REPUBLIC OF RWANDA

MINISTRY OF HEALTH

TREATMENT RESEARCH AIDS CENTER

Guide for Care of People Living with HIV in Rwanda

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CDC

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CONTENTS

Preface

Despite the developments in the last decades in the area of HIV/AIDS control, this pandemic remains a major problem in developing countries.

With more than 200.000 people living with HIV/AIDS in Rwanda, the expansion of antiretroviral treatment among patients who meet the criteria is one of the priorities of the Ministry of Health. There is evidence that shows that putting eligible patients under antiretroviral treatment contributes to the reduction of the suffering of patients and the devastating impact of pandemic.

That also presents a real opportunity for effective response by integrating people living with the HIV/AIDS, their families and the community in the care. This will reinforce the prevention of HIV through increased knowledge, creation of a demand for the counselling and testing and the reduction of stigma and discrimination.

This expansion of antiretroviral treatment is a challenge that can however be surmounted by the participation of all the partners, both national and foreign. Apart from the financial support that is more than essential, other elements include the supply of drugs and the need for regulatory mechanisms. Care providers must be trained, infrastructures installed, the community educated and mobilised. It is also necessary to mobilise various people involved in the fight against the HIV to play their roles.

Human resource capacity building should take an important place in this process to train and coordinate social workers, nurses, doctors as well as other people involved in the fight against HIV. This capacity building must also motivate care providers so that they can provide long-term high-quality care to the patients.

This guide presents new knowledge and directives in the area of care of people living with HIV/AIDS according to latest 2006 WHO recommendations adapted to the national context. It therefore answers the will of the Ministry of Health, which is to improve competence and skills of actors involved in the health sector and to provide high-quality care in the area of antiretroviral therapy both in public and private health facilities in Rwanda.
We are indeed aware that despite the progress made, there is a lot to be done in the area of treatment and prevention in the hope for eradicate the HIV pandemic from our country. May the present guide contribute to the improvement of knowledge of all health actors in the area of HIV/AIDS control and to the improvement of the living conditions of our population.

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Acronyms and Abbreviations

3TC:	lamivudine
ABC:	abacavir
DNA:	Deoxyribonucleic Acid
AES:	Accidental Exposure to Blood
RNA:	Ribonucleic Acid
ARV:	Antiretroviral (drugs)
AUC:	Area under the curve
AZT:	zidovudine
CD4:	lymphocyte variety (T4)
CDC:	Center for Disease Control
CMV:	cytomegalovirus
CTM:	cotrimoxazole
d4t:	stavudine
DdC:	zalcitabine
DdI:	didanosine
EFZ:	efavirenz
HBV:	Hepatitis Virus B
HCV:	Hepatitis Virus C
IDR:	intra-dermoreaction
IDV:	indinavir
NNRTI:	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI:	Nucleoside Reverse Transcriptase Inhibitor
INTRT:	Nucleoside Reverse Transcriptase Inhibitor
OI:	Opportunistic Infection
PI:	Protease Inhibitor
M:	month
NFV:	nelfinavir
NVP:	nevirapine
WHO:	World health Organisation
UNAIDS:	The Joint United Nations Programme on HIV/AIDS
PCR:	polymerase chain reaction
PTCT:	prevention of Mother to Child Transmission
PLWHA:	People living with HIV/AIDS
TV:	Ritonavir
TDF:	Tenofovir
FTC:	Emtricitabine
VCT:	Voluntary Counselling and testing
HIV:	Human immunodeficiency Virus
VZV:	virus varicelle zona

PART I

CHAPTER I. Epidemiology of HIV

Presentation of the situation of the epidemic in 2006

For about three decades until today, the HIV infection has become a pandemic. Despite remarkable developments of the knowledge on HIV during recent years, the epidemiology of the pandemic has not changed, especially in low-income countries. The Sub-Saharan Africa remains the most affected region of the world. The table below describes the HIV/AIDS epidemiology in Rwanda in the more global and regional context.

World Situation	• Fourth cause of mortality in the world. • 39.5 (34.1 – 47.1) million of HIV carriers according to estimates. • New cases of HIV infection in 2006: 4.3 (3.6– 6.6) million. • Deaths due to AIDS in 2006: 2.9 (2.5 – 3.5) million. • About 14000 new cases of HIV infection per day of which 12000 cases among adults (50 % in women) and 2000 cases in children aged less than 15 years. • The majority (90 %) of people do not know that they carry the virus. • Young women are particularly vulnerable due to the fact of the precariousness of their socio-economical status that is often influenced by cultural factors. • At the end of 2006, WHO estimated that there were more than 1.3 million people receiving antiretroviral treatment (ART) in low and middle-income countries, representing 20% of 6.5 million who were estimated to be in need of the treatment.
Sub-Saharan Africa	• The region that is the most affected by the epidemic • HIV is the major cause of mortality in this region • 2.8 (2.4 – 3.2) million of new cases of HIV infections in 2006 according to estimates. • 24.7 million Africans today are HIV carriers and there are 2.41 million (2.1 - 2.7) of deaths (children and adults included) each year.
In Rwanda	Basing on the reference of the Third Demographic and Health Survey (DHS-III) carried out in July 2005, by the Department in charge of statistics in collaboration with Macro-DHS : • With the aim of ensuring national coverage, the 2005 survey was carried out in 5 Provinces of the country with 462 clusters (351 rural and 111 urban). In order to ensure the expected precision of indicators, it became necessary to control the size of the household by limiting the number of each cluster 20 households in an urban cluster and to 24 households in a rural cluster. In total 10,644 households were selected. • Results show that the prevalence is 3 % (confidence Interval is from 2.6 to 3.4). Women with a rate of prevalence of 3.6 % are clearly more than men at 2.3 %.

	• Considering the level of education, the prevalence is higher among the population with secondary education level (5.6 %). • Rates of HIV prevalence vary from 2.2% in Northern Province to 5.6 % in Kigali City. • The average rate in urban areas is 7.3% (CI from 6.2 to 8.4) • The average rate in rural areas is 2.2% (CI from 1.9 to 2.5) • The difference between the prevalence per area may be explained by high-risk behaviour that may contribute to the spread of HIV observed in urban areas. • The rate of HIV prevalence in the group of women aged between 35 and 39 years is high both in urban and rural areas whereas men within the age bracket of 40 to 44 years are the most affected (7.1%). • The proportion of people who tested HIV positive tends to increase with age in both sexes.

Types and sub-types of HIV

Most probably, HIV originates from the evolution of the monkey virus (VIS) which made it pathogenic for man.
Two types of HIV are currently known: HIV-1 and HIV-2. At the world level as well as in Rwanda, the most predominant virus is HIV-1.

The transmission of the two viruses is by sexual contact, by contaminated blood, and by mother to child transmission. The two viruses seem to provoke identical clinical manifestations. However, the HIV-2 is transmitted much easier and the period between the first infection and the onset of the disease is longer in case of HIV-2.

The difference between the two subtypes

The major difference is their genetic composition; and it may be reflected in the biological differences observed in vitro and/or in vivo.

- Many countries report a range of several sub-types.
- A person may be co-infected by different sub-types or be re-infected by a different sub-type.

In total, the sub-type C currently represents more than a half of new cases of HIV infections in the world.

HIV-1	We currently know within the major group (group M) at least ten (10) sub-types of HIV-1 genetically different, of which the sub-type A and a large number of major recombinant forms. (Forms combined with several sub-types). These sub-types are spread in an evenly manner in the world. For example : • The sub-type B is predominant in the Americas, in Japan, in Australia, in the Caribbean Islands, in Europe and in Northern Africa. • The sub-types A and D are predominant in Sub-Saharan Africa. • The sub-type C is predominant in Southern Africa and in India. • The sub-type CRF01AE is predominant in Central African Republic, in Thailand and in other South-Eastern Asian countries • The sub-types F (Brazil and Rumania), G and H (Russia and Central Africa, (Cyprus) and O (Cameroon) have a very low prevalence. • In Africa, there are the majority of the sub-types, although the sub-type B has a lower prevalence. • In Rwanda : Predominance of the sub-types A, C (15 – 20%) and CRF 01AE(See. Appendix I)
HIV-2	• This is another human retrovirus that causes an immunodeficiency similar to that of HIV 1. The two lead to the reduction of the number of CD4 cells. • It is mainly concentrated in Western Africa (Cape Verde Islands and Senegal). • Compared to HIV-1, HIV-2 is less transmissible; it is associated with a less important viral load and a slower evolution of the reduction of the CD4 and clinical progression.

CHAPTER II. Mode of Transmission and Prevention of HIV/AIDS

Efficient prevention of HIV/AIDS is based on the good knowledge of the modes of transmission and on the factors that influence it.

Transmission of HIV

a) Modes of HIV Transmission

There exist three major modes of HIV transmission:

1- Sexual

HIV may be transmitted during unprotected sexual relations, I.e. any sexual activity with penetration during which the partners do not use a condom.
Vaginal and anal sexual relations may transmit the virus from a man infected by HIV to a woman or to another man, or from an infected woman to a man.
The risk of being infected during unprotected sexual relations is conditioned by four major factors:

- Probability that one of the sexual partner may be infected
- The type of sexual activity;
- The quantity of the virus present in the blood or sexual secretions (sperm, vaginal or cervical secretions) of the infected partner ;
- The presence of other sexually transmitted diseases and/or genital lesions in one of the partners.

The age may also constitute a factor, girls being more physiologically vulnerable.

The probability of infection in a partner: in general, your risk of HIV infection through HIV by sexual relations is related to the number of sexual partners and the number of unprotected sexual intercourse that you will have had. In other words, the more sexual partners you have and the greater the number of unprotected sexual intercourse you have, the higher the risk of being infected.

2. Contaminated blood

Each year, blood transfusions save millions of human lives. Where the security of the blood supply is not guaranteed, there is however an increased risk that the blood recPIients may be infected by HIV in the process.

The use of invasive needles or other instruments, if they were contaminated by HIV, may lead to the transmission of the virus. Sharing of syringes and needles among drug users

through injections may lead to a very fast increase in the infection among these groups of the population in many parts of the world.

Certain no medical procedures may also be risky if instruments used are not correctly sterilised. These include among others: the perforation of the part or ear lobe or other parts of the body, tattooing, acupuncture, circumcision in men or women and traditional tattooing through scarification. The effective level of the risk will depend on the local prevalence of HIV infection.

The equipment of injection can as represent a risk of transmission of the HIV within the framework of the health services, as it is because of an inadequate sterilization of the syringes, needles and other instruments like the dental material, or because of accidental punctures by needles or other pointed or cutting instruments.

3. Vertical (= Mother to Child Transmission)

Mother to child transmission (MTCT) is the most common mode of HIV transmission among young children. The virus may be transmitted during pregnancy or childbirth, or after birth during breast-feeding. Among infected children who are not breastfed, MTCT occurs especially at the time of childbirth (immediately before or after childbirth). Among the populations where breast-feeding is a tradition, this could account for more than a third of all cases of MTCT.

b) How is HIV not transmitted?

Families, friends and workmates do not have to fear of infection by occasional contact at home, at work, or in company with a person infected by HIV. There is no risk of transmission during these activities:

- Handshake, embrace, kiss;
- Coughing or sneezing;
- The use of a public phone;
- A visit to the hospital;
- Opening or closing a door;
- Sharing food, or eating or drinking utensils;
- The use of water taps;
- The use of toilets or showers;
- Swimming in public swimming pools;
- Insect bites, including mosquito bites;
- Hairdressing saloons if the clippers are each time disinfected with methylated spirit that is natured at 70%.

c) Clinical and Biological Factors influencing HIV Transmission

FACTORS THAT INCREASE THE RISK OF TRANSMISSION

❖ There are factors **linked to hosts** (transmitter and receptor) :

Hosts	Factors increasing risks of transmission
• **The transmitter**	✓ High viral load (The two periods during which the viral load is the highest are: primo-infection and the terminal stage of AIDS ✓ In the blood ✓ In genital secretions (Man : sperm, seminal liquids; and woman : secretions) ✓ In maternal milk ✓ Traumatising sexual relations ✓ Sexual relations during menstruation period ✓ STI and co-infections (tuberculosis or hepatitis B).
• **The receptor**	✓ Infection or inflammation of genital or rectal mucous membranes ✓ Traumatising sexual relations ✓ Non - circumcision ✓ Sexual relations during menstruation period (increasing the risk in man) ✓ Presence of a local co-infection (STI, ulcerous or non ulcerous)

❖ Factors linked to the virus :

Viruses may be more or less virulent.

FACTORS THAT REDUCE RISKS OF TRANSMISSION

- Protection during sexual relations: regular and correct use of latex condoms (male or female condom);
- Antiretroviral treatment: through the improvement of the immunity status and the reduction of the viral load. This may be reduced but it does not rule out the risk of HIV transmission, since the virus; even when undetectable in the blood, still persists in cell reservoirs (White blood cells).In addition, a virus that cannot be detected in the blood may be present in genital secretions. Therefore, patients under ARV will need intensive counselling and advice in the area of prevention;
- Prevention of HIV/AIDS transmission by antiretroviral drugs has proved efficient in the reduction of vertical transmission from mother to child, especially when it is administered during pregnancy or at the time of labour.
- The treatment of associated infections, particularly genital infections.

d) Socio-economic factors influencing the contamination by HIV

Social Mobility

The situation of the migrants and seasonal workers oblige people concerned to live away from their homes (truck drivers, businesspersons...).

Stigmatization and denial of the reality

Causes of the denial:

- **Death:** HIV used to be a slow and incurable disease, synonymous with death. Today, thanks to antiretroviral treatment, it has become a chronic disease;
- **Fear:** Ignorance generates fear;
- **Moral fault**: HIV is perceived as result of a serious moral fault by the carrier and the community from which he/she comes;
- **Belonging to the risky group:** People tend to stigmatize or blame certain groups for the propagation of HIV, for example; drug addicts, homosexuals, or people with different sexual behaviour.

Consequences of the Denial:

- **Silence:** Stigmatization prevents people from speaking about it or recognizing that HIV is an important cause of morbidity and mortality.
- **Exclusion:** Stigmatization prevents carriers of HIV from accessing treatment and from taking necessary prevention measures. It excludes a patient from the family and the society;
- **The refusal of voluntary testing:** fear of knowing one's HIV status.

Precariousness

The geographical distribution of HIV/AIDS is superimposed on that of precariousness in the world. By its impact on the active members of the society, the HIV/AIDS worsens a situation that is in most cases already precarious.

In that way, HIV has decimated teams of workers. Therefore, the enterprise loses its expertise, knowledge, which seriously hinders its operations. Since women are often victims of economic inequalities, they are sometimes obliged to resort to sexual trade for survival. *This exposes them to unacceeptable risks in the event of refusal by the sexual partner to practise safer sexual relations*. The disease may impoverish a family and gradually destroy the family unit and the social fabric that surrounds it.

Populations in conflict and political instability promoting the propagation of HIV

Conflicts ruin the economy and promote all kinds of exactions. In each country, areas of conflicts are the ones in which HIV is most prevalent. Political instability prevents the

installation of programs and the elaboration and implementation of long-term sustainable programmes.

Cultural Factors

Cultural traditions, beliefs and practices affect the perception of health, the disease and the acceptability of medical conventional treatment. The culture dictates modes of target behaviour according to sex, the country, the religion, the ethnic group, the language, the community and the age. The culture may create barriers that prevent people, in particular women, from taking necessary precautions.

For example, in many cultures, the domination of men on women generates domestic violence. That means that the woman may not easily question the extramarital sexual relations of her husband, she may not ask him to use a condom and she may not refuse to have sexual relations. Prevention is sometimes difficult to accept in certain cultural contexts.
The use of drugs and alcohol lowers vigilance and support the behaviours at the risk. (See. Appendix II)

Prevention of HIV/AIDS

Despite the propagation of HIV/AIDS, several prevention programmes have been crowned with success.

MAJOR ELEMENTS OF THESE PROGRAMMES ARE:

1. Fighting against major risky factors of heterosexual HIV transmission that are:
   - Frequent changes of sexual partners;
   - Unprotected sexual relations;
   - Propagation of STI and inadequate access to STI treatment;
   - Social vulnerability of women and the youth;
   - Poverty in the community;

2. Campaigns for the promotion of voluntary testing and behavioural communication change which include messages on abstinence, faithfulness and the use of the condom. In Rwanda, behavioural change communication is the corner stone of the fight against HIV/AIDS. The reinforcement of the prevention is the first pillar in the National AIDS Control Strategic Framework - CNLS 2002-2006. Therefore, a host of public, private organisations and non-governmental organisations have been carrying out public awareness campaigns against HIV/AIDS in Rwanda.

3. Better access to male and female condoms to reduce the risk of sexually transmitted infection and the vulnerability to HIV;

4. Effective care of STI;

5. Modification of the perception on HIV/AIDS to demystify the disease and to promote behavioural change.

6. Education of the young people and the groups at the risks as regards to sexuality, STI and more particularly to the HIV/AIDS;

7. Reduction in indications of the blood transfusion and reinforcement of transfusion safety. Rigorous application of the universal hygiene precautions (to promote, for example, the use of disposable syringes) and of the PRP (Post-exposure prophylaxis) in health care facilities;

8. The political will to make HIV/AIDS control a priority. In Rwanda, TRAC as well as CNLS were created as an evidence of this political will. The mission of CNLS is to give orientation to the National HIV/AIDS Control Policy, to coordinate all interventions in the area of HIV/AIDS control, to sensitise the population, to promote and reinforce mobilization of leaders at all the levels and in all sectors involved in the fight against HIV/AIDS. In the framework of sensitizing the population, CNLS developed a National Behavioural Change Communication Strategic Framework, in order to facilitate collaboration with its various partners.

MEASURES TO REDUCE THE RISK OF INFECTION:

Measures whose aim is limit high-risk sexual behaviour: identification of groups at risk and strengthening of specific prevention within these groups.

Development of IEC in the general population and target groups. The promotion of measures against inequality and the vulnerability of women and the youth and facilitation of their access to the means of prevention and care.

CONCLUSION

The success of prevention programmes and access to care will depend on a strong political will, which will mobilise means necessary to the implementation of strategies of the fight against HIV/AIDS. Since after genocide, interventions aiming at decreasing the impact of HIV in Rwanda have intensified in several areas, including that of behavioural change communication and the care of HIV patients with antiretroviral drugs. Several stakeholders in the area of behavioural change initiated various types of programmes targeting various brackets of the target population.

In Rwanda, the number of patients under ARV increased in a spectacular way since 2003, thanks to the Ministry of Health that encourages the implementation of a National care and Prevention Programme.
Training of many care providers through TRAC and UPDC has enabled better care of patients in the entire country.

In December 2006, it was estimated that 31,379 adults and 2,757 children had already begun ARV treatment.

CHAPTER III. Physiopathology and Diagnosis of HIV /AIDS

The Immune System

The immune system constitutes the system of defence of the human body. Its role is to protect the organism from lesions caused by the invasion of micro-organisms (bacteria, virus, fungi and parasites). Leucocytes fulfil this defensive function. The lymphoid bodies produce these cells: bone marrow, the lymphatic thymus, and the spleen and lymphatic ganglia. They are found in circulating blood.

There are several varieties of leucocytes of which the lymphocytes are the central cells of the immune system. There are two major types of lymphocytes: the lymphocytes B and the lymphocytes T among the lymphocytes there are the lymphocytes that are carriers of receptors of CD4 (T4 lymphocytes or CD 4 cells) and the lymphocytes that are carriers of CD8 receptors (T8 lymphocytes or CD 8 cells).

The lymphocytes B are responsible for humeral immunity and produce the antibodies.
The lymphocytes T are responsible for cellular immunity and have several functions:

- **Lymphocytes CD4:**
  - The lymphocytes B in their function of the production of antibodies (humeral immunity);
  - Stimulate the CD 8 lymphocytes that can then destroy the cells infected by the virus (cellular immunity).
  - Stimulate the memory lymphocytes.
- CD4 and CD8 lymphocytes can activate macrophages so that they destroy pathogens.

HIV multiplies in a preferential way inside the CD 4 cells. In the host infected by the HIV, CD4 cells are gradually destroyed.

Any function that stimulates the immune system is likely to accelerate this destruction. When the rate of CD 4 cells is low (<500 /mm^3), the organism loses its capacity to efficiently fight against infections (See Figure 1). This person becomes vulnerable to opportunistic infections (tuberculosis, toxoplasmosis, Candida, etc) and may develop certain types of cancer (see. Appendix III).

Structure of HIV

HIV (Human immunodeficiency Virus) is the virus responsible for AIDS in the human being. At present, two types of the virus are known: HIV-1 and HIV-2 (see PART A, CHAPTER 1). These two types of virus are responsible for identical clinical manifestation and a different rate of evolution.

The HIV virus is composed of three essential structures (see. Annex IV):

- The core or nucleus containing the ribonucleic acid (RNAA) which forms the genome;
- The capsid which surrounds the core and contains the þ 24 protein;
- The external membrane of spherical form (envelope) which contains the glycoprotein of the envelope.

The reproduction cycle of HIV

The five phases are the fixation and entry, reverse transcription, integration, replication, budding and maturation (see Annex V).

Fixation and entry phase: The virus by its proteins of gp120 envelope begins in CD4 receptors of the cell. After fixing itself on this receptor, it uses the presence of Co-receptors to stick themselves on the lymphocyte membrane and to amalgamate with it. The membranes of the virus and envelope proteins remain outside the CD4 cell whereas the viral RNA penetrates into the CD4 cell.

Reverse Transcription Phase: The RNA of the virus must be converted into DNA before being built-in in the DNA of CD4 cell. The conversion of the viral RNA into DNA is known as the process of reverse transcription induced by the reverse transcriptase.

Integration Phase: After this stage, the DNA obtained from the viral RNA penetrates in the core of CD4 cell. Under the effect of the viral Integrase enzyme, the viral DNA is integrated into the DNA of the CD4 cell. This process is known under the name of integration.

Replication Phase: The new DNA produced by the integration of viral DNA in the CD4 cell provokes the synthesis of RNA messenger, which will induce the production of the viral RNA and proteins, intended to reconstitute the virus.

Burgeoning and Maturation Phase: The viral proteins and the RNA are synthesized and are assembled around the RNA under the action of protease. They thus produce new viruses in the CD4 cell. These new viruses cross by budding the walls of the CD4 cell and are released in the peripheral blood where they will infect new cells.

HIV can remain latent inside the host cell for one more or less long period (in the form of viral pro-virus DNA) thus making the infection latent.

Biological diagnosis of HIV

The description of the infection may be done either in a direct way by the description of the virus or one of its components, or in an indirect way by the presence of antibodies. The table below defines the determining concepts in the biological diagnosis of HIV:

Markers of the biological course of the natural history of the disease	The viral antigens are called substances that are proteins in nature produced during the viral replication and are liberated in the organism by cells infected by HIV (example: antigens P24). Antibodies are proteins and glycoprotein made by certain cells of the organism (lymphocytes B) to neutralise the effect of antigens (example: antibodies P 24). The antigens and antibodies appear in the organism of the host infected at various periods as indicated in Figure in Appendix VI. Certain antibodies (antibodies directed against antigens of the membrane) have more prolonged life duration than others (such as antibodies directed against the antigens of the nucleus).
The primo infection (1 month)	Following the entry of the virus in the organism, the following happens: a) An important increase of the number of the virus in the organism that is shown by the increase of the highly positive P24 antigenemy. b) The secondary appearance (14 to 21 days) of different antibodies. The period that separates the entry of the virus evidenced by the increase of p 24 cells from the appearance of antibodies is called « Window period » during which the virus is present but the serology is negative.
The phase of Clinical latency (3-12 years)	Past the primo-infection, antibodies are and still remain high and enable the diagnosis of the disease. The quantity of the virus in the organism reduces and is fixed at a platform. In function of the level of the platform, the Agp24 is /or non positive.
The stage of AIDS	Progressively, the rate of antibodies reduces, whereas that of the P 24 antigens increases in parallel to the quantity of the virus.

✓ **Direct Biological diagnosis of the Infection (Identification of the virus itself)**

Specific circumstances (recent primo-infection, child born of an HIV positive mother aged less than 18 months) require the recourse to direct diagnostic methods but those are in practice rarely carried out. Two processes are used for the direct diagnosis: the detection of p 4 antigens and the detection of the viral genetic material (Polymerase Chain Reaction or

PCR). This diagnosis may be difficult for HIV-2 by the absence of PCR to this type of virus in current practice.

✓ **Indirect Biological Diagnosis**

Generally in countries with limited resources, the biological diagnosis of the HIV infection rests primarily on the serological test, which is an indirect diagnosis highlighting the anti-HIV antibodies in the serum of patients. The visualisation methods of the reaction antigen-antibody are the immunological methods of type ELISA or the "rapid" tests, which call upon an agglutination/absorption of the complex on a membrane, then a staining or colouring visible to the eye.

✓ **HIV Testing Strategy (see Appendix VII)**

The HIV biological diagnosis strategy may vary from one country to another by taking into account the estimated prevalence of the HIV infection in the country. The World Health Organisation (WHO) proposes protocols according to the local prevalence. These protocols must be adapted to the local context of each country. In Rwanda in Voluntary Counselling and testing centres and PMTCT sites a sequential strategy using three rapid tests of different principles (DETERMINE, UNI-GOLD and CAPILLUS) was adopted in June 2002.

Evolution and Surveillance of CD4 and the viral load during the natural history of the disease

The plasmatic viral load expresses the quantity of the virus present by ml of plasma. The counting of CD4 expresses CD4 cells per mm^3. As immunological parameters, the rate of CD4 and viral load evolve in three phases (see. Appendix VIII).

✓ Primo infection

CV: Important increase of the viral load
CD4: Moderate and transitory lowering and then rapid return to their initial rate or a bit lower.

✓ The latent Phase

The viral load reduces under the impact of means of the immunity defence and is set on platform. The level of this platform partly determines the long-term prognostic of the disease. It is more derogatory than the level of the highest platform. After this period in platform, CD4 lower only progressively, then experience a more rapid fall before the onset of the symptomatic phase.

✓ Symptomatic Phase

This is expressed by the progressive increase of the viral load and progressive reduction of CD4 that may completely disappear.
In conclusion: the knowledge of the physiopathology of the HIV infection helps in understanding the way different parameters are used for the diagnosis and monitoring of the infection and for modalities of antiretroviral treatment.

For practical reasons, it is the measurement of the CD 4 rates every six months on average (or before) the initiation of the antiretroviral treatment that enables to monitor patients enrolled in care programmes for HIV positive patients in Rwanda.

CHAPTER IV: General Care of patients Living with HIV/AIDS

Definition and Goals

The general care (CG) is a medical, psychological and social care that takes into account the entire host of problems of the patient in order to be able to integrate him/her to a normal family, social and professional life. Its objective is:

- To ensure that all patients concerned get adequate care;
- To reduce mortality and morbidity due to HIV/AIDS;
- To increase the quality of life of the patients concerned to promote prevention by enabling access to testing services, this currently leads to real care.

Principles

The CG is a result of teamwork of all professionals who must act in a complementary and synergistic manner to meet various needs for the patient.

This care requires the installation of structures able to cover each area of intervention (medical, psychological and social) and to equip each activity sector with well-trained adequate personnel in sufficient numbers.

The totality of the work of stakeholders and partners must be carried out with strict respect of confidentiality, the only factor that is able to create and maintain confidence of the patient without which there would be no effective care. The correct operation of CG requires the establishment of an operational framework that enables the promotion of exchanges between various stakeholders and partners: programmed meetings, service meetings.

The CG must ensure the continuity of the care inside the health facilities and outside the walls of this structure. This continuity requires the participation in the CG of the associative and Community sectors.

Medical Care

✓ Prerequisite Conditions for Efficient Medical Care

Good medical care requires:

- Adapted buildings in which confidentiality of patients can be assured, equipped with the technical platform necessary for carrying out basic complementary examinations defined in the national programme;
- A multidisciplinary team available, in a sufficient number and well trained in the care of HIV pathology as well as the management of patients suffering from this pathology;
- The presence of necessary drugs with the organisation of a procurement and distribution circuit able to ensure the treatment of patients without interruption.

✓ Who should ensure the care?

He/she must be multidisciplinary, able to ensure coverage of various problems of the patient.

Within the same service, it is advisable to constitute a care giving team with members of medical personnel supported by the presence of stakeholders and partners from the community or associations: a doctor, nurses, midwives, a pharmacist, a biologist, a nutritionist, social workers, associative mediators...

According to the way the pathology is presented, care can be provided by services of different specialities that must work in complementarity with the core team and take part in meetings intended to progressively monitor patients.

The totality of these structures must be supplemented by a mechanism whose objective is to ensure the continuity of care while working on the interface between the care structure and "the external environment", with the informed consent of the patient.

Finally, it is necessary to consider the development of structures able to providing general home-based care. These structures must work under the supervision and coordination of the core team with which they must elaborate care programmes. The planned activities include regularly planned visits with clinical and support personnel, based on a previously fixed calendar. They must take into account information on patients provided by the core service.

In addition, home-based care requires the participation of the Community and community-based organisations that must, whenever it is deemed necessary, be trained in the administration of certain care services.

✓ Practical achievement of medical care

It is advisable to organize teamwork within the care structure:

- ***Definition of working objectives***: ***collecting and centralising information***, which enables the improvement of the patient by considering him/her in hi/her entirety of an individual with family responsibilities, duties and obligation in the society, etc;
- ***Organization of the restitution and validation meetings:*** to create occasions for meetings and exchange of views and experience between different care providers who intervene in the care giving area.

    - Weekly clinical staff meetings: exchanges Clinicians/biologists/pharmacists… to solve as a matter of priority, emergency or emerging problems.
    - The monitoring and selection committee is an ideal framework to communicate, exchange information, to develop and monitor a programme. It is important, both for clinicians (doctors, nurses, and health workers) and for non-clinicians (health visitors, counsellors and teachers), to attend these meetings. These groups are more effective and efficient when the team leader, often a nurse, a counsellor or a social worker, makes a list of patients, prepares the agenda for the meeting, on a weekly basis, and distributes it in advance to the team.

- ***To define the rules which govern the care giving team:***

    - Confidence;
    - Respect of confidentiality;
    - Secrecy and sharing;
    - Non-stigmatization.

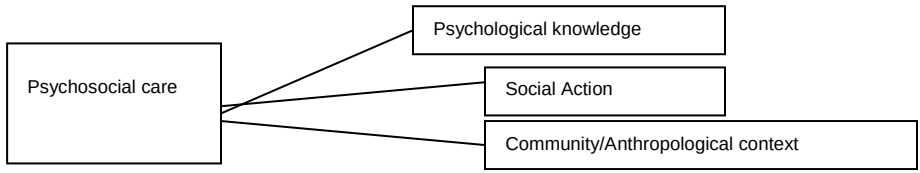
Psychosocial Care

✓ Introduction

HIV/AIDS is a disease that affects various aspects of the human life. The announcement of HIV/AIDS diagnosis is followed by upheavals at the psychic and social level. This requires psychosocial support that takes into account needs and problems of people infected by HIV/AIDS at various stages of the disease.

Care of people infected by HIV/AIDS constitutes general care that takes into account various aspects of the person. i.e. physic, psychological and social aspects. Care and psychosocial support implies continuity of the support to solve psychological, social and spiritual problems of people infected by HIV/AIDS, their partners, their families and their caregivers. This care goes beyond physical needs. It stresses emotional needs for people infected and/or affected by HIV and their needs for interaction and social integration.

Psychosocial care could be seen as an association of psychological knowledge, social action in a community /anthropologic context.
Therefore, there are three interactive actions to be carried out for a person (or a group of people).



✓ Why the psychosocial care in the general care of people living with HIV/AIDS?

Three reasons justify the necessity for psychosocial care of people living with HIV:

HIV /AIDS affects different dimensions of the human life:	○ Physical ○ Psychological /Mental ○ Social ○ Spiritual
To face the problem of stigma and discrimination linked to HIV/AIDS	Counselling and social support considerably contribute to the reduction of stigma and discrimination that people living with HIV /AIDS may be subjected to. This contributes amongst other things to the change of perception of HIV/AIDS by the community and the reduction of self-stigmatization which may be experienced by the people infected by the disease.
To ensure good conformity to antiretroviral treatment and other regimes	The success of antiretroviral treatment is the result of good compliance to treatment. Psychosocial support is a major pillar for adherence to drugs since it consists in eliminating negative factors to compliance to antiretroviral treatment and other medicinal regimes. Counselling and social support help the patient and his/her care givers to face various problems related to HIV/AIDS depending on various stages of the infection and therefore improve the quality of life of infected and affected people.

✓ How to attain psychosocial care objectives?

- Training of the caregivers in the area of psychosocial care of PLWHA;
- Training of volunteers and Community workers by health professionals;
- To elaborate strategies for the establishment of psychological support services for specific groups (children, adolescents, mothers, drug users, drug addicts, caregivers, etc.);
- Training of caregivers in areas of counselling, psychology and psychiatry.

✓ What are the major psychosocial care activities?

The care approach of people living with HIV/AIDS is a global solution in which activities in areas of prevention, fighting against stigma and discrimination, care, treatment and psychosocial support, are systematically integrated.

The care of people living with HIV requires multidisciplinary intervention. The organisation of care therefore depends on the complementarity of various stakeholders and partners. Within the same service, it is advisable to constitute a core care team with members of the care giving personnel reinforced by the presence of stakeholders and partners from the community or community-based associations. It is a team consisting of a doctor, a psychologist /counsellor, a nurse, a pharmacist, a nutritionist, a social worker as well as associative mediators.

Psychosocial Consultations

Psychosocial consultations are organised in form of discussion meetings between a patient and a counsellor to discuss one or the other subject depending on various stages of the care process or an identified problem that requires a quite specific demand.

✓ Preparatory individual Counselling

The very first entry in the care and antiretroviral treatment programme requires certain preparation. A discussion meeting with a counsellor is of great importance.

