HIV Care and Antiretroviral Therapy Guidelines

Second Edition

Fiji Ministry of Health
2013

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Disclaimer

The authors do not warrant the accuracy of the information contained in the guidelines and do not take responsibility for any death, loss, damage or injury caused by using the information in the guidelines.

While every effort has been made to ensure that the contents of the guidelines are correct and in accordance with current evidence-based clinical practice, the dynamic nature of medicine requires that users exercise in all cases independent professional judgement and understand the individual clinical scenario when referring, prescribing or providing information from the guidelines.

Preface

The Fiji Ministry of Health has formulated its National HIV/AIDS Strategic Plan on HIV and STI 2012-2015 that covers care and support of people living with HIV (PLHIV) and their families. The strengthening of an expanded antiretroviral therapy (ART) program has been included in the strategic plan. Standard treatment guidelines are considered to be of crucial importance for the optimal care for PLHIV as well as the cost-effectiveness of the use antiretroviral (ARV) drugs.

Currently, it is universally recognized that ARV drugs do not cure HIV infection but they can suppress viral replication, restore the immune function, reduce HIV-related morbidity and mortality, and improve the quality of life of infected persons. Thus, all possible measures to prevent new infections remain essential and this should remain as the ultimate goal in reversing the epidemic despite the availability of ARV drugs.

This set of guidelines is based on the *WHO Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach* released in June 2013. It was designed to provide a technical basis for the sustainability of the HIV Care/ART Program in Fiji – appropriateness of drug regimens being recommended, clinical and program monitoring, and training of health care professionals. The guidelines should be considered as a basic manual for HIV care and ART in Fiji and not as a comprehensive reference for the complex management of HIV infection. It maintains the WHO "four S's" approach – when to: start drug treatment; substitute for toxicity; switch after treatment failure; and stop.

The focus of the guidelines is primarily directed to health care professionals in Fiji who do not have much experience on ART at the primary and secondary health care levels. As such, it takes into consideration the limited resources available at these levels which is in consonance with the public health approach of WHO in curbing the global HIV epidemic.

Lastly, in as much as HIV medicine is a relatively new and dynamic field, it is recommended that these guidelines should be reviewed in due time and updated appropriately, taking into consideration our local setting.

Dr Neil Sharma
Minister
Ministry for Health
October 2013

Acknowledgment

Abbreviations and Acronyms

ABC	Abacavir
AFB	Acid-fast bacilli
AIDS	Acquired immunodeficiency syndrome
ALT	Serum alanine aminotransferase
AST	Serum aspartate aminotransferase
ANC	Antenatal clinic
ART	Antiretroviral therapy
ARV	Antiretroviral
AZT	Zidovudine
BCG	Bacille Calmette Guerin
BD	*Bis diem* (Latin for "twice a day")
CBO	Community-based organization
CD4+	T-lymphocyte bearing CD4 receptor
CMV	Cytomegalovirus
CNS	Central nervous sytem
CoC	Continuum of care
CTP	Co-trimoxazole prophylaxis
DBS	Dried blood spots
ddI	Didanosine
DNA	Deoxyribonucleic acid
DNA PCR	Deoxyribonucleic acid polymerase chain reaction
DPT	Diphtheria, pertussis, tetanus
d4T	Stavudine
FBC	Full blood count
FBO	Faith-based organization
EFV	Efavirenz
EPI	Expanded program on immunization
FPBS	Fiji Pharmaceutical and Biomedical Services
FTC	Emtricitabine
HBC	Home-based care
Hib	*Hemophilus influenzae* type b
HCW	Health care worker
HIV	Human immunodeficiency virus
INH	Isoniazid
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution inflammatory syndrome
LPV/r	Lopinavir/ritonavir
MCH	Maternal and child health
MOH	Ministry of Health
MR	Measles-rubella (referring to the vaccine)
NACA	National Advisory Committee on AIDS
NGO	Non-governmental organization

NSAID	Non-steroidal anti-inflammatory agent
NRTI	Nucleoside/nucleotide reverse transcriptase inhibitor
NNRTI	Non-nucleoside reverse transcriptase inhibitor
Nocte	At night (Latin)
OD	Once a day
OI	Opportunistic infection
OPV	Oral polio vaccine
PCP	*Pneumocystis jiroveci* pneumonia (formerly *Pneumocystis carinii* pneumonia)
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PLHIV	Person/people living with HIV
PI	Protease inhibitor
PMTCT	Prevention of mother-to-child transmission
PPTCT	Prevention of parent-to-child transmission
PO	*Per orem* (Latin for "by mouth")
RPR	Rapid plasma reagin
SMX	Sulphamethoxazole
SRH	Sexual and reproductive health
TMP	Trimethoprim
TST	Tuberculin sensitivity testing; same as Mantoux test or PPD (purified protein derivative) test
STI	Sexually transmitted infection
TB	Tuberculosis
TDF	Tenofovir
TDS	*Ter die sumendum* (Latin for "three times a day")
UNAIDS	Joint United Nations Program for HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
WHO	World Health Organization

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1 Overview of HIV care and antiretroviral therapy

Figure 1.1 below provides a general overview of care and management of an HIV-positive patient.

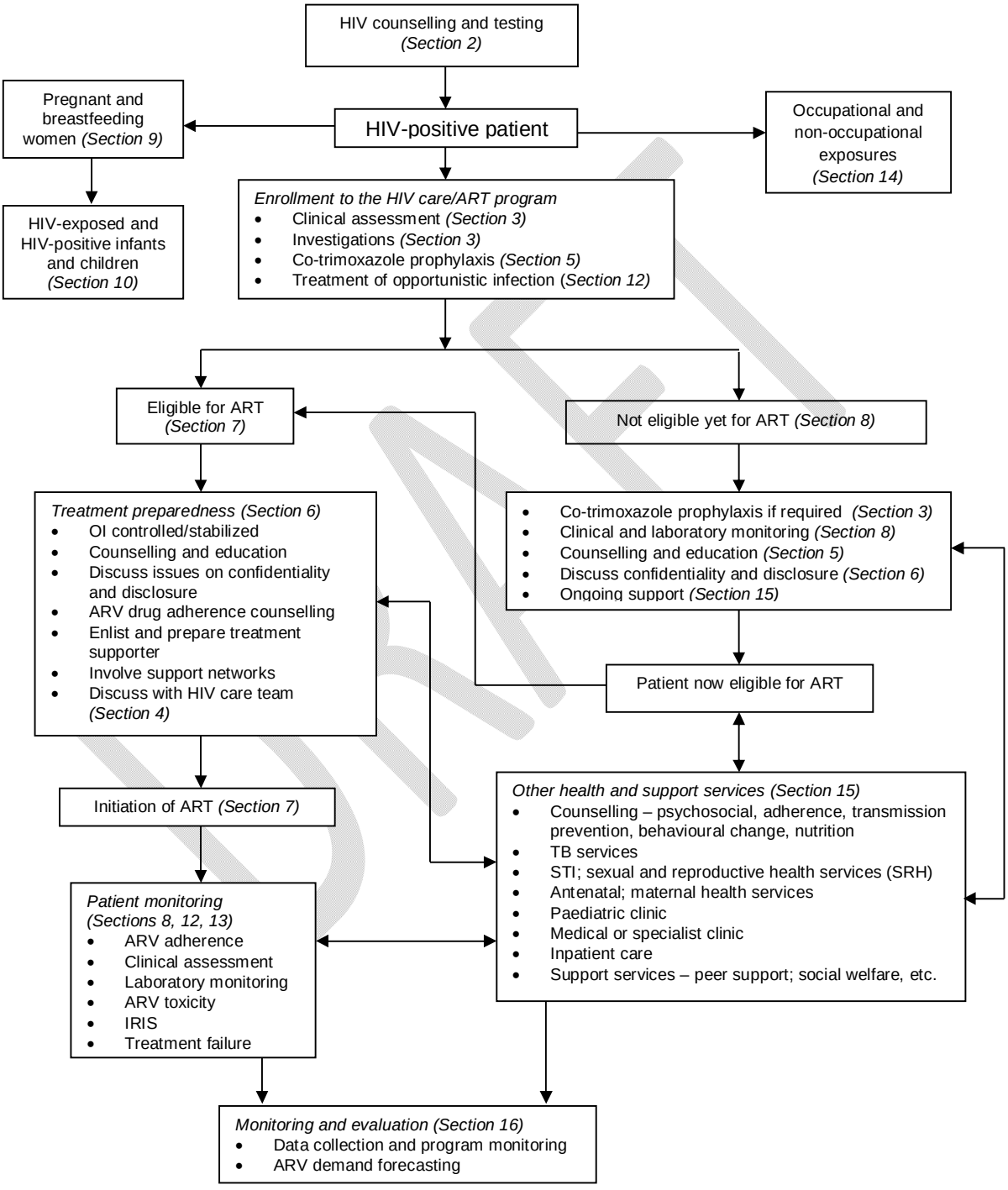


Figure 1.1 Flow diagram for the general management of a newly diagnosed HIV-positive patient.

2 HIV counselling and testing

HIV counselling and testing is the entry point for the continuum of care (CoC) for HIV. Details on continuum of care (CoC) for HIV are discussed in Section 15.

2.1 HIV counselling

HIV counselling and testing services are available in designated health care and community-based facilities around Fiji. There are facilities that offer voluntary confidential counselling and testing (VCCT), also known as client-initiated counselling and testing; and/or provider-initiated counselling and testing (PICT). These models of HIV counselling and testing services should be voluntary and adhere to the five C's: **c**onsent, **c**onfidentiality, **c**ounselling, **c**orrect test results and **c**onnections to care, treatment and prevention services.

- People must give informed consent for HIV testing after being counselled.
- HIV counselling and testing services are confidential, meaning that any information will not be disclosed to anyone else without the expressed consent of the person being tested.
- HIV counselling and testing services must be accompanied by appropriate and quality pre-test and post-test counselling.
- Quality assurance mechanisms must be in place to ensure the provision of correct test results.
- HIV counselling and testing services must have connections or linkage to prevention, care and treatment services that include referral to appropriate follow-up services and long-term prevention and treatment support.

Health care workers who have undergone training on HIV clinical management and prevention ofParent-to-child transmission (PPTCT) are expected to provide HIV counselling and testing services in the health care facilities where they are posted.

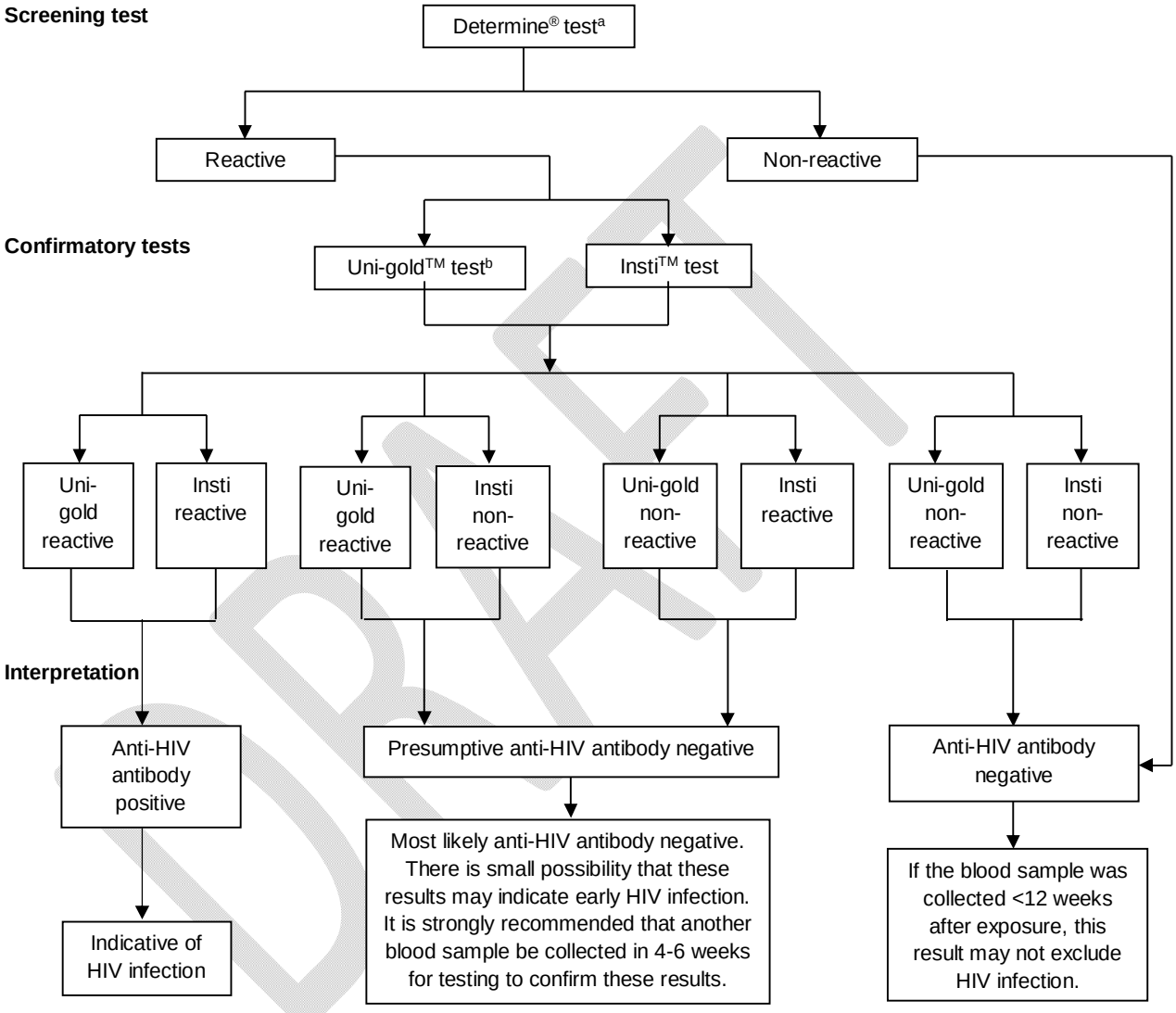
Checklist for pre-test counselling, post-test counselling for HIV-negative test result and post-test counselling for HIV-positive test result are shown in Appendix 1, Appendix 2 and Appendix 3, respectively. Detailed HIV counselling and testing guidelines are beyond the scope of these guidelines and readers are advised to refer to appropriate sources.

2.2 HIV testing

To ensure rapid turnaround time for HIV test results and timely linkage to appropriate treatment, care and support services, the use of rapid diagnostic tests (RDTs) tests are used for screening and confirmation of HIV infection.

2.2.1 HIV testing algorithm in sub-divisional hospitals

Figure 2.1 shows the schematic flow diagram of the HIV testing algorithm[1] used in sub-divisional hospitals. Sensitivity for this HIV testing algorithm is 99.24% while the specificity is 100.00%; positive predictive value is 100.00% while the negative predictive value is 99.82%.



Note: Any blood sample that gives an invalid result should be re-tested in the test(s) in which it was invalid. If the invalid test result persists, no interpretation can be provided and another blood sample should be collected to testing.

[a]Determine® (Inverness Medical Innovations, Inc.), [b]Uni-gold™ (Trinity Biotech USA) and [c]Insti™ (Biolytical Laboratories) are commercial names of HIV rapid tests. Uni-gold and Insti are performed in parallel.

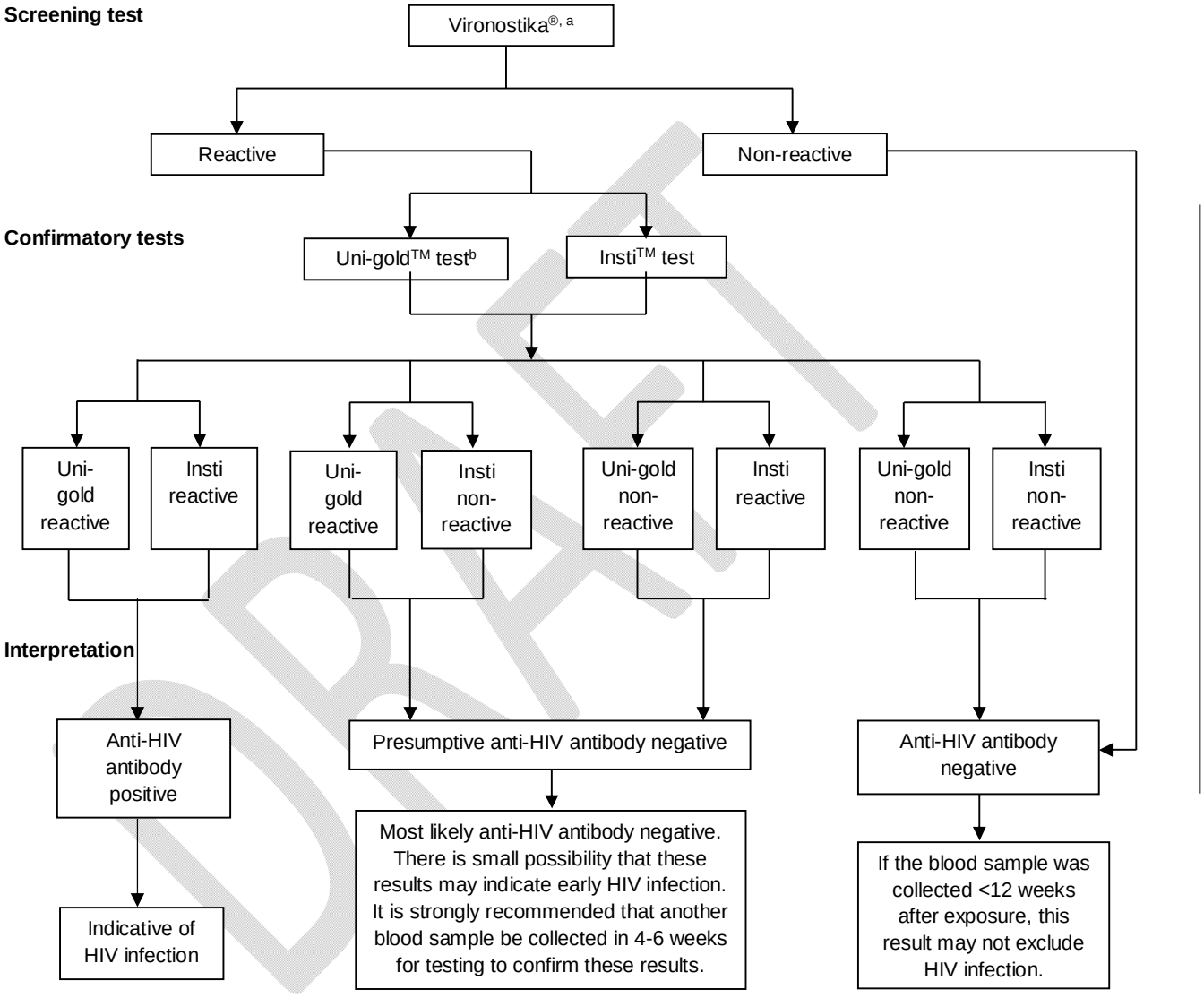
Figure 2.1 HIV testing algorithm for sub-divisional hospitals, MOH, Fiji.

[1] The recommended HIV testing algorithm in some PICTs was mandated by the Regional Level Consultation on HIV Testing (5-6 May 2008, Pago Pago, American Samoa) and validated by the National Serology Reference Laboratory, Melbourne, Australia and recommended by the Pacific HIV Testing Task Force in April 2010.

2.2.2 HIV testing algorithm in divisional hospitals

a. Routine HIV testing

Figure 2.2 shows a schematic flow diagram of the HIV testing algorithm used in divisional hospitals for routine testing.



Note: Any blood sample that gives an invalid result should be re-tested in the test(s) in which it was invalid. If the invalid test result persists, no interpretation can be provided and another blood sample should be collected to testing.

[a] Vironostika® is a manufactured by bioMerieux. [b]Uni-gold™ (Trinity Biotech USA) and [c]Insti™ (Biolytical Laboratories) are commercial names of HIV rapid tests. Uni-gold and Insti are performed in parallel.

Figure 2.2 HIV testing algorithm for divisional hospitals, MOH, Fiji.

b. For urgent HIV testing

For urgent HIV testing in divisional hospitals, the HIV testing algorithm implemented in sub-divisional hospitals will be used (Figure 2.1). Urgent HIV testing is restricted in the following situations:

- Urgent screening of blood donors;
- Unbooked pregnant women presenting in labour;
- Unbooked women presenting immediately post partum; and
- Occupational and non-occupational exposures to HIV.

2.2.3 Diagnostic testing for HIV-exposed infants and children

HIV diagnostic testing for HIV-exposed infants and children is discussed in Section 10.2.

2.3 Linkage to HIV care

After the patient is diagnosed HIV-positive[2] and have received post-test counselling, the patient is referred to the hub centre as early as possible. Figure 2.3 provides a schematic flow diagram for linkage of HIV-positive patients to divisional hub centres.

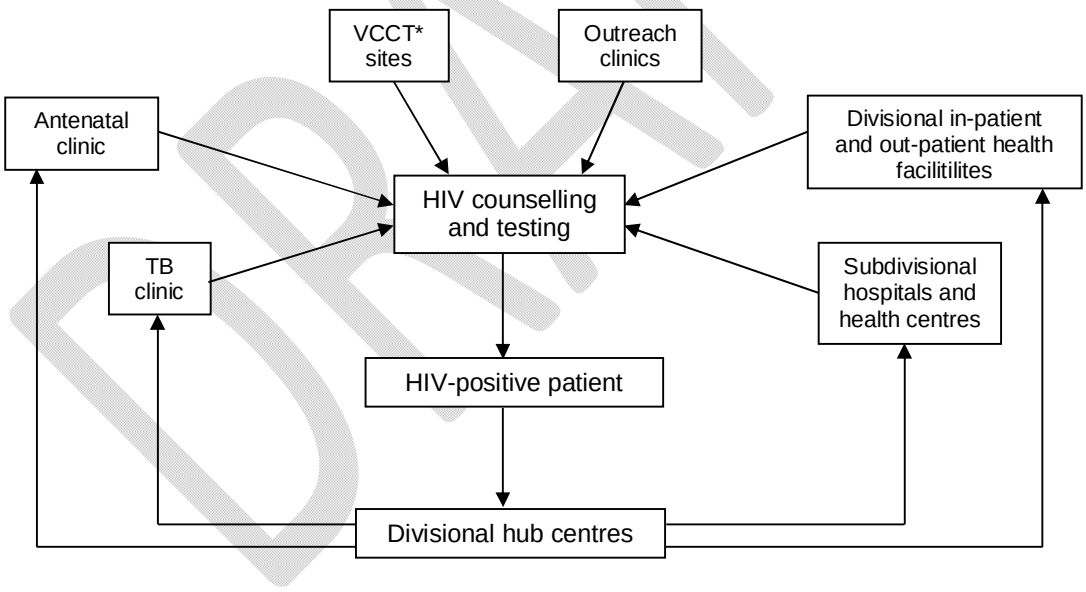


Figure 2.3 Linkage of HIV counselling and testing services to divisional hub centres, MOH, Fij.

* VCCT – voluntary confidential counselling and testing.

[2] WHO HIV case definitions are outlined in Appendix 4.

3 Initial patient assessment

3.1 Clinical assessment and investigations

The recommended baseline clinical assessment and laboratory investigations at the first clinical encounter of an HIV-positive patient in the hub centre are listed in Box 3.1.

Box 3.1 Recommended baseline clinical assessment and investigations at initial clinic visit of HIV-positive patients

Clinical Assessment
Vital signs (blood pressure, pulse rate, respiratory rate, temperature, weight (kg), height (cm)
Physical examination, including eye check (i.e. visual acuity) and oral health assessment
Screening for other sexually transmitted infections (STIs)
Screening for opportunistic infections (OIs) and other HIV-related conditions
Other medical conditions, e.g. jaundice, hypertension, diabetes mellitus, etc.
Immunizations
Functional Status
WRK (normally active: able to work, go to school, do housework)
AMB (ambulatory but bedridden <50% of the day during the last month)
BED (bedridden: >50% of the day during the last month)
Social History
Prior history of taking ARV drugs or any other drugs
HIV status of partner and/or children and history of ART
Desire for family size , future pregnancies, family planning, contraception
Sexual activity (including condom use)
Options for infant feeding (in women desiring pregnancy)
HIV diagnostic testing in infants and children
Tuberculosis (TB) Screening
Coughing >2 weeks
Persistent fever >2 weeks
Night sweats >2 weeks
Weight loss of >3 kg for >4 weeks
Investigations
Full blood count (FBC)
CD4 cell count/%CD4
Urea, creatinine and electrolytes (if required)
Liver function tests (if required)
Blood glucose
Serum cholesterol, triglycerides
Syphilis, hepatitis B and hepatitis C screening
STI screening
Pregnancy test
Paps smear
Urine dipstick for glycosuria
Chest X-ray
Sputum for acid-fast bacilli (if clinically indicated)

3.2 WHO clinical staging

At the initial visit of the patient with confirmed HIV infection (serological and/or virological evidence of infection), the patient is assessed clinically based on the WHO clinical staging system. Table 3.1 provides the clinical stage in simplified terms describing the spectrum of HIV-related symptomatology: asymptomatic, mild symptoms, advanced symptoms, and severe symptoms.

