80% of all sub-counties
3. 80% of women living with HIV provided with family planning services
4. 80% of all pregnant women counselled, tested and given HIV results
5. 80% of HIV negative women within MCH setting counselled and provided information on RH/HIV and STI prevention and treatment services.
6. 50% of the male partners of pregnant and lactating women counselled, tested and given HIV results
7. 80% of HIV +v pregnant women deliver under skilled care. Antiretroviral drugs and Co-trimoxazole for prevention of mother-to-child transmission of HIV provided according to recommended guidelines to 80% of all infected pregnant and lactating women
8. Antiretroviral drugs for mother-to-child transmission of HIV prophylaxis provided according to recommended guidelines to 80% of all exposed infants
9. 80% of all pregnant and lactating mothers provided infant and young child feeding counselling
10. 80% of all pregnant and lactating mothers provided counselling on maternal feeding
11. Co-trimoxazole prophylaxis provided to 80% of HIV exposed infants from 6 weeks of age
12. The first DNA PCR test provided to 80% of all infants born to HIV infected mothers within the first three months of life
13. 80% of eligible HIV positive pregnant and lactating mothers identified under the PMTCT programme referred for or initiated onto HAART
14. 80% of HIV infected infants identified through EID linked to HAART within the first 12 months of age.

6.5 The PMTCT Prongs

This refers to the comprehensive strategy for implementation of PMTCT program globally.

Focusing on one prong or element (particularly prong 3) does not help achieve virtual elimination of MTCT as the HIV infection continues to infect and affect women and men of reproductive age group and therefore closing all the taps as illustrated in **Figure 6.1** below, will be the only way to achieve Virtual elimination of MTCT.

Figure 6.1: The PMTCT pronged approach.



To achieve virtual elimination we need to focus on all the 4 prongs namely:

Prong 1: Primary prevention of HIV infection among women of reproductive/child bearing age

Prong 2: Prevent unwanted pregnancies among women living with HIV

Prong 3: Prevent HIV transmission from women living with HIV to their infants

Prong 4: Provide appropriate treatment, care, and support to mothers living with HIV and their children and families

6.5.1 Prong 1: Primary prevention of HIV infection among women of reproductive age

All women of Reproductive age group and their spouses should be counseled and supported to adopt risk reduction behaviors that protect them from being infected. Great emphasis should be placed on preventing infection among women of reproductive age. They should be encouraged and supported to routinely test for HIV as follows.

- HCT for all women of reproductive age through different approaches especially Provider Initiated Counseling and Testing (PITC), Client Initiated Counseling and Testing (CICT) and Community Outreaches.
- Pregnant women who have tested HIV-negative in the 1st or 2nd trimester of pregnancy should be re-tested in the 3rd trimester (preferably between 28-36 weeks)
- Pregnant women who do not return for testing in 3rd trimester, should be re-tested during labor or just after delivery

- Pregnant women with STIs who have an HIV-negative test result should be re-tested 4 weeks after HIV- negative test
- TB-infected pregnant women with an HIV-negative test result who have had a new potential HIV exposure should be re-tested 4 weeks after the HIV negative test
- HIV-negative pregnant women with ongoing risk of infection (persons with known HIV positive husband/partner, husband/partner of unknown status and injection drug users) should be re-tested at least annually
- Pregnant women with a specific incident of known HIV-exposure within the past 3 months, who test negative at the first testing encounter should be re-tested 4 weeks after initial HIV negative test
- PMTCT messages should be incorporated in school health curriculum and community adolescent health programs for behavioral change and promotion of abstinence
- PMTCT messages should also be incorporated in the pre-marital counseling programs
- Promotion of use of female and male condoms in the general population for prevention of unintended pregnancies, HIV infection and other STI's
- Sexual and Gender Based Violence (prevention and Support). Ensure counseling, psychosocial support, emergency contraception and HIV exposure prophylaxis for women whom have experienced, including sexual assault survivors.

Further linkages should be explored and/or strengthened in regards to

1. Male circumcision
 2. Programming for sero discordant couples
 3. Treatment as prevention
- (See section 2.2.1)

6.5.2 Prong 2: Prevention of unwanted pregnancies among women living with HIV:

The second element of PMTCT is preventing unintended pregnancies in women living with HIV. Family planning for women living with HIV, as with all women, should be based on respect and fulfilment of reproductive rights, and should never be coerced. Women's reproductive choices must be respected and safe guarded. Family planning is a potent instrument in preventing HIV in women and children and provides intrinsic benefits by saving lives and enhancing the health status of women and their families.

Pregnant women living with HIV who do not intend to conceive again should be counseled and supported to avoid a subsequent pregnancy. Women who are HIV-positive have special family planning needs. All HIV-positive women should be made to clearly understand the risks of future pregnancies and of each type of family planning method for their particular situation. HIV-positive women should have access to information, follow-up clinical care and support, including family planning services and nutritional support. Family planning services are particularly urgently needed for HIV-positive women who are not breastfeeding. Women who are not breastfeeding or stop breastfeeding early are at greater risk of becoming pregnant.

6.5.2.1 Factors to consider while starting HIV positive clients on FP

There are a few things to consider when providing Family Planning counseling to HIV positive women. If an HIV positive woman comes for FP and is on ARVs. Find out what specific ARVs she is taking.

- If a client is on nevirapine in whatever combination and wants to start or is using Depo-Provera, emphasize that it is important to return for her next injection on the date indicated on her appointment card. She can also come just before that date in case she cannot make it on the appointment date. The 2 week grace period (providing the injection up to 2 weeks late) is **NOT** advisable for these clients because nevirapine may reduce the progestin in DMPA at the end of the three months
- If a client is taking Nevirapine in whatever combination and wants to start combined oral contraceptives (COCs) emphasize that it's important to take the pills (COCs) regularly everyday or she is more likely to get pregnant.
- Rifampicin that is used for treatment of tuberculosis interferes with combined oral contraceptive pills, progestin only pills and Norplant rendering them less effective. The most effective family planning method for such a client is Depo-provera.
- When a HIV positive client is given Rifampicin, Efavirenz is usually given instead of Nevirapine.
- If a woman is taking efavirenz and wants to start a family, help her to select a **VERY EFFECTIVE** family planning method. She must not get pregnant because efavirenz is a potent teratogen which means it will harm the foetus. If client desires Depo-Provera, advise client to come to the clinic immediately every three months for the repeat injection.
- Dual protection family planning services should be promoted among women living with HIV and their husbands/partners to help them avoid unintended pregnancies, HIV transmission and/or re-infection. Female and male condoms are currently the only barrier devices against transmission or acquisition of HIV. All sexually-active people should be offered “dual protection” against unintended pregnancy and HIV or other sexually transmitted infections.
 - Strategies using “proven” methods to meet this goal include
 - ✓ being in a monogamous relationship in which both partners are free of STIs/HIV and at least one is using effective contraception;
 - ✓ proper and consistent use of a male or female condom; or
 - ✓ dual method use where one method is used to protect against unintended pregnancy (often a hormonal method or other highly effective non-coitally dependent contraceptive) and a second is used to protect against STIs.
- Initiate family planning services as an integral component of ART services as women attending ART clinics have sustained contact with health workers and this can be used as an opportunity to provide them with family planning services

6.5.3 Prong 3: Prevention of HIV transmission from women living with HIV to their infants

6.5.3.1 Routine HCT in the MNCH setting

- All pregnant women and their husbands/partners should be routinely offered counseling and testing for HIV with same day results as part of the basic care package.
- Health workers should offer group pre-test counseling for pregnant and lactating women, women of unknown HIV status and individual post test counseling. Individuals who are not ready to test for HIV during that visit may opt out but should be engaged in the subsequent visits.
- For those who test HIV negative refer to previous section (6.5.1)

6.5.3.2 Laboratory investigations and related services for all pregnant women

- All pregnant women should be screened and treated for syphilis

- All pregnant women should be screened for other STIs and syndromic management should be integrated in antenatal, postnatal and family planning services.
- All pregnant women should be screened and treated for anemia
- All pregnant women should have a blood group test
- All pregnant women should have a urinalysis

6.5.3.3 Laboratory investigations specific to HIV-Positive Pregnant Women

- All HIV positive pregnant women beginning AZT-based prophylaxis or treatment should receive an HB test. Screening for anemia is vital for these women both at the start of the ARV drug and four weeks after initiation.
- All HIV positive pregnant women should receive a CD4 when diagnosed HIV positive or upon first visit to a health facility following pregnancy.

6.5.3.4 Comprehensive Care for Pregnant Women Living with HIV (*Also see section 6.6 below*).

- All pregnant women living with HIV should be given co-trimoxazole for prophylaxis for opportunistic infections and they should **NOT** be given Fansidar for intermittent preventive treatment for malaria (IPT)
- All mothers should be counseled on appropriate feeding practices during pregnancy and while they are breastfeeding (Please see guidelines on Infant and small child feeding below).
- All pregnant women should routinely receive iron, folic acid and multivitamins for supplementation
- All pregnant women should receive Mebendazole during the second trimester for de-worming

6.5.3.5 Risk reduction counseling and support during pregnancy, delivery and lactation

- Consistent and correct use of condoms should be recommended for pregnant and lactating women and their spouses to prevent infection and re-infection.
- All pregnant women should be counseled and encouraged to deliver at the health facilities where safe and appropriate precautions are taken and infection control measures observed at all times
- Immediately after delivery, all mothers should receive vitamin A 200,000 IU supplementation and 50,000 IU for the baby if they intend to give them replacement feeding . (Note: Infants who will breast feed will not receive Vitamin supplementation after birth.)
- All HIV positive children will receive Vitamin A 100,000-200,000 IU every 6 months up to the age of 5 years.

6.5.4: Prong 4: Care and Support for Pregnant Women Living with HIV and their Families

- All pregnant women living with HIV should be provided with appropriate HIV/AIDS care that includes HAART whenever applicable. They should also serve as an entry point for the rest of their family for HIV prevention, testing and care.
- All HIV positive pregnant mothers should be linked into chronic care programs as soon as they are diagnosed HIV positive or as soon as ready.
- All pregnant women living with HIV should be started on co-trimoxazole immediately upon diagnosis.
- All children born to mothers living with HIV should be tested for HIV from 6 weeks of age and offered follow up care and support

- All children born to mothers living with HIV should be started on co-trimoxazole prophylaxis from 6 weeks of age until confirmed to be HIV negative or for life if HIV positive.
- All children aged less than 2 year confirmed to be HIV+ should be started on ART irrespective of their CD4 cell count or viral load
- All HIV positive pregnant mothers and their families should be linked to psychosocial and community groups for on-going support

6.6 Basic integrated MNCH/PMTCT package

For a successful and a cost effective program, the PMTCT intervention should be integrated into the maternal, new born and child health services which include but not limited to the ANC, Labor and delivery and Post Natal Care, Sick child clinic, YCC settings. The recommended ANC protocol is the Goal Oriented (Focused) ANC. It is based on the fact that Goals are different depending on the timing of the visit. Four (4) visits are aimed for uncomplicated pregnancy including the HIV infected pregnant women. If a woman books later than in the first trimester, preceding goals should be combined and attended to. In all visits, address any identified problems, check blood pressure, and measure the Symphysio- Fundal Height (FH).