After the announcement of HIV positive results, the thoughts of the person are dominated by innumerable questions that require reassuring and comforting answers by expert and qualified personnel in the area of counselling. In the majority of cases, patients come with an emotional state that is not yet stable. He/she asks several questions concerning antiretroviral treatment; principles of treatment, and its effectiveness in maintaining their state of health. They also come with false information on antiretroviral treatment and all this requires skilled intervention that responds to various concerns of the patient.

The preparatory counselling also aims at psychosocial evaluation or assessment whose objective is to anticipate factors of conformity to treatment. At this level, the role of the counsellor consists in facilitating the patient to minimize as much as possible factors that may hinder good conformity to antiretroviral treatment.

✓ **The objectives of this discussion session are among others:**

- To give emotional support;
- To evaluate all factors that may block conformity to antiretroviral treatment;
- To provide necessary information on the monitoring and antiretroviral treatment programme;
- To correct the erroneous perceptions and beliefs with respect to antiretroviral treatment of the infection and the disease;
- To encourage positive behaviour of the patient

✓ **Psychosocial Evaluation:**

The psychosocial evaluation of people infected by HIV requires an individual evaluation and if possible of his/her hearth and the rest of the family, of his/her resources and needs. In order to respond to these needs, the community should also be assessed: religious or spiritual belief, social services, and legal resources.

Elements to be evaluated:

- EVALUATION OF THE PSYCHOLOGICAL STATE OF THE PATIENT :

After the announcement of the HIV positive results, the person passes through various stages before accepting and integrating his/her status. The most frequent situation is persistent denial and refusal of the reality and this has considerable impact on the conformity of the patient.

Fear to be known as HIV positive and to be stigmatized by people within one's surroundings characterizes the majority of patients who have just learnt about their HIV status. Thus, the counsellor must evaluate during the first meeting with the patient, the experience lived on knowing one's HIV positive status. The patient that has such difficulties may be supposed to subsequently be poor conformers because they do not feel at ease with the appointments and during the entire monitoring process.

The other category of patients who are likely to be poor conformers is that of people who show neuropsychiatric symptoms related to some factors such as:

- Factors of psychosocial stress;
- Factors related to psychiatric syndromes;
- Factors related to secondary diseases to HIV, or;
- Factors related to the treatment of HIV/AIDS itself.

To respond to these concerns, preparatory counselling must include an evaluation whose aim is to anticipate psychological and social factors to conformity. In the majority of cases, a social worker or a psychologist is responsible for psychosocial evaluation. It is essential that all members of the multidisciplinary team collaborate in this evaluation. However, it is the duty of the psychologist or psychiatrist to evaluate psychological and psychiatric symptoms for the more complicated cases.

- SOCIAL EVALUATION

This evaluation must take into account major elements that affect certain conformity of the patient and/or aiming to his/her integration in the social life:

- To evaluate resources and needs of the patient;
- To evaluate the capacity and the desire of the patient to reveal his HIV status to competent people of the social assistance network;
- To identify Community services and local social services;
- To develop a network of social services;
- To evaluate forms of social support and people or active relay structures surrounding the patient, such as the family, close friends, the community, religious friends (church), associations and others, and of social service agencies.

Caregivers must explore the position of religion and spirituality in the experience of the person.

- To inquire about the religious and spiritual beliefs;
- To evaluate the use of traditional and complementary health systems and to eventually consider as source of support.

Caregivers must probe concerns that may cause stigma and isolation:

- Discrimination of AIDS patients may compromise access to care, security of their employment as well as their household situation;
- To enable patients to talk about their fears, including their recent experience of discrimination;
- To enable patients to identify the most reliable forms of support in their family and within their community;
- Caregivers must also examine their own ideas and their own fears that may contribute to stigma that the patient experiences;
- Caregivers must evaluate the impact that the disclosure of one's HIV status may have on the patient:
    - To ask patients if they have revealed their diagnosis to anyone;
    - To take note of the reactions from their support system;
    - To examine concerns caused by the revelation of their HIV status: to the spouse, to children, members of the family and friends;
    - To elaborate strategies that enable the patient to reveal his/her HIV status, depending on the degree of preparation of the patient;

- To consider forms of social support and needs. To note any change of the level of social activities since the diagnosis, and concerns that could cause self-stigma;
- To refer to support groups depending on cases.

POSITIVE BEHAVIOUR

When the patient presents himself/herself for the first time in a care giving service, the counsellor who receives him/her in the psychosocial service must have the idea in mind that the consulting patient may not be able to control himself/herself and or may be having trouble in changing and maintaining positive behaviour. The counsellor must therefore make sure that the patient is ready to accept and adopt positive behaviour with respect to his/her health and that of others. It is an opportune moment to discuss his/her risk reduction plans. This is very necessary, especially for the case of couples; the patient should be seen together with the spouse and children (if it is a woman who is HIV positive) to find out if they are already tested. It should also be verified whether the patient does not have other occasional sexual partners and explore the possibility of the reduction of the number of partners and the correct and regular use of the condom.

These modes of behaviour include ***inter alia***:

- To avoid re-infecting oneself and infecting others;
- To reduce sexual partners;
- To correctly and regularly use the condom;
- To discuss family planning with one's spouse;
- To avoid the consumption of alcohol or drugs;
- To take personal and food hygiene measures.

FILLING OF THE PSYCHOSOCIAL FILE

All the data received from the patient during this discussion meeting must be recorded in the psychosocial section of the file.

CONCLUSIONS OF THE SESSION

At the end of discussions, the counsellor must make conclusions related to what he/she has heard and observed. These conclusions are primarily related to:

- The psychological experience of the patient vis-à-vis the infection, the disease and treatment;
- Obstacles to conformity anticipated by the Counsellor;
- Specific problems to be monitored with the patient;
- Orientations made after the meeting.

OBSERVATION

These conclusions must be taken into account during the meeting of the selection committee before initiating antiretroviral treatment.
In the event of difficulties of conformity anticipated by the counsellor, he/she must consider particular monitoring whose objective is to help the patient in eliminating negative factors (related to the individual and /or on his/her surroundings) to conformity of the patient in order to enable him/her to begin antiretroviral treatment as early as possible.
It is necessary to note that the initiation of antiretroviral treatment is never regarded as urgency, especially when there are factors that may hinder the conformity of the patient whereas treatment is a lifetime affair.

✓ Treatment education and initiation sessions

The beginning of antiretroviral treatment requires certain education of patients. The acquisition of basic knowledge on antiretroviral treatment is a precondition before starting treatment.

A session of more or less three days is thus necessary to discuss subjects in connection with treatment and behaviour that underlie conformity to antiretroviral treatment.
The facilitation of the meetings must for that matter be supported by appropriate teaching and training materials to facilitate communication and comprehension.

Subjects to be discussed in the meetings of education and initiation of ARV:

Modes of HIV transmission	○ Sexual transmission; ○ Blood transmission; ○ Transmission of HIV from mother to child.
Difference between HIV and AIDS	
Modes of HIV prevention	○ Abstinence; ○ Correct and regular use of the condom (demonstration, male and female condom); ○ Advantages of the use of the condom for people under antiretroviral treatment.
antiretroviral Treatment	○ Principles of action; ○ Importance of antiretroviral treatment; ○ Modes of taking drugs (set time, supporting tools to a good observance); ○ Side effects; ○ Obstacles to good action of treatment; ○ Monitoring of patients under antiretroviral drugs; ○ Indicators of a good evolution for a patient

	under antiretroviral treatment. o
Nutrition	o Balanced diet ; o Food hygiene.
Positive behaviour	o To avoid unplanned pregnancies; o To avoid alcoholic drinks; o To avoid the use of tobacco and drugs; o Personal hygiene and of clothes; o To have sufficient rest; o Spirituality.

✓ Monitoring Individual Counselling:

Definition

Discussion/conversation between the patient and the caregivers with the objective to help the person to overcome stress and to adopt behaviour that enables him/her live positively with HIV/AIDS. Counselling may be individual or in a group depending on the form of selected intervention.

The individual counselling sessions are very important in the care programme of people living with HIV.
As the patient follows antiretroviral treatment, it is necessary for caregivers to consider a monitoring system that ensures not only good conformity to treatment but also which guarantees the maintenance of the psychological and social equilibrium of the patient. This monitoring must be organised in form of meetings of discussion with quite specific goals

Goals of Monitoring individual counselling

To provide psychological support a) Attack on the self and body cohesion	Psychological support for people infected by the HIV from caregivers and one's surroundings is very necessary for various reasons: In the person infected, the infection by HIV from the start attacks the self and corporal cohesion due to its symptoms such as the appearance of lesions, the loss of weight, the fall of lymphocytes, the chronic nature of the infection are the causes of fragmentation of the body and an obstacle in the relation that "oneself" may perceive with regards to the disease. Other symptoms such as slimming, the appearance of cutaneous lesions, sight troubles, constitute a direct attack of the image and vital functions of the body. Eye troubles, even the loss of sight, for an HIV positive person, constitutes a disorganising and destabilising experience. The irruption of a new somatic attack appears
b) Attack on the self esteem and ego	The HIV infection compromises the perception of oneself in that it undermines the structural integrity of the body, its physical and sexual attraction capacity. The attack of self-esteem may have harmful effects on social integration and maintenance of interpersonal relations of the person infected. This contributes to the change of close and marital relations in case of married couples
c) Effect of the chronic	The chronic nature of the HIV infection disturbs the sense of

nature of the infection	temporal continuity by the alternation of attacks and successive recoveries obliging an HIV positive or sick person to make permanent psychological adjustments and these damages the relations in the external world, and even may be the cause of "anticipated self mourning syndrome". This phenomenon is sharpened by consecutive concrete and abstract losses caused by the evolution of health towards the state of the disease of the person: loss of employment, loss of salary, loss of the capacity of attraction, loss of basic security, hope, ambition, the capacity control, ideals. In most cases, these losses are intertwined, coupled by confrontation with losses of friends among close relations, even the loss of the loved partner.
To prevent the infection among people infected by HIV/AIDS	The subject of prevention of the HIV infection among HIV positive people commonly called secondary prevention remains delicate. Counselling of secondary prevention must tackle two problems; consequences of the phenomenon of re-infection in the infected person and the prevention of the transmission of the virus from parents to the child.
To ensure monitoring of the entire family /family Approach	The character of the mode of HIV transmission makes it an epidemic that threatens families and in most cases affects more than one member of the family. Counselling monitoring sessions of the people enrolled in a therapeutic care programme must take into account this dimension. The counsellor must from the very start, during the psychosocial evaluation make sure that all members of the family (children and spouses) have been tested. It is therefore essential to know if the spouse knows the status of his/her partner. It is especially the case of families with children aged less than fifteen years. Here the counsellor must have in mind the family structure (Genogramme in case of need) of the person and know the HIV status of all people who make the family. **NOTE:** Parents are often afraid to have their children tested. It is therefore the duty of the counsellor to provide appropriate psychological support to the parents to enable them overcome this fear to have their children tested.
To recall modalities for examinations and biological and medical monitoring	It is inappropriate to talk about monitoring counselling speaking about efficient medical and biological monitoring. Monitoring counselling enables the counsellor to check if the patient is well monitored, if the examinations and the weightings were made at the desired time. Monitoring is

	necessary for patients who are under treatment and those that have not yet started. Monitoring of people who are under treatment must be done at least each month and every three months for those that have not yet started treatment. For patients who are not yet under antiretroviral treatment, monitoring sessions enable the counsellor to assess if the tests are carried out at the convenient time, to know when it will be necessary to begin antiretroviral treatment.
To reply questions of the patient	As the patient follows the care programme, he/she starts to understand certain important concepts on treatment and the disease. it is therefore essential to adequately answer all their questions in order to avoid false and/or distorted information which they may acquire elsewhere
Help the patient in his/her social integration	One of the objectives of general care is the social integration of people infected by HIV/AIDS. HIV/AIDS is a disease often perceived as being an incapacitating factor both physically and socially. The counsellor, as he/she accompanies the patient must work on his/her social and professional rehabilitation. He/she must encourage the patient to maintain or resume his/her daily work and to avoid any feeling of impotence and uselessness.

Group Counselling or Group discussions / Group Therapy

Demand	It is often difficult for the patient to explicitly ask for it. Prescription: the counsellor after considering it necessary and useful for the patient. The counsellor chooses the form of intervention in agreement with the patient.
The importance of group counselling	**Group**: A privileged place for self exploration and discovery : • It facilitates interpersonal relations; • Enables the patient to be more lively and more expressive; • Enables the patient to know himself/herself and to be assertive (self-esteem); • Enables the sharing of experiences of each one from the point of view of: ➢ The psychological experience of the HIV positive status; ➢ Conformity to treatment (drugs taken) and side effects; ➢ Importance of drugs; ➢ Adoption of positive behaviour; ➢ Mutual support of patients.
Two moments of group counselling	**Before the beginning of treatment:** **Goals**: • To share the psychological experience of the disease and antiretroviral treatment; • To evaluate the attacks of the patients with respect to treatment; • To provide exact information on treatment; • To correct prejudices and erroneous beliefs on antiretroviral treatment. **In the course of Treatment:** **Goals:** • To reinforce conformity by sharing good experiences ; • To acquire more information on treatment; • To avoid the feeling of isolation (mutual support of patients). Organization of group counselling Elements to be considered:

	• To ensure self consent of each participant; • To constitute groups: to bring together patients with similar problems and of the same age bracket; • To respect the rhythm, choice and personality of each participant; • To lay down group rules (Confidentiality, mutual respect etc.) Role of the counsellor: • To guide; • To facilitate; • To support; • To stimulate.

Steps in group counselling	**To target participants** After deeming it necessary to make a patient participate in a group counselling session: • Elimination of all the factors that may obstruct spontaneous expression of the participants: Age difference, the level of comprehension of participants, etc. • To set an appointment (invitation): After identifying participants in a group counselling session, the counsellor should make sure that all the people concerned are well informed and fix a suitable appointment to them. • Choose the topics: The counsellor in agreement with participants may initially propose the discussion topics. It is desirable, in the future, that topics are proposed by participants. The counsellor always remains the facilitator of the meeting. • Conclusion of the session: o To make a summary of the views discussed during the session; o The facilitator must make sure that the objective of the session are attained; o To communicate if necessary, the date for the next appointment. Note: The counsellor must take care not to integrate other participants in the following meetings if they have not been with the group since the beginning.

✓ **Pharmacy and distribution of medicines**

A drug distribution centre is an important place for answering questions on counselling and conformity to antiretroviral treatment. The nurse working with pharmacy must ask questions to know how many tablets the patient missed the previous month. He/she must also know difficulties related to conformity (use of alcohol and drugs, lapses of memory, sleeps, etc) and help the patient to adopt efficient strategies for properly taking drugs. The nurse at the pharmacy must organise and control the respect of appointments and must

report to other members of the multidisciplinary team cases of abandonment, poor conformity, and disappearances to ensure appropriate monitoring.

✓ Data Processing and Record Keeping

Record keeping and data processing must be well organised in order to ensure confidentiality of the patients. All the members of the team must be conscious of the importance of confidentiality of this information.

Important questions:

- Where is documentation on patients preserved?
- Who has access to the documents?
- Is the filing cupboard or room closed to avoid access by unauthorized people?
- Who has access to the database of patients?
- A good filing of data will enable easy and reliable transmission of data to be forwarded to the TRACNet system (further, in the document reference is made on the discussion on the data to be transmitted).

✓ Home-based Monitoring

The care of HIV positive patients must be extended at home. Organization of home visits appears very effective for monitoring of observance and psychological and social support. Home visits are necessary when psychosocial evaluation shows that the patient will have difficulties in conforming to treatment. Home visits are also necessary to be able to identify cases of abandonment of treatment and disappearances. In addition, home-based monitoring contributes to social reintegration of infected people.

✓ Multidisciplinary Care Team

In the same way, caregivers are also confronted with the psychic impact of the epidemic which differs from the impact of other pathologies, not only because it mobilizes defences of caregivers against death, but also because its mode of sexual transmission. By associating sexuality with death, it exposes them to even greater psychic vulnerability and often attacks their personal emotional certainty vis-à-vis values such as love, life, death, sexuality. The repeated exposure of caregivers to the death of their patients has a demoralising and devitalising influence on them.

The care of caregivers must be organised in various forms: meetings of the psychosocial team, supervision sessions, short therapy sessions to avoid the burn out, etc.

▪ CLOSE PEOPLE /SURROUNDINGS.

HIV/AIDS has psychological and social effects on the people surrounding the patient. These people are confronted with shock, despair and problems of stigma.

An important question cannot be avoided. How do we survive a phenomenon that destroys thousands of people? Living in a Community where approximately half of the people are

HIV positive or sick, the HIV positive people are confronted with a form of post-trauma stress that disturbs their emotional life, their social life and their mode of attachment.

Confronted with multiple mourning, they end up living in a psychic state of "anticipated mourning" and experience a feeling of loss at the thought of any possible meeting with a new partner. The processes of mourning are inhibited and prevented by multiple mourning. This often has the consequence of feeling immense guilty vis-à-vis any new emotional attachment and an activation of anxiety of loss:

- *What is the purpose of initiating new emotional attachment to somebody whom I am likely to lose him or her?*
- *How can I develop long-term closer relations whereas I have not yet psychologically separated with my dead friend?*
- *How do I avoid a new loss?*
- *How shall I avoid being invaded by the memory of all these deaths when I fall in love*?

The care of people close to infected people is therefore an important component of psychosocial care of people living with HIV/AIDS.

▪ VOLUNTEERS IN ASSOCIATIONS

The volunteers in associations are confronted with the same difficulties more especially since they sometimes carry out militant work, following mourning and are for that matter exposed to phenomena similar to multiple mourning. In addition, the logic of proximity of associative structures, which is essential to the quality of their services, has long-term psychic exhaustion effects on the people who work in these structures. Volunteers therefore need specific support to be able on one hand, to carry out their essential functions in fighting against the epidemic and on the other hand, to continue their personal development.

Conclusion: The care and psychosocial support of people living with HIV/AIDS are important components of care both at the level of health structures and at the community level.

PART II

CHAPTER I. The ARV Treatment in countries with limited resources and the Approach of Rwanda

Since the discovery of HIV, considerable efforts have been deployed to find drugs that prevent viral replication. For the last ten years, anti retroviral drugs have become powerful weapons of fighting against HIV by inhibiting its replication. Since then, direct and indirect advantages of this treatment has been observed.

Direct Advantages for PLWHA

There is proof that effective care (including ARV treatment) leads to considerable reduction of morbidity mainly due to opportunistic affections and the mortality of PLWHA. The improvement of the quality of life will result in active reintegration of the person into the society.

Indirect Advantages to the introduction of ARV treatment

- Strengthens voluntary Counselling and testing:

In all countries where access to treatment was established, recrudescence of the demand for testing has been experienced. Indeed, if the fact of testing does not lead to concrete care, the interested person finds only disadvantages and refuses to undergo the test. On the other hand, knowledge that knowing one's HIV status can lead to comprehensive care and that a pregnant woman has access to the programme for the prevention of mother to child transmission (PMTCT), which can considerably reduce the transmission of the virus from the mother to the child, encourages candidates for voluntary testing. It was established that a person who has attended a voluntary service would be more likely to change his/her behaviour than a person that has never been tested.

- Modifies the perception of HIV by the population:

Gradually, an evolution is being made on concept of a disease synonymous with death towards a disease that has become chronic. Thanks to treatment, the future is not any longer about getting ready to die but living positively with HIV/AIDS. In the same way, the sticking image of the dying HIV positive is changing. More and more people in good health are known to continue to lead a normal life as HIV positive persons. Access to treatment has enabled the reduction of stigmatization of PLWHA by the population.

- Reinforces the motivation of health workers

Well-trained health workers see the results of their efforts. They are encouraged by the good results obtained in their patients. In addition, they feel strong determination of public authorities to fight AIDS and know that they are major elements of the global efforts in the fight against this pandemic. However, it is essential to take into consideration-increased workload caused by this pathology not to discourage those who devote themselves without forgetting the care of their patients.

- Improves access to care infrastructures and their quality.

Criticisms are frequently made to the extent that too much attention is paid to HIV/AIDS compared to other dominant pathologies (malaria, tuberculosis); it should be noted that any improvement of a structure with respect to a given pathology involves an improvement of the whole care apparatus of pathologies within this structure. All measures taken to facilitate access to the patients in the care structures benefit all the patients using these structures (improved reception, better staff training, improvement of buildings and the technical platform...)

- Reduced the expenses committed to the care of OI

The best prophylaxis of the opportunistic infections is the initiation of ARV. In countries of the North, the generalization of access to ARV has led to a true transformation of HIV pathology in terms of mortality and morbidity in connection with this infection. The very considerable reduction in the frequency of OI involves double advantage: comfort of life for patients and global economy for the health system due to fact of the decrease of the cost of this acre (reduction of consultations and hospital admissions).

- Decreases socio-economic consequences of HIV on families and the society

The major reduction in morbidity and mortality has an important socio-economic repercussion on the family life and secondarily on the society. It improves the family income and indirectly the psychological, relational and educational environment. It also radically decreases the number of orphan children, who are the secondary victims of this disease.

- Has the potential to improve prevention.

Medical and Community mobilization that surrounds access to treatment, has a considerable impact on the general population. It improves its knowledge on HIV/AIDS. The population can therefore be tested and, through the knowledge on the modes of transmission, modify its behaviour to adopt a responsible attitude with respect to the risk.

It has also been currently demonstrated that the successful initiation of ARV, which makes the viral load undetectable, can contribute to considerable decrease of the risk of HIV transmission by infected people. It should however be underlined that it never rules out this

risk and that PLWHA must always maintain responsible sexual behaviour (abstinence and condom).

It should be noted that in developing countries, numerous obstacles might make difficult the establishment of a national initiative in the area of access to treatment due to:

- Lack of financial resources;
- The necessity to negotiate the purchase price of drugs to make them affordable;
- Frequent difficulties encountered in the procurement and storage of drugs;
- Lack of infrastructures;
- Technical platform often insufficient or stock-out conditions in reagents which makes biological monitoring difficult;
- Lack of qualified and adequately trained doctors and nurses;
- Too rapid migration of the personnel and patients;
- Access (geographical and financial) limited;
- Very frequent stigmatisation, even within medical teams.

The experience has shown that effective HIV care achieved in the country with limited resources. Several countries adapted the public health care approach as suggested by WHO and it is based on:

- The integration of this care in the basic care package at the level of medical facilities;
- The development of national standardized norms for this care.

Standards necessary to the accreditation of an ARV Treatment centre

According to the Ministerial Directive determining therapeutic care conditions and procedures for the care of people living with HIV/AIDS, minimal standards of an accredited ART centre are infrastructure, equipment, personnel, and the existence of the selection committee.

Infrastructure	• Reception and filing of files of patients • Paramedical consultation and for distribution of drugs • Two buildings for medical and paramedical personnel consultations' • A reliable distribution pharmacy in the health facility.
Equipments	Consultation Buildings: o A clean and calm room, which enables confidentiality; o Suitable lighting; o An office; o A clean examination table; o A dustbin or waste basket; o A washing basin and hygienic linen; o Weighing scales; o A tensiometer;

	○ A thermometer. For pharmacy: To possess equipment necessary for conservation of antiretroviral drugs according to pharmaceutical standards and ARV stock, OI and STI management tools.
Personnel	○ For consultation, at least to have a doctor trained in the medical care of HIV/AIDS. ○ To have at least two paramedical staff trained in the medical care of HIV/AIDS. This number will be adapted depending on the number of patients. ○ To have set up a selection committee of patients.
Selection Committee	○ The person in charge of the programme in the care facility appointed by the Director of the health Facility; ○ A representative of the medical team who is in charge of treating PLWHA of various age brackets (paediatrics,, internal medicine) appointed by the Director of the health facility; ○ The person in charge of biological data at the level of the treatment centre appointed by the Director of the health Facility; ○ Two representatives of associations of PLWHA located in the geographical area of health facility appointed by the Network of People living with HIV; ○ Persons in charge of psychosocial teams appointed by the Director of the Health facility; ○ The service matron; ○ The person in charge of the pharmacy.

The circuit of patients

The entry points for ARV treatment are VCT, PMTCT, mobile consultations and hospital admissions. It is from these structures that files of patients are submitted to the selection committee. These files must contain the first social, clinical and biological evaluation of the patient that enables his /her selection according to the national criteria of eligibility. This selection enables patients to access ARV treatment and general care measure.

The Biological circuit

It is appropriate that each care structure of patients is equipped with the essential technical platform for carrying out basic examinations. The capacity to make CD4 tests must be developed at least in a Provincial referral structure. It is important to organize the biological circuit so that tests can be done with maximum ease for patients (day and hour of taking the

specimen, respect of confidentiality). It is also important that the biologist is integrated in the care team of PLWHA and can have access to training facilities.

The medicinal circuit

It is desirable that the use of ARV is organized at the national level in public structures. Indeed, it is advisable to have control of the molecules used that only enable the avoidance of uncontrolled prescriptions, which are possible causes of possible resistance. It is in this framework that the Ministry of Health gave Rwanda Central Drug Purchasing Agency (CAMERWA) the exclusiveness of ARV drug imports; in Treatment Research AIDS Centre (TRAC +) the responsibility to formulate the policy and to ensure coordination of the use of these molecules in Rwanda. Permanent control of stocks with the determination of thresholds from which new orders must be renewed is under the co-responsibility of CAMERWA and TRAC +. Officers in charge of stock management must be appointed within each health facility to ensure regular feedback that enables forecasting new orders.

The monthly cost of the family care is determined by the Ministerial Instructions upon the proposal of several technical Government Organs. Revisions of this instruction are provided for at regular intervals. It is essential that this cost does not constitute a hindrance to access to treatment of the indigent and vulnerable groups within the population (see CHAPTER 3).

CHAPTER II. Principles of Antiretroviral Treatment

ARV treatment is an essential element of the care of PLWHA and changes the natural evolution of the HIV infection It results in the reduction from morbidity and mortality.

Key Treatment Factors

It should be known that treatment always highlights three factors each of which will influence its success:

- The virus which can be more or less aggressive depending on the type and the variety of the infecting virus;
- The patient who will largely inflames the success of treatment depending on his/her associated pathologies (Co-infection hepatitis B, tuberculosis...), his/her capacity of conformity to treatment, his/her way of life and the support that he/she receives;
- The drug which ideally has to be effective, in a prolonged manner and with minimum side effects;
- ARV action mechanism: The HIV multiplication cycle (See Appendix VI).

ARV Action Mechanism: The HIV Multiplication Cycle

HIV is an RNA virus which in order to reproduce, must penetrate a CD4 cell. In the cell, it undergoes a series of mutations to give rise to new viruses.
All ARV act by blocking an HIV multiplication cycle stage at the level of the CD4 cell.

Major stages of the multiplication cycle are:

- The penetration of the virus at the level of the CD4 membrane (by fusion with the assistance of Co-receptors).
- The mutation of the viral RNA into DNA under the impulse of an enzyme: Transcriptase reverse;
- The integration of the DNA thus formed with DNA of the nucleus of the CD4 cell under the action of an enzyme: integrase;
- Release of the viral RNA "son" from the DNA;
- Assembly of new viruses from this RNA and proteins synthesized in the CD4 cell under the influence of protease.
- Release of the particles thus reconstituted.

Major ARV used today block the action of two enzymes: Transcriptase reverse and Protease. Molecules able to block the entry of the virus in the CD4 cell (anti Co-receptors) and integrase are available today.

The duration of the of HIV and CD4 in the course of infection :

✓ **HIV :**

When it is free, circulating in plasma, its lifespan is very short with a 6-hour half-life. Conversely, a very small number of viruses can penetrate cells reservoirs or cell sanctuaries (often macrophages) where it hides and can remain in this form for several years. These cells do not respond to treatment.

Given its very short lifespan, the virus continuously seeks to reproduce and an untreated person therefore manufactures 10 000 000,000 new viruses each day with a very high risk of mutations and the possibility of resistance

✓ **LT4 :**

An infected LT 4 has a half-life of 1.6 days (with one normal lifespan of several weeks). This implies that the more LT 4 are infected, the more it will be necessary that the body quickly manufacture new ones so that the number of LT 4 can be maintained. Nevertheless, the organism gets tired and the number of LT 4 drops gradually leading to an immunity deficit.

✓ **Treatment Action:**

By blocking the multiplication of the virus, the treatment will prevent the production of new viruses (whereas the old ones die very quickly) what is going to make the quantity of virus in blood (what is called the viral load) undetectable. However, there is no cure because there is always the dormant virus in cell reservoirs.

When the CD4 are not infected any more by new viruses, they resume a normal lifespan and their number gradually increase, thus improving the immunity situation.

✓ **Therefore the goals of treatment are:**

- To make the viral load undetectable;
- To trigger the increase of the number of CD4;
- To improve the clinical state of the patient.

✓ **Qualities of good treatment for ensuring good conformity:**

Good treatment is that which combines drugs:

- **Powerful:** able to properly block the HIV multiplication. For that matter, it is essential to combine at least 3 drugs (tri-therapy). This association enables to block the virus at its different level of its multiplication or at the same level but in different ways;
- **Prolonged action:** These combinations have to block this multiplication as long as it is possible;
- The majority of conformity to drugs; it is the first cause that should be looked into in any failure of treatment.

The measures intended to create conditions for good conformity to drugs are detailed in the CHAPTER.

Given the importance of conformity for success of treatment and its influence on psychosocial factors on conformity, the health personnel is obliged to leave the simple medical sphere to care for the patient in a general way. This concept was explained in the preceding chapter. For example, when a patient speaks about depression, the care giving personnel will think of a psychiatric disease, side effects of efavirenz, a financial origin, a marital argument... One easily understands the more complicated character (but also more interesting) of such an approach. For this reason, the concept of multidisciplinary team was proposed.

In any case, all these factors will have to be taken into account to establish a general care apparatus of patients, which mechanism must be capable of ensuring efficient monitoring of treatment.

The care of the patient under ARV treatment:

It should be known that the majority of failures of treatment are in connection with poor observance. It is therefore appropriate:

- To adequately prepare the patient before beginning the treatment; He/she must freely conform to it, give informed consent and know the constraints of monitoring it. One period of preparation essential before the patient is put under treatment. The ARV treatment is never urgent, except in the event of BAE (Blood accidental exposure);

- To prescribe treatment to the patient that is well adapted to his/her rhythm of life; treatment with few doses is better monitored than treatment with many doses (A single dose is the most ideal).

- To adequately inform the patient on methods of proper recording of treatment and on possible side effects.
- Important work must be done around the conformity to drugs by various categories of caregivers).

To make sure that the patient has in his/her immediate surroundings, relay people or godfathers able to support him/her with respect to treatment and, if he/she wishes, to provide him/her with associative and Community support (seer. appendix IX).

The lifespan of HIV and CD4 during infection :

✓ The HIV :

Since it is freely circulating in the blood plasma, its life span is very short with half life of 6 hours. Conversely, a small number of virus can penetrate into cells or cells tanks shrines (often macrophages), where they hide and keep for several years. These cells do not respond to the treatment.
Given its very short lifespan the virus seeks constantly to recur and untreated person manufactures as much as 10,000,000,000 new viruses every day with a very high risk of mutations and possible resistance

✓ The LT4 :

One LT 4 infected is half-life of 1,6 day (with a normal lifespan of several weeks) , implying that more infected with LT 4, there is a more need for the body to quickly manufacture more new such that the number of LT4 is maintained. But, organisms get tired and the number of LT4 lessens progressively leading to the immunity deficit.

✓ Action of treatment:

By halting the multiplication of virus, the treatment will hinder the production of new virus (as the old ones die very quickly) that will lead the quantity of virus in blood (what is called viral lord) undetectable. However, there will be no recovery since there is ever the virus sleeping in the cell reserves

When the CD4 are not infected by the new virus, they take a normal life and their number show progressive improvement as well as immunity situation.

✓ Aims of treatment are :

- Leading to undetectable viral load
- Increasing the number of CD4
- Increasing clinic situation of the patient

✓ The qualities of a good treatment to obtain good compliance

A good treatment is the one that combines medicines:

- **Powerful**: capable of blocking the multiplication of HIV. For that it is indispensable to combine at least 3 medicines (tritherapy). This combination permits to block the multiplication of the new virus at several levels but in different manners.
- **Prolonged action**: these combinations must block the multiplication as much as possible.
- The majority of therapeutic failures are related to the problem of compliance; it's the first cause to refer to before any treatment failure.

Measures destined to the creation of conditions of good compliance are detailed in this CHAPTER.

Given the importance of adherence on the success of treatment and the influence of psychosocial factors, health practitioners are obliged to abandon simple medical spheres to care for patients in a global manner.
This concept was explained in the preceding Chapter. For example, when a patient speaks of depression, the care provider will think of a psychiatric illness, a side effect of efavirenz, a financial source, marital dispute...
We easily understand the more complicated nature (but also more interesting) in a given approach; it's for that reason that the concept of multi-disciplinary team was proposed.

In all cases, the set of all these factors must be put into consideration in the establishment of a capable global framework to ensure proper compliance of patients' treatment.

The follow up of patients on ARV treatment:

It must be understood that the majority of treatment failure are related to poor compliance
It is therefore:

- To well prepare the patient before starting treatment; he must freely accept it, give a clear consent and know monitoring constraints. A period of preparation is indispensable before any treatment. The ARV treatment is never an emergency, except in case of AEB (Accident of Exposition to Blood).

- To prescribe him/her the treatment that is adapted to his lifestyle; treatment with few drug takings enables better follow up than treatment many drug takings (the single taking is ideal).

- Explain well to the patient modalities of taking treatment and the possible side effects. An important work must be done on compliance by different categories of caregivers.

- Ensure that the patient has in his immediate entourage relay persons or godfathers able to support him vis-à-vis his treatment and, if he wishes it, provide collective and community support. (See annex IX).