Clinical staging is useful for assessment at baseline (at the time of HIV diagnosis), entry into long-term HIV care, and in the follow-up of patients in care and treatment programs. It should be used to guide decisions on when to start co-trimoxazole prophylaxis and when to start antiretroviral therapy (ART).

The clinical staging events (Appendix 5 for HIV-positive adults and adolescents, and Appendix 6 for HIV-positive infants and children) have been shown to be related to survival, prognosis and progression of clinical disease without ART in adults and children.

Table 3.1 WHO clinical staging of established HIV infection

HIV-associated symptoms	WHO clinical stage
Asymptomatic	1
Mild symptoms	2
Advanced symptoms	3
Severe symptoms	4

Adopted from WHOc 2007:12.

3.3 Immunological assessment

The pathogenesis of HIV infection is largely attributable to the decrease in the number of T cells (a specific type of lymphocyte) that bear the CD4 receptor (CD4+). The immune status of a child or adult living with HIV can be assessed by measuring the absolute number (per mm^3) or percentage of CD4 cells (%CD4)[3]. Progressive depletion of CD4+ T cells is associated with progression of HIV disease and an increased likelihood of opportunistic infections (OIs) and other clinical events associated with HIV.

The normal absolute CD4 count in adults and adolescents ranges from 500 to 1,500 cells/$mm^3$of blood. Measurement of %CD4 is more valuable in children younger than five years of age. Absolute CD4 counts (and less so the %CD4) fluctuate within an individual and depend on inter-current illness, physiological changes or test variability. At times, measuring the trend over two measurements is therefore more informative than an individual value.

In general, the CD4 cell (absolute count or %CD4) progressively decreases as HIV disease advances. The CD4 count usually increases in response to effective combination antiretroviral therapy (ART).

The WHO immunological classification outlines four bands of HIV-related immunodeficiency (Table 3.2). The likelihood of disease progression to AIDS or death without ART increases with increasing immunodeficiency (decreasing CD4). Opportunistic infections and other HIV-related conditions are increasingly likely with CD4 counts <200 cells/mm^3.

[3] To calculate the %CD4+, use the following formula: %CD4+ = (absolute CD4 count [mm^3] × 100) / absolute total lymphocyte count (mm^3).

Table 3.2 WHO immunological classification of established HIV infection

HIV-associated immunodeficiency	Age-related CD4 values			
	<11 months (%CD4)	**12 – 35 months (%CD4)**	**36 – 59 months (%CD4)**	**>5 years (CD4 cells/mm^3 or %CD4)**
None or 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%

Adopted from WHOc 2007:15.

4 The HIV care team

Prescription of ART is complex and requires complete understanding of the rationale, pharmacology, and adverse effects of drugs. In addition, the health practitioner needs to be knowledgeable about the treatment of co-existing conditions and the management of HIV in special groups such as pregnant women and children.

For the above reasons, it is recommended that a multi-disciplinary team (i.e. the HIV care team) should provide care and treatment to HIV-positive patients. Members of the HIV care team (Box 4.1) should have undergone training on HIV care and ART organized by Fiji MOH before providing care to patients. The roles and functions of the HIV care team are outlined below.

- Develop and coordinate comprehensive management plan for people infected with and affected by HIV from the time of diagnosis, treatment and long-term chronic care.
- Serve as the Antiretroviral Treatment Committee.
- Develop training plan, mentorship and support for health care workers involved in HIV care.
- Report to the HIV Board, Permanent Secretary for Health and the National Adviser for Family Health for all decision-making deemed necessary for programmatic purposes.
- Team members should act as HIV advocates.

Box 4.1 'Core' members of the HIV care team

- Physician
- Medical officer-in-charge, Hub centre
- Paediatrician
- Obstetrician
- Head, Accidents and Emergency Unit
- Hub centre clinic nurse
- Midwife
- Infection control officer
- Public health medical officer, Divisional/Sub-divisional Medical Officer
- Pharmacist
- Counsellor
- Laboratory officer
- Person living with HIV (PLHIV)
- Dentist
- TB physician
- Nutritionist

Internal (key personnel from MOH) and external stakeholders (e.g. people working in the public sector with cross-cutting functions with MOH; non-governmental organizations, NGOs; community-based organizations, CBOs; faith-based organizations, FBOs) may be invited *ad hoc* during meetings and activities of the HIV care team for HIV-related issues relevant to the organizations that they represent.

5 Co-trimoxazole prophylaxis

While preparing the patient for ART initiation, primary prophylaxis[4] with co-trimoxazole or co-trimoxazole preventive therapy (CPT) is given if indicated.

Co-trimoxazole, a fixed-dose combination of sulphamethoxazole (SMX) and trimethoprim (TMP), is a broad-spectrum antimicrobial agent that targets a range of aerobic gram-positive and gram-negative organisms, fungi and protozoa. Co-trimoxazole prevents *Pneumocystis jirovecii* pneumonia and toxoplasmosis. It is also active against most *Salmonella*, most methicillin-sensitive *Staphylococcus aureus*, *Streptococcus pneumonia*, *Haemophilus influenzae*, and most gram-negative bacilli. It is also effective in preventing malaria.

Co-trimoxazole is available in both syrup and tablet formulations at low cost and is on the essential medicines list (EML).

5.1 Primary co-trimoxazole prophylaxis

5.1.1 Recommendations for primary co-trimoxazole prophylaxis for HIV-positive adults and adolescents

- *Indications:*
  - WHO clinical stage 2, 3 or 4 if CD4 cell count is not available
  - CD4 cell count of <350 cells/mm^3 regardless of the WHO clinical stage
  - WHO clinical stage 3 or 4 regardless of the CD4 cell count
- *Co-trimoxazole dose:*
  - Two single-strength tablets PO OD (single-strength tablet = SMX 400 mg + TMP 80 mg); *OR* one double-strength tablet PO OD (double-strength tablet = SMX 800 mg + TMP 160 mg)
- *When to discontinue co-trimoxazole:*
  - Co-trimoxazole can be discontinued if the patient is on ART for 6 months and the CD4 count is persistently ≥350 cells/mm^3 in two measurements within a six-month period

5.1.2 Recommendations for primary co-trimoxazole prophylaxis for HIV-exposed and HIV-positive infants and children

- *HIV-exposed infants and children*
  - Start co-trimoxazole at 4 – 6 weeks after birth and maintained until risk of HIV transmission ceases and HIV infection is excluded
- *HIV-positive infants and children <5 years of age*
  - Start co-trimoxazole and continue until 5 years of age regardless of CD4% or WHO clinical stage
- *HIV-positive children* ≥5 years of age (similar to adult recommendations)
  - WHO clinical stage 2, 3 or 4 if CD4 cell count is not available
  - CD4 cell count of <350 cells/mm^3 regardless of the WHO clinical stage
  - WHO clinical stage 3 or 4 regardless of the CD4 cell count
- *Co-trimoxazole doses*: refer to Table 5.1

[4] Primary prophylaxis refers to the treatment given to prevent the development of a particular disease.

Table 5.1 Dosages of commonly used co-trimoxazole formulations for infants and children exposed to or living with HIV[a]

Recommended daily dosage	Suspension (5 ml of syrup 200 mg/40 mg)	Child tablet (100 mg/20 mg)	Single-strength adult tablet (400 mg/80 mg)	Double-strength adult tablet (800 mg/160 mg)
<6 months or <5 kg: 100 mg SMX/ 20 mg TMP	2.5 ml PO OD	One tablet PO OD mixed with feed or small amount of milk or water	¼ tablet PO OD, possibly mixed with feed or small amount of milk or water[b]	–
6 months – 5 years or 5 – 15 kg: 200 mg SMX/ 40 mg TMP	5 ml[c] PO OD	2 tablets PO OD	½ tablet PO OD	–
6 – 14 years or 15 – 30 kg: 400 mg SMX/ 80 mg TMP	10 ml[b] PO OD	4 tablets PO OD	1 tablet PO OD	½ tablet PO OD
>14 years or >30 kg: 800 mg SMX/ 160 mg TMP	–	–	2 tablets PO OD	1 tablet PO OD

[a] Children with history of treated *Pneumocystis* pneumonia (PCP) should be administered secondary co-trimoxazole prophylaxis with the same regimen recommended for primary prophylaxis.
[b] Splitting tablets into quarters is not considered best practice. This should be done only if syrup is available.
[c] Children of these ages (6 months – 14 years) may swallow crushed tablets.
Source: WHO & UNICEF 2009:28.

5.2 Secondary co-trimoxazole prophylaxis

Refer to Section 12.2.1 (adults and adolescents) and Table 5.1 (infants and children) for recommendations for secondary co-trimoxazole prophylaxis[5].

5.3 Co-trimoxazole among HIV-positive pregnant and breastfeeding women

HIV-positive pregnant and breastfeeding women who fulfill the criteria for co-trimoxazole prophylaxis should be given co-trimoxazole. There is no evidence of an increase in co-trimoxazole-related adverse events among pregnant women versus non-pregnant women.

5.4 Adverse effects to co-trimoxazole

Patients should be asked about history of hypersensitivity reaction to sulpha drugs. Severe adverse reactions to co-trimoxazole are uncommon. If non-adverse events occur (Appendix 7), every effort should be made to continue prophylaxis with co-trimoxazole. Except in cases of severe adverse reaction, co-trimoxazole should be temporarily interrupted for two weeks and then desensitization should be attempted in adults and adolescents (Appendix 8), if indicated and feasible. Currently, there is insufficient information in the medical literature on co-trimoxazole desensitization among children in resource-limited settings.

For patients who cannot tolerate co-trimoxazole due to severe adverse reactions, give dapsone 100 mg PO OD for HIV-positive adults and adolescents, and dapsone 2 mg/kg PO OD for HIV-positive children.

[5] Secondary prophylaxis refers to the treatment given to prevent the recurrence or relapse of a disease.

6 Treatment preparedness of HIV-positive patients

Treatment readiness of HIV-positive patients is associated with improved adherence once treatment has commenced. In the context of ART, adherence would mean that there is a collaborative process between the patient and the health care provider. The patient plays a more active role in his treatment and makes a commitment to follow the prescribed regimen as best as possible. Adherence to ART greater than 95% is needed to achieve virologic success. In contrast, compliance implies lack of patient participation in the treatment.

Enrollment into care before the time of ART initiation provides an opportunity for the PLHIV to learn, understand, and prepare for successful lifelong ART. Box 6.1 lists down the important points that need to be discussed with the patient before ART initiation.

Box 6.1 Checklist for patient education and ARV adherence counselling for HIV-positive patients before ART initiation

Patient assessment
Medical history
Knowledge of HIV/AIDS
Prior use of ART and other Drugs
Treatment as prevention
Determine social support
Disclosure – Has the patient disclosed his/her HIV status to anyone?
HIV status of partner and members of the family
Alcohol/drug use/smoking
Mental state
Treatment as Prevention (Discordant Couples)
Review health status
Opportunistic infections and WHO clinical staging
CD4 count, viral load, and other relevant investigations
Review living conditions and employment
Housing
Employment/income
Discuss the treatment program and importance of adherence
Need for continued prevention – condom use, ART
Cost (if applicable)
Side effects of ARVs and what to do
Follow-up – clinical and laboratory investigations, e.g. CD4 count, viral load (if required)
Importance of adherence and consequences of non-adherence
Discuss adherence promotion strategies
Discuss role of treatment support person/caregiver
Adherence tools – pill diary, pill calendar, alarm clocks, mobile phones, pill boxes, etc.
Ongoing adherence counselling
Identify barriers to adherence
Side effects
Poor communication
Low literacy
Inadequate understanding about HIV/AIDS
Lack of social support (family, friends, community)
Failure to disclose HIV status
Alcohol/drug use/smoking
Alternative treatment, e.g. natural/traditional, faith-based
Mental state

7 Antiretroviral therapy

7.1 Goals of ART

Antiretroviral therapy refers to the combination of antiretroviral (ARV) drugs that are active against the human immunodeficiency virus (HIV).

Most of ARV drugs act by inhibiting the enzymes that are needed for HIV replication – reverse transcriptase, integrase, and protease.

The goals of ART are:

- Maximal and durable suppression of viral load;
- Restoration and/or preservation of immunological function;
- Reduction of HIV-related morbidity, mortality and improvement of quality of life; and
- Prevention of HIV transmission.

ART can rapidly suppress HIV replication leading to a rapid fall in the number of viral particles in the blood **(viral load)**. Thus, the impact of HIV on the immune system is reduced and gradual restoration of immune function **(CD4 cell count or %CD4)** occurs.

ART is not a cure, but it suppresses long-term HIV replication in the body. If ART is ceased, HIV replication returns to pre-treatment levels and promptly begins to damage the immune system once again. Therefore, once ART is commenced, it is generally continued for life.

HIV develops spontaneous genetic mutations at a very high rate. As the virus multiplies, the newly-formed virus is often slightly different from the "parent" virus. This is called **mutation**. The mutant viruses are more successful in multiplying and surviving in the presence of ARVs **(viral resistance)**, rendering treatment less effective. Effective ART reduces the rate of development of these mutations (and resistance) by continuously suppressing the viral load.

7.2 ARV drug classes

To date, the currently available ARV drugs can be divided into five classes:

- Entry inhibitors;
- Nucleoside reverse transcriptase inhibitors (NRTIs);
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs);
- Integrase inhibitors; and
- Protease inhibitors (PIs).

Table 7.1 lists down the ARV drug classes, mechanisms of action of ARV drugs and examples for each ARV drug class. Figure 7.1 illustrates the sites of action of currently available ARV drugs in relation to specific stages in the HIV replication cycle.

Table 7.1 Mechanisms of action of antiretroviral drugs[a]

Antiretroviral drug class	Mechanism of action	Examples
1. Entry inhibitors	Prevent HIV from entering into CD4 cells and infecting them	
a. Fusion inhibitors	Prevent conformational change of gp41before fusion of HIV to CD4 target cell occurs	enfuvirtide (T-20)
b. Chemokine receptor antagonists	Blocks the CCR5 co-receptors in CD4 cells which are necessary for HIV entry	maraviroc (MVC)
2. Nucleoside reverse transcriptase inhibitors (NRTIs)	Terminate the growing HIV DNA chain	Tenofovir (TDF)[b], zidovudine (AZT), lamivudine (3TC), emtricitabine (FTC), abacavir (ABC), didanosine (ddI)
3. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Inhibit the conversion of HIV RNA to HIV DNA	efavirenz (EFV), nevirapine (NVP)
4. Integrase inhibitors	Prevents the integration of HIV DNA to the human genome	raltegravir (RAL)
5. Protease inhibitors (PIs)	Prevent maturation of HIV	lopinavir/ritonavir (LPV/r)

[a] Currently, the Fiji Pharmaceutical and Biomedical Services (FPBS) procures ARV drugs that belong to three drug classes: NRTI, NNRTI, and PI.

[b] Strictly speaking, based on its chemical structure, TDF is a nucleotide rather than a nucleoside. For simplicity, in these guidelines, NRTI also refers to nucleotide reverse transcriptase inhibitor (TDF).

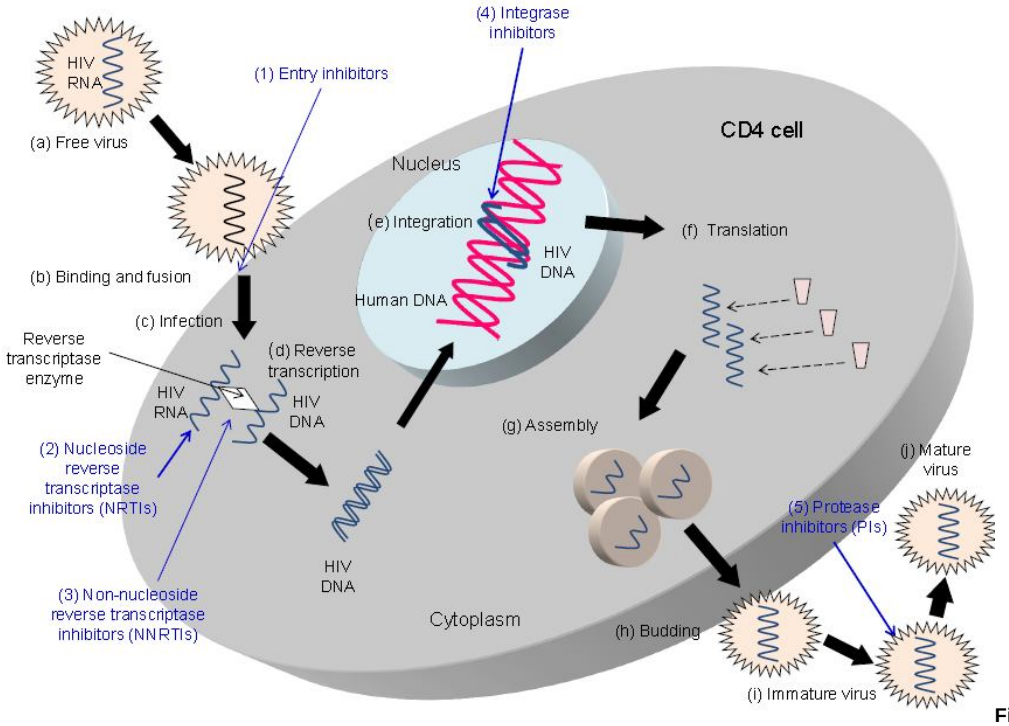


Figure 7.1

The sites of action of antiretroviral drugs in relation to the HIV life cycle.

The stages of the HIV life cycle are denoted by small case letters, while the site of action of antiretroviral (ARV) drug classes are denoted by numbers (that correspond to Table 7.1).

7.3 Principles of ART

A combination of at least three drugs is now the standard treatment for HIV-positive patients. To minimize the potential development of viral resistance, drugs from two ARV classes should be used. The basic backbone of the ARV regimen is a combination of two NRTIs. The third ARV drug will either be a NNRTI or a PI. The combination of two NRTIs + one NNRTI is the preferred combination for first-line ART. The combination of two NRTIs + one PI is reserved for second-line ART. In special circumstances, a triple NRTI regimen may be considered, such as in the treatment of HIV-positive patients co-infected with TB. However, triple NRTI is less effective compared to combinations of three ARV drugs from two ARV drug classes. Single or dual ART is never appropriate due to the rapid development of viral resistance.

Currently, the Fiji Pharmaceutical and Biomedical Services (FPBS) procure ARV drugs that belong to three ARV drug classes: NRTI, NNRTI, and PI. In constructing an ARV drug regimen, health care providers should be guided by the principles of ART outlined in Box 7.1.

Box 7.1 Principles of antiretroviral therapy

- At least three ARV drugs should be used
- The three drugs should belong to two ARV drug classes
- Two NRTIs serve as the backbone of the ART

Possible ART:

ARV regimen 1	2 NRTIs	+	1 NNRTI
ARV regimen 2	2 NRTIs	+	1 PI
ARV regimen 3	3 NRTIs	(does not fulfill all the above pre-requisites; least effective)	

Table 7.2 (for HIV-positive adults and adolescents) and Table 7.3 (for HIV-positive infants and children) list down the ARV drugs that are currently available at FPBS.

Table 7.2 Antiretroviral drugs for HIV-positive adults and adolescents[a]

ARV drug class	Drug	Dose	Drug administration and storage	Adverse effects
Nucleoside reverse transcriptase inhibitors (NRTIs)	Tenofovir (TDF)[a]	300 mg PO OD	No food restrictions; must reduce dose if patient has renal dysfunction	Mild side effects; some nausea, vomiting, loss of appetite, renal impairment, lactic acidosis with hepatic steatosis
	Zidovudine (AZT)	300 mg PO BD	No food restrictions	Anaemia, nausea, vomiting, headache, fatigue, muscle aches, bone marrow toxicity, lactic acidosis with hepatic steatosis, body fat changes[b]
	Lamivudine (3TC)	150 mg PO BD or 300 mg PO OD	No food restrictions	Nausea, vomiting, fatigue, headaches, lactic acidosis with hepatic steatosis, body fat changes[b]
	Abacavir (ABC)	300 mg PO BD or 600 mg PO OD	No food restrictions; alcohol boosts abacavir levels	Hypersensitivity reaction in about 5-8% of patients; if hypersensitivity occurs, do not re-challenge at any time
	Didanosine (ddI)	For body weight ≤60 kg: 250 mg PO OD For body weight >60 kg: 400 mg PO OD	Chew or dissolve in water; take on empty stomach; not within 2.5 hours of ritonavir (RTV)	Diarrhoea, pancreatitis, abdominal pain, neuropathy, nausea and vomiting, lactic acidosis with hepatic steatosis, body fat changes[b]
	Emtricitabine (FTC)	200 mg PO OD	No food restrictions	Headache, diarrhoea, nausea and rash, lactic acidosis with hepatic steatosis, body fat changes[b]
Non-nucleoside reverse transcriptase inhibitor (NNRTIs)	Efavirenz (EFV)	600 mg PO OD	Take on an empty stomach before going to sleep	Headached, dizziness, insomnia, anxiety, vivid dreams, hallucinations (usually transient and lasts for 3 weeks) , rash, nausea, diarrhoea
	Nevirapine (NVP)	200 mg PO OD for the first 14 days then 200 mg PO BD thereafter	No food restrictions	Skin rash, fever, headache, nausea, elevated liver enzymes; be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatotoxicity.
Protease inhibitor (PIs)	Lopinavir/ritonavir (LPV/r)	200 mg lopinavir (LPV) + 50 mg ritonavir (RTV), 2 tablets PO BD	No food restrictions; take liquid formulation with food. Keep at room temperature.	Diarrhoea, fatigue, headache, nausea, taste perversion, perioral and circumoral paresthesia

[a] Fixed-dosed combinations (FDC) of antiretroviral drugs are listed in Appendix 9.

[b] The association with NRTIs with body fat changes varies from drug to drug.

Table 7.3 Antiretroviral drugs for HIV-positive infants and children[a]

ARV drug class	Drug	Formulation	Dose	Side effects	Notes
Nucleoside reverse transcriptase inhibitors (NRTIs)	Zidovudine (AZT)	*Liquid:* 10 mg/ml *Capsule:* 100 mg, 250 mg *Tablets:* 60, 300 mg	*Target dose[b]:* 180 – 240 mg/m^2 per dose given PO BD (total daily dose of 360 – 480 mg/m^2); maximum daily dose of 300 mg PO BD; *PMTCT dose (from birth to 6 weeks):* <2,000 g, starting dose of 2 mg/kg PO OD; 2,000 – 2,499 g, 10 mg PO BD; ≥2,500 g, 15 mg PO BD	Anaemia, neutropaenia, headache, myopathy, myositis, lactic acidosis (uncommon)	Can be given with food; store at room temperature
	Lamivudine (3TC)	*Liquid:* 10 mg/ml *Tablet:* 150 mg	<30 days of life: 2 mg/kg/dose PO BD >30 days of life: 4 mg/kg/dose PO BD Weight >50 kg: 150 mg PO BD	Headache, fatigue, nausea, skin rash, abdominal disturbances; pancreatitis, peripheral neuropathy, neutropaenia, lactic acidosis (uncommon)	Can be given with food; store at room temperature
	Abacavir (ABC)	*Liquid:* 20 mg/ml *Tablet:* 60 mg, 30 mg *Capsule:* none	*Target dose:* 8 mg/kg/dose PO BD for age <16 years or weight <37.5 kg to a maximum dose 300 mg/day PO BD	Nausea, vomiting, fever, headache, diarrhea, anorexia, hypersensitivity rash (5%), pancreatitis, lactic acidosis	Can be given with food; store at room temperature *Do not re-challenge after hypersensitivity*
	Tenofovir (TDF)	*Oral powder:* 40 mg per 1 g of oral powder (1 level scoop = 1 g oral powder; supplied with dosing scoop)	≥2 to <12 years: 8 mg/kg/dose PO OD ≥12 years and weight ≥35 kg (same as adult dose): 300 mg PO OD	Diarrhoea, abdominal pain, nausea, vomiting, peripheral neuropathy, pancreatitis, lactic acidosis, ↑ liver enzymes (uncommon)	Measured oral powder only with the supplied dosing scoop. Mix oral powder with food that does not require chewing. Administer immediately after mixing.
Non-nucleoside reverse transcriptase inhibitor (NNRTIs)	Nevirapine (NVP)[c]	*Liquid:* 10 mg/ml *Tablets:* 50 mg, 200 mg	*Maintenance dose:* 160 – 200 mg/m^2 to maximum dose of 200 mg PO BD *Induction dose:* ½ of the maintenance dose OD for the first 14 days then full maintenance dose BD thereafter *Target dose for PMTCT:* Birth to 6 weeks of age Weight <2.5 kg: 10 mg/day PO Weight >2.5 kg: 15 mg/day PO 6 weeks to 6 months: 20 mg/day PO 6 months to 9 months: 30 mg/day PO 9 months to end of breastfeeding: 40 mg/day PO	Rashes, Stevens-Johnson syndrome, ↑ liver enzymes, hypersensitivity, hepatitis, fulminant hepatitis (less common)	Can be given with food; store at room temperature *Watch for liver toxicity*
	Efavirenz (EFV)[e]	*Liquid:* 30 mg/ml *Tablet :* 600 mg *Capsules:* 50 mg, 100 mg, 200 mg	*Target dose:* Syrup: 19.5 mg/kg/day PO OD Capsule or tablet: 15 mg/kg/day PO OD Weight >40 kg: 600 mg PO OD	Rash (mild), ↑ liver enzymes, somnolence, abnormal dreams, insomnia, confusion, impaired concentration, hallucination, euphoria, amnesia, agitation, abnormal thinking	Can be given with food; store at room temperature; administer at night; contraindicated in children <3 years of age
Protease inhibitor (PIs)	Lopinavir/ ritonavir (LPV/r)	*Liquid:* LPV (80 mg/ml) + RTV (20 mg/ml) *Paediatric tablet:* LPV 100 mg /RTV 25 mg *Adult tablet:* LPV 200 mg/ RTV 50 mg	*Lopinavir target dose:* 230 – 350 mg/m^2 PO BD *Maximum dose:* LPV 400 mg + RTV 100 mg PO BD	Nausea, vomiting, diarrhoea, abdominal pain, headache, anorexia, lipid abnormalities, lipodystrophy syndrome, diabetes mellitus, haemolytic anaemia, pancreatitis, hepatitis (less common)	Give with food; a high fat meal increases absorption; oral suspension should be refrigerated, but remains stable at room temperature for 2 months

[a] If available, fixed-dose combination paediatric formulations are recommended to be prescribed to patients. Formula for calculating body surface area (Mosteller): BSA (m^2) $= \sqrt{\frac{height(cm) \times weight(kg)}{3{,}600}}$.