ANTENATAL Care Package:

Health Promotion & Counseling; Examination & Screening

| | | ANC VISIT 1 | ANC VISIT 2 | ANC VISIT 3 | ANC VISIT 4 |
|---------------------------------|-----------------------|--|---|--|--|
| Period of Visit | | First Trimester (0-16 weeks) | Second Trimester (16-28 weeks) | Third trimester 28-42 weeks | Third trimester 28-42 weeks |
| Timing of Visit | | Anytime < 16 weeks | 24-28 weeks | 32-36 weeks | After 36 weeks |
| Goal | | <ul style="list-style-type: none">Assess risksHealth EducationMake plan for delivery | <ul style="list-style-type: none">Act on abnormal lab resultsCheck foetal growthExclude multiple pregnanciesReview delivery plan | <ul style="list-style-type: none">Check foetal growthAssess for danger signsReview delivery plan | <ul style="list-style-type: none">Check foetal growthAssess for danger signsExclude abnormal presentationReview delivery plan |
| Health Promotion and Counseling | Family Planning | <ul style="list-style-type: none">Counsel and provide information on family planning options at every visitEmphasize dual protection methods for HIV-positive pregnant women, those with unknown status and those with STIsProvide condoms if available and accepted by the pregnant woman/partner | | | |
| | Infant Feeding | <p>Discuss feeding options with the mother at every visit (EBF, MF, RF). Strongly recommend the following:</p> <p><u>HIV-negative mothers:</u> Breastfeed for 24 months (exclusively for the first 6 months, then add complementary feeds)</p> <p><u>HIV-positive mothers:</u> Breastfeed for 12 months with ARV prophylaxis (exclusively for the first 6 months, then add complementary feeds)</p> <ul style="list-style-type: none">If breastfeeding, counsel mother how to properly breastfeed the babyIf replacement feeding, ensure AFASS criteria is met | | | |
| | Danger Signs | Inform client of danger signs to look for <u>during pregnancy</u> : Sensitize to visit the health facility immediately <i>Vaginal Bleeding / Convulsions/ Severe headaches and blurred vision / Severe abdominal pain / Fast or difficult breathing / swelling of fingers, face, or legs</i> | | | |
| | | Inform client of danger signs to look for <u>during labour and delivery</u> : Sensitize to visit the health facility immediately <u>Mother:</u> Not in labour 6 hrs after water breaks / In labour > 24 hrs / Labour pains > 12 hrs / Heavy bleeding / Placenta not expelled 1 hr after <u>Baby:</u> Very small / Difficulty breathing / Fits / Fever / Feels Cold / Bleeding / Not able to feed | | | |
| | PIH | Take <u>Blood Pressure</u> and assess for signs of Pregnancy Induced Hypertention (PIH) at every visit. Indications of PIH are: <i>High BP > 140/90 / High urine protein concentration / Severe headache / Sudden weight gain / Blurred vision</i> <i>If suspecting PIH, treat with Hydralazine (antihypertensive) and refer to clinician urgently for further management.</i> | | | |
| | Anemia | Assess for signs of <u>anemia</u> at every visit: <i>Hb Test < 11.5 g/L / Conjunctival Pallor / Palmar Pallor / Fast or Difficult Breathing / Fatigue / Swelling of Finger Face or Legs</i> <i>If patient has anemia: give an increased dose of Fe and Folic Acid (double dose) and advise on diet. Refer for blood transfusion if severe.</i> | | | |
| | TB | <u>1)</u> Assess for signs and symptoms of <u>tuberculosis</u> at every visit: <i>Cough for > 2 weeks / Persistent Fever / Unexplained Weight Loss / Severe malnutrition / Suspicious lymph nodes / Night sweats</i> <u>2)</u> If any signs of TB or contact with active TB patient, take sputums or refer for CXR <u>3)</u> If patient has active TB, start treatment immediately (start RIPE)..... Do not use Streptomycin for TB-infected pregnant women | | | |
| | Physical Examinations | <ul style="list-style-type: none"><u>Vital observations:</u> If BP > 140/90, provide antihypertensive & determine cause. <i>Look for other signs of PIH.</i> Treat or refer.<u>Symphysis-Fundal Height:</u> SFH should be increasing and approximately the same length as weeks of gestation<u>Abdominal Examination:</u> <i>Presentation</i> (do ECV if not cephalic) and <i>Fetal Heart Rate</i> (do ultrasound if not clearly visible)<u>Vulva/Pelvic Exam (1st and 3rd Trimester):</u> Check for VBACs, previous c-section | | | |
| | Nutritional Status | Discuss mother's diet options and counsel on proper nutrition | Assess diet & counsel on proper nutrition at each visit: <i>Mother is receiving inadequate nutrition if weight fails to increase by at least 2 kg from previous visit</i> | | |
| | HIV Clinical Staging | If mother is HIV-positive, do WHO clinical staging at EVERY VISIT | | | |

ANTENATAL Care Package (continued from previous page):

Lab Investigation; Vaccination, Supplements & Prophylaxis

| | | ANC VISIT 1 | ANC VISIT 2 | ANC VISIT 3 | ANC VISIT 4 |
|---|---------------------------------|---|---|---|--|
| Period of Visit | | First Trimester (0-16 weeks) | Second Trimester (16-28 weeks) | Third trimester 28-42 weeks | Third trimester 28-42 weeks |
| Timing of Visit | | Anytime < 16 weeks | 24-28 weeks | 32-36 weeks | After 36 weeks |
| Lab Investigation | HIV | Test pregnant women & partner for HIV if status unknown | Test for HIV if: <ul style="list-style-type: none">• Pregnant woman or partner have not yet been tested for HIV• Pregnant women or partner tested HIV-negative but > 3 months have elapsed since test | | |
| | CD4 | IMMEDIATELY take CD4 sample if pregnant woman is HIV-positive and has not had CD4 test for 6 months | | | |
| | Syphilis | Do RPR test for syphilis. If positive, treat with single dose of IM benzathine penicillin (injection) | | | |
| | Hb | Conduct Hb test. If Hb < 11.5 g/L, patient is anemic-- Give double dose of Fe/Folate & advise on diet | If pregnant women showing any signs of anemia (especially palor), conduct Hb test For HIV+ pregnant women initiated on AZT, do Hb test at initiation, 4 weeks, 8 weeks, and 16 weeks after Do not give AZT to HIV-positive pregnant woman if Hb < 7.5 g/L (severe anemia) | | |
| | Urine | Conduct urine test for protein and glucose at every visit: <ul style="list-style-type: none">• If protein test is positive, assess for PIH by taking blood pressure. Manage accordingly (see box on PIH).• If glucose or ketones positive, assess for Diabetes Mellitus with random blood sugar test. | | | |
| Vaccination, Supplements, and Prophylaxis | Vaccination | Give first TT dose at first visit | Give second TT dose (if at least 4 weeks after first visit) | Give TT dose if due (if 2 doses not yet received during the pregnancy) | |
| | Fe/Folic Acid | Give 1 tablet of Iron (200 mg) and 1 tablet of Folic Acid (5 mg) daily to all women throughout the course of pregnancy Provide enough supply to last until next ANC appointment For pregnant women showing signs of anemia, give 2 tablets daily as treatment. If severe anemia, transfuse or refer. | | | |
| | Mebendazole | Do NOT give mebendazole during 1st trimester | Give a single dose of Mebendazole (500 mg tablet) to the mother during second or third trimester | | |
| | IPTp for Malaria Prevention | Do NOT give IPT during 1st trimester Counsel mother on ITN use and ITN provide if available | Give 1PT ₁ dose in 2nd Trimester: SP 500 mg/ 25 mg If HIV-positive, give mother Cotrimoxazole instead of IPT | Give 1PT ₂ dose in 3rd Trimester: SP 500 mg/ 25 mg If HIV-positive, give mother Cotrimoxazole instead of IPT | Counsel mother on ITN use and provide ITN if available |
| | Cotrimoxazole & ARV Prophylaxis | If HIV-positive, give mother: <ul style="list-style-type: none">• Cotrimoxazole prophylaxis at every visit (Do not give IPT)• ARV prophylaxis every visit starting from 14 weeks gestation: AZT (Option A) or HAART (Option B)--- Don't wait for CD4 result to start Do NOT give AZT if mother is anemic (Hb < 7.5 g/L) | | | |

L&D and POSTNATAL Care Package:

Health Promotion & Counseling; Examination & Screening

| | | LABOUR & DELIVERY (including the 6-hour postnatal visit) | 1ST POSTNATAL VISIT | 2ND POSTNATAL VISIT | 3RD POSTNATAL VISIT |
|---------------------------------|--|--|---|---|--|
| Period of Visit | | N/A | Within 1 week of delivery | Within 6 weeks of delivery | At 6 months old |
| Timing of Visit | | Labour, Delivery, and 1st 24 hours | 6 days postnatal | 6 weeks postnatal | 6 months postnatal |
| Goal | | <ul style="list-style-type: none"> Safe Delivery for mother and baby Ensure well-being of the newborn Identify problems in newborn baby Ensure comfort & rehydration of mother | <ul style="list-style-type: none"> Maintain physical and psychological well being of the mother and baby; Screen for complications of mother & baby, and for congenital abnormality of the baby Provide health education on nutrition, infant feeding, immunization, family planning, hygiene, STD prevention Promote couple dialogue, partner notification and responsible fatherhood | | |
| Health Promotion and Counseling | Family Planning | <ul style="list-style-type: none"> Counsel on family planning options and agree on method to be used Start contraceptive if appropriate | Counsel on family planning options and agree on method to be used Start contraceptive if appropriate | Counsel on family planning options and agree on method to be used Start contraceptive if appropriate | Counsel on family planning and agree on method to be used Start contraceptive (all methods) |
| | Infant Feeding | <ul style="list-style-type: none"> Discuss and agree with mother on feeding method to be practiced Counsel on infant nutrition and how to feed properly | Assess mother's feeding practice and counsel accordingly. Strongly recommend the following: HIV-negative mothers: Breastfeed for 24 months (exclusively for the first 6 months, then add complementary) HIV-positive mothers: Breastfeed for 12 months with ARV prophylaxis (exclusively for first 6 months, then add) • If breastfeeding, counsel on how to feed properly • If replacement feeding, ensure AFASS criteria is met | | |
| | Danger Signs | <ul style="list-style-type: none"> Inform client of danger signs to look for during <u>postpartum</u> (see postnatal boxes for danger signs). Sensitize to visit the health facility immediately | Inform client of danger signs to look for during <u>postpartum</u> : Sensitize to visit the health facility immediately Mother: Vaginal bleeding / Convulsions / Fast or difficult breathing / Fever & weakness / Abdominal pain / Paleness / Oedema / Vaginal Discharge (Foul Smell) Infant: Reddening of umbilical area / puss from the stump / high fever / jaundice / refusal of breastmilk / convulsions / grunting / chest in-drawing | | |
| Examinations and Screening | Anemia | Assess for anemia before discharge If anemic, give increased Fe/Folate | Assess for signs of anemia at every visit: Hb Test < 11.5 g/L / Conjunctival Pallor / Palmar Pallor / Fast or Difficult Breathing / Fatigue / Swelling If patient has anemia: give double dose of Fe/Folate and advise on diet. Refer for blood transfusion if severe. | | |
| | TB | <ul style="list-style-type: none"> Screen for TB; start on tx if active If mother has positive sputum w/in 2 months of delivery, give baby INH prophylaxis for 6 months | 1) Assess for signs and symptoms of TB at every visit: <i>Cough > 2 weeks / Persistent Fever / Weight Loss / Severe malnutrition / > lymph nodes / Night sweats</i> 2) If signs of TB, take sputums or refer for CXR 3) If active TB, start mother on TB treatment immediately and infant on INH prophylaxis for 6 months | | |
| | Physical Examinations | <ul style="list-style-type: none"> Symphysis-Fundal Height Fetal Heart Rate (120-160 after 30 min) Uterine Contractions (2-4 in 10 min) Cervical dilation (1 cm/hr after 4 cm); | • Mother Abdomen & Vaginal Exam • Mother's Breast and Cervical Exam • Baby's Anterior Fontanelle • Baby's Umbilical Cord Stump | • Mother Abdomen & Vaginal Exam • Mother's Breast and Cervical Exam (Pap Smear or VIA) | • Mother Abdomen & Vaginal Exam • Mother's Breast and Cervical Exam (Pap Smear or VIA) |
| | Nutritional Status | Counsel on proper nutrition & diet for mother and baby postpartum | <ul style="list-style-type: none"> Give mother 200,000IU of Vitamin A within 8 weeks of delivery Assess infant's weight and height for age- if malnourished provide supplements or refer Counsel on proper nutrition and diet | | |
| | ¹³⁴ HIV Clinical Staging | If mother is HIV-positive, do WHO clinical staging | If mother is HIV-positive, do WHO clinical staging at EVERY VISIT | | |

L&D and POSTNATAL Care Package (continued from previous page):