CHAPTER III. The Antiretroviral treatment: the 1st line regime

Different categories of ARV

There are three principle categories of ARV:

- Nucleoside inhibitors and nucleotides of RT (NRTI) that block the reverse transcriptase in a competitive manner (analogues)
- Non nucleotide inhibitors of the RT (NNRTI) that block the reverse transcriptase in a non competitive manner.
- Protease inhibitors (PI) that block protease

A reminder on ARVs molecules used in Rwanda, their abbreviations, and their commercial names is in annex 1.

Other categories of ARV :

The search for new molecules targeting other sites in the multiplication of HIV is constantly evolving. Many medicines exist to day, but they still the subject of clinical trials or are still restricted to certain regions. They are:

- The entrance and fusion inhibitors (at co-receptors level) of HIV in the CD4
- The integrase inhibitors

The choice of ARV: cost and efficiency

At the national level, the choice of ARV is decided by TRAC according to therapeutic directives determined by experts. The latter consider efficiency, tolerance and the cost of the molecules. For that reason, generic ARV and combined forms are chosen in a preferential manner. (See the recommendations first line regime B, b).

At the international level, Rwanda benefits the support of a number of bilateral and multilateral donors.

At the national level, the treatment initiatives supervised by the CNLS and coordinated by the TRAC through the Ministry of Health according to the national plan of access to treatment, enabling at this time to support access to ARV treatment with the principle of equality of care to all Rwandan population.

Principles of regimes selection

The principle of combining several ARV is based on the need to obtain a powerful blockage to multiplication, it is therefore necessary:

- Either blocking the increase at several levels: reverse transcriptase and protease is the case of the combination for NRTI and PI;
- Either, blocking at the same level but in a different and complementary manner: it is the case of combining the NRTI and NNRTI.

It is indeed, indispensable to completely block HIV multiplication since any residual multiplication while the drug is in the blood will lead to the

selection of resistance that virus develops for its survival. It is called tritherapy combination of 3 molecules.

Major combinations

- 2 NRTI + 1 NNRTI (figure of 1st line)
  Or
- 2 NRTI + 1 PI (figure of the 2nd line)
- The combination of 3 NRTI is possible but due to low capacity it should only be used in case of extreme necessity or after the advice of the specialist.

When and how to initiate treatment among adults?

All HIV positive patients do not need to be put on the ARV treatment. In fact, in the period following the primary infection, the rate of CD4 and the level of viral load will form a plateau during a more or less long period. There is a state of balance between the organ and the virus that results from the effective action of defense means of the immune system.

However, at the long term often accelerated by inter-current infections, HIV will gradually multiply, will more and more infect CD4 and break the existing balance.
It is at that time that we notice a progressive increase of viral load and a decrease of CD4. It is therefore, convenient to give a treatment to block artificial multiplication of the virus.

✓ The eligibility criteria:

The initiation to ARV treatment depends on the three criteria: the clinical stage, the immunological stage and especially social status given major impact of this point over adherence.

Thanks to a precise anamnesis and a comprehensive diagnosis of the patient, the clinician identifies the stage of the patient basing on the WHO classification (see annex VIII). This classification is based on two types of arguments enabling to define the stage: retrospective arguments and other

testing arguments present at the diagnosis. Given the important implications at the clinical stage in the therapeutic decisions, it is necessary to carefully understand the retrospective arguments.

Indeed, a patient can declare to have had 2 pneumonias for the last six months, but it possible to deduce 2 severe bronchitis as pneumonia, which shall largely change the attitude of a clinician.

✓ Criteria of clinical and immunological inclusion

- The confirmed HIV positive status and one of the two following criteria
  - All patients at the 4th stage without considering the number of CD4.
  - All patients on stages 1, 2, 3 having the number of CD4 < 350/mm3.

✓ Social Criteria

- To have disclosed his HIV status to a family member or a close friend,
- Accept a home visit by a care-giver,
- Accept the long term medications
- Be supported by a trusted person in order to improve the adherence ; this person is called “Godfather” or “God mother” of the patient
- Have a known residence on the Rwandan territory (at least 6 months in the catchment area of a health facility.
- Be committed to ever have safe sex intercourse
- Never get anti-retroviral through other programs
- Accept the financial contribution in the absence of the certificate of indigence (see annex IX)

✓ A particular case of a pregnant woman

Pregnancy is not an indication against the initiation to ARV treatment See PART C (see PMTCT).

Note: for HIV positive patients who are not eligible, it is advisable:

- If the CD4 are over 500/mm³, see a doctor for consultation all the 3 months (clinical follow up), and carry out the CD4 counts all the 6 months.
- If they are less than 500/mm3, carry out the CD4 counts all the 3 months.

The recommended regimens of the first line

- Adult: The ARV regimen recommended by TRAC in the first line is:
  - AZT + 3TC + NVP : Regimen of the first intention (avoid AZT if HB <9 g/dl)
  - D4T + 3TC + NVP : the second recommended regimen among patients with anemia
  - TDF+3TC+NVP or TDF+FTC+NVP (recommended regimen for the patients with anemia and side effects due to D4T.
- Note: Give EFV in case of allergy to the NVP or to the patients under the anti-tuberculosis treatment.

Given a big number of existing names for each molecule (specialty and generics), it is indispensable to focus on the international naming (e.g: take in the first place the Lamivudine (3TC) and not Avolam nor Epivir)

✓ Table 1: specific dosage of medicines of the 1st line

Class of medicines	Dosage
Zidovudine (ZDV)	300 mg twice a day
Stavudine (d4T)	30 mg twice a day regardless of the weight of the patient.
Lamivudine (3TC)	150 mg twice a day or 300 mg once a day.
Abacavir (ABC)	300 mg twice a day or 600 mg per day
Efavirenz (EFV)	600 mg once a day
Nevirapine (NVP)	200 mg once a day during 14 days, and 200 mg two times a day
Tenofovir (TDF)	300 mg once a day
Emtricitabine (FTC)	200 mg once a day

The Rwandan government is continuously concerned as about providing ARVs approved by a body of reference like WHO. Given the changing list of ARVs recognized by these institutions, the presentation of molecules that a patient will be given risks to, equally evolve. The table bellow aims to help care-givers to more easily manipulate ARVs in their different formulations. Generics and specialty. These figures are based on the lists of currently available generics and specialties.

✓ Therapeutic Table 1: AZT-3TC-NVP.

Initial phase (first 15 days):

Morning	3TC 150mg + AZT300mg+ NVP 200 mg	= Duovir + Nevirapine	=Combivir (1co) +Viramune (1co)
evening	3TC 150mg + AZT 300mg	= Avocomb (1co)	=Combivir (1co)

Contact phase (after 15 first days):

2X/ j (Morning and Evening)	3TC 150mg + AZT300mg+ NVP 200 mg	= Duovir + Nevirapine	=Combivir (1co) +Viramune (1co)

✓ Therapeutic Table 2: D4T-3TC-NVP.

Initial phase (first 15 days):

Morning :	3TC 150mg + D4T 30mg + NVP 200 mg	= Triviro 30(1co) = Triomune 30(1co)	=Epivir (1 co)+ Zerit30(1co)+ Viramune(1co)
evening:	3TC 150mg + D4T 30mg	=Coviro 30	=Epivir (1 co)+ Zerit30 (1co)

Contact phase (after 15 first days):

2X/J (morning and evening)	3TC 150mg + D4T 30mg + NVP 200 mg	= Triviro 30(1co) = Triomune 30(1co)	=Epivir (1 co)+ Zerit30(1co)+ Viramune(1co)

✓ therapeutic diagram 3 : TDF+3TC+NVP

* initial phase 15 days 1x/d (once a day)	TDF 300mg + 3TC 300mg + NVP 200 mg	=	=Tenofovir+ Lamivudine (1 co)+ Nevirapine(1co of 200 mg)
*Contact phase 1x/j (once a day)	TDF 300mg + 3TC 300mg + NVP 400 mg		=Tenofovir+ Lamivudine (1 co)+ Nevirapine(1co of 400 mg)

✓ The HIV-TB Co-infection

- In Rwanda the incidence of tuberculosis has more than doubled during the last ten years due to co- infection cases of TB-HIV. During the first quarter of 2005, 48% of diseases TPM+ patients

were tested for HIV and among them 44.3% were HIV+. Regarding the TPM- patients and TEP, 57% were tested and 66.5% was HIV+. HIV is mainly transmitted through sex intercourse, but also by the contaminated blood transfusion, injections or from an infected pregnant mother to her child, during pregnancy, delivery or breast feeding.

- The HIV infection causes gradual destruction of immunity and favors the opportunistic infections, among which there is tuberculosis. When an HIV infected person develops the opportunistic infections it is said that he has AIDS.
- People infected by HIV have from 10 to 50 times increase of developing active tuberculosis than non infected persons. Indeed, 50% of the co-infected people will develop tuberculosis during their existence (in the absence of ARV treatment) whilst this percentage was ranging from 5 to 10% for the non HIV infected persons.
- As the HIV infected favors the rapid passage of tuberculosis infection to the disease of tuberculosis, this accelerates the progression of HIV infection (by increasing the viral load).

Tuberculosis is the first cause of mortality among HIV infected persons. The systematic detection of tuberculosis among all persons living with HIV and early treatment is the most effective means of prolonging their lives.

✓ HIV Consequences for tuberculosis control

- Increase of the number of cases of tuberculosis linked to the HIV infection.

- Late diagnosis since patients with symptoms of tuberculosis delay to make consultation due to the fear of stigma linked to HIV and TB.

- Difficulties in diagnosis given the different clinical presentations of tuberculosis linked to HIV. Increase of extra-pulmonary cases and TPM- (most frequent presentations at the advanced stage of immunodeficiency).

- The difficulty in treating a single patient with 2 diseases at the same time, in 2 separate care services.

- The difficult to achieve a satisfying success given higher rate of mortality during the treatment as well as more number of abandonment cases linked to the toxic effects of drugs.
- High rate of relapses.
- Risk for the nosocomial infection.
- Overloading work in TB and HIV care services.

Testing of the co-infection

The testing of TB-HIV co-infection aims to:

- To assure early care of co-infected patients
- To monitor the trend of HIV infection among the tuberculosis patients as well as the tuberculosis prevalence among the HIV infected persons

In practice, the testing of the co-infection will be organized as follows:

- Explain at level the every new case of tuberculosis that 2 diseases are frequently associated and advantages of making HIV testing.
- Suggest systematic testing and carry out it, except in case of patient refusal. Results will be confidential.

✓ Advantages of HIV testing (see annex VIII)

- A patient will have the best knowledge of behaviour at risk and precautions to take with a bid to avoid the transmission of the infection.

- In case of positive results, early monitoring will be carried out and the patient will receive the necessary treatments (prevention of opportunistic infections, ARV). He will receive a psychological support enabling him to manage the anxiety linked to the disease

and take important decisions, for example in relation to his reproduction.

✓ Search the tuberculosis in all new HIV positive patients during the follow up consultations, by using the questionnaire (see annex VII)

- In countries of high HIV prevalence, tuberculosis can be the first sign of HIV infection. The disease often develops at the early stage of HIV infection and appears under a pulmonary form to positive smears.
- However, when the HIV infection is at an advanced stage, the tuberculosis diagnosis is more complicated since the spit diagnosis is often negative, the clinic and X-Ray photography are atypical. The pulmonary forms with negative smears and the extra-pulmonary forms are the most frequent.
- The characteristics of the tuberculosis therefore, depend on the level of immunodepression when the disease develops:

Characteristics	HIV premature infection	Late HIV Infection
Clinical forms	Pulmonary TBP	○ disseminated TB or EP ○ TP with negative smearing ○ General predominant signs (fever, loss of weight)
Bacilloscopy	often positive	positive or negative
X-Ray Photography	more frequent cavities	opacities, infiltrations without cavities
CD4	< 500 / mm3	< 100 / / mm3

- The spit examination remains an indispensable diagnostic element of tuberculosis due to its capacity to identify infectious cases with positive smears.

- The differential diagnosis of tuberculosis with negative smears and other pulmonary pathologies linked to HIV is difficult and must follow the program algorithm diagnosis (chapter 1.3).

Care of HIV positive patient infected by tuberculosis

✓ **TB treatment is a priority and must be supervised (DOTS)**

- The response to treatment is similar and the expectoration becomes negative as quick as among the tuberculosis patients who are not infected with HIV.
- However, tuberculosis patients infected by HIV have a higher risk of toxicity related to drugs.
- Mortality during the treatment (often linked to other causes)
- Relapse and re-infection
- Since gastro-intestinal disorders are frequent in patients who are HIV +, bad taking of drugs must be considered when TB persists in spite of adequate treatment.
- In case of re-treatment, it is indispensable to use a sterile syringe and needle for every injection of streptomycin.

✓ **Antiretroviral drugs**

- The clinic and biological criteria of eligibility are confirmed HIV(+) and 1 of the following 2 criteria:
-
- Symptomatic patient, stage 4, without considering the CD4
- Symptomatic patient, stage 1, 2, 3, with some severe signs of (TUBERCULOSIS, Esophageal candidiasis, herpes) + CD4<350 /mm3
- Note : According to WHO classification and of CDC for adults :

- Extra pulmonary tuberculosis = stage 4
- Pulmonary tuberculosis in previous year =stage 3
- Most of HIV positive tuberculosis patients are therefore, eligible for the treatment of ARV and will be referred to a site of ARV accredited treatment.
- For the co-infected patients, the priority is to treat the tuberculosis. The opportune moment to start the tri-therapy is defined in relation to state of clinic and the rate of DC4, as indicated in the following table:
- The ARV treatment can differ in some cases of TBEP (TB ganglionic and uncomplicated pleural attack)

-

TREATMENT OF TB – HIV /AIDS PATIENTS	
SITUATION	RECOMMANDATION
TBP and CD4 < 200 / mm3 or TBEP	Initiate the anti-TB treatment Start the administration of one the combinations of ARV bellow between 2 and 8 weeks after the beginning of the tuberculosis treatment. AZT+3TC+EFV TDF +3TC+EFV TDF+FTC+EFV D4T+3TC+EFV For only pregnant women : AZT+3TC+ABC1,2 D4T+3TC+ABC1,2
TBP and CD4 between 200-350 /mm3	Anti-TB treatment ARV after 2 months (make the CD4 count after two months of anti-tuberculosis treatment to serve as the baseline)
TBP and CD4 >350/mm²	Anti-TB Treatment Make CD4 count after 2 months of anti-tuberculosis treatment, if CD4>350 continue the anti-tuberculosis treatment only; if CD4<350 initiate the ARVs treatment.
Àt the end of TB treatment, the treatment must be modified to come back on the first intention diagram.	

D4T= Stavudine ; AZT : Zidovudine ; 3TC : Lamivudine ; EFV : Efavirenz ; ABC : Abacavir
TDF : Tenofovir ; FTC : Emtricitabine

- In case of anti-TB treatment combined with ARV, we use the EFV 600 mg (no need to increase the dose for EFV) instead of NVP (Nevirapine) since the Rifampicine reduces the effective dose of NVP and increases the risk hepatotoxicity

- The risk of Peripheral neuropathy is increased when taken concomitantly with D4T and the INH. To prevent neuropathies, we will give the pyridoxine or vitamin B6 (1 tablet of 50 mg per day)

- The AZT increases the risk of anemia. Monitor the hemoglobine.
- The ABC is not used in some particular situations among pregnant women to avoid the risk of teratogenicity of the EFV at the first quater of pregnancy.

✓ **ARV Treatment among children under the anti-tuberculosis treatment :**

It is preferable to wait until the end of intensive phase of tuberculosis treatment before initiating ARV treatment. If the ARV treatment is urgent (stage 4 or CD4<15%), the ARV treatment will be initiated in 15 days after the starting of TB treatment (if this one is well tolerated).

If < 10 kg:

AZT or D4T + 3TC + ABC or NVP×2. The dose of NVP will be doubled given the combination with rifampicine. It will be imperative to closely follow the hepatic functioning of the patients (GPT to 2 weeks, 1, 3 and 6 months). These children will be followed up in a referral center.

If > 10 kg:

2 NRTI + EFV. The dose of EFV is increased by a third given the combination with rifampicine (e g: if the normal dose is of 300mg => give 400mgr)

Lpv/r : Lopinavir/ ritonavir

NRTI: nucleoside and nucleotide inhibitors of reverse transcriptase (AZT, 3TC, D4T, DDI, ABC, TDF).

After putting in place ARV treatment, some diseases develop the syndrome of immunity regeneration (SIR), with clinical deterioration and signs like

high fever worsening of respiratory symptomatology, increased adenopathy. This syndrome corresponds to an inflammatory response to the opportunistic infection and must not be considered as a clinical failure. The tuberculosis treatment must be maintained and the patient will be referred to a physician responsible for providing ARV for appropriate treatment.

Patients with tuberculosis and infected by HIV will be served with a comprehensive care made up of:

Correct clinical care
The direct supervision of tuberculosis treatment
The necessary care

The counseling and psychosocial support.

This comprehensive care is organized at each level and must actively incorporate the community and family.

Prevention of tuberculosis among VIH+ persons
All HIV+ patients must be protected from all contacts with tuberculosis patients and be informed of situations that increase risks of tuberculosis contraction.

At the hospital the HIV infected patients must be separated from the suspects and cases of pulmonary tuberculosis.

Ensure the frequent ventilation of waiting hall and hospitalization, emergencies, laboratory and X-Ray Photography service.
Wherever the HIV-infected patients are regrouped (hospital services, hospices, community support groups, prisons etc.) we must pay attention to the possibilities of a tuberculosis onset and assure early testing and opportune treatment of the disease.
Vaccinate children with BCG, even HIV+, except those who have had AIDS or malnourished or <2.5kg.
The INH preventive treatment is recommended by WHO for HIV infected persons. In practice, given the difficulties of excluding active tuberculosis

or even latent among those people with available resources in health facilities, this measure is not recommended by PNILT and TRAC.

Prevention of HIV transmission

Inform all TB patients of the measures of HIV prevention :
Abstinence
Faithfulness (reduce the number of sexual partners)
Condom use (have a stock for TB patients)
Treatment of sexually transmitted infections (STIs)
Use of syringes for any injection.

Refer HIV infected pregnant women to PMTCT, for treatment and prevention of HIV transmission to children.

When ARV therapy is indicated, the Ministry of Health recommends that people suffering simultaneously from TB and are HIV infected complete the initial phase (2 months) of their TB treatment before starting ARV treatment, unless there is a significant risk of evolution of the disease of HIV and death during this period (see Table 2.

If a person requires a simultaneous treatment against TB and HIV, 3 first possible treatment are :

AZT + 3TC + EFV or D4T + 3TC + EFV or TDF + 3TC+EFV
For only pregnant women: AZT + 3TC + ABC or D4T + 3TC + ABC (at the third quarter, a regimen composed of EFV is possible).
If the EFV is at the same time administered with rifampicine, the usual direction for use of the EFV does not change and remains 600mg.
If a patient is treated with a regimen composed of NVP and has tuberculosis. The NVP will be replaced by EFV. How is it done?

The patient will take:
In the morning : AZT or D4T+3TC+NVP as usual
In the evening : AZT or D4T+3TC+EFV 600mg
Or TDF+3TC+EFV

Then the following day :

AZT or D4T+3TC 2x/day +EFV 600mg 1X/day or TDF+3TC+EFV
The NVP is then stopped and we can start anti-tuberculosis in all the serenity.

The combination of PI with the tuberculosis treatment is not advisable and adapting new doses would be necessary after approval by a specialist.

Therapeutic diagram 1: AZT-3TC-EFV.

Morning	3TC 150mg + AZT300mg+	= Duovir	=Combivir (1co)
Evening:	3TC 150mg + AZT 300mg + EFV 600 mg	=Duovir Stocrin 600mg	=Combivir (1co) + Stocrin 600mg

Therapeutic diagram 2: D4T-3TC-EFV

Morning:	D4T 30mg+ 3TC 150mg	Coviro30	=Zerit30 (1co) + Epivir (1co)
Evening :	D4T 30 mg+ 3TC 150mg+ EFV 600mg	Coviro30 Stocrin 600mg	=Zerit30(1co)+ Epivir(1co)+ Stocrin 600mg

Therapeutic diagram 3 : TDF-3TC-EFV

1x/d (a day)	TDF 300mg + 3TC 300mg + EFV 600 mg	=	=Tenofovir (1 co)+ Lamivudine(1co)+ Efavirenz(1co)

The initial assessment, clinical and biological monitoring of a patient under the ARV regimen of the first line

Every patient put under treatment must be strictly monitored on a clinical and laboratory level that is part of the contract he has with his caregiver when he accepts to be put on treatment.

Examinations requested for initial check up of all patients:

Complete clinical examination and screening questionnaire (exclude an active TB) and Lab: the CD4, the NFS and ALAT.

Clinical and biological follow up of patients under treatment: it is important to closely follow the patient (frequency of monitoring see annex 4) during the first month in order to optimize adherence and detect as early as possible the side effects of ARV.
Systematic clinical follow up must be done every three months and make a CD4 control every six months if CD4 are above 500 CD4.

Table 3: clinical and biological follow up of patients under treatment

Date	Clinic	Laboratory
Pre-ARV	+	CD4, NFS (GPT, Creat and Rx thorax according to the alert signs)
J 15	+ adherence	
M 1	+ adherence	NFS if AZT, GPT on clinical indication
M 2	+ adherence	Nothing
M 3	+ adherence	NFS if AZT, GPT if NVP
M 4	+ adherence	Nothing
M 5	+ adherence	Nothing
M 6	+ adherence	CD4, (NFS, GPT on clinic indication)
Before sixth months		
Monthly during 1 year	+ adherence	CD4 : all 6 months GPT : M 12, stop the follow up of GPT from M 12 Some examinations will be directed by clinical data Make viral load for all 12 months

The amylasemia will be controlled only in the event of abdominal pain that could be due to the pancreatitis (possible side effects of D4T).

The creatinine will be monitored before the ARVs if a patient is hospitalized or in the case of toxicity or if HTA or in case of nephrological history.

After treatment of one year, in the absence of a problem, a visit that is paid every six months to the physician is enough whereas a visit to a counselor (a nurse warble for this position) will be maintained to a minimum of three

months. This visit to the counselor will be mixed; the basic medical follow up and monitoring counseling.

The GPT would be done as a pre- ARV check up in relation to NVP and one month control

The viral load will be done in case of clinical failure: appearance of a new opportunistic infection or a malignant infection which shows a clinical evolution of the disease. The reappearance of a previous opportunistic infection. The tendency towards a higher clinical stage, after the exclusion of the immune-regeneration syndrome.

Return of CD4 to the basic pre-therapeutic level or below this level without any concomitant infection that would cause a transitory decrease of CD4.

A drop of more than 50% of the rate of CD4 counts below a maximum value obtained, out of any concomitant infection that would cause a transitory decrease of CD4

The used ARV molecules in Rwanda, their abbreviations, and commercial names (Available in Rwanda)

Name of the molecules	Abbreviations	Commercial Names
the nucleonic inhibitors of the RT (NRTI)		
Zidovudine	AZT	Retrovir®
Lamivudine	3TC	Epivir®
Stavudine	D4T	Zerit®
Emtricitabine	FTC	Emtriva®
Didanosine	DDI	Videx®
Abacavir	ABC	Ziagen®
The nucleoside inhibitors of the RT (NRTI)		
Tenofovir	TDF	Viread®
The nucleoside inhibitors of the RT (NNRTI)		
Nevirapine	NVP	Viramune®
Efavirenz	EFV	Stocrin®
The protease of inhibitors of the (PI)		

Lopinavir /ritonavir	LPV/r	Kaletra®
Nelfinavir	NFV	Viracept®
Indinavir	IDV	Crixivan®
Ritonavir	RTV	Norvir
Associations		
	D4T+3TC+NVP	Triviro/Triomune®
	AZT+3TC	Duovir®, Combivir®
	AZT+3TC	Avocomb®
	D4T + 3TC	Coviro ®

Other available ARVs outside Rwanda

Name of molecules	Abreviations	commercial names
The nucleoside inhibitors		
Zalcitabine	DDC	Hivid®
The Non-Nucleoside inhibitors		
Delavirdine	DLV	RescrPItor®
the inhibitors of the protease		
Amprenavir	APV	Agenerase®
Atazanavir	ATV	Reyataz®
Fosamprenavir	APV	Lexiva®
Saquinavir	SQV	Fortase, Invirase®
the entry inhibitors		
Enfuvirtide	T 20	Fuzeon®

Algorithm of initiation and the monitoring ARV treatment

Before the detail of this algorithm, it is interesting to clarify the role of each member of the team to explain how this will function.

✓ Nurse coordinator:

If we want the consultation to function, it is important that at the minimum, a nurse with a solid experience be permanently appointed to the ARV consultation. This nurse will be the coordinator of psychosocial service.

What will be her/his role?

- S/he will be the first person to be met by a patient who needs to be integrated in the consultation.
- The first contact: s/he will explain how the consultation works, already filling a psychosocial file, will explain the regulations of confidentiality for clinical applications. It will permit to give a hint to the patient. The advantage of this person is that s/he gives a human face to the consultation. S/he Will enable a patient to feel

confident than before. In effect, this first day for the patient seems to be a difficult moment, since during this first day there are no longer questions hiding his/her name as during VCT for instance. S/her must disclose and say things that he perhaps would never tell to any person.

- Selection of patients: this nurse plays a role of sorting out the patients who will be receiving patients on behalf of a physician ever overwhelmed by the work. During the first visit of the patient, s/he can directly evaluate whether the patient can immediately meet the physician or can keep waiting as taking the prescribed CD4 dose before paying a visit to the doctor. This economises the visit of the physician. Then, for other visits of the patient, he could quickly be evaluated if Then during other visits to the patient the nurse will weigh the patient, perform the examination results of biological monitoring and report to the doctor in case of pathological results. In case of normal results, s/he will realize a monitoring counseling and give an appointment for next test. If the patient wishes to see the physician, he will obviously see him/her.

- A patient will be seen by all means, at third month and at the sixtieth month by a physician.

- Individual Counseling: this nurse will carry out (with the help of other colleagues if needed) counseling of patients who must be prepared for ARV. He will thus have a good knowledge of all patients. If there is no any other person, he will also perform group counseling. .
- Data entry: he will be responsible for the data entry to be provided to TRAC and will be supervised by a physician during the monthly report.
- This is a heavy work. It is therefore, interesting that this nurse be assisted by a social worker for the management of files for example.
- It is equally interesting to consider the usage of the agenda to work on the appointment with patients.

✓ Nurse pharmacist:

Ideally, a second trained nurse must be attached to the consultation on a full time basis. This one will be in charge of ARV pharmacy. He/she therefore is the in charge of distributing ARV, procurement and reports of pharmacy (with the supervision of a physician). This person in other words will be helping the coordinator in the group counseling.

However, it is recommended that you set different schedules in order not to get sit a contagious TB patient next to an HIV infected patient.

The nurse of ARV pharmacy can also help the nurse distributing tuberculosis drugs for counseling and HIV testing of TB patients. This will enable better coordination between two services that often serve the same patients.

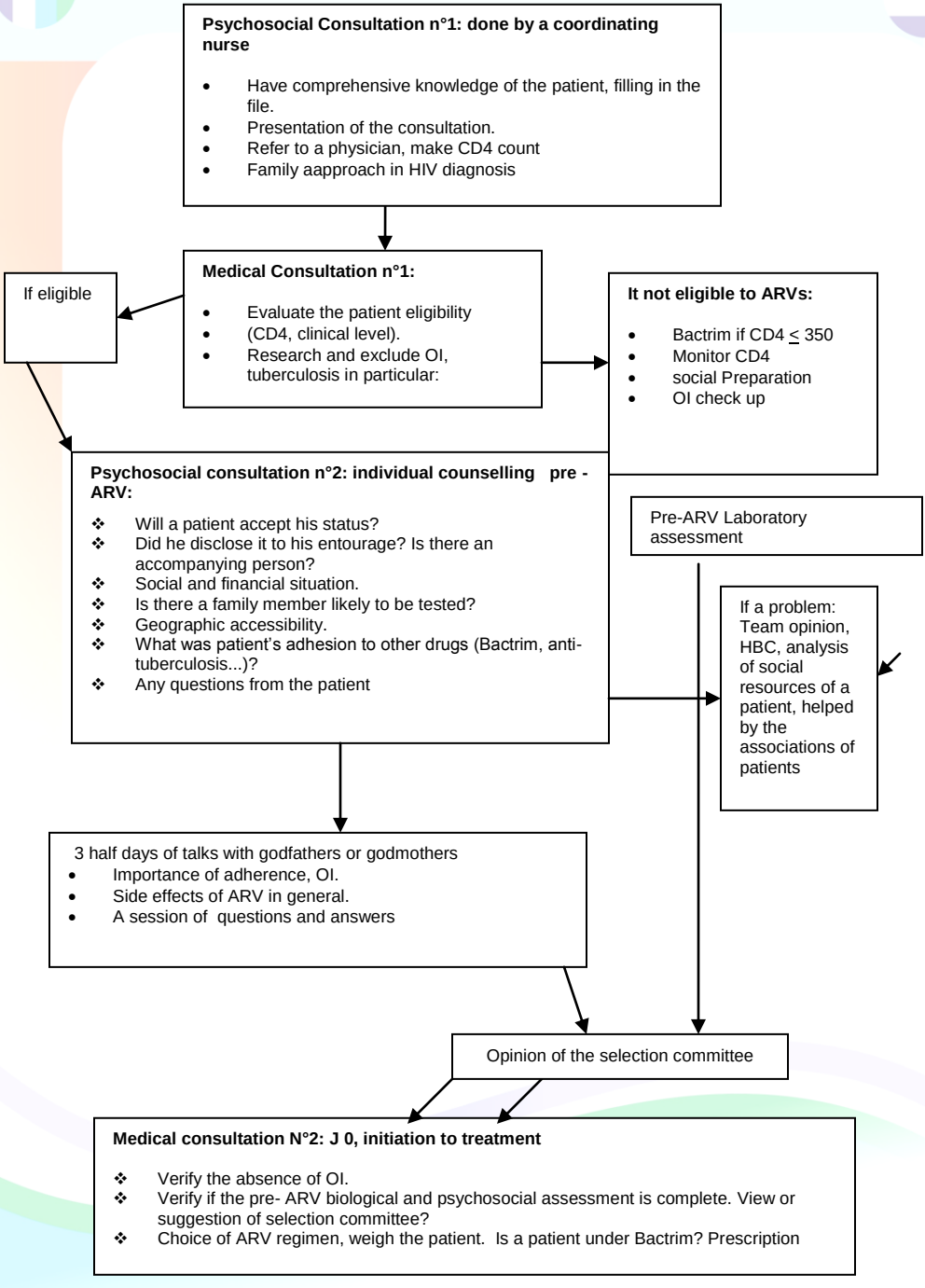
✓ Nurse integrated in the services

Other nurses will necessarily ensure diagnosis (pre and post test counseling) and the follow up of HIV+ hospitalized patients (particularly in maternity and internal medicine).
The team will be extended depending on the number of patients to be treated:

✓ A physician:

S/he will have a heavy task of coordinating clinical activities bearing in mind that delegating tasks to others remain a priority. The ideal leader is that permitting every one to give his best and express himself with full liberty. Coordinating does not mean taking all decisions alone.

In a health center this role could be accomplished by a nurse but the description of tasks will be redefined latter.


Psychosocial Consultation n°1: done by a coordinating nurse
Have comprehensive knowledge of the patient, filling in the file.
Presentation of the consultation.
Refer to a physician, make CD4 count
Family aapproach in HIV diagnosis
Medical Consultation n°1:
Evaluate the patient eligibility
(CD4, clinical level).
Research and exclude OI, tuberculosis in particular:
If eligible
It not eligible to ARVs:
Bactrim if CD4 ≤ 350
Monitor CD4
social Preparation
OI check up
Psychosocial consultation n°2: individual counselling pre - ARV:
Will a patient accept his status?
Did he disclose it to his entourage? Is there an accompanying person?
Social and financial situation.
Is there a family member likely to be tested?
Geographic accessibility.
What was patient's adhesion to other drugs (Bactrim, anti-tuberculosis...)?
Any questions from the patient
Pre-ARV Laboratory assessment
If a problem: Team opinion, HBC, analysis of social resources of a patient, helped by the associations of patients
3 half days of talks with godfathers or godmothers
Importance of adherence, OI.
Side effects of ARV in general.
A session of questions and answers
Opinion of the selection committee
Medical consultation N°2: J 0, initiation to treatment
Verify the absence of OI.
Verify if the pre- ARV biological and psychosocial assessment is complete. View or suggestion of selection committee?
Choice of ARV regimen, weigh the patient. Is a patient under Bactrim? Prescription

Medical or nurse consultation N° 4: Month 1

- Does a patient has a complain? Weight of the patient?
- Adherence: how many tablets have you forgotten last week?
- Tolerance: make important review of the side effects.
- Biological follow up: interpret results of taking blood made the previous day and arrange the following visit.
- Questions of the patient?

Distribution of ARV to the pharmacy N° 3: month 1

- Evaluation of adherence.
- Verify the understanding of taking ARV.
- Evaluate the tolerance.
- This visit must be coupled with the follow up counseling.

Distribution of ARV at the pharmacy N° 4: 6 weeks

- Evaluation of adherence.
- Verify the understanding concerning the taking of ARV.
- Evaluate the tolerance.

Distribution of ARVs at the pharmacy N°5 : 10 weeks
- Evaluation of adherence.
-Verify the understanding concerning the taking of ARV.
-Evaluate the tolerance.

N case the patient is under NVP : at 1 M of medical consultation by a physician or a nurse N° 3 :

- ❖ Has the patient complains ?
- ❖ Weigh the patient
- ❖ Adherence: how many tablets have you forgotten last week?
- ❖ Tolerance: make important review of the side effects.
- ❖ Biological follow up: interpret results of taking blood made the previous day and arrange the following visit.
- ❖ Questions of the patient?