[b] For children suspected of nervous system involvement, it may be beneficial to use a dose at the higher end of the range. [c] Nevirapine (NVP) should be used with caution in postpubertal adolescent boys and girls (considered as adults for treatment purposes) with baseline CD4 count of >250 cells/mm^3 (for girls) or with baseline CD4 count >400/mm^3 (for boys), because of increased risk of developing hypersensitivity and hepatotoxicity.

7.4 Requirements before ART initiation

ART is vital for survival of HIV-positive patients. However, eradication of HIV is not possible with current antiretroviral therapies. Patients and health care workers engaged in HIV care have to deal with life-long treatment. As such, there are requirements that need to be met before ART is initiated (Box 7.2).

Box 7.2 Requirements before initiating ART

- Written documentation of a confirmed positive HIV test result
- Eligibility criteria (refer to Sections 7.5.1 and 7.5.2)
- Assessment and management of opportunistic infections, HIV-related conditions and other medical problems
- Treatment or stabilization of any opportunistic infection
- Patient's readiness for ART
- Supportive team prepared for chronic care of the patient
- Sustainable and available supply of antiretroviral drugs

7.5 When to start ART

7.5.1 When to start ART in HIV-positive adults and adolescents (≥10 years of age)

- WHO clinical stage 3 or 4 regardless of the CD4 cell count
- CD4 cell count ≤500 cells/mm^3 regardless of the WHO clinical stage
- Regardless of the WHO clinical stage or CD4 cell count, initiate ART in
  - Pregnant and breastfeeding women[6]
  - HIV/TB co-infection with active TB disease
  - HIV/hepatitis B co-infection with severe chronic liver disease[a]
  - HIV-positive individuals in an established serodiscordant relationship[b]

[a] Refer to Section 7.7.

[b] The partner is HIV-negative.

7.5.2 When to start ART in HIV-positive infants and children

- Infants and children <5 years of age regardless of the WHO clinical stage or CD4 cell count
- Children ≥5 years of age
  - WHO clinical stage 3 or 4 regardless of the CD4 cell count
  - CD4 cell count ≤500 cells/mm^3 regardless of the WHO clinical stage
  - HIV/TB co-infection with active TB disease
- Any infant or child <18 months of age who has been given a presumptive diagnosis of HIV infection until the child is proven HIV-negative (refer to Section 10.2.1 for further discussion)

[6] For breastfeeding women, they need to be either legal or defacto partners as per definition in the Family Law (amendment) Decree 2012.

7.6 What ART to start

7.6.1 First-line ART recommendations for adults and adolescents (10 – 19 years, ≥35 kg) including pregnant and breastfeeding women

- *Standard first-line ART:*
  - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + efavirenz (EFV) 600 mg PO OD
- *Alternative first-line ART:*
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + efavirenz (EFV) 600 mg PO OD
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + nevirapine (NVP)[b] PO 200 mg OD for the first 14 days then 200 mg BD thereafter
  - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + nevirapine (NVP) 200 mg PO OD for 14 days then 200 mg PO BD thereafter

[a] Emtricitabine (FTC) 200 mg PO OD can be used instead of 3TC. Both drugs have comparable pharmacological profiles.
[b] Be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatotoxicity.

The recommended first-line ART for adults, adolescents and children is a triple therapy consisting of two NRTIs + one NNRTI. The use of fixed-dose combinations (FDC) is recommended to be prescribed to the patient whenever possible to enhance patient's drug adherence.

7.6.2 First-line ART recommendations for infants and children

- *For infants and children <3 years of age:*
  - *Standard first-line ART:*
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + nevirapine (NVP) 160 – 200 mg/m^2/dose PO OD for the first 14 days then BD thereafter
  - *Alternative first-line ARV drug regimen:*
    - Zidovudine (AZT)[a] + 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + lopinavir/ritonavir (LPV/r), LPV target dose: 230 – 350 mg/m^2 PO BD
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + abacavir (ABC) 8 mg/kg/dose PO BD
- *For children 3 years and <10 years of age and adolescents <35 kg:*
  - *Standard first-line ART:*
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + efavirenz (EFV) 19.5 mg/kg/day (liquid) PO OD or 15 mg/kg/day (capsule/tablet) PO OD
  - *Alternative first-line ART:*
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + nevirapine (NVP) 160 – 200 mg/m^2/dose PO OD for the first 14 days then BD thereafter
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + abacavir (ABC) 8 mg/kg/dose PO BD

7.7 HIV/TB co-infection

7.7.1 Decreasing the burden of TB among PLHIV

Tuberculosis (TB) is a leading cause of death and a common presenting illness among PLHIV. Likewise, HIV is more common among TB patients than among the general population. For this reason, HIV/TB co-infection should be diagnosed as early as possible through HIV testing of TB patients TB, and TB screening for PLHIV. Therefore, collaboration between HIV and TB programs through cross-referral of patients is essential (Box 7.3).

Box 7.3 Measures to decrease the burden of TB among people living with HIV (the 3Is)

- ***I**ntensive case finding:*
  - All HIV-positive patients should be screened for TB at each clinical encounter or at each visit at the health care facility.
- ***I**soniazid preventive therapy (IPT)[a, b] for HIV-positive adults and children*
  - If active TB is ruled out, start isoniazid (INH) 5 mg/kg PO OD (to a maximum of 300 mg PO OD) as prophylaxis for 6 months in adults.
  - Children living with HIV >12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case, start isoniazid (INH) at 10 mg/kg/day for 6 months.
  - Children living with HIV <12 months of age who have contact with a TB case and shows no active TB after investigations should receive isoniazid (INH) at 10 mg/kg/day for 6 months.
  - After successful completion of treatment for TB disease, all children living with HIV should receive isoniazid (INH) at 10 mg/kg/day for an additional 6 months.
- *TB **i**nfection control*
  - Prevent PLHIV from being infected or re-infected with TB at health care facilities.

[a] Mantoux test is not a requirement for initiating IPT in PLHIV. PLHIV who have a positive Mantoux test result benefit more from IPT.
[b] Providing IPT to PLHIV does not increase the risk of developing isoniazid-resistant TB.
Adapted from WHO 2013a:160.

7.7.2 Recommendations for treatment of HIV/TB co-infection in adults and adolescents (≥10 years) including pregnant and breastfeeding women

- Start ART in all HIV-positive individuals with active TB regardless of the WHO clinical stage or CD4 cell count
- Start TB treatment first, followed by ART as soon as possible between 2 – 8 weeks
- *Standard first-line ART:*
  - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + efavirenz (EFV) 600 mg PO OD
- *Alternative first-line ART:*
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + efavirenz 600 mg PO OD
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + nevirapine (NVP)[b] 200 mg PO OD for the first 14 days then 200 mg BD thereafter
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + abacavir (ABC) 300 mg PO BD

[a] Emtricitabine (FTC) 200 mg PO OD can be used instead of 3TC. Both drugs have comparable pharmacological profiles.
[b] Be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatotoxicity.

ART in individuals undergoing TB treatment is challenging because of overlapping drug toxicities of ARV drugs and anti-TB drugs, as well as increased pill burden, adherence issues, and possible development of immune reconstitution inflammatory syndrome (IRIS). Health care workers should seek expert advice when faced with these clinical situations.

Studies have shown that co-trimoxazole prophylaxis decreases the morbidity and mortality of adults and children with HIV/TB co-infection.

7.7.3 Recommendations for treatment of HIV/TB co-infection in children

- Start ART as soon as tolerated at 2 – 8 weeks of TB therapy, regardless of the WHO clinical stage or CD4 cell count
- *Children <3 years of age:*
  - Standard first-line ART:
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + nevirapine (NVP)[a] 160 – 240 mg/m^2/dose PO OD for the first 14 days then BD thereafter
  - Alternative first-line ART:
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + abacavir (ABC) 8 mg/kg/dose PO BD
  - If TB develops while on an ART regimen containing nevirapine (NVP) or lopinavir/ritonavir (LPV/r): abacavir (ABC) 8 mg/kg/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD
- *Children >3 years of age:*
  - Standard first-line ART:
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + efavirenz (EFV) 19.5 mg/kg/day (liquid) PO OD or 15 mg/kg/day (capsule/tablet) PO OD
  - Alternative first-line ART:
    - Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + [a]bacavir (ABC) 8 mg/kg/dose PO BD
  - If TB develops while on ART:
    - If receiving efavirenz (EFV), continue the same ARV drug regimen;
    - If receiving nevirapine (NVP), change NVP to efavirenz (EFV); *OR*
    - Change ART to zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + abacavir (ABC) 8 mg/kg/dose PO BD

[a] Ensure that the dose of NVP is 200 mg/m^2.

7.5 Recommendations for treatment of HIV/hepatitis B co-infection

- Regardless of the WHO clinical stage or CD4 cell count, start ART in all patients with HIV/hepatitis B co-infection with severe decompensated chronic liver disease, i.e. clinical evidence of portal hypertension (ascites, variceal haemorrhage and hepatic encephalopathy) or liver insufficiency (jaundice).
- *First-line ART:*
  - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + efavirenz (EFV) 600 mg PO OD

[a] Emtricitabine (FTC) 200 mg PO OD can be used instead of 3TC. Both drugs have comparable pharmacological profiles.

8 Patient monitoring

8.1 Routine monitoring

8.1.1 CD4 cell count monitoring

CD4 cell count should be measured as early as possible. It guides the clinician in deciding when to start ART. It is the best indicator for gauging the status of the immune system and for determining whether the HIV-positive patient is at risk of certain opportunistic infections. The higher the CD4 count, the risk for OIs will be lower. However, HIV-positive patients may be initiated on ART using the WHO clinical staging.

It is recommended to **monitor CD4 cell counts every 6 months**, whether the patient is on ART or not. Patients should be informed that CD4 cell counts are variable. Caution patients not to pin emotions and hopes to a single laboratory result. A change of <30% may not be significant. Implausible CD4 cell count results should be re-checked after 2 to 4 weeks.

8.1.2 Viral load monitoring

It is recommended to **monitor viral load every 6 months**, whether the patient is on ART or not. For most patients on effective ART, the CD4 cell count will rise as the viral replication is suppressed **(decreased viral load)**. Patients should understand that undetectable viral load does not mean that HIV has been completely eradicated or that the patient is not infectious to others.

8.1.3 Clinical monitoring

Clinical assessment of the patient at each clinic visit (whether on ART or not) as well as monitoring the patient's adherence to ARV drugs will provide valuable information on patient's response to ART. CD4 cell count and viral load testing complement clinical monitoring of patients.

Symptom-directed laboratory monitoring for safety and toxicity is recommended for those on ART. For example, serum creatinine and estimated glomerular filtration rate (eGFR) may need to be monitored in patients on tenofovir (TDF); haemogoblin in patients on zidovudine (AZT); and serum alanine transferase (ALT) in those patients on nevirapine (NVP).

HIV-exposed and HIV-positive infants and children will need to be assessed for growth, development and nutritional status at each clinical visit.

Findings of clinical assessment and laboratory findings should be discussed with patients, treatment support persons and caregivers. They should be provided with appropriate advice, management, and referral to the relevant health and support service that are required.

Provide a schedule for the next laboratory tests as well as for the date of the next clinic follow-up.

Table 8.1 provides a recommended schedule for clinical and laboratory monitoring of HIV-positive patients not initiated with ART (i.e. on HIV care) and for those who are on ART.

Table 8.1 Recommende√d schedule of clinical and laboratory monitoring for HIV care and ART

What to monitor	Before ART	At start of ART	Wk[a] 2	Wk 4	Mo[b] 2	Mo 3	Mo 6	Mo 12	As needed
Clinical assessment									
Infants	✓	✓	✓	q[c]	✓	q			✓
Children	✓	✓	✓	✓	✓	q			✓
Adults	✓	✓	✓	✓	✓	q			✓
Weight (and height in children)[d]	✓	✓	✓	✓	✓	q			✓
ART adherence	✓	✓	✓	✓	✓	q			✓
ARV side effects	✓	✓	✓	✓	✓	q			✓
Concomitant medications	✓	✓	✓	✓	✓	q			✓
CD4 cell count (%CD4)	q 6 mo[e]	✓					q		✓
Viral load	Q 6 mo[f]	✓					q		✓
Serum creatinine (if on TDF[g])	✓	✓		✓	✓	q			✓
eGFR (if on TDF[g])	✓	✓		✓	✓	q			✓
Urine dipstick for glycosuria (if on TDF[g])	✓	✓		✓	✓	q			✓
Haemoglobin (if on AZT[h])	✓	✓		✓		q		✓	✓
Serum ALT (if on NVP[i])	✓	✓		✓		✓			✓
Blood sugar	✓	✓						q	
Serum cholesterol & triglycerides	✓	✓						q	
Fundoscopy with eye specialist	✓	✓					✓		
Oral health	✓	✓					✓		
Electrocardiogram (if on LPV/r[k])		✓						✓	
Echocardiogram									q 3 yr[l]
Paps Smear Testing	√							√	√

[a] Wk – week; [b] Mo – month; [c] q – every; for example, "every 4 weeks or every month".

[d] Recalculate doses of ARV drugs at each clinic visit.

[e] Every 6 months before ART is initiated and at start of ART. Once the patient is on ART, monitor CD4 cell count every 6 months and if need arises

[f] Every 6 months before ART is initiatied and at start of ART. Once the patient is on ART, monitor viral load every 6 months.

[g] TDF – tenofovir. A better measurement of kidney function is to estimate the creatinine clearance using Cockroft-Gault formula which, in turn, estimates glomerular filtration rate (GFR) in ml/min (normal: >90 ml/min/1.73 m^2). Cockcroft-Gault formula $= \frac{(140 - age) \times weight(kg)}{serumcreatinine(\mu mol/L)}$. For male patients, multiply result by 1.23; for female patients, multiply result by 1.04. High risk people for adverse events associated with TDF are patients with underlying renal disease, older age group, low body mass index (BMI), diabetes, hypertension and concomitant use of a boosted protease inhibitor (i.e. lopinavir/ritonavir, LPV/r) or potential nephrotoxic drugs.

[h] AZT – zidovudine.

[i] NVP – nevirapine.

[k] LPV/r – lopinavir/ritonavir.

[l] Every 3 years.

8.2 Immune reconstitution inflammatory syndrome (IRIS)

The immune reconstitution inflammatory syndrome (IRIS) is a paradoxical phenomenon that occurs when the patient who has been initiated on ART (usually within 4 to 12 weeks) begins to have immune recovery in the setting of an untreated or not fully treated opportunistic infection or tumour. This may lead to a transient worsening of symptoms or clinical status, despite favourable recovery of the immunological status (improvement in the CD4 cell count or %CD4). When this occurs, all efforts must be made to find, diagnose and treat the opportunistic infection or tumour. The diagnostic criteria for IRIS are outlined in Box 8.1. The general management of IRIS includes treatment of the causative pathogen to decrease the antigenic load, continuation of ART, and the use of anti-inflammatory agents (Figure 8.1).

Box 8.1 Diagnostic criteria for immune reconstitution inflammatory syndrome (IRIS)

- Clinical manifestations are noted usually within the first 4 – 12 weeks after ART initiation
- Documented improvement in the immune status, i.e. increase in CD4 cell count (%CD4)
- No evidence of new infectious process or drug toxicity
- Patient has been previously treated for the HIV-related disease or "unmasking" of a previously undiagnosed infection
- Clinical evidence of inflammatory condition; may present in two forms:
  - *Paradoxical IRIS:* when an opportunistic infection the OI or tumour that was successfully controlled and on continued treatment worsens a few weeks after ART initiation.
  - *Unmasking IRIS:* in which initiating ART triggers disease that was not clinically apparent before ART.

Adapted from Schwarzwald H, Gillespie S 2010:80; WHO 2013a:90.

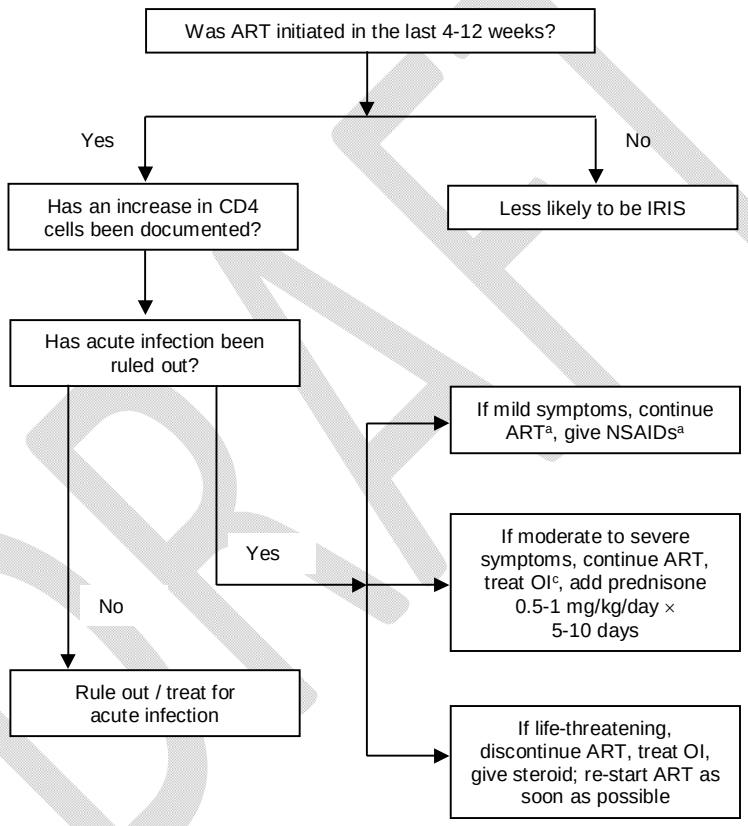


Figure 8.1 Algorithm for the diagnosis and management of immune reconstitution inflammatory syndrome, IRIS (Adapted from Schwarzwald H, Gillespie S 2010:80).

[a] ART – antiretroviral therapy; [b] NSAIDs – non-steroidal anti-inflammatory drugs; [c] OI – opportunistic infection.

8.3 Antiretroviral drug toxicities

8.3.1 General principles

Drug-related toxicities may occur during any stage of ART, and may vary in severity from mild to severe and can be life-threatening. In general, mild toxicities may be managed symptomatically without interruption of treatment. More severe toxicities may require a change in ART regimen. Life-threatening adverse reactions necessitate temporary cessation of the entire ART regimen until the toxicity has resolved (Box 8.2). Before concluding that ARV drugs are the primary cause of toxicity, alternative explanations for toxicity must be excluded. Adverse reactions that have a non-ARV drug etiology do not require changing the drug.

Box 8.2 Guiding principles in the management of ARV drug toxicity

- Determine the seriousness of the toxicity.
- Evaluate concurrent medications and establish whether the toxicity is attributable to an ARV drug or drugs, or to a non-ARV medication taken at the same time.
- Consider other disease processes (e.g. viral hepatitis in an individual on ARV drugs who developed jaundice) because not all problems that arise during treatment are caused by ARV drugs.
- Manage the adverse event according to severity. In general:
  - *Mild reactions:* These are bothersome but do not require change in therapy.
  - *Moderate reactions:* Consider continuing ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitutions. For a few moderate toxicities (e.g. peripheral neuropathy or lipodystrophy), single drug substitution needs to be considered earlier.
  - *Severe reactions:* Substitute the offending drug without stopping ART.
  - *Severe life-threatening reactions:* Immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and re-introduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.
- Stress the maintenance of adherence despite toxicity for mild and moderate reactions.
- If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilized.

Adopted from WHO 2011:80.

Where toxicity is the reason for changing the regimen, and the offending drug is known, this agent alone can be replaced, using another drug that does not have the same toxicity profile. Whenever possible, a single drug substitution because of toxicity should be with a drug belonging to the same ARV drug class.

8.3.2 Management of antiretroviral drug toxicities

Table 8.2 Toxicities associated with selected antiretroviral drugs

Antiretroviral drug	Major types of toxicity	Risk factors	Suggested management
Tenofovir (TDF)	Tubular renal dysfunction, Fanconi syndrome	Underlying renal disease Older age BMI <18.5 (or body weight <50 kg) Untreated diabetes mellitus Untreated hypertension Concomitant use of nephrotoxic drugs or boosted PI	If TDF is being used in first-line ART, substitute TDF with zidovudine (AZT) or abacavir (ABC) If TDF is being used in second-line ART (after AZT use in first-line ART), substitute TDF with abacavir (ABC) or didanosine (ddI)

Antiretroviral drug	Major types of toxicity	Risk factors	Suggested management
	Decreases in bone mineral density	History of osteomalacia and pathological fracture Risk factors for osteoporosis or bone loss	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to NRTIs Obesity	
	Exacerbation of hepatitis B (hepatic flares)	Discontinuation of TDF due toxicity	Use alternative drug for hepatitis B treatment (entecavir)
Zidovudine (AZT)	Anaemia, neutropaenia, myopathy, lipoatrophy or lipodystrophy	Baseline anaemia or neutropaenia CD4 count ≤200 cells/mm^3	If AZT is being used in first-line ART, substitute AZT with tenofovir (TDF) or abacavir (ABC) If AZT is being used in second-line ART, substitute with ddI (didanosine)
	Lactic acidosis or severe hepatomegaly with steatosis	Body mass index (BMI) >25 or body weight >75 kg) Prolonged exposure to NRTIs	
Efavirenz (EFV)	Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion)	Depression or other mental disorder (previous or at baseline) Daytime dosing	Substitute EFV with nevirapine (NVP) If the person cannot tolerate either EFV or NVP, use lopinavir/ritonavir (LPVr)
	Hepatotoxicity	Underlying hepatic disease – hepatitis B and hepatitis C co-infection Concomitant use of hepatotoxic drug	
	Convulsions	History of seizure	
	Hypersensitivity reaction, Stevens-Johnson syndrome Potential risk of neural tube birth defects (very low risk in humans) Male gynaecomastia	Risk factors unknown	
Nevirapine (NVP)	Hepatotoxicity	Underlying hepatitic disease Hepatitis B and hepatitis C co-infection Concomitant use of hepato-toxic drugs CD4 >250 cells/mm^3 in women CD4 >400 cell/smm^3 in men First month of ART (if loading dose of NVP is not used)	Substitute NVP with efavirenz (EFV). If the person cannot tolerate either NPV and EFV, use lopinavir/ritonavir (LPV/r)
	Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	Risk factors unknown	

Antiretroviral drug	Major types of toxicity	Risk factors	Suggested management
Abacavir (ABC)	Hypersensitivity reaction	Presence of HLA-B*5701 gene	If ABC is being used in first-line ART, substitute ABC with tenofovir (TDF) or zidovudine (AZT) If ABC is being used in second-line ART, substitute ABC with tenofovir (TDF)
Didanosine (ddI)	Pancreatitis	Renal failure Alcohol abuse Obesity History of pancreatitis Hypertriglyceridaemia Cholelithiais Concurrent use of hyroxyurea, allopurinol	If ddI is used as second-line ART, substitute with zidovudine (AZT) or TDF (tenofovir)
Lopinavir/ ritonavir (LPV/r)	ECG abnormalities (PR and QT interval prolongation, torsades pointes)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR interval	If LPV/r is used in first-line ART for children, substitute LPV/r with nevirapine (NVP) in children <3 years of age and with efavirenz (EFV) for children ≥3 years of age. If LPV/r is used in second-line ART for adults, use atazanavir/ritonavir (ATV/r).
	QT interval prolongation	Congenital long QT syndrome Hypokalaemia Concomitant use of drugs that May prolong the QT Interval	
	Hepatotoxicity	Underlying hepatic disease Hepatitis B and hepatitis C co-infection Concomitant use of hepatotoxic drugs	
	Pancreatitis	Advanced HIV disease	
	Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidaemia or severe diarrhoea	Risk factors unknown	

Adapted from WHO 2013a:138-141.