Lab Investigation; Vaccination, Supplements & Prophylaxis

| | | LABOUR & DELIVERY (including the 6-hour postnatal visit) | 1ST POSTNATAL VISIT | 2ND POSTNATAL VISIT | 3RD POSTNATAL VISIT |
|---|---------------------------------|--|--|--|--|
| Period of Visit | | N/A | Within 1 week of delivery | Within 6 weeks of delivery | At 6 months old |
| Timing of Visit | | Labour, Delivery, and 1st 24 hours | 6 days postnatal | 6 weeks postnatal | 6 months postnatal |
| Lab Investigation | HIV | Test mother and partner for HIV (if status unknown or more than 3 months since negative test) | Test mother and partner for HIV (if status unknown or more than 3 month since negative test) | Test mother and partner for HIV (if status unknown or more than 3 month since negative test) | Test mother and partner for HIV (if status unknown or more than 3 month since negative test) |
| | CD4 | Take CD4 sample if mother is HIV-positive and has not had CD4 test for 6 months | Take CD4 sample if mother is HIV-positive and has not had CD4 test for 6 months | | |
| | Syphilis | If mother tested positive during pregnancy, give single dose of IM benzathine penicillin to newborn baby | | | |
| | Hb | If pregnant women showing any signs anemia, conduct Hb test. If Hb < 11.5 g/L, double the dose of Fe/Folate | If mother showing any signs of anemia (especially palor), conduct Hb test If Hb < 11.5 g/L, patient is anemic-- give double dose of Fe/Folate & advise on diet | | |
| | Urine | | | | |
| Vaccination, Supplements, and Prophylaxis | Vaccination | Give BCG and OPV-0 to the newborn baby | If not received at birth, give BCG and OPV-0 to the infant | Give DPT-HepB+Hib1 and OPV-1 to the infant at 6 weeks old | Infant should have completed OPV series and DPT-HepB-Hib series |
| | Fe/Folic Acid | Give 1 tablet of iron (200 mg) and folic acid (5 mg) daily to mothers If anemic, give double dose | Give 1 tablet of Iron (200 mg) and 1 tablet of Folic Acid (5 mg) daily to all postnatal mothers for 3 months If anemic, give double dose | | |
| | Mebendazole | If not received during pregnancy, give mother a single dose of Mebendazole | Give mother a single dose (500 mg tablet) of Mebendazole every 6 months | | |
| | IPTp for Malaria Prevention | Counsel mother on ITN use and provide ITN if available | Counsel mother on ITN use and provide ITN if available | | |
| | Cotrimoxazole & ARV Prophylaxis | <ul style="list-style-type: none"> Give mother Cotrimoxazole Give mother sdNVP + AZT for 7 days (Option A) or ART (Option B) Give baby daily NVP syrup (Option A & B) | <ul style="list-style-type: none"> Give HIV-positive mother Cotrimoxazole at each visit Give HIV-exposed infant Cotrimoxazole starting at 6 weeks If mother NOT on ART, give infant daily NVP through breastfeeding (for only 6 weeks if replacement feeding) If mother on ART (either prophylaxis or treatment), give infant NVP for only 6 weeks | | |

6.6.1 Routine quality antenatal, intrapartum & Post partum for all women and additional package of services for HIV positive pregnant & lactating women:

| Routine quality antenatal, intra-partum and postpartum care for all women, regardless of HIV status | Additional package of services for HIV positive pregnant and lactating women |
|--|--|
| <ol style="list-style-type: none"> 1. Health education and information on HIV, including safer sex practices during pregnancy malaria prevention, optimal infant feeding; family planning counseling and related services 2. Provider-initiated HIV testing and counseling, including HIV testing and counseling for women of unknown status at labor and delivery, or postpartum 3. Couple and partner HIV testing and counseling, including support for disclosure 4. Screening and prevention of Anemia 5. Treatment and Prevention of Malaria 6. Promotion and provision of condoms 7. Screening and prevention of HIV-related gender-based violence screening 8. Obstetric care, including history-taking and physical examination 9. Maternal nutritional support 10. Infant feeding counseling 11. Psychosocial support 12. Birth planning, birth preparedness (including pregnancy/postpartum danger signs), including skilled birth attendants 13. Tetanus vaccination 14. Iron and folate supplementation 15. Syphilis screening and management of STIs | <ol style="list-style-type: none"> 1. Ongoing counseling and support to encourage partner testing, adoption of risk reduction and disclosure <ul style="list-style-type: none"> • Special support and follow up of discordant couples 2. Linkage to ART center for lifelong chronic care using referral system 2. Clinical evaluation 3. WHO Clinical staging of HIV disease (refer to staging chart below) 4. Immunological assessment (CD4 cell count) where available 5. ART when indicated 6. Infant feeding counseling and support based on knowledge of HIV status 7. Maternal nutrition include assessment, counseling and support 8. ARV prophylaxis for PMTCT provided during the antepartum, intrapartum and postpartum periods 9. Co-trimoxazole prophylaxis 10. Malaria prevention and treatment 11. Additional counseling and provision of family planning services 12. TB screening and treatment 13. Counsel on other prevention interventions, such as safe drinking water 14. Supportive care, including, psycho social support, adherence support, and palliative care including pain and symptom management 15. Provide outreach services for clients and family members unable to come back for routine follow up.] 16. De-worming 17. Counseling and referral for women with history of harmful alcohol or drug use |

Put in appendix

WHO Adolescent and Adult HIV Clinical Staging

| | WHO Clinical Stage 1 Asymptomatic | WHO Clinical Stage 2 Mild Disease | WHO Clinical Stage 3 Advanced Disease | WHO Clinical Stage 4 Severe Disease (AIDS) |
|--|--|---|---|---|
| Symptoms Treat common opportunistic infections. Consult/refer if required. See the IMAI Acute Care guidelines module. Follow the treatment plan from district clinic. | No symptoms or only: ♦ Persistent generalized lymphadenopathy | ♦ Weight loss 5-10%** ♦ Sores or cracks around lips (angular cheilitis) ♦ Itching rash (seborrhoea or prurigo) ♦ Herpes zoster ♦ Recurrent upper respiratory infections such as sinusitis or otitis ♦ Recurrent mouth ulcers | ♦ Weight loss > 10%** ♦ Oral thrush (or hairy leukoplakia) ♦ More than 1 month: – Diarrhoea or – Unexplained fever ♦ Severe bacterial infections (pneumonia, muscle infection, etc) ♦ Pulmonary TB ♦ TB lymphadenopathy ♦ Acute necrotizing ulcerative gingivitis/periodontitis | ♦ HIV wasting syndrome ♦ Oesophageal thrush ♦ More than 1 month: – Herpes simplex ulcerations ♦ Recurrent severe pneumonia within 6 months ♦ Lymphoma* ♦ Kaposi sarcoma ♦ Invasive cervical cancer* ♦ CMV retinitis* ♦ <i>Pneumocystis</i> pneumonia ♦ Extrapulmonary TB* ♦ Toxoplasma* ♦ Cryptococcal meningitis* ♦ Visceral leishmaniasis* ♦ HIV encephalopathy (Significant neurological impairment interfering with independent functioning and not due to other cause will often improve on ARV treatment) |
| Prophylaxis | Cotrimoxazole prophylaxis if CD4 < 250 INH prophylaxis after excluding TB | ♦ Cotrimoxazole prophylaxis ♦ INH prophylaxis, after excluding TB | ♦ Cotrimoxazole prophylaxis ♦ INH prophylaxis, after excluding active TB | ♦ Cotrimoxazole prophylaxis ♦ INH prophylaxis, after excluding active TB |
| ARV therapy | ♦ Only if CD4 ≤ 350 | ♦ Only if CD4 ≤ 350 | ♦ All in stage 3 are medically eligible for ART, irrespective of CD4 count. | ♦ All in stage 4 are medically eligible for ART, irrespective of CD4 count. |

* Conditions marked with an asterisk require a clinical diagnosis – this could be obtained from records of a previous hospitalization. Muscle infection, *Pneumocystis* pneumonia, or any other severe pneumonia, toxoplasma, cryptococcal meningitis, and Extrapulmonary TB, etc are all infections which should be referred for hospital for diagnosis and treatment.

6.6.2. Essential Package for all newborns, infants and children and Additional package HIV-exposed infants and young children

| Essential Package for all newborns, infants and children | Additional package HIV-exposed infants and young children |
|--|--|
| <ol style="list-style-type: none"> 1 Essential newborn care (thermal care, hygienic cord care, early and exclusive breast feeding) for all and, if needed resuscitation 2 Prophylactic eye care 3 Postnatal follow-up and care regardless of place of delivery to support breast-feeding and identify and manage infection 4 Complete and timely immunization 5 Malaria prevention and treatment including access to malaria control programs and ITNs 6 Case management of diarrhea, pneumonia and sepsis 7 Nutritional assessment, counseling and support, and growth and development monitoring including Vitamin A and other micronutrient supplementation and deworming 8 Interventions to promote safe water, preventive hygiene practices, sanitation and hand-washing with soap 9 Community outreach efforts for follow up and ongoing care 10 TB screening, diagnosis and treatment with urgent HIV testing if TB-positive 11 PITC for every infant or child with signs, symptoms or history suggestive of HIV and rapid return of results to parent/caregiver | <ol style="list-style-type: none"> 1 Completion of ARV prophylaxis regimen as per the national guideline 2 Cotrimoxazole prophylaxis until confirmed HIV negative. 3 Immunizations according to national schedule (provision or referral) 4 Early PCR testing starting at 6 weeks of age, rapid return of results to facility, and provision of results to caregivers^{2nd} PCR done after cessation of breastfeeding, and rapid test done at 18 months of age 5 Regular follow-up visits according to “MOH Exposed Infant Visit Schedule”: <i>monthly visits for the first 6 months of life, and every 3 months thereafter until infant is 24 months of age</i> 6 Diagnostic and Management of HIV related conditions. Comprehensive counseling on the testing process, exposed infant care, and positive living 7 Intensive nutrition assessment and counseling on infant feeding, including a strong recommendation for exclusive breastfeeding 8 Growth monitoring (weight, height, MUAC) and developmental assessment (including milestones and head circumference). (refer to -- - section of IYCF) 9 Nutritional support and care for the HIV exposed infants and young children who are malnourished (ref to Nutrition section) 10 Linkage to ART services for confirmed HIV-positive infants/children, or infants of unknown status showing signs/symptoms of HIV 11 ART initiation for HIV-infected children (ref to ART section) 12 Treatment monitoring for all children receiving ART (refer to ART section) 13 Adherence support counseling for caregivers 14 Malaria prevention and treatment 15 Diagnosis and management of common childhood infections and conditions and integrated management of childhood illness (IMCI) 16 Diagnosis and management of TB 17 Isoniazid (INH) prophylaxis when indicated |