Medical Consultation N° 5: Month3

- Does the patient has a complain?
- Adherence: how many tablets have you forgotten last week?
- Tolerance: make an important review of side effects.
- Biological follow up: interpret the results of blood sampling done the previous day, arrange for examinations and follow-up visit.
- Questions of the patient? Coupled with a follow up counselling
-

The distribution to the pharmacy will continue to be carried out all the months according to the same mode.

Medical Consultation N° 6:6 months

It is a very important moment; it is the time of the first assessment

- Does a patient has complains?
- Clinical evolution: OI? Taking weights? General state?
- Adherence: how many tablets have you forgotten the previous week?
- Tolerance: make an important review of the side effects.
- Biological follow up: interpret the results of CD4
- Questions of the patient?

If during the course of the process, the patient must be hospitalized, he must be followed up during the hospitalization.

A 6 months counseling: time of the assessment

- Explain again that a patient must not abandon his efforts for fear of seeing the sickness recur to the patient, to ensure that the disease recovers
- Discuss with patients the matter of possible pregnancy and the family planning
- Recall that the virus can be transmitted even if it is undetectable.
- Discuss the issue of the condom with the couple.

However, the intercurrence of some OI can delay the initiation to ARV treatment (TB, diarrhea, or vomiting, in general the total acute phase)

If treatment must start or if the patient is already on ARV, the following plan must be followed

During the hospitalization, the counselor must verify the tolerance and adherence by always asking how many tablets remain and by verifying if this corresponds to the number of drug takings. However, it is not a matter of a police investigation

The counseling must be done at the hospital with the godfather and the godmother.

CHAPITER IV. When and how to change the treatment regime?

There exists no founded reason of modifying systematic treatment. Any modification thereof must be decided upon, based on given clinical or biological data. An efficient and well tolerated treatment can not be changed except in case of absolute necessity (stock shortage).

The first ARV therapy must be both active and durable. Once there is adequate adherence, clinical and immunological benefits shall also be durable. ARV treatment need to be changed with precaution.
Regeneration through anamnesis of the ARV sequence may influence therapeutic decisions based on the available data on resistance and cross resistance. Besides, premature changes may exhaust future possible options.

Clinicians may be obliged to carry out modifications in treatment under the following 4 main circumstances :

- Toxicity: a serious side effect
- A therapeutic failure
- Pregnancy
- Medicinal Interaction

In this chapter, we shall tackle changes due to toxicity and failure. The problem of tuberculosis has been dealt with in the previous chapter whereas an insight into pregnancy shall be done in PART C. As for the case of toxicity, just only one type of drug should be substituted.

In case of therapeutic failure, the whole combination should be changed.
The present chapter shall be divided into three (3) parts:

- A. Changes in ARV treatment for reasons of toxicity: Presentation of different ARV molecules and the management of the side effects.
- B. Biological criteria of stopping a treatment regime.
- C. Change in ARV treatment due to failure: Definition and management of therapeutic failure.

Change in ARV treatment due to toxicity: Presentation of different ARV molecules at the management of heir side effects

✓ INTRODUCTION:

When initiating the treatment, opportunistic diseases pose greater threats; and even more hastily, the ARV side effects become the major preoccupation in the care of the PLWHA.

Side effects may be detected symptomatically or through biological check-ups. Some of these symptoms are quite negligible or just come and disappear whereas others need to be treated symptomatically or need a very close clinical follow-up.

Once a serious toxicity appears due to the use of specific ARV treatment, it becomes possible to substitute one molecule. In this chapter, we intend to explain some common side effects of molecules for each class of the ARV and then, study in more details, about each molecule used in Rwanda. The table below summarises the side effects of the drugs appearing on the first line, as well as suggestions for substitution.

✓ Major side effects in the first diagram and recommended treatment for substitution

Regime	Toxicity	Alternatives Molecules
AZT/3TC/NVP	• Persistent gastro-intestinal Intolerance or haematological toxicity linked to AZT • Severe hepato toxicity accrued to NPV • Severe Rash due to NVP that causes no danger to health • Rash due to NVP that leads patients' health to danger(Stevens Johnson)	• Change of ZDV -> d4T • Change of NVP -> EFZ (except during pregnancy) • Change of NVP -> EFZ • Change of NVP -> LPV/r
D4T/3TC/NVP	• Neuropathy and / or pancreatitis due to D4T • Lypodystrophy due to D4T; • Severe Rash due to NVP that causes no danger to health • Rash due to NVP that exposes patients' life to (Stevens Johnson) • Severe hepato toxicity due to NVP	• Change of D4T-> AZT • Change of D4T -> TDF o ABC; • Change of NVP -> EFZ (except during the fist quarte of pregnancy) • Change of NVP -> LPV/r • Change of NVP -> EFZ (except during pregnancy)
AZT/3TC/EFZ	• Persistent gastro-intestinal intolerance or haemalogical toxicity due to AZT • Persistent SNC Toxicity due to the EFZ	• Change of AZT -> D4T • Change of EFZ -> NVP

D4T/3TC/EFV	• Neuropathy or pancreatitis due to D4T • Lypodystrophy due to D4T • Persistent SNC Toxicity due to the EFZ	• Change of d4T -> ZDV • Change of D4T -> TDF (1) • Change of EFZ -> NVP
TDF/3TC/EFV	• Renal Toxicity linked to TDF	Change of le TDF -> AZT ou ABC

Principles of managing side effects :

1° **Knowledge of molecules:** Nursing staff must know very well about each molecule, and must be able to detect the side effects whenever they arise.

2° **Patient's knowledge**: If ever a patient is informed of the major side effects of molecules he is taking, he/she may be able to come for consultations on time in case of arising serious after effects,

3° **Not associated,** in any possible way, with molecules that cause the same side effects (e.g: D4T et DDI).

4° **Change only the molecule responsible for the respective side effects**: This is the most often applied rule. It is sometimes difficult; however, to know which is exactly the responsible molecule. In retrospect, such changes should not be taken lightly, given the limited number of available molecules in Rwanda.

5° **Look into each side effect identified** in the patient's file; as such information remains paramount in the process of choosing which type of regime a patient may finally take.

6° **Remain attentive and accessible**: The nursing staff must interrogate the patient for any arising side effects and assures him/her of a permanent access to services.

Nucleoside inhibitors of the Reverse Transcriptase (NRTI) :

✓ Important side effects:

Lactic acidosis may appear with all nucleosides, although it may be more common among patients on Stavudine (D4T) treatment and aggravates with the mixture of DDI + D4T. Symptoms of lactic acidosis are rare (less than 0.1%) but up to 5% of symptoms among patients under NRTI treatment may have an increased level of lactic acid. Although less common, the syndrome must be familiar to the nursing staff due to its potential danger.

Such symptoms are reflected through fatigue, abdominal pains, nausea/vomiting, dyspnoea and loss of weight.

Medical check-ups show an increased level of lactic acid with or without metabolic acidosis. An increase of the anion-active hole (Na– (Cl+CO2)>16, and the phosphokinase creatinine (CPK), transaminases, and the LDH may also be noticed. Hepatic steatosis may also be objectified through medical imaging.

The best reaction is to interrupt the incriminated anti retroviral agent (particular precaution with the D4T and the DDI). Lactic acidaemia disappears after a period of three to six months. Resumption of the ARV often requires consultation with the experts, as the safe reintroduction of the NRTI has not clearly been demonstrated.

The Lypodystrophy is identified through loss of under skin peripheral fats and the accumulation of fats on the abdomen, on the upper part of the back, on the chest and on some under-skin tissues.

It presently and more frequently meets whenever the D4T is used, he mixture of D4T/DDI (and at least the AZT) during prolonged treatment (see point c). Therapeutic means are limited to physical exercises (with the danger of worsening the Lypodystrophy and change in the ARV treatment. Few data exist on the point, but apparently, premature substitution of D4T by TDF, or by ABC brings about little results.

Zidovudine

Category:

Anti-retroviral Agent, similar to nucleoside, which inhibits reverse transcriptase (NRTI)

Important Information:

Presented in a mixed form with lamivudine (3TC).

Side effects:

- Zidovudine is generally well tolerated. Mostly identified secondary effects (5% of patients) are moderated headache, nausea, vomiting, asthenia and myalgia. Those symptoms disappear frequently after some weeks.

- The myelotoxicity is also possible. After treatment on AZT, the following symptoms that are, extreme fatigue, paleness, dyspenia or dizziness would lead to search for a possible anaemia and the need to conduct a study arises to search for causes of the disease. Anaemia is likely to emerge from 4 to 6 weeks after the beginning of the treatment whereas the neutropenia comes from 3 to 6 months after treatment. The appearance of these problems depends on the duration of the treatment, on medullary pool, and

the evolution of the disease. Our patients frequently being malnourished and being seriously affected by the disease, it is possible that those side effects appear long before than what was stated previously.

- Hepato toxicity, less frequent

- Macrocytosis is common and is therefore not an indication to change the treatment. It is rather a symptom of a good adherence.

- As for other Analogue nucleosides, cases of lactic acidosis and those of Fatty liver have been reported, though that symptom is frequently found with stavudine (D4T). lactic acidosis is rare but should be evoked for patients with fatigue, abdominal pain, nausea, vomiting and/or unexplained breathlelessness

Less frequent hepato toxicity.

- Myopathies, rare.

- Fingernails may be coloured blue but this is not the indication to change the treatment.

Alternatives in case of side effects:

Replace AZT by D4T except in case of lactic acidosis whereby the treatment should be stopped.

Contre-indications:

- Severe anaemia (Hb<7.0g/dl, from 10g/dl, choose one molecule if possible)
- Severe neutropenia (neutrophilic leukocytes<750mm3)
- Severe kidney failure (creatinine <three times normal figures)
- Severe hepatic failure (Functional hepatic tests< 5 times normal figures)

- Well known intolerance
- Zidovudine and should never be prescribed with stavudine (D4T) for they are antagonistic.

Posology for adults:

- A tablet of 300 mg twice a day
- In case of combined tablet with Zidovudine /Lamivudine, the dosage is of one tablet of 300mg/150 2 a day

Posology for children:

- See PART C, CHAPTER 3

Information for the patient:

- Can be taken with or without food
- Can be taken during pregnancy
- The patient has to urgently go the doctor's if the following symptoms appear: Dyspnea, abdominal pain, fatigue, nausea, vomiting

Lamivudine

Category :

Analogue nucleoside antiretroviral agent of the reverse transcriptase inhibitor. (NRTI)

Important information :

- Well tolerated, with little toxicity

- Can be used during pregnancy

Precautions:

Severe kidney failure (creatinine >3 times normal figures)

- Severe liver failure (creatinine >3 times normal figures)
- Severe Hepatic failure (functional hepatic tests>5 times normal figures

Posology for adults:

- One tablet of 150 mg twice a day or 2 tablets of 150 mg once a day
- In case of a combined tablet zidovudine/lamivudine, the dosage is one tablet of 300/150 twice a day.

Posolog for children:

- See PART C, CHAPTER 3

Information for the patient:

- Can be taken with or without food

Emtricitabine (FTC)

Category:

Analogue nucleoside antiretroviral agent of the reverse transcriptase inhibitor(NRTI)

Important notice:

- Well tolerated, with limited toxicity

- Can be taken during pregnancy
- As with other analogue nucleosides, cases of lactic acidosis and of fatty liver have been reported

Precautions:

- Severe kidney failure (creatinine>3 times normal figures)
- Severe hepatic failure (Functional hepatic tests >5 times normal figures

Posology for adults:

- One tablet of 200mg once a day or 10mg/ml for oral solution

Notice for the patient:
Didanosine (DDI)

Category :

Anti-retroviral agent of the analogue nucleoside of the reverse transcriptase inhibitor. (NRTI)

Secondary effects :

- The Didanosine is generally well tolerated. The mostly found side effect is nausea.

- The Didanosine may be associated to a severe pancreatitis. It should not prescribed to alcohol addicted patients and should be stopped in case a patient is suspected of having pancreatitis (pain in the abdomen, amylasemia)or as described in the

antecedents/side effects. The majority of cases of pancreatitis appeared when the DDI is prescribed with the D4T.

- The Didanosine may be the cause of peripheral neuropathies particularly if it is associated with Staduvine (D4T).
- As for all analogue nucleosides, cases of lactic acidosis and fatty liver have been reported. In spite of the fact that that symptom is frequent with Stavudine (D4T). lactic acidosis is rarely found but should be evoked for patients with fatigue , abdominal pain, nausea, patients who vomit or presenting unidentified dyspnea.

- Can be prescribed during pregnancy although there is accrued risk of lactic acidosis and of steatose in case of combined use of didanosine and of stavudine (D4T). We commend to avoid the afore mentioned combination during pregnancy and to use it in absolute necessity. Besides, a clinical and biological monitoring is required.

- Strict use during pregnancy

Alternative treatment in case of side effects:

Specialised caution for molecule of 2nd line

Contra-indications:

- Severe kidney failure (creatinine> 3 times normal
- Severe liver failure (hepatic functional tests > 5 times normal measures)
- Well known intolerance

- Combined use of didanosine and stavudine (D4T) during pregnancy: only to be used in extreme necessity and with caution
- The didanosine should not be used for patients who are alcohol addicted or to patients who have suffered from pancreatitis

Administration and posology for adults:

- For patients over 60 Kg, 2 pills of 200mg per day once or thrice a day
- For patients under 60Kg, one pill of 250mg once a day.
- In case of combination with TFV, DDI dosage should be reduced at 250mg for patients over 60Kg.

Paedriatic posology :

See Part C, Chapter 3

Notice for the patient:

- To be taken in an empty stomach (one hour before eating or 2 hours after eating).

- It is recommended to inform the patient on the possibility or not to concomitantly take other ARV.

Stavudine (D4T)

Category :

Antiretroviral analogue agent of the reverse transcriptase inhibitor (NRTI).

Important information pack :

Frequently prescribed in combination with Lamivudine (3TC).

Side effects:

- Staduvidine can be the cause of peripheral neuropathies, especially if D4T40 is associated with Didanosine (DDI). This effect is not linked to whether the patient is under treatment or not. See annex 5 at the end of the chapter concerning the management of side effects.

- Rising of transaminases
- Pancreatitis (clinical or only biological)
- Lypodystrophy
- As with other analogues nucleosides, cases of lactic acidosis and of fatty liver have been reported.
- Can be taken during pregnancy though the risk of acidose lactique and of stavudine (D4T)is high when using both didonosine and stavudine. We commend to avoid the association and use it only if in extreme necessity. An additional clinical and biological monitoring is therefore required.

Didanosine (DDI)

Category:

Analogue nucleoside anti-retroviral agent of reverse transcriptase inhibitor. (NRTI)

Side effects

- In general the Didanosine is well tolerated. The very frequent side effect is nausea.
- Didanosine may be associated with a pancreatitis that may be acute. It may not be prescribed to patients that abuse alcohol and must be stopped if pancreatitis is suspected (abdominal pain, amilasemy) or described in antecedents. Most cases of pancreatitis happen when DDI was prescribed with D4T.
- Didanosine may be the cause of peripheral neuropathies, especially if it is associated with staduvine (d4T).
- Like all other analogue nucleosides, cases of lactic acidosis and hepatic steatose have been reported. Even if that syndrome is very frequent with stavudine (d4T), lactic acidosis is rare but it must be mentioned in patients showing: tiredness, abdominal pain, nausea, vomiting and/or an inexplicable dyspnea.
- The indicated usage during pregnancy though the risk of lactic acidosis and hepatic steatose may be acute in case of using the combination of didanosine and stavudine (d4T). We recommend avoiding that association during pregnancy and using it only in case of absolute necessity. Clinical and biological supplementary monitoring is therefore required.
- It must never be associated with zidovudine (ZDV) because they are antagonistic

Alternatives in case of side effects:

- In case of neuropathy: replace the D4T by TDF; AZT if there are no other alternatives.
- In case of lactic acidosis: Stop ARV treatment and wait until the patient is clinically and biologically stabilized and then replace D4Tby TDF.
- In case of Lypodystrophy: Replace D4T by TDF or ABC.

Even ABC may replace d4T in case of Lypodystrophy

Contraindications:

- Acute renal deficiency (creatinine>3 times than the normal).
- Acute hepatic deficiency (hepatic functional tests> 5 times than the normal).
- Known Antecedents of intolerance
- Using a combination of stavudine didanosine and stavudine (d4T) during pregnancy: only using it in case of absolute necessity and with cautions.
- Do not use the didanosine in patients who abuse alcohol or with antecedents of pancreatitis.

Adult dosages:

- For patients with more than 60kg, two capsule of 200 mg Once or twice a day.
- For patients with less than 60 kg, a spoonful of 250 mg once a day.
- In case of a combination with TFV, the dose of DDI will be deceased to 250 mg in patients with more than 60 kg.

Paediatric dosage:

See PART C, CHAPTER 3

Information for patient

- To be taken on an empty stomach (an hour before or two hours after the meal)**.**
- It is important to inform the patient about the possibility or not of concomitant taking of other ARV.

Category:

Analogue nucleosidic anti-retroviral inhibitor of reverse transcriptase agent. (NRTI)

Important information:

Sometimes prescribed in form of combination with lamivudine (3TC).

Side effects:

- Staduvine may be the cause of peripheral neuropathies, especially if D4T40 is associated with didanosine (ddi). This effect is dependant dose. See Appendix 5 at the end of chapter on the management of side effects.
- Elevation of transaminases
- Pancreatitis (clinical or only biological)
- Lypodystrophy
- The same with all analogue nucleasidics, cases of lactic acidosis and hepatic steatose have been reported.
- The usage indicated during pregnancy even if the risk of lactic acidosis and hepatic steatose is acute in case of using a combination of didanosine and stavudine (d4T). We recommend avoiding that association and using it only in case of absolute necessity. Clinical and biological supplementary monitoring is therefore required.
- Should never be associated with zidovudine (ZDV) because they are antagonistic.

Alternatives in case of side effects :

- In case of neuropathy: replace D4T by TDF; AZT when there are no other alternatives.
- In case of lactic acidosis: stop the ARV treatment and wait until the patient is clinically and biologically stabilized and after replace D4T by the TDF.
- In case of Lypodystrophy: Replace D4T by TDF or ABC

Even ABC may be replaced by d4T in the case of Lypodystrophy.

Contraindications:

- Acute renal deficiency (creatinine >3 times than the normal)
- Acute hepatic deficiency (hepatic functional tests>5 times than the normal)
- Unknown Antecedents of intolerance
- The use of the combination of stavudine and didanosine (ddI) must be prescribed only in case of absolute necessity, under particular supervision.

Adults dosages:

- A capsule of 30 mg two times a day (Triviro30).

Paediatric dosage:

See PART C, CHAPTER 3

Information for the patient:

May be taken with or without food.

Abacavir (ABC)

Category:

Analogue Nucleoside anti-retroviral agent of reverse transcriptase inhibitor (NRTI)

Important information for the prescription:

- Abacavir is generally well tolerated. The gastrointestinal effects are nausea and diarrhea. The lactic acidosis and hepatic steatose are considered as less frequent than with other analogue nucleosides.

- 3 to 5% of patients taking Abacavir have a reaction of hypersensitivity happening generally in 6 days after beginning to take it (more than 93% of reactions appearing in the first 6 weeks). The symptoms include:

○ Fever ○ Cough ○ Cutaneous erythema ○ Dysponea ○ Headache	○ Fatigue ○ Nausea/vomiting ○ Diarrhoea ○ Abdominal pain ○ Articular or muscular pain

Symptoms disappear as soon as the treatment is stopped, but if the patient is exposed once again, a reaction of terrible hypersensitivity may be observed. Abacavir should never be prescribed to a patient who has had a reaction of suspicious hypersensitivity to abacavir in the past. When abacavir has been stopped for that reason, all remaining capsules should be recovered in order to avoid a new accidental use.

- Before prescribing abacavir, all prescribers should be familiar with the presentation, the diagnosis and therapeutic protocols in connection with that hypersensitivity reaction.

Contraindications:

- Acute renal deficiency (creatinine> 3 times the normal)
- Acute hepatic deficiency (hepatic functional tests> 5 times than the normal)
- Unknown antecedents of intolerance. A patient who has got a hypersensitivity reaction (or simple suspicion) to abacavir should never be exposed to it again.

Adult dosage

A capsule of 300 mg two times a day or 1x600 mg.

Paediatric dosage:

Refer to PART C, CHAPTER 3

Information for patient:

- ABC may be taken with or without food.
- Patients taking abacavir must be warned that it is important to visit the treatment centre the very day if they develop symptoms causing the hypersensitivity syndrome.

Tenofovir (TDF)

Category:
Analogue nucleoside anti-retroviral agent of reverse transcriptase inhibitor (NRTI)

Side effects:

Tenofovir is generally well tolerated:

- Most frequent side effects are nausea and diarrhoea.
- A moderate renal deficiency barely exists. The acute form is exceptional.
- Rare cases of lactic acidosis and hepatic steatose.

Alternatives in case of side effects:
Specialized advice since molecule of 2^{o} line

Containdications:

- Acute renal deficiency (creatinine> 3times the normal)
- Association with other nephrotoxic substances
- Acute hepatic deficiency (hepatic functional tests> 5 times the normal)
- Known antecedents of intolerance

Important notes:

Tenofovir increases concentrations in DDI, it is therefore important tto reduce its dosage if the association is prescribed (1x250 mg).

Adult dosage:
A tablet of 300 mg once a day.

Paediatric dosage:

Is not approved for use to patients aged less than 18 years.

Information for patients:

May be taken with or without food.

The Non Nucleoside reverse transcriptase inhibitor (NNRTI)

Nevirapine (NVP)

Category:

Analogue non Nucleosidic anti-retroviral agent of reverse transcriptase inhibitor (NNRTI)

Side effects:

Most frequent side effect of nevirapine is the skin rash, observed in 20% of patients (especially in black women), most often within 8 first weeks. That rash is usually light or moderate, but requires stopping treatment in 5 to 7 % of patients. Potentially mortal skin reactions have been reported.

The risk must be decreased by taking the drugs with reduced doses during the first 14 days of treatment: The dose is of 200 mg during the first 14 days of treatment and then it goes to 200 mg 2x a day. Table 2 describes different stages of severity of the reaction whereas the algorithm of the management of the dermatologic toxicity is found in Appendix 1.

It should be remembered that NVP must be interrupted if stage 3 is attained.

- Table2.Skin Toxicity

Stage 1	Stage2	Stage3	Stage4
Erythema, pruritus	Outbreak Masculopapular diffuse or dry desquamation	Appearance of vesicles or humid desquamation or ulceration or an association with fever or pain	Appearance of the following symptoms: mucous attack, presumed case of Stevens Johnson, multiformerythema, necrosis, or exfoliator dermatosis

- The hepatotoxic effect is also very frequent appearing often in the first 6 weeks but sometimes until 8 weeks after the beginning of treatment. Factors of risk are: The female sex, hepatic enzymes disturbed, the co-infection with hepatitis B and/ or C and high CD4.

- Usually light, the hepatotoxity may be fatal, and care providers must be warned to monitor their hepatic functions in case of abnormality or pain at level of right hypochondria at the beginning of their treatment and whenever it is deemed necessary. Table 2 describes different stages of severity of the reaction while the algorithm of the hepatic toxicity management is in Appendix 2. Thenevirapine must be completely stopped if stage 3 of toxicity is reached (transaminases> 5 times below the normal limit; see table 3).

Table 3: Hepatic toxicity

	Normal	Stage 1	Stage 2	Stage 3	Stage 4
ALAT5SGPT) (UI/l)	<40	50-100	100-200	200>400	> 400

- Nevirapine reduces plasmatic concentrations of hormonal contraceptives containing estrogens. Alternative or complementary methods of contraception must therefore be used (see PART C, CHAPTER 3 see p93).

Contraindications:

- Acute renal deficiency (creatinine> 3 times than the normal) Note: According to the book of Bartlett, the dose must not be modified in case of renal deficiency.
- Acute hepatic deficiency (hepatic functional tests > 5 times than the normal)
- Known antecedents of intolerance
- Contraindications in case of the use of rifampicine for tuberculosis.

Adult dosage:

- A capsule of 200 mg once a day for the first 14 days of the period of introduction, and again a capsule of 200 mg two times a day.

Paediatricdosage

- See PART C, CHAPTER 3

Information for patients:

- May be taken with or without food.
- The usage is allowed during pregnancy. Biological supervision of hepatic functions is recommended.
- It is necessary to inform the patient during counselling that he/she has to go for checking the very day if he/she shows pruritus a rash. It has been observed that patients in most cases wait or consult health centres lacking adequate training and therefore continuing NVP many days after appearance of Stevens Johnson syndrome.

If a patient stops NVP for more than 2 weeks (for reasons of conformity for example, and if there is no contraindications to the reintroduction, the plan should be taken in the same manner as during the initiation (a half dose for the first 14 first days).

Efavirenz (EFV)

Category:

Analogue non Nucleosidic anti-retroviral agent of reverse transcriptase inhibitor.(NNRTI)

Side effects:

- The skin rash is a side effect appearing in 15 to 25% of patients. That rash is usually light or moderate, but it necessitates an interruption of treatment in 2% of patients. Potentially mortal skin reactions have been reported. The algorithm of dermatologic toxicity management is in Appendix 3.

- Side effects concerning the central nervous system appear in at least 50% of patients, and may include nightmares, dizziness and insomnia. It is therefore preferable to take drugs before going to sleep. These side effects often disappear from the first month and require an interruption of treatment except only in 2 to 5% of patients.

- Hepatotoxicity is less frequent and less acute only with nevirapine but alteration of hepatic functions to 5 times than the normal has been reported in 2 to 6% of patients. The algorithm management of hepatic toxicity is in Appendix 4.

- Efavirenz is teratogenic and may not be used in pregnant women during the first semester.

Contraindications:

- Pregnancy or potential/probable future pregnancy.
- Acute renal deficiency (creatinine> 3 times than the normal) Note: According to the book of Bartlett, the dose must not be modified in case of renal deficiency.
- Acute hepatic deficiency (hepatic functional tests> 5 times more than the normal)
- Known antecedents of intolerance

Adult dosage:

A capsule of 600 mg once a day.

Paediatric dosage

- See PART C, CHAPTER 3

Information to patients:

- May be taken with or without food, but not take with fatty foods.
- To take evening before going to bed.
- Patients must be told that efavirenz may cause nightmare, feeling dizzy, pressure and insomnia and that most often those side effects disappear after three or four weeks. It is capital to make him/her remember to come at the ARV site if those groans appears and never stop the treatment without medical advice.

Important preliminary note:

The NNRTI persist in the blood for a long time after the molecule stopping. It is therefore advised in case of stopping EFV or NVP to continue the NRTI (D4T, 3TC…) for 5 to 7 days after stopping the NNRTI in order to avoid a mono-therapy.

The protease inhibitor (PI)

- **Side effects of Classe:**

Insulin resistance is found in 30 to 90 % of patients under PI and causes diabetes in 1 to 11 %. It happens in the first 2-3 months of treatment, later in the first year. To prevent it, it is important to measure a dose of the glycaemia all the 3 months in that year. In case of known diabetes, a clinical practitioner has two solutions: either he prescribes oral anti-diabetes, or he/she interrupts the treatment. In this case, when choosing the future combination, it will be necessary to take into account possible resistances and make sure he/she maintains a sufficient suppression on the virus. The PI being used in 2° line, specialised advice is necessary at that level as the patient will be most often resistant to other molecules.

Hyperlipidemy (increasing of cholesterol and triglycerides) is a side effect reported for all PI and in particular for ritonavir. This has consequences of

increasing the cardiovascular risk and pancreatitis. Given prohibitive costs of stanines, care will most often be limited to hygienic and nutritional advice.

Hypodystrophy is defined by peripheral loss of subcutaneous fat and the accumulation of fat at level of abdomen, the top of the back, of the chest, and some subcutaneous tissues. In some patients, it is associated with hyperlipidemy and hyperglycaemia. In the long-run, it is observed in many cases (20 to 80 %) and its frequency increases if the PI are associated with the D4T, D4T/DDI and to a lesser extent, AZT. Here again, therapeutic means are limited to physical exercise (with the risk of aggravating the Hypodystrophy) or to change the ARV treatment. Limited data exist at that point, but it seems that premature substitution of D4T by the TDF, or better by the ABC is appreciated by patients.

Hepatoxicity is a side effect common to all ARV. PI are not an exception to the rule, ritonavir being most often the culprit.

Nelfinavir (NFV)

Category:
Anti-retroviral Protease Inhibitor agent (PI)

Side effects:
The most frequent side effects are gastrointestinal (soft stools and or/ diarrhoea) existing in 10 to 30 % of patients. Diarrhoea is so frequent that many prescribers systematically combine to nelfinavir an empiric symptomatic treatment (ex. loperamide immodium®) to use in case of necessity. 2% of patients may be obliged to interrupt the therapy.

Like all other protease inhibitors, nelfinavir may be associated to a resistance to insulin, diabolises, hyperlipidemy or Lypodystrophy.

- Alternatives in case of side effects: specialized advice since molecule of 2^0 line

Important information:

- Like all protease inhibitor, nefinavir is metabolised by the liver and has multiple interactions with other drugs. Particular attention must be paid to drugs to be combined before beginning its use.
- Protease inhibitor may reduce the plasmatic concentration of oral contraceptives, and alternative or complementary control of birth methods must be used.
- The use is indicated during pregnancy.
-

Contraindications:
- Acute renal deficiency (creatinine> 3times than the normal)
- Acute hepatic deficiency (hepatic functional tests> 5 times the normal)
- Known antecedents of intolerance
- Rifampicine-based treatment for tuberculosis

Adult dosage:

Five capsules of 250 mg (1250 mg) two times a day.

Paediatric dosage

See PART C, CHAPTER 3

Information to patients:

- Nelfinavir must be taken with food, ideally during a meal full of fats or a light meal.
- Patients must be warned that diarrhoea is current and must receive instructions on the management of that side effect.

Lopinavir/ritonavir (LPV/r)

Category:

Protease Inhibitor anti-retroviral agent (PI)

Side effects:

- The most frequent side effects are gastrointestinal, including the diarrhoea, existing in 15 to 25 % of patients.
- Like all other protease inhibitor, LPV/r is associated to a resistance with insulin, diabolises, a hyperlipidemy and Lypodystrophy.

➢ **Alternatives in case of side effects: specialized advice since molecule of 2° line:**

Important information

- Like all protease inhibitors, the LP/r is metabolised by the liver and has multiple interactions with other drugs. A particular attention must be paid on drugs to be combined before beginning its use.
- Protease inhibitor may reduce the plasmatic concentration of oral contraceptives, and alternative or complementary birth control methods must be used.
- The use is indicated during pregnancy.

Contraindications:

- Acute renal deficiency (creatinine> 3 times than the normal)
- Acute hepatic deficiency (hepatic functional tests> 5 times than the normal)
- Known antecedents of intolerance
- Rifampicine-based treatment, upon special consultation, the dosage may be modified from Kaletra (double dose Kaletra) or increased to Ritonavir 200 mg (in 2 courses).

Adult dosage:

Three capsules (each of 133 mg of LPV/33 mg of RTV) two times a day.

Or two capsules (each of 200 mg of LPV/50 mg of RTV) two times a day.

Paediatric dosage

See PART C, CHAPTER 3

Information for patients:

- To take with meals.
- To keep capsules in the fridge or in a cool place.
- Currently, there are usually tablets of 200 mg of LPV/50 mg of RTV that are kept at normal temperature.

Indinavir (IDV)

Category:

Protease inhibitor anti-retroviral agent (PI)

Side effects:

- The renal lithiasis is observed in 10 % of patients. Hyper hydration is necessary: drinking 1 5 litres per day.
- Gastrointestinal side effects are less frequent than other protease inhibitor.
- The problem of nephrotoxicity has also been reported.
- Indirect asymptomatic bilirubinemy is observed in 10 to 15 % of patients, and does not constitute an indication for modifying the treatment.

Like all other protease inhibitors, indinavir is associated to resistance to the insulin, diabetes, a hyperlipidemy or a Lypodystrophy.

➢ **Alternatives in case of side effects: specialised advice since molecule of 2° line:**

Important information

- Like all protease inhibitors, indinavir is metabolized by the liver and has multiple interactions with other drugs. A particular attention must be paid to drugs to be combined before beginning its use.

- The protease inhibitor may reduce plasmatic concentration of oral contraceptives, and alternative or complementary birth control methods must be used.

Contraindications:

- Acute renal deficiency (creatinine> 3 times than the normal)
- Acute hepatic deficiency (hepatic functional tests> 5 times than the normal)
- Known antecedents of intolerance
- Rifampicine –base treatment for tuberculosis
- Pregnancy

Adult dosage:

- Four capsules of 200 mg every eight hours, or two capsules of 400 mg every eight hours.
- The dosage is of 3 x 800 mg on an empty stomach.
- When it is used in combination with ritonavir: 800 mg IDV + 100 mg RTV, two times a day.
- In this last case it may be taken with or without food.

Paediatric dosage

- See PART C, CHAPTER 3

Information for patients:

- To take on empty stomach (an hour before or two hours after a meal).
- When it is used in combination with ritonavir, it may be taken with or without food.
- It is important to drink large amount of water or other liquids when indinavir is prescribed, at least 6 big glasses of water a day. Patients must be warned that they must seek medical assistance if they get pain: abdominal pain or haematuria.

Ritonavir

- Is powerful Cytochrome inhibitor P 3A (CYP3A)
- Administered at small dose (100 or 200 mg, 1 to 2 times a day) with other PI, it considerably increases plasmatic concentrations, what enable the ruction of the dosage of PI combined.