8.4 Treatment failure

Treatment failure can be classified as clinical failure, immunological failure, or virological failure (Box 8.3). An individual must be taking ART for at least six months and the drug adherence is assessed to be >95% before it can be determined that a regimen has failed. Clinical events that occur before the first six months of therapy are excluded from the definition of treatment failure because they represent immune inflammatory reconstitution syndromes related to pre-existing conditions.

Before changing to second-line ART, adherence counselling is imperative. Commencement of a second-line ART should be re-considered if there is poor adherence to the first-line ART. Second-line ART is far more complex and likely to fail with poor adherence. Changing to a second-line ART is not the solution for poor drug adherence. Figure 8.2 provide two strategies for viral load testing. Both approaches can guide the clinicians in making a decision to switch to second-line ART.

Box 8.3 WHO definitions of clinical, immunological and virological failure to guide decision to switch to second-line ART

- *Pre-requisites:* Patient should be on ART for six months and ARV drug adherence is assessed to be >95%
- *Definitions*
  - Clinical failure:
    - Adults and adolescents: New or recurrent WHO clinical stage 4 condition and certain WHO clinical stage 3 diseases (pulmonary TB and severe bacterial infections)
    - Children: New or recurrent WHO clinical stage 3 or 4 with the exception of TB
  - Immunological failure:
    - Adults and adolescents:
      - CD4 count falls to the baseline (or below) *OR*
      - Persistent CD4 levels below 100 cells/mm^3
    - Children:
      - <5 years of age: Persistent CD4 levels <200 cells/mm^3 or <10%
      - ≥5 years of age: Persistent CD4 levels <100 cells/mm^3
  - Virological failure: plasma viral load >1,000 copies/ml based on 2 consecutive viral load measurements after 3 months, with adherence support

Adapted from WHO 2013a:134.

8.4.1 Recommendations for second-line ART for adults and adolescents (≥10 years) including pregnant and breastfeeding women

- *If tenofovir (TDF) was used in the first- line ART:*
  - Standard second-line ART:
    - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
  - Alternative second-line ART:
    - Abacavir (ABC) 300 mg PO BD + emtricitabine (FTC) 200 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
    - Didanosine (ddI) 250 mg (for BW[b] <60 kg) PO OD *OR* 400 mg PO OD (for BW ≥60 kg) PO OD + emtricitabine (FTC) 200 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
- *If zidovudine (AZT) was used in the first- line ART:*
  - Standard second-line ART:
    - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
  - Alternative second-line ART:
    - Abacavir (ABC) 300 mg PO BD + emtricitabine (FTC) 200 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
    - Didanosine (ddI) 250 mg (for BW <60 kg) PO OD *OR* 400 mg PO OD (for BW ≥60 kg) PO OD + emtricitabine (FTC) 200 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD
- *HIV/TB co-infection:*
  - Either one of the above relevant regimens + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 4 tablets PO BD
- *HIV/hepatitis B co-infection*
  - Zidovudine (AZT) 300 mg PO BD + tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + lopinavir 200 mg/ritonavir 50 mg (LPV/r), 2 tablets PO BD

[a] Emtricitabine (FTC) 200 mg PO OD can be used instead of 3TC. Both drugs have comparable pharmacological profiles.
[b] BW – body weight.

A boosted protease inhibitor (bPI)[7] plus two NRTIs are recommended for second-line ART in HIV-positive adults, adolescents and children. Lopinavir/ritonavir (LPV/r) is the preferred bPI.

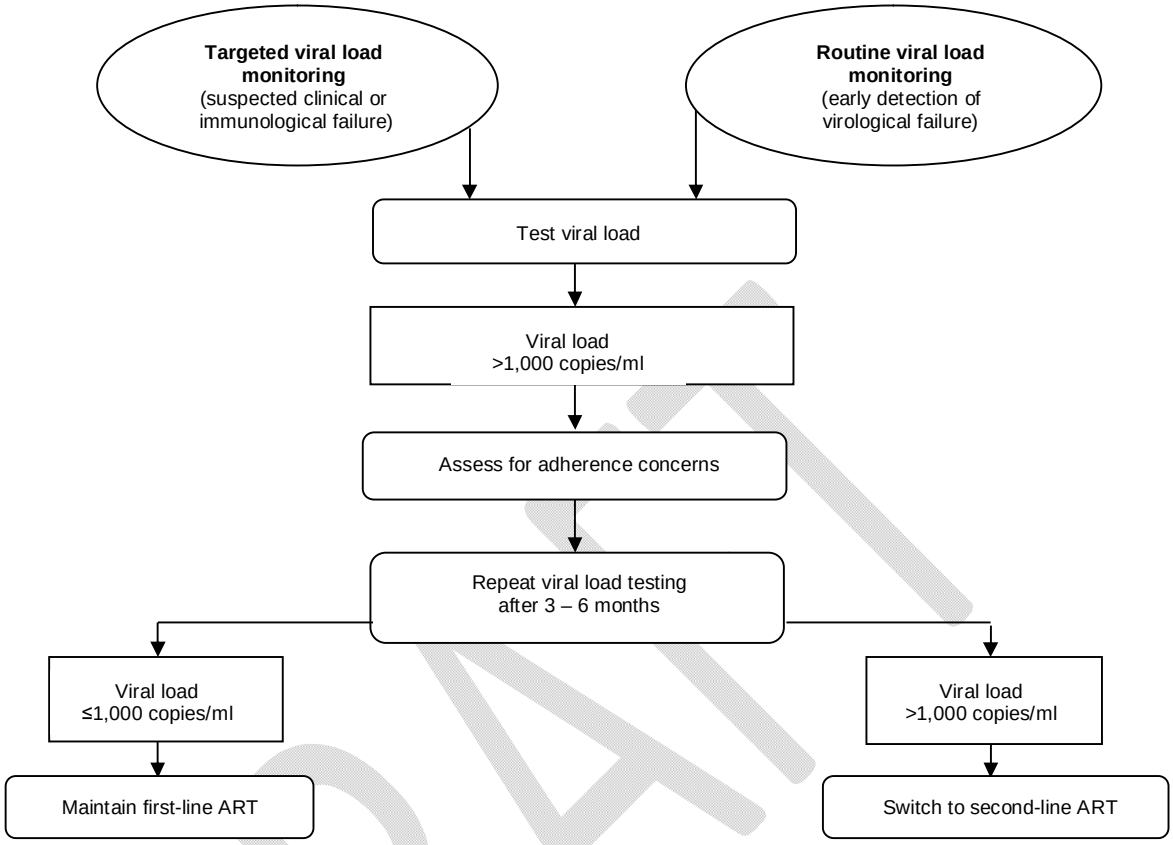


Figure 8.2 Viral load testing strategies to detect or confirm treatment failure and switch to second-line ART in adults, adolescents and children (Adopted from WHO 2013a:136).

[7] A boosted protease inhibitor (bPI) combines ritonavir (RTV) with a second "boosted" PI (lopinavir, LPV). RTV inhibits the enzyme that metabolizes LPV, thus increasing the tissue concentration and bioavailability of LPV, including HIV reservoirs. It overcomes HIV drug resistance and allow less frequent dosing, potentially improving patient's ARV drug adherence.

8.4.2 Recommendations for second-line ART for infants and children

- *Children <3 years of age*
  - If AZT + 3TC + LPV/r was used as first-line ART:
    - Preferred regimen: No change in the first-line ART
    - Alternative regimen: Zidovudine (AZT)[a] 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + nevirapine (NVP) 160 – 200 mg/m^2/dose PO OD for the first 14 days then BD thereafter
- *Children 3 to <10 years of age:*
  - If AZT (or ABC) + 3TC + EFV was used as first-line ART:
    - Preferred regimen: Zidovudine (AZT) 180 – 240 mg/m^2/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + efavirenz (EFV) 19.5 mg/kg/day (liquid) PO OD or 15 mg/kg/day (capsule/tablet) PO OD
    - Alternative regimen: Abacavir (ABC)[b] 8 mg/kg/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + nevirapine (NVP) 160 – 200 mg/m^2/dose PO OD for the first 14 days then BD thereafter
- *If either nevirapine (NVP) or efavirenz (EFV) was used as the NNRTI of the first-line ART:*
  - Preferred regimen: Abacavir (ABC) 8 mg/kg/dose PO BD + lamivudine (3TC) 4 mg/kg/dose PO BD + lopinavir/ritonavir (LPV/r), LPV target dose: 230 – 350 mg/m^2 PO BD
  - Alternative regimen: Tenofovir (TDF) 8 mg/kg/dose PO OD + lamivudine (3TC) 4 mg/kg/dose PO BD + lopinavir/ritonavir (LPV/r), LPV target dose: 230 – 350 mg/m^2 PO BD

[a] Abacavir (ABC) at 8 mg/kg/dose PO BD is an alternative.
[b] Tenofovir (TDF) 8 mg/kg/dose PO OD is an alternative. Refer to Table 7.2.

8.5 Lipodystrophy syndrome

8.5.1 Definition

Lipodystrophy syndrome is the change in body habitus due to fat redistribution. It is associated with long-term use of NRTIs (e.g. zidovudine, abacavir, didanosine); and PIs (e.g. lopinavir/ritonavir). The overlapping toxicities of NRTIs and PIs result in lipodystrophy syndrome causing metabolic abnormalities, i.e. increased blood sugar, serum cholesterol and triglycerides.

There are two mechanisms that occur in lipodystrophy syndrome:

- Lipoatrophy – leading to loss of subcutaneous fat and thinning of subcutaneous fat in the face, buttocks and extremities.
- Lipohypertrophy – deposition of fat tissue subcutaneously in the neck ("bullfrog neck"); dorsocervical spine ("buffalo hump"); breast and upper torso; and abdomen ("pot belly") increasing abdominal girth and waist-to-hip ratio.

8.5.2 Management

- Management is no different from HIV-uninfected patients with metabolic problems, e.g. diabetes mellitus.
- Monitor blood sugar, cholesterol and triglycerides at least once a year.
- Lifestyle changes – reduce saturated fat and cholesterol intake; increased physical activity; smoking cessation.
- Change antiretroviral drugs – currently, the options are quite limited. Among the available NRTIs, the degree of the risk of developing lipodystrophy syndrome is as follows: didanosine (ddI) > abacavir (ABC) > zidovudine (AZT).

- Lipid-lowering drugs – Pravastatin (dose: 20 – 80 mg OD or BD) and atorvastatin (dose: 10 – 80 mg PO OD) are preferable in HIV-positive patients with dyslipidemia.
- Oral hypoglycaemic drugs if patient develops diabetes mellitus – biguanides (metformin).

9 Management of HIV-positive pregnant and breastfeeding women

HIV can be transmitted from an HIV-positive mother to her child during pregnancy, during labour and delivery, and through breastfeeding.

The comprehensive strategy for the prevention of HIV infection in infants and children from their parents (prevention of parent-to-child transmission, PPTCT) of HIV has four prongs:

- Prevention of HIV acquisition among women of childbearing age
- Prevention of unintended pregnancies among women living with HIV
- Prevention of HIV transmission from women living with HIV to their children
- Provision of care, treatment, and support to mothers living with HIV, their children, and their families.

This section will focus on the "third prong" of the strategy, strictly speaking, prevention of mother-to-child transmission (PMTCT) of HIV. In this strategy, ARV drugs are used for HIV-positive pregnant and breastfeeding women for their own health and to prevent the exposed child from becoming infected. It may also offer benefits for preventing the sexual transmission of HIV.

9.1 Maternal services and prevention of parent-to-child transmission of HIV

To reduce mother-to-child transmission of HIV, there is a need to have a unified approach throughout pregnancy, labour and delivery, and the breastfeeding period. Box 9.1 provides a list of the essential health services where information on PPTCT interventions can be provided.

Health care providers should be guided by the principles outlined below for the different clinical situations that they may encounter in delivering care to pregnant patients.

All pregnant women should:

- Be encouraged to book early into antenatal care, as soon as they believe they are or are confirmed to be pregnant.
- Receive routine antenatal care, including micronutrient supplementation, e.g. iron and folic acid.
- Be routinely offered HIV counselling and testing, STI screening (including hepatitis B and syphilis), Paps smear and encourage partner counselling and testing (ideally, couple HIV counselling and testing).
- Be offered information on the availability of PPTCT interventions during all health care facility visits (not only during antenatal clinic visits).
- Be encouraged to involve partners in caring for pregnancy.
- Be counselled on safer sex and provided with condoms.
- Be counselled on safe infant feeding options, assisted in making an appropriate infant feeding choice, and supported on their choice

Box 9.1 PPTCT integration to essential health services

- Health education, information on HIV and STI prevention and care including safer sex practices, pregnancy including ANC, birth planning and delivery options, optimal infant feeding, family planning counselling (including desired family size and future pregnancies) and related services (e.g. contraception, Paps smear)
- HIV counselling and testing, including HIV counselling and testing for women of unknown status at labour and delivery, or postpartum
- Couple and partner HIV counselling and testing, including support for disclosure
- Promotion and provision of condoms
- HIV-related gender-based violence screening
- Obstetric care, including history-taking and physical examination
- Maternal and nutrition support
- Infant feeding counselling
- Psychosocial support
- Birth planning, birth preparedness (including pregnancy/postpartum danger signs)
- Tetanus vaccination
- Iron and folic acid supplementation
- Screening and management for syphilis, hepatitis B and other STIs
- Interventions for PPTCT for HIV-positive pregnant women with referral to appropriate care
- ART adherence counselling for women on treatment

All HIV-positive pregnant women should:

- Receive post-test counselling.
- Receive routine antenatal care, including iron and folic acid supplementation.
- Be offered information on the availability of PPTCT interventions at all health care facility visits (not only during antenatal clinic visits).
- Be referred to the hub centre as early as possible/practicable for:
  - Clinical assessment, CD4 count testing, etc.
  - Screened for STIs, TB and other opportunistic infections, and treated appropriately.
  - Offered co-trimoxazole prophylaxis and isoniazid prophylaxis, if indicated.
  - Started on ART as early as possible, managed appropriately, and monitored regularly.
  - Be counselled on safer sex, family planning, papsmear, postnatal contraception and partner testing (if not yet done); adherence to treatment, HIV care and regular clinic follow-up.

While respecting confidentiality of the mother and the child, information on a patient's HIV status, PMTCT or ART, should be shared among health care personnel that provide direct care to the patient. This is called **shared confidentiality** amongst health care workers, and is essential for maintaining continuum of care (CoC) among women and children.

Pregnant women who test HIV-negative should:

- Receive post-test counselling and counselling on risk reduction interventions including involvement of their partners, mainly focusing on how to maintain their HIV-negative status.
- Continue to receive routine antenatal care and should be encouraged to use condoms.
- Be offered a repeat HIV test 6 weeks after the initial test or at the third trimester of pregnancy, whichever is earlier, to detect those who may have seroconverted during pregnancy.

Pregnant women who initially tested HIV-negative and subsequently test HIV-positive during pregnancy should be referred to the hub centre for appropriate care and management provided for all HIV-positive patients.

Pregnant women who choose not be tested for HIV should:

- Receive another counselling session.
- Be offered HIV testing at every subsequent visit in the antenatal clinic in a non-coercive manner.
- Also be offered HIV testing at the onset of labour; and if this is not possible be offered HIV testing shortly after birth.

Unbooked women presenting in labour should:

- Be counselled and have a rapid HIV screening test.
- Be offered and receive PPTCT intervention as per guidelines if the HIV screening test is reactive.
- Have her HIV screening test confirmed and followed up as early as possible.
- Be informed about the HIV confirmatory test result.
- Be referred to the hub centre for appropriate care and management after delivery if the HIV confirmatory test result is positive.
- Should be offered HIV counselling and testing after delivery if this was not possible during labour.

Women presenting immediately postpartum should:

- Be counselled and have a rapid HIV screening test.
- Be offered PMTCT intervention to her baby if the HIV screening test is reactive.
- Have her HIV screening test confirmed and followed up as early as possible.
- Be informed about the HIV confirmatory test result.
- Be referred to the hub centre for appropriate care and management after delivery if the HIV confirmatory test result is positive.

9.2 First-line ART recommendations for HIV-positive pregnant and breastfeeding women

- *Standard first-line ART:*
  - Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC)[a] 300 mg PO OD + efavirenz (EFV) 600 mg PO OD
- *Alternative first-line ART:*
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + efavirenz (EFV) 600 mg PO OD
  - Zidovudine (AZT) 300 mg PO BD + lamivudine (3TC)[a] 150 mg PO BD + nevirapine (NVP)[b] PO 200 mg OD for the first 14 days then 200 mg BD thereafter

[a] Emtricitabine (FTC) 200 mg PO OD can be used instead of lamivudine. Both drugs have the same pharmacological profiles.

[b] Be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatotoxicity.

9.3 Recommendations for prevention of parent-to-child transmission of HIV

Clinical scenario	Maternal ART	Infant ARV prophylaxis[a]	Duration of infant ARV prophylaxis
Mother diagnosed with HIV during pregnancy	Initiate maternal ART (refer to Section 9.2)	Zidovudine (AZT) – refer to Table 7.3	6 weeks[b]; consider extending AZT to 12 weeks
Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed	Initiate maternal ART (refer to Section 9.2)	Zidovudine (AZT) – refer to Table 7.3	6 weeks[b]; consider extending AZT to 12 weeks
Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding	Refer mother to the hub centre and assess for ART initiation	Zidovudine (AZT) – refer to Table 7.3	6 weeks[b]
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding	Initiate maternal ART (refer to Section 9.2)	Zidovudine (AZT) – refer to Table 7.3	Collect dried blood spots (DBS) for HIV DNA PCR for early infant diagnosis of HIV and then immediately start AZT for 6 weeks; strongly consider extending AZT for 6 weeks
Infant identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding	Refer mother to the hub centre and assess for ART initiation	No drug	Collect dried blood spots (DBS) for HIV DNA PCR for early infant diagnosis of HIV; no infant ART prophylaxis is given; start ART if HIV DNA PCR result is positive
Mother receiving ART but interrupts ART regimen while breastfeeding (such as toxicity, stockouts or refusal to continue ART)	Counsel regarding continuing ART without interruption	Zidovudine (AZT) – refer to Table 7.3	Until 6 weeks after maternal ART is re-started or until one week after breastfeeding has ended

[a] Refer to Table 7.3.

[b] If maternal ART was given less than 4 weeks before delivery, consider extending giving AZT for 12 weeks.

Adapted from WHO 2013a: 120.

9.4 Intrapartum management

- Health care workers should check the woman's HIV status and details of the ARV drugs received during pregnancy. If the woman's HIV status is unknown and she is in the first stage of labour, HIV counselling and testing should be provided. If this is not possible prior to delivery, then HIV counselling and testing should be provided as soon as possible after delivery.

- Standard precautions for infection control should be strictly practiced.

- Caesarean sections should be performed for obstetric and medical indications and are not recommended to reduce mother-to-child transmission of HIV.

- For planned or elective (as well as emergency) caesarean sections for obstetric and medical indications, ensure that HIV-positive pregnant women who are already on ART are adherent to their medications.

- All HIV-positive pregnant women who undergo caesarean sections should receive prophylactic antibiotics as per protocol.

- Mother-to-child transmission of HIV is increased by prolonged rupture of membranes, assisted instrumental delivery, invasive monitoring procedures, and episiotomy. These should be avoided as much as possible.

10 Management of HIV-exposed and HIV-positive infants and children

HIV-exposed infants and children are those born to mothers living with HIV or children breastfeeding from mothers living with HIV until exposure stops, i.e. 6 weeks after complete cessation of breastfeeding and HIV infection is excluded.

Care of HIV-exposed infants should follow standard neonatal care according to safe motherhood practices:

- The baby's mouth and nostrils should be wiped as soon as the head is delivered.
- Only suction the baby's nose and airway when there is the presence of meconium-stained secretions.
- Infants should be handled with gloves until all blood and maternal secretions have been removed (early baby bathing).
- The cord should be clamped after birth, but milking should be avoided.
- Cover the cord with gloved hands and gauze before cutting to avoid blood splattering.
- Initiate feeding within the first hour of birth according to the mother's preferred and informed choice.

HIV-exposed or HIV-positive infants and children should have access to a comprehensive package of care services in addition to child health care services provided to HIV-uninfected children (Box 10.1).

Box 10.1 Comprehensive package of care services for HIV-exposed and HIV-positive infants and children

- Routine newborn and infant care, including growth and development monitoring
- Co-trimoxazole prophylaxis
- Early HIV diagnostic testing and diagnosis of HIV-related conditions
- Diagnosis and management of common childhood illnesses including opportunistic infections, e.g. TB
- Immunizations started and completed
- Nutritional support
- ART for HIV-positive children
- Treatment monitoring for children receiving ART
- Education and ARV drug adherence counselling for family and caregivers
- Continued counselling and support for family and caregivers

10.1 Infant feeding

- HIV-positive mothers should be counselled about infant feeding choices during pregnancy and decide before delivery.

- Infants should exclusively breastfeed (i.e. no water, liquids, or solid foods) immediately after birth up to six months of age.[8]

- Infants should be fed solid food from six months of age as a complement to breast milk (which should continue on demand anytime until at least 12 months).

[8] Refer to Infant Feeding Policy 2010 Ministry of Health Fiji.

- Breastfeeding should only be stopped once a nutritionally adequate and safe diet without breast milk can be provided.
- Breastfeeding HIV-positive mothers should continue taking ART.

- If the HIV-positive mother decides to stop breastfeeding, it should be stopped gradually within one month.

- If commercial infant formula milk is desired as replacement feeding, the infant should be exclusively given formula feeds provided the following conditions are met:
  - Safe water and sanitation are assured at the household level and in the community;
  - The mother or other caregiver can reliably provide sufficient infant formula milk to support the normal growth and development of the infant;
  - The mother or caregiver can prepare it cleanly and frequently enough so that is safe and carries a low risk of diarrhea and malnutrition;
  - The mother or caregiver can, in the first six months, exclusively give infant formula milk;
  - The family is supportive of this practice; and
  - The mother or caregiven can access health care that offers comprehensive child services.

- Mixed feeding (breast milk and formula combined) is the most hazardous form of infant feeding as the risk for mother-to-child transmission of HIV is the highest.

10.2 Early infant diagnosis of HIV infection

Early diagnosis of HIV-exposed infants and children ensures timely treatment and survival. However, making a diagnosis of HIV infection in HIV-exposed infants and children is a challenge.

HIV antibody testing is generally used to diagnose HIV infection in adults and children above 18 months of age. Because of the passive transfer of maternal antibodies (including HIV antibodies) across the placenta to the baby during pregnancy, HIV antibody testing in infancy cannot be used to confirm HIV infection in the infant, but does indicate maternal HIV infection and exposure of the infant.

In order to diagnose HIV infection definitively in infants and children below 18 months of age, assays that detect the virus or its components (i.e. virological tests such as HIV DNA PCR through collection of dried blood spots, DBS) are therefore required.

Infants and children diagnosed with HIV infection should be referred to paediatric specialist care in divisional hospitals as soon as possible where appropriate care and management are provided, in particular ART initiation in HIV-positive infants and children less than 5 years of age.

10.2.1 Presumptive diagnosis of HIV infection

In most instances, virological testing cannot be done readily so a presumptive diagnosis of HIV infection in infants and children less than 18 months of age can be made based on the criteria outlined in Box 10.2. A presumptive clinical diagnosis of severe HIV infection is necessary in order to permit

the early initiation of life-saving ART. The diagnosis of HIV infection should be confirmed as soon as possible using DBS for HIV DNA PCR.

Box 10.2 Criteria for presumptive diagnosis of HIV infection in infants and children less than 18 months of age

- The child is confirmed as being HIV antibody positive (which indicates exposure to HIV but not necessarily HIV infection itself)
  AND
- The child is symptomatic with two or more of the following:
  - Oral thrush
  - Severe pneumonia
  - Severe sepsis
  OR
- A diagnosis of any AIDS-indicator condition(s) can be made (refer to Appendix 6)
- Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive child include:
  - Recent HIV-related maternal death or advanced HIV disease; and
  - Child's %CD4 <20.