Care Guidelines for HIV-Exposed Infants

| Assess for: | Comments: | | At birth | At 6 wks | At 10 wks | At 14 wks | At 5 mo. | At 6 mo. | At 9 mo. | At 12 mo. | At 15 mo. | At 18 mo. | |
|---|---|--------------------|--|---|---|------------------------|--|--|--|--------------------------------|---|---|------------------------------|
| Immunization Status | Assess immunization status and refer if not up-to-date. | | BCG OPV-0 | OPV-1 DPT-HepB+Hib1 | OPV-2 DPT-HepB+Hib2 | OPV-3 DPT-HepB+Hib3 | N/A | Vitamin A | Measles | Vitamin A De-worming | N/A | Vitamin A De-worming | |
| Growth Measures | Check weight, length and MUAC. Compare to standards. If infant is underweight or stunted, refer to ART centre. After 6 months of age, MUAC < 12.5 cm indicates infant has moderate or severe acute malnutrition. | Girls | Under-weight | < 2.5kg | < 3.5kg | 4.5kg or less | 5.0kg or less | 5.5kg or less | 5.75kg or less MUAC < 12.5cm | 6.5kg or less MUAC < 12.5cm | 7kg or less MUAC < 12.5cm | 7.5kg or less MUAC < 12.5cm | 8kg or less MUAC < 12.5cm |
| | | | Stunted | < 45.5cm | < 51cm | < 54cm | < 58cm | < 59.5cm | < 61cm | < 65.5cm | < 69cm | < 72cm | < 75cm |
| | | Boys | Under-weight | < 2.5kg | < 4.0kg | 4.5kg or less | 5.5kg or less | 6.0kg or less | < 6.5kg MUAC < 12.5cm | < 7.0kg MUAC < 12.5cm | < 7.5kg MUAC < 12.5cm | 8.5kg or less MUAC < 12.5cm | < 8.75kg MUAC < 12.5cm |
| | | | Stunted | 46cm or less | < 52.5cm | < 55.5cm | < 60cm | < 62cm | < 63.5cm | 67.5cm or less | 71cm or less | < 74cm | < 77cm |
| Clinical Assessment for Signs and Symptoms of HIV | Evaluate for signs and symptoms suggestive of HIV in infants. Infants with any illness suggestive of HIV must be referred to an ART centre. | | Evidence of HIV is not usually present at birth | Look for signs of poor growth & infection, especially PJP | Check for any of these HIV signs/symptoms at each visit: Skin Rash / Poor growth (height) / Weight Loss / Pneumonia / Oral Thrush / Persistent Diarrhea (> 2wks) Recurrent Diarrhea / Ear Infection / Palpable Lymph Nodes in more than one place | | | | | | | | |
| | Evaluate & manage any sick child, regardless of HIV indication, according to WHO guidelines for Integrated Management of Childhood Illness (IMCI). Refer to a clinician or admit as necessary. | | Inquire about & assess for recent signs and symptoms of childhood illness: Inability to drink or breastfeed / Breathing Difficulty / Coughing / Vomiting / Fever / Diarrhea / Lethargy / Pallor | | | | | | | | | | |
| Developmental Assessment for Evidence of Delay | Failure to meet developmental milestones at each age may be suggestive of HIV. Low head circumference is also an indicator of delay and is suggestive of brain encephalopathy. Infants showing delay must be referred. | Milestones | N/A | Smiling | Controlling the head | Rolling over | Transferring objects from hand to hand | Sitting | Crawling | Standing | Walking with help | Pointing to at least 3 familiar objects (cognition) | |
| | | Head Circumference | < 32cm | < 36cm | < 37cm | < 38cm | < 38.5cm | < 39.5cm | < 41.5cm | < 43cm | < 44cm | < 44.5cm | |
| NVP Prophylaxis | • If mother <u>not on ART</u> and breastfeeding, infant should receive daily NVP until 1 wk after stopping breastfeeding (<i>only for 6 wks if not breastfeeding</i>) • If mother <u>receiving ART</u> either as treatment or prophylaxis, infant should receive daily NVP until 6 weeks old-- irrespective of breastfeeding | | Weight 2 -2.5 kg 1 ml once daily | Daily NVP for breastfeeding infants whose mothers are not receiving ART | | | | Daily NVP for b/feeding infants (if mother not on ART) | Daily NVP until 1 week after cessation of breastfeeding for infants whose mothers are not receiving ART (recommended to stop breastfeeding at 12 months) | | | | |
| | | | Weight > 2.5 kg 1.5 ml once daily | >6 weeks to 6 months 2 ml once daily | | | | >6 mo to 9 mo 3 ml daily | >9 months to end of breastfeeding 4 ml once daily | | | | |
| Cotrimoxazole Prophylaxis | All HIV-exposed infants must receive CTX until confirmed HIV-negative (after breastfeeding) | | Do not give Cotrimoxazole until 6 weeks | Cotrimoxazole Dosing | | | | | < 5.0kg | 5.0 - 14.9kg | | | |
| | | | | Oral Solution (200mg TMP + 40mg SMX per 5ml) | | | | | 2.5ml daily | 5ml daily | | | |
| | | | | Junior Tablet (100mg TMP + 20mg SMX) | | | | | 1 tab daily | 2 tabs daily | | | |
| | | | | Single-strength Tablet (400mg TMP + 80mg SMX) | | | | | 0.25 tabs daily | 0.5 tabs daily | | | |
| HIV Testing | PCR testing is necessary to definitively diagnose HIV in infants. Antibody tests cannot confirm HIV infection until 18 months. | | N/A | Do 1st PCR | Do 1st PCR if not yet completed; Do 2nd PCR 6 weeks after cessation of breastfeeding | | | | | | | Rapid Test confirmation at 18 months | |
| Feeding advice | Mothers should be strongly recommended to breastfeed for 12 months. If mother prefers to replacement feed, ensure AFASS* criteria is met. Counsel to minimize risk of mixed feeding. | | Exclusive breast feeding unless replacement feeding is AFASS*; no mixed feeding *AFASS: Acceptable, Feasible, Affordable, Safe, Sustainable | | | | | Continue breastfeeding while introducing other feeds (Complimentary Feeding) Exclusive replacement feeding only if AFASS | | | No breastfeeding unless necessary (if animal milk is not available) | | |

6.7 Recommended ARV regimens for PMTCT

Following the release of revised PMTCT guidelines by World Health Organization 2010, the Ministry of Health has chosen Option B as the preferred regimen and Option A as the alternate regimen. The Ministry of Health shall transition all sites to alternate regimen and later in a phased manner to the preferred regimen. In general, HIV positive pregnant women who are eligible for HAART (clinical stage III or IV and CD4 \leq 350 cells/mm³) should be initiated and maintained on lifelong treatment.

Currently facilities are advised to implement Option A until they receive communication from MOH to transition to Option B. This communication will occur once MOH has identified sufficient resources and prepared the supply chain to handle the transition”

Table 6.1: Recommended PMTCT regimens

| Alternate Regimen (Option A) | Preferred Regimen (Option B) |
|--|---|
| Mother If CD4 >350 <ul style="list-style-type: none"> Antepartum AZT (from 14 weeks) sdNVP + AZT/3TC at delivery AZT/3TC for 7 days postpartum If CD4 \leq350: Lifelong ART | Mother If CD4 >350 <ul style="list-style-type: none"> ART from 14 weeks of pregnancy until 1 week after breastfeeding has stopped If CD4 \leq350: Lifelong ART |
| Infant <ul style="list-style-type: none"> If breastfeeding: daily NVP from birth until one wk after breastfeeding has stopped If not breastfeeding or mother on ART: NVP for 6 wks | Infant <ul style="list-style-type: none"> NVP for 6 weeks (regardless of whether mother is breastfeeding) |

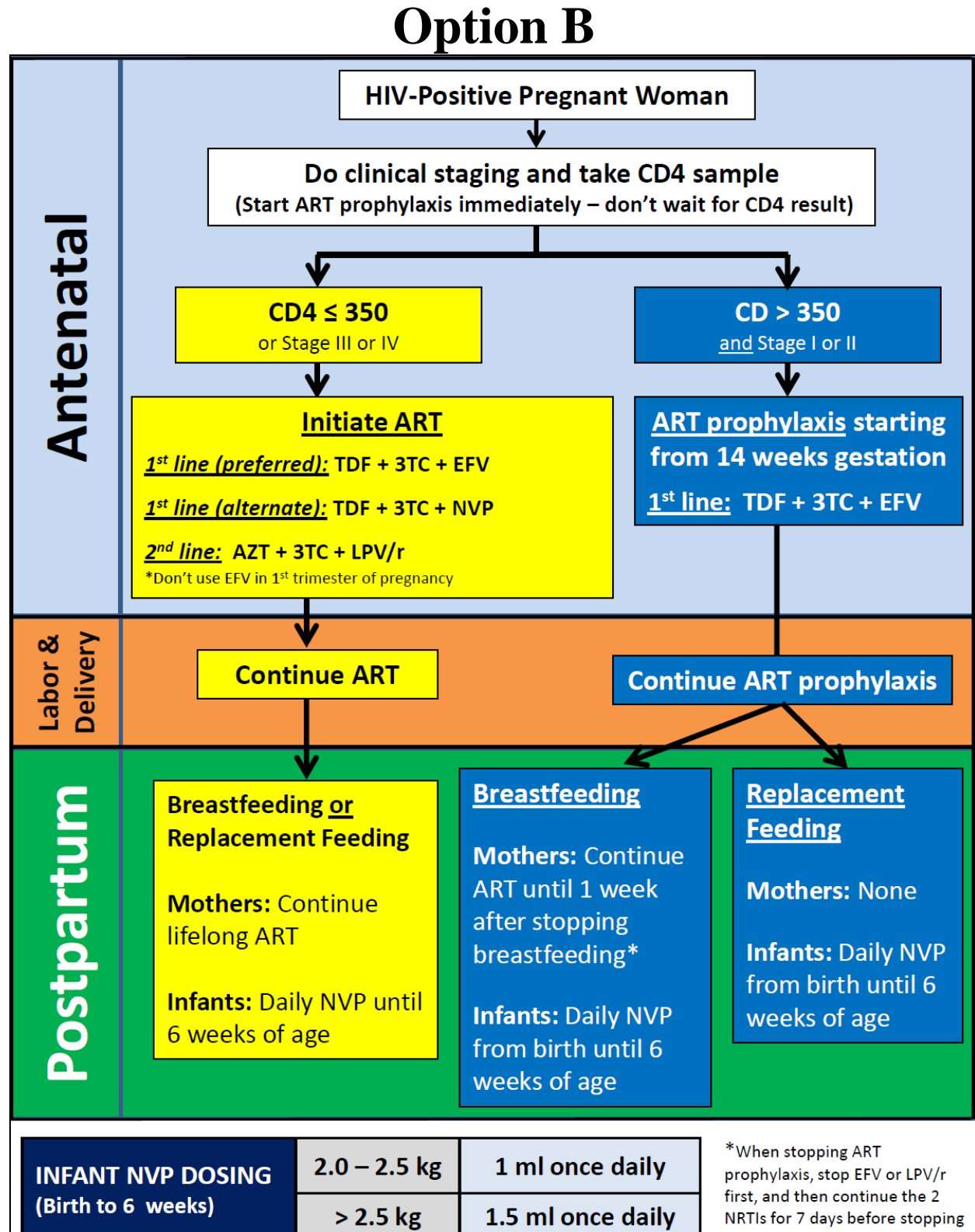
6.7.1 Implementation of the Option B (Preferred Option):

This option is being implemented in a phased manner with guidance from the Ministry of Health.

- The Pregnant Women living with HIV should receive HAART as prophylaxis (regimen according to the adult ART guidelines) from 14 weeks gestation (or as soon as diagnosed) until one week after the cessation of breastfeeding.
- Pregnant women who are already on ART should continue with the same ART regimen during pregnancy, unless the woman is on an Efavirenz-containing regimen and she is before 14 weeks of gestation, where EFZ will be substituted.

- Note: Women above CD4 >350 should not take NVP
 - * All HIV-positive pregnant women should take cotrimoxazole for life
- The HIV-Exposed Babies will receive NVP for six weeks only following birth
 - * All HIV-exposed babies will take cotrimoxazole from six weeks after birth until they are confirmed HIV negative