➢ **Biologic tests for envisaging a change of molecule due to toxicity problems.**

Parameter	**Stage 3 of toxicity**
haemoglobin	< 6,9 g/dL
Neutrophil counting	< 749/mm3
platelets	< 49 999/mm3
chemistry	
Sodium	< 122 mmol/L ou > 159 mmol/L
Potassium	< 2,4 mmol/L ou > 6,6 mmol/L
Bilirubin	> 2,5 x more than the normal
Creatinine	> 3 x more than the normal
Glucose	< 0 ,39 g/L ou > 2,51 g/L (non diabetes on an empty stomach)
ASAT (SGOT)	> 5x more than the normal
ALAT (SGPT)	> 5x more than the normal
Phosphatase alcalin	> 5x more than the normal
Amylase*, lPIase	> 5 x more than the normal

*****In case of gastrointestinal signs or abdominal pains.

Changing the ARV treatment due to failure: defining and management of failure

➢ Introduction

ARV therapies succeeded in bringing clinical and immunologic improvement and thanks to the interruption of HIV reproduction. Symptomatic patient may be reasonably expected to show clinical improvements in three months that follow the beginning of ARV treatment. In six months, the number of CD4 increases in general at least 50 cells/mm3, even if the importance of that increase depends on the basic value of the CD4. The therapeutic failure is most currently combined

with the non-conformity (see chapters on conformity and management of diseases and Appendix 1), and it is imperative to evaluate the conformity to ARV before changing drugs.

➢ Definition of therapeutic failure:

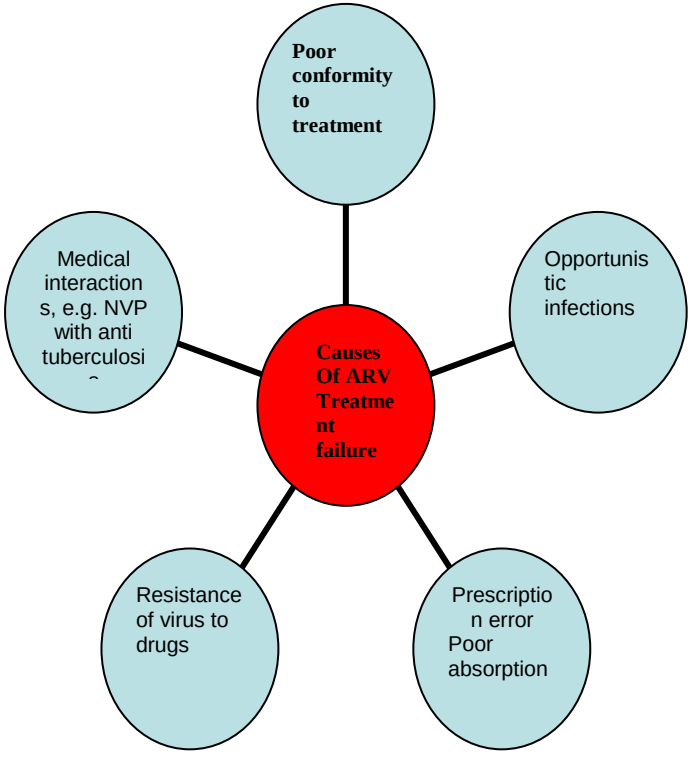
The therapeutic failure may be expressed at three levels:

- The clinical failure: due to new opportunistic infections or to malignant infections that show clinical progression of the disease, recurrence of the previous opportunistic infection, the progression to a higher clinical stage after the exclusion of immuno-reconstitution syndrome, the recurrence of tuberculosis (TB) may not present a progression of the HIV disease as re-infection may happen.

If the patient is asymptomatic of the disease, the therapeutic failure is only defined by the counting criteria of CD4.

- The immunologic failure:
  - Return of CD4 to the basic level of pre-therapeutic or below that level without any concomitant infection that would cause the transitional drop of CD4.
  - Drop of more than 50 % of CD4 rate below the maximum value obtained, without any concomitant infection that would be cause of transitional fall of CD4.
- The virological failure: viral load always detachable to 6 months of treatment in the patient with good conformity to ARV.
- In case of doubt for changing the second-degree ARV, the viral load will enable making appropriate decision.

- **Causes of therapeutic failure:**



- **Management of the problem of therapeutic failure problem: what to do in case of the suspicion of the therapeutic failure?**

Given the costs of the second-line molecule, their most frequent side effects, the more important number of tablets and especially few alternatives that we currently have in Rwanda, sometimes clinical practitioners hesitate to change the regime even if criteria seem to be clear. Therefore, it is strongly advised to be systematic:

- Establish a link of relationshPI with the patient, verifying the conformity of the patient in a specific manner (how many doses have you forgotten in the last 3 days, the last week), then in general manner (the patient must evaluate on the visual scale what percentage of capsules has he taken in the last months), verifying the course schedule.

- Verifying if there is no inter-current opportunistic infection that could transitionally lower the CD4 (ex: TB). If tuberculosis is highlighted, treat it and re-evaluate the CD4 after the intensive stage and at the end of treatment of TB in order to make an appropriate decision.

- Exclude the problem of medicinal interaction in the past

- Exclude the problem of absorption (e.g.: frequent vomiting)

- Repeat the CD4 count in the following month. Meanwhile counselling must be reinforced in order to ensure optimal conformity in the next test. It is important to repeat the test in order to eliminate all laboratory errors; however, it is not advised to spend more time when the failure is real.

- When immunologic failure is confirmed, and after trying to identify the cause, discuss all cases of failure in a team; indeed, seek advice by internet or phone. A physician (or a nurse) should never make decision at his own when passing to the second-degree regime. If the failure is confirmed, the treatment of 3 ARV must be changed. The choice of new ARV must take into account the cross-resistance, compared to ARV already used.

What to do in case of dissociation between those three causes of failure?

- When a patient shows possible clinical improvement despite a deceiving immunologic evolution (increase of CD4 cells < 50 /mm3/6 months) the initial ARV treatment must be continued, control the conformity and the CD4 3 months later. When the patient shows a flagrant immunologic failure, the CV is desirable, when detectable; treatment must be changed, when not detachable, existing treatment must be continued.

It is necessary to specify if CV>10000

- If a patient shows possible clinical and/ or immunologic improvement despite the virologic failure, the initial ARV treatment must be continued. In this case, it is probable that the virologic failure is in connection with poor conformity

and it is important to reinforce the support to the conformity of the patient. It is therefore advised to re-control the CD4 and the CV after 3 months.

- The immune reconstitution syndrome (IRS) is characterised by the appearance of signs and symptoms of an opportunistic infection some weeks after the start of antiretroviral treatment in case of advanced immunodeficiency. It corresponds to an inflammatory response to a preliminary sub-clinical opportunistic infection. It is also possible that that immunologic reconstitution lead to the development of atypical presentations of some opportunistic infections. The aggravation of opportunistic infection constitutes possible evolutions of the disease during the treatment and must not be considered as a clinical failure.

Date	clinical	Labo
Before Second-degree ARV	+	In case of clinical indication NFS, GPT creatinine
D15	+Conformity	Nothing
M1	+Conformity	Nothing
M2	+Conformity	Nothing
M3	+Conformity	GPT and glycaemia
M4	+Conformity	Nothing
M5	+Conformity	Nothing
M6	+Conformity	CD4, NFS, GPT, glycaemia
After six month		
Monthly during 1 year	+Conformity	• CD4 : all six months • GPT : If clinical indication ○ Glycaemia: all the 3 months

Regime of the first line		Second-line Regime recommended	
		Reverse transcriptase Inhibitors	**protease Inhibitor**
Standard strategy	AZT ou d4T+3TC + NVP ou EFV	ddI + ABC ou TDF + ABC ou TDF + 3TC (± AZT)	Lop/r ou IDV/r
	TDF+3TC+NVP ou EFV	ddI + ABC ou ddI + 3TC (± AZT)	
	ABC+3TC+NVP ou EFV	ddI + 3TC (± AZT) c ou TDF + 3TC (± AZT)	
Alternative strategy	AZToud4T+3TC+ TDFou ABC	EFV ou NVP ± ddI	

➢ Detailed recommendations for the change of first-degree regime to the second-degree regime

3TC (lamividine) and FTC (emtricitabine) are interchangeable because they have the same structure, share pharmacologic properties as well as resistance profiles. The 3 TC must be kept in the second line because it has residual effect on the virus, maintains pressure on M1 84 mutation which increases the viral sensitivity to AZT or TDF. In case of failure, the resistance to AZT is less frequent and when it occurs, it hinders viral replication.

Note: In case of intolerance to LPV/r (Kaletra), indinavir is an appropriate alternative.

In this case the patient has been subjected to resistance tests; the second-degree schedule will be adapted in function to the efficiency of each of these ARV.

➢ **Technical form of cotrimoxazole, INH and Fluconazole.**

Cotrimoxazole (TMP-SMX)

Category:

Antibiotics

Side effects:

- The skin rash is most frequent in form of the eruption of maculo-papular pruritic or toxidemy but the reaction may evolve (scarcely) up to the Stevens Johnson Syndrome.
- The frequent side effects are also gastrointestinal (nausea, vomiting, diarrhoea), fever, cough, elevation of transaminase, neutropeny and especially the skin rash and pruritis. Those are normally observed within two weeks following the beginning of treatment.
- Between the beginning of cotrimoxazole and that of zidovudine, it might be duration of four to six weeks, when it is possible.
- Cotrimoxazole may also cause hepatitis or asymptomatic elevation of hepatic enzymes (transaminases). Between the beginning of taking cotrimoxazole and that of nevirapine, it might be a duration of eight to twelve weeks when that is possible.
- Didanosine is prescribed during the duration of pregnancy.
- For HIV positive pregnant women who should receive preventive intermittent treatment to fansidar, a prophylaxis to cotrimoxazole is prescribed if CD4 <350 and fansidar only if CD are > 350.
- In case of doubt regarding the molecule responsible for a side effect (e.g. skin rash, NVP or cotrimoxazole), it is always advised to stop the two,

cotrimoxazole first. In addition, if it is the culprit, it may be reintroduced according to the following of de-sensitization plan:

Syrup of TMP/SMX (40mg TMP + 200 mg SMX/5 ml):

- 1 ml a day for 3 days, thereafter
- 2 ml a day for 3 days, thereafter
- 3 ml a day for 3 days, thereafter
- 5 ml a day for 3 days, thereafter
- 10ml a day for 3 days, thereafter
- 20 ml a day for 3 days, thereafter
- 1 double-dose tablet a day or 1 single-dose tablet a day (if the double-dose tablet cannot be withstood).

Contraindications:

- Allergy to sulphonamides
- Acute renal deficiency (creatinine> 3 times than the normal)
- Acute hepatic deficiency (hepatic functional tests> 5 times than the normal)

Adult dosage:

- The current dosage for the prophylaxis of pneumocystosis is a double tablet (960 mg) a day
- An alternative regime for the pneumocystosis prophylaxis is a double tablet, three times a week.
- Directives for the treatment of pneumocystosis and other acute diseases. (See doc.10)

Paediatric dosage

- See PART C, CHAPTER 3

Information for patients:

- May be taken with or without food.
- Must be taken with water.

Fluconazole

Category:

Anti-fungal agent

Important information for the prescription:

- Well tolerated; side effects are rare but may include nausea, vomiting, headache, and a reversible alopecia
- Inhibit hepatic enzymes P450; medicinal interactions
- To be used with precaution during the first term of pregnancy.

Contraindications:

- Severe renal deficiency (creatinine > times than the normal);
- Severe hepatic deficiency (hepatic functional tests > 5 times than the normal).

Adult dosage:

- The current dosage for side prophylaxis of meningitis with cryptococus is 2 capsules of 200 mg/day for 8 weeks; then 1 capsule of 200 mg/day.
- The current dosage for treatment of oesophageal Candida is of 200 mg x 1/d for 14 days.

Paediatric dosage

- See PART C, CHAPTER 3 H

Information for patients:

May be taken with or without food.

CHAPTER V. medicinal interactions

General Aspects

Medicinal combinations used during the care of HIV infection are capable of many interactions that may be translated by the loss, or conversely the amplification of a therapeutic activity or undesirable side effects.

Medicinal interactions are:

- Either pharmacokinetic: a drug affecting absorption, distribution, metabolism or excretion of another.
- Either pharmacodynamic: two drugs capable of an antagonistic, additive or synergetic action.

These two types of interactions may be combined, hence making the situation more complex.

- Interaction may also be increased by a previous pathologic state: renal, hepatic deficiency, digestive absorption disorders, medullar deficiency, etc.

- Interactions are studied in twos but the final results of poly-drugs are in most cases unknown; as for interactions with illicit products, they are less studied.

The digestive absorption of drugs may also be moderated by some food and therefore condition the daily taking of drugs.

Hepatic metabolism and P450 cytochromes

Most of drugs and food substrates are hydrophobic and may then only be eliminated (through urine or bile) after being transformed into water-soluble metabolites. This mechanism occurs especially in the liver where many enzymatic systems contribute.

➢ Induction _ of cytochromes

It is the increasing of their system that provokes acceleration of oxidation reactions that may lead to the loss of medicinal activity or to the increasing of toxicity of its potential toxic metabolites.

➢ Inhibition of Cytochromes

The fixation of inhibitor molecule on the cytochrome may be non competitive (if it is not metabolized there). Or competitive (if it is metabolized there); in this last case, the result of mutual inhibition varies according to respective affinities of substrates for cytochrome.

Review of major medicinal interactions

Summary of main interactions between ARV molecules and other drugs currently used in Rwanda.

➢ Medicinal interactions

	Nevirapine	Efavirenz	Lopinavir/rit	Nelfinavir	Indinavir
Ketoconazole Fluconazole	Keto ↘63%; Not combine with ; Fluco ok		LPV ↘13%; Keto ↗ x 3	Same dosage	IDV ↗68%; Reduce the dose to 600 mg 3 X/d
Rifampicine	NVP ↘37% ; Not combine ↗hépatotoxicité!	EFV ↘25%; ↗EFV to 800 mg/d	LPV ↘75%; Do not combine	NFV ↘80%; Do not combine	IDV↘89%; Do not combine
Macrolides : Clarythromycine, Erythromycine, Azithromycine	NVP ↗26%; Clari ↘30%; Same dosage	Clari ↘39%; Use alternative			Clari ↗52%; Same dosage
Oral Contraceptives	Oestradiol ↘20%; Use an alternative method	Oestradiol ↗37 % ; Use an alternative method	Oestradiol ↘ 42% ; Use an alternative method	Oestradiol ↘47% ; Use an alternative method	Oestradiol ↘ 37% ; Use an alternative method
Anticonvulsivants : (Phenobarbital, Phenytoin, Carbamazepine)	Unknown effects	Unknown effects	Unknown effects. would decrease the effect of PI…	Unknown effects. Would decrease the effetct of PI…	Unknown effects would decrease the effect of PI…
Antihistamines :		Do not	Not combine	Do not	Do not

(Astemizole, Terfenadine)		combine		combine	combine
Psychotropics* : (Triazolam, Midazolam)		Do not combine	Do not combine	Do not combine	Do not combine
Gastroenterology: Cisapride		Do not combine	D not combine	Do not combine	Do not combine
Anticoagulating: Warfarine		Risk of bleeding ↘ The warfarine and monitor!			
Theophylline			Theophylline ↘47%; Adapter the theo dose Theo.		

Formal contraindication of combining charcoal with all ARV treatment, since the latter inhibits their effects.

Supplements in garlic may not be combined with NVP.
Lopinavir/r potentates the effect of diazepam. A then slightest dose of the latter will be administered.

CFAPTER VI. Conformity to drugs and strategies of application

a) The conformity to drugs is the term used to describe that the patient correctly takes his/her drugs in terms of dose, frequency and time.

b) The patient participates in the conformity by deciding to take drugs or not.

c) The observance means that the patient does what the physician/ pharmacist has told him/her.

d) The conformity is a key factor to the success of treatment.

e) Poor conformity leads to virologic failure, to the evolution to a pharmacological resistance and to subsequent immunologic and clinical failure.

f) Compliance suggests that the patient completely conforms to and respects rules of prescription.

Factors influencing conformity

✓ Factors connected with the patient

- forgetting
- preparation and motivation of the patient
- Negligence
- To be far from one's family
- Life style (excessive consumption of alcohol, etc.)
- Depression
- cultural elements
- Socioeconomic factors (isolation, effective support, job and working rhythm, poverty, etc.)

✓ Factors connected with care providers

- Preparation of care provider (knowledge, capacities)
- Advice

- Educating the patient
- Devices indicating that it is important to take drugs, for example, tables and diaries
- Care providing team responsible for monitoring conformity
- Help to care provider

✓ **Factors connected with treatment and drugs**

- Number of tablets
- Frequency
- Side Effects
- Food restrictions
- Medicinal interactions
- Stock out
- The cost of drugs
- The cost of treatment and monitoring

Operation strategies in the area of conformity to drugs

It is important to give appropriate advice to patients before beginning ARV treatment. That applies to clinical practitioners, nurses, pharmacists, social workers and others. It is important not to begin ARV treatment during the first clinical visit. You should advise the patient about the conformity to treatment in order to maximize it. Once the treatment is begun, you must control it and offer permanent help. The strategies include:

- To prepare and motivate, provide basic information about drugs, the importance of conformity, about the time of taking drugs, medicinal interactions, etc.
- To simplify the treatment
- To adapt the treatment to the life style of the patient.
- To manage side effects and prepare the patient to cope up with those effects.
- To establish a team in charge of conformity monitoring (see part A CHAPTER 4).

- To customise the care in accordance to specificities of each patient.

- To provide support mechanisms in order to promote conformity to treatment (materials, I.E.C).

- To use a relay person (godfather/mother) at home to provide support in monitoring conformity.

Note: advice in the area of conformity implies the capacity to transfer technical aspects of conformity and skills in such a way that the patient is relaxed, that he/she feels at ease and has trust in the care provider. The last point may require more time.

Measures of conformity

- Discussions and auto-evaluation of the patient: practical and cheap ways of counting tablets (requiring manpower)
- Discussion with the godfather/mother
- Pharmacological / control files for the renewal prescriptions.
- Directly Observed Treatment (DOT): theoretically in connection with conformity to 100%. Requiring manpower and less practical outside health facilities.
- Evaluation of therapeutic response (clinical response, CD4): not the first evaluation of conformity; auxiliary marker; may be used when it is used with auto-evaluation of the patient. If available the viral load may be used.

CHAPTER VII: Post-exposure Prophylaxis

Introduction

Any person who becomes a victim of accidental exposure to blood or rape must have access to an urgent early evaluation of the risk and to antiretroviral treatment when the indication may be stated. It has also been demonstrated that early treatment decreases 80% of the risk of contamination in case of exposure.

Accidental blood exposure (ABE)

The risk of HIV after blood exposure is law, compared to exposure to VHB and VHC. However, it is very important to determine if the person exposed requires ARV prophylactic treatment.

It is the role of the employer to train his/her staff in the area of prevention, to provide means of individual protection and make available the security material.
The accident must be declared as early as possible (< 48 hours) in conformity with the regulations in force.

An HIV serology must be carried out in the wounded care provider as soon as possible (ideally before 4 hours). If it reveals negative, serologic monitoring will be carried out, particularly within 3 months and before the end of the 6th month.
If he/she is HIV positive, advise he/him to be referred to the service caring for PLWHA.

Criteria of ARV prophylactic treatment

One of care providers of the institution must evaluate the real risk for a given patient. This evaluation includes:

- The severity of exposure that is related particularly to the depth of the wound and to the type of needle in question:
- Hole for sample taking > hole for injection > full.
- The risk is still lower after the cutaneous-mucous projection.
- With the blood, there is great risk than with other biological liquids (amniotic, serous liquids).

The patient source: is to be taken into account:

- His/her complete serologic status (HIV)
- His/her clinical and immunologic status vis-à-vis the HIV infection
- His/her previous anti HIV treatments

If his status is not known, it is important to obtain his/her consent (any screening without knowledge or forced must be proscribed). However, if the status may not be established within 4 hours, the treatment must be immediately started, according to the criteria of Table 1. If secondarily the source person is proved HIV positive, the prophylactic treatment must be stopped.

Prophylactic treatment

Always immediately clean and wash the wound:

Prick or skin wound:

- Immediately clean the wound with running water and soap,
- Rinse the wound with an antiseptic: solution of Dakin or bleach to 12° chlorometric diluted to 1/10, or if not: spirit diluted to 70°, or iodised dermic polyvidone (betadine).
- Time of contact of at least 5 minutes

Projection on the mucous (in particular conjunctivitis):

- Completely rinse, preferably with physiologic serum or if not with water, at least 5 minutes.
- Do not put disinfectants on the mucous

Recommendations for ARV prophylaxis considering the importance of exposure and state of the source

Source	**Exposure**		
	Massive	**Moderate**	**Minor**
HIV + CD4 low or opportunistic pathology	Recommended	To be recommended	Recommended
HIV + Asymptomatic	Recommended	To be recommended	Is discussed
unknown HIV status, but factor of risk for HIV (≥ 1 argument *)	Recommended	A. To be recommended	Is discussed
Unknown HIV status or unknown source without argument (*)	Recommended	Is discussed	Is discussed

(*) Argument in favour of an infection to HIV to patient source:
Clinical or biological symptomatology compatible with primary infection or a severe immunity deficit; known factors of risk; the prevalence of infection in the institution.
The one who benefit from it is the HIV victim.

ARV treatment

Depends on the state of the source and the importance of exposure.

Evaluation of the importance of the exposure:

- Massive exposure = deep prick, by intravascular device or hollow IV or intra-arterial needle, prick with a laboratory sample.
- Moderate exposure = cutting with lancet through gloves, superficial prick with hollow IV or intra-arterial needle;
- Minor exposure = superficial erosion, with full needle (suture) or hollow of small gauge (IM or SC); skin-mucous contact; prick with an abandoned syringe.

Deadline for prophylactic intervention

Treatment must intervene as soon as possible in the hours following exposure optimally in the first four hours), without waiting for the results of the HIV status of the source person. The deadline of 48 hours seems to be reasonable for maximum effectiveness. However, the doctor may prescribe beyond that deadline but it must not go beyond 72 hours.

Duration of treatment

It is 4 weeks. Initial prescription of 1 to 2 weeks and weekly consultations enable monitoring and psychological support for reinforcing conformity to treatment.

Therapeutic choices

The prophylactic treatment recommended is:

AZT+3TC+LPV/r or d4T+3TC+LPV/r
Give the EFV if there is no LPV/r

If it is a pregnant woman or in case of intolerance or contraindication to EFV, choose: AZT + 3TC + LPV/r in non anaemic persons
D4T + 3TC + LPV/r in anaemic persons
That treatment must be adapted, depending on the advice of an expert if the source patient is under ARV treatment and especially in case of:

- Suspicion of therapeutic failure, or;
- Poor conformity of the source patient.

Monitoring

The person exposed must be informed about:

- The risk of undesirable effects of treatment;
- The importance of conformity to treatment;
- The interest of prevention

He/she must give his/her informed consent about taking the prophylaxis.

A pregnant woman must be informed about the risk of transmission to her child and those linked with taking antiretroviral drugs (the advice of the referring doctor is recommended). To any woman, pregnancy test must be proposed.

Confidentiality must rigorously be respected.

Abstinence from unprotected sexual relations during that period.

Results of evaluation and monitoring

Date	Person that does not receive the prophylaxis	Person receiving the prophylaxis
Initial results in the 4 first hours	- serology HIV +	- HIV status - - NFS - Pregnancy Test
A S2		-NFS (if AZT)
A M1	Between 3 and 6 weeks after exposure : - HIV status	Between 3 and 6 weeks after exposure : - HIV status At the end of treatment: -NFS (if AZT)
A M2		1 month after the end of treatment: -NFS (if anomaly to M1) -HIV status
A M	- HIV status	-HIV status

Rape

Although there is little information about the effectiveness and deficiency of the post sexual exposure prophylaxis, compared to the exposure to blood, data suggest that such prophylactic treatment may reduce the risk of acquiring the HIV infection. The prophylactic treatment must be routinely provided for the victim of rape/defilement.

Evaluation of infectious risks

It is logical to ask the following questions:

- What was the nature of exposure? For example what was the nature of sexual attack? Has actual exposure occurred? (Vaginal anal penetration?)
- The HIV status of the source person (rapist/defiler) is it known or not?

- Is he/she is found out to be HIV positive? If yes, does he/she take ARV treatment?
- Is the source person available for an HIV test? If yes, will he/she accept to be tested?

- The patient exposed (victim of rape/defilement) is already infected. If the state of the patient is unknown, the rapid test must be systematically suggested.

Indications and prophylactic regime

If a person known to be HIV positive rapes an HIV negative person, a post-exposure prophylaxis must be given as soon as possible. The victim must be tested as soon as possible. There are however many circumstances that are very ambiguous. It is the case when the HIV status of the source person is unknown.

Prophylactic treatment is similar to the post-exposure prophylaxis to blood. Care will be taken to add a prophylactic treatment for STI

How to behave in case of rape

HIV status of the source person (rapist)	HIV status of the exposed person (victim of rape)	Recommendation
Positive or negative	known to be positive	No prophylaxis is indicated
known to be positive*	Known to be negative	Indication of immediate prophylaxis
known to be positive	Unknown	Immediate rapid HIV Test for the victim of rape - If HIV negative, give the prophylaxis - If HIV positive, stop the prophylaxis and refer to an HIV care centre
Unknown and accepts to be tested	Known to be negative	Immediate HIV rapid test for the rapist In waiting for the result of the test, give prophylaxis - If the rapist is negative, stop prophylaxis If the rapist is positive, continue prophylaxis
Unknown and accepts to be tested	unknown	. Immediate rapid HIV test for the rapist and the victim Give the prophylaxis while waiting for the results If the rapist is negative, stop the prophylaxis - If the victim is positive, stop prophylaxis and refer to a HIV care centre
Unknown and refuse test or unavailable	Known negative	Counsel the victim and inform him about the risks and interests of prophylaxis and give options and give prophylaxis
Unknown and refuse test or is unavailable	unknown	Rapid HIV test for the victim of rape. If the victim is HIV negative, it is important to give the prophylaxis Counsel him/her, inform on risks and advantages of prophylaxis, and give options.

*If the rapist is positive and is under ARV treatment, consult an experienced person.

Monitoring

The monitoring is similar to the post-exposure prophylaxis to blood.

PART III

CHAPTER I. Care of the pregnant woman

Out of 40.3 million of people living with HIV in the world, 20 million are women; including 14,000 people who are daily infected throughout the world, about 12,000 being adults of whom 50% are women. When the specific vulnerability of women is considered vis-à-vis HIV /AIDS in developing countries due to their position in the couple, their difficulty of access to education and of their socioeconomic vulnerability, it is appropriate to devote a very specific place for their care, especially for those who are pregnant.

The ARV treatment to women

The specificity of women in the area of care of antiretroviral treatment is triple:

- Due to a more frequent appearance of undesirable side effects, which may influence the choice of molecules (risk of severe rash when under nevirapine 7 times more than in man);
- Due to increased frequency of lactic acidosis and hepatic steatoses with analogue nucleosides (83% of 107 first cases reported);
- Due to the possible associated pregnancy.

However, treatment of the woman, including the pregnant woman is still a priority. Family planning will be advised for HIV positive women.
Three possibilities are possible for antiretroviral treatment to woman:

- ARV to a woman within the reproductive age bracket;
- ARV to a pregnant woman who responds to indications of treatment;
- ARV to a woman who is already under the tritherapy and becomes pregnant.

RV to woman with the reproductive age

A double problem occurs:

✓ **Problem of contraception associated with ARV :**

Many ARV (PI and NNRTI) modify the metabolism of hormonal contraceptives and must require particular precautions in using this mode of contraception in case of combined treatment.

The following table gives interactions between ARV and hormone contraceptives:

ARV	Effect on the plasmatic rate of ethnyl – oestradiol	Dosage adaptation
NRTI	No action	
Nelfinavir	Reduction of 47 %	⇑> 30 µg of'EE
Lopinavir/r	Reduction of 42%	⇑ 30 µg of EE
Névirapine	Reduction of 19 %	⇑ 30 µg of EE
Efavirenz	Reduction of 37 %	⇓15 ou 20 µg of EE

In case of difficulty in using ethnyl oestadiol, it is important to refer to another mode of contraception:

- Either using the progestatives: some interactions with ARV exist in the sense of reducing plasmatic concentration of progestatives.
- Either the installation the coil taking into account the increased infectious risk in case of severe immunodeficiency.

In all cases of using condoms (male or female) is recommended since, if it has a limited role in birth control, it has a very important action in avoiding over infection by HIV in case of HIV positive partner and as protection of an HIV negative partner.

✓ Problem of choosing ARV

The choice of ARV to woman within the reproductive age is the same as in the man. However, one will try to avoid molecules that are likely to be teratogenic (efevirenz) or potentially toxic (combination with ddI + d4T). EFV may be used in any woman as long as she uses the contraceptive method and is warned about the necessity of immediately alerting her doctor in case of pregnancy. The doctor will then modify the treatment by replacing EFV by NVP in the 1st semester.

The desire to have a child:

This possibility is of great frequency and is still certainly the most difficult to manage. In fact, it is true that even with current PTMC (PMTCT) programmes; pregnancy would not be encouraged in HIV+ woman. However, it is important to take into account the double reality: that all women want a child before anything else and that of the African cultural context in which a woman must have children to be recognized as a full woman. The physician will therefore have to do his/her best with his/her patient to manage that desire for pregnancy. In the same way, any woman within reproductive age would benefit from counselling before envisaging to become pregnant. (See Appendix XI)

Any health centre offering PMTCT services would therefore provide effective planning services (see Appendix XII).

The first preoccupation concerns the status of the partners: 3 possibilities:

- Either he is positive: it is possible that in that case, the couple will be counselled to use condoms to avoid cross infection but it will be necessary to make choice of window in order to determine the most fertile moment to reduce to the possible minimum the number of unprotected sexual relations.

- Either he is negative what poses the problem of possible contamination during unprotected sexual relations. In this case, "protective" techniques may be advised such as the inoculation of the sperm of the partner using the syringe or even the condom.

- Either the status of the partner is not known. In that case, the situation may be difficult due to double possibility.

- The woman hides her HIV status to her husband. In fact, it is probable in that context that she does frequent unprotected sexual relations and the desire for a child increases the risk of contamination.

- The spouse refuses to know her status and it is important to do in such a way to limit the risk for two couple by restricting where possible the number of unprotected sexual relations.

The second preoccupation concerns the clinical and immunity status of the woman. It is important before anything to evaluate the clinical situation and the level of the CD4 of the woman. In case of unfavourable status (Poor clinical status, decrease of CD4), it is necessary to analyze causes of the failure of treatment.

In short, elements to consider when a woman under ARV treatment wants to become pregnant:

HIV Status of the Partner

- Has the disease stabilised?
  - Good evolution of CD4 (to control if necessary).
  - Favourable clinical evolution.
  - No current opportunistic diseases.

- What is the social support that the patient is receiving?
- Is the ARV regime ideal?
- Information on the risks encountered by the mother, the kid and the partner.

The desire to conceive is often the main concern of HIV positive women. The importance of that desire and may vary with time. A woman may forget that the first months of treatment and then when she passionately wants a baby. Lack of open dialogue may lead to catastrophe (ex. A paraplegic woman patient under EFV without the social support or a husband secretly becomes pregnant as she was forbidden to be pregnant some months early). It is therefore necessary to approach that person regularly during monitoring as patients do not always spontaneously speak about it.

ARV to a pregnant woman who respond to indications of treatment

It is more and more frequent with development of PMTCT programmes that an HIV positive status is discovered during pregnancy. In that case, the team in charge of counselling and proposing the testing must always prepare the wife to the possibility of the initiation of treatment. In the same way, she must discuss the HIV status of the partner with the woman and try to convince her to talk about it with her if that question has never been tackled before.

The first step to carry out when a pregnant woman is discovered to be HIV positive is to do a clinical check up and an evaluation of the CD4 to decide the possible necessity of its transfer to undergo antiretroviral treatment.

Eligibility criteria for ARV are a bit different to pregnant woman:
- Stage 4 whatever is the rate of CD4.
- All patients with less than 350 CD4/mm3, whatever the clinical stage is (1, 2, 3).

Those who are not eligible to treatment will be referred to the PMTCT service.

If treatment is deemed necessary, it is important to treat the woman with the imperative double:

- To choose an effective combination of ARV on viral multiplication
- To take into account of the presence of pregnancy.

When does the treatment begin?

That treatment will start from the beginning of the second term of the pregnancy, the date to which the embryogenesis ends, thus reducing the teratogenic risk of ARV. In case of very severe HIV infection (stage 4 or CD4 < 50/mm3), the treatment may be started before that date.

That treatment can be doubly justified:

- It enables the woman to regain her immunity

- It protects the child from HIV transmission: it is known in fact, that it is the most immunologic depressed women with a rate of CD4 ≤ 200/mm3 who transmits in utero the virus to their child. That rate may attain 25% of mother to child transmission (in addition to the risk related to breast-feeding).

Which ARV to prescribe?

The ARV prescription must conform to the same rules as those of the adult (See part B, CHAPTER 3).

However:

- It will be preferable to promote the prescription of ARV whose efficiency is in PMTC. I.e. AZT, nevirapine and 3TC.

- The ARV known as potentially teratogenic or toxic to the pregnant woman will be avoided. These are: efavirenz (during the 1st term), and the combination ddI+d4T (each of those NRTI may be used individually but the combination is contraindicated due to the importance of the risk of occurrence of hepatic steatose with lactic acidosis that is sometimes mortal).

- Therefore the best choice seems to be the prescription of the combination: AZT+3TC+NVP.in case of intolerance to nevirapine, a PI will be used: LPV/r or Nelfinavir or efavirenz if it is in the second term.

- Clinical and biological monitoring must comprise of tolerance (among others blood formula) and the effectiveness of treatment as for any adult and of pregnancy as for any pregnant woman (see PART B CHAPTER 3 C).