Note: Confirm the diagnosis of HIV infection as soon as possible using dried blood spots (DBS) for HIV DNA PCR.

10.2.2 Diagnosis in breastfeeding infants

Throughout the breastfeeding period, HIV-exposed infants and children are at risk of acquiring HIV infection. However, breastfeeding should not be stopped in order to perform collection of DBS for HIV DNA PCR.

Positive HIV DNA PCR results should be considered to reflect HIV infection. However, interpreting negative results poses a challenge. A six-week window period after the complete cessation of breastfeeding is required before negative HIV DNA PCR test results can be assumed to reliably indicate that the child does not have HIV infection.

10.2.3 Diagnosis in mothers on ART

HIV DNA PCR assays are reliable for diagnosis of HIV infection when the mother or infant has been given ARV drugs. HIV DNA detection in the infant is not affected by maternal ART when the mother is breastfeeding.

10.2.4 Recommended HIV diagnostic testing approaches for HIV-exposed infants and children

Clinical scenario	Test required	Purpose	Action
Well, HIV-exposed infant	DBS for HIV DNA PCR at 4 – 6 weeks of age	To diagnose HIV	Start ART if HIV-positive
Infant – unknown HIV exposure	Maternal HIV antibody test or infant HIV antibody test	To identify or confirm HIV exposure	Need to do DBS for HIV DNA PCR if HIV-exposed

Clinical scenario	Test required	Purpose	Action
Well, HIV-exposed infant at 9 months of age	HIV antibody test (at least immunization, usually 9 months)	To identify infants who have persisting HIV antibody or have seroconverted	Those who are HIV antibody positive, need to DBS for HIV DNA PCR and close follow-up Those who are HIV antibody negative, assume that they are not infected with HIV; repeat testing is required if still breastfeeding
Infant or child with signs and symptoms suggestive of HIV	HIV antibody test	To confirm HIV exposure	Presumptive diagnosis of HIV infection (Refer to Box 10.2) and treat immediately; perform DBS for HIV DNA PCR if <18 months of age
Well or sick child who is HIV antibody positive >9 months and <18 months	DBS for HIV DNA PCR	To diagnose HIV	Reactive – start HIV care and ART
Infant or child who has completely discontinued breastfeeding	Repeat testing 6 weeks or more after breastfeeding cessation – usually initial HIV antibody testing followed by DBS for HIV DNA PCR for HIV antibody positive child and <18 months of age	To exclude HIV infection after exposure from breastfeeding ceases	Infected infants and children <5 years of age need to start HIV care and ART regardless of the WHO clinical stage or CD4%

Adopted from WHO 2013a: 74.

10.3 Infant ARV prophylaxis

Recommendations for infant ARV prophylaxis for PMTCT are discussed in section 9.3.

10.4 Immunizations

- HIV-exposed infants and children should receive, as much as possible, all vaccines under the Expanded Program for Immunization (EPI). However, modification of EPI schedules may be required for infants and children who have HIV infection (Table 10).

- HIV-positive infants and children are considered as severely immunocompromised (and vaccine should not be given) if any of the following conditions are present:
  - <15% CD4;
  - Absolute CD4 count that is lower than normal for age (Table 3.2); and
  - Clinical manifestations of symptomatic HIV infection (refer to WHO clinical staging, Appendix 6).

- Once the immune status of the HIV-positive child has improved, resume immunization schedule as deemed appropriate.

- In general, vaccines with live attenuated organisms (e.g. BCG, measles, oral polio) are not given when the HIV-positive child is severely immunocompromised.

  - BCG vaccine can be given to infants born to mother with an unknown HIV status or those born to HIV-positive mothers but without signs and symptoms suggestive of HIV infection. [9]

  - Measles vaccine should not be given in HIV-positive children who are severely immunocompromised at the time of the immunization schedule.

  - *Haemophilus influenza* type B (Hib) conjugate vaccine should be delayed if the HIV-positive child is severely immunocompromised at the time of the immunization schedule.

Table 10.1 Recommended immunization schedule for HIV-exposed and HIV-positive infants and children

Vaccine	Age					
	At birth	**6 weeks**	**10 weeks**	**14 weeks**	**12 months**	**School entry**
BCG	✓[a]					
Hepatitis B	HBV0	HBV1	HBV2	HBV3		
Poliomyelitis	X[b]	X	X	X		
Diphtheria, pertussis, tetanus		DPT1	DPT2	DPT3		
Haemophilus influenza type B		Hib1[c]	Hib2[c]	Hib3[c]		
Measles, rubella					MR1[d]	MR2[d]

[a] Infants born to mothers with unknown HIV status or those born to HIV-positive mothers but without signs and symptoms suggestive of HIV can receive the vaccine.
[b] Not to be given.
[c] Hib vaccine cannot be given if the HIV-positive child is severely immunocompromised at the time of the immunization schedule.
[d] MR vaccine should be delayed if the HIV-positive child is severely immunocompromised at the time of the immunization schedule.

[9] Refer to EPI Policy 2013 for details

11 Surgical care of HIV-positive patients

This section provides basic guidance for surgeons in the care of HIV-positive patients. It does not cover details on surgical issues on particular opportunistic infections and other HIV-related conditions.

- Retrospective studies have shown that HIV-positive patients have favourable outcomes regardless of extent or duration of surgery.

- Neither CD4 cell count nor HIV viral load should be used as sole determinants of a given patient's surgical risk.

- Pre-operative evaluation of HIV-positive patients is similar to that of the general population.

- It is reasonable to consider all patients to be potentially HIV-infected and infectious. However, pre-operative HIV testing is not mandatory.

- Exposure to blood and body fluids of all patients should always be treated as infectious. Thus, standard precautions for infection control should always be practiced at all times including the use of protective eyewear, masks, and water-impermeable gowns with sleeves, and boots. Wearing two pairs of latex gloves reduces exposure due to glove defects. During procedures involving open fractures, a pair of cloth gloves worn with latex gloves significantly reduces the risk of exposure.

- Knowledge of the HIV status of the patient should not alter the behaviour of health professionals in the operating theatre.

- The surgical team should explore practical ways of reducing the incidence of intraoperative exposure to blood, such as:
  - Avoidance of hand-to-hand passage of sharp instruments;
  - Use of staple devices instead of suturing, if available;
  - Placing sharp instruments on a sterile instrument stand between the scrub nurse and the surgeon, especially in short, low-risk surgical procedures;
  - Use of blunted needles for fascial closure.

- Clinicians should continue ART in the perioperative period with as little interruption as possible. When ART interruption is necessary, all components of the regimen should be stopped and clinicians should consult with the physician. For patients who are able to receive liquids but not solids for more than one week, consideration should be given to converting the ART regimen that is available in liquid formulation temporarily and resume tablet formulations when patient is allowed to take solids.

- Clinicians should assess for potential drug-drug interactions before new medications are introduced. It is recommended to refer to this website: http://www.hiv-druginteractions.org.

- Health care workers who are privileged to be members of the surgical team have a professional responsibility to provide the highest possible quality of care for their patients. Surgeons must weigh the risks to the patient against potential benefits of surgery upon discussion with the patient for an informed choice of the treatment being provided.

12 Management of common opportunistic infections (OI) and other HIV-related conditions

12.1 Opportunistic infections frequently causing skin and mucosal manifestations

12.1.1 Seborrhoeic dermatitis

Clinical features

- Chronic skin infection most likely caused by the dermatophytic fungus *Malassezia furfur* which characteristically incites an intense inflammatory reaction.
- The infection manifests as an erythematous, scaling papule or plaque with an oily or dry surface and an indistinct margin. The usual distribution is the mid-facial region with extension to cover the entire face and scalp.

Management

- **Adults:**
  - Hydrocortisone % cream applied on the skin BD.
  - Selenium sulfphide (Selsun®) shampoo (or tar shampoo, if available) 2-3 times weekly if scalp is involved. Application is easier if hair is cut short.
  - If bacterial superinfection occurs, treat with flucloxacillin 500 mg PO 6-hourly for 7 days. If patient is allergic to penicillin, give erythromycin 500 mg PO 6-hourly for 7 days.
- **Children:**
  - Aqueous cream as soap.
  - Hydrocortisone cream 1% applied on the skin BD.
  - If bacterial superinfection occurs, treat with flucloxacillin 12.5-25 mg/kg PO 6-hourly for 7 days. If patient is allergic to penicillin, give erythromycin 7.5-12.5 mg/kg PO 6-hourly for 7 days.

12.1.2 Papular pruritic eruptions (PPE)

Clinical features

- Etiology is not defined but may be secondary to an abnormal inflammatory reaction to insect bites.
- Presents as chronic, severely itchy rash with (hyperkeratotic and hyperpigmented) dark papules and nodules, and scratch marks.
- Skin lesions heal as dark spots/marks with pale centers or post-inflammatory hypopigmentation.

Treatment

- Rule out scabies; treat empirically if diagnosis is unclear.
- **Adults:**
  - Hydrocortisone 1% cream applied topically BD for 10 days to alternate with emollients (Vaseline®) BD topically for 10 days.
  - For severe itching, give promethazine 10 mg PO nocte to a maximum of 10 mg PO 8-hourly.
  - If bacterial superinfection occurs, apply povidone-iodine solution topically BD. If severe, add flucloxacillin 500 mg PO 6-hourly for 7 day.

- **Children:**
  - Hydrocortisone ointment 0.5-1% cream BD for 7 days to alternate with emollients (Vaseline®) topically BD for 7 days.
  - For severe itching, give promethazine 0.1 mg/kg PO nocte to a maximum of 0.1 mg/kg PO 8-hourly for children >2 years of age.

12.1.3 Fungal nail infections (onychomycosis)

Clinical features

- Also called "tinea unguium".
- The nail becomes thickened and discoloured: white, black, yellow or green. As the infection progresses the nail can become brittle, with pieces breaking off. If left untreated, the skin can become inflamed and painful underneath and around the nail.

Treatment

- **Adults:**
  - *Preferred regimen:* Griseofulvin 500 mg PO OD for 6-9 months for fingernail infections and 12-18 months for toenail infections. (Note: Griseofulvin is contraindicated in pregnancy and the manufacturers caution against men fathering a child for six months after therapy). Cure rates with griseofulvin is better with fingernail infections compared to toenail infections. Monitor serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) regularly during griseofulvin therapy.
  - *Alternative regimen:* Terbenafine 250 mg PO OD for 6 weeks for fingernail infections and for 12 weeks for toenail infections. It is recommended to monitor full blood count (FBC), ALT and AST at baseline, then every 4-6 weeks during therapy.
- **Children:**
  - *Preferred regimen:* Griseofulvin 10 mg/kg PO OD for 6-9 months for fingernail infectios and 12-18 months for toenail infections. Because of the long duration of treatment, it is recommended to monitor serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) regularly.
  - *Alternative regimen:* Terbenafine 4-5 mg/kg/day PO OD for 6 weeks for fingernail infections and 12 weeks for toenail infections. Monitor FBC, ALT, and ALT at baseline, then every 4-6 weeks during therapy.

12.1.4 Angular cheilitis

Clinical features

- It is an inflammatory lesion at the corner of the mouth and often occurs bilaterally.
- The condition manifests as deep cracks or splits. In severe cases, the splits can bleed when the mouth is opened and shallow ulcers or a crust may form.
- The sores eventually get infected with *Candida* species or other pathogens.

Treatment

- Clotrimazole 1% cream applied topically BD for 7-14 days.

12.1.5 Aphthous ulcers

Clinical features

- Aphthous ulcers are painful, punched-out ulcers on the mucosal surface. They are usually covered in purulent exudates and tend to bleed when touched.
- It is difficult to differentiate it with herpetic ulcers caused by Herpes simplex virus (HSV). Syphilitic ulcer (chancre) is another differential diagnosis but the ulcer is painless.

Treatment

- Advise patient to avoid acidic foods.
- Oral hygiene with 0.2% chlorhexidine gluconate aqueous mouthwash, 4 times a day for a variable duration (two weeks to months or even longer until ulcer heals).
- Lignocaine 2% gel applied to oral ulcers 4 times a day for 2 weeks or until ulcers heal.
- Oral analgesics:
  - *Adults:* Paracetamol 1 gm PO 6-hourly; *OR* ibuprofen 400 mg PO 8-hourly.
  - *Children:* Paracetamol 15 mg/kg/dose PO 6-hourly.
- For severe disease (painful persistent ulcers):
  - *Adults:* Prednisone 30-40 mg PO OD to taper over a month.
  - *Children:* Prednisone 1-2 mg/kg PO OD (maximum of 60 mg/day) to taper over a month.

12.1.6 Necrotizing stomatitis, necrotizing ulcerative periodontitis, and necrotizing ulcerative gingivitis

Clinical features

- Stomatitis is inflammation of the mucosa of the oral cavity. It is often associated with poor oral hygiene and bacterial invasion with anaerobes.
- Gingivitis is inflammation of the gums with the gums swollen, red and tend to bleed easily. When pus accumulates in the gingival margin around the teeth it is called pyorrhoea.
- Periodontitis is inflammation of the tissues surrounding the teeth. This is a painful condition in which there is rapid loss of bone and soft tissue surrounding the teeth. Teeth become loose and fall off and there is bleeding from the gums. Ulceration may occur.

Treatment

- Basic oral health is important to prevent infections of the oral cavity, as these occur with increased frequency in PLHIV. This includes:
  - Regular brushing and flossing of teeth.
  - Do not share toothbrush.
  - Regular visit to the dentist.
- Oral hygiene with regular warm saline gargles *OR* chlorhexidine mouthwash.
- Refer to the dentist for possible local debridement of periodontitis and/or pyorrhoea.
- **Preferred regimen: Metronidazole**
  - *Adults:* 200-400 mg PO 8-hourly for 7-10 days.
  - *Children:* 15-35 mg/kg/dose PO 8-hourly for 7-10 days.
- **Alternative regimen: Amoxcillin/clavulanic acid (co-amoxiclav)**
  - *Adults:* Amoxicillin 500 mg/clavulanic acid 125 mg, 1 tablet PO 8-hourly for 7-10 days.
  - *Children:* Dose based on amoxicillin, 22.5 mg/kg/dose PO 8-hourly for 7-10 days.

12.1.7 Oral hairy leukoplakia

Clinical features

- This condition is caused by Epstein-Barr virus (EBV) and presents as asymptomatic white hyperkeratotic corrugations of the lateral border of the tongue. These lesions are classically adherent and cannot be removed with a spatula; in contrast to oral candidiasis, where the white patches can be scraped with a spatula.
- Occurs mostly in adults.

Treatment

- No treatment is necessary. Often disappears after ART is initiated.

12.1.8 Oral, oesophageal, and vaginal candidiasis

Clinical features

- **Oral candidiasis:** creamy-white patches on gums, tongue, or lining of the mouth.
- **Oesophageal candidiasis:** fever, burning retrosternal pain or discomfort, odynophagia, usually in association with oral candidiasis.
- **Vulvo-vaginal candidiasis:** vaginal irritation, itching, burning, and thick white discharge.

Diagnosis

A clinical diagnosis of oral or vaginal candidiasis is usually possible based on the above features. Oesophageal candidiasis may be presumptively diagnosed in an HIV-positive patient with advanced disease and dysphagia or odynophagia, particularly if oral thrush is evident. Gastroscopy is not routinely performed but may be considered if symptoms fail to respond to antifungal therapy.

Treatment

- **Oral candidiasis:**
  - *Adults:*
    - Preferred regimen: Nystatin 500,000 units to be gargled in the mouth four times a day for 10-14 days; *OR* clotrimazole troches (lozenges) 10 mg dissolved in the mouth TDS for 10-14 days.
    - Alternative regimen: Ketoconazole 200 mg PO OD for 7-14 days.
  - *Children:*
    - Preferred regimen: Nystatin 200,000-400,000 units/day divided in 4-6 doses for 14 days; *OR* clotrimazole troches (lozenges) 10 mg dissolved in the mouth TDS for 10-14 days (not recommended in children <3 years of age).
    - Alternative regimen: Ketoconazole 3.3-6.6 mg/kg/day PO OD for 7 days (not recommended in children <3 years of age).
- **Vaginal candidiasis:**
  - *Adults:* Topical therapy usually sufficient. Clotrimazole 100 mg pessary inserted per vaginally nocte for 7 nights; *OR* clotrimazole 500 mg pessary inserted per vaginally nocte single dose.
  - *Children:* Nystatin 100,000 units (one applicatorful) per vagina nocte for 14 days.
- **Oesophageal candidiasis:**
  - *Adults:* Fluconazole 100 mg PO OD for 14-21 days. Start ART once patient can swallow tablets comfortably.

- *Children:* Fluconazole 3-6 mg/kg PO OD.

- **Disseminated (systemic) candidiasis:**
  - *Preferred regimen:* Fluconazole 200 mg PO OD (up to 400 mg/day) for 2-3 weeks.
  - *Alternative regimen:* Amphotericin B 0.3-0.6 mg/kg/day IV for 10-14 days.

Prophylaxis

- Not routinely recommended.

12.1.9 Herpes simplex

Clinical features

- Typical blisters in the oral, genital, or perianal areas.

Diagnosis

- Clinical diagnosis based on history and examination. No laboratory tests required.

Treatment

- **Adults:** Acyclovir 400 mg PO TDS for 7-14 days.
- **Children:** Acyclovir 10 mg/kg PO 4-6 hourly for 7-14 days.
- Herpes simplex can be chronic and invasive (e.g. oesophagitis, encephalitis, disseminated infection). Patients with suspected systemic infection (such as herpes encephalitis) should receive acyclovir 10 mg/kg IV 8-hourly for a minimum of 2 weeks.

Prophylaxis

- **Primary prophylaxis***:* Not recommended.
- **Secondary prophylaxis:** In cases of frequent recurrences of genital herpes, long-term suppressive therapy with acyclovir 400 mg PO BD.

12.1.10 Herpes (varicella) zoster virus

Clinical features

May present as primary varicella infection (chickenpox) or reactivation varicella (shingles).

- Chickenpox presents with a fever, respiratory prodrome, and a diffuse intensely pruritic vesicular rash.
- Shingles presents as typical painful blisters along dermatomes (multiple dermatomal involvement can also occur).
- CNS and respiratory involvement may also occur. It may involve the eyes or the tip of the nose along the trigeminal nerve.

Diagnosis

- Clinical diagnosis based on history and examination. No laboratory tests required.

Treatment

- **Shingles**
  - *Children:* Acyclovir 20 mg/kg PO, 4 times a day for 7 days (maximum of 800 mg PO, 4 times a day)
  - *Adults:* Acyclovir 800 mg, 5 times a day for 7 days (maximum of 800 mg PO, 5 times a day)

- **Chickenpox:** Acyclovir 20 mg/kg PO, 4 times a day for 5 days (maximum dose is 800 mg PO, 4 times a day in children; and 800 mg PO, 5 times a day in adults). Treatment should commence within 72 hours of onset of blisters.
- **Disseminated, ophthalmic nerve involvement, or visceral disease:** Acyclovir 10 mg/kg/day IV 8-hourly for 7-14 days. Adequate hydration is imperative. Acyclovir eye ointment applied to the eye every 4 hours for ophthalmic herpes zoster. Pain relief may be required such as aspirin or paracetamol. If secondary bacterial infection occurs, treat with a suitable antibiotic.

Prophylaxis

- Not required.

12.2 Opportunistic infections frequently causing pulmonary manifestations

The most common pathogens to cause respiratory tract infections in HIV-positive patients are *Pneumocystis jiroveci* (previously *carinii*), *Mycobacterium tuberculosis*, and *Streptococcus pneumoniae*.

12.2.1 *Pneumocystis jiroveci* pneumonia

Clinical features

- Usually presents in advanced HIV disease (CD4 count <200 cells/mm^3); uncommon at higher CD4 counts.
- Generally insidious onset (days to weeks) of progressive shortness of breath, fever, dry cough and fatigue.
- Examination findings commonly include tachypnoea, hypoxia (more marked with exertion), and bilateral fine crackles (chest may be clear on auscultation).
- Unusual in patients adherent to PCP prophylaxis (co-trimoxazole).

Diagnosis

- Chest X-ray: bilateral perihilar interstitial infiltrates; diffuse alveolar shadowing; may be normal. Pneumothorax not uncommon. Pleural effusion rare.
- Presumptive diagnosis based on the characteristic clinical presentation and radiological findings in a patient with known advanced HIV infection.

Treatment

- **Adults:**
  - Co-trimoxazole (sulphamethoxazole [SMX] 75 mg/kg/day + trimethoprim [TMP] 15 mg/kg/day) given in 3-4 divided doses for 21 days. Usually provided by 4 single-strength tablets or 2 double-strength tablets PO, three times a day (TDS).
  - Prednisone 40 mg PO BD for 5 days, followed by 40 mg PO OD for 5 days, then 20 mg PO OD for 11 days) should be given concurrently in patients with severe illness (PaO_2 <70 mm Hg or pulse oximetry reading of <93% where arterial blood gas [ABG] determination is not available).
  - If patient develops intolerance to sulphamethoxazole, the alternative regimen is trimethoprim 15 mg/kg/day PO + dapsone 100 mg/day for 21 days.

- **Children:**
  - Co-trimoxazole (SMX 25 mg/kg + TMP 5 mg/kg) 4 times a day, minimum duration of 21 days.
  - Prednisolone 0.5 mg/kg/dose PO BD for 5 days, then 0.25 mg/kg/dose PO BD for 5 days, then 0.25 mg/kg/dose PO OD for 5 days in children with severe respiratory distress, with or without IMCI signs; or with pO_2 <70 mm Hg in room air; or A-a gradient >35 mm Hg.
  - If there is a severe drug reaction or a history of severe drug reaction to sulphamethoxazole, give trimethoprim (TMP) 5 mg/kg/dose PO 4 times a day + dapsone 100 mg/day PO for 21 days.

Prophylaxis

- **Primary prophylaxis:** Refer to section 4.

- **Secondary prophylaxis[10]:**
  - *Adults:* Patients who have had PCP must continue with maintenance therapy of co-trimoxazole 2 single-strength tablets (SMX 400 mg/TMP 80 mg) PO OD or one double-strength tablets (SMX 800 mg/TMP 160 mg) PO OD. Prophylaxis may be discontinued if the patient is on ART for 6 months and the CD4 count is persistently >250 cells/mm^3 for two measurements within a period of six months.
  - *Children:* Co-trimoxazole prophylaxis dose is based on standard trimethoprim (TMP) dose of 6-8 mg/kg/day PO once a day. Refer to section 4 when to discontinue co-trimoxazole for children <5 years of age. Children >5 years of age, follow adult recommendations as above.

12.2.2 Bacterial pneumonia

Clinical features

- Characteristically rapid onset (within days) of fever, cough productive of purulent sputum, and shortness of breath.

Diagnosis

- Chest X-ray: commonly lobar consolidation.
- Sputum and blood cultures: routine microbiology tests and culture.

Treatment

Refer to Fiji MOH *Antibiotic Guidelines.*

12.2.3 Tuberculosis

Note: This section should be read with section 6.5.3.

Clinical features

- May present at any stage of HIV infection.
- Classically presents with fever, night sweats, productive cough (often with haemoptysis), shortness of breath, and weight loss occurring over weeks to months. However, tuberculosis (TB)

[10] Treatment to prevent the recurrence or relapse of a disease.

in patients with advanced HIV infection frequently presents with atypical pulmonary or extra-pulmonary manifestations.

Diagnosis

- If pulmonary TB is suspected: sputum for acid-fast bacilli (AFB) smear and culture, and chest X-ray.
- If nodal TB is suspected: lymph node biopsy for AFB staining and histopathology.
- If CNS TB is suspected: computed tomography (CT) scan and lumbar puncture (LP) for cerebrospinal fluid (CSF) analysis including AFB smear and culture.
- Alternatively, tissue biopsy of other involved body site for AFB staining and culture, and histopathology.

Treatment

Refer to Fiji MOH TB treatment guidelines.

12.3 Opportunistic infections frequently causing headache and/or neurological manifestations

12.3.1 Toxoplasmosis *(Toxoplasma gondii)* encephalitis

Clinical features

- Usually presents in advanced HIV infection (CD4 count <50 cells/mm^3).
- Most commonly presents with fever, headache, altered mental state (confusion, delusional behavior), with or without focal neurological signs (e.g. hemiparesis, seizures, and coma).
- It can also affect the eye causing eye pain and reduced vision.

Diagnosis

- CT scan: usually multiple ring-enhancing lesions (may be single) with associated cerebral oedema. The diagnosis is confirmed by a documented clinical and radiological response to empirical therapy (as below) over 2 weeks.