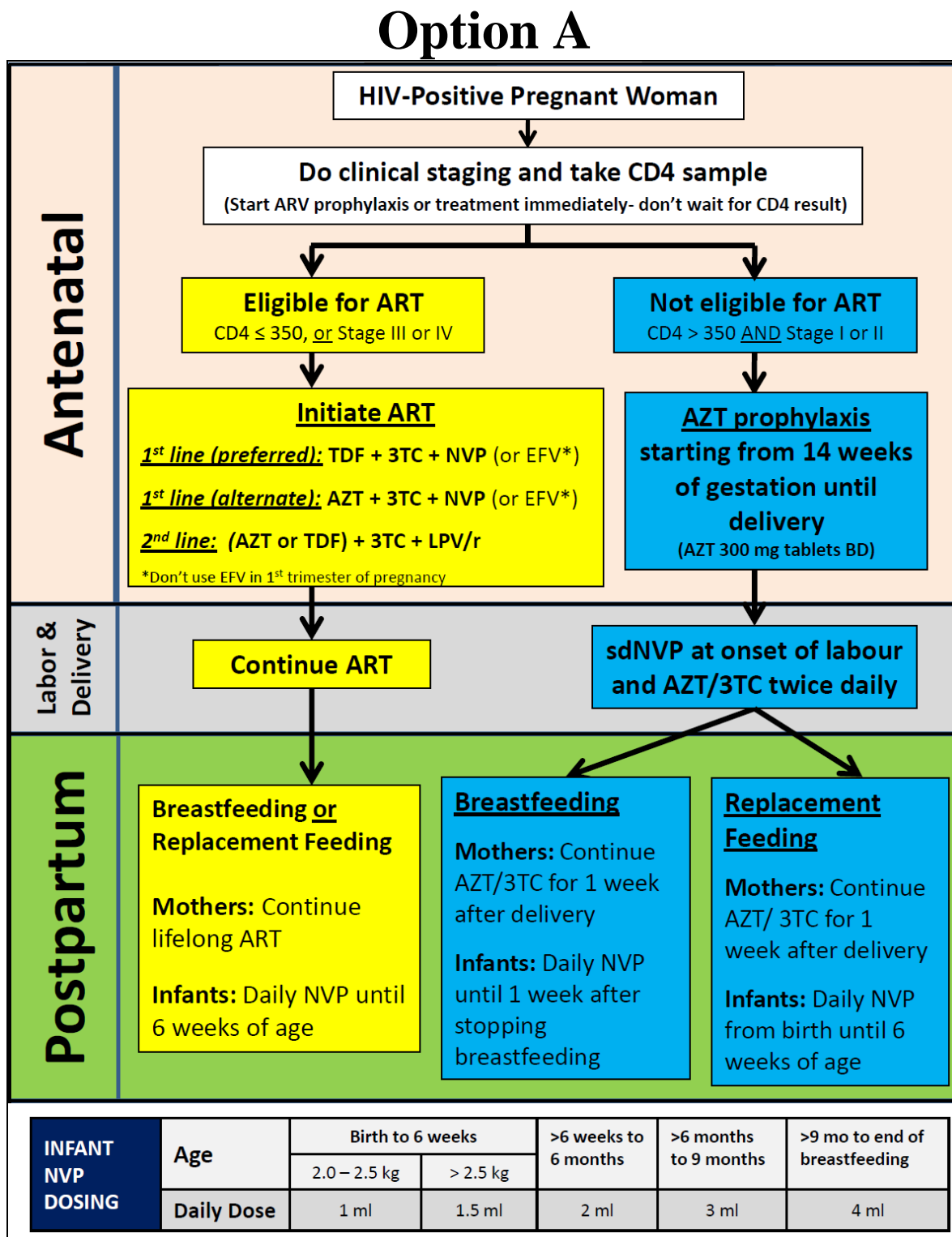
Figure 6.2 Preferred (Option B) ARVs for PMTCT



6.7.2 Implementation of the Alternate Option (Option A):

Ministry of health is currently transitioning all sites to this option while preparations for the preferred options are being finalized. Currently facilities shall implement Option A until they receive communication from MOH to transition to Option B. This communication will occur once MOH has identified sufficient resources and prepared the supply chain to handle the transition”

Figure 6.3 Alternative (Option A) ARVs for PMTCT



6.7.2.1 HIV-Positive Pregnant Women *Not Eligible for HAART*

This option is recommended if the following apply:

- The woman presents for antenatal care at or after 14 weeks of gestation
- She is not eligible for ART treatment by the WHO staging criteria (i.e. she is stage 1 or 2) AND she is not eligible for treatment by immunological criteria (i.e. CD4 >350)
- If she is eligible for treatment by the WHO staging or immunological criteria but HAART is *not available and it is not feasible for this woman to be referred.*
- There is no capacity for WHO HIV disease staging and it is not feasible for the HIV-positive woman to be referred for further HIV disease evaluation

ARV Recommendation for the mother:

- AZT 300mg twice daily from 14 weeks of gestation (or thereafter) until onset of labor
- Boosted by Nevirapine 200mg single dose at the onset of labor.
 - If single dose NVP is swallowed during false labor, **repeat the dose again when in actual labor.**
- and AZT 300mg + 3TC 150mg at onset of labor and every 12 hours until delivery
- Continue with AZT 300mg + 3TC 150mg twice daily for seven days after delivery

* Note: Nevirapine as a single dose shall be given during labor irrespective of the duration of AZT use.

** Begin a mother on ARV prophylaxis whenever she is first diagnosed or even if it is during labor.

*** All HIV-positive pregnant women shall take co-trimoxazole for life

ARV Recommendation for the infant:

If breastfeeding: Give Nevirapine syrup once daily from birth until one week after cessation of breastfeeding

If not-breastfeeding: Give Nevirapine syrup once daily for six weeks only after delivery

*All HIV-exposed babies shall take cotrimoxazole from six weeks after birth until they are confirmed HIV negative.

6.7.2.2 HIV+ Pregnant Women *Eligible for HAART*

This intervention is recommended if the following apply:

- Woman is already on HAART
- Woman is eligible for ART by the WHO staging criteria (stage 3 or 4)
- A CD4 cell count has been done, and it is ≤ 350 and/or she has a high viral load
- Woman is co-infected with tuberculosis

ARV Recommendation for the Mother:

- Start woman on the ART regimen recommended in the Adult ART Guidelines (**see section -- on Adult ART guidelines – Chapter 3.0**)

- Women who are already on ART will continue with the same ART regimen, unless the woman is on an Efavirenz-containing regimen AND she is before 14 weeks of gestation

* Note: Nevirapine as a single dose shall not be added during labor.

** Begin mother on HAART whenever she is first diagnosed, even if it is during labor or within one week after labor.

*** All HIV-positive pregnant women should take co-trimoxazole for life

ARV Recommendation for the infant:

- All exposed infant should receive Nevirapine syrup - once daily for six weeks, whether breastfeeding or not
- * All HIV-exposed babies should take Cotrimoxazole from six weeks after birth until they are confirmed HIV-negative

6.7.2.3 Recommended ARVs use for PMTCT under Special Circumstances:

- Elective Caesarian Section: Give the HIV positive woman ARV's (NVP tablet and AZT+3TC or HAART) at least 2 hours before the Elective C/section.
- Precipitate Delivery: If the baby is delivered less than two hours after the mother receives NVP tablet, the baby should be given Nevirapine syrup *immediately* after birth.
- Mother Missed Antenatal ARV's: Where the mother did not receive ARVs for prophylaxis during pregnancy or did not deliver at a health facility, the baby will be given:
 - NVP syrup at first contact, throughout the breastfeeding period and until one week after cessation of all breastfeeding or until HIV status is confirmed.
 - If baby is on replacement feeding, give NVP syrup for six weeks only
- All infants and children aged less than 2 years diagnosed HIV-positive, shall begin immediately on the appropriate ART regimen
- Born Before Arrival (BBA): All BBA's (Born Before Arrival) shall be treated like all other exposed babies with respect to NVP syrup.
- HIV-TB Co-infection: Women with TB co-infection on rifampicin, will not take NVP or any PIs (ATV or LPV) containing regimen
- Anemia: A woman with anemic (Hb<7.5) and has a CD4>350, she will not be put on AZT. She will be referred to ART clinic and, put on TDF-based HAART (See preferred option above)

6.8 Community PMTCT

Community involvement is necessary for successful implementation, scale-up and utilization of PMTCT & EID services in the country. Community mobilization and education has been going on albeit at a comparatively lower level. The PMTCT & EID service are now widely availability at the lower levels where community mobilization and education should improve uptake and create appropriate demand for these services. The programme has revised its communication strategy for mobilization all stakeholder support these services. The Village Health Team system will be strengthened, facilitated and utilized to deliver key community PMTCT interventions. In addition existing community programmes will be utilized

Key community PMTCT interventions will include;

1. Community mobilization and sensitization to utilize RH/PMTCT services.
2. Promote pro-active male participation in RH/PMTCT services
3. Peer mothers for PMTCT. ----
4. Psycho-social support groups. ---
5. Health Education and Promotion.---
6. Mother-Baby Pair follow up.---
7. Home based HIV Counseling and Testing.
8. Community distribution of family planning commodities.
9. Community linkages and tracking to care and support groups.
10. Community growth promotion and development monitoring.---
11. Sexual and Gender Based Violence (Sensitization, prevention and Support)

6.9 Monitoring the PMTCT Interventions

6.9.1 Monitoring of HIV positive pregnant and lactating women and exposed babies

- Women who attend all the four focused Antenatal visits.
- Women who deliver under skilled care.
- Women shall receive a CD4 test every six months. If the CD4 drops below 350, she should be started on HAART.
- Regular assessment of drug adherence is recommended for women and children under PMTCT prophylaxis or ART treatment
- Additional clinical and laboratory monitoring of adverse reactions related to ARV drugs shall be based on potential adverse reaction of the drugs used. Mothers on NVP should be monitored for Jaundice, skin rash and Liver function tests. Those on AZT should be monitored for anemia while those on TDF shall have renal function tests (use table format).
- All mothers and babies receiving ARVs should receive standard ART monitoring (Un pack ART monitoring or if it's in the ART section, refer to it)

Health workers should use existing PMTCT/ART monitoring tools

6.9.2 PMTCT program monitoring


Subsequent implementations of PMTCT interventions shall be based on evidence obtained from data and information collected from all participating health units. Integrated Reproductive Health/PMTCT registers are used for primary data collection. The program has identified and recommended that the following core indicators be used for monitoring the output as incorporated in the Health Management Information System (HMIS).

These core indicators include:

- Number of pregnant women counseled, tested and received results for HIV
- Number of pregnant women who tested positive for HIV
- Number of mothers who received ARVs for PMTCT by regimen
- Number of mothers who received HAART during pregnancy
- Number of babies who received ARVs for PMTCT
- Number of exposed babies tested for HIV

- Number of exposed babies initiated on Cotrimoxazole prophylaxis
- Number of HIV exposed babies tested HIV positive
- Number of HIV positive babies linked to ART

The data collected shall be forwarded to heads of health sub-districts, the district directors of health services and to the MoH headquarters at the AIDS Control Program (ACP) at the end of each month. Information generated should be used to inform planning for the drugs, reagents and other logistics procurement processes, estimate staff requirements, identify bottlenecks in the PMTCT program and find solutions at the source of data (health facility), Health Sub-district and District.



7.0 Guidelines on feeding the Infant/Young child who is exposed to HIV

7.1 Introduction

Infant feeding in the context of HIV has implications for child survival. Balancing the risk of infants acquiring HIV through breast milk with the higher risk of death from malnutrition, diarrhea and pneumonia among non-breastfed infants is a challenge. Protecting the infant from the risk of death from these causes is as important as avoiding HIV transmission through breastfeeding. Replacement feeding unquestionably prevents all postnatal transmission but has been associated with increased risk of death from other causes.

MTCT accounts for the vast majority of new infections in children. Infants can acquire HIV from their infected mothers during pregnancy, at the time of delivery, or after birth through breastfeeding. Transmission through breastfeeding accounts for up to 20% of MTCT. It is estimated that more than 20,000 children in Uganda are infected with HIV annually through MTCT if there is no intervention, but with various PMTCT interventions this rate can be reduced by 50-95%. Among the key strategies in PMTCT is routine HIV counseling and testing during pregnancy labor and lactation, antiretroviral drug (ARV) prophylaxis and treatment for HIV-infected pregnant women, lactating mothers and their infants and appropriate infant and young child feeding practices.

Current evidence indicates that exclusive breastfeeding and the use of antiretroviral drugs greatly reduce MTCT. The effectiveness of ARV interventions with continued breastfeeding by HIV infected mothers until the infant is 12 months of age capitalizes on the maximum benefit of breastfeeding to improve the infant's chances of survival while reducing the risk of HIV transmission.

Early diagnosis of HIV in children has made it possible to classify HIV- exposed children into four categories:

- HIV-exposed but not HIV-infected
- HIV-exposed and HIV-infected
- HIV exposed and HIV infected on ARV treatment
- HIV-exposed but with unknown HIV status

These categories are useful for deciding appropriate care, treatment and feeding for these children.

7.2 Aims and objectives

This section aims at ensuring optimal feeding for the four categories of infants and young children exposed to HIV.

The objectives are to:

1. Promote optimal feeding for the HIV-exposed children
2. Minimize HIV transmission through breastfeeding

7.3 Implementation

7.3.1 During pregnancy

Pregnant women who are infected with HIV are at higher risk of anemia, malnutrition, opportunistic infections and death. To maintain their nutrition and health status, they need to eat twice the usual amount of high energy foods (e.g., potatoes, cassava, cereal meals, matooke), protein giving foods (peas, beans, fish, meat, chicken), fruits (papaya, sweet banana, pineapple, mangoes) and green leafy vegetables (Nakati, dodo, bugga, sukuma-wiki, spinach) to meet all these extra demands of energy, protein, vitamins and minerals.