Care of a woman already under triple therapy and who discloses her pregnancy

This possibility will be more and more frequent with the development of access to antiretroviral treatment. When a woman under ARV treatment becomes pregnant, it is important to carry out double control:

- To ensure the efficiency of current treatment: it means carrying out a complete clinical check up and the evaluation of CD4. It is in that context that it is interesting to assess the viral load if it is available. Indeed, the lower the level of CD 4 and the higher the viral load, the higher the risk of transmission to the child, if the treatment does not properly improve the immunity situation, it is better to change it, in conformity to the general rules.

- It is necessary to verify that the current treatment does not contain ARV contraindication in case of pregnancy. The presence of such molecule must lead to its immediate withdrawal. If it is efavirenz, it will be substituted for by nevirapine if it is in the 1st term, if it is the combination of d4T+ddI, one of the two NRTI will be dropped to be replaced by another one chosen in relation with those already used in the patient.

Family planning

The availability of a FP service is essential in a health structure that provides PMTCT services.
The service provider must:

- Remind the woman in the immediate post partum of the importance of family planning.
- Provide appropriate information and help each of his/her patients to make an informed decision whether or not to become pregnant.
- To tale particular interest in the HIV positive woman and her partner by enabling them access to safe contraceptive methods, depending on their choice.
- To explain that the fact of using another contraceptive method does not exclude the use of the condom and does not protect against HIV transmission.
- If the contraception is requested, ensure that the woman or preferably the couple has all information and necessary counselling for safe contraception.

CHAPTER 2: Prevention of Mother-to-Child Transmission (PMTCT)

PMTCT.

It is the first area in which ARV has proved their real effectiveness. Following the therapeutic test that was evaluating the impact of AZT against a placebo in order to prevent mother to child HIV transmission from, it has been found that AZT reduces 2/3 of the rate of HIV transmission, compared to the placebo. Since then, numerous tests have been carried out throughout the world, particularly in developing countries (sub-Saharan Africa and South East Asia) seeking to attain the most efficient, cost-effective prevention method, with the simplest procedure possible that enables wider dissemination of its application.

Stages of PMTCT

Any PTMC programme comprises 5 application periods:

- The primary HIV prevention: to avoid that the woman becomes HIV positive
- The prevention of unwanted pregnancy: it is the gamily planning.
- Prevention of transmission in utero.
- Prevention of the transmission prevention during labour or child birth (per partum)
- Prevention of the transmission in post partum by the mother's milk.

The two first periods will not be dealt with in this chapter since they belong to the area of counselling.

✓ Different stages and rate of mother to child transmission (without treatment)

The mother to child transmission occurs anytime but particularly during the time of child birth or labour. Out of one hundred HIV positive women, total transmission of 30 to 50% may occur in the following manner:

- Before giving birth: in utero (5 to 10%)
- During labour (10 to 20 %)
- After giving birth: the risk is related to the mother's milk and ranges from 15 to 20 %, depending on duration of breast-feeding. The risk of contamination during breast-feeding is major in case of primary infection during this period (up to 30%).

The average rate of mother to child HIV transmission ranges from 40 to 50% in the Sub-Saharan African Region (i.e. one child out of 2 contaminated). It is about 15 to 30% in Europe (i.e. about 1 child out of 4 contaminated).

Differences between those two situations are in connection with:

- The unfavourable clinical status of the mother in Africa during the period of pregnancy and inadequate care;
- The practice of breastfeeding is quite discouraged even forbidden for positive women in Europe.
- Frequent food shortage in Africa that increases the importance of immunity deficiency.
- STI are more frequent and treated late.
- Childbirths are often complicated, at home.
- A high frequency of young parturient.

This shows that to improve the situation in Africa, it is important to concentrate efforts on:

- The improvement of care of women in general, but more particularly the screening, early diagnosis and access to PMTCT or ARV treatment,
- To suggest a suitable and accessible alternative to breast-feeding;
- To improve the feeding situation of pregnant women.

Factors favoring Mother-to-Child transmission

In general, the more mothers are immunodepressed, the higher the risk of mother–to-child transmission, particularly in utero as from the second term.
Three types of elements favouring mother to child transmission:

- The clinical status of the mother
- The childbirth conditions.
- Breast-feeding.

- **Clinical status of the mother:**

The risk of transmission is as high if:

- The viral load is high;
- The clinical status is poor (stage 3 or 4 WHO): symptomatic women, in particular the presence of opportunistic infection.
- The existence of infections generally associated (tuberculosis, hepatitis B or C, malaria…) or local (genital infections).
- The rate of CD4 is lower with the considerable risk in below 200 CD4 /$mm^{3.}$

- **Delivery**

Aggravating factors surrounding delivery are:

- Adequate child birth measures that are not respected
- Long labour beyond 12 hours;
- A premature rupture of the membrane beyond 4 hours;
- Home-based child delivery;
- A Dystocic childbirth;
- Existence of haemorrhagic or meconial liquid

- **Breast-feeding:**

As it will be explained below in more details, mixed breast-feeding is the mode of nutrition that most promotes mother to child HIV transmission through the mother's milk.

Different interventions to reduce Mother to Child HIV transmission

This chapter shows mother to child HIV transmission prevention strategies with particular emphasis on tests and interventions which have shown evidence of that effectiveness.

That prevention is divided into four main axes:

- Primary prevention of the HIV infection: Ensures that future parents do not become infected
- Prevention of unwanted pregnancy in HIV positive women
- Prevention of transmission by medicinal intervention (ARV):
    - In utero
    - per partum
    - post partum
- The care of infected woman , her child and her family

Note: The antiretroviral try therapy will be recommended, depending on the status of the mother.

1. Primary HIV/AIDS infection prevention

The primary prevention consists in starting information, education and communication (IEC) programme, as well as the screening and treatment of sexually transmitted infection that are subsequently associated to HIV. Primary prevention also includes the promotion of the condom both male and female as well as HIV counselling in order to propose testing.

The objective of this strategy is to promote the prevention of the infection to parents through the improvement/reinforcement of their knowledge in the area of HIV/AIDS, the adoption of less risky behavioural, the use of condoms, and the possibility of knowing their HIV status.

2. The prevention of unwanted pregnancy in women infected by HIV.

The HIV infection poses a real problem besides when faced with the desire of having children existing in most women, especially in Africa where child birth is still an important social and cultural value. In a woman infected by HIV who does

not want pregnancy, it is a matter of reinforcing family planning services for effective prevention of pregnancy. It is in that context that double protection is more and more considered (strategy enabling simultaneous protection both against STI and unwanted pregnancy). Therefore, the choice of contraception must be made bearing in mind those risks of pregnancy and STI/HIV.

On the contrary, in case of the desire for a child, the woman must be advised on the possibility of the least risk for her and for her child. It is in that context that complete clinical evaluation is carried out to assess the status of the mother and the level of CD4. It is from this set of information that is possible to determine the risk for the child and the best preventive strategy to be adopted.

In some cases, poor clinical status combined with a low rate of CD4 ($<200/mm^3$) may lead to temporarily advise against pregnancy while waiting for the restoration of immunity by putting the patient under treatment to make the situation less compromising.

3. The prevention of in utero transmission:

That time of prevention is important because it is accompanied in most cases by severe forms when children are infected in that period. This period of prevention consists in treating, by antiretroviral drugs (triple therapy) women who respond to criteria of eligibility for treatment.

In fact, whether pregnant or not, an HIV positive woman should be under anti-retroviral triple therapy on basis of medical indication. In a pregnant woman, it is necessary to begin the treatment from the beginning of the second term (end of embryogenesis period with high teratogenic risk). If that stage is passed, it is important to quickly begin the treatment.

This treatment must exclude the combination with DDI – D4T more toxic for the liver of a pregnant woman with the risk of severe lactic acidosis (each of these ARV may be used in isolation). Efavirenz (Stocrin) whose teratogenic effect has been proved may be used in the third term. The treatment prescription will have also to contain preferably molecules whose effect on the reduction of mother to child HIV transmission has been proved as AZT, 3TC, NVP. A good combination of the first line may be constituted as follows: AZT + 3TC + NVP.

4. Medicinal and obstetrical interactions (ARV) in the context of PMTCT

Medicinal interventions

The long AZT regime (ACTG 076): The test carried out for the first time in 1994 in the USA and in Europe indicated the reduction of mother to child transmission by 66%. That regime uses AZT by oral means administered to the pregnant woman from the fourth week of pregnancy in perfusion, from labour until childbirth and by oral means administered to the child during the six first weeks of life.

The short AZT regime (Thai): the test carried out in 1998, uses AZT in a short regime by oral means from the 36th week of pregnancy until child birth. Those regimes lead to the reduction of transmission by 50%.

The regime AZT + TC (PETRA): jointly carried out in South Africa, Tanzania and Uganda in 1996-1999. It consists in administering to the mother AZT and 3TC from the 36th week of pregnancy until a week after pregnancy. In that regime, four arms have been individualized of which the arm A and B. In A, the prophylaxis is given three times, per and post partum, the arm B alone in per and in post partum. The arms A and B have led the reduction of mother to child HIV transmission by 50%.

The NVP regime *(HIVNET 012)*: The test carried out in 1997 in Uganda, the regime uses by oral means a single dose of NVP 200 mg at the beginning of labour administered to the pregnant woman and 2 mg/kg to the new born baby in 72 hours that follow birth. For the woman, if labour is very longer > 24, a second dose of NVP must be administered. If she takes the dose of NVP 4 hours before giving birth, it will be necessary to administer NVP to the child immediately after birth since very good trans-placenta passage for that product will not have had time to be carried out perfectly. In that case it will be necessary to administer a second dose to the child on the third day. That regime led to the reduction of the rate of mother to child HIV transmission by 47%. The important problem posed by NVP is that of the occurrence of resistance in 20% of women after a single dose. It has been found that in general, this resistance occurs in the first year but reappears in case of next reintroduction of NVP. These cases of resistance are due to the long period of life of NVP that is prolonged for about 7 days after being taken. The impact of this resistance on the effectiveness of the molecule is still to be established but that problem must certainly not be neglected.

The regime AZT + *NVP (DITRAME- Plus)*: carried out between 1998 and 2003. It combines NVP as it is administered in the HIVNET 012 regime (1 tablet of 200 mg administered at the beginning of labour to the mother and 1 dose of 2 mg/kg of solution of NVP administered to the child in the first 3 days) and AZT according to the short schedule (to the mother: 300 mg 2 times a day from the 28^{th} to 36^{th} week, at the beginning of labour: 300 mg/kg 2 times a day until the 7^{th} day after birth). The advantage of that protocol is double: it has proved the effectiveness (The rate of transmission to 6.2%) and considerably reduces the occurrence of resistance to NVP by the fact of combining NVP with AZT.

When the mother has not received the prophylaxis and is HIV positive, it is important to propose a prophylaxis to the child after birth for the first 3 days of its life. Several tests begin by documenting that question, including the one carried out in Malawi that shows a rate of 20.9% of transmission at 6 weeks when only NVP is administered in the second hour of life and the rate of 15.3% when NVP is combined with AZT for 7 days. The rate of transmission without treatment is 30%.

Several recent research works have proved the superiority of the prophylaxis combining 2 or 3 ARV.

- **The current protocol proposed in Rwanda**

The age of pregnancy: before 34 weeks:

- ❖ Level of CD4 the earliest possible and clinical categorisation.
- ❖ The patient comes with the results of CD4:

  - The patient is eligible: stage 4 or < 350 CD4/mm^3 regardless of the clinical stage: refer to an ARV treatment centre or begin the earliest possible the triple therapy following the initial classic initial assessment: D4T or AZT-3TC-NVP (automatically the cheapest triomune)
    If Hgb < 7 gr/dl: D4T-3TC-NVP

  - If the patient does not conform to eligible criteria, she will receive the combination of AZT+NVP:

- The mother will receive AZT 2x300 mg a day from the 28th week of pregnancy or the earliest possible, until the beginning of labour and a dose of NVP at the beginning of labour as well as a tablet of AZT+3TC (Duovir) to follow 7 days after giving birth.

- After giving birth, the woman will receive AZT 300 mg + 3TC 150 mg 2x a day for seven days.

- The new born baby will receive syrup of NVP in a single dose (2mg/kg) in the 72 hours following the birth combined with the AZT syrup 2x4 mg/kg a day for a month after birth.

The monitoring of haemoglobin must be carried out as the treatment by ARV is contraindicated if the haemoglobin is lower than 7gr/dl.

- The patient has not yet received the results of CD4:
  Begin the plan above but it is important to reconsider the plan after receiving the CD 4 results.

Age of pregnancy: more or equal to 34 weeks

- Refer to an ARV treatment centre or begin the triple therapy, whatever the rates of CD4:
  D4T or AZT-3TC-NVP.
  If Hgb< 7gr/dl: D4T-3TC-NVP.

- Whatever happens, the patient should begin ARV in the week so as to reduce the viral load to the minimum and therefore reduce the risk of transmission the earliest possible!

- To achieve this, the ARV centre, during the first visit for each 34-week pregnant or more, on that day, it is advised to:

  - See the physician
  - Carry out counselling on the treatment
  - Assess the pre-ARV status
  - Measure the level of CD4 if possible or give ARV

- The following day, ideally, the patient will begin ARV if a second individual counselling session is favourable and if the pre-ARV assessment is correct even if the CD4 results are not accessible. Then, the patient will receive group counselling and will appear before the selection committee even if she has already begun ARV.

Important note: The risk of hepatitis and rash is considerably increased if the CD4 >250/ mm3 and we recommend very attentive clinical and biological monitoring (hepatic tests) for the patients concerned.

- The analysis of the CD 4 results will sometimes be carried out after beginning of ARV. The doctor will then decide if it is necessary to stop or continue the triple therapy after giving birth:

  - The patient who conforms to the criteria of initiating ARV to the pregnant women will continue the triple therapy after giving birth.
  - The patient who does not conform to the criteria of initiating ARV to the adult, will stop ARV the following day after giving birth and will continue AZT-3TC (2 times a day) for 7 days and then will stop all ARV.

If an ARV treatment centre is not available or if the patient may not go to the ARV treatment centre, she will begin AZT300 mgr 2 xs/ day as soon as possible. Then she will receive a single dose of nevirapine (200mg) at the beginning of labour. After giving birth she will receive AZT 300mg + 3TC 150 mg (Duovir) 2x/d for 7 days.

The child will also receive treatment as soon as possible (within 72 hours) a single dose of NVP(2mg/kg, that is to say ~ 1 ml) combined with the AZT syrup (2x4 mg/kg, i.e. ~ 2 times 1 ml) a day for a month.

The patient is diagnosed at the time of giving birth:

- She will receive a single dose of nevirapine (200 mg) at the beginning of labour. After giving birth she will receive:
  - AZT 300mg+ 3TC 150 mg 2x/d for 7 days.

- The child will receive as soon as possible (within 72 hours) a single dose of NVP (2mg/kg) combined with the AZT syrup 2x4 mg/kg a day for a month.

- The HIV positive patient whose husband is HIV+ will equally receive the same regime: NVP single dose and AZT+3TC for a week after giving birth. That is important as she may be re-infected between the period of the test and that of giving birth.

Measures surrounding delivery « safe delivery »

During delivery, it is important to avoid anything that is likely to increase blood interchange from mother to child or cause a lesion of teguments or the mucous membranes. The risk is major when the membranes are cut, the placenta is detached and the child reaches the genital membrane at the contacts of maternal secretions.

Safe childbirth comprises of four orders of measures:

- **Avoid invasive actions:** artificial rupture of amniotic sac, episiotomy, laying of precepts…
- Limiting the practice of artificial rupture of membranes in the following cases: (failure or poor evolution of labour, foetal distress, cervical expansion more or equal to 7 cm)
- Avoid inopportune vaginal touches, especially after rupture of membranes.
- Clean the genital epithelia, the skin and mucous membranes of the child at birth with chrorhexidine 0/.25%).
- Do not draw the umbilical cord towards the child.
- Avoid any lesion of teguments or mucous membranes of the child.

The prophylactic caesarean section programmed at 38 weeks has been proposed but the risk of morbidity and mortality associated with it should be avoided in that indication in developing countries.

✓ Post partum prevention:

One of the most causes of differences observed between the rate of MTCT in Africa and in Europe is due to breast-feeding, which alone is responsible for 14% of MTCT, and it may rise up to 30% in the case of maternal primary infection during breast-feeding. Faced with that situation, alternative substitute feeding will eliminate the risk of MTCT after delivery. However, socio-cultural and economic conditions (acceptability, feasibility, cost, sustainability) of families may make impossible the choice of artificial feeding. A possible alternative is in exclusive

breast-feeding for a short period but it is better to bear in mind that breast-feeding carried out under good conditions is still ideal.

Counselling the HIV positive mother concerning the choice of mode of child feeding will depend on her means and capacity to apply the type of feeding chosen for her child.

The health worker must explain to the woman the advantages and disadvantages of breast-feeding, compared to those of alternative artificial feeding, in order to enable her to make an informed choice on the mode of feeding her child. Therefore, health care providers must support and accompany the mother in choosing and applying the mode of feeding of her child, bearing in mind that mixed feeding increases the risk of MTCT.

If the mother chooses breast-feeding, she has to respect the following conditions:

- Breast-feeding must be exclusive; it means that the child should not be given another type of food or drink, including water;
- Exclusive breast –feeding does not exclude oral administration of drugs to the child;
- Breast-feeding must be short, not going beyond 6 months;
- The counsellor must explain how to accurately position the baby onto the breast in order to avoid breast-feeding that risks causing cuts or abscess. Those constitute a severe risk of the virus transmission;
- Stopping breast-feeding must be early enough (6 months) with a safe transition. The transition is to accustom the child to receive mother/ milk on a spoon or cup, while preparing for quick weaning. Premature weaning is not advised except if the child and mother are comfortable with bottle feeding;
- In order to avoid the swelling of the mammary glands, an injection of 5 mg of oestadiol will be proposed to the mother that does not want to breastfeed her baby, who wishes wean the child.

If the mother chooses substitute feeding, the child must be fed exclusively on the substitute food other than the mother's milk, for the 6 first months of the child' life. From the age of 6 to 24 months, supplement milk meals by adequate additional foods locally available. The success of artificial feeding depends on:

- The quality of the advice that has been given upstream; it happens that the problem of breast-feeding must be tackled as soon as possible since the announcement of the HIV positive status.

- Facilities that will be given by PTMC care programmes in the area of breast-feeding: free supply of milk and feeding bottles for 6 months. It is important to provide clear explanations on how feeding bottles or cups are cleaned and sterilised using hot water. Access to clean water is an indispensable element to evaluate before envisaging bottle feeding;

- Family and/ or community support received by the woman;

- The quality of mother/child monitoring carried out by the nursing or care providing team.

PTMC Plus or PMTCT Plus :

We insist much more on all stages of PMTCT (at level of its 4 stages) so that actions are not limited to the mother-child couple but also to the entire family cell: spouses, all brothers and sisters as well as other members of the family. Particularly, this concerns counselling for testing and the general care of the entire family. It is important to mention that active participation of the spouse considerably facilitates different stages of a pregnant woman whether it is at level of her treatment if she needs to be treated as well as the choice of mode of child feeding.

The child whether it is infected or affected by HIV will be dealt with in the CHAPTER on the child.

Children are concerned by HIV/AIDS too. The December 2006 AIDS UN figures revealed that 2.3 million (1.7- 3.5 million) children < 15 years worldwide are infected with HIV and that 530.000 (between 410.000- 660.000) out of 4.3 million new cases registered in 2006, 530,000 (between 410,000 and 600,000) were children. About 380.000 children died of HIV/AIDS in 2006.

Modes of contamination and the evolution of a child.

Modes of Contamination.

The major mode of contamination in children is from parents-child transmission. This is examined in the corresponding section **(PARTC, CHAPTER 2.).**

The modes of contamination include among others:

- Blood transfusion
- Use of non sterilised injection materials.
- Surgical practices with non sterilised materials (circumcision…).
- Sexual abuses.
- Some ritual practices (extraction of the emerging of babies, resection of the uvula palatine, excision, tattooing, scarification, piercing…).

NATURAL CLINICAL EVOLUTION IN A CHILD

The evolution of the HIV infection that is transmitted from mother to foetus is characterised by the following 3 major modes of evolution:

- A severe form (30 - 50 of cases in Africa) with the risk of mortality 50% within the first 2 years of life (without treatment), especially for children infected in utero.
- A moderate symptomatic form without opportunist infection.
- A slow progressive form (rare).

Given important mortality in children, it is essential to carry out early diagnosis to start antiretroviral treatment early before the age of 6 months and to drastically reduce mortality and morbidity due to the HIV infection.

DIAGNOSIS OF HIV BIOLOGICAL INFECTION IN A CHILD.

Warning symptoms suggesting the necessity to verify whether the child is not infected with HIV or not.
Automatically: malnourished children (compulsory, Ministerial instruction), children under anti-tuberculosis treatment, multiple hospital admissions, children whose mothers are HIV positive.
Suggestive symptoms of the HIV infection in a child: oral Candida, low height, under height or underweight and mental retardation, dermatitis and frequent ENT infections, peritonitis, recurrent infections.

In Children aged < 18 months

Maternal antibodies (included those of HIV) during pregnancy go across the placental barrier and may still be detectable in a child up to the age between 15-18 months. Any child born of an HIV positive mother, whether contaminated or not, shows an HIV positive status within the first few months of its life.

In fact, among non HIV contaminated children, born of HIV positive mothers:

- 75% will have lost their antibodies between the age of 9-12 months.
- Most of them (90%) have lost them at the age of 15 months.
- 10% conserve an HIV positive status between 15-18 months.

The certainty of the diagnosis of the infection in a child aged > 18 months is PCR (DNA PCR diagnosis or RNA PCR= viral load) which enables the highlighting the genome of the virus. The PCR is expensive and is not widely available in Rwanda even if easy to be carried out and conserved with DGS5 (Dried blood spot).

The fact that these techniques are lacking does not constitute an obstacle to the treatment of those young children. Clinical diagnosis is feasible (even if its sensitivity and specificity are low) to confirm the child infection and decide an antiretroviral tri-therapy of a child aged > 18 months and with a positive status but keeping clinical symptoms of HIV infection (see presumptive diagnosis of WHO). Before giving ARV without assurance by PCR to children aged <18 months, it is important to ensure that the child has benefited from supplementary nutrition and verify the response to anti-tuberculosis treatment (same symptoms as HIV of the child, especially if immune depression is caused by malnutrition).

In the Child aged >18 months.

Any positive status in a child aged > 18 months is equal to an HIV infection. It's not necessary to carry out the PCR diagnosis (difficult). A negative status excludes at any age the HIV diagnosis, except if a child is in sero-conversion. Indeed, the mother may be infected during breastfeeding where a child may be infected through other ways (Blood transfusion, sexual abuses, needles and other tools contaminated by blood…). That is why; it is necessary to verify the HIV status, 3 months after breastfeeding or blood transfusion.

It is always necessary to exclude HIV infection in a clinically suspected child (Cf. warning symptoms) of being immune-depressed even if her mother is said to be HIV negative. It is necessary to verify the status of the mother or infant (even if the results of the child aged < 18 months is the same as that of its mother and indicates the child is exposed).

To summarise:

Interpretation of HIV test of the child born of an HIV positive mother.

.Age	HIV Status of the Child	Interpretation
< 9 months	The serological test serves only to verify the maternal status (exposure). The options of diagnosis are PCR and in case of its absence: the percentage of CD4 and dg clinical presumptive WHO.	
9-15 months	HIV + status	A child may be HIV + or -, the only way of determining its status is the PCR test. In case of its absence: the percentage of CD4 and presumptive clinical dg WHO. . Repeat the test at the age of 18 months
	HIV – status	For a non-HIV infected child (viral test not necessary) in case it is not breastfed.
15-18 months	HIV + status	The child is probably HIV +, but this is to be confirmed by serological test at the age of 18 months or PCR. When PCR absent: the CD4 percentage and presumptive clinical dg WHO. The test to be repeated at the age of18 months.
	Status HIV -	For a non-HIV infected child (viral test not necessary) in case of the child is not breastfed.
> 18 months	HIV + Status	For an HIV infected child (PCR viral test not necessary).
	HIV - Status	For a non-HIV infected child (viral test not necessary) in case the child is not on breastfeeding.

The diagnosis of HIV for monitoring of children aged< 18 months is carried out as follow in Rwanda:

The first PCR in 6 weeks at PMTCT centre (= the 1st vaccination date and the beginning of prophylaxis of Cotrimoxazole so that the mother can remember this date. The aim of this PCR detecting children infected in utero or during per partum. Those children often present fast mortal evolution of sickness without ARV treatment. If it is positive, the result will be confirmed by the other PCR test if possible. This time does not post pose the beginning of treatment if the child's state is worse. However WHO agrees a diagnosis with one PCR+ for we have problems to realize 2nd PCR.

NB: If a Child didn't benefit from the 2nd PCR of confirmation for many reasons, he will be considered as infected until the verification is carried out (status to be controlled between 9-18 months).

Second PCR: Objective: To exclude infection of children nourished by maternal breastfeeding. These children however have less risks of death than those infected at an earlier age.

This is why, given limited means to realize those PCR, if the child has had the first PCR within sixth weeks, the second PCR will only carried out only when:

- There is poor clinical evolution with the status +
- There is positive control of the 1st PCR.
- The mother wishes to stop breastfeeding at sixth week but this poses the risk of malnutrition and bacterial infection. It is therefore necessary to verify whether the child was not infected during weaning at the sixth week= PCR at 5 months and if PCR negative: counselling and health education to maintain maternal breastfeeding at 6 months, but supplementary nutrition is given in case of indigence.
- An infected child should continue maternal feeding.

Before carrying out PCR, it is advised to verify the status of a child who is loosing its maternal antibodies from the age of 6 months. PCR is carried out if and only the HIV status in a child aged<18 months, is positive.

❖ In case of the absence of PCR but accessible doses of CD4:
- The child is declared infected by HIV until it is proved otherwise, if at least two arguments on the list below are present (WHO, August 2006):
  - Sepsis (choc notion in severe infection context.)
  - Severe pneumonia requiring oxygeno-therapy
  - Chronic Oral Candida beyond the age of 1 month
    OR
  - Symptoms of stage 4 (AIDS) for WHO
    Most frequently: persistent unexplained severe malnutrition.

SUGGESTIVE SYMPTOMS:
CD4<20%
= <1200 CD4/mm3 between 0 and 11months and < 750/mm between 12 -17 months).

Any child aged <18 months diagnosed HIV + without PCR, will benefit from an HIV status at 9 and/or 18 months or (3 months after the end of breastfeeding.

Miasma makes HIV clinical diagnosis difficult for those children are also immuno-depressed (oral Candida, frequent infections…)
Is the severe malnutrition problem caused by a lack of food, tuberculosis, HIV or other chronic disease?

To response this question there is need to proceed by the exclusion method:

- ❖ Admit a child in nutritional feeding centre and begin a careful nutrition treatment.
- ❖ Actively search for tuberculosis (see, appendix 6, diagnosis score accepted by the National Tuberculosis Control Programme -NTCP) :
  - For anamnesis: cough> 3 weeks or T^O not responding to large-spectrum antibiotics.
  - Look for the tuberculosis story in the family, particularly in parents, brothers and neighbours.
  - Carry out a thorough chest X ray radiography in every child and mother and search for BK by gastric probe (2 series of probes)

- Intra-dermoreaction.
- Unexplained malnutrition (disseminated tuberculosis)

❖ If there is no response to nutritional care nor for tuberculosis arguments, the HIV infection is probable but disseminated tuberculosis (also possible (the child being exposed to 2 diseases), and it's important to observe the response to anti-tuberculosis drugs before prescribing ARV without PCR before the age of 18 months.

The only sign of extra pulmonary tuberculosis may be malnutrition without pulmonary symptom; cachectic children often show signs of fever and cough less, the intra-dermoreaction is negative (anergy due to cellular immunity deficiency related to malnutrition).

Exclusion of the diagnosis of HIV infection in a child born of an HIV+ mother.

A Child aged > 18 months: negative status outside of breastfeeding that has ended at least 3 months before.

Child aged < 18 months: Negative status of child born of HIV+ mother may be negative from the age of 9 months; however, it may remain positive until 18 months. Verify if the child has not been exposed (breastfeeding) within 3 months before the HIV status.
2 negative PCR (of which 1, one month after weaning)
If the infection is excluded, bactrim will be stopped.

Care & treatment of a child born of an HIV + mother

Close clinical and biological monitoring will be established for every child born of an HIV + mother to diagnose and treat patients who need ARV before 18 months.

Clinical monitoring (to be carried out, if possible, in a PMTCT centre).

Any child born of an HIV+ mother will be completely examined (weight, height, neurological evolution, search for Candida, skin problems, lymph nodes, liver, spleen…) every month till the age of 6 months, and then every 3 months until the HIV infection is excluded; either by a negative status 3 months after the end of breastfeeding, or by a negative PCR, one month after weaning. Those data are recorded on the purple medical file.

If the child presents growth or neurological retardation, or any symptom mentioned above, please refer it to a doctor.

If HIV infection is confirmed, this trimester follow-up will be going on in ARV centre (green folder).

Biological monitoring of a child born of an HIV + mother (Cf. PMTCT and Cf. diagnosis: recall.

- **The first PCR within 6 weeks** :(= the first date of vaccination and the start of cotrimoxazole prophylaxis. NB: The PCR within 6 weeks is indicated to child whose mother opted for artificial milk feeding or who presents immuno-depression symptoms.

- **The second PCR:** for asymptomatic child: 1 month before weaning, this will be often done at fifth month of the child life. If the child presents clinical symptoms, the second PCR will be carried out whenever possible after the first one.

  If the infection is confirmed by PCR, the patient is treated stage by stage and CD4 trimester monitoring will be carried out to decide ARV treatment, if the child does not present the 4th & 5thstages symptoms.

Child clinical stages according to WHO (August 2006 revised guidelines).

Thanks to specific anamnesis and full patient examination, the clinician establishes the stages of the child basing on WHO classification.

There are 4 children clinical stages < (teenagers> 15 years: utilisation of WHO old people classification.

✓ Stage 1 :

Asymptomatic
Generalized persistent polyadenopathy

✓ Stage 2 :

Coetaneous-mucous manifestations: Popular prurigo, seborrheic dermatitis, mucotic, perleche, linear gingival erythema, molluscum disseminated infection (> 5% coetaneous surface), disseminated cattle warts, frequent oral ulcerations (2 episodes or more within 6 months, frequent herpes zoster (1 episode or more within 6 months).
Hepato-splenomegaly.

Frequent ENT infections: 2 episodes (sinusitis, acute otitis) or more within 6 months, chronic peritonitis.

✓ Stage 3

- A moderated weight and height retardation (<-2 scores for a child aged< 5 years in the WHO curve and < percentile 5 for children > 5 years (CDC curve) without other medical evident pathology (TB, persistent malnutrition even nutrition ingestion was given);
- Persistent unexplainable diarrhoea (>14 days);
- Persistent unexplainable, intermittent or constant fever (> 1 month);
- Oral Candida (neonatal period excluded);
- Gingivitis and necrotic peritonitis;
- Hairy Leucoplasia;
- Pulmonary tuberculosis;
- Tuberculosis's lymphadenitis;
- Repetitive pulmonary bacterial infections (assumed), (2 or more episodes within 6 months;
- LIP: pulmonary interstitial neuropathy (Rx thorax);
- Chronic unexplainable anaemia (<8 gr/dl) or chronic neutropenia 1000/ mm3) or thrombocytopenia (<30,000/ mm3) during a period >1 month (blood collection);
- Chronic pulmonary pathology related to HIV, including bronchiectasis;

✓ **Stage 4 :**

- Severe persistent unexplainable malnutrition not responding to adequate nutritional treatment: (< 3 scores for a child < 5 years (CDC curves) without other evident medical pathology (TB, persistent malnutrition despite nutritional treatment);
- Pneumocystis to jirovenci Pneumopathy (carinii).
- Severe presumed bacterial infections, 2 or more episodes/ year (emphysema, pyomyositis, osteomelitits, arthritis, meningitis, but the pneumonia is excluded of this list).
- Chronic labial infection (>1 month) or cutaneous-mucosis infection to HSV
- Extra pulmonary tuberculosis.
- Kaposi's sarcoma.
- Mycotic oesophagus.
- Toxoplasmosis cerebral
- Encephalopathy caused by HIV.
- Cryptococcus meningitis or other ultra pulmonary location.
- CMV infection (retinitis or other spleen, liver and lymph nodes infections).
- Disseminated mycosis (histo-plasmosis, coccidioidomicosis, and penicilliosis): laboratory.
- Cryptosporidiosis or isosporosis (with persistent diarrhoea, feces analysis).
- Recto-vesical fistula related to HIV.
- HIV's Cardiomyopathy (heart diagnostic ultrasound)
- HIV's nephropathy (loin's diagnostic ultrasound, loin's clearance, ECBU, butts to detect the proteinuria.

Child immunity stage to be confirmed:

Severe immune suppression according to WHO is a function of the age and the CD4 percentage summarized in the following table.

TABLE 5. CD4 CRITERIA FOR SEVERE HIV IMMUNODEFICIENCY

Immunological marker[a]	Age-specific recommendation to initiate ART[b] [A (I)]*			
	≤11 months	12 months to 35 months	36 months to 59 months	≥5 years
%CD4+[c]	<25%	<20%	<15%	<15%
CD4 count[c]	<1500 cells/mm^3	<750 cells/mm^3	<350 cells/mm^3	<200 cells/mm^3

ANNEX C: WHO CLASSIFICATION OF HIV-ASSOCIATED IMMUNODEFICIENCY IN INFANTS AND CHILDREN

Classification of HIV-associated immunodeficiency	Age-related CD4 values			
	≤11 months (%)	12–35 months (%)	36–59 months (%)	≥5 years (cells/mm^3)
Not significant	>35	>30	>25	>500
Mild	30–35	25–30	20–25	350–499
Advanced	25–29	20–24	15–19	200–349
Severe	<25	<20	<15	<200 *or* <15%

✓ **Prophylaxis for pneumocystis jiroveci (lastly called carinii) (PCC) and other infections (diarrhoea, malaria, toxoplasmosis, bacterial infections):**

The pneumopathy to pneumocytosis has a high mortality for an HIV infected child, especially during the first life year, but the risk still remains high until 24 months, often with a good immunity.