Treatment

- **Standard therapy:** Co-trimoxazole (sulphamethoxazole [SMX] 75 mg/kg/day + trimethoprim [TMP] 15 mg/kg/day) given in 3-4 divided doses for 4-6 weeks. Usually provided by 4 single-strength tablets or 2 double-strength tablets PO, three times a day (TDS).
- **Alternative therapy:** If intolerant to sulfadiazine, clindamycin 600 mg IV or PO 6-hourly; *OR* dapsone 100 mg PO OD may be substituted for 6 weeks.

Prophylaxis

- **Primary prophylaxis:** Refer to Section 4.
- **Secondary prophylaxis:** Co-trimoxazole 2 single-strength tablets (SMX 400 mg/TMP 80 mg) PO OD; *OR* one double-strength tablet (SMX 800 mg/TMP 160 mg) PO OD. Prophylaxis may be discontinued if the CD4 count rises on ART to >250 cells/mm^3 for two measurements within a period of six months.

12.3.2 Cryptococcal *(Cryptococcus neoformans*) meningitis

Clinical features

- Usually presents in advanced HIV infection (CD4 count <50 cells/mm^3).
- Characteristically presents with an acute (i.e. days) or subacute (i.e. weeks to months) onset of fever and headache, with or without photophobia, neck stiffness, fatigue, irritability, or altered mental state.
- Patients may also present with non-specific CNS symptoms including dementia and seizures.

Diagnosis

- CT scan: Lumbar puncture analysis including opening pressure (usually elevated), fungal stain and culture, and cryptococcal antigen (Ag). Serum cryptococcal Ag and fungal blood culture may also be performed.
- Where the above investigations are not available, a presumptive diagnosis may be made based on the characteristic clinical presentation, CSF findings of leucocytosis with a lymphocyte predominance, and exclusion of a likely alternate diagnosis.

Treatment

- **Preferred regimen:** Amphotericin B 0.7 mg/kg/day intravenously (IV), with or without 5-flucytosine 100 mg/kg/day PO for 14 days ("induction phase"), then fluconazole 400 mg/day PO for 8 weeks ("consolidation phase"). Refer to Appendix 6 for administration of amphotericin B.
- **Alternative regimen:** If amphotericin B is not available, fluconazole 800 mg/day PO for 4 weeks, then 400 mg PO OD for 8 weeks.
- An important adjuvant to antifungal therapy is the lowering of raised intracranial pressure by serial lumbar puncture, if required.

Prophylaxis

- **Primary prophylaxis:** Not required.
- **Secondary prophylaxis:** Patients should be on maintenance therapy with fluconazole 200 mg/day PO ("suppressive phase"). This can be discontinued if the patient is on ART for 6 months, the CD4 count is persistently >250 cells/mm^2 in two measurements within a period of six months, and the patient has been on fluconazole for six months.

12.4 Opportunistic infections frequently causing diarrhoea

Common causes

- **Viruses:** Rotavirus, enterovirus, cytomegalovirus (CMV), HIV
- **Bacteria:** *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli*, *Mycobacterium tuberculosis*, *Mycobacterium avium* complex
- **Parasites:** *Entamoeba histolytica*, *Giardia lamblia*, *Isospora belli*, *Cryptosporidium*, *Microsporidium*, *Strongyloides*
- **Non-infectious:** Kaposi sarcoma, non-Hodgkin's lymphoma

Diagnosis

Clinical manifestations with supportive stool and blood cultures. Identification of the causative organism frequently requires multiple stool examinations for routine microscopy and culture (ova,

cysts, and parasites) and modified AFB stain. Endoscopy and biopsy should be considered early where diarrhea persists and the diagnosis remains unclear.

Treatment

- **Symptomatic**
  - *Rehydration:* Oral or IV fluids with electrolytes.
  - *Anti-motility agents:* Co-phenotrope (diphenoxylate hydrochloride 2.5 mg, atropine sulfate 25 micrograms) PO, 2 tablets as stat dose followed by one tablet PO 8-hourly for each loose stool (exclude bacterial infection first).
- **Organism specific:**
  - **Salmonellosis:**
    - *Adults:* Ciprofloxacin 500 mg PO BD for 7-14 days; *OR* ceftriaxone 2 g IV OD for 7-14 days. Consider 4-6 weeks therapy if bacteraemic.
    - *Children:* Chloramphenicol 12.5-25 mg/kg IV/PO 6-hourly for 7-14 days.
  - **Shigellosis:**
    - *Adults:* Chloramphenicol 500 mg PO/IV 6-hourly for 7-14 days, *OR* ciprofloxacin 500 mg PO BD for 7 days. Consider 2 weeks therapy if bacteraemic.
    - *Children:* Chloramphenicol 12.5-25 mg/kg IV/PO 6-hourly for 7-14 days.
  - **Campylobacter:**
    - *Adults:* Erythromycin 500 mg PO, 4 times a day for 7 days; *OR* ciprofloxacin 500 mg PO BD for 7 days.
    - *Children:* Erythromycin 10 mg/kg PO, 4 times a day for 7 days.
  - **Giardiasis:**
    - *Adults:* Metronidazole 400 mg PO TDS for 7 days.
    - *Children:* 10 mg/kg TDS for 7 days.
  - **Amoebiasis:**
    - *Adults:* Metronidazole 400-800 mg PO TDS for 7-10 days.
    - *Children:* Metronidazole 15 mg/kg (maximum 800) every 8 hours for 7-10 days.
  - **Isosporiasis:**
    - *Adults:* Co-trimoxazole 2-single strength tablets *OR* one double-strength tablet PO, 4 times a day for 7 days.
    - *Children:* Co-trimoxazole (SMX 25 mg/kg + TMP 5 mg/kg) PO, 4 times a day for 7 days.
  - **Helminth infestation:**
    - *Adults:* Mebendazole 100 mg PO TDS for 3 days.
      - *Children:* Mebendazole; for children >6 months and <10 kg, 50 mg PO 12-hourly for 3 days; for children >10 kg, 100 mg PO 12-hourly for 3 days.
  - **Stronglyloidiasis:**
    - *Adults:* Thiabendazole 25 mg/kg BD for 3 days.
    - *Children:* Thiabendazole 25 mg/kg BD for 3 days.
  - **Cryptosporidiasis:** No organism-specific therapies have been proven consistently effective. Hydrate and maintenance of fluid and electrolyte balance. Anti-motility drugs may also be useful. Start ART as soon as possible when patient can tolerate.
  - Salmonellosis, shigellosis, campylobacteriosis, and isosporiasis in HIV-infected patients often relapse. If relapse occurs after an initial course of antimicrobial therapy, a 6- to 12-week course therapy should be administered. These conditions (especially if recurrent) may respond to immune reconstitution with ART.

12.5 Other common opportunistic infections and HIV-related diseases

12.5.1 Cytomegalovirus (CMV)

Clinical features

Usually presents in advanced HIV infection (CD4 count <50 cells/mm^3), most commonly with CMV retinitis but occasionally with disseminated disease, or with other localized end organ involvement. Symptoms are related to the organ system involved.

- **Retinitis:** may be asymptomatic, or present with floaters, scotomatas or visual field defects. Central lesions may cause decreased visual acuity and can lead to blindness. Involvement may be uni- or bilateral.
- **Colitis:** fever, abdominal pain, bloody diarrhea, weight loss.
- **Oesophagitis:** pain and difficulty in swallowing, fever.
- **Pneumonitis:** fever, dry cough, shortness of breath.
- **Encephalitis:** confusion, fever, altered mental state, dementia.

Diagnosis

- **Retinitis:** Characteristic appearance on ophthalmologic examination.
- **Oesophagitis and colitis:** Endoscopy and biopsy for histopathology.
- **Pneumonitis:** Pulmonary insterstitial infiltrates on chest X-ray. Lung biopsy required for definitive diagnosis. Exclude more common pathogens, especially PCP, pulmonary TB, and bacterial pneumonias.
- **Encephalitis:** CT scan and LP for CSF examination to exclude other causes.

Treatment

- Induction dose: ganciclovir 5 mg/kg IV BD, OR valganciclovir (the drugs that is most likely available) 900 mg PO BD for 21 days for CMV retinitis.
- Commence ART early.

Prophylaxis

- **Primary prophylaxis:** Not required.
- **Secondary prophylaxis:** Ganciclovir 5 mg/kg IV OD, *OR* valganciclovir 900 mg PO OD.
- Patients should have a visual acuity test at least once every 6 months and a fundoscopic examination yearly.

12.5.2 *Mycobacterium avium* complex (MAC)

Mycobacterium avium and *Mycobacterium intracellulare* are two non-tuberculous mycobacteria that collectively form a group of organisms known as *Mycobacterium avium* complex (MAC). MAC disease in HIV-infected persons is generally a disseminated multi-organ infection seen in advanced HIV infection (CD4 count <50 cells/mm^3). Localized disease may also be seen, most commonly lymphadenitis or pulmonary disease.

Clinical features

Disseminated MAC infection presents as a systemic illness characterized by persistent fever, night sweats, fatigue, weight loss, cough, anaemia, abdominal pain, and diarrhea.

Diagnosis

- Confirmed by isolation of the organism (AFB smear and culture) from blood or bone marrow or another normally sterile site, or by histopathology and culture of an appropriate tissue specimen (e.g. lymph node or liver biopsy).
- Where the above investigations are not available, a presumptive diagnosis may be made based on the characteristic clinical presentation and the presence of typical laboratory (anaemia, elevated alkaline phosphatase [ALP]) and radiological (hepatomegaly, splenomegaly, and mediastinal or intra-abdominal lymphadenopathy) parameters, and exclusion of an alternate likely diagnosis (especially disseminated TB or lymphoma).

Treatment

Azithromycin 500 mg PO OD + ethambutol 15 mg/kg/day PO with or without rifabutin 300 mg PO OD for a minimum of 12 months.

Prophylaxis

- **Primary prophylaxis:** Azithromycin 1,200 mg PO per week + rifabutin 300 mg PO OD.
- **Secondary prophylaxis:** Patient should remain on maintenance therapy on the above doses of clarithromycin and ethambutol unless the CD4 count rises on ART to $\geq$100 cells/mm^3 for at least two measurements within a period of six months and the patient is on ART for 12 months.

12.5.3 Cervical cancer

Clinical features

- Often asymptomatic.
- May also present with vaginal discharge, vaginal bleeding, and pelvic pain.

Diagnosis

- Annual Papanicolaou (Pap) smear is recommended for all HIV-positive women as they are at increased risk of cervical dysplasia and cancer. Pap smear will detect human papilloma virus (HPV), the cause of most cervical cancers, cervical dysplasia, and cancer.
- Colposcopy and cone biopsy where indicated.
- Further investigations may be considered (e.g. ultrasonography for hepatic metastases or CT scan for lymph node or bone metastases).

Treatment

- Patients with Pap smear reports of dysplasia or intraepithelial neoplasia require colposcopy and cone biopsy or surgery. Adjuvant therapy may be required.

13 Management of symptoms related to OI, ART and IRIS

Table 13.1 Symptomatic management of HIV infection related to OI, ART and IRIS

Symptom	Management of symptoms of OI or HIV-related illness	Side effects of ARV or OI prophylaxis	IRIS
Abdominal or flank pain and/or jaundice	Pancreatitis and intestinal perforation (due to CMV); hepatociliary disease (due to MAC and cryptosporidiosis)	**ART:** Didanosine (ddI) may cause pancreatitis which requires stopping these drugs. NVP (and less commonly EFV) may cause liver dysfunction which necessitates discontinuation of these drugs. Stop ART if lactic acidosis suspected. **Cotrimoxazole and INH:** If jaundice occurs, stop these drugs.	Hepatitis B and C can occur with IRIS. Suspect if nausea, vomiting, and jaundice occur.
Anxiety, bizarre dreams, psychosis, depression	Counselling and referral to specialist	**ART:** This may be due to efavirenz (EFV). Usually lasts for <3 weeks. Advise patient to take the drug at night. Needs counseling and support. Amitriptyline: adults – 25 mg (increasing gradually to 100 mg) PO or at bedtime in adults; children – 1 mg/kg/day PO in divided doses 8-hourly. Call for advice or refer if severe depression, suicidal, or psychotic symptoms occur.	These CNS effects are not due to IRIS.
Cough, difficulty in breathing	For wheezing: salbutamol 2 puffs every 20 minutes for 3 doses, then 2 puffs every 4 hours, thereafter. If symptoms persist or worsen, common causes are PCP, TB, bacterial, or fungal pneumonias.	**ART:** Stop if lactic acidosis is suspected.	IRIS can be associated with PCP, TB, fungal, or bacterial pneumonias.
Diarrhoea	Drink extra fluids, in addition to usual fluid intake after each loose stool, e.g. oral rehydration solution (ORS). If diarrhoea persists or worsens, investigate and treat cause.	**ART:** Lopinavir/ritonavir (LPV/r) commonly causes diarrhoea. Co-phenotrope: adults – 2 tablets as stat dose followed by one tablet 8-hourly for each loose stool; children – 1 tablet TDS.	Temporary flare ups of MAC or CMV may cause diarrhoea. Continue ART and treat symptomatically.
Fatigue, pallor	If symptoms persist or worsen, check haemoglobin (Hb) for anaemia (caused by HIV or by MAC). Transfuse as necessary (Hb <8 g/dL).	**ART:** Common during 4-6 weeks after starting ART. Stop zidovuidne (AZT) if severe pallor or symptoms or anaemia or low Hb (<8 g/dL). **Co-trimoxazole:** Stop the drug if Hb <8 g/dL.	Suspect MAC if fever, fatigue, and anaemia occur. Continue ART once CD4 count >50 cells/mm^3.

Symptom	Management of symptoms of OI or HIV-related illness	Side effects of ARV or OI prophylaxis	IRIS
Fever	Paracetamol: adults – 1 gm PO 6-hourly; children 10-15 mg/kg/day PO 4-hourly. If symptom persists or worsens, investigate cause and treat or refer.	**ART:** Stop all drugs when hypersensitivity reaction of abacavir (ABC) is suspected.	Fever soon after commencing ART could be due to IRIS (MAC, TB, CMV, HBV, HCV, cryptococcus, herpes zoster).
Headache	Paracetamol: adults – 1 gm PO 6-hourly; children 10-15 mg/kg/day PO 4-hourly. If symptom persists or worsens, the most common causes are cryptococcal meningitis and toxoplasmosis.	**ART:** If on zidovudine (AZT) or efavirenz (EFV), reassure that this is common and usually self-limiting but can last 4-8 weeks. If it persists more than 2 weeks or worsens, call for advice or refer.	Assess for cryptococcal meningitis or toxoplasmosis.
Indigestion	Adults and children: magnesium sulphate tablets 1-2 tablets every 6 hours. If symptom persists or worsens, treat as oesophageal candidiasis. If no response, refer.	**ART:** Take ART with food except didanosine (ddI).	Oesophageal candidiasis requires treatment.
Nausea, vomiting	Metoclopramide : adults – 10-20 mg PO TDS ; children – 0.1-0.2 mg/kg PO 8-hourly. Prochlorperazine 2.5 mg BD or TDS. Chlorpromazine: adults – 25-50 mg PO every 6-12 hours; children – 0.5 mg/kg 4-6 hourly.	**ART:** Take ART with food except didanosine (ddI); usually self-limiting if on zidovudine (AZT). Treat symptomatically. Stop ART if lactic acidosis is suspected. **Co-trimoxazole:** Take with food. **Isoniazid (INH):** Take at bedtime. If vomiting still occurs, stop INH.	Hepatitis B and C can occur with IRIS. Suspect if there is concomitant jaundice.
Neuropathy	Amitriptyline: adults – 25 mg (increasing gradually to 100 mg) PO or at bedtime in adults; children – 1 mg/kg/day PO in divided doses 8-hourly + Paracetamol: adults – 1 gm PO 6-hourly; children 10-15 mg/kg/day PO 4-hourly. It takes 3 weeks before amitriptyline takes effect. If symptom persists or worsens, commencing ART may help.	**ART:** Commonly caused by ddI. Add amitriptyline PO at increasing disease. Replace ARV. **Isoniazid (INH):** Give pyridoxine 10 mg PO OD.	Not an IRIS symptom.
Skin rash, itch	Emollient lotion; calamine lotion; mild steroid creams (1% hydrocortisone, 0.01% triamcinolone); oral antihistamines. If symptoms persist or worsens, investigate cause and treat or refer.	**ART:** If on EFV, give oral antihistamines and review daily. Rash is often self-limiting. If on nevirapine (NVP) or abacavir (ABC), assess carefully. Stop drug if rash is moderate or severe (generalized peeling, muscosal involvement). **Co-trimoxazole and isoniazid (INH):** Stop if rash is moderate or severe.	Skin infections which can flare up due to IRIS in the first 3 months of ART: herpes simplex, herpes zoster, papilloma virus warts, fungal infections, atopic dermatitis. Treat as necessary.

14 Post-exposure prophylaxis to HIV

This section covers consideration and initiation of antiretroviral post-exposure prophylaxis (PEP) in occupational and non-occupational settings.

The aim of PEP is to reduce the likelihood of HIV, hepatitis B (HBV), and hepatitis C (HCV) transmission. Post-exposure prophylaxis (PEP) should be offered to a person (i.e. health care workers and non-health care workers) who is eligible to receive it after a thorough risk assessment of the possible source, the exposed person, and the circumstances surrounding the exposure to HIV.

14.1 Management of occupational exposures

Prevention is vital. Health care workers should practice standard precautions for infection control in delivering care for all patients. The risk of exposure to HIV via the percutaneous (needlestick injuries) route is 0.3%, and 0.09% via the mucous membrane and non-intact skin[11]. It is advisable that health care workers should ensure that they have received and completed hepatitis B (HBV) vaccination series.

14.1.1 Immediate management

- Needle stick injuries and cuts should be washed immediately with soap and running water. Aspiration, forced bleeding and wound incision are not recommended. Do not use any strong solutions (i.e. iodine) as these may irritate the wound and make the injury worse. If running water is not available, clean the site with an alcohol-based hand rub solution. Cover with a sterile dressing.
- Splashes to the nose, mouth or non-intact skin should be flushed with water.
- Splashes to the eyes should be irrigated with clean water, saline or sterile water. If wearing contact lenses, leave them in place while irrigating, remove after the eye is cleaned, and cleanse the lenses in the usual manner. Do not use soap or disinfectant in the eye.
- Splashes to the mouth or nose should have the fluid immediately spat or blown out and the site should then be rinsed thoroughly with water or saline and spat or blown out again. Repeat this several times. Do not use soap or disinfectant in the mouth or nose.
- Seek medical attention immediately.

14.1.2 Report the occupational exposure

- Report occupational exposure incident immediately to the supervisor or manager.
- The supervisor should arrange with the infection control officer or the medical officer for assessment of the occupational exposure.

14.1.3 Assess the occupational exposure

- Complete the prescribed form indicating the following information:
  - The name of the health care worker;
  - Where the incident occurred;
  - Description of the exposure site, body site, and the initial care provided;

[11] This data is relates to an injury where the source is known to be HIV-positive.

- Determine whether the exposure occurred while the health care worker was officially working or not; and
- Determine the body fluid type (Box 14.1) and, exposure type, and volume of exposure (Box 14.2).

Box 14.1 Body fluid type and risk of blood-borne pathogen transmission

- *Body fluids that pose a risk for blood-borne pathogen transmission*

Blood	Semen	Vaginal secretions
Cerebrospinal fluid	Synovial fluid	Pleural fluid
Peritoneal fluid	Pericardial fluid	Amniotic fluid

- *Body fluids that do not pose a risk of blood-borne pathogen transmission*

Urine	Stool	Tears
Saliva	Vomitus	Sweat
Non-purulent sputum	Nasal discharge	

Box 14.2 Type and volume of exposure to body fluids and risk of blood-borne pathogen transmission

- *Percutaneous injuries*
  - Occur when the skin is penetrated by a contaminated sharp object, i.e. needle or instrument.
    - *Less severe* – superficial injury; penetration with a solid needle, e.g. suture needle.
    - *More severe* – deep puncture; penetration with a large bore, hollow needles; blood visible on device; needle was used in a patient's artery or vein.
- *Mucous membrane exposures*
  - Can be inside the eyes, nose or mouth or exposure to non-intact skin, e.g. dermatitis, abrasion, open wound.
    - *Small-volume exposure* – a few drops
    - *Large-volume exposure* – larger splash
- *Exposure of intact skin to blood and other body fluids does not constitute an exposure.*

- The completed form should be sent to the infection control officer who then carries out the risk assessment of the occupational exposure as guided by the algorithm in Figure 14.1.

- In the risk assessment of the occupational exposure, the infection control officer should be guided by the algorithm in Figure 14.1.

- The exposed HCW should be counselled by the infection control officer and/or the immediate supervisor in a confidential, sensitive, and non-judgmental way. This will also be an opportune time for the exposed HCW to be re-educated on standard infection control precautions at the health care facility.

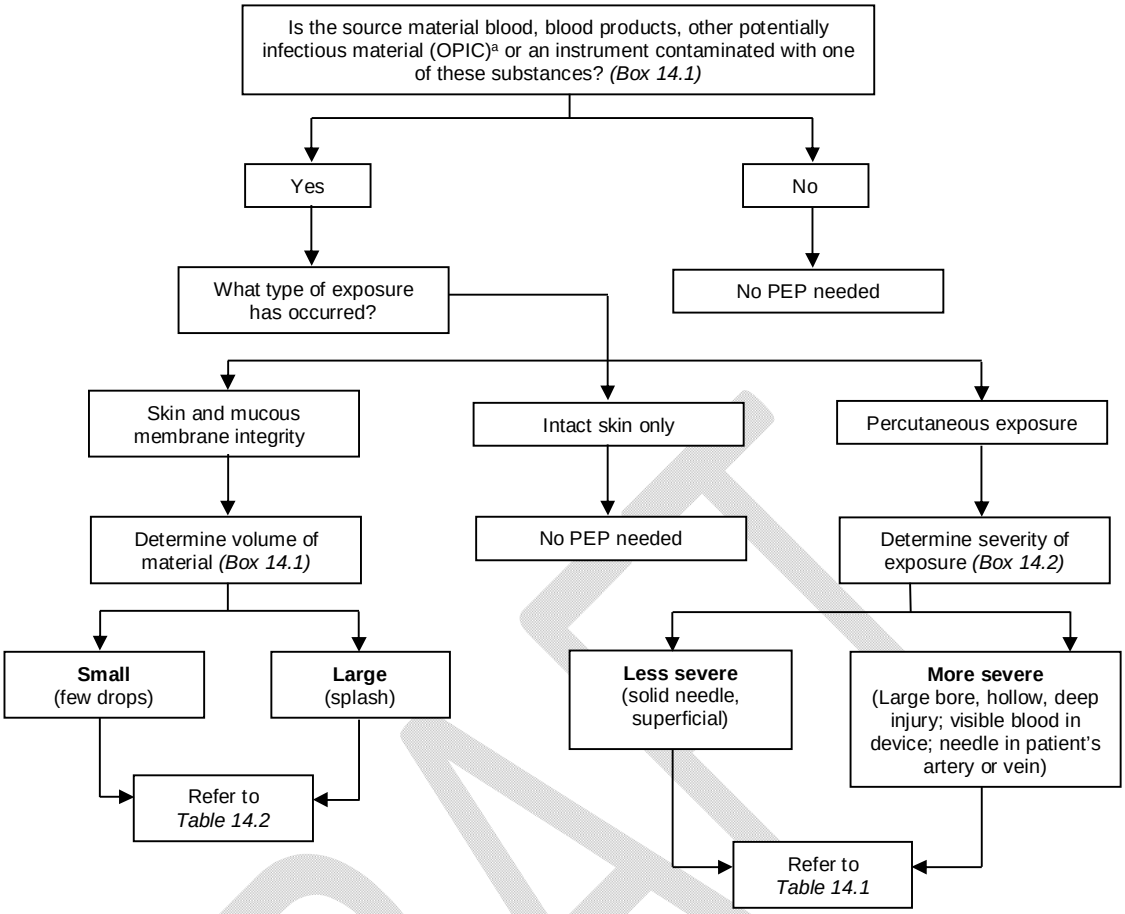


Figure 14.1 Risk assessment for occupational exposure to HIV. (Adapted from CDC; 1998).

14.1.4 Assess the source person

- If the source person is HIV-positive, assess the patient (WHO clinical staging; CD4 count).
- If on antiretroviral therapy (ART), review drug adherence; viral load and drug resistance testing are not recommended.
- If HIV status of the patient is unknown:
  - HIV counselling and testing, including testing for hepatitis B (HBV surface antigen, HBsAg) and hepatitis B antibody (anti-HBs); hepatitis C virus (HCV) antibody (anti-HCV); rapid plasma reagin (RPR) for syphilis (if not previously done).
- If the patient refuses HIV testing, decide on considering the assumption that the source patient might be HIV-positive based on the risk assessment during pre-test counselling.