- Educate and counsel women on the recommended feeding practices during pregnancy and breastfeeding.
- Counsel HIV-infected pregnant women on the recommended infant feeding practices.
- Ensure that the pregnant woman starts ARVs as per the PMTCT guidelines
- Assess all pregnant women for anemia and malnutrition at facility at every visit and community level
- Health workers providing the counseling on infant and Young child feeding should endeavor to undergo training in maternal, infant and young child feeding counseling.

7.3.1.1 Key messages to HIV infected pregnant and breastfeeding mothers on maternal nutrition

- Counsel on;
 - Adding at least two extra meals per day during pregnancy to regular meals, and three extra meals during breastfeeding.
 - Eating plenty of fruits and vegetables with every meal. Women should drink enough liquids every day (8 glasses or 3 tumpecos).
 - Eating foods rich in vitamin C such as oranges, pawpaws, mangoes, avocados, bananas to enhance absorption of iron.
 - Differing from drinking tea or coffee close to (less than 1 hour) or with meals as this may interfere with absorption of iron causing anemia.
 - Sleeping under an insecticide-treated mosquito net and provide presumptive anti-malarials in accordance with the national guidelines on malaria prevention and treatment to prevent malaria which may result in anemia
 - Consumption of iodized salt to prevent pregnancy complications (abortions, miscarriages and stillbirths), fetal, infant and young child brain damage, cognitive and physical growth retardation, maternal goiter.
 - Avoiding consumption, of alcohol, narcotics or tobacco products and medicines that are not prescribed by a trained health care provider
 - Maintaining high levels of personal and food hygiene and food safety to prevent infections.
- Provide and encourage adherence to iron and folic acid supplementation in accordance with the maternal nutrition and Reproductive health guidelines
- Provide vitamin A capsule to the postpartum mothers immediately after delivery or within 8 weeks to help build your baby's immunity.
- Provide de-worming tablets as prescribed to treat worms and to prevent anemia from the 2nd trimester as per reproductive health guidelines.
- Encourage mothers to attend antenatal care at least four times during pregnancy and always follow your health worker's recommendations.

- Pregnant adolescent mothers need extra care, more food and more rest than an older pregnant or breastfeeding mother to enable their bodies to grow fully and ensure that it produces enough milk for their baby

Box 7.1

The Ministry of Health Recommends the following feeding practices for HIV exposed infants

a) HIV negative infants and those of unknown status

- i) Exclusive breastfeeding for the first 6 months and continued breastfeeding up to 12 months of life while their mothers receive HAART or ARV prophylaxis.
- ii) From six months, the infant should be started on appropriate complementary feeding. Breastfeeding should then only stop once a nutritionally adequate and safe feed (without breast milk) can be provided. The following conditions must be met; Affordable, Feasible, Acceptable, Safe and Sustainable (AFASS).

b) Infants and young children known to be already HIV-infected

Exclusive breastfeeding for the first six months of life and continued breastfeeding up to two years of age or beyond.

Mothers known to be HIV positive should be provided with lifelong ART if eligible or ARV prophylaxis to reduce HIV transmission through pregnancy, labor, delivery and Breastfeeding.

- Actively promote and support Baby Friendly Health facility Initiative through implementation of the key requirements:
- Counsel all pregnant women about the benefits and management of breastfeeding; MTCT, Importance of adhering to ARV regimen.
- Counsel on the benefits of exclusive breastfeeding for the first six months regardless of the HIV sero status.
- Demonstrate to mothers how to position the infants when breastfeeding, and how to maintain lactation even if they should be separated from their infants. Pay particular attention to the positioning and attachment to prevent conditions such as cracked nipples, mastitis which increases the risk of HIV transmissions.
- Give newborns and infants up to six months of age only breast milk; no food or drink other than breast milk should be given, unless medically indicated.
- Link the mothers to support systems such as mother support groups, lactation clinics on discharge from the hospital or clinic.
- The National Regulations on marketing of Infant and Young Child Foods prohibits advertising, receiving and promoting breast milk substitutes in health facilities / by the companies and health workers.

7.3.2 During labor and delivery

- Mothers who are not on ARV drugs should receive ARV for prophylaxis in accordance with the ART and PMTCT guidelines.

- Help mothers initiate breastfeeding within an hour of birth including cases of caesarian section
- Newborn infants should be fed on only colostrum (the first milk) and not be given pre-lacteal feeds such as glucose, dill/ gripe water, mushroom soup; herbal extracts, etc
- ARV prophylaxis should be administered to the baby as per the PMTCT guidelines
- Continue to counsel on demand feeding, Exclusive breastfeeding, ways of holding and putting the baby to the breast (positioning and attachment) to enhance breastfeeding

7.3.3 During lactation

7.3.3.1 All HIV exposed infants should be EBF for the first six months.

- **HIV exposed but not HIV infected**
 - ✓ From six months continue BF until the infant is 12 months old. After 12 months, BF should be stopped only if nutritionally adequate and safe diet which includes source of milk can be provided. From birth and throughout the breastfeeding period, both the mother and baby should receive ARVs as per PMTCT guidelines
- **HIV exposed and HIV infected**
 - ✓ Continue BF as per the general population until the child is 24 months and beyond.
- **HIV exposed and HIV infected on ARV treatment**
 - ✓ Continue BF as per the general population until the child is 24 months and beyond.
- **HIV exposed and unknown HIV status**
 - ✓ Endeavour to establish the status of the infant. In the meantime, Encourage exclusive BF for the first six months, introduce complementary feeds at six months with continued BF until the infant is 12 months old. During this period both the mother and baby should receive ARV prophylaxis as per PMTCT guidelines. Once the infant's HIV status is established, follow the above 1), 2) or 3) guidelines as appropriate
 - ✓ Mothers known to be HIV positive should be provided with life long ART if eligible or ARV prophylaxis to reduce HIV transmission through pregnancy, labor, delivery and Breastfeeding. When ARVs are unavailable, mothers should be counseled to exclusively breastfeed for the first six months; the HIV sero-status for the infant should be established.
 - ✓ If negative, the mother should consider discontinuing breastfeeding and use replacement feeding if affordable, feasible, acceptable, sustainable and safe (AFASS).
 - ✓ If infant is positive continue to breastfeed up to two years
 - ✓ Complementary feeds should be started at six months of age

7.3.4 Complementary feeding 6-12 months

- The mother should be encouraged breastfeed as often as the infant wants
- HIV positive mothers who have decided to stop breastfeeding should feed their infants at least 500 ml of milk every day. (A full NICE cup is 500 ml.)
- When counseling mothers on complementary feeding; consider the following:
 - **F=Frequency**, (Feed your baby 3-5 times a day increasing frequency as the baby grows).
 - **A = Amount**, Start with 2-3 heaped tablespoons per feed. Gradually increase the amount of food to at least one-third (1/3) of a NICE cup. (A full NICE cup is 500 ml.)

- **T = Thickness** (consistency), mothers should mash and soften the food for easy swallowing and digestion. Meat should be minced, fish flaked and bean skin removed. Animal milk or margarine/ ghee/oil (not water) can be used to soften and enrich the food. Food thickness should be gradually increased as the infants grow.
- **V = Variety** (different kinds of foods). Encourage mothers to include at least one type of food from the food groups below daily:
 - ✓ a) **STAPLE FOODS**: Millet flour, sorghum flour, maize flour, potatoes, matooke etc.
 - ✓ b) **LEGUMES**: Fresh or dry beans, peas, groundnuts
 - ✓ c) **ANIMAL SOURCE**: Milk, Meat, chicken, fish, eggs
 - ✓ d) **VEGETABLES**: dark green leafy vegetables (dodo, nakatti, buga), tomato, eggplant, carrot, etc.
 - ✓ e) **FRUITS**: Passion fruit, mango, pawpaw, orange, banana, watermelon, pineapple, avocado, sugarcane juice etc.
 - ✓ f) **FATS AND OIL**: ghee, shea butter, margarine, palm oil
- **A = Active/responsive feeding**. Mothers should be encouraged to patiently and actively feed their infants and young children and to use separate plate for the infant to ensure adequate intake.
- **H = Hygiene** Counsel Mothers on hygienic food preparation and handling to avoid Foods given to contamination leading to diarrhea and illness. This includes:
 - Use of clean open cups. Discourage use of feeding bottles, teats or spouted cups as they are very difficult to clean

7.3.5 Complementary feeding 12-24 months

- Discourage breastfeeding for mothers, whose infants are HIV negative at 12 months. Alternative forms of milk should be given; of at least 500ml a day. (1 TUMPECO)
- Encourage mothers to feed their children 5 times a day - 3 main meals and 2 extra foods between meals (snacks).

7.3.5.1 Complementary feeding 12-24 months who are HIV infected

- Encourage mothers to continue breastfeeding on demand, day and night up to 24 months and beyond to maintain the baby's health and nutrition.
- Counsel caregivers to:
 - Give 1 extra snack to well children and 1 extra meal (or 2 snacks) at onset of sickness.
 - Give 3 extra meals (or 2 extra meals and 1 snack) when sick and losing weight

7.3.6 Feeding a child 2– 6years

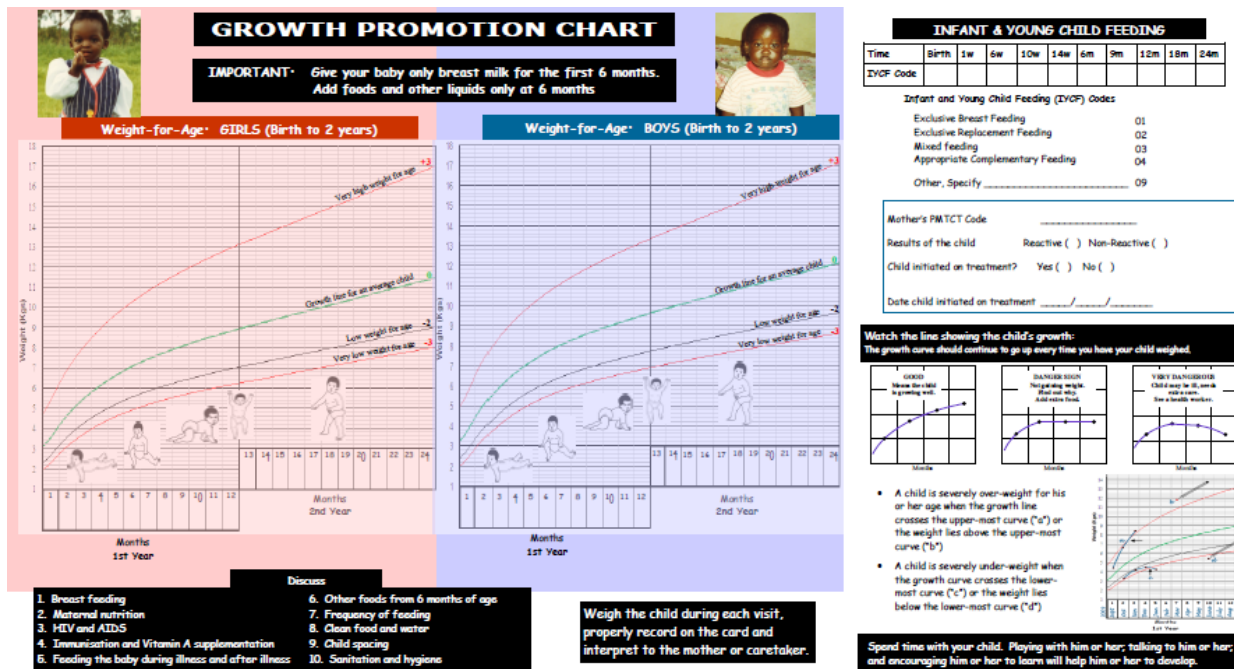
- Encourage mothers to give a variety of foods prepared from the family meal (each meal should consist of a carbohydrate, protein, vegetables) at least 3 main meals a day.
- Encourage care givers to give nutritious snacks between meals e.g. a fruit (banana, pawpaw, orange, mangoes) egg, bread, enriched thick porridge or a glass of milk.