✓ **CRITERA OF INITITION:**

- Any child born of an HIV+ mother without non infection verification.
- From the age of sixth weeks or more.

IN CONCLUSION:
Any baby born of HIV+ mother whose diagnosis is not formally excluded (status- or PCR-) has to take TMP-SMX (Timetoprim+ Sulfamethoxazole) = cotromoxazole= Bactrim® = Eusaprim® for25/5 mg/kg 1x/day.

✓ **An HIV infected child :**

- Whatever the clinical stage or CD4 percentage for every infected child until 5 years.
- - > 5 years with CD4 < 350/mm3

Daily recommended dosing based on child weight:

Weight in kg	Dose	3-3,9 kg	4-4,9 kg	5-5,9 kg	6-6,9 kg	7-7,9 kg	8-8,9kg	9-9,9 kg	10 kg
Bactrim® syrup 200 mg/40 mg/5ml	25/5 mg/kg once a day	2 ml	2,5 ml	3 ml	4 ml	4,5 ml	5 ml	5,5 ml	6 ml
Bactrim® tab	25/5 mg/kg once a day	/	1 tab 100/20 mg	1 tab 100/20 mg	1,5 tab 100/20 mg	1,5 tab 100/20 mg	1/2 tab 400/80 mg	1/2 tab 400/80 mg	1/2 tab 400/80 mg

Kg/ child	Dose	10-11 kg	12-14kg	15-16 kg	17-19 kg	20 - 24kg	25-29 kg	30-34 kg	35-39 kg	40 kg
Bactrim® tab	25/5 mg/kg 1X/day	½ tab 400/80 mg	1 tab 400/80 mg	1tab 400/80 mg	1 tab 400/80 mg	1 tab 400/80 mg	1 ½ tab 400/80 mg	1 tab 800/160 mg	1 tab 800/160 mg	1 tab 800/160 mg

Tuberculosis Prophylaxis.

In Rwanda the INH's prophylaxis is controversial for old people but not for a young baby. The IHN prophylaxis for 5mg/kg within 6 months remains the recommendation of the national programme for children < 5 years living with tuberculosis patient. It is necessary to exclude active tuberculosis diagnosis before initiating the prophylaxis (Rx thorax, gastric probing or expectorations, IDR, Crofton's score.)

What to do before putting any HIV child infected under ARV treatment:

- Prophylaxis with SMX/TPM
- Actively check suggestive symptoms of tuberculosis and if possible carry out thorax Rx (scheduled in the basic plan) immediately before prescribing ARV. Tuberculosis may easily be unobservable and the child may easily be contaminated (close contact with its surroundings).
- Nutritional supplement.
- Vitamin A: 50,000 UI between 0-6 months- 100,000 UI between 6-12 months and 200,000 UI after 1 year every 6 months.
- To assure if the child has followed the vaccination plan. Encourage supplementary vaccination: pneumococcus, meningococcal infection, salmonella typhi.
- Systematically think about anti-helminth for any child under nutritional treatment (mebendazole 100 mg 2 x day for 3 days) 1x year.

When and how t0 initiate child treatment:

- If the PCR is available, start ARV if :
  - 3rd and 4th clinical stages whatever the rates of CD4.
  - 1st and 2nd stage according t0the CD4 count.

N.B : For children aged 5 years the same criteria of old people are followed when initiating ARV treatment (stage 4 whatever CD4 count, stages 1,2,3 if CD4 < 350°.

Immunological indicator	Specific Recommendation about the age of initiating ARV.		
	< or = 11 months	12 -35 months	36 - 59 months
% CD 4	< 25 %	< 20 %	< 15%
CD 4 (absolute figure)	< 1500 cells/mm^3	< 750 cells/mm^3	< 350 cells/mm^3

The first line recommended ARV regimen:

The same for babies having received a prophylaxis with nevirapine

2 NRTI + 1 NNRTI: D4T + 3TC + NVP and AZT + 3TC+ NVP (si Hb > 8)

From 12 kgs, it is recommended to prescribe tablets and avoid syrups (cost and difficulties to conform to treatment): < 12 Kg: AZT + 3TC + NVP in syrup.

If under Anti-tuberculosis drugs:

If < 8kg: AZT or DT+ 3 TC +ABC or NVP X 130%. The NVP dose will double in case of association with rifampicine. It is imperative to closely monitor hepatic function of the patient: GPT to 1, 3, and 6 months, those children.
If > 8kg 2NRTI +EFV. Remember that effavirenz has a reduced blood rate to 20% during the enzymatic stimulation of the cytochrom P450 by the rifampicine.

It's preferable to wait till the end of the intensive phase of tuberculosis treatment before you start ARV treatment. If ARV treatment is urgent (stage 4 where CD4 % < 15%, ARV treatment will start 15 days after the beginning of anti TB treatment (if this is well tolerated.

Initial balance and clinico-biological monitoring of a child under the 1st degree ARV child.

The same monitoring as in the adult. (PART B CHAPITER 3) surveillance of the child growth.

Date	Clinic	Laboratory
Pre-ARV	+	CD4, NFS, RX thorax systematic lf possible
J 15	+ compliance	
M 1	+ compliance	NFS if AZT, GPT if NVP
M 2	+ compliance	nothing
M 3	+ compliance	NFS if AZT, GPT if NVP
M 4	+ compliance	nothing
M 5	+ compliance	nothing
M 6	+ compliance	CD4, NFS, GPT immediately
Beyond 6 months		
Every 6 months	+ compliance	CD4: every 6 months. Some tests will be guided by clinical data.

A weight and height curve must be recorded on the child file. New WHO international height and weight curves for children under years will be used. For children> 5 years, CDC curves must be used (WHO are unpublished curves beyond 5 years).

Psychomotor evolution is also an important element to monitor.

Major stages of psychomotor development for a child aged from 1 month to1year.

1 month	2 months	3 months	4-5 months	6 months	8-9 months	1 year
- staring in the face - Ocular following of the face - Broad smile.	- Response smile. - Turns the head for a while - Scanning objects and materials with the eye	- Keeps the head in one position when seated - Head upright when spinal cord in ventral decubitus	- Voluntary pretension - Head in sitting position. - All the lower limbs upright.	- Keeps seated with support	- Seats without support - Stands up with support - Starts crawling or walking on a seat (“Shuffle’’) - Sucks of index thumb. - Disyllabism	- Walks alone (N =12 -18 months) - Holds and releases objects when asked. - Utters a few words

When and how to change the regime of treatment.

Toxicity.

The change of the treatment in case of toxicity:

If neuropathy severe with D4T: AZT + 3TC + 1 INNRT
If anaemia (Hb < 9gr/dl): D4T + 3TC + 1 INNRT
If hepatoxicity or severe skin allergy: see (PART B CHAPITER 4)

Therapeutic failure:

Definitions:

Clinical failure :	- Lack of clinical improvement (weight and height stagnation and /or psychomotor after 6 months of ARV treatment. - Appearance of new opportunistic infection or malignant affection that shows the progress of a clinical disease. Recurrence of previous opportunistic infection. Progression towards the pathology defining stages 3, 4 of WHO. - Recurrence of tuberculosis (TB) may not indicate HIV disease progression for a re-infection may occur. - If the patient is suffering from an asymptomatic disease, therapeutic failure is defined by the criterion of the CD4 count only.
Immunological failure	- The return of CD4 to the basic pre-therapeutic level or below this level without any concomitant infection, which should be the cause of the decrease of the CD 4 - Exfoliation of more than 50% of CD4 below the maximum value, without any concomitant infection which should be the cause of CD4 transitory decrease.
Viral failure	The Viral load always detectable at 6 months of treatment in a patient with good compliance. The 2nd degree regime recommended. DDI+Abacavir+ 1 IP (LPV/r).

Paediatric ARV and major side effects.

INRT:

ARV Molecule	Dosing	Major side effects
Zidovudine (AZT)	200 mg/m2 eithert~8 mg/kg (0,8 ml/kg) X 2/J	Verify anaemia
Stavudine (D4T)	1 mg/kg (1ml/kg) X2	Neuropathy (more rare for adults)
Lamivudine (3T)	4 mg/kg (0,4 ml/kg) X2/J	
Abacavir (ABC)	8 mg/kg (0,4 ml/kg) X2 /J	Allergy rare but grave
Didanosine (DDI)	180 mg/m2 either ~ 8 mg/kg 1 X/ day for young (½ h before eating or 2 h after)	Rare pancreatitis

INNRT:

ARV Molecule	Dosing	
Nevirapine (NVP)	5 mg /kg (or 0,5 ml/kg) X 1/day during 15 J ; then 200 mg/m2 either ~ 8-10 mg/kg X2/day (or 0,8 at 1 ml/kg)	Rash, hepatitis
Efavirenz (EFV)	For children of height > 10 kg only 1X/day with dosage according to height.	Nightmare, vertigo especially the 15 days (occurring at beginning evening of the 1st month).
	10-15 kg: 200 mg	
	15-20 kg: 250 mg	
	20-25 kg: 300 mg	
	25-30 kg: 350 mg	
	30-40 kg: 400 mg	
	35-40 kg: 450 mg	
	>40 kg: 600 mg	

PI:

ARV Molecule	Dosage	
Lopinavir/R (LPV/r)	230 / 57,5 mg / m2 or ~10mg of lopi/kg 2 X/day	Digestive troubles
Nelfinavir (NFV)	55 mg/kg X2 (tablets of 250 mg to break)	Diarrhoea
Indinavir/R (IDV/r)	Indinavir 400 +Ritonavir 100 X 2 /day for children > 25 kg	

Galenic and ARV non simplified paediatric dosage

Generic noun	Available Forms	Dosage
AZT	Syrup 1 ml = 10 mg capsules 100 mg	Premature < 36s 1.5 mg / Kg x 2 N born : < 3 months : 2 mg / Kg x 4 or IV 1.5 mg x 4 New born : > moths : 5 mg / Kg x 4 children : 5 - 8 mg x 2
D4T	Syrup : 1 ml = 1 mg	New born: Evaluation ACTG 332 child (< 30 kg) : 1 mg / kg x 2 teenagers and adults: < 60 kg : 30 mg x 2 > 60 kg : 40 mg x 2
3TC	Solution : 1 ml = 10 mg	N born < 1 months : 2 mg / kg x 2 child: 4 mg / kg x 2 teenagers : < 50 kg : 2 mg / kg x 2 Possibility: 1 taking of 300 mg /j
DDI	tablets : 100, 150 et 200 mg gastro-resistant capsules : Vindex EC : 125, 200, 250 et 400 mg Powder for paediatric solution 10 mg / ml WITHOUT FOOD +++	New born< 3 months 50 mg / m2 x 2 child : 200 mg / m2 x 1 Adolescents < 60 kg : 125 mg x 2 or 250 mg x 1 / j
Abacavir	Oral Solution 20 mg/ml Cp 300 mg	< 3 months limited data 3 months – 12 years 8 mg/kg x 2 > 12 years 300 mg x 2/j
Efavirenz	Oral solution 30 mg/ml (?) capsules 50,100 and 200 mg	Do not give it to children < 10 kg child: 10 – 15 kg : 200 mg x 1 15 – 20 kg : 250 mg x 1 20 – 25 kg : 300 mg x 1 25 – 32.5 kg : 350 mg x 1 32.5 – 40 kg : 400 mg x 1 > 40 kg : 600 mg x 1 Teenagers and adults : 600 mg x 1 AT EVENING +++
Nevirapine	Syrup : 1 ml = 10 mg	New Born < 2 months : 14 days 5 mg / kg or 120 mg / m2 x 1 14 days: 5 mg / kg or 120 mg / m2 x 2 Then: 200 mg / m2 x 2 child: 2 months to< 8 years : 14 days : 7 mg / kg x 1 Then : 7 mg / kg x 2 > 8 years :

		14 days 4 mg / kg x 1 Then: 4 mg / kg x 2 Teenagers and adults : 14 days: 200 mg x 1 Then : 200 mg x 2
Lopinavir / ritonavir	Oral solution 80 mg + 20 mg / ml Pipette of 5 ml	< 2 years limited data > 2 years (230 + 57.5) mg/m2 x 2/j If associated with EFV or NVP : (300 + 75) mg/m2 x 2/j
Nelfinavir	Tablets 250 mg When eating	New Born 40 mg / kg x 3 or 55 mg / kg x 2 < 2 years : 75 mg / kg x 2 2 - 3 years : 50 mg / kg x 2 3 -13 years : 45 mg / kg x 2 > 13 years and adults : 1250 mg x 2

Simplified paediatric dosages based on kg.

Dosage for children of 3 -10 kg (formulation of syrup)

weight in kg	**Dose**	**3 kg**	**4 kg**	**5 Kg**	**6 kg**	**7 kg**	**8 kg**	**9 kg**	**10 kg**	**12 kg**
T in cm		50 cm	57 cm	63 cm	63 cm	68 cm	72 cm	77 cm	81 cm	92
SC in m2		0,2 m2	0,25 m2	0,3 m2	0,32 m2	0,36 m2	0,4 m2	0,44 m2	0,5 m2	0,55 m2
Age for P and T to Perc 5		0-1 mois	~ 3 m	~4 m	~6 m	~9 m	~12 m	~18 m	~24 m	~36 m
AZT = Retrovir® syrup 10mg/ml	8 mg/kg or 180-300 mg/m2 2X/day	4 ml	5 ml	6 ml	6,5 ml	7 ml	8 ml	9 ml	10 ml	11 ml

Weight in kg	**Dose**	**3 kg**	**4 kg**	**5 kg**	**6 kg**	**7 kg**	**8 kg**	**9 kg**	**10 kg**	**12 kg**
3 TC = Epivir® = Lamivir Syrup 10 mg/ml	4 mg/kg 2X/day	1,2 ml	1,6 ml	2 ml	2,5 ml	3 ml	3,2 ml	3,5 ml	4 ml	5 ml
D4T =Zerit® syrup 1mg/1ml = Stavudine	1 mg/kg 2X/day Max : 40mg 2Xday (>40kg)	3 ml	4 ml	5 ml	6 ml	7 ml	8 ml	9 ml	10 ml	12 ml
DDI= Videx® syrup 10 mg/ml	180-220 mg/m2 1X/day A jeun	3,6 ml	4,5 ml	5,4 ml	6 ml	6,5 ml	7,2 ml	8 ml	9 ml	11 ml
Abacavir = Ziagen® syrup 20 mg/ml	8 mg/kg 2X/day max 300mg 2X/day	1,2 ml	1,6 ml	2 ml	2,4 ml	2,8 ml	3,2 ml	3,6 ml	4 ml	5 ml

Wight en kg	**Dose**	**3 kg**	**4 kg**	**5 kg**	**6 kg**	**7 kg**	**8 kg**	**9 kg**	**10 kg**	**12 kg**

Efavirenz = Sustiva = Stocrin® 30 mg/ml	Max : 600mg 1 X/day	/	/	/	/	/	/	/	9 ml	9 ml 1 X/day
NVP = nevirapine = Viramune® 10 mg/ml	5 mg 1 X/day during 15days then 2 X/day	4 ml	5 ml	6 ml	6,5 ml	7 ml	8 ml	9 ml	10 ml	10 ml 2 X/day
Lopinavir + Ritonavir = Kaletra® Syrup 80/20mg/ml	230/ 57,5mg/m² 2X/day	0,6 ml 2X /day	0,7 ml 2X /day	0,9 ml 2X /day	0,9 ml 2X /day	1ml 2X /day	1,2 ml 2X /day	1,3 ml 2X /day	1,5ml 2X/day	1,6 ml 2 X/day
Nelfinavir = Viracept® co of 250mg	55mg/Kg 2X/day	1 tab 2X /day	1 tab 2X day	1 tab 2X /day	1,5 tab 2X /day	1,5 tab 2X /day	2 tab 2X /day	2 tab 2X /day	2 tab 2X/day	3 tab 2 X/day
Bactrim® SMX/TMP 200mg/40mg/5ml Syrup	25/ 5 mg/ kg 1X/day	2 ml	2,5 ml or1 co 100/20 mg	3 ml or 1co 100/20 mg	4 ml or1 ,5 tab 100/20	4,5 ml or 1,5 tab 100/20	5 ml or 1 tab 400/80 mg	5,5 ml or1 tab 400/80 mg	6 ml or 1 tab40 0/80 mg	7,5 ml or 1,5 tab40 0/80

Dosage for children weighing - 40 kg (tablet formulation)

child Kg (5th perc)	**Dose mg/kg or mg/m2 2X/days**	**10 kg**	**12 kg**	**15 kg**	**17 kg**	**20 kg**	**25 kg**	**30 kg**	**35 kg**	**40 kg**
Age with P and T 5th perc)		~ 2 a	~ 3 years	~5 years	~7 years	~ 8-9 years	~10-11 years	~12 years	~14 years	~15 years
T cm-5thperc		87 cm	92 cm	104 cm	112 cm	120 cm	130 cm	140 cm	147 cm	150 cm
SC (m2)		0,5 m2	0,55 m2	0,66 m2	0,72 m2	0,82 m2	0,9 m2	1,1 m2	1,2 m2	1,3 m2
Kg child	Dose	10 kg	12 kg	15 kg	17 kg	20 kg	25 kg	30 kg	35 kg	40 kg
AZT 300= Zidovudine = Retrovir®	8 mg/kg 180-300 mg/m2 2X/day	/	/	½tab 2X/day	½ tab 2X/day	½ tab 2X/day	/	/	1 tab 2X/day	1tab 2X/day

AZT 100= Zidovudine = Retrovir®	Max 300mg 2X/day	1 tab 2X/day	1 tab 2X /day	/	/	/	2 tab 2X/day	2tab 2X/day	/	/
3 TC= Lamivudine = Lamivir =Avolam = Epivir® 150 mg	4 mg/kg 2X/day	/	/	½ tab 2X/day	½tab 2X/day	½tab 2X/day	¾tab 2X/day	¾ tab 2X/day	1 tab 2X/day	1tab 2X/day

child Kg	**Dose**	**10 kg**	**12 kg**	**15 kg**	**17 kg**	**20 kg**	**25 kg**	**30 kg**	**35 kg**	**40 kg**
D4T 30 = Stavudine = Zerit ®30	1 mg/kg 2X/day max 30mg 2X/day if <60Kg	/	½ cap (dilute in 4 ml and give 2 ml) 2X/day	½ cap 2X/day	½ cap 2X/day	/	/	1 cap 2Xday	1 cap 2X/day	1 cap 2X/day
Kg child	Dose	10 kg	12 kg	15 kg	17 kg	20 kg	25 kg	30 kg	35 kg	40 kg
DDI Didanosine= Videx®	180-220 mg/m2 1X/day A jeun.	100mg 1X/day	100mg 1X/day	150mg 1X/day	150mg 1X/day	150mg 1X/day	200mg 1X/day	200mg 1X/day	250mg 1X	250mg 1X

	Max 400mg1X/ day								/day	/day
ABC 300 Abacavir = Ziagen®	8 mg/kg 2X/day max 300 mg 2 X/J day	/	/	½ tab 2X/Jday	½ tab2X /day	½ tab 2X/day	¾ tab2X /day	1 tab 2X/taby	1 tab 2X /day	1 tab 2X /day
AZT 300 mg + 3T150 mg = Combivir® =Avocomb = Duovir	Max 1 tab 2X/day	/	/	½ tab 2X/day	½tab 2X/day	½ tab 2X/day	¾tab 2X/day	¾ tab 2X/day	1 tab 2X /day	1 tab 2X /day

Dosage for children weighing between 10 - 40 kg (tablet formulation)

Kg child	**Dose**	**10 kg**	**12 kg**	**15 kg**	**17 kg**	**20 kg**	**25 kg**	**30 kg**	**35 kg**	**40 kg**
3 TC 150 mg + D4T 40 mg = Coviro 40		/	/	/	/	½ cap 2X/day	¾cap 2X/day	/	/	/
Efavirenz 50- 200-600 = Stocrin® = Sustiva®	~15 mg/kg	200 mg	200 mg	250 mg	250 mg	300 mg	350 mg	350 mg	400 mg	600 mg
Nevirapine =Viramune® 200 mg	5 mg/m2 1X/day for 15days then 200 mg/m2 2X/day	/	½ tab	½ tab	¾ tab	¾ tab	¾ tab	1tab	1tab	1tab
Child Kg		10 kg	12 kg	15 kg	17 kg	20 kg	25 kg	30 kg	35 kg	40 kg
3TC 150 mg + NVP 200 mg+ D4T 30 mg = Triviro 30 =Triomune		/	½ cap 2X/day	½cap + ¼ gel de NVP 2X/day*	½capl + ¼ NVP tab 2X/d	/	/	1 cap 2X/d	1 cap 2X/d	1 cap 2X/d
3TC 150 mg + NVP 200 mg+ D4T 40 mg = Triviro 40 =Triomune		/	/	/	/	½ cap + ¼ NVP tab 2X/d*	¾ cap 2X/day	/	/	/

Nevirapine is often under dosed for children in combined tablets but tablets are difficult to break with exactitude.

child Kg		**10 kg**	**12 kg**	**15 kg**	**17 kg**	**20 kg**	**25 kg**	**30 kg**	**35 kg**	**40 kg**
AZT 300 mg + 3TC 150 mg + NVP 200 mg = Duovir N		/	½ tab 2X/day	½ tab + ¼ NVP tab 2X/day*	½ tab + ¼ NVP tab 2X/day*	½ tab + ¼ NVP tab 2X/day*	¾ tab 2X/day*	¾tab + ¼ NVP tab 2X/day*	1tab 2X/day	1 tab 2X/day
Lopinavir + Ritonavir = Kaletra®= capsules unsectile and bitter syrup	230mg/ 57,5mg/ m² 2X/day	1 capl (= 1,5ml) 2X/day	1 cap (=1,6 ml) 2X/day	2 cap (= 3ml) 2X day	2 cap (=3,2ml) 2X/day	2 cap (=3,5ml) 2X/day	2 cap (=3,5 ml) 2X/day	2 cap (= 4 ml) 2X/day	2cap (=4,5 ml) 2X/day	3 cap (= 5ml) 2X/day
Nelfinavir = Viracept®	55mg/Kg 2X/day	2,5 tab2X/day	3 tab 2X/day	3 tab 2X/day	4 tab 2X/day	4 tab 2X/day	5 tab2X/day	5 tab2X/day	5 tab 2X/day	5 tab 2X/day
SMX-TMP	25/5	½ tab	1 tab	1tab	1 tab	1 tab	1 ½	1 tab	1 tab	1

Bactrim®	mg/kg 1X/day	480 mg	480 mg	480 mg	480 mg	480 mg	tab 480 mg	960 mg	960 mg	tab 960 mg

NB:

For the only non dryable capsules are those of Kaletra (enveloped capsules); it is preferable, if the child cannot swallow these big capsules, to prescribe the syrup which is unfortunately bitter.

Concerning other forms of treatment, it's advised from 12 kg to prescribe tablets (to be broken according to the recommendations above) since it is simpler for all than to be obliged to carry large quantities of syrup wherever one goes.

Recommended dosage in WHO guidelines per molecule:

Lamivudine: Recommended dosing based on weight bands				
Weight range (kg)		Formulation	Dose (ml, tablets)	
Bottom	Top	Target dose 4 mg/kg/dose twice daily to a maximum 150mg/dose twice daily	a.m.	p.m.
5	5.9	10 mg/ml solution	3 ml	3 ml
6	6.9	10 mg/ml solution	3 ml	3 ml
7	7.9	10 mg/ml solution	4 ml	4 ml
8	8.9	10 mg/ml solution	4 ml	4 ml
9	9.9	10 mg/ml solution	4 ml	4 ml
10	10.9	10 mg/ml solution	5 ml	5 ml
11	11.9	10 mg/ml solution	5 ml	5 ml
12	13.9	10 mg/ml solution	6 ml	6 ml
		or 150 mg tablets	0.5	0.5
14	16.9	150 mg tablets	0.5	0.5
17	19.9	150 mg tablets	0.5	0.5
20	24.9	150 mg tablets	1	0.5
25	29.9	150 mg tablets	1	1
30	34.9	150 mg tablets	1	1

Stavudine: Recommended dosing based on weight bands				
Weight range (kg)		Formulation	Dose (ml or capsules)	
Bottom	Top	Target dose 1 mg/kg /dose twice daily up to 30 mg/dose twice daily	p.m.	p.m.
5	5.9	1 mg/ml syrup	6 ml	6 ml
6	6.9	20 mg capsules	0.5	0.5
		or 1 mg/ml syrup	7 ml	7 ml
7	7.9	20 mg capsules	0.5	0.5
		or 1 mg/ml syrup	8 ml	8 ml
8	8.9	20 mg capsules	0.5	0.5
		or 1 mg/ml syrup	9 ml	9 ml
9	9.9	20 mg capsules	0.5	0.5
		or 1 mg/ml syrup	10 ml	10 ml
10	10.9	15 mg capsules	1	1
11	11.9	15 mg capsules	1	1
12	13.9	15 mg capsules	1	1
14	16.9	20 mg capsules	1	1
17	19.9	20 mg capsules	1	1
20	24.9	20 mg capsules	1	1
25	29.9	30 mg capsules	1	1
30	34.9	30 mg capsules	1	1

'Stavudine 20 mg capsule can be dissolved in a measured quantity of water and half the quantity administered to provide dose shown in table'

Zidovudine: Recommended dosing based on weight bands; Range of tablets, capsules and syrup available				
Weight range (kg)		Target dose 180–240mg/m^2/dose twice daily	Dose (ml or capsules or tablets)	
Bottom	Top	Formulation	a.m.	p.m.
5	5.9	10 mg/ml syrup	6 ml	6 ml
6	6.9	10 mg/ml syrup	7 ml	7 ml
7	7.9	10 mg/ml syrup	8 ml	8 ml
8	8.9	10 mg/ml syrup	9 ml	9 ml
		or 100 mg capsules	1	1
9	9.9	10 mg/ml syrup	10 ml	10 ml
		or 100 mg capsules	1	1
10	10.9	10 mg/ml syrup	10 ml	10 ml
		or 100 mg capsules	1	1
11	11.9	10 mg/ml syrup	10 ml	10 ml
		or 100 mg capsules	1	1
12	13.9	10 mg/ml syrup	11 ml	11 ml
		or 100 mg capsules	1	1
14	16.9	100 mg capsules	2	1
		or 300 mg tablets	0.5	0.5
17	19.9	100 mg capsules	2	1
		or 300 mg tablets	0.5	0.5
20	24.9	100 mg capsules	2	2
		or 300 mg tablets	0.5	0.5
25	29.9	100 mg capsules	2	2
		or 300 mg tablets	1	0.5
30	34.9	100 mg capsules	3	3
		or 300 mg tablets	1	1

Zidovudine: recommended dosing based on weight bands; 100-mg capsules and syrup available					
Weight range (kg)		Target dose 180–240mg/m^2/dose twice daily		Dose (ml or capsules)	
Bottom	Top	Formulation		a.m.	p.m.
5	5.9	10 mg/ml syrup		6 ml	6 ml
6	6.9	10 mg/ml syrup		7 ml	7 ml
7	7.9	10 mg/ml syrup		8 ml	8 ml
8	8.9	10 mg/ml syrup		9 ml	9 ml
		or	100 mg capsules	1	1
9	9.9	10 mg/ml syrup		10 ml	10 ml
		or	100 mg capsules	1	1
10	10.9	10 mg/ml syrup		10 ml	10 ml
		or	100 mg capsules	1	1
11	11.9	10 mg/ml syrup		10 ml	10 ml
		or	100 mg capsules	1	1
12	13.9	100 mg capsules		1	1
14	16.9	100 mg capsules		2	1
17	19.9	100 mg capsules		2	1
20	24.9	100 mg capsules		2	2
25	29.9	100 mg capsules		2	2
30	34.9	100 mg capsules		3	3

Zidovudine: Recommended dosing based on weight bands; 300-mg tablets and syrup available				
Weight range (kg)		Target dose 180–240mg/m^2/dose twice daily	Dose (ml or tablets)	
Bottom	Top	Formulation	a.m.	p.m.
5	5.9	10 mg/ml syrup	6 ml	6 ml
6	6.9	10 mg/ml syrup	7 ml	7 ml
7	7.9	10 mg/ml syrup	8 ml	8 ml
8	8.9	10 mg/ml syrup	9 ml	9 ml
9	9.9	10 mg/ml syrup	10 ml	10 ml
10	10.9	10 mg/ml syrup	10 ml	10 ml
11	11.9	10 mg/ml syrup	10 ml	10 ml
12	13.9	10 mg/ml syrup	11 ml	11 ml
14	16.9	300 mg tablets	0.5	0.5
17	19.9	300 mg tablets	0.5	0.5
20	24.9	300 mg tablets	0.5	0.5
25	29.9	300 mg tablets	1	0.5
30	34.9	300 mg tablets	1	1

Abacavir: Recommended dosing based on weight bands					
Weight range (kg)		Target dosing <16 years or <37.5 kg: 8 mg/kg/dose given twice daily Maximum dose >16 years or ≥37.5 kg: 300 mg/dose given twice daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	a.m.
5	5.9	20 mg/ml syrup		2 ml	2 ml
6	6.9	20 mg/ml syrup		3 ml	3 ml
7	7.9	20 mg/ml syrup		4 ml	4 ml
8	8.9	20 mg/ml syrup		4 ml	4 ml
9	9.9	20 mg/ml syrup		4 ml	4 ml
10	10.9	20 mg/ml syrup		5 ml	5 ml
11	11.9	20 mg/ml syrup		5 ml	5 ml
		or	300 mg tablet	0.5	0.5
12	13.9	20 mg/ml syrup		6 ml	6 ml
		or	300 mg tablet	0.5	0.5
14	16.9	300 mg tablet		0.5	0.5
17	19.9	300 mg tablet		0.5	0.5
20	24.9	300 mg tablet		1	0.5
25	29.9	300 mg tablet		1	1
30	34.9	300 mg tablet		1	1

Didanosine: Recommended dosing based on weight bands Once-daily EC capsules			
Weight range (kg)		Target dose Maximum dose: >13 years or >60 kg: 400 mg once daily	Dose (capsules)
Bottom	Top	Formulation	a.m. or p.m.
10	10.9	125 mg EC capsule	1
11	11.9	125 mg EC capsule	1
12	13.9	125 mg EC capsule	1
14	16.9	200 mg EC capsule	1
17	19.9	200 mg EC capsule	1
20	24.9	250 mg EC capsule	1
25	29.9	250 mg EC capsule	1
30	34.9	250 mg EC capsule	1

Didanosine: Recommended twice-daily dosing based on weight bands					
Weight range (kg)		Target dosing <3 months: 50 mg/m^2/dose twice daily 3 months to <13 years: 90–120 mg/m^2/dose twice daily Maximum dose: ≥13 years or >60 kg: 200 mg/dose twice daily or 400 mg once daily		Dose (ml or tablets)	
Bottom	Top	Formulation		a.m.	p.m.
5	5.9	10 mg/ml suspension		4 ml	4 ml
		or	25 mg chew tablet	2	2
6	6.9	10 mg/ml suspension		5 ml	5 ml
		or	25 mg chew tablet	2	2
7	7.9	10 mg/ml suspension		6 ml	6 ml
		or	25 mg chew tablet	2	2
8	8.9	10 mg/ml suspension		6 ml	6 ml
		or	25 mg chew tablet	2	2
9	9.9	10 mg/ml suspension		6 ml	6 ml
		or	25 mg chew tablet	2	2
10	10.9	10 mg/ml suspension		6 ml	6 ml
		or	25 mg chew tablet	3	2
11	11.9	10 mg/ml suspension		7 ml	7 ml
		or	25 mg chew tablet	3	3
12	13.9	10 mg/ml suspension		7 ml	7 ml
		or	25 mg chew tablet	3	3
14	16.9	10 mg/ml suspension		8 ml	8 ml
		or	25 mg chew tablet	4	3
17	19.9	10 mg/ml suspension		9 ml	9 ml
		or	25 mg chew tablet	4	4
20	24.9	25 mg chew tablet		5	5
25	29.9	25 mg chew tablet		5	5
30	34.9	25 mg chew tablet		5	5

Note: 25 mg chew tablets can be substituted with other strengths to the same mg amount but each a.m. and p.m. dose must always be made up of at least **two** tablets.