14.1.5 Assess the exposed health care worker

- Do HIV counselling and testing, HBsAg, anti-HBs, anti-HCV, RPR for syphilis, full blood count, liver function tests, serum creatinine, estimated glomerular filtration rate (eGFR) and urine diptick for glycosuria.
- Assess hepatitis B immune status of the exposed HCW:

- If the source patient's status is unknown and the exposed HCW is immune (positive anti-HBs) or known responder – the exposed HCW is protected.
- If the exposed HCW is non-immune (anti-HBs negative), administer hepatitis immune globulin (0.06 ml/kg intramuscularly) stat; and start hepatitis B immunization (20 µg intramuscularly per dose) as soon possible at 0, 1 and 6 months.
- Consider tetanus immunization.

14.1.6 Recommend post-exposure prophylaxis for HIV

- After risk assessment of the occupational exposure, determine the recommended antiretroviral regimen for post-exposure prophylaxis to HIV using Table 14.1 and Table 14.2.

- Not all occupational exposures of HCW will receive PEP for HIV. The decision for treatment will be based on the risk assessment process that will evaluate the risk of exposure (Figure 14.1). If the HCW is eligible for PEP, it should be offered immediately without waiting for the results of the HIV test of the source person of the exposure. There is greater benefit if PEP is initiated within 36 hours after exposure and none if given after 72 hours.

14.1.7 Counselling, education, and support to the exposed health care worker

Counselling should be provided regarding PEP and this should be continued until follow-up is completed (i.e. for 6 months). The following issues should be discussed during counselling:

- Confidentiality and disclosure
- HIV, HBV and HCV infection and their respective consequences
- Procedure of HIV testing and the meaning of results
- Assessment of risk related to past and current sexual and other risk behaviours, as well as any previous exposures
- Assessment of risk related to the current exposure
- Explanation of risk of transmission associated with exposure
- Assessment of anxiety level and coping mechanisms
- Obtaining informed consent for testing (including stat pregnancy test)
- Planning for precautions while awaiting test results (and while taking PEP, if indicated) including:
  - Safe sexual practices, e.g. provide condoms
  - Cessation of breast feeding, if lactating
  - Any required modification of occupational duties, if indicated
  - Not to donate blood
  - Wound management.
- Providing information about the need to take PEP; when to start and what are the drugs to take; duration of PEP; PEP side effects and management
- Repeat blood tests:
  - HIV antibody: 6 weeks, 3 months, and 6 months
  - Anti-HBs: 1-2 months after the last dose of HBV vaccine, if administered
  - Anti-HCV: 4 months (with serum alanine transferase, ALT)
- Regular follow-up
- Arranging support while awaiting results and while taking PEP, if PEP is indicated
- Provision of exposure risk reduction education in a sensitive and non-judgmental way
- Referral for appropriate care and management if repeat blood test is confirmed HIV-positive.

Table 14.1 Recommendations for occupational post-exposure prophylaxis to HIV for percutaneous injuries

Exposure type and volume	Status of source person		
	Source person HIV-positive and low risk[a]	Source person HIV-positive and high risk[b]	HIV status of source person is unknown
Less severe: solid needle, superficial	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days[b]	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + efavirenz (EFV) 600 mg PO OD for 28 days	Usually none; consider tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days if source is high risk for HIV or HIV infection is most likely
More severe: large bore, deep injury, visible blood in device, needle in patient artery/vein	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + efavirenz (EFV) 600 mg PO OD for 28 days[c]	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + efavirenz (EFV) 600 mg PO OD for 28 days[c]	Usually none; consider tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days if source is high risk for HIV or HIV infection is most likely

[a] Low risk – asymptomatic HIV or viral load <1,500 copies/ml

[b] High risk – symptomatic HIV, AIDS, acute seroconversion, and high viral load.

[c] Concern for drug resistance – initiate prophylaxis without delay and consult an expert.

Table 14.2 Recommendations for occupational post-exposure prophylaxis to HIV for mucous membranes and non-intact skin[a]

Exposure type and volume	Status of source person		
	Source person HIV-positive and low risk[b]	Source person HIV-positive and high risk[c]	HIV status of source person is unknown
Small volume: drops of blood or other potentially infectious body materials	Consider tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days[†]	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days	Usually none; consider tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days if source is high risk for HIV or HIV infection is most likely
Large volume: Splash of blood or other potentially infectious body materials	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days	Tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + efavirenz (EFV) 600 mg PO OD for 28 days[4]	Usually none; consider tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD for 28 days if source is high risk for HIV or HIV infection is most likely

[a] Non-intact skin: Dermatitis, abrasion, wound

[b] Low risk: Asymptomatic HIV or viral load <1,500 copies/ml.

[c] High risk: Symptomatic HIV, AIDS, acute retroviral syndrome (seroconversion) and high viral load.

14.2 Post-exposure prophylaxis for non-occupational exposures

Post-exposure prophylaxis for HIV infection (PEP-HIV) will be provided to the person who has been raped and/or sexually abused by a known HIV-positive person and also to individual cases where a high risk of transmission has been identified (Box 14.3). The victim should receive medical care and other support services:

- Initial crisis intervention (such as emotional support) and first aid;
- Explain to the victim the care and interventions that will be provided;
- Obtain medical history;
- Conduct a general examination, including overall status and recording injuries;

- Assess the risk of HIV transmission (see below);
- HIV counselling and testing;
- Baseline full blood count, liver function tests, serum creatinine, estimated glomerular filtration rate (eGFR) and urine diptick for glycosuria.
- STI screening and treatment, including hepatitis B, hepatitis C, and syphilis;
- Pregnancy test, emergency contraceptive, and other sexual and reproductive health services; and
- Psychosocial support.

The individual risk of HIV transmission depends on the type of exposure. Co-factors such as sexually transmitted infections (STIs), viral load, and trauma may affect the risk estimate. The estimated per-act probability of acquiring HIV from an infected source, by exposure act is as follows: receptive anal intercourse, 0.5%; receptive penile-vaginal intercourse, 0.1%; insertive anal intercourse, 0.065%; insertive penile-vaginal intercourse, 0.05%. Accurate risk estimates for receptive oral or insertive oral intercourse are not available.

Box 14.3 Eligibility criteria for post-exposure prophylaxis (PEP) among people who have been sexually assaulted

- Less than 72 hours has elapsed since exposure; *AND*
- The exposed individual is not known to be HIV-positive; *AND*
- The person who is the source of the exposure is HIV-positive or has unknown HIV status*; *AND*
- A defined risk of exposure, such as:
  - Receptive vaginal or anal intercourse without a condom or with a condom that broke or slipped; *OR*
  - Contact between the perpetrator's blood or ejaculate and mucous membrane or non-intact skin during the assault; *OR*
  - Receptive oral sex with ejaculation; *OR*
  - The person who was sexually assaulted was drugged or otherwise unconscious at the time of the alleged assault and is uncertain about the nature of the potential exposure; *OR*
  - The person was gang-raped.

* Attempts should be made, where possible, to establish the HIV status of the source with informed consent.
Adopted from WHO 2007:52.

The use of PEP following potential sexual exposure to HIV is only recommended where the victim presents within 72 hours of exposure. Within that time frame, it is recommended that HIV-PEP (if given) should be administered as early as possible. HIV-PEP is not appropriate in the context of chronic exposures to HIV such as regular and ongoing unprotected sex with an intimate partner.

It is recommended that a three-drug ARV regimen should be used: tenofovir (TDF) 300 mg PO OD + lamivudine (3TC) 300 mg PO OD + efavirenz (EFV) 600 mg PO OD; all three drugs to be taken for 28 days.

The exposed person should be counselled on:

- The need to take PEP; when to start, what drugs to take and for how long; adherence to PEP; the side effects of PEP and how to manage them
- How to prevent HIV transmission
- Repeat laboratory tests:
  - Repeat pregnancy test 4 weeks after exposure
  - HIV antibody: 6 weeks, 3 months, and 6 months
  - Anti-HBs: 1-2 months after last dose of HBV vaccine, if vaccination was administered
  - Anti-HCV: 4 months (with serum alanine transferase, ALT)
- Referral for appropriate care and management if repeat blood test is confirmed HIV-positive.

15 Continuum of care for HIV

15.1 The concept of continuum of care for HIV

Throughout the course of HIV infection, people living with HIV will face a number of consequences of HIV infection including:

- Deterioration of physical health – opportunistic infections, ARV drug adverse reactions;
- Mental health issues – fear of rejection and isolation;
- Economic issues – inability to work and health care costs leading to poverty; and
- Social and legal issues – stigma, discrimination, human rights violation.

In addition to or prior to initiation of ART, PLHIV should have access to care and "positive prevention" interventions that:

- Promote physical and mental health;
- Address diseases that most impact the quality and duration of their lives;
- Reduce vulnerability and risk behaviours;
- Reduce the risk of HIV transmission to others; and
- Greater involvement in community activities.

For health care workers, positive prevention interventions should focus on prevention of initial illness or episodes of opportunistic infections and other HIV-related conditions or prevention of recurrence. Also, HIV care should not only focus on medical care but requires a wide range of services and activities, such as psychological, social, and legal support; economically productive activities; and creation of enabling environments.

HIV is now considered a chronic disease because of increasing accessibility of PLHIV to effective ART. As with other chronic diseases, the continuum of care (CoC) for HIV is the system that provides humane, effective, quality, comprehensive and continuous care for PLHIV as well as their families. CoC is a network that links, coordinates and consolidates care, treatment, and support services for PLHIV (Figure 15.1). These services are provided in their homes, in the communities where they live, and in the health facilities that serve them. CoC is a valuable approach to comprehensive care for PLHIV with greater involvement amongst them because:

- It enhances the quality of life of PLHIV;
- It promotes better ARV adherence and retention in HIV care;
- It reduces stigma and discrimination; and
- It reduces service delivery costs.

The CoC Committee in each hub centre coordinates the linkage of these services. CoC members include health service providers, key personnel from MOH as well as relevant government agencies, representatives from civil society organizations (CSOs), PLHIV, and other stakeholders. The CoC Committee, with guidance and support from the HIV Board, shoud strive to provide a package of CoC interventions for PLHIV as recommended in Box 15.1.

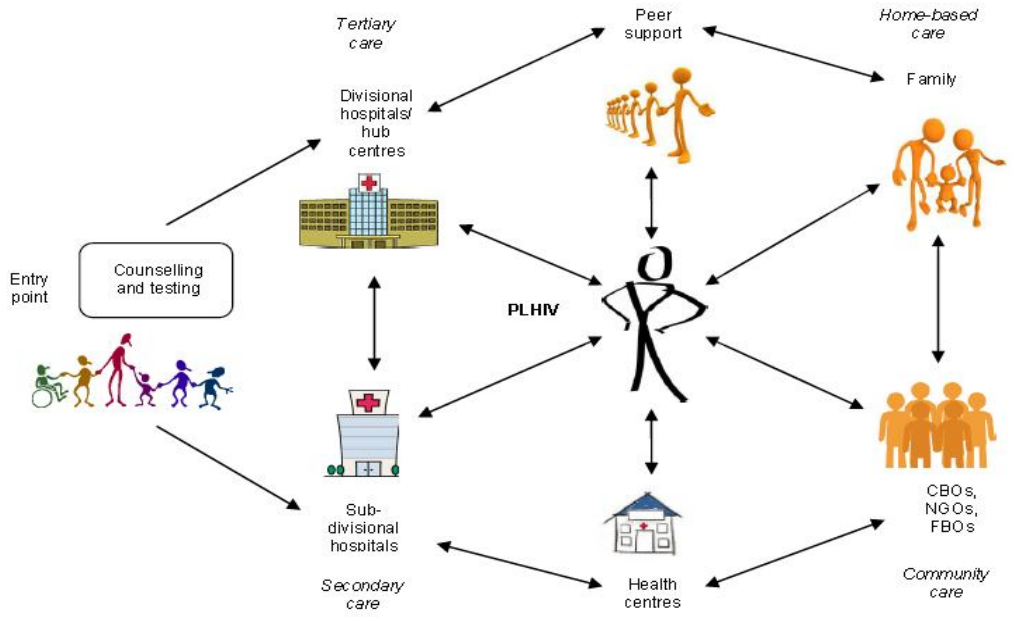


Figure 15.1 A model for continuum of care for HIV

CBOs – community-based organizations; NGOs – non-governmental organizations; FBOs – faith-based organizations.

Box 15.1 Package of continuum of care interventions for people living with HIV

- Counselling and testing – to prevent new infections; refer and retain PLHIV to treatment, care and support services; disclosure; partner management
- Co-trimoxazole prophylaxis
- Prevention, early detection and treatment of TB
- Diagnosis and treatment of other sexually transmitted infections
- Prevention and treatment of opportunistic infections and other HIV-related conditions
- Antiretroviral therapy and adherence counselling and support
- Immunizations
- Antenatal (ANC), maternal and child health (MCH), sexual and reproductive health (SRH) services
- Prevention of mother-to-child transmission (PPTCT) for HIV-positive pregnant women linked to ANC, MCH and SRH (e.g. family planning, contraception)
- Infant feeding and ongoing support
- Care and diagnostic testing for HIV-exposed infants
- Adolescent health and development (AHD) and peer support services
- Nutritional therapy
- Palliative care
- PLHIV support groups
- Psychosocial support
- Care and support of orphans
- Financial and legal support
- Prevention services for those most at risk – sex workers, men having sex with men (MSM), prisoners, etc.
- Support services for gender-based and domestic violence
- Spiritual support
- Respite for caregivers
- Business Partners (Coalition)

The following sections are relevant CoC interventions not discussed elsewhere in the guidelines. The reader is advised to refer to the relevant sources for detailed discussion on other CoC interventions.

15.2 Psychosocial issues across the HIV disease spectrum

Consideration for psychosocial, psychiatric and neurological issues is fundamental to HIV medicine. Health care workers can maximize treatment and care by assessing the patient holistically within the context of their social environment. The experience of living with HIV will vary from patient to patient; and the experience for each individual patient will likely change over time and with disease progression.

Health care workers should be sensitive to the common psychosocial issues experienced by PLHIV, such as the following:

- Issues on confidentiality
- Difficulty accepting diagnosis
- Issues on disclosure
- Stigma and discrimination
- Emotional reactions – shock, denial, anger, fear, guilt, depression, hopelessness, suicidal thoughts
- Changes in physical appearance
- Illness/deterioration in health
- Loss of control
- Impairment in cognitive function – poor mental function such as confusion, forgetfulness, inattention or difficulty in concentrating
- Death and dying
- Loss and grief
- Changes in relationships – partner, family, friends
- Financial difficulties
- Sexual difficulties
- Employment difficulties or loss of job
- Treatment issues – access, adherence, side effects
- HIV-related psychiatric and neurological disorders.

In addressing the PLHIV's psychosocial issues, health care workers should be guided by the possible interventions that they can advise and, subsequently, refer the patient to the appropriate support services that are required.

- Psychosocial interventions – preventive counselling; counselling for adjustment, loss and grief issues; training in specific skills such as relaxation, stress management, assertiveness/negotiation skills and problem solving; psychological therapies for specific disorders (depression and anxiety).

- Education – verbal or written information; behaviourally-based education.

- Support groups – can be facilitated professionally by a counsellor or by peer support groups. They may be helpful in addressing a range of issues including isolation and stigma by enabling PLHIV to build support networks with each other.

- Other interventions – spiritual support; economic support; welfare interventions; nutritional care; palliative care; home-based care; family planning services; community activities; assistance to orphans and vulnerable children.

15.3 Nutrition counselling

ART can improve nutritional status by reducing HIV viral burden and increasing immune function, thereby reducing infections that alter metabolism or decrease nutrient intake/absorption. Conversely, optimal nutritional status has the potential to enhance ART efficacy through providing the body with the building blocks for immune system growth and repair.

HCWs are advised to refer the patient to the dietician for appropriate counselling. Table 14.1 outlines general principles on when and what nutritional advice or interventions can be provided to PLHIV.

Table 15.1 When and what nutritional advice/interventions to provide for PLHIV

When	What
WHO clinical stage 1	• Healthy eating to enhance immune function • Food and personal hygiene for prevention of infections
WHO clinical stage 2	• Weight gain advice (if the weight loss is unintentional) • Modified textured (minced or mashed moist food) diet, e.g. for oral ulcers
WHO clinical stage 3 and 4	• Diet strategies to manage existing nutrition-related problems including diarrhoea, weight loss, sore mouth
During first 6 weeks of treatment	• Identification and provision of dietary strategies to manage symptoms related to ART if present, e.g. diarrhoea, nausea, reflux, loss of appetite, taste changes, weight loss
At treatment reviews or when treatment changes	• Nutritional assessment and dietary modification if indicated.

Adapted from WHO 2004b: Mod 6, Submod 3:2.

During clinical encounters with the patient, health care workers should take the opportunity to remind patients about basic food hygiene.

- Cook food thoroughly.
- Food should be "steaming" hot when served.
- Eat cooked food immediately.
- Store food carefully.
- Re-heat food thoroughly.
- Avoid contact between raw and cooked food.
- Wash hands thoroughly before and after cooking, before and after eating, before and after using the washroom.
- If possible, prepare salads personally to ensure that vegetables are washed thoroughly.
- Wash fruits thoroughly. Eat fruits that need to be peeled.
- Keep kitchen surfaces clean.
- Protect food from rodents, insects and animals.
- Use clean, potable water.

15.4 Palliative care

The aim of palliative care is to provide the best quality of life both for people approaching the end of life and for their families and carers. It begins when:

- Medical treatment is no longer effective and side effects outweigh the benefits;
- The patient does not want to continue aggressive therapy; or
- The patient's vital organs fail.

As with any chronic, terminal illness, palliative care for HIV-positive patients follow the basic principles as outlined below.

- Provide effective pain relief – In the providing pain control for the patient, HCWs are advised to follow the WHO analgesia ladder (Box 14.2).
- Keep the patient nourished and hydrated.
- Maintain basic physical care.
- Provide medications for confusion or dementia.
- Clean and treat skin ulcers and abscesses.
- Address emotional distress appropriately.

Box 15.2 WHO analgesia ladder

- Step 1: Paracetamol
  - *Adults:* Paracetamol 1 gm PO 6-hourly.
  - *Children:* Paracetamol15 mg/kg/dose PO 6-hourly.
- Step 2: Codeine, with or without NSAIDs
  - *Adults:* Codeine 30 mg PO 8-hourly PRN; ibuprofen 400 mg PO 8-hourly.
  - *Children:*
    - <12 years old: Paracetamol with codeine elixir (paracetamol 120 mg + codeine 12 mg/5 ml) at a dose of codeine 0.5-1 mg/kg/dose PO 6-hourly *OR* paracetamol 10-15 mg/kg/dose PO 6-hourly.
    - >12 years old: Paracetamol with codeine elixir (paracetamol 120 mg + 12 mg codeine/5 ml) 15 ml PO 6-hourly.
- Step 3: Morphine
  - *Adults:* Morphine 5 mg PO 8-hourly and increase by 5-10 mg increments. Add ibuprofen 400 mg PO 8-hourly if needed.
  - *Children:* Morphine 0.2-0.4 mg/kg/dose PO 6-hourly.

HCWs should also be aware of the counselling issues that need to be addressed in the palliative care of terminally ill HIV-positive patients. These include:

- Fear of death
- Loneliness and depression
- Feelings of guilt and regret
- Spiritual support
- Making a will (if this is relevant)
- Preparation for death
- Provide care for caregivers
- Bereavement counselling – patient, partner, family.

16 Data collection and program monitoring

With the advent of antiretroviral therapy, HIV is now considered as a chronic disease similar to non-communicable diseases (NCDs). As such, it is critical for the health system to provide and sustain effective long-term HIV care with ART and prevention. This requires an effective patient monitoring system (PMS) integrated with care, prevention and treatment at the health facility.

Patient monitoring captures data on patients over time and across health facilities that provide HIV care/ART services. Aggregated patient data from HIV care/ART sites (i.e. the hub centres) will provide routine tracking information about the program and its intended outcomes.

Figure 16.1 provides an overview of the recording and reporting forms in the patient monitoring system. Description of the forms is provided in Table 16.1.

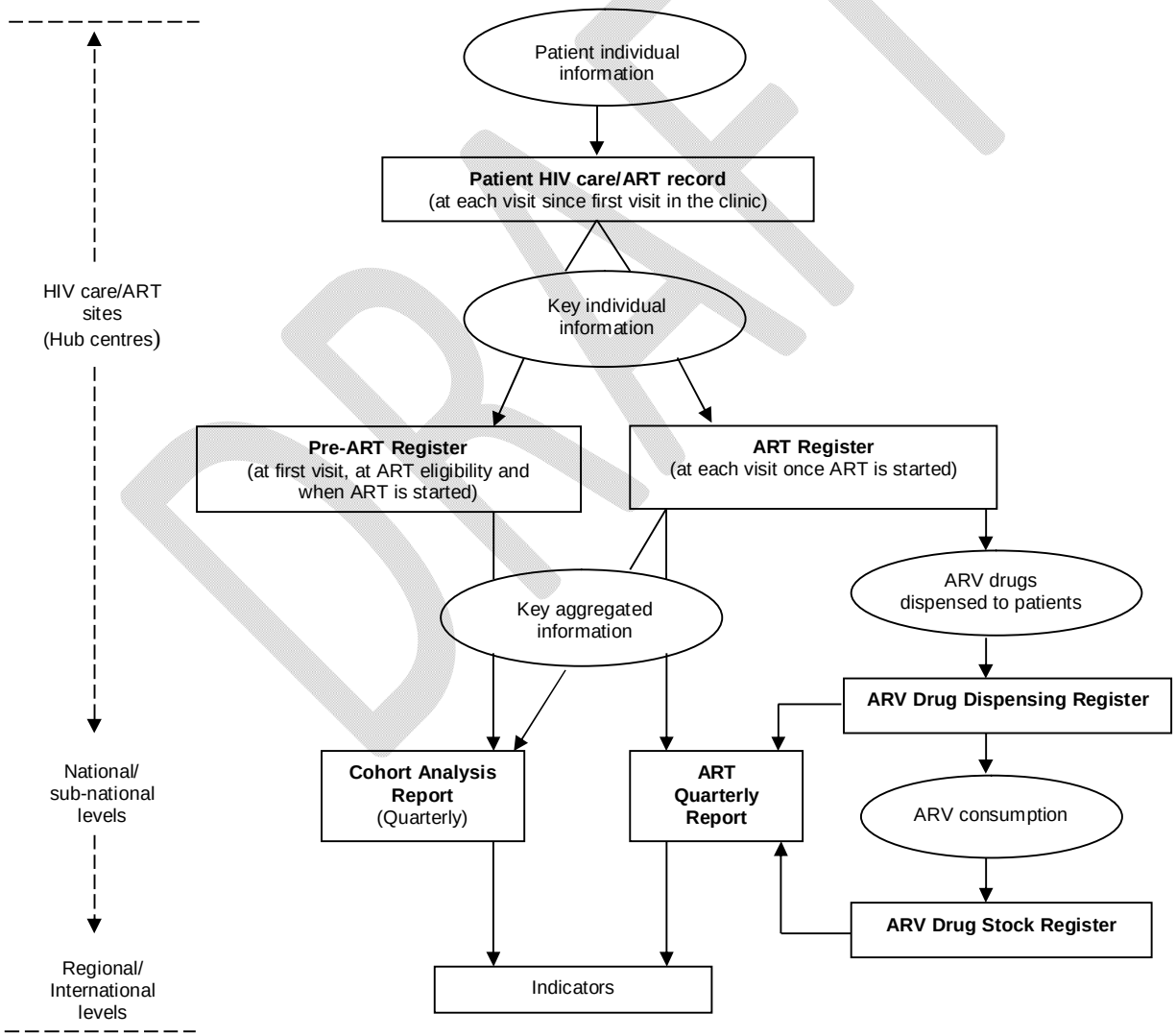


Figure 16.1 Recording and reporting in the patient monitoring system for HIV care and ART, and data flow for program monitoring (Adapted from WHO 2006b:6)

Table 16.1 Recording and reporting forms for the patient monitoring system for HIV care and ART and program monitoring

Form	What information?	For what purpose?	When to complete?
Patient HIV Care/ ART Record	Demographic information, ART and clinic follow-up information	• *Patient management:* to ensure appropriate lifelong follow-up • *Patient monitoring:* to obtain key individual variables for future analysis	• At each patient visit, starting from the first visit to the clinic
Pre-ART Register	Standardized and systematic key variables on each patient before ART is started	• *Patient monitoring:* to report key variables on each patient • *Program monitoring:* to facilitate calculation of indicators	• At the first visit • At the start of tuberculosis (TB) treatment and co-trimoxazole prophylaxis • At ART eligibility • When starting ART • At the end of follow-up, if needed
ART Register	Standardized and systematic key variables on each patient under ART	• *Patient monitoring:* to report key variables on each patient • *Program monitoring:* to facilitate calculation of indicators	• At each visit once ART is started
ARV Drug Dispensing and Stock Registers	• Drugs and number of tablets dispensed • Drug stocks	• *Patient monitoring:* accounting for number of tablets dispensed • *Program monitoring:* drug consumption and available stocks	• At the time of drug dispensing to each patient • Daily basis
Quarterly HIV Care/ART Clinic Report	• Indicators	• *Program monitoring:* to calculate and analyze indicators	• Quarterly
Cohort Analysis Report	• Indicators	• *Program monitoring:* to analyze and calculate indicators at 6, 12, 24 months of ART	• Every 6 months

Adapted from WHO 2006b:7.