Sick and recuperating infants and children should be fed on small, frequent meals which include porridge enriched with milk/g.nut paste/margarine/honey/oil/cooked, skinned, mashed beans; thickened soups, etc

7.4 Growth promotion and monitoring

- All HIV exposed children should be monitored for growth and development monthly.
- Weight should be plotted and interpreted on the child health card at least once a month.
- Counsel the mother/ caregiver on the child's growth trend and take appropriate action where necessary.

Figure 7.1: Growth promotion chart



7.4.1 Additional support messages

- HIV positive mothers who decide to stop breastfeeding at anytime should stop gradually. This transition period should be between one to two weeks which is not too long to increase exposure and not too short to cause physical and psychological trauma to the mother and baby.
- Mechanism of transition includes:
 - Expressing BM and feeding infant/child by cup
 - Heat treating the expressed breast milk if Infant is HIV uninfected and mother and infant are not on ARV prophylaxis
 - Substituting the expressed BM with suitable replacement feed gradually
- Replacement feeding (using alternative milk other than breast milk in the first 6 months of life) should be recommended only in extreme circumstances such as: mother absent, dead or mentally disabled, in accordance with the Regulations on the Marketing of Infant and Young Child Foods.

- Follow up all HIV-exposed infants, and continue to offer infant feeding counseling and support to mothers/caregivers.
- If an HIV-exposed child falls sick, counsel the mother/caregiver to feed the child even more frequently than usual in order to meet that child's nutritional requirements.

8. Appendices

APPENDIX 1: WHO Staging for HIV Infection and Disease in Adults & adolescents

| |
|--|
| <p>Clinical Stage I:</p> <ol style="list-style-type: none"> 1. Asymptomatic 2. Persistent generalised lymphadenopathy <p><i>Performance Scale 1: Asymptomatic, normal activity</i></p> |
| <p>Clinical Stage II:</p> <ol style="list-style-type: none"> 1. Moderate weight loss (less than 10% of presumed or measured body weight) 2. Minor mucocutaneous manifestations (seborrhoeic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular stomatitis) 3. Herpes zoster within the last 5 years 4. Recurrent upper respiratory tract infections, e.g., bacterial sinusitis, tonsillitis, otitis media and pharyngitis <p><i>And/or Performance Scale 2: Symptomatic but normal activity</i></p> |
| <p>Clinical Stage III:</p> <ol style="list-style-type: none"> 1. Severe weight loss (more than 10% of presumed or measured body weight) 2. Unexplained chronic diarrhoea for more than 1 month 3. Unexplained prolonged fever, intermittent or constant, for more than 1 month 4. Oral candidiasis 5. Oral hairy leukoplakia 6. Pulmonary tuberculosis (current) 7. Severe bacterial infections such as pneumonias, pyomyositis, empyema, bacteremia or meningitis 8. Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis 9. Unexplained anemia ($<8\text{gm/dl}$), neutropenia ($<0.5 \times 10^9$ per litre), or chronic thrombocytopenia ($<50 \times 10^9$ per litre) <p><i>And/or Performance Scale 3: Bed-ridden for less than 50% of the day during the last month</i></p> |
| <p>Clinical Stage IV:</p> <ol style="list-style-type: none"> 1. HIV wasting syndrome – weight loss of more than 10%, and either unexplained chronic diarrhoea for more than 1 month, or chronic weakness or unexplained prolonged fever for more than 1 month 2. <i>Pneumocystis pneumonia</i> (PCP) 3. Recurrent severe bacterial pneumonia 4. <i>Toxoplasmosis of the brain</i> 5. Cryptosporidiosis with diarrhoea for more than 1 month 6. Chronic isosporiasis 7. Extrapulmonary cryptococcosis including meningitis 8. Cytomegalovirus infection (retinitis or infection of other organs) 9. Herpes simplex virus (HSV) infection, mucocutaneous for more than 1 month, or visceral at any site 10. Progressive multifocal leukoencephalopathy (PML) 11. Any disseminated endemic mycosis such as histoplasmosis, coccidioidomycosis 12. Candidiasis of the oesophagus, trachea, bronchi or lungs 13. Atypical mycobacteriosis, disseminated 14. Recurrent non-typhoid salmonella septicaemia 15. Extrapulmonary tuberculosis 16. Lymphoma 17. Invasive cancer of the cervix 18. Kaposi's sarcoma 19. HIV encephalopathy – disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing slowly over weeks or months, in the absence of concurrent illness or condition other than HIV infection that could account for the findings 20. Atypical disseminated leishmaniasis 21. Symptomatic HIV-associated nephropathy or symptomatic HIV associated cardiomyopathy <p><i>And/or Performance Scale 4: Bed-ridden for more than 50% of the day during the last month</i></p> |

APPENDIX 2: WHO Clinical Staging of HIV for infants & children with HIV infection

| |
|---|
| Clinical Stage I: <ol style="list-style-type: none"> 1. Asymptomatic 2. Persistent generalised lymphadenopathy |
| Clinical Stage II: <ol style="list-style-type: none"> 1. Unexplained persistent hepatosplenomegaly 2. Papular pruritic eruptions 3. Extensive wart virus infection 4. Extensive molluscum contagiosum 5. Recurrent oral ulcerations 6. Unexplained persistent parotid enlargement 7. Lineal gingival erythema 8. Herpes zoster 9. Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) 10. Fungal nail infections |
| Clinical Stage III: <ol style="list-style-type: none"> 1. Unexplained moderate malnutrition not adequately responding to standard therapy 2. Unexplained persistent diarrhoea (14 days or more) 3. Unexplained persistent fever (above 37.5 °C, intermittent or constant, for longer than one month) 4. Persistent oral candidiasis (after first 6 weeks of life) 5. Oral hairy leukoplakia 6. Acute necrotizing ulcerative gingivitis/periodontitis 7. Lymph node TB 8. Pulmonary TB 9. Severe recurrent bacterial pneumonia 10. Symptomatic lymphoid interstitial pneumonitis 11. Chronic HIV-associated lung disease including bronchiectasis 12. Unexplained anaemia (<8.0 g/dl), neutropenia (<0.5 x 10⁹/L³) or chronic thrombocytopenia (<50 x 10⁹/L³) |
| Clinical Stage IV: <ol style="list-style-type: none"> 1. Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy 2. Pneumocystis pneumonia (PCP) 3. Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) 4. Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site) 5. Extrapulmonary TB 6. Kaposi sarcoma 7. Oesophageal candidiasis (or Candida of trachea, bronchi or lungs) 8. Central nervous system toxoplasmosis (after the neonatal period) 9. HIV encephalopathy 10. Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over 1 month 11. Extrapulmonary cryptococcosis (including meningitis) 12. Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis) 13. Chronic cryptosporidiosis (with diarrhoea) 14. Chronic isosporiasis 15. Disseminated non-tuberculous mycobacteria infection 16. Cerebral or B cell non-Hodgkin lymphoma 17. Progressive multifocal leukoencephalopathy 18. HIV-associated cardiomyopathy or nephropathy |

APPENDIX 3: ART-Associated adverse clinical events

Hepatotoxicity

- Usually an otherwise unexplained elevation of ALT that may be asymptomatic or may be associated with symptoms of hepatitis (e.g. jaundice, anorexia, dark urine).
- May be caused by any ARV drug and may be more frequent or severe in those with chronic hepatitis such as HBV or HCV
- Worst offender is usually Nevirapine especially in women with CD4 greater than 250

Hyperglycemia

- Results from peripheral and hepatic insulin resistance, insulin deficiency, and a reduced capacity of the liver to extract insulin
- It occurs with all PIs in 3-17% and within the first 60 days.
- When this occurs, hyperglycemia should be treated and continue with the drug

Lactic acidosis

- Probably due to mitochondrial toxicity. NRTIs inhibit DNA polymerase gamma, which is responsible for mitochondrial synthesis
- Presentation includes unexplained gastrointestinal symptoms (abdominal pain, nausea, vomiting, anorexia, diarrhea, hepatomegaly, distension), wasting, dyspnoea, ascending weakness, and/or paraesthesias
- Lab shows elevated lactate ($>2\text{-}5\text{ mmol/ml}$), elevated anion gap ($\text{Na} - [\text{Cl} + \text{CO}_2] >16$,
- Treatment may require life support and intravenous bicarbonate

Fat redistribution

- Lipodystrophy syndrome includes visceral or central fat accumulation ("buffalo hump", visceral, abdominal fat collection, breast enlargement, and lipomas) and/or peripheral fat atrophy (thin extremities, facial thinning, buttock thinning)
- Treatment involves exercise programs and cosmetic surgery

Hyperlipidaemia

- Changes in blood lipids including cholesterol and triglycerides usually attributed to PIs. The mechanism is unclear, but may be due to PI interference with lipid metabolism. Very high levels may lead to pancreatitis and related cardiovascular disease.
- Preferred intervention is diet and exercise but some patients may need additional medication
- Where possible, patients on PIs should have baseline fasting lipid profiles and repeated every 6 months

Skin rash

- Rash reactions are most common with NNRTIs, especially Nevirapine 10-20%. Most rash reactions are mild, maculopapular and occur within the first 12 weeks without systemic findings. Severe reactions occur in 1% and include:
 - Stevens-Johnson syndrome
 - Toxic epidermal necrolysis (TEN)
 - Drug rash, eosinophilia, and systemic syndromes (DRESS) with fever and multiple organ involvement
- Discontinue drug if rash is wet and associated with fever, desquamation, mucous membrane involvement, blistering, or arthritis

APPENDIX 4: Antiretroviral Drug Toxicity

| Antiretroviral Drug | Primary toxicities | Minor toxicities | Monitoring/Management |
|---------------------|---|---|--|
| Zidovudine (ZDV) | Hematological (Anemia, neutropenia, thrombocytopenia), myopathy, GI intolerance | Blue to black discoloration of nails, nausea and headache | For severe anemia: <ul style="list-style-type: none"> Reduce dose or change to d4T or transfuse For myopathy: <ul style="list-style-type: none"> Discontinue if CPK high |
| Lamivudine (3TC) | Painful peripheral neuropathy, pancreatitis | Skin rash, headache | Do serum amylase. Stop if elevated. Restart when resolved or change to ABC |
| Stavudine (d4T) | Painful neuropathy, lipoatrophy, lactic acidosis, hepatitis, pancreatitis | Insomnia, anxiety, panic attacks | Severe peripheral neuropathy, abnormal serum amylase and transaminases, discontinue therapy |
| Didanosine (ddI) | Pancreatitis, painful peripheral neuropathy | Abdominal cramps, diarrhea | Discontinue if neuropathy severe, raised serum amylase and transaminases |
| Tenofovir (TDF) | Renal dysfunction | | Monitor renal function at baseline, and every 6 months. Avoid use in pregnant women except if other alternatives are not available. |
| Abacavir (ABC) | Hypersensitivity reaction, | Lactic acidosis | Discontinue therapy and don't restart when resolved |
| Nevirapine (NVP) | Skin rash, Stevens-Johnson syndrome, hepatotoxicity | | Low-dose over first 2 weeks minimizes rash occurrence. If mild or moderate continue cautiously or substitute with EFV. If severe stop NVP and permanently if hepatitis +ve |
| Efavirenz (EFV) | Nightmares, rash, hepatitis | Dizziness, | Rash in 10% but rarely severe <1%; CNS symptoms often resolve 2-4 weeks. Stop if hepatitis is confirmed. |
| Lopinavir/Ritonavir | Diarrhea, skin rash | Headache, weakness | Diarrhea rarely severe |
| Nelfinavir (NFV) | Diarrhea, lipid, glucose & liver abnormalities, | | Diarrhea occurs 10-30% at start of therapy but often resolves on its own |
| Indinavir (IDV) | Nephrolithiasis, hepatitis, lipid, glucose abnormalities | Headache, rash, retinoid-like effects, alopecia, | Ensure adequate re-hydration (1.5 L/day). Monitor liver enzymes |
| Emtricitabine (FTC) | Lactic acidosis with hepatic steatosis | Hyperpigmentation Skin coloration | Do serum lactate if suspicious symptoms exist |