B. Efavirenz: Recommended once-daily dosing based on weight bands			
Weight range (kg)		Target dose 15 mg/kg/day (capsule/tablet) Weight >40 kg: 600 mg once daily	Dose (capsules, tablets) Once daily, 3 years and above
Bottom	Top	Formulation	
10	10.9	200 mg capsule	1
11	11.9	200 mg capsule	1
12	13.9	200 mg capsule	1
14	16.9	mg capsule	200 mg + 50 mg
17	19.9	mg capsule	200 mg + 50 mg
20	24.9	mg capsule	200 mg + 100 mg
25	29.9	mg capsule	200 mg + 100 mg + 50 mg
30	34.9	200 mg capsule	2
35	39.9	200 mg capsule	2
>40		600 tablet	1

Nevirapine: Recommended induction dosing based on weight bands				
Weight range (kg)		Target dose Half of daily maintenance dosing (160–200 mg/m^2/dose to max 200 mg.)		Dose (ml or tablets)
Bottom	Top	Formulation		Once daily
5	5.9	10 mg/ml syrup		6 ml
6	6.9	10 mg/ml syrup		7 ml
7	7.9	10 mg/ml syrup		8 ml
8	8.9	10 mg/ml syrup		9 ml
9	9.9	10 mg/ml syrup		9 ml
		or	200 mg tablets	0.5
10	10.9	10 mg/ml syrup		10 ml
		or	200 mg tablets	0.5
11	11.9	10 mg/ml syrup		10 ml
		or	200 mg tablets	0.5
12	13.9	10 mg/ml syrup		11 ml
		or	200 mg tablets	0.5
14	16.9	200 mg tablets		0.5
17	19.9	200 mg tablets		1
20	24.9	200 mg tablets		1
25	29.9	200 mg tablets		1
30	34.9	200 mg tablets		1

Nevirapine: Recommended maintenance dosing based on weight bands				
Weight range (kg)		Target dosing 160–200 mg/m^2 to max 200 mg per dose twice daily	Dose (ml or tablets)	
Bottom	Top	Formulation	a.m.	p.m.
5	5.9	10 mg/ml syrup	6 ml	6 ml
6	6.9	10 mg/ml syrup	7 ml	7 ml
7	7.9	10 mg/ml syrup	8 ml	8 ml
8	8.9	10 mg/ml syrup	9 ml	9 ml
9	9.9	10 mg/ml syrup	9 ml	9 ml
		or 200 mg tablets	0.5	0.5
10	10.9	10 mg/ml syrup	10 ml	10 ml
		or 200 mg tablets	0.5	0.5
11	11.9	10 mg/ml syrup	10 ml	10 ml
		or 200 mg tablets	0.5	0.5
12	13.9	10 mg/ml syrup	11 ml	11 ml
		or 200 mg tablets	0.5	0.5
14	16.9	200 mg tablets	1	0.5
17	19.9	200 mg tablets	1	0.5
20	24.9	200 mg tablets	1	0.5
25	29.9	200 mg tablets	1	1
30	34.9	200 mg tablets	1	1

Lopinavir/ritonavir: Recommended dosing based on weight bands						
Weight range (kg)		Target dosing See table over for lopinavir and ritonavir target doses			Dose (ml or tablets)	
Bottom	Top	Formulation			a.m.	p.m.
5	5.9		80 mg lopinavir/20 mg ritonavir per	ml solution	1 ml	1 ml
6	6.9		80 mg lopinavir/20 mg ritonavir per	ml solution	1.5 ml	1.5 ml
7	7.9		80 mg lopinavir/20 mg ritonavir per	ml solution	1.5 ml	1.5 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	1	1
8	8.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	1	1
9	9.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	1	1
10	10.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	1	1
11	11.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	1	1
12	13.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	2	1
		or	200 mg lopinavir/50 mg ritonavir per	tablet	1	1
14	16.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2 ml	2 ml
		or	133 mg lopinavir /33 mg ritonavir per	capsule	2	1
		or	200 mg lopinavir/50 mg ritonavir per	tablet	1	1
17	19.9		80 mg lopinavir/20 mg ritonavir per	ml solution	2.5 ml	2.5 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	2	1
		or	200 mg lopinavir/50 mg ritonavir per	tablet	1	1
20	24.9		80 mg lopinavir/20 mg ritonavir per	ml solution	3 ml	3 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	2	2
		or	200 mg lopinavir/50 mg ritonavir per	tablet	1	1

Weight range (kg)		Target dosing See table over for lopinavir and ritonavir target doses			Dose (ml or tablets)	
Bottom	Top	Formulation			a.m.	p.m.
25	29.9		80 mg lopinavir/20 mg ritonavir per	ml solution	3.5 ml	3.5 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	2	2
		or	200 mg lopinavir/50 mg ritonavir per	tablet	2	1
30	34.9		80 mg lopinavir/20 mg ritonavir per	ml solution	4 ml	4 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	3	3
		or	200 mg lopinavir/50 mg ritonavir per	tablet	2	2
35	39.9		80 mg lopinavir/20 mg ritonavir per	ml solution	5 ml	5 ml
		or	133 mg lopinavir/33 mg ritonavir per	capsule	3	3
		or	200 mg lopinavir/50 mg ritonavir per	tablet	2	2

Treatment of opportunistic infections and paediatric dosage.

A reminder plan of the national first degree tuberculosis treatment.

The diets are the same as those for adults

Name	Abbreviation	Daily Mean dosing (min-max)	Presentations
Rifampicine	R	10 mg/Kg (8-12)	tab 100 mg ,300mg
Isoniazide ou INH	H	5 mg/Kg (4-6)	tab 100 mg 300mg
Pyrazinamide	Z	25 mg /kg (20-30)	tab 400 mg
Ethambutol	E	15 mg /kg (15-20)	tab 400 mg
Sreptomycine	S	15 mg /kg (12-18)	1 g

Treatment plan for children < 6 years.

	Months / N doses	Medication	Administration	Dosage based on weight					
				5-7 kg	8-9 kg	10-14 kg	15-19 kg	20-24 kg	25-37 kg
Intensive phase	2 months 56 doses	(R60h30z 150)	every day	1 tab	1½tab	2 tab	3 tab	4 tab	5 tab
Ongoing phase	4 months 48 doses	(R150h150)	3 times a week	½ tab	½ tab	¾ tab	1 tab	1½ tab	2 tab

Wait for 15 days before initiating ARV, verify hepatic tests

Pneumocystis Jiroveci's pneumopathy (previously called Carinii)

- Symptoms: respiratory distress, especially for the young baby.
- Diagnosis: clinical and Rx thorax (in frosted lens aspect).
- Treatment: TMP-SMPX25/100 per kg /day for 4 days, for 21 days + corticotherapy in the first days (predinosolone 2mm/kg/day; oxygen if possible, feeding by catheter).

Oesophageal Candida

- Fluconazole : 12mg/Kg the 1st day, then 6mg/kg/day or 21 days
- or
- Ketoconazole : 3mg/Kg/day for 7 days
- Nystatine 100 000 UI/ml : 2,5ml X 5/day for 7 days
- Nutrition-feeding
- Analgesia: Paracetamol: 20mg/Kg X 3 (+ morphine 0,1mg/Kg X 8 SN).

Fever of unknown origin.

Ignoring meningitis, pneumonia and bacterial septicaemia: Haemophilic Influenza, Pneumococcus, Salmonellosis, Neisseria meningitis.
If treatment IV: high-dose penicillin=500000UI/Kg/day in 6X + Chloramphenicol PO or Ampicilline + Gentamycine.

Or Cephalosporin 3rd generation.

Pyodermitis, furunculosis:

Local disinfection + AB (Oxacilline IV: 100mg/Kg/day or Erythromycin PO: 50mg/Kg/day or Cloxacilline PO 50mg/Kg/day).

Contagious Molluscum:

Full resection as soon as possible (with curettes)
Reduce child's pain with encephalopathy.

- Valium (diazepam) : 0,1mg/Kg/4H
- Antalgiques : Paracétamol : 15mg/Kg/6H +/- Morphine : 0,1mg/Kg/4H PO, IV, SC, IM
- Mobilisation: physiotherapy.

Cryptococcus:

- Meningitis septicaemia, pleurisy
- Staining by Indian ink + Ag
- Amphotericine B: 0,8mg/Kg/day – 15 days or Fluco 12mg/Kg (max: 800mg/day, then Fluconazole: 8mg/Kg/day (max: 400mg/day) during 60 days.
- Prophylaxis: Fluco 4mg/Kg/d (max: 200mg/d).

Toxoplasmosis

- Neurological asymmetry.
- Pyrimethamine : 1 mg/Kg/day (max : 75 mg/day)
- Sulfadiazine : 85 mg/Kg/J en 2X (max : 2 gr/2X/j)
- Folic acid: 10 mg/Kg/day (max : 25 mg/day)
- Treatment from 3 - 6 weeks
- Cortico-therapy if pain of HTIC
- In case of lack of Sulfadiazine/Pyr: Bactrim 80 mg/20 mg/Kg/day for 1 month.
- Dosage Ac Toxo.

Isosporosis:

- Bactrim: 80 mg/20 mg/Kg/day for 3 weeks.

Herpes zoster:

- Analgesic : Paracetamol +/- codeine + ibuprofen
- Eosin
- Acyclovir: 800 mg 5X/day for 7 days.

Herpes simplex: 200 mg 5X/day for 5 days.
- (1/2 dose if < 2 years).

Compliance of a Child :

In children, like in adults, the success of antiretroviral treatment requires before everything else, good compliance.
The success of compliance depends on level of the implementation of the following 3 key compliance principles by the patient or his/her "guardian".

- The knowledge: To possess all the knowledge required and full understanding of these skills in order to take the treatment in the appropriate manner.
- The will: To have the will and commitment to take medicines.
- The capacity: To have the capacity to realize what is required.

Specificities of Compliance in Children.

Before a certain age, which varies from a child to another, the success of antiretroviral treatment child's compliance utterly depends on its guardian. This can be one or two of its biologic parents but in case of death or abandonment, a relay person (sponsor): close relative, guardian, foster family or institution.

It is this relay person that must be convinced of the necessity for compliance. That's why, it's necessary to work hand in hand with him/her on the following 3 key principles described above:

- **The knowledge**: concerns especially the guardian who must have received adequate answers to all questions he asks himself/herself about the treatment.
- **The will : This principle in this particular case will have two levels:**

- The level of the guardian: He/she must scrupulously respect instructions on the treatment of the child. This means he/she has accepted all its constraints.
- T the level of the child: his/her will is shown by his/her willingness to take his/her treatment. This compromises the galenic form which must be adapted (liquid), taste (the child often refuses or accepts according to taste) the times and units of taking the treatment (many times and unity larger units are often refused by the child).

▪ **The capacity:** It's necessary, in collaboration with the guardian, to prepare all material conditions for the success of treatment. His/her availability in comparison with time-tables (which must respect the rhythm of the child's vigilance/ sleeping of a child), his/her relationship with the child (the child accepts some things from certain persons only), the possibility of respect, if possible confidentiality (the remaining part of the family must not kwon the child is concerned.

In an older child.

It is appropriate to be attentive if the child has to be properly accustomed. This is carried out into two stages from the previous phase:

- The time during which the guardian wants progressively to accustom the child
- The time during which the child takes its treatment alone, under the supervision of the guardian.

The capacity of the child to accustom itself differs considerably from child to child.
For some, this may start from 5 years while for others they will wait for a more advanced age to attempt it.

Here again, the 3 key principles of compliance must be considered:

✓ **The knowledge**: Little by little, the child will wonder about the reasons of its treatment. It's necessary to detect this query from the child which does not express itself by direct questions. It is, in most cases, the signs indicated by the child (through its behaviour, drawings and words…) which reveal it. It is also fundamental that the answers to these questions be adapted to the child's age.

They must use the vector he/she prefers: history, drawings, images…This questioning about treatment always leads to the nature of the disease and then after to its origin. It's the most difficult problem of the announcement of the diagnosis that must be done as soon as possible but must be conditioned by the existence of the query of the child. Pay attention, during these phases we must be sure that we are understood by the child and therefore use proper tools adapted to his/her age.

✓ **The will**: It is necessary that the child accepts the reality of his/her treatment. Pay attention: a child often forgets when he/she is busy. For taking medicines, it is necessary to create landmarks in relation to his/her compulsory activities in his/her daily life: for i.e. tooth brushing, breakfast. Never stop surveillance even when the child is taking his treatment alone.

✓ **The capacity: T**he landmarks defined for a young child concerning medicine remain identical, the new problems will occur when the child is obliged to adapt his/her treatment to the rhythm of her/his new life He/she must never take his/her medicines at school. In most cases, the school may not know he/she is ill (which is not necessary).

Working as a team: The basis of good compliance.

Compliance is the major element in the general treatment and requires support and participation of every caregiver. Any intervention must not be isolated but integrated in synergy and complementarity with others.

Caregivers must adapt their interventions the area of children:

- The Doctor: must have paediatric knowledge and if possible practice in children treatment.
- The same for all health caregivers: nurses, health assistants,…
- Appropriate psychological support is necessary and that is why in this regards, one or more persons must be trained.
- The person in charge of the pharmacy must be sure that all paediatric forms of drugs are available and participate to counselling (for guardian and the child) when dispensing medicine.
- Social workers should be careful and be sure that families have minimum requirements for treatment of their children, i.e.: to enable them come for consultation or the ability to pay consultation fees, if necessary.
- Community support is essential for the families where these children live are often made more vulnerable by the disease and financially weak because of the consequences of disease. The existence of support persons or sponsors is therefore crucial.
- All caregivers must have appropriate tools adapted to children in their different areas of intervention.
- Conclusion: Good compliance is the result of team work where all caregivers work in complementarily to create the essential physical, psychological and material conditions for a child and guardian, which conditions are indispensable for the success of treatment.
- Tools for the analysis of the infection adapted to age utilized in many countries worldwide and designed at CUH St Peter in 1999 (story, images, comic strips) available in Rwanda and currently used by TRAC while waiting for specific adaptation (ESTHER project- lux Development).

Evaluation of Sate of immunity of the child:

Therapeutic indications are based on clinical test data (with WHO criteria evaluation) and on the importance of immunity deficiency evaluated by the CD4 count.

In fact, before the age of 6 years the child's blood formula undergoes important physiological changes to move from leukocyte's predominance formula at birth towards poly-nuclear predominance formula reached at the age of 6 years.

In a non-HIV child, the CD4 rate always presents more than 25% of the total rates of lymphocytes. If these are physiologically elevated to 6000 at birth, the normal is 1500 CD4, which presents 25% of the

whole total. As the total number decreases, the CD4 normal rate decreases too but remains always 25%. It's only at the age of 6 years that the adult situation is reached with a total rate of lymphocytes of 2000 and a CD4 normal rate of 500 (25%) see appendix XIV.

System of score for tuberculosis diagnosis in a child (NTCP).

According to the book entitled ***«Treatment and Prevention of Opportunistic Infections, Referral Hospitals in Countries with Limited Resources»,*** IMT2004, Lut Lunen- adaptation of Crofton score. Reiterated in the TB National Control Programme.
The score of 7 or more indicates the high probability of tuberculosis. A score between 3 and 7 indicates the probable tuberculosis to be confirmed by Rx Thorax.
A score < 3: less probable tuberculosis.

Characteristics	**0**	**1**	**2**	**3**	**4**	**T**
Duration of disease(week)	<2	2 to 4		>4		
Nutrition (% Weight for age)	>80 %	60-80%	60%			
Family TB history	none	Told by the family		Positive sputum or clear profs		
Malnutrition				no improvement after 4 weeks		
TB's test				positive		
Unexplainable fiver and night sweats.			No antimalaria's response or antibiotics .			
				Adenopathies >1cm		
				abdominal mass-ascites		
				LCR's defects		
				.Joint or bone inflammation		
					Angular vertebral column defect	
Total Score						

TRAC NET FOR HIV TREATMENT.

Introduction / Evolution of TRACnet

HIV/AIDS remains, in Rwanda as well as all over the entire world, a major public health problem. From the onset of this pandemic, Rwanda has been adopting different strategies to face HIV/AIDS. It is in this regards that in 2003 Rwanda launched a national care and treatment programme for people living with HIV/AIDS. Currently about 90,000 people receive care under this programme and about 40,000 are under antiretroviral treatment.

In order to guarantee efficient monitoring of the programme, the government of Rwanda initiated consultations in 2003 with various partners to set up a national electronic monitoring and reporting system of information on HIV/AIDS patients.

It was in2004, that TRAC Net became operational in certain health centres in the country. TRAC Net is a technology developed by VOXIVA funded by CDC (Centres for Disease Control and Prevention) in the PEPFAR framework programme (US President's Emergency Plan for AIDS Relief). The technology enables electronic monitoring and reporting of information on monitoring of HIV/AIDS patients using telephones or internet.

Its innovation, compared with other existing ones, is to facilitate rapid and instant transmission and monitoring of data even from remote regions of the country with limited communicational infrastructures. The major problems of the information systems in developing countries are: the delay in the transmission of information, the fullness of data and the lack of top-down feed-back. This causes the deformation of information and especially hinders the use of system to inform the programme.

TRAC Net system enables all healthy workers, even those operating remote health facilities, far from capital, to transmit data on the progress of patients under ARV treatment to coordinators of national programmes using one’s mobile telephone only.

By doing so, coordinators of national programmes can access health information data on TRAC Net Web Site.

Major modules of TRAC Net include:

- A module for routine programmatic management indicators, using report and graphic forms.
- A module for monitoring of drug supply in health centres, districts and provinces to avoid shortages and stock outs.
- A module for prompt monitoring crucial information of the patient such as weights, WHO categorisation…
- Laboratory module.

Why TRAC Net system ?

The information collected by the Health Information System (HIS) is not enough for monitoring and evaluation of all vertical programmes of Ministry of Health. This situation requires, in most cases, other types of reports from various partners involved in the area of health in the country, to coordinate, monitor and evaluate their activities. Those partners are in most case donors supporting some programmes of Ministry of Health, such as National Integrated Programme against Leprosy and Tuberculosis (NTCP), National Malaria Control Programme, National Vaccination programme…Therefore, there are a considerable number of reports required by programmes involved in HIV/AIDS control.

Even if those parallel systems provide detailed and very useful information, additional work is required from health workers because in most cases the required reporting formats are not standardised. The standardisation of the reporting system would reduce the work of the personnel of health facilities.

Following the extension of the HIV/AIDS treatment programme, it has been necessary to set up a system that enables the collection of information related to HIV. It is in this respect that TRAC Net provides an HIV easy data collection at the level of sites that implement ARV programmes (VCT, PMTCT and treatment). Given the recorded success of this initiative, discussions are going on to extend it and connect it to the National health information System and other parallel systems (CAMERWA, National laboratory…

The following chapter describes in details indicators collected by the TRAC Net system on monitoring and evaluation of HIV treatment service.

For every indicator, the definition, the methodology of data collection, the presentation of various indicators and programmatic implications are also detailed.

A separated manual of procedures will provide in details the use of TRAC Net system.

Indicators utilised in treatment

The Cumulative total number of HIV+ patients under the treatment programmeme

Definition/ calculation Method:

The total number of all HIV+ patients who are treated in health facilities from the beginning of HIV services in health facilities. Those patients often arrive through the front doors of health facilities (which are external consultation services, hospital admissions, VCT and PMTCT) and have been tested positive and transferred to health care services of these health facilities.

Method of collection/ Data sources.

Normally any patient tested positive in VCT and PMTCT services, through outpatient consultations or hospital admission is directed to a care service where he/she is registered in a registration book « PRE-ARV), it is the same for other patients transferred from other health facilities with a positive test. Other sites use a registration book for HIV patients. The sites use a registration book of all HIV+ patients that they have received. The cumulative total number will be obtained by considering the previous monthly registration number in the «PRE-ARV» registration book.

Periodicity of collection

The periodicity of this indicator collection is done monthly.

Different presentations of indicator.

This indicator will be reported for all patients (generally) then after, a categorisation based on sex and age will be done. The following indicators will be reported:

- *The cumulative total number HIV+ adult patients (>15years) in the care programme.*
- *The cumulative total number of HIV+ adult patients (male) in the care programme.*
- *The cumulative total number of HIV+ adult patients (female) in the care programme.*
- *The cumulative total number of paediatric HIV+ patients (>15 years) in the care programme*
- *The cumulative total number of paediatric HIV+ patients (<2 years) in the care programme*
- *The cumulative total number of paediatric HIV+ patients (2-5 years) in the car programme*
- *The cumulative total number of paediatric HIV adult patients (>6-15 years) in the care programme*
- *The total number of HIV+ paediatric patients (male) in the care programme.*
- *The total number HIV+ paediatric patients (female) in the care programme.*

This indicator provides a general idea about the number of HIV+ patients to be treated by a given health facility. The difference between paediatric patients and adults, male and female and other brackets, they have the important programmatic implication in terms of ARV treatment coverage of various groups. In fact, it enables detecting the less represented groups and provides orientation for sensitization and monitoring strategies. The 1st weakness is that it is difficult for health facilities to take into account cases of abandonment, transfers and deaths among HIV positive patients. We shall discuss later how the problem is not very serious for patients who are monitored for prophylaxis or who are under ARV treatment. The second weakness is that this indicator does not provide the exact number of HIV+ patients who come to the health facility. In fact, there is an important number of HIV+ patients who are transferred from VCT & PMTCT for treatment but who never report and consequently who are not registered in «PRE-ARV» registration book.

Cumulative total number of patients currently under ARV treatment

Definition/ Method of calculation :

The total number of all HIV positive patients who are under ARV programme in a health facility from the beginning of the HIV service at the time of reporting.

Method of collection/ Sources of data

The HIV positive patients monitored in health facility (registered in PRE-ARV) will be transferred in «ARV» Register if they meet the criteria to be put under ARV treatment. The cumulative total number of patients currently under ARV treatment will be obtained by considering the cumulative total number of patients under ARV during the previous month **PLUS** new cases under ARV available at the time of reporting **PLUS**« transfers in» **MINUS «** transfers out». Even if the sites use their proper registration books, It's crucial to differentiate among patients under ARV; those transferred (in and out), those who abandoned deaths and new cases in the month.

Periodicity of collection

The periodicity of collection of indicators of patients under ARV is monthly. The reporting is on the cumulative total number of all patients under ARV from the beginning of the programme until the end of the current month according to calculation described above.

Different presentations of indicator.

This indicator has to be reported for all patients (generally) then after, the distinction will be done based on age, sex and diet (1st or 2nd degrees) The following indicators will be reported:

- The cumulative total number of adult patients (male) under 1st degree diet?
- The cumulative total number of adult patients (female) under 1st degree diet?
- The cumulative total number of adult patients (male) under 2nd degree diet?
- The cumulative total number of adult patients (female) under 2nd degree diet?
- The new registered total number in the current month (ARV+ prophylaxis)
- The cumulative total number of HIV+ paediatric patients <2 years) under ARV treatment
- The cumulative total number of HIV+ paediatric patients <2-5 years) under ARV treatment
- The cumulative total number of HIV+ paediatric patients <6-15 years) under ARV treatment
- The total number of paediatric patients (male) under 1st degree regimen?
- The total number of paediatric patients (female) under 1st degree regimen?
- The total number of paediatric patients (male) under 2nd degree regimen?
- *The total number of paediatric patients (female) under 2nd degree regimen?*

Importance of this indicator/ Analysis.

This indicator provides a general idea about the number of HIV positive patients under ARV. It is an important indicator for the quantification of ARV drugs and projection of the rate of consulting patients monitored in the ARV treatment programme. It also enables monitoring of the coverage trends, but its objective is not to distinguishing between different ARV treatment forms or to measure the quality or the efficiency of the treatment.

The degree of the use of ARV treatment will depend on existing care providing infrastructures, their quality, availability, the attendances of voluntary Counselling and testing services, the perception of the efficiency and possible side effects to treatment.

The number of new patients who have started ARV treatment in the current reporting month.

Definition/ Method of calculation :

In the framework of monitoring HIV positive patients, there is every month, a number of patients treated in the HIV programme that become eligible for antiretroviral treatment or transferred patients from other sites. The present indicator provides numbers of new patients who are under ARV during the reporting month.

Method of collection/ Sources of data.

The number of new patients under ARV during the reporting moth will be registered in an ARV registration book from the beginning until the end of the month.

Periodicity of collection.

The periodicity of the collection of indicator of new patients under ARV is one month. The number of patients under ARV per month is reported (this is done at the end of the month).

Various presentations of this indicator :

This indicator will be reported for all patients (generally) thereafter, the distinction will be done, based on age, sex and WHO stages. For women, the number of new pregnancies will equally be recorded. The following indicators will be reported:

- The number of patients (>15 years male) who have started ARV treatment in the current month
- The number of patients (>15 years female) who have started ARV treatment in the current month.
- The number of new pregnancies in women under ARV reported this month.
- The number of new adult patients (>15years) who are at WHO stage 4 this month.
- The number of new adult patients who are at WHO stage 3 this month.
- The number of new adult patients who are at WHO stage 2 this month.
- The number of new adult patients who are at WHO stage 1 this month.
- The number of new adult patients who are at an unknown WHO stage this month.
- The number of new paediatric patients (< 15 years) who are at WHO stage 4 this month.
- The number of new paediatric patients who are at WHO stage 3 this month.
- The number of new paediatric patients who are at WHO stage 3 this month.
- The number pf new paediatric patients who are at WHO stage 1 this month.
- The number of new paediatric patients who are at an unknown WHO stage this month.

Importance of this indicator/ Analysis

The advantage of this indicator is that it enables monitoring of the trend of the ARV treatment coverage. It therefore provides an idea about the utilisation of ARV services by the population covered by the health facility. It also provides the proportion of HIV positive people with an advanced stage of the infection and it is a base for progressive evaluation of the efficiency of the ARV.

Its major weakness is that it does not distinguish various types of ARV drugs offered. In addition, it

does not cover preventive ARV treatment in case of the prevention of PMTCT or post-exposure prophylaxis.

The total number Patients under prophylactic treatment.

Definition/ Method of calculation :

The HIV positive patients at stages 1,2or 3 still with the CD4 rate of 350/mm3 may develop opportunistic infections. They must accordingly be put under prophylaxis to prevent the onset of those opportunistic infections. Drugs used in Rwanda for the prophylaxis of opportunistic infections are cotrimoxazole, Dapsone (in case of allergy for Bactrim) and Fluconazole. The isoniazide is prescribed for children < 5 years of whom at least one parent presents an active TB.

Method of collection/ Sources of data.

The cumulative total number of patients under prophylaxis is obtained in the pre-ARV registration book. The number in the reporting month is added to the past total cumulative number but we subtract patients who stopped the prophylaxis (for different reasons).Some sites have specific registration books for patients under the prophylaxis. There are some who are under cotrimoxazole (dapsone) and others under fluconazole (Diflucan). These registration books enable the monitoring of patients under prophylaxis. Consequently the total number of patients under prophylaxis is equal to the number of all complying patients (= **total number-deaths-transfers- deserted.**

Periodicity of collection

The periodicity of the collection of the indicator of new patients under ARV is one month.

Different presentations of indicator.

The number of adults patients (> 15 years) under Bactrim (or dapsone), under isoniazide and under Fluconazole will be separately reported. For children (< 15 years) children under Bactrim (or dapsone), and those under Fluconazole will be separately reported.

- The total number of adult' patients under cotrimoxazole prophylaxis
- The adults' patients' total number under dapsone prophylaxis
- The total number of adult patients under Fluconazole prophylaxis
- The cumulative total number of paediatric patients under dapsone prophylaxis
- The cumulative total number of paediatric patients under cotrimoxazole prophylaxis
- The cumulative total number of paediatric patients under INH (isoniazide) prophylaxis
- The cumulative total number of paediatric patients under fluconazole prophylaxis

Importance of this indicator/ Analysis

This indicator provides a general idea on the number of patients monitored in this programme and who will be potentially under ARV in coming months or years. It is also a good indicator of monitoring patients. Patients already monitored at level of sites for prophylaxis will probably have a more considerable ARV treatment compliance than those who have attained the advanced stage of the disease.

The number of patients under ARV who deserted the programme.>(3months)

Definition/ Method of calculation

The ARV treatment is heavy, constraining and its compliance is not easy because it is the treatment for the entire life. For several reasons, it happens that patients under ARV abandon the treatment. The patient is considered as deserted when he/she does not appear on the list for 3 months or more and he/she has not been found during home visits.

Method of collection/ Sources of data.

In ARV registration book, there is a column « out of programme» reserved for comments related to monitoring patients under ARV. In that place, it will be noted if the patient has deserted, died, stopped the treatment or been transferred. In the column « out of the programme of ARV registration book, the number of deserted patients is recorded (differentiate them from deaths, those who stopped and transfers). To fulfil this column, it is advised to classify the nursing files of patients (including pharmacy form) according to appointments. The green files of patients will then be classified according to their TRAC Net ID (or if not according to the identification number of sites). Every appointment day, the caregiver will verify all absent patients and will monitor to classify them correctly in the appropriated column.

Periodicity of collection.

The periodicity of collection of this indicator is one month. Patients will be considered as deserted when they do not appear on the list for 3 months or more.

Various presentations of this indicator.

This indicator will be presented by age and sex (male and female).

- The number of adult patients (male) of under ARV who deserted (> 3 months).
- The number of adult patients (female) of under ARV who deserted (> 3months).
- The number of paediatric patients (male) of under ARV who deserted (> 3months).
- The number of paediatric patients (female) of under ARV who deserted (> 3 months).

Importance of indicator/ Analysis

This indicator enables the control of the onset of the resistance of the virus to antiretroviral drugs.
In case of a high number of abandonment of patients under ARV, the criteria of the ARV treatment will be questioned. The ARV treatment will have more chances of success for a treatment in a «naive» patient since he/she has less chances of having strains of resistant viruses. Poor compliance to treatment is a major factor of the development of multi resistant strains and consequently the failure of treatment.

The number of patients admitted in a month.

Definition/ Method of calculation :
The number of patients under ARV that have been admitted in hospitals during the reporting month.

Method of collection/ Sources of data.
The ARV registration book monitors patients under ARV and it will each time be recorded in the column« out of programme» and « comments» patients who will have been hospitalised during the reporting month. Note this number.

Periodicity of collection
Monthly

Different presentations of this indicator.
This indicator will be presented by age and sex (female and male).

- The number of patients (male) under ARV hospitalized this month.
- The number of patients (female) under ARV hospitalised this month.
- The number pf paediatric patients (male) under ARV hospitalised this month.
- The number of paediatric patients (female) under ARV hospitalised this month.

Importance of indicator/ Analysis
The ultimate goal of ARV treatment is to stabilise the immunity level of patients and therefore prevent or at least delay the onset opportunistic infections. The number of patients under ARV hospitalised is a major indicator. The indicator may be considered as a proxy of a therapeutic response for ARV.

The total number of patients registered in the programme that died in the reporting month.

Definition/ Method de calculation :
The total number of patients monitored by the programme that lost their lives within the reporting month

Method of collection/ Sources data.
In ARV registration book, the columns« out of programme» and «comments» are recorded patients who died during the reporting month. Write this number.

Periodicity of collection
Monthly

Different presentations of this indicator.

This indicator will be based age and sex presentation (male and female).

- The number of adults patients (male) under ARV who died this month
- The number of adults patients (female) under ARV who died this month
- The total number of paediatric patients who died this month.
- The number of paediatric patients (male) under ARV who died this month
- The number of patients (female) under ARV who died this month.

Importance of indicator/ Analysis

The number of patients registered in the programme who died is a good indicator of the impact of all interventions that are undertaken to improve the heath of people living with HIV/AIDS.

The number of patients transferred / or received as transfers in the current month
Definition/ Method of calculation : The patients' number followed by the programme and transferred/or received as transfers towards other health facilities during the month of report. .
Method of collection/ Sources of data. In ARV registration book, in the column « patients out of programme» and «Comments» patients that have been transferred to other health facilities within the reporting month are recorded. Write the total number of patients transferred or received as transfers within the reporting month.
Periodicity of collection Monthly
Different presentations of this indicator. The following indicators will be reported **:** • The number of ARVP patients received as transfers. • The total number of patients registered in treatment programme transferred to other health facilities this month. • The total number of patients transferred or received this month. • The total number of paediatric patients transferred / received this month • The total number of paediatric patients under ARV transferred received this month • The total number of paediatric patients transferred to another health facility this month. • The total number patients under ARV transferred towards another health facility.
Importance o this indicator/ Analysis. Since not all sites provide all HIV service package, a high rate of transfers/referrals of patients from one site to another is a good sign of efficient functioning of a health system of a country. Patients may be registered under ARV in a given site and then be transferred to another site to ensure good compliance to the treatment.

Indicators of individual information of patients

General information of patients.

The TRAC Net system collects general information on all patients monitored by the ARV treatment programme. Variables such as health facility, age, sex and marital status enable the description of the population monitored by the programme. Deep analysis of these variables will enable a detection of the least represented various categories in the programme. The results of the discussions by site, districts and provinces will provide tangible recommendations for the programme of the treatment of HIV positive patients.

For example, it will be possible to realise that the youth aged between 15-25 years do not frequent health facilities to seek HIV services. It would then be advisable to find out the reason of this situation and design attractive strategies for the youth.

It should be noted that the single identification number for every patient is recorded in the general information (TRAC Net ID). Children will be identified, not only by their own TRAC Net ID, but also

by names of their parents. This identification number is very important for the management and analysis of data because it enables the linkage between different data modules (general information, patient monitoring and laboratory).

In addition, general information of patients provides basic data tat enables the monitoring of patients in time. This information is:

- Date of registration in the programme.
- Date of the 1st positive test
- WHO stage of the patient at the time of enrolment
- Weight of the patient at the time of enrolment.

This information is crucial for the analysis of the therapeutic response by the patient because it depends on the initial state of the patient at the enrolment in the programme. A more detailed module will describe different phases of collection, processing and compilation of data to prepare analysis. Here we present only the possible tables which can be produced thanks to this information.

The analysis of data from individual information of patients will produce the following descriptive tables:

- Description of the age of patients registered in the programme by a health facility.
- The distribution of Patients registered in the programme by age brackets (we will chose any category).
- The patients distribution registered based on sex
- The distribution of patients registered based on marital status.
- The patients distribution registered based on WHO stages.

Information on monitoring of patients

Several kinds of information and data which enable monitoring of patients are collected and processed in the TRAC Net system. Concerning monitoring of patients, the following tables will be produced for data collected from individual files of patients.

- The ongoing treatment: determine patients under ARV and those under prophylaxis.
- For patients under ARV, classify them according to treatment regimes.

- Characteristics related to prophylaxis and ARV treatment of monitored patients.
- The evolution of the gain of weight by children / children under ARV from the beginning of treatment (the weight of patients is recorded every 6 months from the start of treatment).
- The distinction of patients under ARV according to the age brackets.
- The evolution of the count of CD4 for patients under ARV (the CD4 count for patients every 6 months is recorded from the beginning of treatment).

APPENDICES

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