In keeping with the principle of continuum of care for HIV, it is recommended that the patient monitoring system for HIV care and ART should be interlinked with MCH/PMTCT and HIV/TB collaborative program as early as feasible and practicable.

Appendices

Appendix 1. Checklist of minimum pre-test counselling for informed consent for HIV testing

When recommending HIV testing to a patient, the health care provider should at a minimum provide the patient with the following information:

- ☐ Health information on HIV and STIs, transmission, prevention and care, safer sex practices.
- ☐ The reasons why HIV counselling and testing is being recommended.
- ☐ The process of HIV testing; when and how to get the results.
- ☐ The clinical and prevention benefits of HIV testing and the potential risks, such as discrimination, abandonment or violence.
- ☐ The services that are available in the case of either an HIV-negative or an HIV-positive test result, including the availability of ART.
- ☐ The fact that the HIV test result will be treated confidentially and will not be shared with anyone other than the health care providers directly involved in providing services to the patient.
- ☐ The fact that the patient has the right to decline the test.
- ☐ The fact that declining an HIV test will not affect the patient's access to services.
- ☐ In the event of an HIV-positive result, encouragement of disclosure to other persons who may be at risk of exposure to HIV.
- ☐ An opportunity to ask questions from the health care provider.

In addition, pre-test information for women who are or may become pregnant should include:

- ☐ The risks of transmitting HIV to the infant.
- ☐ The need for ART for the patient's own health and to prevent mother-to-child transmission.
- ☐ Options for infant feeding.
- ☐ The benefits to infants of early diagnosis of HIV.
- ☐ Contraceptive method, if desired.

Adapted from WHO 2004c:34-35; WHO & UNAIDS 2007:31.

Appendix 2. Checklist for post-test counselling for HIV-negative persons

Counselling for individuals with HIV-negative test results should include the following minimum information:

- ☐ An explanation of the HIV test result, including information about the window period for the appearance of HIV antibodies and a recommendation to re-test in case of a recent exposure or ongoing risk behaviour.
- ☐ Basic advice on methods to prevent HIV transmission.
- ☐ Provision of male and female condoms and guidance on their use.

Adapted from WHO 2004c:38-39.

Appendix 3. Checklist for post-test counselling for HIV-positive persons

The focus of post-test counselling for people with HIV-positive test results is psychosocial support to cope with the emotional impact of the test result, facilitate access to treatment, care and prevention services, prevention of transmission and disclosure to sexual partners. Health care providers should:

- ☐ Inform the patient of the test result simply and clearly.
- ☐ Ensure that the patient understand the result.
- ☐ Allow the patient to ask questions.
- ☐ Help the patient cope with emotions arising from the test result.
- ☐ Discuss any immediate concerns and assist the patient to determine who in his/her social network may be available and acceptable to offer immediate support.
- ☐ Describe follow-up services that are available in the health facility and in the community, with special attention to available treatment, PMTCT, and care and support services.
- ☐ Provide information on how to prevent transmission of HIV, including provision of male and female condoms and guidance on their use.
- ☐ Provide information on other relevant preventive health measures such as good nutrition, use of co-trimoxazole, positive prevention, etc.
- ☐ Discuss possible disclosure of the result.
- ☐ Encourage and offer referral for counselling and testing of partners and children.
- ☐ Assess the risk of violence (particularly women) or suicide.
- ☐ Arrange specific date and time for follow-up visits or referrals for treatment, care, counselling, support and other services as appropriate.

In addition to the above information, post-test counselling for pregnant women whose test result is HIV-positive should address the following:

- ☐ Child birth plans.
- ☐ Initiation of ART for the patient's own health and to prevent mother-to-child transmission.
- ☐ Adequate maternal nutrition, including iron and folic acid supplementation.
- ☐ Infant feeding options.
- ☐ HIV diagnostic testing for the infant and the follow-up that will be necessary.
- ☐ HIV care, ART, monitoring immediate postpartum and long-term care.
- ☐ Encourage and offer referral for HIV counesllling and testing of partners and children.

Adapted from WHO 2004c:38-39.

Appendix 4. WHO HIV case definitions

1.1 WHO case definition of HIV infection

A case of HIV infection is defined as an individual with HIV infection irrespective of clinical stage confirmed by laboratory criteria.

Adults and children 18 months old or older
HIV infection is diagnosed on:

- Reactive screening test for HIV antibody using rapid test (Determine) or laboratory-based enzyme immunoassay
  AND
- Confirmed by reactivity to HIV antibody using two rapid tests (Uni-Gold and Insti) performed in parallel
  OR
  Two laboratory-based enzyme immunoassay performed in parallel
  OR
  Western blot technique.

Children younger than 18 months
HIV infection is diagnosed based on:

- Positive HIV-DNA PCR test using dried blood spots (DBS) taken more than 6 weeks after birth and confirmed by second determination.

1.2 WHO case definition of advanced HIV infection or disease for reporting

Advanced HIV infection is diagnosed based on clinical and/or immunological (CD4) criteria among people with confirmed HIV infection.

Clinical criteria for diagnosis of advanced HIV in adults and children with confirmed HIV infection:

- Presumptive or definitive diagnosis of WHO clinical stage 3 or 4 condition

AND/OR;
Immunological criteria for diagnosing advanced HIV in adults and children 5 years or older with confirmed HIV infection:

- CD4 count <350/mm^3 in an HIV-infected adult or child.

AND/OR;
Immunological criteria for diagnosing advanced HIV in a child younger than 5 years of age with confirmed HIV infection:

- %CD4 <30 among those younger than 12 months;
- %CD4 <25 among those aged 12-35 months;
- %CD4 <20 among those aged 36- 59 months.

1.3 Definition of acquired immunodeficiency syndrome (AIDS) in adults and children

Clinical diagnosis (presumptive or definitive) of any WHO clinical stage 4 with confirmed HIV infection;
OR
Immunological diagnosis in adults and children with confirmed HIV infection and >5 years, first ever documented CD4 count <200/mm^3 or %CD4 <15;
OR
Among children with confirmed HIV infection aged 12–35 months, first ever documented %CD4 <20;
OR
Among children with confirmed HIV infection and <12 months of age, first ever documented %CD4 <25.

AIDS case reporting for surveillance is no longer required if HIV infection or advanced HIV infection is reported. Providing antiretroviral therapy (ART) to persons prior to the development of AIDS will result in fewer persons progressing to AIDS. Consequently, AIDS reporting can no longer provide a stable way of monitoring the HIV epidemic.

Adapted from WHO 2007c:8-9.

Appendix 5. WHO clinical staging of HIV for adults and adolescents with confirmed HIV infection

Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2
Moderate unexplained loss (<10% of presumed or measured body weight)
Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrhoeic dermatitis
Fungal nail infections
Clinical stage 3
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (intermittent or constant for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis
Severe bacterial infections (e.g. pneumonia, empyema, meningitis, pyomyositis, bone or joint infection, bacteraemia, severe pelvic inflammatory disease)
Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
Unexplained anaemia (<8 g/dL), neutropaenia (<0.5 × 10^9/L) or and/or chronic thrombocytopaenia (<50 × 10^9/L)
Clinical stage 4
HIV wasting syndrome
Pneumocystis jiroveci pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi sarcoma
Cytomegalovirus disease (retinitis or infection of other organs, excluding liver, spleen and lymph nodes
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacteria infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis
Chronic isosporiasis
Disseminated mycosis (histoplasmosis, coccidiomycosis)
Recurrent septicaemia (including non-typhoidal *Salmonella*)
Lymphoma (cerebral or B cell non-Hodgkin)
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

Adopted from WHO 2007c:15-16.

Appendix 6. WHO clinical staging of HIV for infants and children with established HIV infection

Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2
Unexplained persistent hepatosplenomegaly
Papular pruritic eruptions
Extensive wart infection
Extensive molluscum contagiosum
Recurrent oral ulcerations
Unexplained persistent parotid enlargement
Lineal gingival erythema
Herpes zoster
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
Fungal nail infections
Clinical stage 3
Unexplained moderate malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5^0C, intermittent or constant, for longer than one month)
Persistent oral candidiasis (after the first 6 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis or periodontitis
Lymph node tuberculosis
Pulmonary tuberculosis
Severe recurrent bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including bronchiectasis
Unexplained anaemia (<8 g/dL), neutropaenia (<0.5 × 10^9/L) and/or chronic thrombocytopaenia (<50 × 10^9/L)
Clinical stage 4
Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
Extrapulmonary tuberculosis
Kaposi sarcoma
Oesphageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (after the neonatal period)
HIV encephalopathy
Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset of age more than one month
Extrapulmonary cryptococcosis including meningitis
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
Chronic cryptosporidiosis (with diarrhoea)
Disseminated non-tuberculous mycobacterial infection
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
HIV-associated cardiomyopathy or nephropathy

Adopted from WHO 2007c:17-18.

Appendix 7. Co-trimoxazole toxicity grade scale for adults and adolescents

The potential side effects associated with co-trimoxazole can be monitored among people living with HIV who are taking co-trimoxazole, either as prophylaxis or treatment for certain opportunistic infections.

Patients must be provided with adequate information on the potential side effects of co-trimoxazole and advised to stop the drug and report to the nearest health facility if co-trimoxazole-related adverse events are suspected.

Toxicity	Clinical description	Recommendation
Grade 1	Erythema	Continue co-trimoxazole prophylaxis with careful repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines.
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue co-trimoxazole prophylaxis with careful repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines.
Grade 3	Vesiculation, mucosal ulceration	Co-trimoxazole should be discontinued until the adverse effect has completely resolved (usually two weeks), and then re-introduction or desensitization can be considered.
Grade 4	Exfoliative dermatitis, Stevens-Johnson syndrome or erythema multiforme, moist desquamation	Co-trimoxazole should be permanently discontinued.

Adopted from WHO 2006b:24.

Appendix 8A. Protocol for co-trimoxazole desensitization among adults and adolescents

Given the importance of co-trimoxazole and the lack of an equally effective and widely available alternative, desensitization is an important component of managing adults and adolescents with HIV infection.

Desensitization can be attempted two weeks after a non-severe (grade 3 or less) co-trimoxazole reaction that has resulted in a temporary interruption of co-trimoxazole. Desensitization should not be attempted in individuals with grade 4 reaction to previous co-trimoxazole or other sulfa drugs.

It is recommended to commence an antihistamine regimen of choice one day prior to starting the desensitization and continue daily until completing the dose escalation. If a severe reaction occurs, the desensitization regimen is terminated. If a minor reaction occurs, repeat the same step for an additional day. If the reaction subsides, advance to the next step; if the reaction worsens, the desensitization regimen is terminated.

Step	Dose (sulfamethoxazole [SMX] + trimethoprim [TMP])	Amount to be administered
Day 1	80 SMX + 16 mg TMP	2 ml of oral suspension*
Day 2	160 mg SMX + 32 mg TMP	4 ml of oral suspension
Day 3	240 mg SMX + 48 mg TMP	6 ml of oral suspension
Day 4	320 mg SMX + 64 mg TMP	8 ml of oral suspension
Day 5	400 mg SMX + 80 mg TMP	one single-strength tablet
Day 6 onwards	800 mg SMX + 160 mg TMP	two single-strength tablets or one double strength tablet

* Co-trimoxazole oral suspension is 200 mg sulfamethoxazole (SMX) + 40 mg trimethoprim (TMP) per 5 ml.
Adopted from WHO 2006b:25.

Appendix 8B. Protocol for co-trimoxazole desensitization in children

Day	Dose
Day 1 – 3	0.2 mg
Day 4 – 6	0.4 mg
Day 7 – 9	1.6 mg
Day 9 – 12	3.2 mg
Day 13 – 15	4.8 mg
Day 16 – 18	9.2 mg
Day 19 – 21	20 mg
Day 22 thereafter	40 mg/day for one week

De Groot H, Mulder WMC 2010:1306.

Appendix 9. Fixed-dose combination of antiretroviral drugs in adults

Short form	Available dosage forms	Usual dose	Dosing instructions	Common adverse effects
AZT/3TC	zidovudine 300 mg + lamivudine 150 mg	1 tablet PO BD	Take with or without food	See individual components
TDF/3TC	tenofovir 300 mg + lamivudine 300 mg	1 tablet PO OD	Take with or without food	See individual components
TDF/FTC	tenofovir 300 mg + emtricitabine 200 mg	1 tablet PO OD	Take with or without food	See individual components
ABC/3TC	abacavir 600 mg + lamivudine 300 mg	1 tablet PO OD	Take with or without food	Risk of hypersensitivity reaction See individual components
TDF/3TC/EFV	tenofovir 300 mg + lamivudine 300 mg + efavirenz	1 tablet PO OD	Recommend taking on an empty stomach as high-fat/high caloric meals increase plasma concentrations	See individual components
TDF/FTC/EFV	tenofovir 300 mg + emtricitabine 200 mg + efavirenz 600 mg	1 tablet PO OD	Recommend taking on an empty stomach as high-fat/high caloric meals increase plasm concentrations	See individual components
AZT/3TC/NVP[a]	zidovudine 300 mg + lamivudine 150 mg + nevirapine 200 mg	1 tablet PO BD	To be taken after loading dose of AZT 300 mg/3TC 150 mg, 1 tablet PO BD + NVP 200 mg PO OD for 14 days	See individual components

[a] Be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatotoxicity.

Appendix 10. Simplified dosing of child-friendly solid and oral liquid formulations for twice-daily dosing

Drug	Strength of tablets (mg) or oral liquid (mg/ml)	Number of tablets by weight band morning and evening										Strength of adult tablet (mg)	Number of tablets by weight band	
		3 – 5.9 kg		6 – 9.9 kg		10 – 13.9 kg		14 – 19.9 kg		20 – 24.9 kg			25 – 34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Solid formulations														
Lamivudine (3TC)	Tablet (dispersible) 30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	150	1	1
Zidovudine (AZT)	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1
Abacavir (ABC)	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1
Nevirapine (NVP)[a]	Tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1
Lopinavir/ritonavir (LPV/r)[b]	Tablet (heat stable) 100 mg/25 mg	-	-	-	-	2	1	2	2	2	2	100 mg/ 25 mg	3	3
Liquid formulations														
Zidovudine (AZT)	10 mg/ml	6 ml	6 ml	9 ml	9 ml	12 ml	12 ml	-	-	-	-	-	-	-
Lamivudine (3TC)	10 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	-	-	-	-	-		
Abacavir (ABC)	20 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	-	-	-	-	-	-	-
Nevirapine (NVP)[a]	10 mg/ml	5 ml	5 ml	8 ml	8 ml	10 ml	10 ml	-	-	-	-	-	-	-
Lopinavir/ritonavir (LPV/r)[b]	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	-	-	-

[a] NVP dose escalation with half dose for 2 weeks when initiating ART is still recommended to avoid toxicity from high initial NVP levels.

[b] LPV/r liquid requires a cold chain during transport and storage. The LPV/r heat-stable formulation must be swallowed whole and should not split or crushed.

Adopted from WHO 2013a:247.

Appendix 11. Simplified dosing of child-friendly solid formulations for once-daily dosing in children

Drug	Strength of tablets (mg)	Number of tablets or capsules by weight band once daily					Strength of tablet (mg)	Number of tablets or capsules by weight band once daily
		3 – 5.9 kg	6 – 9.9 kg	10 – 13.9 kg	14 – 19.9 kg	20 – 24.9 kg		25 – 34.9 kg
Efavirenz (EFV)[a]	Tablet (scored) 200 mg	-	-	1	1.5	1.5	200	2
	Table (double scored)[b] 600 mg	-	-	one third	one half	Two thirds	600	2/3
Abacavir/lamivudine (ABC/3TC)	Tablet (dispersible) 60mg/30 mg	2	3	4	5	6	600 mg + 300 mg	1

[a] EFV is not recommended for children younger than 3 years and weighing <10 kg.

[b] The double-scored tablet has two score lines on one side of the tablet and one score line on the other side, enabling the tablet to be divided into thirds and halves as needed.

Adopted from WHO 2013a:246.

Appendix 12. Simplified dosing of child-friendly fixed-dose formulations for twice-daily dosing among children

Drug	Strength of tablets	Number of tablets by weight band morning and evening										Strength of adult tablet (mg)	Number of tablets by weight band	
		3 – 5.9 kg		6 – 9.9 kg		10 – 13.9 kg		14 – 19.9 kg		20 – 24.9 kg			25 – 34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Zidovudine/lamivudine (AZT/3TC)	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/ 150 mg	1	1
Zidovudine/lamivudine/ nevirapine (AZT/3TC/NVP)	Tablet (dispersible) 60 mg/30 mg/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/ 150 mg/ 200 mg	1	1
Abacavir/zidovudine/ lamivudine (ABC/AZT/3TC)	Tablet (dispersible) 60 mg/60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/ 300 mg/ 150 mg	1	1
Abacavir/lamivudine (ABC/3TC)	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600 mg/ 300 mg	0.5	0.5

Adopted from WHO 2013a:245.

Appendix 13. Simplified harmonized dosing for currently available tenofovir formulations for children

Drug	Size of powder scoop (mg) or strength of tablet (mg)	Number of scoops or tabelts by weight band once daily					Strength of tablet (mg)	Number of tablets or capsules by weight band once daily
		3 – 5.9 kg	6 – 9.9 kg	10 – 13.9 kg	14 – 19.9 kg	20 – 24.9 kg		25 – 34.9 kg
Tenofovir (TDF)[a]	Oral powder scoops 40 mg/scoop	-	-	3	-	-	300 mg	1 (200 mg)[b] or 1 (300 mg)
	Tablets 150 mg or 200 mg	-	-	-	1 (150 mg)	1 (200 mg)		

[a] Target does: 8 mg/kg or 200 mg/m^2 (maximum 300 mg).

[b] 200-mg tablets should be used for weight 25 – 29.9 kg and 300-mg tablets for 30 – 34.9 kg.

Adopted from WHO 2013a:246.

Appendix 14. Protocol for amphotericin B administration

Preparation: Injection (vial) 50 mg (powder)

Caution

- Under no circumstances should a total dose of 1.5 mg/kg be exceeded. If therapy is interrupted for 7 days or more, resume at lowest dose level.
- Must not be given by intramuscular route or direct IV injection.

Reconstitution

- Add 10 ml of water for injection (without preservative) only to vial.
- Shake vial immediately until solution is clear (concentration = 5 mg/ml).

Test dose

- 100 ml of dextrose 5% in a chamber + 1 mg (10 ml) of reconstituted solution of amphotericin B as above

Pre-medications before administration of test dose

- Paracetamol 1 gram PO + prochlorperazine 5 mg PO
- Hydrocortisone 25 mg IV

Administration of recommended dose

- 0.25 mg/kg/day to be added to 1 liter of dextrose 5% to be infused for 6 hours.
- If above dose is tolerated, dose can be gradually increased to 1 mg/kg/day the next day to a maximum of 1.5 mg/kg/day in the succeeding day.

Stability (after reconstitution and dilution)

- Protect from light (cover with aluminum tin foil).
- The reconstituted solution contains no preservative and should be stored in a refrigerator and discarded 24 hours after preparation.
- Discard any solution not used within 24 hours of preparation.

Compatibility Data

- Compatible with 5% glucose only.
- Do not mix with 0.9% sodium chloride.
- Do not mix with any other medications or IV fluids.
- Do not inject medications into infusion line.

Appendix 15. Important drug-drug interactions of selected antiretroviral drugs

Given the complex and sometimes unpredictable nature of ARV drug-drug interactions, patients should be encouraged to inform prescribers if they are taking other drugs as well as herbal and traditional medicine compounds. The list of drug interactions of some ARV drugs outlined below is not exhaustive. Health care workers are encouraged to refer to this website for further information: http://www.hiv-druginteractions.org.

ARV drug class	Drug	Drug interactions
Nucleoside reverse transcriptase inhibitors (NRTIs)	Zidovudine (AZT)	• AZT is primarily eliminated by hepatic conjugation to an inactive glucuronidated metabolite. Active substances which are primarily eliminated by hepatic metabolism especially via glucuronidation may have the potential to inhibit metabolism of AZT. • Phenytoin levels are not predictable – some patients will have increased levels while others will be low. If possible, check serum phenytoin levels in relation to control of seizures. • Renal excretion of AZT is reduced in the presence of probenecid. • AZT has antagonistic effect if used together with stavudine (d4T). • Aspirin, codeine, morphine, indomethacin, ketoprofen, naproxen, lorazepan, cimetidine and clofibrate inhibit hepatic metabolism of AZT, and therefore, may potentially increase drug levels of AZT.
	Lamivudine (3TC)	• Rarely, co-trimoxazole increases the blood levels of 3TC.
	Tenofovir (TDF)	• If didanosine (ddI) and antacids are administered, they should be taken at least 2 hours apart. • TDF increases the levels of didanosine (ddI); hence, TDF is preferably not co-administered with ddI. • TDF levels are increased by lopinavir/ritonavir (LPV/r).
	Abacavir (ABC)	• Ethanol decreases the elimination of ABC causing an increase in overall exposure; care must be taken when co-administered with lopinavir/ritonavir (LPV/r) solutions in children.
	Didanosine (ddI)	• Do not administer stavudine (d4T) together with ddI because of the risk of acute lactic acidosis and death. • Do not administer with tenofovir (TDF) and allopurinol – inferior virological and CD4 count responses and drug interactions. • Decreases the absorption of ritonavir (RTV), fluroroquinolones, dapsone, itraconazole, ketoconazole (separate administration: at least 2 hours before or after ddI).
	Emtricitabine (FTC)	• No clinically significant drug interactions with other antiretroviral (ARV) drugs, i.e. zidovudine (AZT) and tenofovir (TDF).
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Efavirenz (EFV)	• EFV should not to be taken with these drugs: clarithromycin, ergotamine and similar alkaloids, garlic supplements, midazolam, terfenadine and triazolam. • EFV levels are decreased by rifampicin. No dose adjustment in EFV (600 mg OD) is required when co-administered with rifampicin. • EFV increases the levels of ritonavir (RTV). • EFV decreases the levels of clarithromycin, lopinavir (LPV), and rifabutin. • Potential interactions with anticonvulsants (levels are potentially decreased), statins, oral contraceptives (levels of estradiol are decreased; consider alternative or additional method of contraception), tricyclic antidepressants, and oral anticoagulants.

ARV drug class	Drug	Drug interactions
Non-nucleoside transcriptase inhibitors (NNRTIs)	Nevirapine (NVP)	• NVP should not be taken with these drugs: ketoconazole (levels are decreased by NVP) and garlic supplements. • NPV levels are decreased by rifampicin and rifabutin. In patients with HIV/TB co-infection and receiving rifampicin, an EFV-containing regimen is preferred. If EFV is unavailable or cannot be used in a particular patient, standard doses of NVP may be used with rifampicin but sub-therapeutic NVP levels may occur in some patients. However, dose increase in NVP is not recommended due to the risk of hepatotoxicity. • NVP decreases the levels of clarithromycin, lopinavir (LPV), and ritonavir (RTV). • Potential interactions with anticonvulsants (levels are potentially decreased), statins, oral contraceptives (levels of estradiol are decreased; consider alternative or additional method of contraception), tricyclic antidepressants, and oral anticoagulants.
Protease inhibitors (PIs)	Lopinavir/ritonavir (LPV/r)	• If didanosine (ddI) or antacids are administered, they should be taken at least one hour apart. • LPV should not be taken with these drugs: amiodarone, ergotamine and similar alkaloids, garlic supplements, lovastatin, midazolam, propafenone, rifampicin, simvastatin, terfernadine and triazolam. • Rifampicin should not be used in combination with LPV/r because co-administration may cause large decreases in LPV concentrations which may in turn significantly decrease the therapeutic effect of LPV. • LPV levels are increased by ritonavir (RTV). • LPV levels are decreased by carbamazepine, dexamethasone, efavirenz (EFV), ketoconazole, nevirapine (NVP), phenobarbital, phenytoin, rifampicin, and tenofovir (TDF). • LPV increases the levels of amiodarone, atorvastatin, calcium-channel blockers, clarithromycin, ketoconazole, lidocaine (systemic), quinidine, rifabutin, sildenafil and tenofovir (TDF). • Potential interactions with anticonvulsants (levels are potentially decreased), statins, oral contraceptives (levels of estradiol are decreased), tricyclic antidepressants, oral anticoagulants, and immunosuppressants.

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