APPENDIX 5: Antiretroviral dosage regimens for adults and adolescents

| Drug Class | Drug | Dose | Comments |
|-----------------------------|------------------------------|---|---|
| Nucleoside RTIs | Zidovudine (ZDV) | 300 mg twice daily | |
| | Lamivudine (3TC) | 150 mg twice daily or 300mg once daily | Well tolerated No food restrictions Also active against hepatitis B |
| | Didanosine (ddI) | 400 mg once daily | 250mg once daily if <60 kg or with TDF |
| | Abacavir (ABC) | 300 mg twice daily | |
| | Emtricitabine (FTC) | 200 mg once daily | |
| Nucleotide RTI | Tenofovir (TDF) | 300 mg once daily | |
| Non-nucleoside RTIs | Efavirenz (EFV) | 600 mg once daily | Should be taken at bedtime |
| | Nevirapine (NVP) | 200 mg once daily for 14 days, then 200 mg twice daily | This is the 'lead in dosing' |
| | Delavirdine (DLV) | 400 mg three times a day | It has several drug interactions |
| | Etravirine (ETV) | 200 mg twice daily | |
| | Rilpivirine (RPV) | 25 mg once daily | |
| Protease Inhibitors | Lopinavir/ritonavir (LPV/r) | 400 mg/100 mg twice daily | 533 mg/133 mg twice daily if combined with EFV or NVP |
| | Nelfinavir (NFV) | 1250mg twice daily | |
| | Indinavir/ritonavir (IDV/r) | 800 mg/100 mg twice daily | Dose adjustment when combined with an NNRTI may be required |
| | Saquinavir/ritonavir (SQV/r) | 1000 mg/100 mg twice daily or 1600 mg/100 mg once daily | Dose adjustment when combined with an NNRTI may be required |
| | Atazanavir (ATV) | 400 mg once daily | ART/r 300 mg/100 mg once daily |
| | Tipranavir (TPV) | 500 mg twice daily | |
| | Duranavir (DRV) | 600 mg/100 mg twice daily | |
| Fusion Inhibitors | Enfuvirtide (T-20) | 90 mg (1 ml) twice daily | Injected subcutaneously into the upper arm, thigh or abdomen |
| Integrase Inhibitors | Raltegravir (ISENTESS) | 400 mg twice daily | |
| Fixed combinations | ZDV/3TC/ABC (Trizivir) | 300 mg/150 mg/300 mg as 1 tablet twice daily | Use tablet with d4T 30 mg |
| | TDF+FTC+EFV (Atripla) | 300mg/ 200mg/600mg as 1 tablet daily | Take at bedtime because of efavirenz |
| | ZDV/3TC (Combivir) | 300 mg/150 mg as 1 tablet twice daily | |

APPENDIX 6: Antiretroviral dosing for infants and children

Paediatric ART Dosing by Formulation and Weight Range. Feb 2011

| | 3-5.9 Kg | 6-9.9 Kg | 10-13.9 Kg | 14-19.9 Kg | 20-24.9 Kg | 25-29.9 Kg |
|--------------------------------|--|--------------------------------------|---------------|----------------|----------------|----------------|
| Fixed-Dose Combination Tablets | AZT/3TC/NVP 60/30/50mg | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | AZT/3TC 60/30mg | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | ABC/3TC 60/30mg | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | d4T/3TC/NVP 6/30/50mg (Baby) | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | d4T/3TC 6/30mg (Baby) | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | d4T/3TC/NVP 12/60/100mg (Junior) | 0.5 BD | 1 AM / 0.5 PM | 1 BD | 1.5 AM / 1 PM | 1.5 BD |
| Single-Dose Tablets/Capsules | d4T/3TC 12/60mg (Junior) | 0.5 BD | 1 AM / 0.5 PM | 1 BD | 1.5 AM / 1 PM | 1.5 BD |
| | AZT 300mg | nr | nr | nr | 0.5 BD | 1 AM / 0.5 PM |
| | ABC 300mg | nr | nr | nr | 0.5 BD | 1 AM / 0.5 PM |
| | ABC 60mg | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | 3TC 150mg | nr | nr | nr | 0.5 BD | 1 AM / 0.5 PM |
| | NVP 200mg | nr | nr | nr | 1 AM / 0.5 PM | 1 AM / 0.5 PM |
| | NVP 50mg | 1 BD | 1.5 BD | 2 BD | 2.5 BD | 3 BD |
| | EFV 200 - 100 - 50mg | nr | nr | 200mg daily | 300mg daily | 300mg daily |
| | ddI 25mg (buffered) | 3-4.9kg NR 5-5.9kg 2 BD | 3 AM / 2 PM | 3 BD | 4 AM / 3 PM | 4 BD |
| | ddI 125 - 200 - 250mg (enteric-coated) | nr | nr | 125mg: 1 daily | 200mg: 1 daily | 250mg: 1 daily |
| Oral Solutions | LPV/r 100/25mg | nr | nr | 2 AM / 1 PM | 2 BD | 2 BD |
| | LPV/r 200/50mg | nr | nr | nr | 1 BD | 1 BD |
| | AZT 10mg/ml | 6ml BD | 9ml BD | 12ml BD | nr | nr |
| | d4T 1mg/ml | 6ml BD | 9ml BD | nr | nr | nr |
| | 3TC 10mg/ml | 3ml BD | 4ml BD | 6ml BD | nr | nr |
| | NVP 10mg/ml | 5ml BD | 8ml BD | 10ml BD | nr | nr |
| | ABC 20mg/ml | 3ml BD | 4ml BD | 6ml BD | nr | nr |
| | LPV/r 80/20 mg/ml | 3-3.9kg: 1ml BD 4-5.9kg: 1.5ml BD | 1.5ml BD | 2ml BD | 2.5ml BD | 3ml BD |

Cotrimoxazole Dosing by Formulation and Weight Range

| | < 5 Kg | 5-14.9 Kg | 15-29.9 Kg | > 30 Kg |
|---------------|------------------------------|-------------|------------|------------|
| Cotrimoxazole | 200+40mg/5ml (Oral Solution) | 2.5ml daily | 5ml daily | 10ml daily |
| | 100+20mg (Tablet) | 1 daily | 2 daily | 4 daily |
| | 400+80mg (Tablet) | 0.25 daily | 0.5 daily | 1 daily |
| | 800+160mg (Tablet) | nr | nr | 0.5 daily |

APPENDIX 7: Routine Follow up visits for children on ART

| PARAMETER | Issues to Evaluate |
|---------------------------------|---|
| Review Interim medical History | <ul style="list-style-type: none"> Assess for TB exposure |
| Assess growth and nutrition | <ul style="list-style-type: none"> Weight , height, head circumference and Mid upper arm (for children after 6 months of age) |
| Perform physical exam | <ul style="list-style-type: none"> As directed by symptoms |
| Assess development progress | <ul style="list-style-type: none"> Evaluate the developmental milestone. Look out for encephalopathy characterized by delayed or loss of milestones |
| Identify concomitant conditions | <ul style="list-style-type: none"> Opportunistic infections e.g. TB, Monitor for decrease or increase in frequency of OIs For adolescents always monitor for pregnancy |
| Do HIV disease staging | <ul style="list-style-type: none"> Assessment for OIs will guide the staging |
| Check adherence to ART | <ul style="list-style-type: none"> Evaluate the child's and caregivers understanding of ART Adherence can be done by <ul style="list-style-type: none"> ✓ Pill counts at the clinic or an announced pill count at home ✓ Self reporting by patient can also be used to assess adherence though it is limited by recall bias. ✓ In advance care centers, patient drug levels can be used to assess adherence. It more expensive but more reliable. |
| Prescribe correct ARV dose | <ul style="list-style-type: none"> Use the ARV dosing guide to prescribe the right dose (<i>see appendix 6</i>) |
| Review concomitant medication | <ul style="list-style-type: none"> Consider drug interaction Check out cotrimoxazole and INH therapy. Make dose adjustments |
| Discuss findings | <ul style="list-style-type: none"> Always explain the findings from the visit mean |
| Provide referral as needed | <ul style="list-style-type: none"> For support services and other required clinical services like Lab |
| Advice and guide | Re enforce and support adherence to ART, nutrition, when to seek medical care and medication side effects |
| Schedule lab tests if indicated | <p>See table 5.8 for schedule for Lab test</p> <p>Infants and children started on ART on the basis of presumptive diagnosis of severe HIV disease should have confirmation of their HIV status as soon as possible</p> |
| Schedule Next visit | Frequency of follow up visits depends on the response to ART |

Appendix 8: TB management recommendations

| CATEGORY | DIAGNOSTIC CATEGORY | ANTI-TB DRUG REGIMENS | |
|------------|--|--------------------------------|--------------------|
| | | INTENSIVE PHASE | CONTINUATION PHASE |
| Category 1 | NEW PATIENT REGIMEN <ul style="list-style-type: none"> New smear positive Smear negative PTB with extensive parenchymal involvement Severe forms of EPTB⁹ other than TB meningitis and TB spine | 2HRZE | 4HR |
| | NEW PATIENT REGIMEN <ul style="list-style-type: none"> TB meningitis TB Spine | 2HRZS | 7HR |
| Category 2 | RETREATMENT REGIMEN <ul style="list-style-type: none"> Relapse Treatment after interruption (Defaulter) Treatment failure | 2HRZES/1HRZE | 5HRE |
| Category 3 | NEW PATIENT REGIMEN <ul style="list-style-type: none"> Smear negative PTB without extensive parenchyma involvement Less Severe forms of EPTB¹⁰ | 2HRZ | 4HR |
| Category 4 | MDR REGIMEN <ul style="list-style-type: none"> MDR-TB | Individualized regimens | |

⁹ Severe TB: TBM, Pericarditis, Miliary TB, Abdominal TB, Peritonitis, Intestinal TB, obstructive adenitis & TB spine.

¹⁰ Less severe TB: TB adenitis, adrenal TB, Pleural effusion (Unilateral) and TB bone.

Appendix 9: Intensified TB Case Finding Form

*Use the form to suspect:
TB in People living with HIV, contacts of smear positive cases and in HIV care settings*

This form should be administered by either a health care provider or lay provider at the health facility (The form should not be self-administered)

Date of TB Assessment _____

Name of district: _____

Name of Health facility: _____

Location: _____ (e.g. OPD, HIV Clinic etc.)

Patient ID/Registration number: _____

1. Has the patient been coughing for 2 weeks or more? **Yes** ☐ **No** ☐
2. Has the patient coughed up sputum stained with blood? **Yes** ☐ **No** ☐
3. Has the patient had persistent fevers for 3 weeks or more? **Yes** ☐ **No** ☐
4. Has the patient had noticeable weight loss (more than 3 kg) in the last one month? **Yes** ☐ **No** ☐
5. Has the patient had night sweats for 3 weeks or more? **Yes** ☐ **No** ☐

Guide for Actions to take

- If **yes to question 1 or 2**; request for sputum test and refer to clinician for further investigations. ***Direct the patient to a designated area for people with chronic cough.***
- If **no to question 1 and 2 and yes to any other question**; refer to clinician for further investigations

If no to all questions: repeat TB Assessment at subsequent visits

Record of Information at Health facility level

1. *If you are in a clinic attending to patients enrolled in HIV care record this information on the comprehensive ART card; this information should then be transferred to the Pre ART or ART register.*
2. *If you are in any HIV care setting (not attending to patients enrolled in HIV care e.g. OPD) and the patient is found to be a TB suspect record this information in a TB suspect register.*

Appendix 10: Karnofsky (Performance) Score [KS]

| | | |
|---|-----|--|
| Able to carry on normal activity, No special care is needed | 100 | Normal; no complaints; no evidence of disease |
| | 090 | able to carry on normal activity; minor signs or symptoms of disease |
| | 080 | Normal activity with effort; Some signs or symptoms of disease |
| Unable to work; able to live at home and care for most personal needs; a varying amount of assistance is needed | 070 | Cares for self; unable to carry on Normal activity or to do active work |
| | 060 | Requires occasional assistance And frequent medical care |
| | 050 | Requires considerable assistance and frequent medical care |
| Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly | 040 | Disabled; requires special care and assistance |
| | 030 | Severely disabled; hospitalization is Indicated, though death is not imminent |
| | 020 | Very sick; hospitalization is necessary; Active supportive treatment is necessary |
| | 010 | Moribund; fatal processes are progressing rapidly |
| | 000 | Dead |

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